Edible Medicinal and Non-Medicinal Plants

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Volume 5, Fruits

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Contents

Introduction

This book continues as volume 5 of a multi-compendium on *Edible Medicinal and Non-Medicinal Plants*. It covers edible fruits/seeds used fresh, cooked or processed into other by-products, or as vegetables, cereals, spices, stimulant, edible oils and beverages. It covers selected species from the following families: Apiaceae, Brassicaceae, Chenopodiaceae, Cunoniaceae, Lythraceae, Papaveraceae, Poaceae, Polygalaceae, Polygonaceae, Proteaceae, Ranunculaceae, Rhamnaceae, Rubiaceae, Salicaceae, Santalaceae, Xanthorrhoeaceae and Zingiberaceae. However, not all the edible species in these families are included. The species with edible fruits dealt with in this work include lesser-known, wild and underutilized crops and also common and widely grown crops.

As in the preceding four volumes, topics covered include: taxonomy (botanical name and synonyms); common English and vernacular names; origin and distribution; agro-ecological requirements; edible plant part and uses; plant botany; nutritive and medicinal/pharmacological properties with up-to-date research findings, traditional medicinal uses; other non-edible uses; and selected/cited references for further reading.

Apiaceae or more commonly known as the parsley or carrot family comprises about 434 genera and 3,700 species. Most species are temperate, aromatic herbs with hollow stems and sheathing petioles. Four species with edible fruit/seed used as spices, namely *Carum carvi*, *Cuminum cyminum*, *Foeniculum vulgare* and *Trachyspermum ammi*, are covered in this volume. All have essential oils and various pharmacological properties. The fruits, seeds, flowers, leaves, shoots, stems, sprouted seedlings of fennel, together with the swollen petiole bases (*F. vulgare* subspecies var. *azoricum*) and swollen roots are all edible.

Brassicaceae commonly refer to as the mustard, cabbage or crucifer family is a medium-sized but economically important family of flowering plants with over 338 genera and 3,709 species (Warwick et al. 2006). In their Brassicaceae Species Checklist Database approximately 14,000 taxonomic names are listed and 39 *Brassica* species have been accepted. The family consists of economically well-known species such as the mustards (*Brassica nigra* – black mustard, *B. juncea* – brown mustard and white mustard *Sinapis alba*), *Brassica oleracea* (broccoli, Brussels sprouts, cabbage, cauliflower, kale, etc.), *Brassica rapa* (turnip, Chinese cabbage, etc.), *Brassica napus* (rapeseed/canola, etc.), *Brassica napobrassica* (rutabaga/swede), *Raphanus sativus* (common radish), *Armoracia rusticana* (horseradish), and *Matthiola* (stock) ornamental species. Only two species with edible seeds are covered in this volume, *B. nigra* a well known spice and *B. napus* the seeds are also used a spice but is better known for its oil, canola/rapeseed oil. Both species are rich in nutrients, glucosinolates, flavonoids and volatiles that posses important pharmacological properties that include anticancer, antimicrobial, antihyperlipidemic

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activities to name a few. Other edible species of this family used as leafy, flower or root vegetables are covered in subsequent volumes.

Chenopodium quinoa or quinoa, a psuedocereal, is the only member of the flowering plant family Chenopodiaceae, the goosefoot family, covered in this volume. The family has about 100 genera and 1,400 species of annual herbs or subshrubs, rarely small trees, in temperate and subtropical regions of both hemispheres in all continents except the polar ones. Quinoa is a highly nutritious, gluten-free grain, containing more proteins than other cereals with a good balance of all 8 essential amino acids, high in fibre and has a low glycaemic index (GI). Other important economic edible species include *Beta vulgaris* and *Spinacea oleracea* which are covered in later volumes.

Cunoniaceae is a lesser known, small family of flowering trees, shrubs and liana with 265 species in 29 genera. The species are found in tropical and temperate regions especially in the southern hemisphere – Australasia, South Africa, South America and in Central America and Malaysia. One species *Davidsonia pruriens* or locally called Davidson's plum is indigenous to Australia and is covered in this volume. This species has edible fruit that makes excellent jams, sauces, cordial and a full-flavoured, dry red wine. Like members of the family it has anthocyanins that can be used as food colorants.

Poaceae a large and cosmopolitan family of monocotyledonous annual or perennial flowering plants, herbaceous, sometimes tall woody culms (bamboos) usually cylindrical, jointed, often hollow in the internodes, closed at the nodes. The family has been called grass family and represent the fifth-largest plant family with 777 plant genera and 11,461 species name names being accepted (The Plant List 2010). Grasses are of major economic significance as they provide about 60% of food for human consumption, for animal feed, industry and lawns. The principal cereals are, in order of importance, wheat, rice, maize, barley, oats, sorghum, rye and several grasses usually grouped together and termed 'millets'. Rice is grown largely in the tropics and subtropics, is the staple diet for half the world's population, while wheat is the preferred cereal crop in temperate regions and maize in Central and South America. Grasses are of prime importance to the meat, poultry, dairy and wool industries as they provide feed for animals in the form of grazing pastures, fodder and grains. Ten cereal species are covered in this volume: *Avena sativa*, *coix lachryma-jobi*, *Echinochloa frumentacea*, *Hordeum vulgare*, *Oryza sativa*, *Setaria italicum*, *Sorghum bicolor*, *Trticum aestivum*, *Zea mays* and *Zizania palustris*.

Papaveraceae or commonly known as the poppy family, is an economically important family of flowering plants with 44 genera and about 770 species. The family is cosmopolitan, occurring in temperate and subtropical climates but almost non-existent in the tropics. Unripe capsules of *Papaver somniferum* is the source of commercial opium, and numerous species from *Papaver*, *Eschscholtzia*, *Meconopsis*, *Argemone*, etc. are cultivated as ornamentals. *P. somniferum* is included in this volume as poppy seeds are an important food item providing poppy seed spice and the healthful edible poppy seed oil.

Polygalaceae, the milkwort family, comprises about 17 genera and 900–1,000 species of herbs, shrubs and trees, in tropical and subtropical regions of both hemispheres. One species with edible fruit indigenous to Malaysia, Indonesia and the Philippines, *Xanthophyllum amoenum* is treated in this volume. The fruit has been used in local folkloric medicine.

Polygonaceae is a family of flowering plants commonly known as knotweed family, smartweed family and buck-wheat family. It has about 1,200 species in about 50 genera of herbs, shrubs, or rarely trees found worldwide but with greatest diversity in the northern temperate zone. Economically important genera with edible species include *Rumex* (sorrel), *Persicaria* (e.g. Vietnamese mint), *Fagopyrum*, *Coccoloba*, and *Rheum* (rhubarb). *Coccoloba uvifera*, sea-grape with edible fruit and *Fagopyrum esculentum* buckwheat with edible grains are treated in this volume. The other remaining genera consumed as vegetables and potherbs are treated in later volumes.

Proteaceae family comprises 80 genera and about 1,780 species of mainly flowering shrubs

and trees (exception *Stirlingia* herbaceous plant). The species are widespread in the southern hemispheres with a few species in the northern hemisphere. Together with the Platanaceae and Nelumbonaceae, they make up the order Proteales. In Australia, well known genera include *Protea*, *Banksia*, *Embothrium*, *Grevillea*, *Hakea*, *Dryandra* and *Macadamia*. Many are cultivated by the nursery industry for their prominent and distinctive flowers and foliage. Some are cultivated for the fresh and dried cut-flower industry. Others are cultivated for their edible nuts like *Gevuina avellana* (Chilean hazelnut) in Chile and New Zealand and Macadamia species in Australia, South Africa and Hawaii. *Macadamia integrifolia* and *M. tetraphylla*, indigenous to Australia are covered in this volume.

Rubiaceae, the coffee or madder family, is the fifth largest family of flowering plant by number of genera, and the fourth or fifth largest by number of species with about 611 genera and 13,000 species. The species are shrubs (mostly), trees, lianas and herbs with the greatest diversity in the warm, humid, tropical climates. Following molecular phylogenetic studies by the Angiosperm Phylogeny Group, a number of traditionally accepted families (Dialypetalanthaceae, Henriqueziaceae, Naucleaceae, and Theligonaceae) are now subsumed under Rubiaceae. Economically important crops are coffee (world's second most important economic commodity after petroleum), noni, cinchona (whose bark yields quinine), and ornamental plants like *Ixora*, *Pentas*, *Coprosma* and *Gardenia*. Included in this volume are four species with edible fruits, *Nauclea orientalis*, *Morinda citrifolia* (noni), *Coffea arabica* (Arabica coffee), *C. canephora* (robusta coffee) and *C. liberica* (liberica coffee). The pharmacological impact of coffee consumption and health are elaborated under the three *Coffea* chapters.

Ranunculaceae (buttercup or crowfoot) family comprises about 60 genera and 2,500 species distributed globally. Most are herbaceous plants, but with some woody climbers (such as *Clematis*) and subshrubs (e.g. *Xanthorhiza*). Many are common and well-known ornamentals such as many genera are well known as cultivated flowers, such as *Aconitum* (monkshood), *Clematis*, *Consolida* (larkspur), *Delphinium* (larkspur), *Helleborus* (Christmas rose), *Ranunculus* (Buttercup), *Trollius* (globeflower). One species with edible seeds used as spice in Asian and Middle Eastern cuisine, *Nigella sativa* or black cumin, is treated in this volume. Black cumin has been used in herbal folk medicine and has various pharmacological attributes like anticancer, antiinflammatory, antiarthritic, antimicrobial, antidyslipidemic, hypotensive, cardioprotective, antinociceptive, anxiolytic antidiabetic activities etc. A volatile oil and fixed oil are obtained from the seeds.

Rhamnaceae, the Buckthorn family contains 50–60 genera and about 900 species of flowering plants distributed globally but mostly in tropical or subtropical areas. Members are deciduous or evergreen often thorny trees, shrubs, woody climbers, or lianas, rarely herbs. Economically important plants include some *Rhamnus* species used as medicine, source of dyes and drugs; *Alphitonia*, *Colubrina*, *Hovenia*, and *Ziziphus* species providing timber for construction, fine furniture, carving, lathe work, and musical instruments; *Hovenia*, *Paliurus*, and *Rhamnus* species cultivated as ornamentals and *Ziziphus* and *Hovenia* spp yielding edible plant parts. *Z. jujuba* (Chinese jujube) and *Z. mauritania* (Indian jujube) yielding edible fruit and *Hovenia dulcis* (Chinese raisin tree) cultivated for its edible fruit and fleshy inflorescence stalks are included in this volume. All three also have medicinal attributes.

Salicaceae or the willow family is placed under the order Malpighiales. Recent phylogenetical studies by the Angiosperm Phylogeny Group (APG) has greatly expanded the circumscription of the family to contain 55 genera and about 1,210 species. Many members of the Flacourtiaceae including the type genus *Flacourtia*, have now been transferred to the Salicaceae in the molecular phylogeny-based classification, known as the APG II system. Other members have been transferred mostly to Achariaceae and Samydaceae. Thus, the botanical family, Flacourtiaceae, is now defunct. The species in Salicaceae are mostly evergreen (deciduous) trees and less often shrubs, distributed

pan-tropically to temperate and to arctic zones. Seven species with edible fruit, namely *Dovyalis hebecarpa*, *Flacourtia indica*, *Flacourtia inermis*, *Flacourtia jangomas*, *Flacourtia rukam and Pangium edule* are covered in this volume. Several of these species have been used in traditional medicine.

Santalaceae comprises about 36 genera and 500 species distributed world wide but chiefly in tropical and warm dry regions. They are partially parasitic on other plants and grow as shrubs, tree and herbs, semiparasitic on the roots of host plants. *Santalum album* or sandalwood tree is of economic importance providing valuable fragrant timber used in carving and carpentry, and as a form of incense and for joss sticks. Sandalwood oil is used in soap, perfumes, and massage oils. *Exocarpos cupressiformis* called the Australian cherry has edible fruit. Another species with edible fruit *Santalum acuminatum* (sweet quandong) is indigenous to Australia. It has been used in folkloric medicine by Australian aborigines and is treated in this volume.

Xanthorrhoeaceae is a small family of flowering plants in the order Asparagales. The family comprises 24 genera and 456 accepted species name although 1,318 species names have been recorded. The family has a wide but scattered distribution in the tropics and temperate regions. Many species are cultivated as ornamentals and for cut-flowers. Several species of *Aloe* are cultivated for their leaf sap with medicinal and cosmetic uses. One species with edible fruit, *Dianella caerula*, found in Australia and New Guinea is treated in this volume.

Zingiberaceae, the ginger family, contains about 52 genera and more than 1,300 species distributed pantropically in Africa, Asia and the Americas with greatest diversity in southeast Asia. The species are aromatic, perennial herbs with distichous leaves with basal sheaths that overlap to form a pseudostem and creeping horizontal or tuberous rhizomes. At the Third Symposium on Zingiberaceae, Dr. W. John Kress proposed a new classification of Zingiberacea based on recent research, including molecular phylogenetic analyses and morphological features. He has proposed four subfamilies and six tribes: Siphonochiloideae with tribe Siphonochileae, Tamijioideae with tribe Tamijieae, Alpinioideae with tribes Akpinieae and Riedelieae, Zingiberoideae with tribes Zingibereae and Globbeae. The family include many important ornamental, spices and medicinal plants. Ornamental species include the shell gingers (*Alpinia* spp.), Siam or summer tulip (*Curcuma alismatifolia*), *Globba* spp., ginger lily (*Hedychium* spp.), *Kaempferia* spp., torch-ginger *Nicolaia* spp., *Renealmia* spp. and ginger (*Zingiber* spp.). Spices include ginger (*Zingiber* spp.), galangal or Thai ginger (*Alpinia galanga* and others), melegueta pepper (*Aframomum melegueta*), myoga (*Zingiber mioga*), turmeric (*Curcuma longa*) and cardamom (*Amomum* spp., *Elettaria* spp.). Six species with edible fruits are covered in this volume: *Amomum aromaticum*, *A. compactum*, *A. longiculare*, *A. subulatum*, *Amomum taso-ko* and *Elletaria cardamomum*. Other edible members are treated in subsequent volumes.

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Carum carvi

Scientific Name

***Carum carvi* L.**

Synonyms

Bunium carvi (L.) M. Bieb., *Carum aromaticum* Salisb., *Carum carvi* f. *gracile* (Lindl.) H. Wolff, *Carum carvi* var. *gracile* (Lindl.) H. Wolff, *Carum carvi* f. *rhodochranthum* A.H. Moore, *Carum carvi* subsp. *rosellum* (Woronow) Vorosch., *Carum carvi* f. *rubriflora* H.Wolff, *Carum carvi* f. *rubriflorum* H. Wolff, *Carum decussatum* Gilib. (Inval.), *Carum gracile* Lindl., *Carum officinale* Gray, *Carum rosellum* Woronow, *Carum velenovskyi* Rohlena, *Carvi careum* Bubani, *Falcaria carvifolia* C.A. Mey., *Foeniculum carvi* (L.) Link, *Karos carvi* Nieuwl. & Lunell, *Lagoecia cuminoides* Soy.-Will., *Ligusticum carvi* Roth, *Pimpinella carvi* Jess., *Selinum carvi* E.H.L. Krause, *Seseli carum* Scop., *Seseli carvi* Spreng., *Sium carum* F.H. Wigg., *Sium carvi* Bernh.

Family

Apiaceae

Common/English Names

Caraway, Carum, Carvies, Medidein Fennel, Persian Cumin, Wild Cumin.

Vernacular Names

Albanian: Qimnoni;
Arabic: Al-Karawya, Kammûn Armanî, Karaway, Karawiaa, Karawiya;
Azeri: Adi Cirə;
Armenian: Chaman, Chaman;
Basque: Xarpoil;
Belarusian: Kmen;
Brazil: Alcarávia (Portuguese);
Bulgarian: Kim;
Burmese: Ziya;
Catalan: Comi De Prat;
Chinese: Goht Leuih Ji (Cantonese), Fang Feng, Ge Lü Zi, Yuan Sui (Mandarin);
Croatian: Kim;
Czech: Kmín, Kmín Kořenný, Kmín Luční;
Danish: Almindelig Kommen, Karve, Kommen, Vild Kommen;
Dutch: Echte Karwij, Karwij, Karwijzaad, Kummel, Wilde Komijn;
Eastonian: Harilik Köömen;
Egypt: Karawyâ;
Esperanto: Karvio;
Farsi: Miweh Zireh;
Finnish: Kumina, Saksan Kumina, Tavallinen Kumina;
French: Anis Des Vosges, Carvi, Cumin De Montagne, Cumin Des Prés, Carvi, Faux Anis, Faux Cumin, Grains De Carvi, Kummel;
Gaelic: Carbhaidh, Carvie, Cearbhas, Lus Dearg;
Galician: Alcaravea, Alcaravía;
Georgian: T'mini;

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German: Echter Kümmel, Feldkümmel, Feld-Kümmel, Gemeiner Kümmel, Kümmel, Mattenkümmel, Wiesenkümmel;
Greek: Κάρο, Καρβί, Karo, Karon, Karvi;
Hebrew: Cravy Tarbutit, Kravyah, Kimel, Kimmel, Kravyah, Qimel;
Hungarian: Kömény, Köménymag, Konyhakömény, Réti Kömény;
Icelandic: Kúmen;
India: Jira (Bengali), Farili Dhamui (Dhivehi), Gunyan, Jangi Dhania, Jeerka, Jeero, Kaalaa Jiiraa, Kalazera, Kalazira, Kalazird, Shiajira, Siya Jeera, Vilayati jira, Zira (Hindu), Gonyorog (Lahaul), Sajiragam, Sajirakam (Malayalam), Shahajire (Marathi), Sahajira (Oriya), Bahugandha, Bhedanika, Bhedini, Hridya, Jarana, Jiraka, Kalajiraka, Kalameshi, Karavi, Karavi Asitajiraka, Karunjiraka, Krishna, Krishnajaji, Krishnajeeraka, Krishnajiraka, Krsnajiraka, Mashmirajiraka, Nila, Nilakana, Patu, Raka, Ruchya, Sugandha, Sushavi, Syahajira, Udgarashodhini, Vantishodhini, Varshakali (Sanskrit), Gonyod (Spiti), Appakaccaccompucceti, Appakacam, Cimai Compu, Cimai Peruncirakam, Cimaiccirakam, Cimaiccompu, Cimaivitai, Karuncirakam, Kekku Vitai, Kekkuvirai, Kekkuvitai, Keturuvirai, Malaiccompu, Pilappu-Chirakam, Shimayi-Shombu, Simaishembu (Tamil), Seema Jeeraka, Seemai Sompu, Shimaisapu (Telugu), Karawiyah, Syah Zira, Zeera Siyah, Zira Siyah (Urdu);
Indonesia: Jintan;
Italian: Caro, Carvi, Comino, Comino Tedesco, Cumino, Cumino Dei Prati, Cumino Tedesco, Finocchio Medionale, Kümmel, Seme Di Carvi;
Japanese: Himeuikyō, Kyarawei;
Korean: Kaereowei, Kaerowei;
Latin: Careum, Carvum;
Latvian: Pļavas Ķimene, Ķimenes;
Lithuanian: Paprastasis Kmynai;
Macedonian: Kim, Kimel;
Malaysia: Jintan;
Mongolian: Gon'd;
Morocco: Faux Cumin;
Norwegian: Karve, Karvi, Karving, Kømming, Kyrdd;
Pashto: Carabia;
Persian: Karoya, Kharawjá;
Polish: Kminek, Kminek Zwyczajny;
Portuguese: Alcaravia, Semente De Alcarávia, Cominho;
Romanian: Chimion, Chimen;
Russian: Tmin, Tmin Obyknovennyi;
Serbian: Kim, Divlji Kumin;
Slovašcina: Kumina, Kumina Navadna, Navadna Kumina;
Slovencina: Rasca Lúčna, Rasca, Kmin;
Spanish: Alcarahueya, Alcaravea, Alcaravia, Carvi, Comino De Prado, Hinojo De Prade, Hinojo De Prado;
Swahili: Kisibiti;
Swedish: Brödkummin, Karven, Kommel, Kommen, Kumin, Kummil, Kummin, Kumming;
Thai: Hom pom, Tian takap;
Tibetan: Go-snyod, Gonyod, Zi Ra Nag Po;
Turkish: Frenk Kimyonu, Hakiki Kimyon, Karaman Kimyonu;
Ukrainian: Dikyj Anis, Kmyn, Kmyn Zwychajnyj;
Vietnamese: Ca Rum;
Yiddish: Kimmel, Kiml.

Origin/Distribution

This species is native to Europe and West Asia but its exact origin is unclear. It is cultivated in many areas of Europe, the Mediterranean, South-west, Middle and temperate Eastern Asia, India and North America. Major producing countries are Norway, Sweden, Finland, Great Britain, the Netherlands, Germany, Poland, Czech Republic, Austria, Hungary, Ukraine, Russia, Morocco, Egypt, Syria and India. The Netherlands is usually the main exporting country. Within India, it is found growing wild in Himachal Pradesh and is cultivated in the hills and plains of North India and in the hills of South India.

Agroecology

Its natural habitat includes forests, brushy alpine meadows, riparian grasslands, fields, ruderal areas from 1,500 to 4,300 m. The plant prefers

warm, sunny locations and well-drained soil rich in organic matter. In warmer regions it is planted in the winter months as an annual. In temperate climates, it is planted as a summer annual or biennial.

Edible Plant Parts and Uses

Caraway fruit have a pungent, aromatic anise-like flavour and is used as a spice in culinary dishes, confectionery, bread, beverages and liquors. The whole fruit, or powder or the essential oil is used. Caraway is widely used in southern German and Austrian cuisine, with meat (roast pork *Schweinsbraten*), vegetable or rye bread. It is also popular in Scandinavia particularly in the Baltic states, but is hardly known in Southern European cuisine. Caraway is commonly added to *sauerkraut* (fermented cabbage). It is also used to add flavor to cheeses such as *bondost*, *pultost*, *nøkkelost* and *havarti*. Caraway is also used in casseroles, curries, salads and other foods. In Britain, it has been used to make '*seedy cake*' similar to a Madeira cake. Caraway is also important in cuisines of North Africa, particularly in Tunisia and Yemen, in Tunisian *harissa* (fiery paste with chillies) and Yemenese *zhoug*. The essential oil is used as a flavouring in ice creams, candy, soft drinks, liquors. It is used in the traditional Scandinavian spirit '*Akavit*,' and other liquors like kümmel.

The crushed fruits and leaves are brewed into a tea, with a soothing effect on digestion. The leaves are eaten raw or cooked as a flavouring in soups and dishes or as spinach. Young leaves are less spicy than the seeds and are used in salads. The roots are used as a root vegetable like parsnip.

Botany

A glabrous, branched plant, 30–70 (120) cm tall with elongated fusiform taproot. Leaves are green, bipinnatisect with ultimate segments linear or linear-lanceolate, 3–5 × 1–2 mm; lower leaves petiolate, upper sessile, base sheathing, and leaves reduced upwards. ultimate segments linear or linear-lanceolate, 3–5 × 1–2 mm. Leaves reduced upwards. Umbels 2.5–6 cm across, rays 3–10, 0.6–4 cm, extremely unequal; bracteoles absent; umbellules 4–15-flowered. Calyx teeth obscure, petals white or pinkish. Fruits ellipsoid to crescent-shaped yellowish brown achenes, 4–6 mm long by 1–1.5 mm wide, with five prominent pale ridges (Plate 1), furrows 1-vitta; commissure 2-vittae.

Plate 1 Caraway fruits

Nutritive/Medicinal Properties

The nutrient value of caraway seeds per 100 g edible portion had been reported to be: water 9.87 g, energy 333 kcal (1,393 kJ), protein 19.77 g, total lipid (fat) 14.59 g, ash 5.87 g, carbohydrate 49.90 g, total dietary fibre 38.0 g, total sugars 0.64 g, Ca 689 mg, Fe 16.23 mg, Mg 258 mg, P 568 mg, K 1,351 mg, Na 17 mg, Zn 5.50 mg, Cu 0.910 mg, Mn 1.300 mg, Se 12.1 μg, vitamin C 21.0 mg, thiamin 0.383 mg, riboflavin 0.379 mg, niacin 3.606 mg, vitamin B-6 0.360 mg, total folate 10 μg, total choline 24.7 mg, β- carotene 206 μg, α- carotene 8 μg, β-cryptoxanthin 6 μg, vitamin A 18 μg RAE, vitamin A 363 IU, lycopene 20 μg, lutein + zeaxanthin 454 μg, vitamin E (α-tocopherol) 2.50 mg, total saturated fatty acids 0.620 g, 10:0 (capric acid) 0.010 g, 12:0 (lauric acid) 0.010 g, 14:0 (myristic acid) 0.040 g, 16:0 (palmitic acid) 0.400 g, 18:0 (stearic acid) 0.110 g, total monounsaturated fatty acids 7.125 g, 16:1

undifferentiated (palmitoleic acid) 0.090 g, 18:1 undifferentiated (oleic acid) 7.035 g, total polyunsaturated fatty acids 3.272 g, 18:2 undifferentiated (linoleic acid) 3.122 g, 18:3 undifferentiated (linolenic acid) 0.150 g, tryptophan 0.244 g, threonine 0.756 g, isoleucine 0.826 g, leucine 1.218 g, lysine 1.031 g, methionine 0.361 g, cystine 0.329 g, phenylalanine 0.867 g, tyrosine 0.642 g, valine 1.037 g, arginine 1.252 g, histidine 0.550 g, alanine 0.914 g, aspartic acid 2.084 g, glutamic acid 3.169 g, glycine 1.322 g, proline 0.917 g, and serine 0.946 g (USDA 2012).

Caraway oil is the essential oil obtained by distillating the fruit. The components of caraway fruit oil were: *cis*-carveol, carveol, dihydrocarveol, isodihydrocarveol, neodihydrocarveol (Rothbaecher and Suteu 1975); α-pinene, α-phellandrene, β-phellandrene, α-thujene, β-fenchene, camphene, sabinene, β-pinene, myrcene, *p*-cymene (Salveson and Svendsen 1976); anethofuran (Zheng et al. 1992); main components carvone, limonene (Tewari and Mathela 2003; Iacobellis et al. 2005) and germacrene D, and *trans*-dihydrocarvone (Iacobellis et al. 2005); monoterpenoids and their glucosides: *p*-menthane-2,8,9-triol (Matsumura et al. 2001): *p*-menth-8-ene-1,2-diol, *p*-menthane-1,2,8,9-tetrol, 8,9-dihydroxy-8,9-dihydrocarvone, *p*-menth-ene-2,10-diol 2-*O*-β-D-glucopyranoside, *p*-menthane-1,2,8,9-tetrol 2-*O*-β-D-glucopyranoside, 7-hydroxycarveol-7-*O*-β-D-glucopyranoside (Matsumura et al. 2002b); 2-methoxy-2-(4′-hydroxyphenyl)ethanol, junipediol A 2-*O*-β-D-glucopyranoside and L-fucitol (Matsumura et al. 2002a); flavonoids quercetin 3-glucuronide, isoquercitrin, quercetin 3-*O*-caffeylglucoside and kaempferol 3-glucoside (Kunzemann and Herrmann 1977).

Besides the volatile components in the fruit, caraway oil also contained carvacrol (De Martino et al. 2009) which had been reported to be converted from carvone during the storing process (Rothbaecher and Suteu 1978). Essential oil yields were relatively low and ranged from 0.86 to 1.20% (w/w). Forty-one volatile compounds were identified, the main ones being carvone (76.78–80.53%) and limonene (13.05–20.29%). The main components of the caraway essential oil were identified to be (R)-carvone (37.98%) and D-limonene (26.55%) followed by α-pinene (5.21), *cis*-carveol (5.01%) and β-myrcene (4.67%) (Fang et al. 2010). Twelve major constituents were found in Canadian caraway oil, with a corresponding percentage of 93.9% (Embong et al. 1977). D(+)-carvone and D(+)-limonene accounted for 87.5% of the oil. There were 23 minor and at least 13 trace constituents. FT-Raman spectroscopy showed characteristic bands that could be assigned to lignin, unsaturated fatty acids, and polysaccharides in caraway fruit (Seidler-Lozykowska et al. 2010). Additionally, the essential oil composition showed a great variation in carvone and limonene content among European and breeding accessions.

Total fatty acid (TFA) proportion of caraway seeds varied from 2.95 to 5.68% (w/w) (Laribi et al. 2010). The fatty acid composition of Tunisian caraway seed oil was rich in an unusual fatty acid, petroselinic acid (31.53 and 38.36% of TFA).

Caraway seed oil was found to contain petroselinic and *cis*-vaccenic acid (Reiter et al. 1998).

The following flavonoids were found in caraway leaves: quercetin 3-glucuronide, isoquercitrin, quercetin 3-*O*-caffeylglucoside, kaempferol 3-glucoside, and also isorhamnetin glycosides in low amounts (Kunzemann and Herrmann 1977). Caraway flower was found to contain flavonoids: kaempferol, isoquercetrin, astragalin, hyperoside (Khaleel 2005). Roots of caraway have also been found to contain flavonoids (mean 0.312 mg/g dry weight) (Najda et al. 2008). The seed and root of caraway showed the presence of polyacetylenic compounds (Nakano et al. 1998).

Antioxidant Activity

Cold-pressed black caraway (*Carum carvi*), carrot, cranberry and hemp seed oil extracts exhibited significant antioxidant activities (Yu et al. 2005). The ORAC (oxygen radical absorbing capacity) value ranged from 28 to 220 μmol TE (trolox equivalent)/g oil for the cold-pressed hemp, carrot, and black caraway seed oils, whereas the $ABTS^{\cdot+}$ – scavenging capacity ranged from 8.9 to 30.8 μmol TE/g oil. The great-

est total phanolic content, 3.53 mg gallic acid equivalent (GE) per gramme of oil, was detected in the cold-pressed black caraway seed oil extract. Caraway oil extract significantly suppressed the lipid peroxidation in human LDL, with TBARS (thiobarbituric acid-reactive substance) reduction of 3.77 mg/g. Results suggested that the cold-pressed black caraway seed oil may be used as a natural antioxidative food additive for improving food quality and stability and as a dietary source of natural antioxidants for health promotion and disease prevention. The amount of aqueous extract of caraway fruit needed for 50% scavenging of superoxide radicals was found to be 105 μg, for 50% inhibition of lipid peroxide was 2,100 μg and the amount needed for 50% inhibition of hydroxyl radicals was 1,150 μg (Satyanarayana et al. 2004).

Caraway essential oil was found to reduce on 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals in a dose and to neutralize hydrogen peroxide, reaching 50% neutralization with IC_{50} values of < 2.5 μl/mL (Samojlik et al. 2010). Caraway essential oil strongly inhibited lipoid peroxidation in both systems of induction. Caraway essential oil appeared promising for safe use in folk medicine and the pharmaceutical and food industries.

Anticancer Activity

Three monoterpenes, anethofuran, carvone and limonene, potential cancer chemopreventive agents, were isolated from caraway oil (Zheng et al. 1992). These compounds induced the detoxifying enzyme glutathione S-transferase in several mouse target tissues. The α, β-unsaturated ketone system in carvone appeared to be critical for the high enzyme-inducing activity. Caraway oil, supplemented in diet or painted on the skin, inhibited 7,12-dimethylbenz[a]anthracene- (DMBA) and croton oil-induced skin tumors in female BALB/c mice (Shwaireb 1993). The inhibition was manifested by disappearance of carcinomas, reduced incidence and number of papillomas, delay of their appearance, retardation of their development, and regression of already established papillomas. Caraway oil was more effective when topically applied than when supplemented in the diet. The fruit and root of caraway was found to have antiproliferative polyacetylenes (Nakano et al. 1998). The antiproliferative activity was determined by MTT assay using the tumor cell lines MK-1 (human gastric carcinoma), HeLa (human epithelial carcinoma) and B16F10 (mouse cutaneous melanoma).

Studies showed that caraway seed extract containing high levels of both flavonoids and steroid-like substances and prepared in three different organic solvents suppressed cytochrome P450 1A1 (CYP1A1) enzyme activity in rat hepatoma cells in a dose-dependent manner (Naderi-Kalali et al. 2005). The extracts added above 0.13 μM could significantly inhibit ethoxy resorufin dealkylation (EROD) activity and higher levels of each extract (1.3 and 13 μM) caused approximately tenfold suppression in the enzyme activity. The data showed that substances in caraway seeds extractable in organic solvents could potentially reverse the TCDD (2, 3, 7, 8-tetrachlorodibenzo-*p*-dioxin)-dependent induction in cytochrome P450 1A1.

Studies in rats showed that caraway supplementation significantly reversed diminished levels of intestinal, colonic and caecal lipid peroxidation products, such as conjugated dienes, lipid hydroperoxides and thiobarbituric acid reactive substances (TBARS) and also the antioxidants superoxide dismutase, catalase, reduced glutathione and glutathione reductase caused by subcutaneous injection of the carcinogen, 1,2-dimethylhydrazine (DMH) (Kamaleeswari and Nalini 2006). Additionally caraway supplementation significantly reduced enhanced activity of intestinal, colonic and caecal glutathione peroxidase, glutathione S-transferase and colonic ascorbic acid and α-tocopherol levels observed in carcinogen-treated rats. Thus, the study showed that caraway supplementation at a dose of 60 mg/kg had a modulatory role on tissue lipid peroxidation, antioxidant profile and prevented DMH-induced histopathological lesions in colon cancer rats. In further studies, caraway supplementation to 1,2-dimethylhydrazine (DMH)-induced colon cancer rats significantly reduced aberrant crypt foci development and also

decreased the levels of fecal bile acids, neutral sterols, and tissue alkaline phosphatase activities and modulated oxidative stress significantly as compared to the unsupplemented DMH-treated group (Deeptha et al. 2006; Kamaleeswari et al. 2006). The histological alterations induced by DMH were also significantly improved. The results showed that all three doses, 30, 60, and 90 mg/kg body weight, of caraway inhibited tumorigenesis though the effect of the intermediary dose of 60 mg/kg body weight was more effective than the other two doses. In a recent study, the number of aberrant crypt foci (ACF) and aberrant crypt (AC) induced by 1,2-dimethylhydrazine (DMH) were found to be significantly inhibited in colon of rats treated with caraway essential oils in diet (0.01 and 0.1%) (Dadkhah et al. 2011). Histopathological and biochemical data clearly showed that inhibition of colon premalignant lesions induced by DMH in rats was mediated by interference of caraway oil components in the activities of the main hepatic xenobiotic metabolizing enzymes, cytochrome P4501A1 (CYP1A1) and glutathione S-transferae.

The apoptotic activity of caraway ethanol extract was determined against human leukaemic cell lines: ML-1 – human acute myeloblastic leukaemia, J-45.01 – human acute T cell leukaemia, EOL -human eosinophilic leukaemia, HL-60 – human Caucasian promyelocytic leukaemia, 1301 – human T cell leukaemia lymphoblast, C-8166 – human T cell leukaemia, U-266B1 – human myeloma, WICL – human Caucasian normal B cell, and H-9 – human T cell (Bogucka-Kocka et al. 2008).

Antimutagenic Activity

Hot water, methanol and hexane extracts of caraway were not mutagenic for *Salmonella typhimurium* strains TA98 and TA100 by the Ames assay (Higashimoto et al. 1993). However, when the extracts were treated with nitrite, samples of the water and methanol extracts were mutagenic for strain TA100 without metabolic activation. Its hot water extract (equivalent to 1–2 mg of spice powder) exhibited antimutagenic activity, it reduced the mutagenicity induced by 2.7 nmole (397 ng) of N-methyl-N′-nitro-N-nitrosoguanidine by more than 84%, and that induced by dimethylnitrosamine (1.48 mg) or acridine mustard ICR-170 (10 ng) by 30–60%. However, they did not inhibit the mutagenic activity of 1-nitropyrene, 3-nitrofluoranthene, AF-2, methyl methanesulfonate, N-ethyl-N′-nitro-N-nitrosoguanidine, 2-aminoanthracene, 2-acetylaminofluorene, benzo[a]pyrene or IQ (2-amino-3-methylimidazo[4, 5-f]quinoline).

Hot water extract of caraway seeds inhibited N-methyl-N′-nitro-N-nitrosoguanidine (MNNG)-induced mutation only in the ogt+strains of *Salmonella typhimurium* (Mazaki et al 2006). In the presence of caraway extract, O6-methylguanine DNA adducts in strain YG7100 were decreased in proportion to the decrease of MNNG-induced mutagenesis. Caraway had no effect on cellular concentrations of acid-soluble thiols. These results indicated that caraway did not directly inactivate MNNG and that Ogt-O6-methylguanine-DNA methyltransferase may be involved in the antimutagenic activity of caraway.

Antiulcerogenic Activity

Extracts from the plants *Iberis amara*, *Melissa officinalis*, *Matricaria recutita*, *Carum carvi*, *Mentha x piperita*, *Glycyrrhiza glabra*, *Angelica archangelica*, *Silybum marianum* and *Chelidonium majus*, singly and combined in the form of a commercial preparation, STW 5 (Iberogast) and a modified formulation, STW 5-II, lacking the last three plant constituents, produced a dose dependent anti-ulcerogenic activity associated with a reduced acid output and an increased mucin secretion, an increase in prostaglandin E2 release and a decrease in leukotrienes (Khayyal et al. 2001). The most beneficial effects were observed with the combined formulations STW 5 and STW 5-II in a dose of 10 mL/kg b.w., comparable with cimetidine in a dose of 100 mg/kg b.w. The anti-ulcerogenic activity of the extracts was also confirmed histologically. The cytoprotective effect of the extracts could be partly due to their flavonoid content and to their free radical scavenging properties.

Antihyperlipidaemic Activity

After a single oral administration, caraway fruit extract produced a significant decrease on triglycerides levels in normal rats (Lemhadri et al. 2006). In streptozotocin (STZ)-induced diabetic rats, cholesterol levels were decreased significantly 6 h after caraway treatment. Further, repeated oral caraway extract administration exhibited a significant hypotriglyceridemic and hypocholesterolemic activities in both normal and STZ diabetic rats 15 days after caraway treatment. The authors concluded that the aqueous extract of *Carum carvi* (20 mg/kg) exhibited a potent lipid lowering activity in both normal and severe hyperglycemic rats after repeated oral administration of the extract.

AntihyperglycemicActivity

Aqueous extracts of caraway exhibited a potent anti-hyperglycaemic activity in streptozotocin diabetic rats without affecting basal plasma insulin concentrations (Eddouks et al. 2004). After a single dose or 14 daily doses, oral administration of the aqueous caraway extract (20 mg/kg) produced a significant decrease on blood glucose levels in STZ diabetic rats; the blood glucose levels were nearly normalised 2 weeks after daily repeated oral administration of the extract. No changes were observed in basal plasma insulin concentrations after treatment. Results of another study showed that the normal control, the caraway control and the diabetic rats treated with 10 mg/kg body weight of black caraway oil showed progressive and steady increase in the percent mean weekly body weights, while the diabetic untreated rats and the other test groups showed decreasing and alternating increments respectively in the percent mean weekly body weights (Ene et al. 2007). The blood glucose level in the 10 mg caraway treatment group was significantly reduced compared to the diabetic control and the other treatment groups. They inferred the 10 mg/kg B.W. of caraway oil to be the safe dose that can be used in managing diabetes mellitus. Recent studies showed that caraway had both antihyperglycemic and hypolipidemic activity in diabetic rats (Haidari et al. 2011). Oral administration of caraway caused a significant decrease in blood glucose level of treated rats and alleviated their body weight loss. Further, it caused significant decrease in total cholesterol, and low-density lipoprotein cholesterol levels in the treated animals compared with the diabetic control rats, and with no significant change in triglyceride and high-density lipoprotein cholesterol levels.

Antibacterial Activity

Caraway seed essential oil exhibited antibacterial activity against eight pathogenic bacteria, causing infections in the human body (Singh et al. 2002). The oil was equally or more effective when compared with standard antibiotics, at a very low concentration. The MIC (minimum inhibitory concentration) value of caraway essential oil against *Escherichia coli* was 0.6 and 0.5% against *Staphylococcus aureus* (Mohsenzadeh 2007). The MBC (minimum bactericidal concentration) values were 0.8 and 0.6% for *Escherichia coli* and *Staphylococcus aureus* respectively. Caraway essential oil possessed stronger antifungal and antibacterial potential than did citronella oil when tested 19 fungal and 7 bacterial species, food contaminants, spoilage fungi, as well as plant or fungi and animal pathogens (Simic et al. 2008).

Caraway was one of four essential oil that was found promising for the treatment of intestinal dysbiosis (Hawrelak et al. 2009). The essential oil displayed the greatest degree of selectivity, inhibiting the growth of 12 potential pathogens at concentrations that had no effect on the beneficial members of the human gastrointestinal tract microflora. Caraway seed was found to be inhibitory to the gram-negative bacterium, *Helicobacter pylori* now recognized as the primary etiological factor associated with the development of gastritis and peptic ulcer disease (Mahady et al. 2005). It had an MIC of 25 μg/mL. Caraway, ajowan and *Xanthium brasilicum* exhibited highest in-vitro activity of ten active plants against ten clinical isolates of *Helicobacter pylori* (Nariman et al. 2009). Of three essential oils, caraway oil exhibited the most potent antioxidant activity, due to its content of carvacrol and

was most effective against *Bacillus cereus* and *Pseudomonas aeruginosa* but was ineffective against *Lactobacillus* strains (De Martino et al. 2009). Carvacrol proved most active against *Escherichia coli*, and completely inhibited the growth of *Penicillium citrinum*. Caraway volatile oil was found to have antibacterial activity against *Pseudomonous aeruginosa* but not *Proteus vulgaris* (Deb et al. 2010). Caraway effectively inhibited aflatoxin (AFB1) production without any obvious effect on growth of *Aspergillus parasiticus* (Razzaghi-Abyaneh et al. 2009).

Antidyspeptic Activity

Holtmann et al. (2001) using a multicenter, placebo-controlled, double-blind, randomized trial showed that a fixed peppermint oil/caraway oil combination (FPCO) (2×1 capsule daily) improved the NDI (Nepean Dyspepsia Index) subscores for pain and discomfort of the patients (primary efficacy variables) as well as the NDI symptom score and the NDI total score (secondary efficacy variables) compared to the placebo. They also demonstrated that not only patients with severe pain but also patients with severe discomfort responded significantly better to FPCO than to placebo (Holtmann et al. 2002). Overall, efficacy of FPCO combination appeared comparable to chemically defined treatment, e.g. with prokinetics (Holtmann et al. 2003). Due to its good tolerability and safety the fixed peppermint oil/caraway oil could be considered an alternative for the long-term management of these patients.

Ethanol caraway extracts reduced significantly the response of dispersed guinea pig smooth muscle cells to acteylcholine in a dose-dependent manner (Al-Essa et al. 2010). This response may partly explain the beneficial effect of caraway in relieving gastrointestinal symptoms associated with dyspepsia.

Diuretic Activity

Studies in normal maleWistar rats demonstrated that aqueous caraway extract exhibited strong diuretic action confirming their ethnopharmacological use in traditional medicine (Lahlou et al. 2007). From the pattern of excretion of water, sodium and potassium, it was postulated that there were at least two types of active principals present in these extracts, one having a furosemide-like activity and the other a thiazide-like activity.

Adaptogenic Activity

Daily administration of caraway at doses of 100, 200 and 300 mg/kg body weight 1 h prior to induction of stress inhibited the stress induced urinary biochemical changes in a dose dependent manner in rats (Koppula et al. 2009). However no change in the urinary excretion of vanillylmandelic acid and ascorbic acid was observed in normal animals at all the doses studied. The conditioned avoidance response of rats administered with the caraway extract or vehicle increased gradually to 95% over 7–11 days. The cognition, as determined by the acquisition, retention and recovery in rats was observed to be dose dependent. Caraway extract produced significant inhibition of lipid peroxide formation in comparison with ascorbic acid in a dose dependent manner in both liver and brain. The results provided scientific support for the antistress (adaptogenic), antioxidant and nootropic activities of *Carum carvi* extract and substantiates its traditional use as in combating stress induced disorders.

Nephroprotective Activity

High dose of *Carum carvi* aqueous seeds extract (60 mg/kg) showed renoprotection against STZ induced diabetic nephropathy in rats (Sadiq et al. 2010). Administration of caraway extract decreased the elevated levels of glucose, urea, creatinine, total urinary volume, and protein microalbuminuric levels in diabetic rats and increased the decreased body weight of diabetic rats.

Elevated kidney lipid peroxidation and plasma urea/creatinine ratio levels were readily reversed in septic rats treated with caraway essential oil but not in those treated with

hydroalcoholic extract (Dadkhah and Fatemi 2011). Unlike lipid peroxidation, the heart and kidney GSH levels were not affected in all treated groups. The data implied that caraway oil probably had a protective role in kidney tissue against oxidative injury in advanced stages of sepsis.

Antiasthmatic and Antianaphylatic Activities

Intragastric administration of carveol and carvone produced protective effects against histamine and acetylcholine -induced asthma in guinea pigs (Tang et al. 1988, 1999). Aerosol administration produced relaxation effect on isolated guinea pig trachea and antagonized the carbachol-induced contractions. Carveol and carvone also inhibited the release of slow-reactive substances (SRS-A) in ovalbumin sensitized guinea pig lung tissue and antagonized SRS-A-induced contractions of isolated guinea pig ileum and inhibited the Dale Schultz reaction of isolated guinea pig trachea.

Antispasmodic Activity

Caraway essential oil inhibited isolated rat uterus contraction to KCl (80 mM) and the phasic contraction to acetylcholine (320 nM) in a concentration-dependent manner, reducing the response to zero at their highest used concentrations. The results indicated that the essential oil may be useful for control of uterus spasm (Sadraei et al. 2003).

Drug Potentiating Activity

CC-1a, chemically standardized butanolic fraction from caraway seed, enhanced the plasma levels of anti-TB drugs, rifampicin, pyrazinamide, and isoniazid in Wistar rat, resulting in increased bioavailability indices (C(max) and AUC) of the drugs (Sachin et al. 2009). A permeation-enhancing property of CC-1a across small intestinal absorptive surface was found to be a contributing factor in its bioavailability enhancing profile.

Insecticidal Activity

Caraway essential was one of five aromatic plants that showed significant larvicidal activity after 24 h exposure against *Anopheles dirus*, the major malaria vector in Thailand, and *Aedes aegypti*, the main vector of dengue and dengue hemorrhagic fever (Pitasawat et al. 2007).

Traditional Medicinal Uses

Caraway has a long history of traditional medicinal use (CSIR 1950; Grieve 1971; Chopra et al. 1986; Bown 1995; Chevallier 1996). Caraway fruit is antispasmodic, antiseptic, aromatic, carminative, digestive, emmenagogue, expectorant, galactogogue and stimulant. It can be chewed raw for immediate relief of indigestion and can also be made into infusions, decocotions or tisanes. It is used in the treatment of bronchitis and as an ingredient in cough remedies for children. The fruit is also used as a remedy for colic, loss of appetite, digestive disorders and as a galactogogue to promote lactation in nursing mothers. A tea made from the fruits or leaves is a stomachic, carminative and is drank to treat flatulence. An infusion of fruits and foliage is used as a vermifuge to dispel intestinal worms. Caraway fruit is one of many plants most commonly used for the treatment of diabetes and hypertension in Moroccan traditional medicine (Tahraoui et al. 2007) and as a diuretic in Moroco (Lahlou et al. 2007). The pungent fruit is used in Tibetan medicine where it is regarded to have an acrid taste and a heating potency.

Other Uses

Caraway seed essential oil is used as a fragrance component in soaps, lotions, and perfumes and as a parasiticide.

The antibacterial activity of caraway essential oil was particularly high against the genera *Clavibacter*, *Curtobacterium*, *Rhodococcus*, *Erwinia*, *Xanthomonas*, *Ralstonia*, and *Agrobacterium*,

which are responsible for plant or cultivated mushroom diseases worldwide (Iacobellis et al. 2005). In general, a lower activity was observed against bacteria belonging to the genus *Pseudomonas*. These results suggested the potential use of the caraway essential oil for the control of phytobacterial diseases.

Caraway seed powder exhibited molluscicidal activity in a time and dose dependent manner against the snail *Lymnaea acuminata* with an LC_{50} of 140.58 mg/L at 96 h (Kumar and Singh 2006). The 96 h LC_{50} of column purified fraction of seed powder of *C. carvi* was 5.40 mg/L suggesting the product may be uses as potent molluscicides. Caraway essential oil also showed insecticidal activity. Among the essential oils tested, strong insecticidal activity against the Japanese termite *Reticulitermes speratus* was observed with the essential oils of ajowan (*Trachyspermum ammi*), allspice (*Pimenta dioica*), caraway (*Carum carvi*), dill (*Anethum graveolens*), geranium (*Pelargonium graveolens*), and litsea (*Litsea cubeba*) (Seo et al. 2009). Among the bioactive compounds, phenol compounds exhibited the strongest insecticidal activity among the test compounds. The alcohol and aldehyde groups were more toxic than the hydrocarbons. Responses varied in a dose-dependent manner for each compound. Caraway essential oil was found to possess strong contact toxicity against *Sitophilus zeamais* and *Tribolium castaneum* adults, with LD_{50} values of 3.07 and 3.29 μg/adult, respectively, and also showed strong fumigant toxicity against the two grain storage insects with LC_{50} values of 3.37 and 2.53 mg/L, respectively (Fang et al. 2010). Components of the essential oil, (R)-Carvone and D-limonene showed strong contact toxicity against *S. zeamais* (LD_{50} = 2.79 and 29.86 μg/adult) and *T. castaneum* (LD_{50} = 2.64 and 20.14 μg/adult). (R)-Carvone and D-limonene also possessed strong fumigant toxicity against *S. zeamais* (LC_{50} = 2.76 and 48.18 mg/L) and *T. castaneum* adults (LC_{50} = 1.96 and 19.10 mg/L). Caraway seed essential oil was one of eight plant essential oils that exhibited good insecticidal activity (>90%) against larvae of *Lycoriella ingénue* at 20×10^{-3} mg/mL air (Park et al. 2008).

Comments

The species is a declared terrestrial noxious weed and/or noxious-weed seed in some states in USA.

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Cuminum cyminum

Scientific Name

***Cuminum cyminum* L.**

Synonyms

Cuminia cyminum J. F. Gmel., *Cuminum aegyptiacum* Mérat ex DC., *Cuminum hispanicum* Bunge, *Cuminum odorum* Salisb., *Cuminum officinale* Garsault (Inval.), *Cuminum sativum* J. Sm., *Cyminon longeinvolucellatum* St.-Lag., *Ligusticum cuminum* (L.) Crantz, *Selinum cuminum* E.H. Crantz.

Family

Apiaceae

Common/English Names

Cumin, Cummin, Roman Caraway.

Vernacular Names

Arabic: Al-Kamuwn, Kamoun, Kamun, Kamműn, Cammun, Kamoun, Kammoon, Sannűt;
Brazil: Cominho;
Bulgarian: Kimion, Kimion Rimski, Kimion Italianski;
Burmese: Ziya;
Chinese: Ou Shi Luo, Ma Qin, Ma Ch'in, Xian Hao, Xiang Han Qin, Zi Ran;
Croatian: Kumin;
Czech: Římský Kmín, Šabrej Kmínovitý;
Danish: Spidskommen, Kloeftsvoeb;
Dutch: Komijn;
Eastonian: Juustuköömen, Vürtsköömen;
Ethiopia: Kemun;
Finnish: Juustokumina, Kumina, Maustekumina, Roomankumina;
French: Cumin, Cumin De Malte, Cumin Blanc, Cumin Du Maroc, Faux Anis;
German: Kreuzkümmel, Römischer Kümmel, Weißer Kreuzkümmel;
Greek: Kimino, Kiminon;
Hebrew: Camon, Kamon, Kamoon, Kammon, Kammun, Camon Tarbuti;
Hungarian: Borsos Kömény, Egyiptomi Kömény, Kuminmag, Római Kömény;
Icelandic: Ostakúmen, Kummin;
India: Jira (Bengali), Jiru (Guerati), Jiiraa, Jeera, Zeera, Zira, Ziira, Safed Ziiraa, Safed Zira, Safed Jiiraa, Safaid Jeera (Hindu), Jeerige (Kannada), Jeerakam (Malayalam), Jire (Marathi), Jiira (Punjabi), Ajaji Jarana, Jiraka, Jirana, Jirna, Sugandha (Sanskrit), Jirakam, Cirakam, Seeragam (Tamil), Jiraka, Jilakarra (Telugu), Jirah, Zeera, Ziraa (Urdu);
Iran: Zeera, Zirah;
Italian: Comino, Comino Bianco, Comino Romano, Cumino;
Indonesia: Jintan Putih, Jintan Bodas;
Japanese: Hime Unikyoo, Kumin;
Khmer: Ma Chin;

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Laotian: Thien Khaw;
Malaysia: Jintan Putih;
Nepalese: Jiiraa, Jeera, Jira;
Norwegian: Spisskarve, Spisskummen;
Pakistan: Zeera;
Persian: Zireh, Zeera, Zire, Zira, Zireye Sabz, Zireh Sabz;
Polish: Kmin, Kmin Rzymski, Kminek;
Portuguese: Cominho;
Russian: Kmin, Kmin Rimskii, Kmin Tminovyi, Kmin Tminovyj;
Sri Lanka: Suduru, Duru. Maduru (Sinhala);
Slovašcina: Kumin, Kumina, Laški Kumin, Orientalske Kumina, Rimska Kumina, Zamorska Kumina;
Slovenia: Džíra, Rasca Rímska;
Spanish: Comino, Comino Blanco;
Swahili: Jamda, Jira, Kisibiti;
Swedish: Pepparkummin, Romerks Kummin, Spiskummin, Vit Kummin;
Thai: Yee Raa, Thian Khao;
Turkish: Kimyon;
Ukrainian: Кмин, Kmin.

Origin/Distribution

Cumin is probably native to the Eastern Mediterranean region and southwest Asia; and occurs elsewhere as an escape. It has been cultivated since antiquity in Europe and Egypt. The primary cultivation of cumin is in Europe, Asia, the Middle East, and North Africa with India and Iran as the largest cumin producers and exporters.

Agroecology

Cumin prefers a Mediterranean climate with daytime temperatures of around 30°C and annual rainfall of 300–2,700 mm. The plant needs mild temperatures during a 3–4 month growing season and is intolerant of long periods of dry heat. It thrives best in fertile, well-drained sandy loam with a soil pH of 4.5–8 in a sheltered sunny position. It is frost sensitive and drought tolerant.

Edible Plant Parts and Uses

Cumin is the second most popular spice in the world after black pepper. Cumin fruits are widely used as a spice for its distinctive flavour, strong and warm aroma in various cuisines around the world in Asian (Indian, Pakistani, Western China- Sichuan and Xinjiang), Malaysian, Indonesian Middle Eastern, North African, Cuban, Brazilian and Mexican cuisines. Cumin is used whole in powdered form or as an essential oil. Cumin is used for seasoning soups, stews, couscous, rice, meat-dishes, cheese (e.g. Leyden), bread, biscuits, cakes, enchiladas, tacos, salsa, pickles and chutney. Cumin mixed with coriander constitutes an important condiment referred to as *ketumbar-jintan* which is commonly used for preparing meat dishes, curries and *kimlo* in Indonesia and Malaysia. Cumin mixed with coriander constitutes an important condiment refereed to as ketumbar-jinten which is commonly used for preparing meat dishes, curries and kimlo in Indonesia and Malaysia. It is an essential ingredient of curry and chilli powders such as *achiote* (*Bixa orellana*) blends, *adobos* (marinade sauce), *sofrito* (culinary seasoning mix), *garam masala* (pungent spice mixture) and *baharat* (Arabic spice blend). In Ethiopia, cumin is used in the *bebere* spice mix. The essential oil is used as a food flavouring and for flavouring liquors.

Botany

An erect, slender herbaceous, subglabrous annual growing to 50 cm high with a long slender taproot. Leaves 2–3-pinnatisect; 4–6 cm long; ultimate segments filiform 3–6 × 0.05 cm; petiole bases with narrow membranous wings. Inflorescence a long stalked, compound, 3–15-rayed umbel, bracts and bracteoles 3-lobed at apex, slightly hairy; umbellules 6-flowered; bracteoles subulate, 7–10 mm long. Flowers with 5-fid calyx segment unequal, linear-lanceolate, petals oblong-ovate, white or pink, 1 mm. Fruit ellipsoid to fusiform non-dehiscent achene, 4–6 mm long, yellowish-brown, sparsely pubescent; with longitudinal pale ribs (Plate 1).

Plate 1 Cumin fruits

Nutritive/Medicinal Properties

The nutritive value of cumin fruit per 100 g edible portion was reported as: water 8.06 g, energy 375 kcal (1567 kJ), protein 17.81 g, fat 22.27 g, ash 7.62 g, carbohydrate 44.24 g, total dietary fibre 10.5 g, total sugars 2.25 g, Ca 931 mg, Fe 66.36 mg, Mg 366 mg, P 499 mg, K 1788 mg, Na 168 mg, Zn 4.80 mg, Cu 0.867 mg, Mn 3.333 mg, Se 5.2 mcg, vitamin C 7.7 mg, thiamine 0.628 mg, riboflavin 0.327 mg, niacin 4.579 mg, vitamin B-6 0.435 mg, total folate 10μg, choline 24.7 mg, vitamin A 64 mcg RAE, vitamin A 1270 IU, β-carotene 762μg, lutein + zeaxanthin 448μg, vitamin E (α-tocopherol) 3.33 mg, vitamin K (phylloquinone) 5.4μg, total saturated fatty acids 1.535 g, 10:0 (capric) 0.018 g, 12:0 (lauric) 0.018 g, 14:0 (myristic) 0.018 g, 16:0 (palmitic) 1.137 g, 18:0 (stearic) 0.344 g, total monounsaturated fatty acids 14.040 g, 16:1 undifferentiated (palmitoleic) 0.212 g, 18:1 undifferentiated (oleic) 13.618 g, 20:1 (gadoleic) 0.212 g, total polyunsaturated fatty acids 3.279 g, 18:2 undifferentiated (linoleic) 3.103 g, 18:3 undifferentiated (linolenic) 0.176 g and phytosterols 68 mg (USDA 2012). The Bulgarian cumin showed the highest content of crude protein (23%) whereas the Egyptian seeds contained the lowest percentage (18%) (Badr and Georgiev 1990). Generally, 18 amino acids were identified in all cumin seeds of which 8 were essential amino acids. The first limiting amino acid was tryptophan.

Fourteen flavone glycosides were found in cumin seeds, seven belong to apigenin group, five to luteolin group and two to the chrysoeriol group (El-Negoumy and Mansour 1989).

From the water-soluble portion of the methanol extract of cumin fruit, 16 monoterpenoid glucosides, including 12 new compounds, were isolated (Ishikawa et al. 2002). Their structures were characterised as (8R)-9-hydroxycuminyl β-D-glucopyranoside (1), (8S)-8,9-dihydroxycuminyl β-D-glucopyranoside (2), 8-hydroxycuminyl β-D-glucopyranoside (3), (3S,4S,6R)-*p*-menth-1-ene-3,6-diol 6-*O*-β-D-glucopyranoside (4), (3*R*,4*S*,6*R*)-*p*-menth-1-ene-3,6-diol 6-*O*-β-D-glucopyranoside (5), (3R,4S,6R)-*p*-menth-1-ene-3,6-diol 3-*O*-β-D-glucopyranoside (6), (4*S*)-*p*-menth-1-ene-4,7-diol 4-*O*-β-D-glucopyranoside (7), (4*R*,6*S*)-*p*-menth-1-ene-4,6-diol 4-*O*-β-Dglucopyranoside (8), (4S,6S)-pmenth-1-ene-4,6-diol 4-*O*-β-D-glucopyranoside (9), (4R)-*p*-menth-1-ene-7,8-diol 8-*O*-β-Dglucopyranoside (10), (4R)-*p*-menth-1-ene-7,8-diol 7-*O*-β-Dglucopyranoside (11), (3R,4R)-*p*-menth-1-ene-3,4-diol 3-*O*-β-D-glucopyranoside (12), *p*-menth-1-ene-3_{eq},4_{ax},6_{ax}-triol 3-*O*-β-lucopyranoside (13), (1S,2R,4R)-*p*-menth-5-ene-1,2-diol 2-*O*-β-D-glucopyranoside (14), (1S,2R,4R)-*p*-menth-5-ene-1,2-diol 1-*O*-β-D-glucopyranoside (15) and(1S,2R,4S)-*p*-menth-5-ene-1,2,4-triol 2-*O*-β-D-glucopyranoside (16). Kitajima et al. (2003) isolated glycosides of 2-C-methyl-D-erythritol from cumin fruit, clarified as 3-*O*-β-D-glucopyranoside, 4-*O*-β-D-glucopyranoside, and 1-*O*-β-D-fructofuranoside. From the polar portion of the methanolic extract of cumin fruit two sesquiterpenoid glucosides, cuminoside A and B, and two alkyl glycosides were isolated together with five known compounds (Takayanagi et al. 2003). Their structures were elucidated as (1S,5S,6S,10S)-10-hydroxyguaia-3,7(11)-dien-12,6-olide β-D-glucopyranoside, (1R,5R,6S,7S,9S,10R,11R)-1,9-dihydroxyeudesm-3-en-12,6-olide 9-*O*-β-D-glucopyranoside, methyl β-D-apiofuranosyl-(1 → 6)-β-D-glucopyranoside and ethane-1,2-diol 1-*O*-β-D-apiofuranosyl-(1 → 6)-β-D-glucopyranoside, respectively. Cumin seed was found to contain a nonspecific lipid transfer protein nsLTP1 with a molecular weight of 9.7 kDa and a primary

structure of 92 amino acids with 8 conserved cysteine residues (Zaman and Abbasi 2009). Plant nsLTPs are small basic proteins involved in transport of lipids between membranes and participate in plant defense mechanism.

Harborne and Williams (1972) found that of the 25 flavone and flavonol glycosides detected in Apiaceae, by far the most common were luteolin 7-glucoside and quercetin 3-rutinoside. Isorhamnetin was found to occur regularly in two tribes, Peucedaneae and Apieae. The researchers asserted that the discovery of apigenin and luteolin 7-glucuronosylglucosides in *Cuminum cyminum* supported its removal from the Apieae and transfer to the tribe Caucalideae.

Cumin fruit was found to be rich in essential oil (3–4%) that contained appreciable amount of cuminaldehyde (35–60%), and also contained α-pinene, β-pinene, δ-3-carene, 1,8-cineole, α-phellandrene, β-phellandrene, *p*-cymene, limonene, α-terpinene, γ-terpinene, α-terpineol, terpinene-4-ol cuminyl alcohol, *trans*-dihydrocarvone (menthane type monoterpenoids), myrcene, linalool (acyclic monoterpenoids), β-caryophyllene, β-farnesene, β-elemene (sesquiterpenoids) and other minor compounds (El-Hamidi and Ahmed 1966; Baser et al. 1992).

The yield of solvent extracted oil of *Cuminum cyminum* was 18.7% (Shahnaz et al. 2004). The oil was classified into hydrocarbon 1%, wax esters 1%, sterol ester 25%, triglycerides 55%, 1,3 diglycerides 1%, 1,2 diglycerides 1%, monoglycerides 2%, free fatty acid 10%, phosphatidyl-ethanolamines2.0%,phospatidylcholine1.2%, lysophosphatidyl eth-anolamines 0.6% and phosphatidyinositol 0.2%. The oil was considered as a good source of petroselinic acid (51.7%) in the fatty acid composition. The range of fatty acid was found from C10 to C20. In a recent study, essential oil yields for Tunisian cumin and Indian cumin were 17.77 and 15.40% respectively (Bettaieb et al. 2011b). Petroselinic acid (C18:1n-12) was the major fatty acid in both varieties, with a higher proportion being found in Tunisian cumin (55.90% of total fatty acids (TFA)) than in Indian cumin (41.42% TFA). Moreover, the most predominant fatty acids were palmitic, petroselenic and linoleic acids, accounting for more than 91% TFA in both varieties. The unsaturated fatty acid content was high: 70.95% TFA in Tunisian cumin and 62.17% TFA in Indian cumin. A total of 40 compounds were identified, 34 of which were present in both essential oils. The two varieties displayed different chemotypes: γ-terpinene/1-phenyl-1,2-ethanediol for Tunisian cumin and cuminaldheyde/γ-terpinene for Indian cumin. The study revealed that the biochemical composition of cumin seeds was origin-dependent and that cumin seeds were rich in an unusual fatty acid, petroselinic acid and other compounds, including cuminaldehyde and γ-terpinene. The overall results suggested the potential of exploiting cumin seeds as a low-cost renewable source for industrial processing in the fields of cosmetics, perfumes and pharmaceuticals.

The main flavor-impacting components in cumin volatile oil were found to be cuminal, *p*-mentha-1, 3-dien-7-al, *p*-mentha-1, 4-dien-7-al, phellandrene, 1,8-cineole, linalool, limonene, and small amounts of other aromatic aldehydes (Sahana et al. 2011). Among the methods employed for the isolation of volatile oils, microwave-assisted as well as supercritical extraction methods provide a better quality essential oil. The essential oil of cumin was found to contain 20 compounds that comprised 95.8% of the total oil (Rehman et al. 2000). The major constituents found were: cuminaldehyde (37.4%), *p*-cymene (16.5%), and *p*-mentha-1,3-dien-7-al (15%). Others components included: β-pinene (9.8%), γ-terpinene (8.1%), *p*-mentha-1,4-dien-7-al (5.5%), less than 1% – α-pinene (0.4%), α-thujene (0.1%), sabinene (0.1%), myrcene (0.4%), limonene (0.2%), 1,8-cineole (0.1%), *cis*-isopulegone (0.2%), terpinen-4-ol (0.4%), α-terpineol (0.6%), phellandral (0.2%), *p*-cymen-8-ol (0.1%), cumin alcohol (0.3%), *cis*-*p*-menth-4-en-1,2-diol (0.2%) and *p*-isopropylphenol (0.2%). Among the 49 compounds were identified from steam distilled cumin oil, comprising 16 hydrocarbons and 32 oxygenated compounds (Yan et al. 2002). The main components were cuminal and safranal accounting for 32.26 and 24.46% respectively. The other nine compounds with contents all over 1%, were monterpenes, sesquiterpenes, aromatic aldehydes and aromatic oxides etc. The other components with relatively small amounts were chiefly terpenes, terpenols, terpenals, terpenones, terpene esters and aromatic

compounds. In another study, main components of *C. cyminum* oil found were *p*-mentha-1,4-dien-7-al, cumin aldehyde, γ-terpinene, and β-pinene (Iacobellis et al. 2005). Thirty-seven components were identified in the hydrodistilled essential oil of cumin seeds, representing 97.97% of the oil (Li and Jiang 2004). Cuminal (36.31%), cuminic alcohol (16.92%), γ-terpinene (11.14%), safranal (10.87%), *p*-cymene (9.85%) and β-pinene (7.75%) were the major components. More than could be identified as essential volatiles, responsible for the pleasant fresh, clean, spicy (typical cumin-like) odour of a high quality product. Jirovetz et al.(2005) identified >60 constituents of cumin oil among which cumin aldehyde (36%), β-pinene (19.3%), *p*-cymene (18.4%) and γ-terpinene (15.3%) were the principal compounds found.

The hydrodistilled essential oil of cumin was found to contain α-pinene (29.1%), limonene (21.5%), 1,8-cineole (17.9%), linalool (10.4%), linalyl acetate 4.85% , α-terpineole (3.17%), methyl eugenol (1.6%), α-terpinyl acetate (1.3%), geraniol (1.1%), isobutyl isobutyrate (0.8%), a-thujene (0.3%), sabinene (0.6%), myrcene (0.2%), d-3-carene (0.2%), *p*-cymene (0.3%) (*E*)-ocimene (0.1%), g-terpinene (0.6%), terpinolene (0.3%), a-campholenal (0.03%), *trans*-pinocarveole (0.07%), d-terpineole (0.09%), terpinene-4-ol (0.5%), *trans*-carveole (0.07%), methyl geranate (0.2%), neryl acetate (0.09%), b-caryophyllene (0.2%),a-humulene (0.2%), spathulenol (0.07%), caryophylleneb epoxide (0.1%), humulene epoxide 11 (0.08%), and acetocyclohexane dione (0.4%) (Gachkar et al. 2007). The main constituents identified in cumin seed essential oil at different harvesting time were found to be cumin aldehyde (19.9–23.6%), *p*-mentha-1,3-dien-7-al (11.4–17.5 5) and *p*-mentha-1,4-dien-7-al (13.9–16.9%) (Kan et al. 2007). Major constituents in cumin oil were γ-terpinene (15.82%), 2-methyl-3-phenyl-propanal (32.27%) and myrtenal (11.64%) (Jalali-Heravi et al. 2007). The major components identified in cumin essential oil were *p*-menta-1,3-dien-7-al, cuminaldehyde, γ-terpinene and *p*-cymene, (Hashemi et al. 2009).

Twenty-one components were identified from Tunisian cumin essential, comprising monoterpene hydrocarbons 42.42%, oxygenated monoterpenes 56.61%, sesquiterpene hydrocarbons 0.33%: cuminaldehye 39.48%, γ-terpinene 15.21%, *o*-cymene 11.82%, β-pinene 11.13%, 2-caren-10-al 7.93%, *trans*-carveol 4.49%, myrtenal 3.50%, limonene 1.42%, β-myrcene 0.785%, sabinene 0.56%, δ-3-carene 0.42%, α-pinene 0.4%, phellandral 0.39%, *cis*-sabinene hydrate 0.34%, β-caryophyllene 0.33%, terpinene-4-ol 0.30%, *trans*-pinocarveol 0.25%, α-thujene 0.20%, α-phellandrene 0.18%, verbenol 0.18%, and linalool 0.08%. (Hajlaoui et al. 2010). The major compounds in cumin oils from four different regions in Germany were monoterpenes β-pinene, *p*-cymene and γ-terpinene and the terpenoid aldehydes cuminic aldehyde and the isomeric menthadien carboxaldehydes (Wanner et al. 2010). The abundant components in cumin fruit essential oil were found to be cumin aldehyde, pinenes, and *p*-cymene, and a fraction of oxygenated compounds such as alcohols and epoxides (Romagnoli et al. 2010). The major constituents of cumin essential oil were cuminaldehyde (30.2%), *p*-cymene (14.1%), γ-terpinene (12.8%), and safranal (9.4%) (Oroojalian et al. 2010). A total of 12.72 mg of cuminaldehyde and 10.61 mg of *p*-menta-1,4-dien-7-al were obtained from 50 mg of the essential oil of *C. cyminum* with purities of 95.42 and 97.21%, respectively (Chen et al. 2011). Pajohi et al. (2011) found that cumin aldehyde (29.02%) and α-terpinen-7-al (20.70%) constituted the highest amount of cumin essential oil. Important aroma compounds of toasted cumin are the substituted pyrazines, 2-ethoxy-3-isopropylpyrazine, 2-methoxy-3-*sec*-butylpyrazine, and 2-methoxy-3-methylpyrazine (Vasundhara and Parihar 2006; Hajlaoui et al. 2010).

The volatile oil yield, after pre-treatment of cumin seeds with cellulase, pectinase, protease and Viscozyme, was in the range 3.2–3.3% compared to 2.7% in a control sample (Sowbhagya et al. 2011). The total hydrocarbon content was 63.7, 66.1 and 70.1% in control, cellulase and Viscozyme treated samples, respectively. However, there was no change in the content of cuminaldehyde, the principal flavour-impact constituent, in any of the volatile oils. Enzymatic pre-treatment of cumin seeds resulted in higher yield of volatile oil and did not affect

physico-chemical quality of oil. The percentage increase in yield of oil with enzyme pre-treatment was 18–22%. Studies indicated that the microwave-heated samples of cumin seeds afforded volatile oils that showed better retention of characteristic flavour compounds, such as aldehydes, than did the conventionally roasted samples (Behera et al. 2004).

Cumin essential oil yields were 0.03% in roots, 0.1% in stem and leaves, and 1.7% in flowers (Bettaieb et al. 2010). Major components of the oils were bornyl acetate (23%), α-terpinene (34%), and γ-terpinene (51%) in roots, stems and leaves, and flowers, respectively. In all cumin plant parts, total phenolics content varied from 11.8 to 19.2 mg of gallic acid equivalents per gram of dry weight (mg of GAE/g of DW). Among the polyphenols studied, 13 were identified in roots, 17 in stem and leaves, and 15 in flowers. The major phenolic compound in the roots was quercetin (26%), whereas in the stems and leaves, *p*-coumaric, rosmarinic, *trans*-2-dihydrocinnamic acids and resorcinol were predominant. In the flowers, vanillic acid was the main compound (51%).

Spent cumin from spice industries was found to have a carbohydrate content of 23%, protein 19%, fat 10% and soluble dietary fibre 5.5%, along with vitamins such as thiamine (0.05 mg/100 g), riboflavin (0.28 mg/100 g) and niacin (2.7 mg/100 g) (Milan et al. 2008). It was also a rich source of minerals, having Fe (6.0 mg/100 g) and Zn (6.5 mg/100 g) (mg/100 g). Different concentrations of phytase were used to improve the bioavailability of iron and zinc. Results showed that phytase (ratio of 1:1000), in the presence of 20 mM citric acid, increased iron and zinc bioavailability significantly. The saline and hot aqueous extracts of spent cumin showed enzymatic activities similar to that of native cumin. maximum increases in amylase, protease, lipase and phytase activities in the presence of saline and hot aqueous extracts, along with high antioxidant activity. Thus, the spent cumin can find potential use in various health food formulations, showing improved digestibility and a good nutrient composition.

Cumin has been reported to possess many pharmacological properties as elaborated below.

Antioxidant Activity

The IC_{50} values for aqueous extract of cumin in scavenging of superoxide radicals was found to be 220 μg, for inhibition of lipid peroxide was 4,300 μg, and for inhibition of hydroxyl radicals was 470 μg (Satyanarayana et al. 2004). The strong antioxidant activity of the extract was superior to known antioxidant ascorbic acid and indicated its intake may be beneficial as food additives. The IC_{50} values for aqueous extract of cumin in scavenging of superoxide radicals was found to be 220 μg, for inhibition of lipid peroxide was 4,300 μg, and for inhibition of hydroxyl radicals was 470 μg (Satyanarayana et al. 2004). The strong antioxidant activity of the extract was superior to known antioxidant ascorbic acid and indicated its intake may be beneficial as food additives. Cumin essential oil notably reduced the concentration of DPPH free radical, with an efficacy slightly lower than that of trolox (Gachkar et al. 2007). The lipid peroxidation inhibitory activities of the essential oils as assessed by the β-carotene bleaching test showed cumin to have higher activity than rosemary oil.

Methanol, ethanol, dichloromethane and hexane extracts of cumin were found to have antioxidant properties namely chelating activity, reducing power and free radical scavenging activity (Bukhari et al. 2009). The antioxidant activities of cumin essential oils and acetone extracts obtained from the flowers, stems and leaves were assessed using four tests [1,1-diphenyl-2-picrylhydrazyl (DPPH)], β-carotene/linoleic acid, reducing power, and chelating power assays (Bettaieb et al. 2010). The acetone extract of flowers was strongly effective as a DPPH radical scavenger, lipid peroxidation inhibitor, and reducing agent, with IC_{50} values of 4, 32, and 8 μg/mL, respectively. Moreover, the acetone extract of stems and leaves showed the highest chelating power. However, the essential oils exhibited moderate activities in the different tests.

In the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay, *Rosmarinus officinalis*, *Cuminum cyminum*,

Pimpinella anisum, *Thymus serpyllum* and *Liquidamber orientalis* essential oils obtained by supercritical carbon dioxide extraction showed higher antioxidant activity than steam distillation extracts, with radical scavenging activities ranging from 87.1 to 92.0% compared with the butylated hydroxytoluene positive control (91.4%) (Topal et al. 2008). The DPPH (2,2′-diphenyl-1-picrylhydrazyl) radical scavenging activity of the extracts in decreasing order was: *Pimpinella anisum* > *Trachyspermum copticum* > *Cuminum cyminum* > *Foeniculum vulgare* > or = *Bunium persicum* > or = *Coriandrum sativum* > *Heracleum persicum* (Nickavar and Abolhasani 2009). The decreasing order of the flavonoid content of the extracts was: *Cuminum cyminum* > *Trachyspermum copticum* > *Pimpinella anisum* > or = *Heracleum persicum* > or = *Buniumpersicum* > or = *Foeniculum vulgare* > or = *Coriandrum sativum*.

Cumin essential oil exhibited a higher antioxidant activity than BHT in each antioxidant system especially in the β-carotene bleaching test (IC_{50}: 20 μg/mL), reducing power (EC_{50}: 11 μg/mL), DPPH assay (IC_{50}: 31 μg/mL) and superoxide radicals (IC_{50}:16 μg/mL) (Hajlaoui et al. 2010). Of ginger and cumin volatile oils, the highest yield was obtained for cumin 2.52% and the major components were cuminal, γ-terpinene and pinocarveol (El-Ghorab et al. 2010). In non-volatile extracts the highest yield was obtained by the methanol extract of cumin (4.08% w/w), while the n-hexane extract of fresh ginger showed the lowest yield (0.52% w/w). The hexane extract of cumin showed the lowest total phenolic content (10.6 mg/g dry extract). The DPPH method showed the highest antioxidant activity for cumin essential oil (85.44%) followed by dried ginger essential oil (83.87%) and fresh ginger essential oil (83.03%). The FRAP of essential oils showed almost comparative results with DPPH. Cumin essential oil was found best in reducing Fe^{3+} ions, followed by dried and fresh ginger. The total phenol content of cumin essential oil was estimated to be 33 μg GAE/mg of the oil (Allahghadri et al. 2010). The oil showed higher antioxidant activity compared with that of BHT and BHA. The cumin essential oil exhibited a dose-dependent scavenging of DPPH radicals and 5 μg of the oil was sufficient to scavenge 50% of DPPH radicals/mL.

Studies by Bettaieb et al. (2011a) found that water deficit could impact fatty acid and essential oil composition and antioxidant activities of cumin. Total fatty acid content decreased significantly with severity of water deficit. Drought reduced considerably the proportions of major fatty acids and the unsaturated to saturated fatty acid ratio. The essential oil yield was 0.14% (based on the dry weight); it increased by 2.21-fold at moderate water deficit (MWD) but decreased by 42.8% under severed water deficit (SWD) in comparison to the control. Drought resulted in the modification of the essential oil chemotype from 1-phenyl-1-butanol to 1-phenyl-1,2-ethanediol. The highest antioxidant activity as determined by two complementary test systems, namely, DPPH and β-carotene/linoleic acid was exhibited by moderately stressed plants and was reduced significantly under SWD. In control plants, the total phenolic amount was 10.23 mg GAE/g DW, which increased by 1.5-fold under MWD and decreased by 42% under SWD. Irradiation was found to non-significantly increase and/or maintain all antioxidant parameters, total polyphenol content of cumin seeds and the electron spin resonance signal intensity was found to be increased in cumin seeds (Kim et al. 2009).

Antimicrobial Activity

Of seven essential oil tested, cumin essential oil showed the most significant activity against *Pseudallescheria boydii* (88.2%), and *Aspergillu flavus* (66.7%). It also showed activity against *Microsporum canis* (51.6%) and *Trichophyton simii* (25%) (Rehman et al. 2000). Cumin exhibited in-vitro antifungal activity against *Candida albicans* (Pai et al. 2010). Cumin oils and cuminic aldehyde exhibited a considerable inhibitory effect against all the Gram-positive and Gram-negative bacteria isolated from different sources of food (pork fillet, minced meat and sausages) and clinical isolates, as well as three different *Candida albicans* isolate tested, except *Pseudomonas* spp. (Wanner et al. 2010).

Cumin fruit essential oil exhibited antifungal activity against dermatophytes, yeast and some *Aspergillus* spp. (Romagnoli et al. 2010). *Trichophyton rubrum* was the most susceptible fungus, being inhibited at the lowest dose of 5 μL. The oil was less inhibitory to the phytopathogens. *C. cyminum* essential oil exhibited high inhibitory activity against the mold *Aspergillus niger*, the Gram (+) bacteria *Bacillus subtilis* and *Staphylococcus epidermidis* as well as the yeast *Saccharomyces cerevisiae* and *Candida albicans* (Jirovetz et al. 2005).

The essential oil of seven spices including cumin were found to be effective against eight pathogenic bacteria, causing infections in the human body (Singh et al. 2002). The oils were equally or more effective when compared with standard antibiotics, at a very low concentration. *C. cyminum* oil exhibited stronger antimicrobial activity than did rosemary oil against *Escherichia coli*, *Staphylococcus aureus* and *Listeria monocytogenes* (Gachkar et al. 2007). Complete death time on exposure to cumin and rosemary oils were 20 and 25 min, 180 and 240 min, and 90 and 120 min for *Escherichia coli*, *Staphylococcus aureus* and *Listeria monocytogenes*, respectively. Both essential oils may be considered as potent agents in food preservation. Cumin oil was also found to inhibit growth of *Klebsiella pneumoniae* strains. Growth of *Klebsiella pneumoniae* strains exposed to subminimum inhibitory concentrations of cumin extracts resulted in cell elongation and repression of capsule expression and decreased urease activity (Derakhshan et al. 2008). The bioactive constituent of the oil was determined to be cumin aldehyde. Cumin essential oil exhibited antibacterial activity against several food-borne pathogens, namely *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Salmonella enteritidis*, and *Listeria monocytogenes* with MIC values of 0.37–3.0 mg/mL (Oroojalian et al. 2010).

Cumin essential oil exerted substantial antibacterial activity against 24 bacterial species/isolates that included gram positive *Staphyloccocus epidermidis*, *Staphyloccocus aureus*, *Micrococcus luteus*, *Bacillus cereus* (2), Gram negative *Escherichia coli*, *Listeria monocytogenes*, *Enterococcus feacalis*, *Pseudomonas aeruginosa*, *Salmonella typhimirium*, and *Vibrio* species : *Vibrio cholerae*, *Vibrio alginolyticus* (2), *Vibrio parahaemolyticus* (2), *Vibrio proteolyticus*, *Vibrio furnisi* (2), *Vibrio fluvialis*, *Vibrio carhiaccae*, *Vibrio vulnificus*, *Vibrio mimicus* and five yeast species : *Candida albicans*, *Candida glabrata*, *Candida parapsilosis*, *Candida krusei*, *Sacchormyces cerevisae* (Hajlaoui et al. 2010). Based on in-vitro-growth inhibition diameter, Gram positive bacterial species were more sensitive to cumin oil especially *Micrococcus luteus* than Gram negative bacteria species. MIC and MBC values obtained with cumin oil was effective against all tested bacteria with MIC value about 0.078 mg/mL for Gram positive bacteria, and MICs of 0.078–0.15 mg/mL for Gram negative bacteria and MICs of 0.078–0.31 mg/mL for *Vibrio* species. MBC values were also low and low concentration was sufficient to halt growth of *M. luteus* (MBC 0.15 mg/mL), *Enterococcus feacalis* and *Escherichia coli* both with MBC of 0.625 mg/mL, and MBC value of 1.25 mg/mL for *V. cholerae*, *V. parahaemolyticus* and *V. vulnificus*. The effectiveness of some spice essential oil in complete inhibition of both mycelial growth and aflatoxin production of *Aspergillus parasiticus* followed the sequence: thyme > cumin > clove > caraway > rosemary > sage (Farag et al. 1989). The major components of the essential oils produced an inhibitory effect at minimum inhibitory concentrations equal to those obtained with the oils.

In a recent study, the lowest concentration of cumin essential oil significantly affected the growth of the bacteria, *Bacillus cereus* and *Bacillus subtilis* at 8°C but not at 25°C (Pajohi et al. 2011). Synergistic effect of cumin essential oil in combination with the lowest concentration of nisin was observed on the bacteria at 8°C. The essential oil of cumin seed showed the most bactericidal effects on *B. cereus* at 8°C. Ultrastructural studies of vegetative cells confirmed the synergistic destructive effects of the essential oil and nisin on membrane and cell wall of the bacteria. Studies showed a significant in-vitro effect of cumin plant extract against *Helicobacter pylori* and may contribute to the development of new and safe agents for inclusion

in anti-*H. pylori* regimens (Nostro et al. 2005). The ethanolic cumin extract expressed a MIC_{90} value of 0.075 mg mL. Cumin essential oil exhibited antibacterial activity against *Streptococcus mutans* and *Streptococcus pyogenes* and biofilm-formation preventive properties (Shayegh et al. 2008). *Escherichia coli*, *Staphylococcus aureus*, and *Staphylococcus faecalis* were sensitive to various cumin oil dilutions (Allahghadri et al. 2010). Antibacterial and in vivo biofilm preventive efficacies of all the concentrations of *Mentha piperita* oil were significantly higher. The biofilm inhibitory properties in planktonic cultures were in the order of *Mentha piperita*>chlorhexidine>cumin.

Anticancer Activity

In-vivo studies showed that cumin seed mixed diet significant inhibited of stomach tumor burden (tumors per mouse) (Gagandeep et al. 2003). Tumour burden was 7.33 in the benzo(a)pyrene-induced control group, whereas it reduced to 3.10 by a 2.5% dose and 3.11 by a 5% dose of cumin seeds. Cervical carcinoma incidence, compared with the 3-methylcholanthrene (MCA)-induced control group (66.67%), reduced to 27.27% by a diet of 5% cumin seeds and to 12.50% by a diet of 7.5% cumin seeds. Cumin diets also altered the status of on carcinogen/xenobiotic metabolizing phase I and phase II enzymes, antioxidant enzymes, glutathione content, lactate dehydrogenase (LDH), and lipid peroxidation in the liver of Swiss albino mice. Levels of cytochrome P-450 (cyt P-450) and cytochrome b5 (cyt b(5)) were significantly augmented by the 2.5% dose of cumin seed diet. The levels of cyt P-450 reductase and cyt b(5) reductase were increased by both doses of cumin. Among the phase II enzymes, glutathione S-transferase specific activity increased by the 5% dose, whereas that of DT-diaphorase increased significantly by both doses used (2.5 and 5%). In the antioxidant system, significant elevation of the specific activities of superoxide dismutase and catalase was observed with the 5% dose of cumin. The activities of glutathione peroxidase and glutathione reductase remained unaltered by both doses of cumin. The level of reduced glutathione measured as nonprotein sulfhydryl content was elevated by both doses of cumin. Lipid peroxidation measured as formation of MDA production showed significant inhibition by both doses of cumin. LDH activity remained unaltered by both doses of cumin. The results strongly suggested the cancer chemopreventive potentials of cumin seed and could be attributed to its ability to modulate carcinogen metabolism. At a concentration of 0.1 μL/mL, cumin essential oil destructed Hela cells by 79% (Allahghadri et al. 2010). The antioxidant activity of cumin essential oil might contribute to its cytotoxic activity. Acute and subchronic toxicity was studied in a 30-day oral toxicity study by administration to Wistar rats of cumin essential oil. A 17.38% decrease in WBCs count, and 25.77, 14.24, and 108.81% increase in hemoglobin concentration, hematocrit, and platelet count, respectively, were observed (Allahghadri et al. 2010). LDL/HDL ratio was reduced to half, which adds to the nutritional effects of cumin.

Hepatoprotective Activity

In-vivo studies showed that rats administered alcohol, thermally oxidized sunflower oil (rich in polyunsaturated fatty acids) and alcohol + thermally oxidized oil, had increased activity of aspartate transaminase (AST), alkaline phosphatase (ALP) and gamma glutamyl transferase (GGT) in the plasma and increased levels of cholesterol, triglycerides and phospholipids in the plasma and lever and kidney tissues compared to the control group (Aruna et al. 2005). These levels were decreased when cumin was given along with alcohol and thermally oxidized oil. Cumin also elevated the significantly reduced level of phospholipids and phospholipase activity in the liver and kidney of groups given alcohol, thermally oxidized oil and alcohol + thermally oridized oil. The results obtained indicated that cumin could decrease the lipid levels in alcohol and thermally oxidized oil induced hepatotoxicity.

Gastroprotective Activity

Perfusion of the stomach of pentobarbitone-anesthetized rats with an aqueous extract of cumin increased acid secretion by a cholinergic mechanism (Vasudevan et al. 2000). Cumin extract also increased gastric acid secretion in stomach with aspirin-induced mucosal injury.

Nephroprotective Activity

Studies showed that the aqueous cumin seed extract had a protective action against gentamicin induced nephrotoxicity in rats (Mahesh et al. 2010). The cumin extract at 200 mg/kg showed marked decrease in the gentamicin-induced elevated levels of serum urea, creatinine, lipid peroxidation, and increased clearance of urea and creatinine compared to the 100 mg/kg cumin extract.

Antidiabetic and Antiphyperlipidemic/ Antihyperchlolesterolemic Activities

Cuminaldehyde isolated from cumin seeds was found to be an inhibitor of lens aldose reductase and α-glucosidase isolated from Sprague-Dawley male rats (Lee 2005). The IC_{50} value of cuminaldehyde was 0.00085 mg/mL against aldose reductase and 0.5 mg/mL against α-glucosidase, respectively. Cuminaldehyde was about 1.8 and 1.6 times less in inhibitory activity than acarbose and quercitin, respectively. Nonetheless, cuminaldehyde may be useful as a lead compound and a new agent for antidiabetic therapeutics.

An 8 week dietary regimen containing cumin powder (1.25%) was found to be remarkably beneficial, as indicated by reduction in hyperglycaemia and glucosuria (Willatgamuwa et al. 1998). This was also accompanied by improvement in body weights of streptozotocin diabetic animals on the cumin diet. Dietary cumin also prevented other metabolic alterations as revealed by lowered blood urea level and reduced excretions of urea and creatinine by diabetic animals.

Oral administration of cumin (0.25 g/kg body weight) for 6 weeks to diabetic rats resulted in significant reduction in blood glucose and an increase in total haemoglobin and glycosylated haemoglobin (Dhandapani et al. 2002). It also prevented a decrease in body weight. Cumin treatment also produced a significant reduction in plasma and tissue cholesterol, phospholipids, free fatty acids and triglycerides and fatty changes and inflammatory cell infiltrates. *C. cyminum* supplementation was found to be more effective than glibenclamide in the treatment of diabetes mellitus. Animal studies showed that ingestion of cumin prevented the changes in fatty acid composition produced by ingestion of ethanol (20%) and thermally oxidized sunflower oil (15%) (Kode et al. 2005). The elevated levels of 16:0, 16:1, 18:0, 18:1 and 20:4 induced by ethanol and thermally oxidized sunflower oil were restored to near normal in cumin treated rats. In-vitro studies indicated that cumin inhibited free radicals and advanced glycated end (AGE) products formation (Jagtap and Patil 2010). Treatment of streptozotocin-diabetic rats with cumin methanol extract and glibenclamide for 28 days caused a reduction in blood glucose, glycosylated hemoglobin, creatinine, blood urea nitrogen and improved serum insulin and glycogen (liver and skeletal muscle) content when compared to diabetic control rats. Significant reduction in renal oxidative stress and AGE was observed with cumin when compared to diabetic control and glibenclamide. Cumin and glibenclamide improved antioxidant status in kidney and pancreas of diabetic rats. Though the antidiabetic effect of cumin was comparable to glibenclamide, it had better effect in controlling oxidative stress and inhibiting the advanced glycated end formation in the pathogenesis of diabetic microvascular complications.

The spices cumin (*Cuminum cyminum*), cinnamon (*Cinnamomum zeylanicum*), ginger (*Zingiber officinale*), mustard (*Brassica nigra*) and tamarind *(Tamarindus indica*) did not show any cholesterol lowering effect when included in the diet of normal and hypercholesterolemic rats at about fivefold the normal human intake level (Sambaiah and Srinivasan 1991). However, recent

studies showed that treatment with estradiol and methanol cumin extract both significantly decreased total cholesterol levels in serum in ovariectomized rats (Shirke and Jagtap 2009). The decrease in total serum cholesterol caused by cumin extract was significantly greater than that caused by standard drug estradiol. It was observed that total cholesterol levels in cumin extract treated rats were lower but not significantly than sham operated control rats. The results indicated that estradiol as well as methanol cumin extract protected ovariectomize rats against increased cholesterol levels due to ovariectomy while cumin extract was better than estradiol. Thus the methanolic extract of *Cuminum cyminum* could be useful for the treatment of menopausal disorders, especially cardiovascular disorders in postmenopausal women.

Antiplatelet Activity

Ethereal extracts of both cumin and turmeric inhibited arachidonate-induced platelet aggregation (Srivastava 1989). Both extracts inhibited thromboxane B2 production from exogenous (14C) arachidonic acid (AA) in washed platelets. Both extracts reduced the formation of (14C) TxB2 from AA-labelled platelets when they were challenged with A23187.

Antityrosinase Activity

Cuminaldehyde (*p*-isopropylbenzaldehyde) from cumin was identified as a potent mushroom tyrosinase inhibitor (Kubo and Kinst-Hori 1998). It inhibited the oxidation of l-3,4-dihydroxyphenylalanine (l-DOPA) by mushroom tyrosinase with an ID_{50} of 7.7 μg/mL (0.05 mM). Its oxidized analogue, cumic acid (*p*-isopropylbenzoic acid), also inhibited this oxidation with an ID_{50} of 43 μg/mL (0.26 mM).

Osteoprotective Acitivty

Methanol extract of cumin fruit at a dose of (1 g/kg, p.o.) significantly reduced urinary calcium excretion and significantly increased calcium content and mechanical strength of bones in comparison to control ovariectomized adult Sprague Dawley rats (Shirke et al. 2008). Cumin extract showed greater bone and ash densities and improved microarchitecture of bones. The osteoprotective effect was comparable with estradol but unlike estradiol it did not affect body weight gain and weight of atrophic uterus in ovariectomized animals. Cumin extract prevented ovariectomy-induced bone loss in rats with no anabolic effect on atrophic uterus.

Antiepileptic Activity

Administration of cumin essential oil protected mice against maximal electroshock -induced and pentylenetetrazole-induced tonic seizures (Sayyah et al. 2002a). Additionally, at certain anticonvulsant doses, cumin essential oil produced sedation and motor impairment. Studies demonstrated that extracellular application of the essential oil of *Cuminum cyminum* (1 and 3%) to F11 neuronal cells of *Helix aspersa* dramatically decreased the frequency of spontaneous epileptiform activity induced by pentylenetetrazol in a time and concentration dependent manner (Janahmadi et al. 2006). Further cumin exhibited protection against pentylenetetrazol-induced epileptic activity by increasing the duration, decreasing the amplitude of after hyperpolarization potential (AHP) following the action potential, the peak of action potential, and inhibition of the firing rate.

Analgesic Activity

Cumin fruit essential oil at does of 0.0125 and 0.2 mL/kg exhibited a significant dose-dependent analgesic effect in the rat model of chronic and inflammatory pain (Sayyah et al. 2002b). However, the essential oil was devoid of nay anti-inflammatory effect. The oil had no analgesic effect in tail flick test as a model of acute pain. The LD_{50} value was 0.59 mL/kg.

Antispasmodic/Bronchodilation Activity

Studies demonstrated that macerated and aqueous extracts of cumin seeds exhibited a potent relaxant effect on guinea pig tracheal chains which may be due to a stimulatory effect of the plant on β-adrenoceptors and/or an inhibitory effect on histamine H1 receptors (Boskabady et al. 2005).

Adaptogenic Activity

Results of the study by Koppula and Choi (2011) provided scientific support for the antistress, antioxidant, and memory-enhancing activities of cumin extract and substantiated its traditional use as a culinary spice in foods and in combating stress and related disorders. They found that daily administration of cumin (100, 200, and 300 mg/kg body weight) 1 h prior to induction of stress inhibited the stress-induced urinary biochemical changes in a dose-dependent manner. The cognition, as determined by the acquisition, retention, and recovery in rats, was observed to be dose-dependent. The extract also produced significant lipid peroxidation inhibition in comparison with known antioxidant ascorbic acid in both rat liver and brain.

Antitussive Activity

Studies showed that the aerosols of aqueous and macerated cumin extract exhibited antitussive effect comparable to that of Codeine (Boskabady et al. 2006). Exposing guinea pigs to the aerosols, produced significant reduction in cough number for the aqueous and macerated cumin extracts and Codeine.

Antifertility Activity

Studies by Gupta et al. (2011) showed that *C. cyminum* treatment resulted in the inhibition of spermatogenesis and fertility without producing apparent toxic effects. Cumin methanol extract fed to male rats for 60 days did not cause any alterations in the body weight, whereas the weight of testes, epididymides, seminal vesicles and ventral prostate were significantly reduced. Animals treated with the extract showed a marked reduction in sperm density in the cauda epididymis and testes and sperm motility in the cauda epididymis. Reduction in fertility was 69.0 and 76.0% in 100 and 200 mg/rat/day dose levels, respectively. The circulatory hormones were also reduced significantly. Testicular biochemical analysis of protein, sialic acid, glycogen, ascorbic acid and fructose indicated a marked decline, whereas testicular cholesterol content was significantly increased, which showed altered biochemistry of the reproductive organs. After cumin treatment, significant decreases were observed in the number of testicular cells (i.e., spermatogonia, primary spermatocytes, secondary spermatocytes and round spermatids); nonsignificant change was observed in the Sertoli cell count. The treatment had no effect on levels of serum protein, cholesterol, bilirubin, glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), blood urea and hematological indices.

The acetone extract of cumin exerted estrogenic activity in immature ovariectomized rats (Malini and Vanithakumari 1987). Cumin fruits had been reported to contain estrogenic compounds like β-sitosterol, stigmasterol, apigenin and luteolin and studies showed that the methanol extract of cumin fruit exhibited in-vitro and in-vivo estrogenic activity (Jagtap et al. 2007). The methanol extract significantly increased MCF-7 breast cancer cell line proliferation over the concentration range of 1 ng/mL to 100 μg/mL with the maximum increase of 115.78% at 1 μg/mL. At 200 mg/kg, the extract caused significant increase in absolute and relative weight of uterus along with the increase in uterine peroxidase (UPO) activity and significant increase in total protein content in ovariectomized rats. All the various fractions with n-hexane, diethyl ether, chloroform and water were also found to be estrogenic in-vitro. The estrogenic potential of the most active chloroform fraction was confirmed by in-vivo uterotropic assay, showed significant increase in absolute and relative weight of uterus

and increase in glycogen content with no effect on uterine peroxidase activity at 25 mg/kg; higher doses 50 and 100 mg/kg did not show any estrogenic activity. The results suggested that cumin could be used as an uterotropic or antifertility herbal drug.

Amelioration of Morphine Tolerance

Studies in mice showed that cumin fruit essential oil, at the dose of 2%, significantly attenuated the development of morphine tolerance and dependence (Haghparast et al. 2008). Cumin (0.001–2%) did not show any analgesic effect. Studies showed that cumin fruit essential oil reduced the acquisition and expression of morphine-induced conditioned place preference in mice. Administration of cumin oil 60 min before the test decreased the conditioning scores at the doses of 1 and 2% while i.p. injection 60 min before morphine injection during 3 days of conditioning session (acquisition) significantly resulted in decrement of rewarding properties of morphine in dose-dependent manner.

Antiglycating Activity

Kumar et al. (2009) investigated the antiglycating potential of cumin by feeding streptozotocin (STZ)-induced diabetic rats with diet containing 0.5% cumin powder. The aqueous extract of cumin was found to prevent in-vitro glycation of total soluble protein, α-crystallin and bovine serum albumin. Supplementation of cumin delayed progression and maturation of STZ-induced cataract in rats. Cumin was effective in preventing glycation of total soluble protein and α-crystallin in diabetic lens. Feeding of cumin to diabetic rats not only prevented loss of chaperone activity but also attenuated the structural changes of α-crystallin in lens. These results indicated that cumin had antiglycating properties that may be attributed to the modulation of chaperone activity of α-crystallin, thus delaying cataract in STZ-induced diabetic rats.

Drug Potentiating Activity

An aqueous extract derived from cumin seeds produced a significant enhancement of rifampicin (drug for tuberculosis) levels in rat plasma (Sachin et al. 2007). This activity was found to be due to a flavonoid glycoside, 3′,5-dihydroxyflavone 7-*O*-β-D-galacturonide 4′-*O*-β-D-glucopyranoside. The altered bioavailability profile of rifampicin could be attributed to a permeation enhancing effect of this glycoside. Cumin seed essential oil decreased biofilm formation by *Klebsiella pneumoniae* and enhanced the activity of the antibiotic ciprofloxacin in-vitro (Derakhshan et al. 2010).

Immunomodulatory Activity

Oral administration of cumin (25, 50, 100 and 200 mg/kg) to Swiss albino mice subjected to Cyclosporine-A induced immune-suppression, significantly increased T cells (CD4 and CD8) count and Th1 predominant immune response in a dose dependent manner thereby suggesting immunomodulatory activity through modulation of T lymphocytes expression (Chauhan et al. 2010). In restraint stress induced immune-suppressed mice, cumin compound 1 countered the depleted T lymphocytes, decreased the elevated corticosterone levels and size of adrenal glands and increased the weight of thymus and spleen. The results suggested cumin to be a potent immunomodulator and may be developed as a lead to recover the immunity of immuno-compromised individuals.

Traditional Medicinal Uses

Cumin has been used in traditional medicine in Asia especially in traditional Chinese, Indian and Pakistani medicine.

Cumin is reported to be antispasmodic, aphrodisiac, astringent, carminative, galactagogue, stimulant and stomachic. It is used as a general tonic to the whole digestive system, in the treatment of flatulence and bloating, for reducing

intestinal gas and relaxing the gut, for improving liver function and is useful in dyspepsia and diarrhoea. It has been used in the treatment of minor digestive complaints, chest conditions and coughs, as a pain killer and to treat rotten teeth. In India, it is also used in the treatment of insomnia, colds and fevers and to improve milk production in nursing mothers. The seeds when ground into a powder and mixed into a paste with onion juice, has been applied to scorpion stings. Cumin has been used externally as a poultice to relieve stitches, wounds and pains. Cumin also acts as a stimulant to the sexual organs. The essential oil is also used as an antiseptic. In South Asia, cumin tea (dry seeds boiled in hot water) is used to distinguish false labour (due to gas) from real labour. In Sri Lanka, toasting cumin seeds and then boiling them in water makes a tea used to soothe acute stomach problems.

Other Uses

Cumin is strongly aromatic and the essential oil is used in perfumery and in veterinary medicine.

The antibacterial activity of cumin essential oil was particularly high against the genera *Clavibacter*, *Curtobacterium*, *Rhodococcus*, *Erwinia*, *Xanthomonas*, *Ralstonia*, and *Agrobacterium*, which are responsible for plant or cultivated mushroom diseases worldwide (Iacobellis et al. 2005). In general, a lower activity was observed against bacteria belonging to the genus *Pseudomonas*. These results suggested the potential use of the cumin essential oil for the control of phytobacterial diseases.

Cumin essential oil was found to have acaricidal activity (Martinez-Velazquez et al. 2011). Cumin displayed high toxiciological effect producing 100% mortality in all tested concentrations on *Rhipicephalus microplus* (cattle tick) larvae. The most common compounds detected in cumin essential oil were cuminaldehyde (22.03%), γ-terpinene (15.69%) and 2-caren-10-al (12.89%). Results indicated that *C. cyminum* essential oil could be used as an effective, friendly alternative for *R. microplus* cattle tick control.

Comments

Cumin is traded as whole product, in ground form, or as an essential oil. The regulatory status of cumin and cumin oil is regarded generally as safe (GRAS2340 and GRAS2343) (Sahana et al. 2011).

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Foeniculum vulgare

Scientific Name

Foeniculum vulgare **Miller**

Family

Apiaceae

Synonyms

Anethum dulce DC., *Anethum foeniculum* L., *Anethum minus* Gouan, *Anethum panmori* Roxb., *Anethum panmorium* Roxb. ex Fleming, *Anethum pannorium* Roxburgh, *Anethum piperitum* Ucria, *Anethum rupestre* Salisb., *Foeniculum azoricum* Mill., *Foeniculum capillaceum* Gilib. (Inval.), *Foeniculum divaricatum* Griseb., *Foeniculum dulce* Mill., *Foeniculum foeniculum* (L.) H. Karst. (Inval.), *Foeniculum giganteum* Lojac., *Foeniculum officinale* All., *Foeniculum panmorium* (Roxb.) DC., *Foeniculum piperitum* (Ucria) C.Presl, *Foeniculum rigidum* Brot. ex Steud., *Foeniculum scoparium* Quézel, *Foeniculum vulgare* subsp. *piperitum* (Ucria) Cout., *Foeniculum vulgare* var. *sativum* C.Presl, *Foeniculum vulgare* subsp. *sativum* (C.Presl) Janch. ex Holub, *Ligusticum foeniculum* (L.) Crantz, *Meum foeniculum* (L.) Spreng., *Meum piperitum* Schult., *Ozodia foeniculacea* Wight & Arn., *Selinum foeniculum* (L.) E.H.L. Krause, *Seseli dulce* Koso-Pol., *Seseli foeniculum* (L.) Koso-Pol., *Seseli piperitum* Koso-Pol., *Tenoria romana* Schkuhr ex Spreng.

Common/English Names

Aniseed Weed, Bitter Fennel, Bronze Fennel, Common Fennel, False Dill, Fennel, Finnochio, French Fennel, Green and Bronze Fennel, Garden Fennel, Roman Fennel, Sweet Cumin, Sweet Fennel, Wild Fennel.

Vernacular Names

Albanian: Kopër, Marac, Maraja;
Arabic: Badyan, Badiyan, Bikhe Badian, Bisbas, Razianaj, Raziyan, Shamaar, Shamar, Shamraa, Shoumar, Shumar;
Armenian: Samit, Samiţ;
Azerbaijani: Разjана, Razĵana, Razyana;
Basque: Mehul, Mieloi, Miur Belar;
Brazil: Erva-Doce, Funcho;
Bulgaria: Morach, Morač, Rezene;
Burmese: Samong-Saba;
Catalan: Fonoll, Fonollera, Herba De Les Vinyes;
Chinese: Hui Xiang, Hui Xiang, Huai-Xiang, Hsiang-Su-Ts'ai, Huai-Hsiang, Hui-Hsiang, Shih-Lo, Siao-Hiu, Tian Hi Xiang, Tzu-Mo-Lo, Xiao Hui Xiang, Xiang-Si-Cai;
Croatian: Komorač, Koromač;

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Czech: Fenýkl Obecný, Fenykl Obecný Pravý, Fenykl, Římský Kopr, Sladký Kopr, Vlašský Kopr;
Danish: Almindelig Fennikel, Fennikel, Sød Fennikel;
Dutch: Knolvenkel, Venkel;
Eastonian: Apteegitilliseemned, Harilik Apteegitill, Venkel;
Esperanto: Fenkolo;
Farsi: Razianeh;
Finnish: Fenikeli, Fenkoli, Maustefenkoli, Maustevenkoli, Saksankumina, Salaattifenkoli, Venkoli;
French: Anet, Aneth, Aneth Doux, Anis Doux, Fenouil, Fenouil Amer, Fenouil Commun;
Galician: Fiuncho;
Georgian: Kama;
German: Brotsamen, Echter Fenchel, Enis, Fenchel, Fehnkohl, Femis, Fenicht, Fenikl, Fenis, Fenkel, Finchel, Frauenfenchel, Gartenfenchel, Gemeiner Fenchel, Gewürzfenchel, Mutterwurz;
Greek: Finókio, Finokio, Maratho, Máratho;
Hebrew: Shumar;
Hungarian: Bécsi Fű, Bécsi Kapor, Édeskömény, Közönséges Édeskömény;
Icelandic: Fennika, Fenniku;
India: Sap Guti (Assamese), Mauri, Mouri (Bengali), Variyali (Gujerati), Saumph, Mauti Sanf, Saunf (Hindu), Badhesoppu, Dodda Jeerige, Badesopu, Badisopu, Dodda Sompu (Kannada), Perincirakam, Perumjirakam (Malayalam), Hop (Manipuri), Badishep, Fumh (Marathi), Madhura, Madhurika, Methica, Misi, Misreya, Satahva, Satapuspa (Sanskrit), Cokikkirai, Compu, Kacicciram, Peruncheeragam, Sombu, Shombu, Sohikirai, Sompu, (Tamil), Peddajilakarra, Peddajeekaramu, Peddajeela Koora, Sopu (Telugu), Arq Badiyan, Badi Saunf, Badiyan, Badiyan Nim Kofta, Badiyan Saunf, Badiyan Biryan, Badiyan Khatai, Badyan, Bikh Badiyan, Mauti Saunf, Roghan Badiyan, Roghan-I-Badyan, Saunf, Sonf, (Urdu) ;
Indonesia: Das Spicy (Aceh), Popoas (Alfurese), Fennel (Bali), Porotomo (Baree), Papaato (Boeol), Adase (Bugis), Denggu-Denggu (Gorontalo), Adas, Adas Landa, Adas Landi, Adas Londa, Fennel Londa, Fennel Landi (Javanese), Adhas (Madura), Paapang, Paampas (Manado), Adeh, Manih (Minangkabau), Adasa, Rempasu (Napier), Kumpasi (Sangir Talaud), Adeh Manih (Sumatran), Wala Wunga (Sumba), Hades (Sundanese);
Irish: Finéal;
Italian: Finocchio, Finocchio Commune, Finocchio Di Lucca, Finocchio Di Roma, Finocchio Selvatico, Finocchione;
Japanese: Fenneru, Uiky, Uikyo, Uikyou;
Korean: Hoe-Hyang, Hoe-Hyang-Pul, Hoehyang, Hoehyang-Pul, Pen-Nel, Pennel, So-Hoe-Hyang, So –Hoehyang;
Laos: Phak Si;
Latvian: Fenhelis, Fenheļi Parastie;
Lithuanian: Paprastasis Pankolis, Pačiolis;
Malaysia: Adas, Adas Pedas, Jintan Manis;
Maltese: Bużbież;
Nepalese: Madesi Sauf;
Norwegian: Fenikkel, Fennikel, Finkel;
Pakistan: Barisaunf, Madhurika;
Persian: Razýanh, Razianeh;
Polish: Fenku, Fenkuł, Fenkuł Włoski**,** Koper Woski, Koper Włoski;
Portuguese: Funcho;
Provencal: Fenoun;
Romanian: Anason Dulce, Fenicol, Merulă Obişnuită, Molura, Molură;
Russian: Fenchel´ Obyknovennyj, Aptechnyj Ukrop, Aptečnyj Ukrop, Fenhel', Fenchel' Obyknovennyj, Fenkhel, Sladkij Ukrop, Ukrop Sladki, Ukrop Sladkij;
Scottish Gaelic: Lus An T'saiodh;
Sri Lanka: Maduri;
Slovaščina: Komarček Navadni, Navadni Komarček, Sladki Komarek, Sladki Komarček;
Slovencina: Fenikel, Fenikel Obyčajný;
Spanish: Hinojo, Hinojo Común;
Swahili: Tamari;
Swedish: Besk Fänkål, Bitter Fänkål, Fänkål, Finocchio, Florentinsk Fänkål, Fransk Fänkål, Kryddfänkål, Romersk Fänkål, Söt Fänkål, Tysk Fänkål, Vanlig Fänkål;
Philippines: Anis, Haras (Tagalog);
Portuguese: Erva-Doce, Fiolho, Fionho, Funcho, Funcho-Doce, Funcho-Amargo;
Russian: Fenchel' Obyknovennyj
Thai: Pak Chi Duanha, Phak Chi, Phak Chi Duen Ha, Phak Chi Lom, Phong Karee, Thian Klaep, Thian-Kaupeluengk, Thian-Klaep, Yira, Yira (Central Thailand);
Tibetan: Ma Tog Brgya Pa, Su Ti;
Turkey: Arapsaçı, Bahçe Rezenesi, Mayana, Raziyane, Rezene, İrziyan;

Ukrainian: Fenḫel' Zvičajnij, Fenkhel Zvychajniy; ***Vietnam***: Cay Thi La, Cây Thì Là, Hồi Hương, Hoi Huong, Tiêu Hồi Hương, Tieu Hoi Huong; ***Welsh***: Ffennigl.

Origin/Distribution

Fennel is considered native to the Mediterranean region and has widely naturalised and escaped from cultivation worldwide. It is extensively grown for its fruits and leaves mainly in the Mediterranean area, Western and Central Europe, southern and eastern Asia, New Zealand, Ethiopia, South Africa and the Americas.

Agroecology

Fennel is adapted to a Mediterranean, sub-temperate climatic regime with diurnal temperature range of 12–28°C. Fennel is frost sensitive. In the tropics it is cultivated in the highlands above 600 m. It thrives in full sun in well-drained, light, moderately fertile soils, especially in sandy loams nut needs supplemental watering during the dry seasons.

Edible Plant Parts and Uses

The fruits, seeds, flowers, leaves, shoots, stems, sprouted seedlings, essential oil together with the swollen petiole bases (*F. vulgare* subspecies var. *azoricum*) and swollen roots are all edible.

The tender shoots, leaves and stems are used in snacks, salads, soups, stews, or as spices. They are usually used in egg recipes, omelette, with grilled fish and cooked on fish dishes and bouillons, stewed with different kinds of beans and chickpeas and in various soups and sauces. They are also used fresh or dried in brochettes and herbal teas. These plant parts are also used to aromatize olive brines, fig preserves and brandy. The young leaves serve as flavouring or as a garnish on raw or cooked dishes and make a very pleasant addition to salad. The inflorescences and flowers are used to flavour beverages and spirits and also used as a spice. The yellow flowers have a mild anise flavour and are used with desserts or cold soups, or as a garnish with entrees or in fennel and watercress soup.

The fruit (mericarps) of sweet fennel (*F. vulgare* subspecies *vulgare*) are used for flavouring fish and other sea food dishes and can be used to make a pleasant-tasting herbal tea. The fruits and seeds are used for flavouring sweets, cakes, bread, biscuits, stuffings ordinary dishes, stews and dainties. The fruit mericarp called 'Jintan manis' or 'Adas pedas' is a common spice used in Malaysian cuisine such as dried grounded prawn curry powder, satay peanut sauce, and in chicken curries. Fennel seed is a common ingredient in Italian sausages, meatballs and northern European rye bread. The sprouted seeds can be added to salads. An essential oil from the fully ripened and dried seed is used as a food flavouring in similar ways to the whole seed.

The swollen, fleshy petiole bases of Florentine fennel are eaten cooked or raw as an accompaniment to cheese in England. It forms a key ingredient in some Italian and German salads, often tossed with avocado and chicory. It can also be braise, or blanched or marinated and cooked in risotto. Sliced fennel with avocados and oranges make for a delightful salad. Sliced fennel is often added to the traditional toppings of lettuce and tomato in sandwiches. Thinly sliced fennel slices are also eaten with plain yogurt and mint leaves. Fennel combines very well with salmon and braised fennel is a wonderful complement to scallops. Healthy sautéed fennel and onions make a wonderful side dish. The thick roots are also cooked and eaten. Florence fennel is one of three ingredients used in the preparation of absinthe, a popular alcoholic beverage in Europe especially in the nineteenth century. The plant is cultivated commercially in several European countries for the production of anethol which is used in food, cordials and liquors such absinthe.

Pectins extracted from fennel were found to compose of uronic acid and traces of rhamnose, galactose, and arabinose (Giosafatto et al. 2007). The extracted pectins were characterised for use as a carbohydrate source to prepare biopolymer films in the absence and in the presence of phaseolin protein.

Plate 1 Fennel plant with finely-divided foliage

Plate 2 Sheathing leaf bases

Botany

An erect, aromatic, glabrous, much-branched, biennial herb with erect, robust, glabrous stem filled with white spongy pith, growing up to 2 m high. Basal and cauline leaves up to 15 cm, broadly triangular-ovate in outline; ultimate segments 5–40 × 0.5 mm; petiole 7–14 cm. The bases of the petioles are broad and inflated in var. *azoricum*. Upper leaves alternate, 2–4 × pinnately divided, ultimate segments filiform, 1–6 × 0. 6 mm, petiole broadly sheathing at base (Plates 1–2). Flower pale yellow, tiny, 2 mm across, in compound umbels, 4–10 cm across; bracts and bracteoles absent, sepals inconspicuous, petals yellow, ovate, inflexed at apex, stamens exerted, ovary obconic and stigma on short style (Plates 3–4). Fruit ovoid-oblong to oblong (Plate 5), schizocarpic, of mericarps (2, dorsally flattened, each with 5 prominent ribs), non-fleshy, 4–10 mm long by 1.5–2 mm wide (Plate 6).

Foeniculum vulgare is divided into two subspecies: subspecies *vulgare* which include the sweet fennel and var. *azoricum* which has swollen bulbs. The other subpecies *F. vulgare* spp. *piperitum* (Ucria) Countinho also referred to as 'carosella' has stiffer and narrower leaf lobes and sharp-tasting mericarps which are used to flavour herb liqueurs.

Nutritive/Medicinal Properties

Fruit Nutrients and Other Phytochemicals

Fennel seed and bulb is an excellent source of vitamin C which is the body's primary water-soluble antioxidant. Fennel seed is a very good source of dietary fibre, potassium, manganese, folate, niacin, phosphorous, calcium, magnesium,

Plate 3 Young compound umbel

Plate 5 Cluster of young fennel fruits

Plate 4 Compound umbel with mature flowers

Plate 6 Fennel mericarps (seeds)

iron, copper and vitamins like thiamine, riboflavin and niacin and amino acids.

The proximate value per 100 g edible portion of fennel seed was reported as: water 8.81 g, energy 345 kcal (1,443 kJ), protein 15.8 g, total lipid 14.87 g, ash 8.22 g, carbohydrate 52.29 g, total dietary fibre 39.8 g, minerals – Ca 1,196 mg, Fe 18.54 mg, Mg 385 mg, P 487 mg, K 1,694 mg, Na 88 g, Zn 3.70 mg, Cu 1.067 mg, Mn 6.533 mg, vitamins – vitamin C 21 mg, thiamine.0.408 mg, riboflavin 0.353 mg, niacin 6.050 mg, vitamin B-6 0.47 mg,vitamin A 135 IU, vitamin A 7 µg RAE, total saturated fatty acids 0.480 g, 16:0 (palmitic acid) 0.480 g; total monounsaturated fatty acids 9.910 g, 18:1 undifferentiated (oleic acid) 9.910 g; total polyunsaturated fatty acids 1.690 g, 18:2 undifferentiated (linoleic acid) 1.690 g; phytosterols 66 mg, tryptophan 0.253 g, threonine 0.602 g, isoleucine 0.695 g, leucine 0.996 g, lysine 0.758 g, methionine 0.301 g, cystine 0.222 g, phenylalanine 0.647 g, tyrosine 0.410 g, valine 0.915 g, arginine 0.680 g, histidine 0.331 g, alanine 0.789 g, aspartic acid 1.833 g, glutamic acid 2.956 g, glycine 1.107 g, proline 0.900 g and serine 0.900 g (USDA 2012).

Oil content obtained in sweet and bitter fennels was 12.22 and 14.41%, respectively (Coşge et al. 2008). The C18:1 c6, C18:2, C18:1 c9 and C16:0 acids were principal fatty acids and constituted about 97% of total oil. The ratios of essential oil from sweet and bitter fennels were found similar (average 3.00%). *trans*-anethole, estragole and fenchone were found to be the major constituents in both fennels. The compound with the highest value in the two oil samples was *trans*-anethole 95.25% in sweet fennel and 75.13% in bitter fennel. Estragole (15.51%) was also high in bitter fennel but low in sweet fennel oil (2.87%).

Sweet fennel had <1% fenchone while bitter fennel had about 5%. Trace amounts <1% of *p*-anisaldehyde was found in bitter fennel oil, while α-pinene and γ-terpinene were not found in sweet fennel essential oil. During fruit development, anethole continuously increased in both bitter and sweet varieties of *Foeniculum vulgare* to about 22 mg/100 fruits (Betts 1986). Fenchone was present at all stages of fruit development of both varieties, and continuously increased to about 10 mg and 2 mg/100 fruits in both varieties respectively. Greater oil yields were obtained from the bitter fruit due to their higher fenchone content and lower weight. Two diglucoside stilbene trimers and a benzoisofuranone derivative were isolated from fennel fruit together with nine known compounds (De Marino et al. 2007).

Eighteen constituents, with estragole, *trans*-anethole, fenchone, limonene and α-pinene as the major components were identified in the hexane extract of fennel ripe mericarps of 11 indigenous population of fennel in Israel (Barazani et al. 1999). Based on the level of estragole and *trans*-anethole, four different groups were obtained: (1) highest estragole (63%) and the lowest *trans*-anethole (3%) characterized the population of Mt. Meron; (2) estragole (39–47%) and *trans*-anethole (17–29%) in 3 mountainous populations; (3) estragole (21–29%) and *trans*-anethole (38–49%) in the coastal and lowland populations; (4) two exceptional populations with the lowest content of estragole (ca. 8%) and high content of *trans*-anethole (55 and 74%). In habitats of high precipitation, the content of estragole was high and that of *trans*-anethole was low, and vice versa under limited rainfall. It was proposed that the composition of oleoresins of fennel could be governed by environmental conditions. The following major volatile constituents were found in fennel fruits: α-pinene, α-phellandrene, limonene, fenchone, estragole and *trans*-anethole (Križman et al. 2006). Anisaldehyde, a degradation product of *trans*-anethole was also found. 4-[1-propenyl] benzaldehyde was selectively isolated from fennel fruit volatile oil (Wang et al. 2003).

Fennel oil was found to comprise 8.9% hydrocarbon compounds, 77.1% oxygenated compounds, 8.9% hydrocarbon monoterpenes, 76.8% oxygenated monoterpenes, 0.3% oxygenated sesquiterpenes, 0.3% oxygenated sesquiterpenes (Lahhit et al. 2011). The major components were limonene (20.8%) and β-pinene (17.8%). followed by myrcene (15%) and fenchone (12.5%), piperitenone oxide 12.5%, α-pinene 8%, terpinolene 2.4%, *p*-cymene 1.5%, piperitenone 1%, sabinene 1%, γ-terpinene 0.8%, 3-carene 0.7%, nepetalactone 0.7%, α-phellandrene 0.3%, linalool 0.3%, α-terpineol 0.3%, geranyl acetate 0.2%, α-thujuene 0.1% and camphre 0.1%.

Fourteen components, representing the 99.98% of fennel essential oil, were identified: *trans*-anethole (64.08%), α-phellandrene (14.54%), and α-pinene (9.38%), fenchone (3.48%), estragole (2.77), β-phellandrene (2.51%), myrcene (0.83%), β-pinene (0.75%), *p*-cymene (0.61%), fenchil acetate (0.35%), β-ocimene (0.25%), γ-terpinene (0.23%), sabinene (0.12%), camphene (0.08%) (Araque et al. 2007). Fifteen components were identified in fennel essential oil, among them, *trans*-anethole (81.1%) and fenchone (9.2%) were the major components (Fariba et al. 2006). The main constituents of fennel oils obtained by different hydrodistillation conditions were: (E)-anethole (72.27–74.18%), fenchone (11.32–16.35%) and methyl chavicol (3.78–5.29%) (Mimica-Dukić et al. 2003). The method of distillation significantly affected the essential oil yield and quantitative composition. Fennel and *Pimpinella anisum* (anise) extracts were obtained by Soxhlet, cold percolation, ultrasound assisted extraction, and centrifugal extraction using ethanol as solvent; anise extracts were also obtained by steam distillation (Leal et al. 2011). Soxhlet gave the highest yields for both fennel and anise seed (16.8 and 23.3%, respectively). The highest anethole content among ethanolic extracts was obtained for centrifugal extraction (6.8 and 143 mg/g for fennel and anise extracts, respectively). Steam distillation afforded low yield (0.26%), but high anethole content (68–98%, area). The essential oil yield of fennel fruits (*Foeniculum vulgare* subsp. *vulgare* var. *vulgare*) was 12.5% v/w, whereas 1.8% v/w volatile fraction (corresponding to plant material) was obtained by hydrodistillation of the fennel infusion, equivalent to 14.5% of the initial fennel essential oil (Tschiggerl and Bucar 2010). The main

constituents of the volatile fraction of the fennel infusion were (hydrodistillation/solid phase extraction): *trans*-anethole (56.4%/54.8%), fenchone (36.2%/39.5%) and estragole (2.5%/2.2%), which were also the major compounds of the genuine bitter fennel essential oil. In infusions, the proportion of ethers vs. ketones was shifted significantly towards a higher proportion of the latter compared with the essential oil obtained from the fruits.

The essential oil content of all *F. vulgare* samples was 5–51 mL/kg and between 22 and 51 mL/kg in fruits. A total of 34 compounds were identified (Raal et al. 2012). The major component was *trans*-anethole (34.8–82.0%); the other major constituents were fenchone (1.6–22.8%), estragole (2.4–17.0%), limonene (0.8–16.5%), and *cis*-anethole (0.1–8.6%). The yield of essential oil (5.0 mL/kg) and content of *trans*-anethole was very low (34.8%) in the Turkish spice sample. Maximum yield of essential oil was found in fennel from Norway and Austria (50.7 and 50.5 mL/kg, respectively); these samples were rich in fenchone (21.2 and 22.8%), but contained less *trans*-anethole (64.6–63.7) than samples from Estonia and Moldova (82.0 and 80.9%).

In both fennel fruits and tea, *trans*-anethole, anisaldehyde, and *trans*-4,5-epoxy-2(E)-decenal showed high flavor dilution (FD) factors followed by fenchone, 1,8-cineole, (R)-α-pinene, estragole, and β-myrcene (Zeller and Rychlik 2006). The highest odor activity value (OAV) was found for *trans*-anethole, followed by estragole, fenchone, 1,8-cineole, (R)-α-pinene, β-myrcene, and anisaldehyde. From a comparison of the concentrations of odorants in fruits and tea, *trans*-anethole and estragole showed similar extraction rates of approximately 10–15%, whereas the extraction rates for (R)-α-pinene, β-myrcene, and limonene were below 2%. In contrast to this, fenchone, camphor, linalool, and carvone showed higher extraction rates (26–50%), whereas the high apparent extraction rates of anisalcohol (393%) and vanilline (480%) were attributed to the formation from precursors. Estragole had no odor impact on the overall flavor of fennel tea, and, therefore, a reduction of estragole in fennel products would have no negative impact on their sensoric quality. In contrast to this, *trans*-anethole and fenchone were found to be character impact compounds of fennel.

Zhang et al. (2009) reported that frying of fennel fruits in accordance with different Chinese medicine frying recipes altered the contents of the volatile fennel oil. *Trans*-anethole still predominated but the contents of all 24 ingredients were changed. Additionally 18 new compounds were formed after frying; among them were linalylacetate, farnesene, *p*-allyiphenyl aromatic oxide, menthone, and hexyl octanoate.

Fennel seed oil extracted by simultaneous distillation-extraction (SDE) and supercritical fluid extraction (SFE) showed similar compositions, with *trans*-anethole, estragole, and fenchone as the main components (Diaz-Maroto et al. 2005). Key odorants of fennel seeds determined by gas chromatography-olfactometry (GC-O) showed similar patterns when applying SDE and SFE. *trans*-Anethole (anise, licorice), estragole (anise, licorice, sweet), fenchone (mint, camphor, warm), and 1-octen-3-ol (mushroom) were the most intense odor compounds detected in fennel seed extracts. *Trans*-anethole was the main volatile compound found in wild fennel (*Foeniculum vulgare* Mill.) stems (Diaz-Maroto et al. 2006).

The main components of the flower and unripe and ripe fruit oils of bitter fennel (*Foeniculum vulgare* ssp. *piperitum*) were estragole (53.08, 56.11, and 61.08%), fenchone (13.53, 19.18, and 23.46%), and α-phellandrene (5.77, 3.30, and 0.72%), respectively (Ozcan et al. 2006).

Fennel seed methanolic extract was found to contain flavonoids, terpenoids, alkaloids, phenols, and sterols; estragole (71.099%) was the predominant alcohol, gallic acid was the phenolic compound (18.895%), and L-limonene was the most prevalent monoterpene hydrocarbon (11.967%) (Mohamad et al. 2011).

Nutrients and Other Phytochemicals in Other Aerial Plant Parts

The nutrient compostion of fennel aerial plant parts (shoots, stems, leaves and inflorescenes) were reported by Barros et al. (2010). Among

the sugars, most abundant sugars were fructose and glucose, in fennel shoots, leaves, stems and inflorescence). Twenty one fatty acids were found with polyunsaturated fatty acids being the main group in all the fennel parts; linoleic acid predominated in shoots, stems and inflorescences, while α-linolenic acid predominated in leaves. The higher levels of ω-3 fatty acids found in leaves contributed to its lowest ratio of ω-6 to ω-3 fatty acids. Also, the lower levels of ω-3 fatty acids found in inflorescences contributed to its highest ratio of ω-6 to ω-3 fatty acids. The detailed nutrient composition (g/100 g) reported were as follows:

Shoots: moisture 73.88 g, ash 2.39 g, fat 0.49 g, protein 1.33 g, carbohydrate 21.91 g, reducing sugars 1.14 g, fructose 1.51 g, glucose 4.71 g, sucrose 0.35, total sugars 6.57 g, energy 97.37 kcal; total SFA 19.95%, caproic acid (C6:0) 0.06%, caprylic acid (C8:0) 0.33%, capric acid (C10:0) 0.06%, undecanoic acid (C11:0) 0.07%, lauric acid (C12:0) 0.21%, myristic acid (C14:0) 0.75%, pentadecanoic acid (C15:0) 0.18%, palmitic acid (c16:0) 12.78%, heptadecanoic acid (C17:0) 0.24%, stearic acid (C18:0) 1.53%, arachidic acid (C20:0)1.06%, behenic acid (C22:0) 1.12%, tricosanoic acid (C23:0) 0.36%, lignoceric acid (C24:0) 1.20%; total MUFA 2.72%, myristoleic acid (C14:1) 0.17%, oleic acid (C18:1n9c) 2.55%; total PUFA 77.33%, linoleic acid (C18:2n6c) 39.99%, α-linolenic acid (C18:3n3) 36.84%, *cis*-11,14-eicosadienoic acid (C20:2c) 0.38%, *cis*-11,14,17-eicosatrienoic acid + heneicosanoic acid (C20:3n3 + C21:0) 0.12%; omega 3 (ω3) fatty acids 39.96%, omega 6 (ω6) 39.99 and ω6/ω3 ratio 1.08 (Barros et al. 2010).

Leaves: moisture 76.36 g, ash 3.43 g, fat 0.61 g, protein 1.16 g, carbohydrate 18.44 g, reducing sugar 0.72 g, fructose 0.49 g, glucose 0.76 g, sucrose 0.04 g, total sugars 1.29 g, energy 83.9 kcal, total SFA 27.99%, caproic acid (C6:0) 0.02%, caprylic acid (C8:0) 0.08%, capric acid (C10:0) 0.04%, undecanoic acid (C11:0) 0.25%, lauric acid (C12:0) 0.31%, myristic acid (C14:0) 1.43%, pentadecanoic acid (C15:0) 0.17%, palmitic acid (C16:0) 20.15%, stearic acid (C18:0) 1.61%, arachidic acid (C20:0) 0.56%, behenic acid (C22:0) 0.77%, tricosanoic acid (C23:0) 0.82%, lignoceric acid (C24:0) 1.03%; total MUFA 4.96%, myristoleic acid (C14:1) 0.61%, oleic acid (C18:1n9c) 4.35%; total PUFA 67.05%, linoleic acid (C18:2n6c) 23.25%, α-linolenic acid (C18:3n3) 43.55%, *cis*-11, 14-eicosadienoic acid (C20:2c) 0.08%, *cis*-11,14,17-eicosatrienoic acid + heneicosanoic acid (C20:3n3 + C21:0) 0.16%; omega 3 (ω3) fatty acids 43.72%, omega 6 (ω6) 23.25 and ω6/ω3 ratio 0.53 (Barros et al. 2010).

Stems: moisture 77.46 g, ash 1.62 g, fat 0.45 g, protein 1.08 g, carbohydrate 19.38 g, reducing sugar 1.49 g, fructose 1.49 g, glucose 3.43 g, sucrose nd, total sugars 4.92 g, energy 85.91 kcal; total SFA 33.81%, caproic acid (C6:0) 0.19%, caprylic acid (C8:0) 0.48%, capric acid (C10:0) 0.13%, undecanoic acid (C11:0) 0.04%, lauric acid (C12:0) 0.11%, myristic acid (C14:0)0.49%, pentadecanoic acid (C15:0) 0.41%, palmitic acid (C16:0) 25.43%, heptadecanoic acid (C17:0) 0.61%, heptadecanoic acid (C17:0) 0.74%, stearic acid (C18:0) 1.99%, arachidic acid (C20:0) 0.84% behenic acid (C22:0) 1.20%, tricosanoic acid (C23:0) 0.68%, lignoceric acid (C24:0) 1.21%; total MUFA 4.78%, myristoleic acid (C14:1) 0.37%, oleic acid (C18:1n9c) 4.35%, eicosanoic acid (c20:1c) 0.06%, total PUFA 61.41%, linoleic acid (C18:2n6c) 38.22%, α-linolenic acid (C18:3n3) 22.86%, *cis*-11,14-eicosadienoic acid (C20:2c) 0.14%, *cis*-11,14,17-eicosatrienoic acid + heneicosanoic acid (C20:3n3 + C21:0) 0.19%; omega 3 (ω3) fatty acids 23.04%, omega 6 (ω6) 38.22 and ω6/ω3 ratio 1.66 (Barros et al. 2010).

Inflorescences: moisture 71.31 g, ash 3.23 g, fat 1.28 g, protein 1.37 g, carbohydrate 22.82 g, reducing sugar 1.20 g, fructose 1.10 g, glucose 2.94 g, sucrose 0.03, total sugars 4.07 g, energy 108.23 kcal; total SFA 37.47%, caproic acid (C6:0) 0.41%, caprylic acid (C8:0) 0.37%, capric acid (C10:0) 0.09%, undecanoic acid (C11:0) 0.29%, lauric acid (C12:0) 0.43%, myristic acid (C14:0)1.68%, pentadecanoic acid (C15:0) 0.35%, palmitic acid (C16:0) 23.89%, heptadecanoic acid (C17:0) 0.58%, stearic acid (C18:0) 2.62%, arachidic acid (C20:0)1.78%, behenic acid (C22:0) 1.52%, tricosanoic acid (C23:0)

1.89%, Lignoceric acid (C24:0) 1.58%; total MUFA 5.59%, myristoleic acid (C14:1) 0.28%, oleic acid (C18:1n9c) 5.05%; eicosanoic acid (C20:1c) 0.26%,total PUFA 56.94%, linoleic acid (C18:2n6c) 38.94%, α-linolenic acid (C18:3n3) 17.55%, *cis*-11,14-eicosadienoic acid (C20:2c) 0.31%, *cis*-11,14,17-eicosatrienoic acid + heneicosanoic acid (C20:3n3 + C21:0) 0.15%; omega 3 (ω3) fatty acids 17.6917.69%, omega 6 (ω6) 38.94 and ω6/ω3 ratio 2.20 (Barros et al. 2010).

A chemical classification based on the amount of estragole, *trans*-anethole, limonene and fenchone was proposed for the different varieties and chemotypes of *F. vulgare* subsp. *vulgare* (Muckensturm et al. 1997). Different populations of *F. vulgare* were found to contain 10-nonacosanone as a specific chemical marker. *p*-Butylanisole occured in traces in fennel which contained a large amount of *trans*-anethole. *Foeniculum vulgare* subsp. *piperitum* was characterized by the presence of rotundifolone.

Forty-two phenolic substances were identified from fennel plant materials, 27 of which had not previously been reported in fennel, including hydroxycinnamic acid derivatives, flavonoid glycosides, and flavonoid aglycons (Parejo et al. 2004a). Eight antioxidant compounds with strong antiradical scavenging activity were isolated and identified in fennel waste: 3-caffeoylquinic acid, 4-caffeoylquinic acid, 1,5-*O*-dicaffeoylquinic acid, rosmarinic acid, eriodictyol-7-*O*-rutinoside, quercetin-3-*O*-galactoside, kaempferol-3-*O*-rutinoside, and kaempferol-3-*O*-glucoside (Parejo et al. 2004b). *Foeniculum vulgare* var. *azoricum*, *Foeniculum vulgare* var. *dulce* and *Foeniculum vulgare* var. *vulgare* revealed the presence of 18 major monoterpenoids but their content in each oil were greatly different (Shahat et al. 2011). *Trans*-anethole, estragole, fenchone and limonene were abundant in all the examined oils.

The major phenolic compounds identified in fennel plant material were: 3-*O*-caffeoylquinic acid (3-CQA), chlorogenic acid, 4-*O*-caffeoylquinic acid (4-CQA), eriocitrin, rutin, miquelianin, 1,3-*O*-dicaffeoylquinic acid (1,3-diCQA), 1,5-*O*-dicaffeoylquinic acid (1,5-diCQA), 1,4-*O*-dicaffeoylquinic acid (1,4-diCQA) and rosmarinic acid (Krizman et al. 2007). The limits of detection (LOD) and the limits of quantitation ranged from 0.05 to 1.0 μg/mL and from 0.15 to 2.5 μg/mL, respectively. The following compounds were isolated from fennel stem: dillapional (a phenyl propanoid derivative), scopoletin (a coumarin derivative), dillapiole (a phenylisopropylamine), and furocoumarins bergapten, imperatorin and psolaren (Kwon et al. 2002).

The flavon(ol)-*O*-glycosides found in fennel leaves and fruit were identified as quercetin 3-glucuronide, isoquercitrin, rutin, quercetin 3-arabinoside, kaempferol 3-glucuronide and kaempferol 3-arabinoside (Kunzemann and Herrmann 1977). Leaves in addition contained isorhammetin glycosides in low concentration. Fennel leaf was found to contain the following flavanol glycosides quercetin 3-arabinoside, kaempferol 3-arabinoside, kaempferol 3-glucuronide and quercetin 3-glucuronide (Harborne and Saleh 1971). Chlorogenic acid, quercetin-3-*O*-β-D-glucuronide, *p*-anisaldehyde and *trans*-anethole were identified by HPLC-DAD and HPLC-MS as main constituents of fennel herbal and instant teas (Bilia et al. 2000).

The major component of bitter fennel (*Foeniculum vulgare* var. *vulgare*) oil samples was *trans*-anethole (29.70, 37.07, 54.22, 61.08, 64.71% in the leaf, stem, flowering umbel, flower, fruit, respectively) (Akgül and Bayrak 1988). The other main components were α-pinene in the leaf, stem, flowering umbel, flower; α-phellandrene in the leaf, stem, flowering umbel; fenchone in fruit oil. The volatile oils of flowering umbel, flower and fruit contained high amounts of oxygenated compounds, in gradually increasing percentages.

The essential oils obtained from inflorescence, leaf stems, and whole aerial parts of *Foeniculum vulgare* var. *azoricum* contained (E)-anethole (59.28–71.69%), limonene (8.30–10.73%), apiole (trace to 9.23%), β-fenchyl acetate (3.02–4.80%), and perillene (2.16–3.29%) as the main components (Cetin et al. 2010). Similarly, the hexane plant extract exhibited a similar chemical composition, and it contained (E)-anethole (53.00%), limonene (27.16%), γ-terpinene (4.09%), and

perillene (3.78%). However, the hexane extract contained less volatile components such as n-hexadecanoic acid (1.62%), methyl palmitate (1.17%), and linoleic acid (1.15%).

The *F. vulgare* leaf essential oil yield was 0.97%, and its major constituents were methyl clavicol (46.3%), α-phellandrene (18.2%), fenchone (10.6%), (E)-anethole (11.3%), myrcene (3.4%), and α-pinene (2.1%) (Chung et al. 2011).

Fennel contains a range of unique pythonutrients that include the flavonoids *rutin*, *quercitin*, and various *kaempferol glycosides* – that give it strong antioxidant activity and *anethole* – the primary component of its volatile oil. The phytonutrients in fennel extracts compare favorably in research studies to BHT (*butylated hydroxytoluene*), a potentially toxic antioxidant commonly added to processed foods. In animal studies, the *anethole* in fennel has repeatedly been shown to reduce inflammation and to help prevent the occurrence of cancer.

Antioxidant Actvity

Fennel oil demonstrated antioxidant capacities as evaluated by two lipid model systems: a modified thiobarbituric acid reactive species (TBARS) assay and a spectrophotometric detection of hydroperoxydienes from linoleic acid in a micellar system, comparable to that of reference antioxidants α-tocopherol and butylated hydroxytoluene (BHT), used as reference antioxidants (Ruberto et al. 2000). The water and ethanol extracts of fennel seeds showed strong antioxidant activity exhibiting 99.1 and 77.5% inhibition of peroxidation in linoleic acid system, respectively, and greater than the same dose of α-tocopherol (36.1%) (Oktay et al. 2003). Both extracts exerted effective reducing power, free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, and metal chelating activities in a dose dependent manner. The amount of aqueous extract of *Foeniculum vulgare* fruits and ascorbic acid needed for 50% scavenging of superoxide radicals was found to be 205 μg for fennel versus 260 μg for ascorbic acid (Satyanarayana et al. 2004). The amount needed for 50% inhibition of lipid peroxide was 4,600 μg for fennel versus 5,000 μg for ascorbic acid. The quantity needed for 50% inhibition of hydroxyl radicals was 700 μg for fennel versus 4,500 μg for ascorbic acid. The data revealed strong antioxidant activity of *Foeniculum vulgare* extracts that was superior to known antioxidant ascorbic acid and indicated its intake may be beneficial as food additives. Wild fennel was found to exhibit a radical scavenging activity, as well as a total phenolic and total flavonoid content, higher than those of both medicinal and edible fennels (Faudale et al. 2008).

Trans-Anethole (31–36%), α-pinene (14–20%) and limonene (11–13%) were the main components of the essentials oil isolated from *F. vulgare* dried aerial parts, whereas methyl chavicol (= estragole) (79–88%) was dominant in fennel fruit oils (Miguel et al. 2010). With the DPPH (2, 2′-diphenyl-1-picrylhydrazyl) method fennel plant oils showed better antioxidant activity than fennel fruits oils. With the TBARS method and at higher concentrations, fennel essential oils showed a pro-oxidant activity. None of the oils showed a hydroxyl radical scavenging capacity >50%, but they showed an ability to inhibit 5-lipoxygenase. The essential oils showed a very low antimicrobial activity.

Antioxidant activities of the essential oils of *Foeniculum vulgare* var. *azoricum*, *Foeniculum vulgare* var. *dulce* and *Foeniculum vulgare* var. *vulgare* evaluated using the DPPH radical scavenging, lipid peroxidation and metal chelating assays indicated that the *azoricum* and *dulce* varieties were more effective antioxidants than that from the *vulgare* varieties (Shahat et al. 2011).

The DPPH radical scavenging activity of the extracts in decreasing order was: *Pimpinella anisum* > *Trachyspermum copticum* > *Cuminum cyminum* > *Foeniculum vulgare* > or = *Bunium persicum* > or = *Coriandrum sativum* > *Heracleum persicum* (Nickavar and Abolhasani 2009). The decreasing order of the flavonoid content of the extracts was: *Cuminum cyminum* > *Trachyspermum copticum* > *Pimpinella anisum* > or = *Heracleum persicum* > or = *Buniumpersicum* > or = *Foeniculum vulgare* > or = *Coriandrum sativum*.

Antimicrobial Activity

Oils from the 2 samples of *F. vulgare* showed a higher and broader degree of inhibition against 25 genera of bacteria, including animal and plant pathogens, food poisoning and spoilage bacteria than that of *Crithmum maritimum* (Ruberto et al. 2000). A phenyl propanoid derivative, dillapional (1) from fennel stem was found to be a antimicrobial with MIC values of 125, 250 and 125/against *Bacillus subtilis, Aspergillus niger* and *Cladosporium cladosporioides*, respectively (Kwon et al. 2002). A coumarin derivative, scopoletin (2) was also isolated as marginally antimicrobial agent along with inactive compounds, dillapiole (3), bergapten (4), imperatorin (5) and psolaren (6) from fennel plant. The compounds 1–6 were not active against *Escherichia coli*.

Fennel essential oil exhibited in-vitro antibacterial activity against *Escherichia coli*, *Bacillus megaterium*, and 27 phytopathogenic bacterial species and 2 mycopathogenic ones responsible for cultivated mushroom diseases (Lo Cantore et al. 2004). Fennel essential oil exhibited a very strong antibacterial activity against foodborne pathogens *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Salmonella typhimurium*, and *Staphylococcus aureus* (Dadalioglu and Evrendilek 2004). Fennel essential oil exhibited strong inhibitory against 30 strains of multiresistant Gram-negative bacilli (15 *Pseudomonas aeruginosa*, 10 *Acinetobacter* spp. and 5 *Alcaligenes faecalis*) resistant to wide-spectrum β-lactam antibiotics and aminoglycosides and isolated from patients with nosocomial infections (Araque et al. 2007). Fennel essential oil displayed antibacterial activity in nutrient broth culture (Mohsenzadeh 2007). The MIC value against *Escherichia coli* was 1% and MBC value was 2%. The MIC value against *Staphylococcus aureus* was 2% and MBC value 4%. All fennel oil samples exerted good activity against *Escherichia coli* and *Staphylococcus aureus* at low concentrations but were inactive against *Bacillus cereus* and *Pseudomona aeruginosa* (Aprotosoaie et al. 2008). The fennel oil samples were generally bactericidal at a concentration up to twofold or fourfold higher than the MIC value. Significantly showed all fennel samples showed synificant synergistic activity with amoxicillin or tetracycline against *E. coli*, *Sarcina lutea* and *B. subtilis* strains. Fennel oil samples also had high activity against *Candida albicans*. The most important identified compounds in all fennel volatile oil samples were *trans*-anethole, estragole, fenchone, limonene, α-pinene and γ-terpinene.

Fennel essential oil was found to possess antibacterial effect against all 48 antibiotic resistant isolates of *Acinetobacter baumannii* (Jazani et al. 2009). Fennel herbal extract was on of several herbal extracts that showed strong inhibition against *Campylobacter jejuni*, the most common cause of enteric infections, particularly among children, resulting in severe diarrhoea (Cwikla et al. 2010).

In-vitro antimicrobial assays showed that *Foeniculum vulgare* var. *azoricum* essential oil, anethole, and hexane extract were effective against most of the foodborne pathogenic, saprophytic, probiotic, and mycotoxigenic microorganisms tested (Cetin et al. 2010). The results revealed that (E)-anethole, the main component of Florence fennel essential oil, was responsible for the antimicrobial activity and that the essential oils as well as the hexane extract can be used as a food preservative against probiotic bacteria. *Foeniculum vulgare* var. *azoricum*, *Foeniculum vulgare* var. *dulce* and *Foeniculum vulgare* var. *vulgare* showed similar antimicrobial activity against two species of fungi, two species of Gram negative and two species of Gram positive bacteria (Shahat et al. 2011). Fennel exhibited in-vitro antifungal activity against *Candida albicans* (Pai et al. 2010). *Foeniculum vulgare* essential oils from aerial plant parts and seeds inhibited growth of *Aspergillus* spp. (Alizadeh et al. 2010).

Antiplatelet Activity

Studies demonstrated that the main constituent of the fennel essential oil, anethole, tested in guinea pig plasma was as potent as fennel oil in inhibiting arachidonic acid-, collagen-, ADP- and U46619-induced aggregation (IC_{50} from 4 to 147 μg/mL) (Tognolini et al. 2007). It also prevented

thrombin-induced clot retraction at concentrations similar to fennel oil. The essential oil and anethole, tested in rat aorta with or without endothelium, displayed comparable NO-independent vasorelaxant activity at antiplatelet concentrations which had been proven to be free from cytotoxic effects in-vitro. In-vivo, both fennel essential oil and anethole orally administered in a subacute treatment to mice (30 mg/kg/day for 5 days) showed significant antithrombotic activity preventing the paralysis induced by collagen-epinephrine intravenous injection (70 and 83% protection, respectively). At the antithrombotic dosage they were free from prohemorrhagic side effect at variance with acetylsalicylic acid used as reference drug. In addition, both fennel essential oil and anethole (100 mg/kg oral administration) provided significant protection toward ethanol induced gastric lesions in rats. The results demonstrated fennel essential oil, and its main component anethole, to have a safe antithrombotic activity attributable to their broad spectrum antiplatelet activity, clot destabilizing effect and vasorelaxant action.

Anticancer Activity

Fennel and its major component, anethole had been reported to have anticancer activity (Chainy et al. 2000; Aggarwal et al. 2008; Kaileh et al. 2007; Singh and Kale 2008; Choo et al. 2011). Fennel possessed mmunomodulatory effects on nuclear transcription factor NFκB that regulates the expression of various genes that play critical roles in apoptosis and immunomodulation (Kaileh et al. 2007). Anethole suppressed TNF-induced both lipid peroxidation and ROI generation and also blocked the NF-kappaB activation induced by a variety of other inflammatory agents (Chainy et al. 2000). Results of studies demonstrated that anethole inhibited TNF-induced cellular responses, which may explain its role in suppression of inflammation and carcinogenesis anethole analogues eugenol and isoeugenol also blocked TNF – mediated signalling. Despite weak cytotoxicity against HT-1080 human fibrosarcoma tumour cells s, anethole inhibited the adhesion to Matrigel and invasion of HT-1080 cells in a dose-dependent manner (Choo et al. 2011) Anethole was also able to down-regulate the expression of matrix metalloproteinase (MMP)-2 and -9 and up-regulate the gene expression of tissue inhibitor of metalloproteinase (TIMP)-1. In addition, anethole suppressed the phosphorylation of AKT, extracellular signal-regulated kinase (ERK), p38 and nuclear transcription factor kappa B (NF-κB) in HT-1080 cells. Taken together, their findings indicated anethole to be a potent anti-metastatic drug that functions through inhibiting MMP-2/9 and AKT/mitogen-activated protein kinase (MAPK)/NF-κB signal transducers. Studies showed that fennel seed methanolic extract had remarkable anticancer potential against a breast cancer cell line (MCF7) and liver cancer cell line (HepG-2) (Mohamad et al. 2011). The mean 50% inhibitory concentrations of in fennel seed methanolic extract were 50 μg/mL for the MCF7 breast cancer cell line and 48 μg/mL for the HepG-2 liver cancer cell line. The significant increase in malondialdehyde levels and the significant decrease in Ehrlich ascites carcinoma were ameliorated after fennel seed extract administration. It also showed strong free radical-scavenging activity (100%). Administration of the fennel extract before irradiation exerted a cytoprotective effect against gamma irradiation, as manifested by a restoration of the malondialdehyde level, catalase activity, and GSH content to near-normal levels. The results indicated that the extract may reduce oxidative stress and protect mouse cells from damage caused by reactive oxygen species. In addition, it could be used as a safe, effective, and easily accessible source of natural antioxidants to improve the oxidative stability of fatty foods during storage. The extract also exhibited an antitumor effect by modulating lipid peroxidation and augmenting the antioxidant defence system in Ehrlich ascites carcinoma-bearing mice with or without exposure to radiation.

Fennel was found to contain minor amount of polyacetylenes in nonpolar extracts, which showed cytotoxicity against different lymphoblastic cell lines (Zidorn et al. 2005). The ethanol extracts from fruits of seven species of Apiaceae including fennel were found to have apoptotic activity

on some human leukaemia cell lines (Bogucka-Kocka et al. 2008).

Fennel seeds exhibited a significant reduction in DMBA-induced skin and B(a)P-induced forestomach tumour incidence and tumour multiplicity as compared to the control group (Singh and Kale 2008). A significant enhancement in the activities of antioxidant enzymes were observed especially at 4 and 6% test diets of Fennel. Glyoxalase I activity and the content of reduced glutathione were significantly elevated. The levels of peroxidative damage along with lactate dehydrogenase activity, exhibited a significant reduction at all three doses of test diets. The findings were indicative of chemopreventive potential of fennel against carcinogenesis. Studies by Celik and Isik (2008) found that fennel infusion exhibited a chemopreventive effect in rats against the carcinogen trichloroacetic acid that may be attributable to its antioxidative properties.

Five herbal supplements, designated FB, FM, PP, HF and FBL101, containing different combinations of various natural herbs such as liquorice, black cohosh, Dong Quai, false unicorn and vitex berry root extracts, fennel seed extract, red clover blossoms extract as well as genistein and gamma oryzanol, were found to inhibit the growth of prostate tumour xenografts in immunodeficient mice, possibly in part by antiangiogenic mechanisms (Ng and Figg 2003).

Antimutagenic Activity

Chromosomal aberration assay in mice bone marrow cells revealed slight insignificant effect of fennel hot water extract on aberrant mitosis rate, while it gave remarkable significant dose-dependent reduction of the mitomycin C induced chromosomal aberrations (Ebeed et al. 2010). Further, random amplified polymorphismof DNA (RAPD) showed clear variation between different classes of treated and non treated animals against mitomycin C treatment, which reflected DNA protective effect of fennel extract. Nucleic acids system (RNA, DNA, RNAase, DNAase and total soluble protein of liver), also the serum uric acid, urea and creatinine (kidneys function) and liver function (GOT and GPT activities) were slightly affected by mitomycin C, but were improved by the ingestion of fennel extract, indicating fennel extract alleviated mitomycin C toxic effects. In *Drosophila,* fennel extract significantly decreased the frequency of cholchicine induced aneuploidy and chromosomal aberrations in post and pre-treatments.

Hepatoprotective Activity

Studies showed that fennel essential oil had a potent hepatoprotective action against carbon tetrachloride-induced liver fibrosis in rats as evidenced by decreased levels of serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and bilirubin (Ozbek et al. 2003). Histopathological findings also suggested that fennel essential oil prevented the development of chronic liver damage.

Antiinflammatory Activity

Fennel has been used traditional Iranian medicine to cure inflammatory illnesses and has been shown to possess anti-inflammatory and immunomodulatory effects (Amirghofran 2010). Oral administration (200 mg/kg) of fennel fruit methanolic extract produced inhibitory effects against acute and subacute inflammatory diseases and type IV allergic reactions and showed a central analgesic effect (Choi and Hwang 2004). Plasma superoxide dismutase and catalase activities and the high density lipoprotein–cholesterol level were enhanced but malondialdehyde level was significantly decreased in fennel extract group compared to the control group. The results supported the use of *F. vulgare* fruit extract in relieving inflammation.

Hypoglycaemic Activity

Studies showed that administration of fennel essential oil (250 mg/kg) to healthy albino rats markedly reduced blood glucose compared to the 500 mg/kg dose essential oil and estradiol valerate (5 mg/kg) (Javadi et al. 2008).

Antiobesity Activity

Treatment of obese white male albino rats induced by a high fat diet with L-carnitine, or an Egyptian herbal mixture formulation (HMF) (consisting of *Terminalia chebula*, senna, rhubarb, black cumin, aniseed, fennel and liquorice) ameliorated obesity and its associated metabolic problems (elevated lipid profile, defective antioxidant stability, and high values of insulin resistance parameters) in varying degrees (Amin and Nagy 2009). Also HMF was found to have antioxidant, hypolipidaemic insulin sensitizing effects. Additionally, HMF might be a safe combination way to surmount the obesity state as it had a distinct anti-obesity effect.

Antidysmenorrhoea Activity

Administration of different doses of fennel essential oil to rats reduced the intensity of oxytocin and prostaglandin E(2) PGE(2) induced contractions significantly (Ostad et al. 2001). The oil also reduced the frequency of contractions induced by PGE(2) but not with oxytocin. The estimated LD_{50} was 1,326 mg/kg. No obvious damage was observed in the vital organs of the dead animals. The results indicated that fennel essential oil was safe and effective in treating dysmenorrhea.

In a study of 30 female patients with moderate to severe dysmenorrhea, mefenamic acid and fennel fruit extract effectively relieved menstrual pain as compared with the control cycles (Namavar et al. 2003). The mean duration of initiation of action was not significant 67.5 min for mefenamic acid and 75 min for fennel. Mefenamic acid had a more potent effect than fennel on the second and third menstrual days, however, the difference on the other days was not significant. No complication was reported in mefenamic acid treated cycles, but five cases (16.6%) withdrew from the study due to fennel's odor and one case (3.11%) reported a mild increase in the amount of her menstrual flow. A randomised study of high-school girls (55 mean age 13 years) suffering dysmenorrhoea, showed that administration of fennel extract resulted in 80% of the girls having complete pain relief or pain decrease compared to 73% administered mefenamic acid drug (Modaress and Asadipour 2006). Further, 80% in the fennel group and 62% in the mefenamic acid group no longer needed to rest.

Oculohypotensive Activity

The aqueous fennel seed extract exhibited significant oculohypotensive activity, which was found to be comparable to that of timolol (Agarwal et al. 2008). The aqueous fennel seed extract exerted 17.49, 21.16 and 22.03% reduction of intraocular pressure (IOP) in normotensive rabbits at 0.3, 0.6 and 1.2% (w/v) concentrations respectively. A maximum mean difference of 31.20% was observed between vehicle treated and fennel extract treated eyes in water loading model while a maximum mean IOP lowering of 31.29% was observed in steroid induced model of glaucoma.

Osteoprotective Activity

Fennel essential oil exerted a preventive effect on development of osteoporosis in ovariectomized rats assessed on the basis of bone mineral density and uterine weigh (Fariba et al. 2006). This protective effect of fennel extract on early post-ovariectomy bone loss was dose dependent and at the dose of 1000 mg/kg it was even more than estradiol of 0.082 g/cm^2.

Gastroprotective Activity

Studies showed that pretreatment of rats with an aqueous fennel extract exhibited a protective effect against ethanol-induced gastric mucosal lesion (Birdane et al. 2007). Fennel extract significantly reduced the malondialdehyde levels, while significantly increased GSH (reduced glutathione), nitrite, nitrate, ascorbic acid, and retinol and β-carotene level. This effect of was highest and statistically significant in 300 mg/kg fennel group compared with the control.

Hypotensive Activity

An intravenous administration of the lyophilized boiled water extract of fennel leaves in produced a significant dose-related reduction in arterial blood pressure, without affecting the heart rate or respiratory rate (Abdul-Ghani and Amin 1988). The non-boiled aqueous extract elicited very little hypotensive activity. The hypotensive effect of the boiling water extract appeared not to be mediated via adrenergic, muscarinic, ganglionic or serotonergic receptors; however, histamine antagonists inhibited the hypotensive effect in a dose-related manner. In another study, oral administration of the fennel aqueous extract lowered the systolic blood pressure of spontaneously hypertensive rats (SHR) and in normotensive Wistar-Kyoto rats (El Bardai et al. 2001). In SHR, fennel treatment increased water, sodium and potassium excretion, vascular effects of fennel were less pronounced and were blocked by N-nitro-L-arginine. The results indicated that hypotensive activity of fennel appeared to act mainly as a diuretic and a natriuretic and not via a vascular relaxant activity.

Antihirsutism Activity

In a double blind study of 38 female patients, the efficacy of treatment in suppressing idiopathic hirsutism with the cream containing 2% fennel was better than the cream containing 1% fennel and these two were more potent than placebo (Javidnia et al. 2003). The mean values of hair diameter reduction was 7.8, 18.3 and −0.5% for patients receiving the creams containing 1, 2 and 0% (placebo) respectively.

Nootropic Activity

Methanolic extract of fennel plant administered for 8 successive days ameliorated the amnesic effect of scopolamine (0.4 mg/kg) and aging induced memory deficits in mice (Joshi and Parle 2006). The passive avoidance paradigm served as the exteroceptive behavioral model for assessing memory. Fennel extract increased step-down latency and acetylcholinesterase inhibition in mice significantly. The findings suggested that *F. vulgare* could be employed in treatment of cognitive disorders such as dementia and Alzheimer's disease.

Estrogenic Activity

Fennel, and anise (*Pimpinella anisum*), have been used as estrogenic agents for millennia (Albert-Puleo 1980). Specifically, they have been reputed to increase milk secretion, promote menstruation, facilitate birth, alleviate the symptoms of the male climacteric, and increase libido. The main constituent of the essential oils of fennel and anise, anethole, has been considered to be the active estrogenic agent. However, further research suggested that the actual pharmacologically active agents were polymers of anethole, such as dianethole and photoanethole.

Following oral administration of fennel fruit acetone extract for 15 days in male rats, total protein concentration was found to be significantly decreased in the testes and vas deferens and increased in seminal vesicles and prostate gland (Malini et al. 1985). Acid and alkaline phosphatase activities in all these areas, except that alkaline phosphatase was unchanged in vasa. In female rats, oral administration of fennel extract for 10 days led to vaginal cornification and oestrus cycle. While moderate doses caused increase in weight of mammary glands, higher doses increased the weight of oviduct, endometrium, myometrium, cervix and vagina also. The results confirmed the estrogenic activity of fennel extract.

Infantile Colic Activity

In a randomized, placebo-controlled study, fennel oil emulsion eliminated colic, according to the Wessel criteria, in 65% (40/62) of infants in the treatment group, which was significantly better than 23.7% (14/59) of infants in the placebo control group (Alexandrovich et al. 2003). There was a significant improvement of colic in the fennel treated group compared with the control group, and no side effects were observed suggesting that

fennel seed oil emulsion was superior to placebo in decreasing intensity of infantile colic. In another study, Savino et al.(2005) showed in a randomized double-blind placebo-controlled trial that colic in breastfed infants improved within 1 week of treatment with an extract based on *Matricaria recutita*, *Foeniculum vulgare* and *Melissa officinalis.* Crying time reduction was observed in 85.4% colicky infants for the herbal extract and in 48.9% colicky infants for the placebo. No side effects were reported. Perry et al. (2011) conducted a systematic review of 15 randomized clinical trials in relation to treatment for infantile colic. Although some encouraging results were found for fennel extract, mixed herbal tea, and sugar solutions, all the trials had major limitations. Thus, the notion that any form of complementary and alternative medicine was effective for infantile colic current findings from the included randomized clinical trials did not support this.

Antidiabetic Activity

Administration of essential oil of *Foeniculum vulgare* to diabetic rats rectified the hyperglycemia from (162.5 mg/daily) to (81.97 mg/daily) and the activity of serum glutathione peroxidase from (59.72 U/g Hb) to (99.60 U/g Hb) (El-Soud et al. 2011). It also improved the pathological changes in their kidney and pancreas.

Anxiolytic Activity

The crude ethanolic fennel extract at doses of 200 and 400 mg/kg were found to possess significant anti-anxiety activity in albino mice as assessed by the elevated plus-maze model (Divekar et al. 2011). The crude ethanolic fennel extract contained anisic acid, anisic aldehyde, dpinene, fenchone, organic phellandrine, anethole, volatile oils (50–60%). The fennel extract (400 mg/kg) exhibited maximum anti-anxiety effect. At a high dose (400 mg/kg) the extract showed increase number of entries and time spent in open arm of elevated plus-maze model. The effect produced by the extract was comparable to that of diazepam, a prototype of anxiolytic agent.

Laxative Activity

A phytotherapeutic formulation containing *Pimpinella anisum*, *Foeniculum vulgare*, *Sambucus nigra* and *Cassia augustifolia*, largely used in Brazil for the treatment of constipation was found to have laxative efficacy in randomized, crossover, placebo-controlled, single-blinded trial of 20 patients (Picon et al. 2010). Mean colonic transit time assessed by X ray was 15.7 h in the active herbal treatment period and 42.3 h during the placebo treatment. Number of evacuations per day increased during the use of active herbal tea. Patient perception of bowel function was improved, but quality of life did not show significant differences among the study periods.

Bronchodilatory Activity

Studies using isolated tracheal chains of the guineapig confirmed the bronchodilatory effects of the ethanol extract and essential oil of fennel (Boskabady et al. 2004). Diltiazem, ethanol extract, and essential oil from fennel exerted a significant relaxant effect on methacholine-induced contraction of tracheal chains compared to those of negative controls. The effect of the ethanol extract was significantly greater than that of diltiazembur but aqueous fennel extract was devoid of any relaxant activity. The results also indicted that the inhibitory effect of ethanol extracts and essential oil of fennel on calcium channels was not contributing to their relaxant (bronchodilatory) effects on guinea pig tracheal chains. However, the results suggested a potassium channel opening effect for fennel which may contribute to its relaxant effect on guineapig tracheal chains.

Mosquito Repellency and Larvicidal Activity

The biologically active constituents of fennel fruits (+)-fenchone and (E)-9-octadecenoic acid elicited different repellency activity against *Aedes aegypti* mosquitoes (Kim et al. 2002). In a skin test with female mosquitoes, at a dose of 0.4 mg/cm^2, (+)-fenchone and (Z)-9-octadecenoic acid

exhibited moderate repellent activity at 30 min after treatment, whereas deet provided >1 h of protection against adult mosquitoes at 0.2 mg/cm^2. (Z)-9-Octadecenoic acid was a more potent repellent agent than (E)-9-octadecenoic acid.

In a laboratory study with female *Aedes aegypti*, fennel oil exhibited good repellency in a release-in-cage test and repellency in skin and patch tests of the oil was comparable with those of citronella and geranium oils (Kim et al. 2004). In paddy field tests with five human volunteers, 5 and 8% fennel oil-containing aerosol and cream produced 84 and 70% repellency, respectively, at 90 min after exposure, whereas Baby Keeper cream (containing IR3535) and MeiMei cream (containing citronella and geranium) gave 71 and 57% repellency respectively, and Repellan S containing 19% N,N-diethyl-m-toluamide (DEET) aerosol gave 89% repellency at 210 min. The species and ratio of mosquitoes collected were the genera *Culex* (44.1%), *Anopheles* (42.2%), *Aedes* (7.8%) and *Armigeres* (5.9%). The results suggested that fennel oil-containing products could be useful for protection of humans and domestic animals from vector-borne diseases and nuisance caused by mosquitoes. Essential oils extracted from six Mediterranean plants (*Achillea millefolium*, *Lavandula angustifolia*, *Helichrysum italicum*, *Foeniculum vulgare*, *Myrtus communis*, and *Rosmarinus officinalis*) exhibited insecticidal activity against the larvae the Culicidae mosquito *Aedes albopictus*, with differences in mortality rates as a function of both oil and dosage (Conti et al. 2010). At the highest dosage (300 ppm), essential oils from *H. italicum*, *A. millefolium*, and *F. vulgare* caused higher mortality than the other three oils, with mortality rates ranging from 98.3 to 100%.

F. vulgare leaf essential oil had a significant toxic effect against early fourth-stage larvae of *Aedes aegypti* with an LC_{50} value of 41.23 ppm and an LC_90 value of 65.24 ppm (Chung et al. 2011). Also, its constituents methyl clavicol (≥98.0%), α-phellandrene (≥95.0%), fenchone (≥98.0%), (E)-anethole (≥99.0%), myrcene (≥99.0%), and α-pinene (≥99.0%) were tested against the F(21) laboratory strain of *A. aegypti*. Fenchone (≥98.0%) and (E)-anethole (≥99.0%) exhibited medium activity with an LC_{50} value of 73.11 and 102.41 ppm.

Acaricidal Activity

Fennel fruit oil was found to have acaricidal activity against two species of house dust mites (Lee 2004). Its acaricidal activity could be attributed to its constituents (+)-fenchone and *p*-anisaldehyde; (+)-Fenchone was 20.3 times more abundant in the oil than *p*-anisaldehyde. On the basis of LD_{50} values, the compound most toxic to *Dermatophagoides farinae* was *p*-anisaldehyde (11.3 mg/m^2) followed by (+)-fenchone (38.9 mg/m^2), (−)-fenchone (41.8 mg/m^2), benzyl benzoate (89.2 mg/m^2), thymol (90.3 mg/m^2), and estragol (413.3 mg/m^2). Against *Dermatophagoides pteronyssinus*, *p*-anisaldehyde (10.1 mg/m^2) was much more effective than benzyl benzoate (67.5 mg/m^2), thymol (68.5 mg/m^2), and estragol (389.9 mg/m^2).

Antigentoxicity Activity

Pretreatment of mice with *trans*-anethole and eugenol led to significant antigenotoxic effects against cyclophosphamide (CPH), procarbazine (PCB), N-methyl-N′-nitro-N-nitrosoguanidine (MNNG) and urethane (URE) (Abraham 2001). In addition, *trans*-anethole inhibited the genotoxicity of ethyl methane sulfonate (EMS). Both *trans*-anethole and eugenol exerted dose-related antigenotoxic effects against PCB and URE. There was no significant increase in genotoxicity when *trans*-anethole (40–400 mg/kg body weight) and eugenol (50–500 mg/kg body weight) were administered alone.

Toxicity Studies

Acute (24-h) and chronic (90-day) oral toxicity studies on the ethanolic extracts of fennel fruit in mice showed that the extracts caused no significant acute or chronic mortality as compared to controls (Shah et al. 1991) and had no spermatotoxic effects. The treated male mice gained significant

weight during chronic treatment while a loss or no significant change in weight was noticed in the female mice treated with the same extracts. Findings of in-vitro studies of rat embryo limb bud rnesenchymal cells suggested that the fennel essential oil at the studied concentrations may have toxic effect on fetal cells, but there was no evidence of teratogenicity (Ostad et al. 2004)

Drug-Drug Interaction Activity

Oral administration of aqueous fennel herbal extract was found to impact on ciprofloxacin absorption and disposition in the rat (Zhu et al. 1999). Significant interaction between ciprofloxacin and fennel was observed in this study. Compared with the control, maximum plasma concentration, area under the curve and urinary recovery of ciprofloxacin were significantly lower, by 83, 48 and 43%, respectively, in rats receiving concomitant dosing of the two agents. The relative bioavailability of ciprofloxacin, under the influence of fennel, was estimated to be 0.52. In addition, its apparent volume of distribution and terminal elimination half-life were significantly increased. These changes might be attributed to the formation of a more lipophilic ciprofloxacin chelate in the presence of relatively large amounts of metal cations in the fennel extract. The authors cautioned that the concurrent use of the two therapeutic dugs should incorporate an adequate dosing interval to ensure efficacy of ciprofloxacin.

Thirteen compounds isolated from a methanol extract of fennel were tested for their inhibition on cytochrome P450 3A4 (CYP3A4) (Subehan et al. 2007). Among them, 5-methoxypsoralen (5-MOP) showed the strongest inhibition with an IC_{50} value of 18.3 μM and a mixed type of inhibition. The inhibitory activity of CYP3A4 by 5-MOP was found to be a mechanism-based inactivation.

Adverse Effects

Türkyilmaz et al. (2008) reported that long-term use of preparations such as *Foeniculum vulgare*, which is used to eliminate gas and regulate intestinal function in children, may cause premature thelarche, and thus, the use of such preparations should be limited. Isolated premature thelarche is a common disorder characterized by breast development, usually younger than 2 years, with no other signs of puberty. Thelarche is usually associated with adrenal or ovarian disorders, hypothyroidism, and use of exogenous hormones or drugs, it may also be associated with long-term use of herbal medicine.

In a review paper on the risk assessment of estragole in fennel tea, Iten and Saller (2004) questioned the advice issued by the German Federal Institute for Consumer Heath Protection and Veterinary Medicine (BgVV) to consumers to reduce their intake of foods containing estragole and methyleugenol, e.g. tarragon, basil, anis, star anise, Jamaica pepper, nutmeg, lemon grass as well as bitter and sweet fennel fruits for reasons of health in 2001. Their contentions concerned the transfer of data obtained in animal models to the human situation as well as the high doses of the applied monosubstance, which did not at all represent the amounts humans were exposed to as consumers of estragole-containing foods and phytopharmaceuticals. They asserted that the findings based on experiments with rats and mice where estragole, a natural ingredient of fennel fruits, proved to be carcinogenic should not be directly transposed to human situations as studies on estragole metabolism revealed at least quantitative differences between the estragole metabolism of mice and men. In addition, it had been shown that an agent when administered in its isolated form may have significantly different effects and side effects than the same agent applied as a constituent in naturally occurring multicomponent mixtures. Thus, a multicomponent mixture such as fennel tea contains various antioxidants known to be protective against cancer. Based on long traditional use of fennel tea and the total lack of epidemiological and clinical studies indicating a well founded cancerogenic potential, they asserted that the probability of a serious risk connected with the consumption of fennel tea appeared to be negligibly small. The following concentration levels of estragole were found in fennel teas obtained from different

types of commercial products in Italy: teas from teabags 241–2,058 μg/L, diluted instant teas 9–912 μg/L, and teas from not packaged seeds 251–1,718 μg/L (Raffo et al. 2011). Based on these data and considering the daily consumption of three portions of herbal tea, a maximum exposure to estragole for adults of 10 μg/kg bw/day was calculated. Estimated exposure in infants was up to 51 μg/kg bw/day for teas from teabags, and up to 23 μg/kg bw/day for instant teas. A generalization of the use of suitable technologies in production processes of instant teas could substantially reduce the exposure to estragole in the vulnerable population groups (infants, young children, pregnant and breastfeeding women) who consume these products.

Traditional Medicinal Uses

The seeds, leaves and roots can be used medicinally, but the seeds are most active medicinally and are the part commonly used (Burkill 1966; Grieve 1971; Chiej 1984; Bown 1995; Chevallier 1996).

Fennel seed is carminative, aromatic, antispasmodic, anti inflammatory, galactogogue, hepatic, diuretic and emmenagogue. Fennel is an excellent stomach and intestinal remedy which relieves flatulence and colic whilst also stimulating the digestion and appetite. In India, fennel water is given in colic and flatulence of children. A hot infusion of the fruit is useful in amenorrhoea and in cases where the lacteal secretion is suppressed. The oil is useful in flatulence. The juice of the fennel fruit has been used to improve the eye-sight and a paste of the seeds is used in a cooling drink in fevers and in scalding urine. Extracts of fennel seed have been shown in animal studies to have a potential use in the treatment of glaucoma. In Madras, fennel seed are employed in venereal diseases; in Mexico a decoction of fennel seeds is administered as a galactagogue; in Antilles they are used as a stimulant. It is similar to aniseed in its calming effect on bronchitis and coughs. It may be used to flavour cough remedies. It has been reported to increase the flow of milk in nursing mothers. Externally the oil eases muscular and rheumatic pains. The infusion may be used as an eye wash or compress to treat conjunctivitis and inflammation of the eyelids (blepharitis). Crushed seeds are inhaled for fainting.

Fennel is widely used in Egyptian traditional medicine for its estrogenic, lactagogue, diuretic, antioxidant, immune booster and its usefulness in dyspepsia (Ebeed et al. 2010). In Lebanese traditional societies, fennel is used as a digestive stimulant (Jeambey et al. 2009). *Foeniculum vulgare* is an ancient common herb and spice known to the ancient Egyptians and Greeks, traditionally used as a carminative, a weak diuretic and lactation stimulant (El-Soud et al. 2011). Fennel, *Foeniculum vulgare*, and anise, *Pimpinella anisum*, have been used as estrogenic agents for millennia (Albert-Puleo 1980). Specifically, they have been reputed to increase milk secretion, promote menstruation, facilitate birth, alleviate the symptoms of the male climacteric, and increase libido (Grieve 1971).

The leaves are also reported to be diuretic, increasing the secretion of urine and perspiration and the shoots of the young plant as carminative and respiratory. The roots are employed as an aperative and purgative and used to treat urinary disorders. In India, an infusion of the roots is given for toothache and to relieve pains following childbirth. An essential oil obtained from the seed is used in aromatherapy The essential oil is bactericidal, carminative and stimulant but should no be administered to pregnant women.

The plant is analgesic, anti-inflammatory, antispasmodic, aromatic, carminative, diuretic, emmenagogue, expectorant, galactogogue, hallucinogenic, laxative, stimulant and stomachic. An infusion is used in the treatment of indigestion, colic, abdominal distension, stomach cramps. It is used in the treatment of kidney stones and, when combined with other urinary disinfectant makes an effective treatment for cystitis. It can also be used as a gargle for sore throats and as eyewash for sore eyes and conjunctivitis.

Fennel is used in home beauty cosmetics often in combination with buttermilk and honey, as a cleansing lotion and skin freshener and in toothpaste. An infusion of the ground seeds is used as

a facial steam bath. Fennel in combination with other ingredients is used as anticellulite massage oil. Fennel is also the basis of weight loss recipes.

Other Uses

The essential oil extracted from fennel seeds is used in toothpastes, soaps, perfumery, air fresheners etc. The dried plant is an insect repellent while the crushed leaves are effective for keeping dogs free of fleas. Yellow and brown dyes are obtained from the flowers and leaves combined. A bicyclic ketone isolated from the plant is used as an odour-making agent for use in air fresheners because of its camphor-like aroma. The plant stubble in the field is used for grazing animals.

Studies found that fennel fruit derived compounds the phenylpropenes (E)-anethole and estragole, and the monoterpene (+)-fenchone, could be useful for managing field populations of *Sitophilus oryzae, Callosobruchus chinensis* and *Lasioderma serricorne* (Kim and Ahn 2001). Fennel oil was found to have corrosion inhibition activity of carbon steel (Lahhit et al. 2011). Fennel oil acted as a mixed-type inhibitor. The inhibition efficiency attained a maximum of 76% at 3 mL/L, but decreased with the rise of temperature. Essential oil of *F. vulgare* showed significant insecticidal activity against *Sitophilus zeamais*, a stored foot insect pest (Bertoli et al. 2011).

The flower and unripe and ripe fruit oils of bitter fennel (40 ppm) exerted varying levels of antifungal effects on in-vitro mycelial growth of *Alternaria alternata*, *Fusarium oxysporum*, and *Rhizoctonia solani* (Ozcan et al. 2006). Among the essential oil of seven plants, *F. vulgare* showed most potent activity against second-stage juveniles (J2) of *Meloidogyne incognita* nematode in an immersion bioassay (Ntalli et al. 2011). Its consituents *trans*-anethole and estragole also exhibited nematicidal activity against second-stage juveniles.

Comments

Major producing countries of fennel fruits are Egypt, Syria, India, Argentina, Bulgaria, China, Indonesia and Pakistan.

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Trachyspermum ammi

Scientific Name

***Trachyspermum ammi* (L.) Sprague ex Turrill**

Synonyms

Ammi copticum L., *Ammi glaucifolium* Blanco, *Ammios muricata* Moench, *Apium ammi* (L.) Urb. (illeg.), *Athamanta ajowan* Wall., *Bunium copticum* (L.) Spreng., *Carum ajowan* Benth. & Hook.f., *Carum aromaticum* Druce, *Carum copticum* (L.) Benth. & Hook.f. ex C.B.Clarke, *Carum copticum* (L.) Benth. & Hook. f., *Carum korolkowii* Lipsky (illeg.), *Carum panatjan* Baill., *Cyclospermum ammi* (L.) Lag., *Daucus anisodorus* Blanco, *Daucus anisodorus* Blanco, *Daucus copticus* (L.) Lam., *Daucus copticus* (L.) Pers., *Helosciadium ammi* (L.) Oken, *Helosciadium ammi* (L.) Britton, *Ligusticum ajawain* Roxb. ex Fleming, *Ligusticum ajawain* Spreng., *Ptychotis ajowan* DC., *Ptychotis coptica* (L.) DC., *Selinum copticum* E.H.L.Krause, *Seseli ammoides* Jacq., *Seseli foeniculifolium* Poir., *Sison ammi* L., *Trachyspermum copticum* (L.) Link.

Family

Apiaceae

Common/English Names

Bishop Weed, Carom, Ajwan Seed, Ajwain, Ajowan Seed, Falsely Lovage Seeds.

Vernacular Names

Arabic: Ajwân, Al-Yunan, Anîsûn Barrî, Kammûn Hhabashî, Nakhwah, Taleb El Koubs;
Amharic: Netch Azmud;
Armenian: Hounastan;
Azeri: Yunanistan;
Burmese: Sa.mwat;
China: Xi Ye Cao Guo Qin, Yìn Dù Zàng Huí Xiāng (Mandarin),Yan Douh Jòhng Wùih Hèung (Cantonese);
Czech: Adžvajen;
Danish: Ajwan;
Dutch: Ajowan;
Eastonian: Lõhnav Karusköömen;
Ethiopia: Netch Azmud;
Finnish: Koptilainen Kumina;
French: Ammi De L'inde, Ajouan, Ajowan, Ammi, Anis De L' Inde, Sison;
German: Adiowan, Ajowan, Ägyptischer Kümmel, Herrenkümmel, Indischer Kümmel, Königskümmel;
Hebrew: Yavan;
Hungarian: Ajova;

T.K. Lim, *Edible Medicinal and Non-Medicinal Plants: Volume 5, Fruits*,
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India: Joan, Joni-Guti (Assamese), Jowan, Juvani, Yamani (Bengali), Hithi Dhamui (Dhivehi), Ajamo, Jawain, Yavan, Yavano (Gujarati), Ajawa, Ajmud, Ajowa, Ajowan, Ajwain, Carom, Omum , Randhuni (Hindu), ajamoda, Ajamodhavoma, Oma Omakki, Omu (Kannada), Omam Ayamodakam (Malayalam), Owa, Vova, Ova (Marathi), Juani (Oriya), Aijavain, Ajowan (Punjabi), Ajmoda, Ajamoda, Ajmodika, Yavanaka, Yavaanika , Yavani, Yawani, Ugragandha, Brahmadarbha, Deepyaka Yavsaha (Sanskrit), Asampadam, Asamtavomam, Amam, Omam (Tamil), Ajumoda, Omamu, Vamu, Vayu (Telugu), Buranikataya (Urdu);
Italian: Ajowan, Ammi, Sisone;
Japanese: Ajowan;
Korean: Ayowan;
Lithuanian: Tikrasis Šventkmynis;
Malay: Mungsi;
Nepalese: Agnimanthaa, Javano, Jvaanuu;
Persian: Nanavva, Zenyân, Zenian;
Philippines: Lamudio (Bikol), Damoro (Pampangan), Damoro, Lamudio (Tagalog);
Polish: Ajowan, Kminek Koptyjski;
Portuguese: Ajowan; Orégano-Semente, Semente-De-Orégano;
Russian: Ažgon, Ajovan Dušistyj;
Slovak: Falsely Ligurčekové Semeno;
Spanish: Ajowan, Ayowam;
Sri Lanka: Asamodagam (Sinhala);
Swedish: Ajowan;
Taiwan: Yin Du Zang Hui Xiang;
Tajikistan: Yunon;
Thai: Phak Chi;
Turkish: Emmus, Mısır Anason, Mısır Anisonu, Nanavah.

Origin/Distribution

Ajowan is indigenous to Eastern Mediterranean and perhaps also to Egypt and Ethiopia. It is cultivated as a spice and medicinal plant from Egypt to Ethiopia, SW and Middle Asia, Crimea, Afghanistan, India and China. The main production areas today are Iran, Iraq and India.

Agroecology

In India it is found in dry open ruderal areas, lowland plains and hills in the arid areas. The plant is drought tolerant.

Edible Plant Parts and Uses

The fruits are used as a spice in savoury dishes, including curries, pickles, pastry snacks, pulses and bread. The strong aroma is enhanced by toasting or frying. Ajowan goes well with fish, potatoes, lentils and beans these legumes are commonly flavoured with a perfumed butter frequently containing ajowain.

Ajwain also enjoys some popularity in the Arabic world and is found in *berbere*, a spice mixture of Ethiopia which both shows Indian and Arabic heritage. In some parts of India, ajawan is used for specific types of salty pastry, e.g., the Rajasthani biscuits called mathari and similar ajwain-favoured pastry in Ladakh and Nepal called *nimki*. In India, ajowan is popularly used in *tadka* a lentil puree dish.

Botany

An erect, glabrous and corymbosely branched annual growing to 20–90 cm high. Leaves are petiolate, 2–3-pinnate, ultimate segments linear-filiform to 15 × 0.2–0.5 mm; petioles narrowly sheathing at base. Umbels compound, 2.5–5 cm across; bracts 3–8, linear-subulate, 5–7 mm; rays 6–20, 1–3 cm; bracteoles 5–10, linear, 2–3 mm. Calyx teeth minute or obsolete. Petals white, 1.3 by 1.3 mm, obovate emarginate or acuminate and inflexed at apex. Stylopodium domed; styles reflexed in fruit. Fruit broadly ellipsoid to ovoid, slightly compressed laterally, 1.2 × 2 mm to 1.0 × 1.8 mm, mericarps densely covered with fine short hairs or papillae, 5-ribbed (Plate 1).

Plate 1 Ajowan fruits

Nutritive/Medicinal Properties

Twenty-seven compounds were identified in the steam distilled ajowan fruit oil predominated by thymol (61%) *p*-cymene (15.6%) and gamma-terpinene (11.9%) (Chialva et al. 1993). The principal oil constituents of *T. ammi* were carvone (46%), limonene (38%), and dillapiole (9%) (Choudhury et al. 1998). Analysis of the volatile oil of ajowan seeds showed the presence of 17 constituents of which thymol (39.36%), γ-terpinene (30.97%), ρ-cymene (19.47%) and β-pinene (5.45%) and α-pinene (1.48%) were the major constituents (Nagalakshmi et al. 2000). The yield of the oleoresin was 24.66% containing 12.15% volatile oil and 87.85% non-volatile material. Eight compounds were identified in the hydrodistilled essential oil of ajowan (Khajeh et al. 2004). The major components were thymol (49.0%), γ-terpinene (30.8%), *p*-cymene (15.7), β-pinene (2.1%), myrcene (0.8%) and limonene (0.7%). GC and GC-MS analysis of ajwain essential oil showed the presence of 26 identified components which accounted for 96.3% of the total amount (Singh et al. 2004). Thymol (39.1%) was found as a major component along with *p*-cymene (30.8%), γ-terpinene (23.2%), β-pinene (1.7%), terpinene-4-ol (0.8%). In contrast, the acetone extract of ajwain showed the presence of 18 identified components which account for 68.8% of the total amount. The major component was thymol (39.1%) followed by oleic acid (10.4%), linoleic acid (9.6%), γ-terpinene (2.6%), *p*-cymene (1.6%), palmitic acid (1.6%), and xylene (0.1%). Major constituents of the ajowan oil were thymol (54.50%), γ-terpinene (26.10%) and *p*-cymene (22.10%) (Mohagheghzadeh et al. 2007). Comparison of the result from this study with other reports indicated ajowan to have thymol and carvacrol chemotypes. The major constituents of ajowan essential oil were thymol (48.4%), *p*-cymene (21.8%), γ-terpinene (21.3%) (Oroojalian et al. 2010).

The oil from immature green seeds of *Trachyspermum ammi* was composed of nine monterpenes which include seven hydrocarbons (97.1%) and two alcohols (2.9%) (Singh et al. 2008). The major monoterpenes were γ-terpinene (35%), α-phellandrene (31.4%), δ-carene (19.3%), *p*-mentha-1,3,8 triene (8.8%), *p*-cumin-7-ol (2.7%), β-pinene (1.9%), β-myrcene (.4%), *cis*-myrtenol (0.2%), and α-pinene (0.3%).

The phenolic compounds umbelliferone, psoralen, and eugenol were purified from ajowan dried fruits (Dhalwal et al. 2007). The average percentage recovery was found to be 98.88% for umbelliferone, 100.104% for psoralen, and 99.33% for eugenol. The seeds also contain 6-*O*-β-glucopyranosyloxythymol, a glucoside (Garg and Kumar 1998).

Almost pure thymol (98%) was isolated from ajowan fruits, but the leaf oil was found to compose of monoterpenoids and sesquiterpenoids: 43% cadinene, 11% longifolene, 5% thymol, 3% camphor and others (Minija and Thoppil 2002). In the essential oil distilled from ajowan aerial parts (flowers, leaves) isothymol (50%) was found to be the dominant constituent followed by *p*-cymene, thymol, limonene and γ-terpinene (Kambouche and El-Abed 2003). However, isothymol had not been well characterized and might refer to both 2-isopropyl-4-methylphenol and 3-isopropyl-6-methylphenol (carvacrol). Recent studies in Algeria found that isothymol was the major component of ajowan aerial plant parts at the beginning of the flowering stage, in other cases thymol was the predominant constituent (Bekhechi et al. 2010).

Ajowan besides being used as a culinary spice, is also used as a medicinal plant and has many pharmacological attributes.

Antioxidant Activity

Thymol and its siomer carvacrol, important constituents of ajowan seeds were found to decrease peroxidation of phospholipid liposomes in the presence of iron(III) and ascorbate (Aeschbach et al. 1994). The compounds were good scavengers of peroxyl radicals (CCl_3O_2). Data suggested that thymol and carvacrol possessed useful antioxidant properties and may become important in the search for 'natural' replacements for 'synthetic' antioxidant food additives. The acetone extract of ajowan showed better antioxidative activity for linseed oil as compared with synthetic antioxidants such as butylated hydroxyl toluene and butylated hydroxyl anisole (Singh et al. 2004). The methanol fraction of ajowan fruits showed highest antioxidant activity by phosphomolybdenum (2087.7 μmol) and DPPH assay (90.2%) followed by other fractions comparable to ascorbic acid and BHT (Zahin et al. 2010).

Antiplatelet Aggregation Activity

An extract of *Trachyspermum ammi* was found to inhibit platelet aggregation induced by arachidonic acid (AA), epinephrine and collagen (Srivastava 1988). The extract was most effective against AA-induced aggregation. Inhibition of aggregation by omum could be elucidated by its effect on platelet thromboxane production.

Antifertility Activity

Human sperm treated with ajowan essential oil showed a significant decrease in viability and a significant loss of functional mitochondria, membrane integrity and antioxidant enzyme, catalase when compared to control (Paul and Kang 2011a, 2012). The cholesterol:phospholipid ratio was also increased in treated sperm when compared to control, which indicated the loss of binding ability of human spermatozoa to the zona pellucida. The morphological deformities of sperm plasma membrane were characterised by vaculation, detachment of heads and tail coiling. The minimum effective dose (MED) of the essential oil that induced instant immobilization of human spermatozoa in vitro was 125 μg/mL. The motility was also irreversible. The observations indicated the spermicidal property of essential oil of *T. ammi* fruits, which could be helpful to develop medicinal preparations as a male contraceptive.

Antimicrobial Activity

The essential oil of ajowan fruits exhibited fungitoxicity against *Epidermophyton floccosum, Microsporum canis* and *Trichophyton mentagrophytes* at 900 ppm concentration (Singh et al. 1986). Thymol was isolated as fungitoxic factor and it exhibited toxicity against the test fungi at 1,000 ppm concentration.

Hot water extract of ajowan seeds exhibited antibacterial activity against *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomans aeruginosa*, *Salmonella typhimurium* and *Shigella flexneri* (Kaur and Arora 2009). Among the organic solvents used, the hexane, ethyl acetate, acetone and ethanol extracts of ajowan exhibited good inhibitory activity against all the tested bacteria *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae* 1, *K. pneumoniae* 2, *Pseudomonas aeruginosa* 1, *P. aeruginosa* 2, *Salmonella typhi*; *Salmonella typhimurium* 1, *S. typhimurium* 2 and *Shigella flexneri*. Bactericidal activity using viable cell counts showed that ajowan hot water extract killed 90–92% of *S. areus* after 8 h incubation. *S. typhi* was least sensitive to aqueous extracts, with the longest time for complete inhibition. Phytochemical analysis of ajowan seeds showed the presence of 4.23% alkaloids, 8.58% flavonoids, 22.77% tannins and 0.71% saponins. The essential oil of ajowan rich in phenols exhibited the highest antimicrobial activity with minimum inhibitory concentration

(MIC) <2% (v/v) against 55 bacterial strains except *Pseudomonas aeruginosa* (Mayaud et al. 2008). Ajowan essential oil exhibited antibacterial activity against several food-borne pathogens, namely *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Salmonella enteritidis*, and *Listeria monocytogenes* with MIC values of 0.03–0.5 mg/mL (Oroojalian et al. 2010).

A naphthalene derivative, (4aS, 5R, 8aS) 5, 8a-di-1-propyl-octahydronaphthalen-1-(2H)-one, isolated first time from *T. ammi* seeds exhibited antibiofilm activity against *S. mutans*, a major causal organism of dental caries (Khan et al. 2010b). It was found effective against adherent cells *of S. mutans*. It reduced water-insoluble glucan synthesis and inhibited the reduction in pH. Around 50% reduction was observed in adherence at 39.06 μg/mL and in biofilm at 78.13 μg/mL. The petroleum ether fraction of *T. ammi* (least MIC- 625 μg/mL) showed best inhibitory activity against multidrug resistant (MDR) strains of *Candida albicans*, *Candida krusei*, *Candida tropicalis*, *Candida glabrata*, *Escherichia coli* and reference strains of *Streptococcus mutans* and *Streptococcus bovis* when compared to its other fractions (Khan et al. 2010a). Ajowan essential oil displayed maximum activity against *Bacillus subtilis* and least activity against *Staphylococcus aureus* among the Gram positive bacteria tested (Wadhwa et al. 2010). The oil, and extracts of hexane, chloroform, ethyl acetate and methanol of *T. ammi* fruits exhibited significant anti-bacterial effects against *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Enterobactor aerogens* and *Staphylococcus aureus* (Paul et al. 2011). The scanning electron microscopic studies also demonstrated inhibitory effect of the oil on the morphology of *B. subtilis* at the MIC concentration, along with the potential effect on cell viabilities of the tested bacteria.

Ajowan was one of four essential oil that was found promising for the treatment of intestinal dysbiosis (Hawrelak et al. 2009). The essential oil displayed the greatest degree of selectivity, inhibiting the growth of 12 potential pathogens at concentrations that had no effect on the beneficial members of the human gastrointestinal tract microflora.

Antiviral Activity

The methanol extract of eight plant extracts including ajowan were found to be the most inhibitory against hepatitis C virus (HCV) with 90% or more inhibition at 100 μg/mL (Hussein et al. 2000).

Anticancer Activity

A significant reduction in murine skin as well as the forestomach tumour multiplicity with respect to all doses of ajowan seed diet (2, 4, and 6%) was found as compared to the control group (Singh and Kale 2010). A concomitant increase in the activities of the phase II enzymes and antioxidant enzymes were observed in ajowan treated groups. The content of reduced glutathione was significantly elevated, whereas the peroxidative damage along with lactate dehydrogenase activity exhibited a significant reduction with all the three doses of test diet. The findings were indicative of chemopreventive potential of *Trachyspermum ammi* seeds against carcinogenesis.

Antimutagenic Activity

Antimutagenic activity of the methanolic ajowan fruit extract was recorded with inhibition of mutagenicity ranging from 10.8 to 83.1% in a concentration dependent manne ragainst direct acting mutagens sodium azide (NaN3) and methyl methane sulphonate (MMS) and indirect acting mutagens 2-aminofluorene (2-AF) and benzo(a) pyrene (B(a)P), using Salmonella typhimurium (TA97a, TA98, TA100, and TA102) tester strains (Zahin et al. 2010). The methanolic fraction showed no sign of mutagenicity at tested concentrations (25–100 μg/plate). The extract was found to contain a high content of phenolic terpenoids.

Antilithiatic Activity

A novel calcium oxalate crystal growth inhibitor was purified from the seeds of *Trachyspermum ammi* (Kaur et al. 2009b) The anticalcifying

protein was found to have a molecular weight 107 kDa and an isolectric point 6.2. It possessed abundant acidic amino acids (Asp and Glu). The protein exhibited significant similarity with unnamed protein product of *Vitis Vinifera*. Using a urolithiatic rat model, the antilithiatic potential of *Trachyspermum ammi* anticalcifying protein was confirmed by its ability to maintain renal functioning, reduce renal injury and decrease crystal excretion in urine and retention in renal tissues (Kaur et al. 2009a).

Antihyperlipidaemic Activity

The results of studies suggested that 2 g/kg *T. ammi* seed powder produced hypolipidaemic activity in albino rabbits rendering 49, 53, 71 and 63% reduction in total lipids, triglycerides, total cholesterol and LDL-cholesterol, respectively (Javed et al. 2006, 2009). Ajowan at this dose caused 62% increase in the value of HDL-cholesterol. *T. ammi* seed powder at the rate of 2 g/kg and simvastatin (0.6 mg/kg body weight) were equally effective in treating hyperlipidaemia in albino rabbits but not at lower dosages. However, the chloroform and water extracts had no hypolipidaemic activity. Additionally, the petroleum ether extract appeared to be more effective than methanol extract in increasing the level of HDL-cholesterol and lowering the LDL-cholesterol. The petroleum ether extract reduced atherogenic index (total cholesterol/HDL-cholesterol) more effectively than methanol extract. Studies also suggested that the beneficial effects of ajowan on fat metabolism may be due to the considerable amounts of fibre in ajowan (Kumari and Prameela 1992).

Antiinflammatory Activity

The alcoholic and aqueous extract of ajowan seeds in 100 mg/kg doses exhibited significant antiinflammatory activity in both the animal models (Thangham and Dhananjayan 2003). In the carragenan induced rat paw oedema, both extracts showed an inhibition of 38.32 and 41.11% respectively. In the cotton pellet induced granuloma studies also they produced 38.05 and 43.87% inhibition of the pellets weight respectively. The weights of the adrenal glands were found to be significantly increased in extract treated animals (25.53 and 32.2%). The anti-inflammatory effects in rats was comparable to aspirin and phenylbutazone.

In an open prospective multicentre clinical trial conducted in patients suffering from various ophthalmic disorders namely, conjunctivitis, conjunctival xerosis (dry eye), acute dacryocystitis, degenerative conditions (pterygium or pinguecula) and postoperative cataract patients. An improvement was observed with the treatment of the herbal eye drop preparation (Ophthacare) in most cases (Biswas et al. 2001). Ophthacare conatins a mixture of different herbs which have been conventionally used in the Ayurvedic system of medicine, namely *Carum copticum*, *Terminalia belirica*, *Emblica officinalis*, *Curcuma longa*, *Ocimum sanctum*, *Cinnamomum camphora*, *Rosa damascena* and meldespumapum. There were no side effects observed during the course of the study and the eye drop was well tolerated by the patients. The herbal eye drop Ophthacare may have a useful role in a variety of infective, inflammatory and degenerative ophthalmic disorders.

Antinociceptive Activity

Studies in mice showed that ajowan fruit extract had antinociceptive activity especially in the late than early phase (Hejazian et al. 2008).

Studies showed that ethanolic extract of ajowan fruit produced significant increase in tail-flick latency during 2 h post-extract administration (Dashti-Rahmatabadi et al. 2007). The peak of the effect was observed at 45 min post injection, which was comparable to that of 1 mg/kg morphine (i.p.). The positive results indicated that the antinociceptive action may be of the opoid type, supporting the claim of Iranian traditional medicine showing that ajowan extract possessed a clear-cut analgesic effect.

Cholinomimetic Activity

An aqueous extract from roasted ajowan seeds exhibited cholinomimetic effects (Devasankaraiah et al. 1974). It showed muscarinic effects on rabbit duodenum, guinea-pig ileum and rat jejunum, and on the blood pressure of rat and cat. These effects were blocked by atropine. It also exhibited a nicotinic action on the frog rectus preparation and atropinized cat blood pressure. Its effect was potentiated by physostigmine and antagonized by cholinesterase or alkalinization. The presence of acetylcholine and choline were confirmed in the roasted ajowan seed extract.

Anticholinergic Activity

Studies demonstrated that ajowan extract and essential exhibited a competitive inhibitory effect on histamine (H1) receptors of isolated guinea-pig tracheal chains (Boskabady and Shaikhi 2000). A β-adrenergic stimulatory effect of essential oil and an anti cholinergic property of ajowan were also suggested. The results elucidated the relaxant and anti-cholinergic of ajowan observed in earlier studies.

Hypotensive Activity

Animal studies showed that thymol (the bioactive component of ajowan) exerted a blood pressure-lowering action, suggesting a channel-blocking mechanism and possibly elucidating the hypotensive and bradycardic effects observed in in-vivo studies (Aftab et al. 1995). The aqueous-methanolic extract of ajowan seeds (3–100 mg/kg) caused a dose-dependent fall in arterial blood pressure in anaesthetized rats (Gilani et al. 2005).

Antispasmodic/Bronchodilation Activity

In isolated rabbit aorta and jejunum preparations, the aqueous-methanolic extract of ajowan seeds (0.1–3.0 mg/mL) caused an inhibitory effect on the K^+-induced contractions (Gilani et al. 2005). The calcium channel blocking effect was confirmed when the extract shifted the Ca^{2+} dose–response curves (DRCs) to right similar to verapamil. In isolated guinea-pig tracheal preparations, it caused inhibition of carbachol and K^+-induced bronchoconstriction at 0.1–1.0 mg/mL as well as shifted the DRCs of carbachol and histamine to the right with suppression of maximum response suggestive of non-specific bronchodilator effect mediated possibly through calcium channel blocking.

Ajowan extract exhibited an inhibitory effect on acetylcholine induced contraction in rat's ileum (Hejazian-Y et al. 2009). One percent aqueous ajowan extract reduced the basal contractile activity of rat's ileum. The extract also reduced acetylcholine induced contraction to 40% of its maximum response. Ajowan's inhibitory action on acetylcholine induced contraction was similar but slower than that of atropine sulfate.

Hepatoprotective Activity

Pretreatment of rats with aqueous-methanolic extract of ajowan seeds (500 mg/kg orally for 2 days at 12 h intervals) prevented paracetamol (640 mg/kg) and CCl_4 (150 mL/kg)-induced rise in serum alkaline phosphatase (ALP) and aminotransferases (AST and ALT) (Gilani et al. 2005). The same dose of the extract was able to prevent the CCl4-induced prolongation in pentobarbital-induced sleeping time in mice confirming its hepatoprotectivity.

Antitussive Activity

Animal studies showed significant reduction of cough number obtained in the presence of both concentrations of aqueous and macerated ajowan extracts and codeine (Boskabady et al. 2005). The cough number obtained in the presence of higher concentration of aqueous and macerated ajowan extracts was significantly less than those of lower concentrations. In addition the cough number obtained in the presence of both concentrations of aqueous and macerated

extracts was significantly lower than that of codeine. However, carvacrol did not show any antitussive effect.

Antimalarial Activity

Essential oil of ajowan seeds and its pure constituent thymol showed promising larvicidal, oviposition-deterrent, vapor toxicity, and repellent activity against malarial vector, *Anopheles stephensi* (Pandey et al. 2009). Thymol was 1.6-fold more toxic than the oil toward fourth-instar larvae with LD_{50} values of 48.88 and 80.77 μg/mL, respectively. Egg laying by female adults was significantly reduced when exposed to vapors of thymol compared to the oil, and similar effects were recorded for subsequent egg hatching and larval survival. Vapor toxicity assay showed LC_{50}value of 79.5 mg/mat for thymol against adults, whereas the crude oil exhibited the LC_{50} value of 185.4 mg/mat. Thymol provided complete repellency toward adults at the dose of 25.0 mg/mat after 1 h duration, whereas same degree of repellency was obtained by the oil at the dose of 55.0 mg/mat, indicating thymol double-fold activity over the oil.

Antifilarial Activity

The crude extract of ajowan fruits and the active fraction showed significant activity against the adult bovine filarial *Setaria digitata* by both a worm motility and MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] reduction assays (Mathew et al. 2008). The isolated active principle was identified as a phenolic monoterpene. It exhibited in-vivo antifilarial activity against the human filarial worm *Brugia malayi* in *Mastomys coucha*, showing macrofilaricidal activity and female worm sterility in-vivo against *Brugia malayi*. The findings provide a new lead for development of a macrofilaricidal drug from natural products. Lymphatic filariasis is caused by infection with the parasitic filarial nematodes *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*, transmitted by mosquitoes.

Protease Activity

Ajowan seed was found to have high protease activity and to be an effective digestive aid in the stomach and small intestines (Ali et al. 2003). The protease was found to be thermostable.

Anthelmintic Activity

Ajowan seeds exhibited appreciable anthelmintic activity against human roundworm, *Ascaris lumbricoides* (Raj 1974). Crude ajowan seed powder (3 g/kg body weight) administered to sheep naturally infected with mixed species of gastrointestinal nematodes resulted in a maximum (79.1%) in eggs per gram (EPG) of faeces recorded on day 14 post treatment (Lateef et al. 2006). Increases in the reduction of EPG were observed with increasing dosage of ajowan seeds administered as crude powder, crude aqueous extract or crude methanol extract. However, the anthelminthic activity was not comparable with levamisole (99.2% reduction in EPG).

Detoxification of Fungal Toxins

Ajowan seed extract exhibited maximum degradation (up to 65%) of aflatoxin G1 (AFG1) (Velazhahan et al. 2010). The dialyzed ajowan seed extract was more effective than the crude extract, degrading >90% of the toxin. After treatment with ajowan extract, AFG1 failed to induce chromosomal aberration demonstrating the degradation of AFG1 by the extract. Significant levels of degradation of other aflatoxins viz., AFB1 (61%), AFB2 (54%) and AFG2 (46%) by the dialyzed *T. ammi* extract was also observed. The findings suggested that ajowan extract may provide a biologically safe method to protect poultry or livestock feeds and other agricultural commodities from aflatoxins. The application of

ajowan ethanolic extract in food samples resulted in considerable inhibition of the growth of toxigenic fungus, *Aspergillus ochraceus* in foods such as maize and poultry feed at 125 mg/g and no detectable amount of ochratoxin was found at a high moisture level of 20%, even after 7 days (Murthy et al. 2009).

Chromium Toxicity Protective Activity

Treatment of human bronchial epithelial cells (BEAS-2B) and isolated human peripheral blood lymphocyte (PBL) with ajowan methanol extract prior to potassium dichromate treatment exhibited an increase in cell viability and decrease of DNA damage as compared to potassium dichromate treatment alone (Deb et al. 2011). Further, ajowan methanol extract administration 1 h prior to graded doses of potassium dichromate significantly decreased reactive oxygen species (ROS) level, increased the mitochondrial membrane potential, reduced apoptosis and caspase 3 activity. Ajowan methanol extract also ameliorated potassium dichromate induced decrease in superoxide dismutase (SOD), glutathione peroxidase (GPx) antioxidant enzyme levels in BEAS-2B and PBL cells accompanied by reduction in lipid peroxides with maximum effect at 50 μg/mL. The study provided strong evidence to support the beneficial effect of ajowan methanol extract in preventing chromium induced toxicity in BEAS-2B and PBL cells.

Traditional Medicinal Uses

In traditional medicine the seed, and especially the essential oil in the seed, is regarded to be strongly antiseptic, antispasmodic, aromatic, bitter, diaphoretic, digestive, diuretic, expectorant, and tonic. It also have antibacterial and spermaticidal, antifungal and anti coagulant properties. It is used internally in the treatment of colds, coughs, influenza, asthma, diarrhoea, cholera, colic, indigestion, flatulence, dyspepsia, wind, oedema, arthritis and rheumatism. The root is carminative, abortive and diuretic. They are employed in traditional medicine as remedy for asthma, diarrhoea and cholera.

Ajowain is much used as a medical plant in Ayurvedic medicine in India, mainly, in treating diseases of the digestive tract and fever. In the West, thymol is used in medicines against cough and throat irritation.

Other Uses

Fruits and essential oils are also used for perfumery in India.

Ajowan essential oils also showed insecticidal and nematicidal activity.

Among the essential oils tested, strong insecticidal activity against the Japanese termite *Reticulitermes speratus* was observed with the essential oils of ajowan (*Trachyspermum ammi*), allspice (*Pimenta dioica*), caraway (*Carum carvi*), dill (*Anethum graveolens*), geranium (*Pelargonium graveolens*), and litsea (*Litsea cubeba*) (Seo et al. 2009). Among the bioactive compounds, phenol compounds exhibited the strongest insecticidal activity among the test compounds. The alcohol and aldehyde groups were more toxic than the hydrocarbons. Responses varied in a dose-dependent manner for each compound. The essential oil of ajowan was one of seven spices death of adults and larvae of the pulse beetle, *Callosobruchus chinensis* when fumigated with a 24 h LC_{50} of 15.6 mul (Chaubey 2008). The essential oil reduced the oviposition potential, egg hatching rate, pupal formation and emergence of adults of F(1) progeny of the insect when fumigated with sublethal concentrations. Fumigant activity of essential oil vapor distilled from *Carum copticum* was toxic against eggs, larvae and adults of the grain storage pest, *Callosobruchus maculatus* (Sahaf and Moharramipour 2008). The lethal concentration of ajowan essential oil to kill 50% of the population (LC_{50}) for egg, larvae and adult were found to be 1.01, 2.50 and 0.90 μL/L. Ajowan essential oil and its compounds exhibited good activity against the pinewood nematode *Bursaphelenchus xylophilus* (Park et al. 2007).

Sublethal treatment (20 and 60% of LC_{50}/24 h) of plant-derived molluscicides, viz. *Polianthes tuberosa*, *Trachyspermum ammi*, *Allium sativum* powder; *Azadirachta indica* oil; oleoresin of *Zingiber officinale* and their active molluscicidal component viz. tigogenin, hecogenin, azadirachtin, allicin, thymol, and [6]-gingerol in combination (1:5) with MGK-264 (*N*-Octyl bicycloheptene dicarboximide) or piperonyl butoxide caused a significant reduction in fecundity, hatchability, and survival of young *Lymnaea acuminata* snails (Singh and Singh 2000). In-vivo exposure of *Lymnaea acuminata* to thymol (active molluscicidal component of *Trachyspermum ammi*) significantly alter edacetylcholinesterase, lactic dehydrogenase, succinic dehydrogenase and cyto-oxidase activity in the nervous tissue of snails (Singh et al. 1999). Sublethal exposure to thymol reduced the levels of 5-hydroxytryptamine (5-HT) and dopamine (DA) in the nervous tissue of *Lymnaea acuminata*.

The essential oil from *Trachyspermum ammi* fruits exhibited toxicity at 800 ppm against *Aspergillus flavus* and *A. niger* (Tripathi et al. 1986). *Arachis hypogea* seeds when treated with oil at 5,000 ppm and stored for 12 months did not show the appearance of any fungi indicating the grain protectant activity of the oil. Thymol and *p*-cymene were isolated as antifungal principles of the oil exhibiting toxicity against the test fungi at 1,000 ppm. Among the various plant parts of ajowan, the ethanol (95%) extract of the seeds was moderately effective against the following test fungi: *Aspergillus niger*, *Aspergillus flavus*, *Fusarium solani*, *Alterranria alternata* and *Helminthosporium* sp. (Rizki et al. 1997). Benzene and petroleum ether extracts also showed some activity. Ajowan essential oil exhibited a broad spectrum of fungitoxic behavior against all tested fungi such as *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus oryzae*, *Aspergillus ochraceus*, *Fusarium monoliforme*, *Fusarium graminearum*, *Pencillium citrium*, *Penicillium viridicatum*, *Pencillium madriti*, and *Curvularia lunata* (Singh et al. 2004).

Comments

Ajowan is readily propagated from seeds.

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Brassica napus

Scientific Name

***Brassica napus* L.**

Synonyms

Brassica campestris f. *annua* Schübl. & G. Martens, *Brassica campestris* var. *bullatopetsai* Makino, *Brassica campestris* var. *dentatopetsai* Makino, *Brassica campestris* var. *dichotoma* Duthie & Fuller, *Brassica campestris* var. *glauca* (Roxb.) Duthie & Fuller, *Brassica campestris* f. *glauca* (Roxb.) Prain, *Brassica campestris* f. *luteoalba* Makino, *Brassica campestris* var. *napobrassica* (L.) Prain, *Brassica campestris* var. *napobrassica* (L.) DC., *Brassica campestris* subsp. *napus* (L.) Hook.f., *Brassica campestris* var. *napus* (L.) Bab., *Brassica campestris* var. *nippo-oleifera* Makino, *Brassica campestris* var. *oleifera* (Moench) Prain, *Brassica campestris* var. *pabularia* DC., *Brassica campestris* var. *quadrivalvis* (Hook.f. & Thomson) Duthie & Fuller, *Brassica campestris* f. *quadrivalvis* (Hook.f. & Thomson) Prain, *Brassica campestris* f. *simplex* Prain, *Brassica campestris* f. *spontanea* Makino, *Brassica campestris* var. *toria* Duthie & Fuller, *Brassica campestris* var. *trilocularis* (Roxb.) Duthie & Fuller, *Brassica campestris* f. *trilocularis* (Roxb.) Prain, *Brassica carinatua* var. *saharensis* A. Chev., *Brassica gongylodes* Mill., *Brassica napobrassica* Mill., *Brassica napus* var. *aestiva* Endl., *Brassica napus* f. *alba* DC., *Brassica napus* var. *annua* K. Koch, *Brassica napus* var. *arabica* O.E. Schulz, *Brassica napus* var. *biennis* (Schübl. & Mart.) Rchb., *Brassica napus* var. *brevirostris* Borbás, *Brassica napus* f. *dissecta* Peterm., *Brassica napus* f. *dolichocarpa* O.E. Schulz, *Brassica napus* var. *edulis* Delile, *Brassica napus* var. *esculenta* DC., *Brassica napus* f. *flava* DC., *Brassica napus* var. *glauca* (Roxb.) O.E. Schulz, *Brassica napus* var. *hiemalis* Döll, *Brassica napus* var. *italica* Alef., *Brassica napus* var. *leptorhiza* Spach, *Brassica napus* f. *micrantha* O.E. Schulz, *Brassica napus* var. *napobrassica* (L.) Rchb., *Brassica napus* subsp. *napobrassica* (L.) Jafri, *Brassica napus* subsp. *napobrassica* (L.) Hanelt, *Brassica napus* f. *nigricans* DC., *Brassica napus* subsp. *oleifera* (Moench) DC., *Brassica napus* var. *oleifera* (Moench) Delile, *Brassica napus* var. *pabularia* (DC.) Rchb., *Brassica napus* var. *quadrivalvis* (Hook.f. & Thomson) O.E. Schulz, *Brassica napus* subsp. *rapifera* Metzg., *Brassica napus* var. *rapifera* Metzg., *Brassica napus* var. *rossica* Alef., *Brassica napus* f. *rubescens* Peterm., *Brassica napus* var. *rutila* Alef., *Brassica napus* var. *sarcorhiza* Spach, *Brassica napus* var. *schebalinae* Bondartseva & Pivov., *Brassica napus* var. *syntomocarpa* O.E. Schulz, *Brassica napus* var. *trilocularis* (Roxb.) O.E. Schulz, *Brassica napus* var. *trimestris* Boenn., *Brassica napus* var. *ulti* (Prain) O.E. Schulz, *Brassica oleifera* Moench [Illeg.], *Brassica oleracea* var. *arvensis* Duchesne, *Brassica oleracea* var.

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hongnoensis H. Lév., *Brassica oleracea* var. *napobrassica* L., *Brassica oleracea* f. *praecox* Spreng., *Brassica praecox* Kit. ex Hornem., *Brassica praecox* Waldst. & Kit. ex DC., *Brassica rapa* subsp. *napus* (L.) Briq., *Brassica rutabaga* (DC.) Druce, *Brassica rutabaga* DC. ex H. Lév., *Brassica sativa* subsp. *napus* (L.) Clavaud, *Brassica stricta* Nestl. ex DC., *Braya campestris* f. *rutabaga* DC., *Crucifera napus* E.H.L. Krause.

Family

Brassicaceae

Common/English Names

Argentine Canola, Canola, Coleseed, Colza, Colza Rape, Oilseed Rape, Rapaseed, Rapeseed, Rappi, Summer Rape.

Vernacular Names

Argentina: Nabo, Rape;
Austria: Raps;
Bulgarian: Panc, Rapica, Raps;
Catalan: Colza;
China: Ou Zhou You Cai, Yang You Cai;
Croatia: Repica;
Czech: Brukev Řepka Olejka;
Danish: Raps;
Dutch: Koolzaad;
Eastonian: Raps;
Finnish: Rapsi;
French: Chou Colza, Colza, Colza D'hiver, Navette;
German: Kohlsaat, Kolza, Lewat, Ölraps, Raps, Winterraps;
Greek: Kolysa, Rapitsa;
Hungarian: Repce;
Icelandic: Blaðrepja;
India: Toria (Hindu);
Italian: Cavolo Colza, Colza, Napo Oleifera, Ravizzone;
Japanese: Inabana, Nanohana, Seiyou Aburana;
Korean: Yuchae;
Norwegian: Raps;
Polish: Rzepak;
Portuguese: Colza, Grelos, Nabiça;
Romanian: Colza, Rapiță, Rapiță Colza;
Russian: Рапс, Сурепица – Raps, Surepica;
Slovenia: Ogrščica;
Spanish: Colza, Nabino, Nabo, Nabo Colza;
Thai: Phak Kat Kan Khao;
Vietnamese: Cải Dầu.

Origin/Distribution

The centre of origin of *Brassica napus* is uncertain but is regarded to be in Mediterranean Europe. Evidence based on either chloroplast or nuclear markers has strongly suggested that *B. napus* is an amphiploid and appeared to have resulted from several independent hybridisation events (Song et al. 1988; Song and Osborn 1992; Allender and King 2010). Evidence suggested that most cultivated forms of *B. napus* were derived from a cross in which closely related ancestral species of *B. rapa* and *B. oleracea* was the maternal donor (Song et al. 1988; Song and Osborn 1992). Phylogentic relationships based on nuclear RFLPs (restriction fragment length polymorphism) clearly separated *B. napus* accessions having different cytroplasm types providing further evidence for multiple origins of *B. napus* (Song and Osborn 1992). *B. oleracea* or any of the C genome species are closely related to the maternal progenitor of most *B. napus* accessions. Based on recent evidence from chloroplast haloptypes and nuclear AFLP (simplified fragment length polymorphism) markers, Allender and King (2010) concurred with the findings of Song et al. (1988), that *B. rapa* 'spring broccoli raab' may be the closest extant relative of the maternal ancestor of *B. napus*.

Based on 2010 global production volume in tonnes, rapeseed (59, 071,197) ranked fifth

among the primary oil crops cultivated: after soybeans (261,578,498), oilpalm fruit (210,917,078), seed cotton (68,299,244), and coconuts (62,451,506) (FAO 2012). The leading rapeseed producing countries in tonnes for 2010 in descending order are: China 13,082,010; Canada 11,866,200; India 6,410,000; Germany 5,697,600; France 4,815,520; Australia 2,180,600; Poland 2,077,630; Ukraine 1,469,700 and the United States 1,113,620.

Agroecology

Canola is a relatively cool season crop in that its best growth occurs above 12°C and below 30°C. The optimum temperature for maximum canola growth and development has been reported at 21–25°C. Canola is susceptible to heat stress (32°C or more) during grain fill that can lower yields (Potter et al. 1999) and reduce oil content. High temperatures (32°C/26°C; day/night) can also induce both male and female sterility as shown by reduced stamen and anther size and abnormal microsporogenesis and in the gynoecia aberrant ovule development and no seed set (Polowick and Sawhney 1988). Canola is relatively frost tolerant, however, damage can occur at the cotyledon stage and seedlings affected are injured and may die. Plants become more frost tolerant as they aged. Lower temperatures during flowering may cause flower abortion. Higher temperatures, drought and long days hasten maturity, and, in combination, can severely affect the formation of pods, seeds, seed size and oil content. Canola is grown in areas receiving from 325 to 700 (2000) mm annual rainfall. Canola thrives on medium textured, well-drained fertile soils with pH of 6.2–7.7. Canola is tolerant of a soil pH as low as 5.5 and saline conditions (pH 8.3) (Colton and Sykes 1992). On strongly acid soils with a pH of less than 5.5, canola yields are often reduced considerably. Canola is intolerant of waterlogging. Sodic and dispersing soils that surface seal will significantly reduce emergence of canola seedlings (Potter et al. 1999).

Edible Plant Parts and Uses

Rapeseed /Canola is grown primarily for its seeds which yield between 40 and 50% oil. Canola oil is widely used as cooking oil, for making margarine and as salad oil.

In Europe young sprouted seedlings of *Brassica napus* are occasionally eaten in salads and used as garnish, replacing white mustard (*Sinapis alba*) and garden cress (*Lepidium sativum*). The leaves and young tender leafy shoots are eaten as vegetables in the same way as other *Brassica* leafy vegetables raw in salads, cooked as potherbs and in stir fries on its own with salt, garlic, oil with or without added spices or stir-fries with meat or seafood. The seed is also used as a mustard flavouring.

Rapeseed flowers produce abundant nectar, and honeybees produce a light coloured, peppery honey from it. The honey is usually blended with milder honeys, if used for table use or sold as bakery grade.

Botany

An annual, herbaceous plant, 80–120 cm high with a slender erect, glabrous, stem arising from taproot, stem sparsely branching above (Plate 1). Lower leaves alternate, often lyrate-pinnatifid, petiolate, glaucous, 5–25 (–35) long by 2–7(10) wide, with large, ovate terminal lobe, entire or dentate, lateral lobes much smaller, entire or dentate. Upper and middle cauline leaves sessile, lanceolate, ovate or oblong, 9 cm by 3.5 cm, glaucous, base amplexicaul, auricles rounded, margin entire, repand (Plates 1 and 3). Flowers in branched terminal racemose clusters with buds overtopping open flowers. Flowers bisexual, 10–15 mm across; sepals 4 oblong, subequal, yellowish-green and glabrous, petals 4 yellow to pale yellow, obovate, narrowed towards the base (Plates 2 and 4); stamens 6 with yellow anthers; ovary glabrous, green, terete 4–5 mm long with 1.7 mm long style and capitate stigma persistent in fruit. Fruit a glabrous, linear, terete siliqua, 4.5–11 cm × 3–4 mm, with a tapering beak 1–3 cm long, ascending (Plates 3, 4, 5, and 6),

Plate 1 Flowering rapeseed plants

Plate 2 Close-up of yellow flower cultivar

Plate 3 Immature fruits (siliqua) of yellow-flowered cultivar

Plate 4 Pale yellow-flowered rapeseed cultivar

dehiscent, up to 30-seeded. Seeds globose, 1.5–2.5 mm in diameter, finely reticulate, bluish black to dark brown.

Nutritive/Medicinal Properties

Nutrients and Phytochemicals in Rapeseed Oil/ Seeds

Proximate nutrient value per 100 gm edible portion for low erucic rapeseed oil (canola) had been reported by USDA (2012) as follows: energy

Plate 5 Ascending fruits of pale-yellow flowered cultivar

Plate 6 Close-up of rapeseed siliqua

884 kcal (3,699 kJ), total lipid 100 g, total choline 0.2 mg, vitamin E (α-tocopherol) 17.46 mg, β-tocopherol 0.01 mg, γ-tocopherol 27.34 mg, δ-tocopherol 0.99 mg, vitamin K (phylloquinone) 71.3 μg, total SFA 7.365 g, 16:0 (palmitic acid) 4.298 g, 18:0 (stearic acid) 2.087 g, 20:0 (arachidic acid) 0.650 g, 22:0 (behenic acid) 0.330 g, total monounsaturated fatty acids (MUFA) 63.276 g, 16:1 undifferentiated (palmitoleic acid) 0.214 g, 18:1 undifferentiated (linoleic acid) 61.744 g, 18:1 c (linoleic acid *cis*) 61.714 g, 18:1 t (linoleic acid *trans*) 0.030 g, 20:1 (gadoleic acid) 1.317 g, total polyunsaturated fatty acids (PUFA) 28.142 g, 18:2 undifferentiated (linoleic acid) 19.05 g, 18:2 n-2 c,c 18.640 g, 18:2 t,t 0.365 g, 18:3 undifferentiated (linolenic acid) 9.137 g, 18:3 n-3 c,c,c (ALA) (α-linolenic acid) 9.137 g, total *trans* fatty acids 0.395 g, total *trans*-monenoic fatty acids 0.030 g, stigmasterol 3 mg, campesterol 241 mg, β-sitosterol 413 mg, δ-5-avenasterol 11.721 mg, β-sitostanol 0.925 mg, and campestanol 0.811 mg. Egosterol, a fungal metabolite indicating spoilage, was detected in canola seed (Abramson and Smith 2003).

Germination was found to enrich the content of tocopherols and phytosterols in canola (*B. napus*) seeds (Zhang et al. 2007). The total tocopherol content of oil extracted from 20-day-old seedlings was 4.3- to 6.5-fold higher than that of intact seeds. On a dry seedling basis, the content and composition of phytosterols did not change significantly over the sprouting period, but the concentration of total phytosterols in the oil fraction increased 4.2- to 5.2-fold. Tocopherols were mainly concentrated in the leafy seedling tops rather than in the non-photosynthesizing bottoms, whereas phytosterols were equally distributed across both sections. Earlier they found that diminution of proteins and lipids in whole canola seedlings and their top (leaf/cotyledons) and bottom parts (stem/roots/seed coat) was independent of light, whereas the protein solubility increased at a faster rate under an illuminated environment than in the dark (Zhang et al. 2004). A rapid rise in free fatty acids but a net decline of dry matter content in seedlings grown in the dark was observed. The dry matter content of canola seedlings grown in the illuminated environment increased due to photosynthetic biomass accumulation.

Molecular distillation from rapeseed oil deodoriser distillate (RODD), a by-product of vegetable refining edible oil yielded a fraction, containing mainly hydrocarbons, ketones and aldehydes (Jiang et al. 2006). The second fraction

contained mainly fatty acid methylesters (FAME) (above 90%) and another fraction yielded tocopherol (nearly 35%).

Field studies indicated that seed yield from canola regrowth was 67% of uncut plots (1,349 vs. 2,020 kg/ha) (Bhardwaj and Hamama 2009). The oil content in regrowth plots was significantly lower than that in uncut plots (34.7 vs. 37.1%). However, the oil from regrowth plots was considered healthier since, it contained less saturated and more unsaturated fatty acids. With regards to the C16:1 (7.42 vs. 7.53% for uncut), C18:0 (2.05 vs. 2.36% for uncut), C18:3 (6.39 vs. 8.09% for uncut), C20:0 (0.67 vs. 0.87% for uncut), C20:1 (1.39 vs. 1.64% for uncut) and C24:0 (0.14 vs. 0.41% for uncut) fatty acids, the seeds produced on regrowth had significantly lower contents as compared to the uncut plots whereas, the content of C18:1 fatty acids was significantly increased by the cut regrowth treatment (61.96 vs. 59.91% for uncut). Also the content of 22:1 (erucic acid) was lower in the regrowth (0.29%) compared to uncut 0.34%. The content of total unsaturated fatty acids in the seed produced on the regrowth (89.4%) was significantly greater than that in the seed produced on uncut plants (88.5%) whereas the content of total saturated fatty acids in the seed produced on regrowth (10.6%) was significantly lower than that produced on uncut plants (11.5%). The content of polyunsaturated were 25.04% for regrowth and 25.98% for uncut.

El-Beltagi and Mohamad (2010) found oleic acid (18:1) to be the predominating fatty acid accounting for 56.31–58.67% in the seeds of five Egyptian rapeseed cultivars followed by linoleic acid (18:2) 10.52–13.74%, stearic acid (18:0) 11.09–14.93%, α-linoleic acid 8.83–10.32%, palmitic acid (16:0) 2.18–7.91% and gadoleic acid 0.93–1.69%. Erucic acid (22:1) ranged from 0.15 to 0.91% and nervonic acid (24:1) ranged from 0.12 to 0.34%. Total saturated fatty acids ranged from 15.85 to 20.50%, total unsaturated fatty acids from 78.99 to 84.33%, total MUFA from 58.22 to 60.27% and total PUFA from 19.35 to 24.06%. Total amino acids in mg/100 g N ranged from 103.8 to 105.01 among the five cultivars, comprising 47.16–48.34 mg essential amino acids namely 3.02–3.60 mg isoleucine, 7.29–7.62 mg leucine, 6.33–6.82 mg lysine, 4.21–4.50 mg cysteine, 3.91–4.94 mg methionine, 2.71–3.30 mg tyrosine, 3.66–4.10 mg phenylalanine, 4.24–4.97 mg threonine, 5.70–5.87 mg valine and 4.50–4.75 mg histidine. Total non-essential amino acids ranged from 56.00 to 57.12 mg comprising 7.56–7.90 mg arginine, 16.83–17.91 mg aspartic acid, 8.47–8.94 mg glutamic acid, 5.09–5.86 mg serine, 4.52–.03 mg proline, 6.08–6.96 mg glycine and 5.47–5.82 mg alanine. Total tocopherol contents ranged from 90.0 to 138.3 mg/100 g oil and total phenolic contents varied from 28.0 to 35.4 mg/g dw. The five rapeseed cultivars also contained glucosinolates with mean content of 5.03 μmol/g dw; the major glucosinolates found were progoitrin, gluconapin and glucobrassicanapin. The glucosinolate profile comprised aliphatic glucosinolates viz glucoberin (3-methylsulfinylpropyl glucosinolate) 0.002 μmol, glucobrassicanapin (4-pentenyl glucosinolate) 0.44 μmol, progoitrin (2-(r)-2-hydroxy-3-butenyl glucosinolate) 2.83 μmol, epi-progoitrin (2-(s)-2-hydroxy-3-butenyl) 0.036 μmol, sinigrin (2-propenyl glucosinolate) 0.004 μmol, glucoalyssin (5-methylsulfinylpentyl glucosinolate) 0.002 μmol, gluconapoleiferin (2-hydroxy-4-pentenyl glucosinolate) 0.002 μmol, glucoerucin (4-methylthiobutyl glucosinolate) 0.004 μmol, gluconapin (3-butenyl glucosinolate) μmol, 1.58 μmol, indoyl glucosinaltes viz. glucobrassicin (3-indolylmethyl glucosinolate) 0.006 μmol, neoglucobrassicin (1-methoxy-3-indolylmethyl glucosinolate) 0.002 μmol, 4-hydroxyglucobrassicin (4-hydroxy-3-indolylmethyl glucosinolate) 0.038 μmol, and aromatic glucosinolates viz. gluconasturtiin (2-phenylethyl glucosinolate) 0.082 μmol and 4-methoxygluconasturtiin (4-methoxy2-phenylethyl glucosinolate) 0.002 μmol. The presence of health-promoting compounds showed nabicol to be a good source of glucosinolates and phenolic antioxidants. Earlier, (−)-5-allyl-2-thiooxazolidone (napoleiferin) was isolated from rape (*Brassica napus* var. *oleifera*); it was found to have a similar absolute configuration to that of goitrin isolated from the same tissue (Tapper and MacGibbon 1967). A new glucoside,

2-hydroxy-4-pentenyl-glucosinolate, was also detected in fresh tissues.

Oil bodies from rapeseed (*Brassica napus*) consist of a triacylglycerol (TAG) core surrounded by a phospholipid monolayer embedded with integral proteins which confer high stability to oil bodies in the mature dry seed (Jolivet et al. 2011). They assessed lipid and protein accumulation patterns throughout seed development (from 5 to 65 days after pollination [DAP]) both in the whole seed and in purified OBs. The major protein component of oil body organelles are oleosins, low molecular weight (15–26 kDa) basic proteins, embedded in the phophol lipid monolayer (Katavic et al. 2006). Major seed oil body proteins identified, included 19 oleosins, 5 steroleosins and 9 caleosins (Jolivet et al. 2009). Two rapeseed oleosin orthologs appeared acetylated on their N-terminal alanine residue and both caleosins and steroleosins displayed a low level of phosphorylation. Accumulation of oleosins and caleosins was observed starting from early stages of seed development (12–17 DAP), while steroleosins accumulated later (~25 DAP) onwards (Jolivet et al. 2011). In situ electron microscopic observations of maturing seed suggested that plant seed oil bodies were formed through the 'budding' of the endoplasmic reticulum (Katavic et al. 2006). Major differences were observed in the fatty acid composition of polar lipid fractions between two *B. napus* cultivars: high erucic, low glucosinolate cultivar (cv.) Reston and low erucic, low glucosinolate cv. Westar (canola) oil bodies. The polar lipids isolated were primarily phosphatidylcholine, phosphatidic acid and phosphatidylethanolamine. Neutral lipid composition confirmed erucic acid and oleic acid accumulation in Reston and Westar seed oil. They also identified in addition to olerosins, proteins that could be classified into groups including 11-β-hydroxysteroid dehydrogenase like proteins, putative embryo-specific protein (ATS1), short chain dehydogenase/reductase, myrosinases, myrosinase binding proteins, myrosinase associated proteins, β-glucosidases, storage proteins, heat shock proteins and putative seed maturation protein (Katavic et al. 2006). Three oleosin proteins: oleosin type 4, 1803528A and oleosin BN-V, with experimental molecular masses of 24, 21 and 19 kDa and pI valuesof 9.5, 10, and 9.5 respectively, were identified. The short chain dehydrogenase/reductase, is similar to a triacylglycerol-associated factor from narrow-leafed lupin while the other, a protein annotated as a myrosinase associated protein, shows high similarity to the lipase/hydrolase family of enzymes with GDSL-motifs. Two other proteins showing high homology with seed oil body proteins described in other species were identified including 11-β-hydroxysteroid dehydrogenase-like protein similar to steroleosin from sesame oil bodies and putative embryo-specific protein (ATS1) similar to caleosins described in oil bodies from sesame and rice. In addition, a short chain dehydrogenase/reductase was identified from cv. Reston oil bodies. They also found protein contaminants namely storage proteins cruciferin and napin (found in protein storage vesicles) and import inner membrane translocase and ATP synthase α-chain (mitochondrial proteins). Analysis of cultivars Reston and Westar oil body protein preparations by Multidimensional Protein Identification Technology (MudPIT) revealed the same group of proteins identified as well as aspartic protease, protein disulfide isomerase, luminal binding protein, and a LEA (late embryogenesis abundant) domain-containing protein.

Accessions of winter hardy rapeseed (*B. napus*) had significantly higher mean oil content in the seeds (37.4%) than *Brassica rapa* (36.6%) (Bhardwaj and Hamama 2000). The glucosinolate content was higher in *B. napus* than *B. rapa* meal (49.2 vs. 43.8 μmol/g). The erucic acid content was higher in *B. rapa* (32.6%) than *B. napus* accessions (26.1%). The results indicated that plant material from either *B. napus* or *B. rapa* species could be used in breeding for increasing erucic acid content. Accessions with high, medium, and low contents of oil, erucic acid, and glucosinolate contents were identified. The US industry uses ≈18 million kg of high erucic acid oil annually, mostly from imports. The oil content in both the high and low-glucosinolate rapeseed lines increased approximately by a factor of 4 from 26 to 52 days after

flowering (DAF) (Bhardwaj and Hamama 2003). Erucic acid content in the oil was significantly higher in low glucosinolate lines compared with high glucosinolate lines on 28 and 40 DAF. The glucosinolate contents in high glucosinolate lines started to increase significantly at 26 DAF and continued up to 33 DAF. However, the glucosinolate content in the low glucosinolate lines increased only from 33 to 35 DAF. Thus the greatest accumulation of glucosinolate in developing rapeseed seeds may occur at approximately 26 DAF.

Brassica napus varieties with low glucosinolate, experimentally grown in Brazil were found to have 43–45% lipids with an erucic acid content lower than 1% and proteins (18–20%) were the main components (Lajolo et al. 1991). Mineral contents were high, dietary fibre in rapeseed meals comprised 23.7–27.5% and also contained phytic acid which could compromise the availability of minerals. Sinapine and esters were found at a mean content of 3.4%. Total aliphatic plus indolyl glucosinolates values varied between 26 and 43 μmol/g for air-dried, defatted seed meals, roughly similar to glucosinolate contents and with 26–37 μmol/g glucose. Individual glucosinolate analysis showed predominance of progoitrin. Earlier studies showed that intact glucosinolates progoitrin, gluconapin, and glucoalyssin and oxazolidinethiones were found to combine with the rape seed meal proteins to a very small extent, independently of pH; but the isothiocyanates reacted readily with the proteins at pH values higher than 6 (Björkman 1973). Fractionation of the rape seed protein conjugates showed that isothiocyanates particularly reacted with the basic low molecular weight proteins. A 12 S rapeseed globulin, a neutral protein , containing high contents of glutamic (19%) and aspartic (10%) acid and a low content of sulphur containing amino acids and sugar (0.5%), was isolated from the seed (Schwenke et al. 1981).

In a comparative study of lipid polyester composition of *Arabidopsis thaliana* and *Brassica napus* seeds, Molina et al. (2006) found in *Arabidopsis* seeds, the major C16 and C18 monomers identified included ω-hydroxy fatty acids and α,ω-dicarboxylic acids derived from palmitate, oleate and linoleate, and 9,10,18-trihydroxyoctadecenoic acid. Among monomers, docosan-1-ol, docosane-1,22-diol, 22-hydroxydocosanoic acid, 24-hydroxytetracosanoic acid, tetracosane-1,24-dioic acid and ferulic acid were the major species. Compared to *Arabidopsis, Brassica* seeds showed a roughly similar proportion of monomer classes, with the exception that alkan-1ols were threefold higher. Also, there were much less C24 aliphatic species and significant amounts of C14–C16 alkan-1ols, including iso-methyl and anteiso-methyl branched compounds. Dissection and analysis of mature *Brassica* seeds showed that the trihydroxy C18:1 fatty acid was found mainly in the embryo, while ferulate, fatty alcohols and C22 and C24 species were specific to the seed coat plus endosperm.

Phenolic compounds range from simple, low molecular-weight, single aromatic-ringed compounds to large and complex tannins and derived polyphenols. They can be classified based on the number and arrangement of their carbon atoms into flavonoids (flavonols, flavones, flavan-3-ols, anthocyanidins, flavanones, isoflavones and others) and non-flavonoids (phenolic acids, hydroxycinnamates, stilbenes and others) and they are commonly found conjugated to sugars and organic acids (Cartea et al. 2011). The most widespread and diverse group of polyphenols in *Brassica* species including *B. napus* are the flavonoids (mainly flavonols but also anthocyanins) and the hydroxycinnamic acids.

Fifteen sinapate esters constituents were isolated and identified in seeds of oilseed rape (*Brassica napus*) (Baumert et al. 2005). These include glucose, gentiobiose and kaempferol glycoside esters as well as sinapine (sinapoylcholine), sinapoylmalate and an unusual cyclic spermidine amide. One of the glucose esters (1,6-di-O-sinapoylglucose), two gentiobiose esters (1-*O*-caffeoylgentiobiose and 1,2,6′-tri-*O*-sinapoylgentiobiose) and two kaempferol conjugates [4′-(6-*O*-sinapoylglucoside)-3,7-di-*O*-glucoside and 3-*O*-sophoroside-7-*O*-(2-*O*-sinapoylglucoside)] were new plant products. Serine carboxypeptidase-like (SCPL) acyltransferases were found to catalyze the formation of sinapine and sinapoylmalate accepting 1-*O*-β-acetal esters

(1-*O*-β-glucose esters) as acyl donors. The formation of the complex pattern of these esters in *B. napus* seeds was dependent on sinapoylglucose. Phenylpropanoids found in the transgenic low-sinapine oilseed rape were elucidated to be 4-*O*-glucosides of syringate, caffeyl alcohol and its 7,8-dihydro derivative as well as of sinapate and sinapine, along with sinapoylated kaempferol glycosides, a hexoside of a cyclic spermidine alkaloid and a sinapine derivative with an ether-bridge to a C(6)-C(3)-unit (Wolfram et al. 2010). Silencing the expression a key enzyme of sinapate ester biosynthesis (UDP-glucose:sinapate glucosyltransferase, encoded by the UGT84A9 gene) in oilseed rape seeds disrupted the metabolic flow through sinapoylglucose and altered the amounts and nature of the phenylpropanoid end-products.

Among the commercially cultivated Brassicaceae (Cruciferae) plants, *Brassica juncea*, *Brassica napus*, *Brassica rapa*, and *Sinapis alba* store significant amounts of oil and protein in the seed (Wanasundara 2011). Cruciferin (11S) and napin (2S) are the predominant storage proteins of these Brassicaceae seeds that contribute to different properties and functions. Both proteins were found in the embryo axis and cotyledons and in smaller amounts in the endosperm of *B. napus* seeds (Höglund et al. 1992). In germinating seeds, napin and cruciferin were rapidly degraded and after 4 days hardly any cells contained napin or cruciferin.

The yellow seed characteristic in *Brassica napus* is desirable because of its association with higher oil content and better quality of oil-extracted meal (Akhov et al. 2009). Seed-coat pigmentation in YN01-429, a yellow-seeded canola-quality germplasm developed in Canada after several years of research, was attributed to oxidized proanthocyanidins (condensed tannins) derived from phenylpropanoids and malonyl CoA.

Rapeseed hulls were found to contain no free phenolic acids and relatively low levels of soluble ester and bound phenolics (Krygier et al. 1982). Sinapic acid was the principal phenolic acid released by hydrolysis of the soluble esters in the hulls while protocatechuic acid was the major phenolic acid in the residues. Rapeseed flours contained 698 mg/100 g of free phenolic acids, 768–1,196 mg/100 g of phenolic acids from hydrolyzed esters, and no phenolic acids in the residues. Sinapic acid accounted for a high proportion of the free phenolic acids and 99% of acids released from esters in the flours. Minor phenolic acids included *p*-hydroxybenzoic, vanillic, gentisic, protocatechuic, syringic, *p*-coumaric, and ferulic acids in the various fractions and cultivars.

The use of oilseed rape/canola (*Brassica napus*) protein in the meal for human nutrition is presently not feasible due to the presence of major antinutritive compounds such as dietary fibre, dark-coloured tannins and bitter-tasting sinapate esters (Lipsa et al. 2009). Yellow coloured seeds were found to be of particular interest for oilseed rape breeding because of their association with a thinner seed coat resulting in reduced dietary fibre and condensed tannin content which considerably improved the feed and protein quality of rapeseed meal after oil extraction. Plant tannins have the ability to complex strongly with proteins, starch, cellulose and minerals. Chemically three groups of tannins are distinguishable: phlorotannins, hydrolysable and condensed tannins (syn. proanthocyanidins). In rapeseed (*Brassica napus*) condensed tannins were found to be largely responsible for the dark colour of the seed coat, where they accumulated predominantly in the endothelium cell layer between the outer integument and the aleuronic layer. In contrast, the proportion of condensed tannins in the cotyledons of *B. napus* seeds was comparatively low (0.1–0.5% of dry weight), condensed tannins in dark-seeded *B. napus* could comprise up to 6% of the seed coat. Condensed tannins compounds found in double haploid populations of *B. napus* included flavonoids, oligomeric proanthocyanidins, F2PA2, F2PA3, F2PA6 and polymeric proanthocyanidins F3PA3, F3PA4, F3PA6. A significant proportion of the total seed flavonoids are non-coloured flavonoids.

Canola seed was found to typically contain 35–45% oil content depending on varieties and environmental conditions and a minimum of 35% protein at 13% moisture (AOF 2007). The hull comprised approximately 16% of the seed weight

(approximately 30% of the oil-free seed meal) (Bell 1984). Canola varieties with <7 μmol of total glucosinolates per g of whole seed, equating to 11 μmol/g of oil-free meal and well less than the canola standard of 30 μmol/g of meal had been developed through breeding and selection. The composition of seed meal depended on the method of oil extraction (AOF 2007). Rape seed meal was found to contain 42.8% crude protein (N×6.25), 12.1% crude fibre, 7% ash, 34% nitrogen free extract and 4,300 kca/kg total energy (Bell and Jeffers 1976). Vitamin content in mg/kg of rapeseed meal comprised: 160 mg niacin, 9.5 mg pantothenic acid, 5.2 mg thiamine, 3.7 mg riboflavin, 2.3 mg folic acid, 0.9 mg biotin and 0.67% choline (Clandinin et al. 1986). The mineral content (dry matter basis) of rapeseed meal was reported as: ash 7.4–7.6%, Ca 0.68%, P 1.2–3%, phytin-phosphorus 0.8–0.9%, K 1.3%, Mg 0.64%, S 0.8–1.7%, Na 6–7 mg/kg, Zn 72 mg/kg, Mn 32–80 mg/kg, Cu 7–10 mg/kg, Fe 7–8 mg/kg, Ni 1.5–4.3 mg/kg, Se 1 mg/kg, Cd 0.02–0.13 mg/kg, B 18–24 mg/kg (Bragg and Seier 1974; Elson et al. 1979; Clandinin et al. 1986; Bell 1984). Major glucosinailates found in *B. napus* rapeseed meals included progoitrin (2-OH-3-butenyl-glucosinolate), gluconapin (3-butenyl- glucosinolate), glucobrasicanapin (4-pentenyl-glucosinolate),napoleiferin(2-OH-4-pentenyl-glucosinolate), glucobrassicin (3-indolyl-methyl-glucosinolate) and neoglucobrassicin (1-methoxy-3-indolyl-methyl glucosinolate) (Bell 1984).

Rapeseed hull contained (dry matter basis) 12–16% crude protein, 44% crude fibre, 4–5% ash, 34% nitrogen free extract and 4,230 kca/kg total energy, 14.5% pentosan, 32% cellulose, 12–24% lignin, 6–12% polyphenols, 1.5% tannins, 3.8% sugars (2.3–2.9% sucrose, 0.4–0.5% stachyose, 0.05–0.16% each of fructose, glucose, raffinose, 0.1% each of arabinitol, galactilol, myo-inositol, and traces of galactose and galactinol) (Bell 1984). Dehulled rapeseed oil free dry matter contained 14.5% pectins, 7% cellulose residue, amyloid (mainly fuco-amyloid) 4.5%, arabinan 2%, arabinogalactan 1%, lower molecular weight carbohydrates (fructose, glucose, galactose, myo-inositol, sucrose, galactinol, raffinose and stachyose) 3.2%, lignin (permanganate) 2.6%, ash 3.7%, lipids (bound) 5.5, phytates 2%, glucosinolates 1% and protein (N×6.24) 52% (Bell 1984).

Phytochemicals in Seeds, Leaves and Roots

In a comparative study of glucosinolate profile of leaves and seeds of 33 *Brassica napus* crops, including leafy crops, forage, rutabaga, and oilseed crops, Velasco et al. (2008) found that glucosinolate concentration was higher in seeds than in leaves, ranging from 3.8-fold in oilseed crops to 7.1-fold in root vegetable crops. Aliphatic glucosinolates predominated in both plant parts. In seeds, aliphatic glucosinolates varied between 91 and 94% in the different groups, whereas in leaves there was more variation. For root vegetable crops, aliphatic glucosinolates comprised 80% of the total glucosinolate concentration. For leafy and forage types, aliphatic glucosinolates comprised approximately 90% and for oilseed crops 92%. Indole glucosinolates were higher in leaves (5–17%) than in seeds (5–8%). The total glucosinolate content in leaves varied from 14 to 24 μmol/g dry weight (DW) in oilseed and forage types, respectively, whereas in the seeds, it varied from 55 to 115 μmol/g DW in oilseed and forage types, respectively. Significant differences were noted among the four groups in glucosinolate concentration and glucosinolate composition. In the seeds, progoitrin was found as the main glucosinolate in all groups. In the leaves, two different glucosinolate profiles were found depending on the crop: forage and root vegetable crops showed high levels of progoitrin, whereas glucobrassicanapin was the main glucosinolate for oilseed and leafy crops.

Nutrient/Phytochemicals in Leaves, Inflorescences

Pre-flowering canola foliage or canola greens were found to possess nutritional quality that compared favourably with mustard and turnip

greens (Bhardwaj et al. 2003). The canola greens contained 89.10% water, 3.4% oil, 30.6% protein and ash 8.19% on a dry weight basis. Canola greens contained per 100 g dw: 0.52 g P, 4.14 g K, 0.35 g Mg, 1.59 g Ca, and 0.20 g Na 0.94 mg S, 2.22 mg B, 5.47 mg Zn, 14.65 mg Mn, 28.61 mg Fe, 0.74 mg Cu, and 321.92 mg Al. The oil in canola greens contained 18.79% saturated fatty acids, 14:0 (myristic acid) 2.48%, 16:0 (palmitic acid) 14.77%, 18:0 (stearic acid) 1.52%; 80.39% unsaturated fatty acids, 15.36% MUFA, 18:1 (oleic acid) 6.66%, 22:1 (erucic acid) 5.11%; 65.78% PUFA , 18:2 (linoleic acid) 13.85%, and 18:3 (linolenic acid) 43.78.

Some of the flavonoids identified in nabicol (*B. napus*) leaves included K-3-*O*-sophoroside-7-*O*-glucoside; K-3,7-di-*O*-glucoside; K-3-*O*-(caffeoyl)sophoroside-7-*O*-glucoside; K-3-*O*-(methoxycaffeoyl)sophoroside-7-*O*-glucoside; K-3-*O*-(sinapoyl)-sophoroside-7-*O*-glucoside; K-3-*O*-(feruloyl)-sophoroside-7-*O*-glucoside; K-3-*O*-(*p*-coumaroyl)-sophoroside-7-*O*glucoside; K-3-*O*-(methoxycaffeoyl)-sophoroside; K-3-*O*-(sinapoyl)-sophoroside; K-3-*O*-(feruloyl)-sophoroside (Velasco et al. 2011). Among the 8 hydroxycinnamic acids identified namely: 3-caffeoyl quinic acid; 3-*p*-coumaroyl quinic acid; sinapylglucoside; ferulic acid; sinapic acid; 1,2-disinapoylgentiobiose; 1-sinapoyl-2-feruloyl-gentiobiose; 1,2,2′-trisinapoylgentiobiose and 1, 2′-disinapoyl-2-feruloylgentiobiose; sinapic acid was the most abundant.

In oilseed rape plants subjected to cold and then to freezing treatments, the levels of soluble *p*-coumaric, sinapic and ferulic acids increased about three-, four- and fivefold, respectively. The level of caffeic acid practically did not change in the leaves but it increased by about 70% after the frost-thaw treatment (Solecka et al. 1999). Acclimation of plants in cold and the frost-thaw treatment resulted in the promotion of phenolic esterification.

Separate headspace samplings of *Brassica napus* flowers and leaves in-situ showed that 6 volatiles were emitted from the flowers only, 12 compounds were common to both flowers and leaves, and 11 compounds were emitted from the leaves only (Jakobsen et al. 1994). Floral rhythmic emission was shown for sabinene and limonene, both emitted from flowers and leaves. In contrast, no rhythm of emission was detected for the major compounds emitted from the flowers only, i.e. α-farnesene, linalool and 3-carene. During flowering of *B. napus* along with intensive radiation and high temperatures, a higher production and emission of biogenic volatile organic (VOC) compounds was observed (Müller et al. 2002). The emissions of terpenes and high concentrations of organic carbonyl compounds were observed. Limonene, α-thujene and sabinene were the most important compounds (about 60% of total terpenes). The detected carbonyl compound concentrations were unexpectedly high (maximum formaldehyde concentration was 18.1 ppbv (parts per billion by volume) and 3.4 ppbv for butyraldehyde) for an open field.

Compared to “tronchuda” cabbage (*Brassica oleraceae* L. var. *costata*), the inflorescence of rape (*Brassica napus* L. var. *napus*) had higher contents of ash, carbohydrates, sugars (including fructose, glucose, sucrose and raffinose), essential n-3 fatty acid α-linolenic acid, and the best ratios of PUFA/SFA and n-6/n-3 fatty acids, tocopherols, lycopene, chlorophylls, phenolics, flavonoids, and also the highest antioxidant properties (Batista et al. 2011). Both are nutritionally well-balanced traditional cultivated vegetables highly consumed among Northern Portuguese regions.

Twenty-two volatile compounds were identified as being emitted during the flowering period of oilseed rape (Butcher et al. 1994). The main constituents were α-farnesene (a sesquiterpene); β-myrcene (a monoterpene); linalool (a monoterpene alcohol) and the ‘green leaf’ volatile (E)-3-hexen-1-ol acetate. These compounds constituted between 50 and 87% (mean 68%) of the total volatiles emitted in all of the entrainments carried out with flowering oilseed rape plants. The remaining constituents consisted of a range of compounds including other terpenoids, the characteristic ‘green leaf’ volatile (E)-3-hexen-1-ol, short chain alcohols and ketones, organic sulphides and nitrogen-containing compounds. These were generally present as minor constituents but some plant entrainments revealed that higher relative amounts could be emitted as was particularly

apparent for dimethyl disulphide, 3-methyl-2-pentanone, 3-hydroxy-2-butanone, sabinene, isomyrcenol and (E)-3-hexen-1-ol.

The profile of volatile chemicals emitted by flowering oilseed rape confirmed field emissions to be broadly similar to those found previously in laboratory studies (McEwan and Macfarlane Smith 1998). The major constituents identified were the monoterpenes limonene, sabinene, β-myrcene, and *cis*-3-hexen-l-ol acetate, a 'green leaf' volatile. The minor constituents included monoterpenes, sesquiterpenes, short chain aldehydes and ketones, other 'green leaf' volatiles and organic sulphides including the respiratory irritant, dimethyl disulphide.

Antioxidant Activity

No significant differences in plasma malondialdehyde or conjugated diene concentrations were found in 59 subjects fed a rapeseed oil-based diet rich in monounsaturated fatty acids (MUFA) and a sunflower oil-based diet rich in polyunsaturated fatty acids (PUFA) in a cross-over fashion for three and a half weeks (Turpeinen et al. 1995). Plasma alpha-tocopherol significantly increased from 4.8 to 6.4 mg/L following the canola oil diet and no changes were noted after the sunflower oil diet. In a second study, small but significant decrease in both lipid hydroperoxides and TBARS was observed in the LDL fraction after the sunflower oil diet. The in-vitro oxidation gave opposite results, showing increased oxidation after the sunflower oil diet. The results suggested that moderate changes in the fatty acid composition of a Western style diet may be adequate to affect lipoprotein susceptibility to oxidation in vitro. However, the authors concluded that results from lipid peroxidation studies must be viewed with caution as there appeared to be disparity with some measurements of in-vivo lipid peroxidation.

Kozlowska et al. (1990) tested the phenolic constituents isolated from the polar fraction of rapeseed oil for antioxidative activity in various lipid oxidation models. The amount of phenols was greatest in the post-expelled crude rapeseed oil, decreasing with an increasing degree of refining. The polar phenol content correlated with oxidative stability. The most active antioxidant component of the polar fraction was identified as vinylsyringol, a decarboxylation product of sinapic acid. It was abundant in the post-expelled crude oils and apparently responsible for their high phenol content and oxidative stability. Some vinylsyringol was present in the super degummed oil but not in the fully refined oils. The cold-pressed low erucic acid rapeseed oils were more easily oxidized, partly attributed to their higher contents of polyunsaturated fatty acids (Koski et al. 2002). The rapeseed oils were rich in γ-tocopherol and had low initial peroxide values (PVs), but their hydrophilic phenol content was low, only 3–4 ppm. Lutein and β-carotene were found in the oil. The extracts obtained from the rapeseed oils had either moderate or no antioxidative effect in methyl linoleate. Testing of the extracts for their 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity yielded similar results. It was conclude that phenolic compounds contributed significantly to the oxidative stability of cold-pressed oils.

Wakamatsu et al. (2005) isolated a highly potent alkylperoxyl radicals (ROO*) scavenger designated canolol, from crude canola oil (rapeseed). Its chemical structure was identified as 4-vinyl-2,6-dimethoxyphenol. The canolol content of crude canola oil increased appreciably after the seed was roasted as compared with that from unroasted seed, but it decreased in highly purified oil. This anti-ROO* activity was highest in crude oil, deceased after each refining step, and was lowest in highly purified refined oil. Canolol was thus generated during roasting. ROO* are biochemically reactive and damage nucleic acids and proteins, thereby harming living cells. The potency of canolol was much greater than that of well-known antioxidants, including alpha-tocopherol, vitamin C, β-carotene, rutin, and quercetin. Studies found that α-tocopherol significantly lowered peroxide values and headspace oxygen consumption of canola oil under singlet oxygen, and its antioxidant activity was increased by the co-presence of phosphatidylcholine (PC) or phosphatidylethanolamine (PE) (Lee and Cho 2011).

PC and PE increased chemical quenching of singlet oxygen by tocopherol in decreasing the oil oxidation.

The presence of *Arabidopsis* regulatory gene Production of Anthocyanin Pigment 1 (AtPAP1) in *Brassica napus* (canola) enhanced the antioxidant capacity in transgenic leaves up to four fold (Li et al. 2010). They identified derivatives of quercetin, kaempferol, sinapic acid, cyanidin and pelargonidin and also found that all of them, except for the kaempferol derivatives were dramatically increased in the leaves of transgenic plants as compared to the non-transgenic controls. Transgenic plants had intense purple coloration, cyanidin and pelargonidin levels were enhanced 50-fold, and quercetin and sinapic acid were 5-fold higher.

Hypocholesterolemic/Antihyperlipidemic Activity

Animal Studies

Compared to rats fed a cholesterol-rich diet or standard balanced diet, rats fed a canola oil diet (rich in n-3 fatty acid) had smallest cardiac weight and greatest numerical density of the myocytes (Aguila et al. 1998; Aguila and Mandarim-de-Lacerda 1999). The aorta and artery pulmonary internal diameters were smaller in the cholesterol diet group. The HDL-C serum was about 40% greater in canola oil group. The length density of blood vessels was greater in the canola oil group than in the other groups. The cross sectional area of myocyte and cross sectional area of vessels were greater in group cholesterol group and smaller in the canola oil group suggesting that the canola oil diet (n-3 fatty acid rich) rats preserved the myocardium more than the standard and cholesterol-rich diets. Bell et al. (1997) found that mice fed the low fat or canola oil diet had lower body weight and significantly less body fat than the non-exercising mice fed beef fat. Voluntary exercise did not affect lean body mass but did result in significantly lower body fat in all diet groups. The amount of body fat of mice fed the monounsaturated canola oil was significantly less than that of mice fed the beef fat diet, suggesting that the type of fat as well as the amount of fat influences body fat stores. Also, voluntary exercise decreased body fat in all mice and prevented diet-induced obesity in mice fed diets high in fat.

Clinical Studies

McDonald et al. (1989) found in an 18-day study of normolipidemic men that canola and sunflower oil diets produced similar significant decreases in plasma total cholesterol (20 and 15%, respectively) and LDL-C (25 and 21%, respectively). Plasma HDL-C, VLDL-C and triglyceride concentrations were not altered by either fat source. Bleeding times were significantly longer following both diets in comparison to the mixed fat diet. However, in-vivo 6-keto-PGF1 production and the stable blood metabolite of the anti-thrombotic eicosanoid prostacyclin, was significantly greater only following the canola diet. Mean levels of the pro-thrombotic eicosanoid, thromboxane B2, decreased following both diets and mean systolic blood pressure was also lower. The hypocholesterolemic and antithrombotic effects of the canola diet were equivalent to those of the sunflower diet. In a randomized, blind study of 16 men, safflower- or canola-oil–oil-based diets reduced serum total cholesterol 9–15%, low-density-lipoprotein (LDL)-cholesterol 12–20% and apolipoprotein B-100 21–24% compared with baseline (Wardlaw et al. 1991). There were no significant changes from baseline to the end of the study in serum triglycerides, total high-density-lipoprotein (HDL) cholesterol, HDL3 cholesterol, HDL2 cholesterol, or apolipoprotein A-I.

In a 4-month study of 36 hypercholesterolemic and/or hypertriglyceridemic subjects, canola-oil based diet was found to decrease serum low-density-lipoprotein cholesterol (LDL-C) decreased from 173 to 160 mg/dL (Bierenbaum et al. 1991). Blood pressure, total cholesterol, and high-density-lipoprotein cholesterol (HDL-C) did not change significantly even though the HDL subfractions did, HDL2 decreasing and HDL3 increasing. In another randomised blinded crossover design study of 30 women and 29 men, Valsta et al. (1992) compared the effects a diet

rich in high oleic and low erucic acid monounsaturated rapeseed oil (total energy content of fat, 38%; saturates, 12.4%; monounsaturates, 16%; n-6 polyunsaturates, 6%; and n-3 polyunsaturates, 2%) and one rich in polyunsaturated sunflower oil (total energy content of fat, 38%; saturates, 12.7%; monounsaturates, 10%; n-6 polyunsaturates, 13%; and n-3 polyunsaturates, 0%). Both test diets reduced serum total cholesterol (TC) and low density lipoprotein (LDL) cholesterol levels from baseline, the monounsaturated rapeseed oil diet more than the polyunsaturated sunflower oil diet. Very low density lipoprotein (VLDL) cholesterol and total, VLDL, and LDL triglyceride levels were lower during the sunflower oil diet compared with the rapeseed oil diet. Total high density lipoprotein (HDL) cholesterol levels remained unchanged by both diets. The consumption of rapeseed oil resulted in a more favourable HDL2 to LDL cholesterol ratio and an apolipoprotein A-I to B ratio than did the sunflower oil.

Seppänen-Laakso et al. (1992) studied the effects of zero-erucic acid rapeseed oil and rapeseed oil-containing margarine on plasma fatty acid composition and serum cholesterol were studied in 43 butter users. They found that reduction in saturated fatty acids elicited a significant increase in the proportion of n-3 and n-6 polyunsaturated fatty acids (PUFA) with the rapeseed oil diet, whereas rapeseed-margarine caused a significant rise in n-6 PUFA only. When butter was replaced by rapeseed oil, low-density-lipoprotein-cholesterol decreased by an average of 9.1% without a reduction in high-density-lipoprotein-cholesterol. During rapeseed-margarine substitution the mean reduction was 5.2%. Of the plasma phospholipids, alpha-linolenic acid and the linoleic:stearic acid ratio, but not oleic acid, were the components most significantly correlated with serum cholesterol levels or the decrease in these levels. Their results showed that rapeseed oil could act primarily as a source of essential fatty acids, rather than that of monoenes, in the diet of butter users.

Lichtenstein et al. (1993) compared the effects of canola, corn, and olive oils on fasting and postprandial plasma lipoproteins in humans as part of a National Cholesterol Education Program Step 2 diet in a 32-day randomized, double-blinded study of 15 male and female subjects (mean age 61 years). Plasma cholesterol concentrations declined after consumption of diets enriched in all the test oils; however, the declines were significantly greater for the canola (12%) and corn (13%) than for the olive (7%) oil-enriched diet. Mean plasma LDL-C concentrations declined after consumption of diets enriched in all the test oils (16, 17, and 13% for canola, corn, and olive oil, respectively), and the magnitude of the declines was statistically indistinguishable among the test oils. Mean plasma high-density lipoprotein cholesterol (HDL-C) concentrations declined after consumption of the baseline diet, and these declines were significant for the canola (7%) and corn (9%) oil-enriched diets. Changes in LDL apolipoprotein (apo)B concentrations paralleled those of LDL-C. Switching from the baseline to the vegetable oil-enriched diets had no significant effect on plasma triglyceride, apoA-I, and lipoprotein(a) concentrations or the total cholesterol to HDL-C ratio. LDL apoB to apoA-I ratios were significantly reduced when the subjects consumed the vegetable oil-enriched diets.

In a 3-week randomised controlled study of 95 subjects with moderate hyperlipoproteinemia, total serum, low-density- and high-density-lipoprotein cholesterol concentrations decreased by 15, 16, and 11%, respectively, on the rapeseed oil diet and by 16, 14, and 13% on the sunflower oil diet (Gustafsson et al. 1994). Serum triglycerides decreased more significantly (by 29%) on the sunflower oil than on the rapeseed oil diet (14%). The n-3 fatty acids (20:5 and 22:5) in the serum phospholipids increased significantly on the rapeseed oil diet but decreased on the sunflower oil diet. There was an increase in the alpha-tocopherol concentrations after both diets. The findings indicated that low erucic acid rapeseed oil can replace oils and fats rich in polyunsaturated fatty acids in a lipid-lowering diet.

The replacement of margarine on bread by zero erucic acid rapeseed oil and olive oil accounted, on average, for 16% of the total fat and 7% of the total energy intake in 46 margarine users (Seppänen-Laakso et al. 1993). Fatty acid

analysis of total plasma indicated a dose-dependent rise in alpha-linolenic (alpha-LLA) and oleic acid (OA) levels during rapeseed and olive oil substitutions, respectively. Rapeseed oil substitution increased the proportion of eicosapentaenoic acid, an omega-3 fatty acid (0.4%-units, on average) in plasma phospholipids. A slight decrease in low-density lipoprotein cholesterol (LDL-C) and an increase in high-density lipoprotein cholesterol (HDL-C) generated a significantly higher HDL-C/total cholesterol (TC) ratio (1.9%-units). The results suggested a marked competitive effect for alpha-LLA, not only among plasma phospholipid fatty acids, but also in the relationships with serum lipids, since the changes in alpha-LLA, rather than in OA, governed the HDL-C/TC ratio. No competitive action of polyunsaturated acids comparable to rapeseed oil was found during olive oil substitution. Contrariwise to the rapeseed oil diet, the reduced proportion of linoleic acid (LA) in plasma phospholipids was not restored; this may be unfavourable if the habitual intake of LA were low. However, the effects on LDL-C levels were beneficial: the level decreased by 5.9%, correlating inversely with the increase in OA. Additionally, the HDL-C level remained unchanged during olive oil substitution.

Miettinen and Vanhanen (1994) found in a study of 18 male subjects (mean age 50) that dietary rapeseed oil mayonnaise reduced serum concentrations of total cholesterol, LDL cholesterol, and triglyceride concentrations by 9, 10 and 19%, respectively during a 6-week baseline period from initial values. HDL cholesterol concentrations increased by 9%. VDL cholesterol levels decreased. Addition of 1 g squalene in rapeseed oil for 9 weeks caused net increases in serum total, VLDL-, IDL-, and LDL-cholesterol concentrations by 12, 34, 28, and 12%, respectively; squalene by five times; and cholesterol precursor sterols by up to 60%. Faecal squalene was 15% of the dietary intake, cholesterol absorption was unchanged, faecal neutral sterols were significantly increased, whereas, in contrast to the precursor sterols, the increase in cholesterol synthesis was insignificant. LDL apolipoprotein B was increased by 14% with unchanged removal but enhanced transport of LDL apolipoprotein B. A negative correlation between the changes in LDL apolipoprotein B removal and LDL cholesterol suggested that LDL receptor activity was down-regulated, allowing more of the LDL precursor lipoproteins to be converted to LDL. A subsequent 6-week period on 0.5 g squalene/d normalized serum sterols.

Nydahl et al. (1994) conducted a randomised double-blind cross-over study for two 3-week periods to compare the effects of rapeseed oil and sunflower oil, enriching a normal diet, on the lipoprotein and fatty acid composition in healthy 101 subjects(mean age 29.2 years). They found that in both treatment periods the serum cholesterol (−4%), LDL cholesterol (−5 to −7%) and apolipoprotein B (−5%) concentrations decreased significantly and to the same extent, while serum triglycerides, HDL cholesterol, apolipoprotein A-1 and lipoprotein (a) remained virtually unchanged. The content of 18:2 n-6 serum phospholipids was increased after the sunflower oil-enriched diet, and the contents of oleic acid (18:1 n-9), alpha-linolenic acid (18:3 n-3), and eicosapentaenoic acid (20:5 n-3) were increased after the rapeseed oil-enriched diet. The concentration of alpha-tocopherol increased and gamma-tocopherol decreased after the sunflower oil-enriched diet, less so after the rapeseed oil-enriched diet. They concluded that substitution of mono- and polyunsaturated fats for saturated fats without any other dietary changes caused a significant improvement of the lipoprotein profile in healthy subjects. The rapeseed oil and sunflower oil fats were equally effective in this respect. In a cross-over study comprising two consecutive 3.5-week treatment periods of 22 hyperlipidemic patients, both low erucic rapeseed (canola) oil or olive oil reduced total serum cholesterol, low-density lipoprotein low-density/high-density lipoprotein cholesterol ratio, apolipoproteins B, A-I and Lp(a) to the same extent (Nydahl et al. 1995). However, there was a slightly greater decrease in low-density lipoprotein cholesterol with the diet containing rapeseed oil (−17%) than with the olive oil diet (−13%). The intravenous glucose tolerance improved to a similar extent on both diets.

In a double-blinded randomized cross-over study (3-week intervention period) of 18 young, healthy men, consumption of rapeseed oil and sunflower oil had more favourable effects on blood lipids and plasma apolipoproteins as well as on the number and lipid content of LDL subfractions compared with olive oil (Pedersen et al. 2000). Some of the differences may be attributed to differences in the squalene and phytosterol contents of the oils. In a double blind randomized cross over study of 18 healthy males, aged 20–28 years, consumption of rapeseed oil and sunflower oil diets lowered postprandial cholesterol and triacylglycerol concentrations compared with olive oil, while rapeseed oil and olive oil diets resulted in similar and lower in-vitro susceptibility to oxidation of lipoproteins than sunflower oil (Nielsen et al. 2002). In a study of 17 children and adolescents with familial hypercholesterolemia, rapeseed oil diet for 5 months decreased serum triglycerides by 29%, VLDL-cholesterol by 27%, LDL-cholesterol by 7% compared to classical cholesterol reduction diets (step I) (Gulesserian and Widhalm 2002). HDL-cholesterol and lipoprotein a Lp (a) were not changed significantly.

In an open and balanced crossover study of 37 men, compared to butter, administration of cold-pressed turnip rapeseed oil (CPTRO) was followed by a reduction of total cholesterol by 8% and LDL cholesterol by 11% (Palomäki et al. 2010). The level of oxidized LDL was 16% lower after oil period. Minimal differences in arterial elasticity were not statistically significant. The cold-pressed turnip rapeseed oil (CPTRO) had favourable effects on circulating LDL cholesterol and oxidized LDL, which may be important in the management of patients at high cardiovascular risk. In a randomised cross-over study of 28 men and women with mean levels of total and low density lipoprotein cholesterol of 6.0, and 4.1 mmol/L, respectively and a mean body mass index (BMI) of 26.9 kg/m^2, a 30 g serving of nuts, or a serving of a Canola oil enriched cereal with a similar fatty acid composition reduced total and LDL cholesterol to a similar extent when consumed as part of a lipid lowering diet (Chisholm et al. 2005). The results suggested that foods with a similar fatty acid composition to nuts can produce comparable decreases in lipoprotein mediated cardiovascular risk.

Studies in 15 volunteers showed that palm oil and partially hydrogenated soybean oils, compared with soybean and canola oils, adversely altered the lipoprotein profile in moderately hyperlipidemic subjects without significantly affecting HDL intravascular processing markers (Vega-López et al. 2006). Partially hydrogenated soybean and palm oils resulted in higher LDL-cholesterol concentrations than did soybean (12 and 14%) and canola (16 and 18%) oils. Apolipoprotein B and A-I concentrations mirrored the pattern of LDL- and HDL-cholesterol concentrations, respectively. No significant effect on the total-to-HDL cholesterol ratio was observed for palm oil compared with the other dietary fats. HDL3 cholesterol was higher after palm oil than after partially hydrogenated and soybean oils. A 6-week randomized, crossover study found that phytosterols mixed within a medium-chain triglycerides- and high-oleic canola-rich matrix lowered total cholesterol, plasma LDL-C, without significantly changing the high-density lipoprotein cholesterol concentrations, in hyperlipidemic, overweight men, and may therefore decrease the risk of cardiovascular events (Rudkowska et al. 2006).

In a 2 × 3-week randomized, controlled, crossover trial of 20 free-living hyperlipidemic subjects, replacing a diet rich in saturated fat from dairy foods (DF diet) with a rapeseed oil diet rich unsaturated fatty acids 18:1n-9, 18:2n-6 and 18:3n-3, caused a rapid and clinically relevant improvement in serum lipoprotein profile including lowering of triglycerides (Iggman et al. 2011). The rapeseed oil diet, but not the dairy food diet, reduced the levels of serum cholesterol (−17%), triglycerides (−20%) and low-density lipoprotein cholesterol (−17%), cholesterol/high-density lipoprotein (HDL) cholesterol ratio (−21%), apolipoprotein (apo) B/apo A-I ratio (−4%) and factor VII coagulant activity (FVIIc) (−5%) from baseline. The rapeseed oil diet, but not the dairy food diet, modestly increased serum lipoprotein(a) (+6%) and tended to increase the glucose disappearance rate (K-value, +33%). HDL cholesterol, insulin sensitivity, fibrinogen

and tissue plasminogen activator inhibitor-1 levels did not change from baseline or differ between the two diets.

Gillingham et al. (2011) conducted a randomised, controlled, crossover trial, 36 hypercholesterolemic subjects consumed three isoenergetic diets for 28 days each containing approximately 36% energy from fat, of which 70% was provided by high-oleic canola oil (HOCO), canola oil blended with flaxseed oil (FXCO) or atypical Western diet (WD). They found after 28 days, compared with WD, LDL-cholesterol was reduced 15.1% with FXCO and 7.4% with HOCO. Total cholesterol was reduced 11% with FXCO and 3.5% with HOCO compared with WD. Endpoint total cholesterol differed between FXCO and HOCO. FXCO consumption reduced HDL-cholesterol by 8.5% and LDL:HDL ratio by 7.5% and E-selectin concentration compared to WD. They concluded that consumption of high-oleic canola oil alone or when blended with flaxseed oil was cardioprotective through lipid-lowering effects. The incorporation of flaxseed oil may also target inflammation by reducing plasma E-selectin.

Platelet Function Activity

In a study in rats, the (n-3) fatty acids (vegetable: corn, rapeseed; or fish: cod liver, maxepa) added in small amounts to a saturated fat diet (from 78 to 90%) over a period of several months induced drastic changes in platelet lipid metabolism and composition without comparable effects on platelet behaviour (Nordøy et al. 1985). In a crossover study of 20 healthy male subjects, average age 29 year (range 20–46 year), the effects of two diets rich in monounsaturated fatty acids differing in their linoleic/alpha-linolenic acid ratio on platelet aggregation were compared (Freese et al. 1994). Fatty acid compositions of the diets were as follows (saturated/monounsaturated/polyunsaturated fatty acids): low-erucic acid rapeseed oil (RO) diet 12.4/18.6/8.9% of total energy (en%) (linoleic/alpha-linolenic acid ratio 2.8) and high-oleic acid Trisun sunflower oil (TSO) diet 11.8/17.8/8.3 en% (linoleic/alpha-linolenic acid ratio 28), respectively. Plasma cholesterol ester fatty acid composition proved compliance to the experimental diets. Platelet aggregations induced by ADP (1, 2 and 3 μM) or thrombin (0.12, 0.15 and 0.18 NIH/mL) were significantly enhanced and collagen-(1.5, 2.5 and 5.0 μg/mL) induced aggregation tended to be enhanced after the TSO diet compared with the RO diet. The diets had no effect on antithrombin III activity. Results show that platelet aggregation in-vitro decreased as the ratio of linoleic acid to alpha-linolenic acid decreased in diets rich in monounsaturated fatty acids.

In a study of 30 healthy male subjects who ate a controlled-saturated-fatty-acid (baseline) diet for 3 weeks and then consumed either safflower oil or canola oil as a major fat source for 8 weeks, a 35% decrease in arachidonic acid was observed in platelet phospholipids of the canola-oil diet group while long chain n-3 fatty acids rose 7–26% compared with baseline (Kwon et al. 1991). Compared with baseline both unsaturated-fatty-acid diets reduced platelet aggregation at 3 week of oil-based diet feeding whereas only canola oil influenced platelet function (lowered ATP secretion) at 8 week. No significant difference was observed in thromboxane B2 concentrations between oil-treatment groups at 8 week. Both oil-based diets had short-term beneficial effects on platelet function but the effect of canola oil persisted longer. In a highly controlled, blind crossover design study of 26 healthy men (average age 28 years, range 18–60), Mutanen et al. (1992) found that rapeseed and sunflower oil diets enhance platelet in-vitro aggregation and thromboxane production in healthy men when compared with milk fat or habitual diets. Their findings conflicted with a number of other studies in which consuming vegetable oils were found to be anti-thrombotic.

In a 6-week, parallel design study of 42 volunteers (35 women, 7 men, 16–62 years) (Seppänen-Laakso et al. 2010) found that elevated plasma fibrinogen caused by inadequate alpha-linolenic acid intake could be reduced by replacing fat with canola-type rapeseed oil. The intake of alpha-linolenic acid (alpha-LLA) was doubled. Efficient competitive

inhibition by alpha-LLA was seen as a decrease in long-chain n-6 PUFA at 3 weeks. Elevated fibrinogen (2.6–3.9 g/L) decreased by 0.95 g/L at 6 weeks. Docosahexaenoic acid (22:6n-3) in plasma phospholipids increased at low fibrinogen levels only. Elevated fibrinogen levels (that is, a protein that promotes blood clotting) would be associated with an increased risk of heart attack.

Cardioprotective Activity

Studies suggested consumption of canola oil, a major dietary source of oleic acid additionally containing the (n-3) polyunsaturated fatty acid alpha-linolenic acid [18:3(n-3)], could reduce vulnerability to cardiac arrhythmia in rats (McLennan and Dallimore 1995). Incidence of ventricular fibrillation, mortality and arrhythmia score during reperfusion were significantly lower in rats fed the diet containing canola oil than in those fed the olive oil diet. No difference in the severity of arrhythmias was seen in groups fed diets containing soybean or sunflower seed oils. Analysis of myocardial phospholipid fatty acids showed that consumption of canola oil decreased the ratio of (n-6)/(n-3) polyunsaturated fatty acids relative to the other diets. The results suggested that regular substitution of canola oil for other dietary lipid sources may assist in reducing the likelihood of a transient ischemic event leading to life-threatening cardiac arrhythmias, but the effectiveness of alpha-linolenic acid is reduced by high levels of linoleic acid. Fuhrman et al. (2007) found that supplementation of mice diet with a novel dietary formula (PS-CO) of plant sterol esters of fatty acids, produced by enzymatic interesterification of plant sterols with canola oil (CO), in a CO matrix containing 1,3-diacylglycerol was beneficial in reducing serum lipid levels, and serum and macrophage oxidative stress, thus contributing to the reduction in atherogenic risk factors.

Lemaitre et al. (2003) investigated the association of the dietary intake of n-3 polyunsaturated fatty acids, i.e., docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) from fatty fish and alpha-linolenic acid (ALA) from vegetable oils, with ischemic heart disease among older adults. They conducted a case–control study nested in the Cardiovascular Health Study, with a cohort study of adults aged > or = 65 years comprising 54 incident fatal myocardial infarction and other ischemic heart disease death, 125 incident nonfatal myocardial infarction and 179 randomly selected matched controls. They found a higher concentration of combined DHA and EPA was associated with a lower risk of fatal ischemic heart disease, and a higher concentration of alpha-linolenic acid with a tendency to lower risk, after adjustment for risk factors (odds ratio: 0.32 and 0.52 respectively). In contrast, n-3 polyunsaturated fatty acids were not associated with nonfatal myocardial infarction. The association of n-3 polyunsaturated fatty acids with fatal ischemic heart disease, but not with nonfatal myocardial infarction, was consistent with possible antiarrhythmic properties of these fatty acids.

Epidemiological studies and dietary trials in humans suggest that alpha-linolenic acid is a major cardio-protective nutrient (de Lorgeril and Salen 2004). Like other n-3 fatty acids from marine origin, it may prevent cardiac arrhythmias and sudden cardiac death. The optimal dietary intake of alpha-linolenic acid appear to be about 2 g per day or 0.6 to 1% of total energy intake. Obtaining an optimal ratio of the two essential fatty acids, linoleic and alpha-linolenic acids that is a ratio of <4–1 in the diet-is a major issue. The main sources of alpha-linolenic acid for the European population should be canola oil (and canola-oil based margarine if available), nuts (English walnut), ground linseeds and green leafy vegetables such as purslane.

In a randomised study of 40 patients with peripheral arterial occlusive disease, canola diet supplementation was found to lower LDL-cholesterol and improve endothelial function (Stricker et al. 2008). Heart rate variability and plasmatic coagulation, fibrinolysis, platelet activation, inflammation, and lipid and homocysteine levels did not change.

Hypotensive Functional Food Activity

Wu et al. (2009) found that Alcalase 2.4 L and protease M "Amano" were the most efficient enzymes in releasing angiotensin I-converting (ACE)-inhibitory peptides from defatted canola meal among 13 tested enzymes. The IC_{50} values of canola protein hydrolysates ranged from 18.1 to 82.5 μg protein/mL. Ion-exchange chromatography of canola protein hydrolysate increased the protein content greater than 95% without loss of ACE-inhibitory activity. This fraction was resistant to the degradation of gastrointestinal enzyme and ACE during in-vitro incubation and may be a useful ingredient in the formulation of hypotensive functional food products.

Animal studies by Begg et al. (2010) showed that different sources of alpha-linolenic acid (canola oil or flaxseed oil) were effective in preventing hypertension related to omega-3 fatty acid deficiency. However, there were other marked differences between the omega-3 fatty acid deficient (DEF) animals and, in particular, the weaned rats fed 10% canola oil-(SUF-C) rich in omega-3 fatty acids had lower body weight, adiposity, leptin and food intake. Animals fed 7% safflower oil + 3% flaxseed oil containing omega-3 fatty acids (SUF-F) also had lower, but less marked reductions in adiposity and leptin compared with DEF animals. The differences observed between DEF, SUF-F and SUF-C phenotypes indicated that body fat and leptin may be involved in omega-3 fatty acid deficiency hypertension.

Using data on infant weight and length gain from a prospective randomized double-blind trial in full-term infants in the German Infant Nutritional Intervention study (GINI), Rzehak et al. (2011) found that absolute and standardized weight and length measures did not differ between the formula groups with or without canola oil. This was true for both, analyses within each of the three anthropometric measurement periods (4–6 weeks, 3–4 months, 6–7 months) and for the longitudinal analyses over the whole period from 4 weeks to 7 months of life. Power analyses confirmed that sample size was sufficient to detect a difference of 3 g per day between 14 and 120 days between the two formula groups. They concluded that infant formula containing canola oil supported normal infant growth as assessed by weight and length gain.

Renoprotective Activity

Usual blood pressure increase, glomerulosclerosis, glomerular enlargement, and glomeruli loss in spontaneously hypertensive rats was prevented by long term administration of fish, canola and palm oils or attenuated by olive and soybean oils (Aguila et al. 2005). The most favourable effect was observed for the fish oil administration (source of n-3 polyunsaturated fatty acids, PUFA, eicosapentaenoic and docosahexaenoic acids), followed by both canola and palm oils (source of n-3 PUFA plus n-9 monounsaturated, MUFA, and saturated fatty acid, respectively), and finally by both olive and soybean oils (source of n-9 MUFA and n-6 PUFA, respectively).

In a 30 week study, administration of high n-3 PUFA canola diet to streptozotocin-induced diabetic Sprague-Dawley rats (D + canola) significantly decreased diabetes-associated increases in urine albumin excretion (non diabetic (ND) 17.8; diabetic (D) 97.3; D + canola 8.3 mg/day); systolic blood pressure (ND 153; D 198 ; D + canola 162 mmHg); glomerulosclerosis (ND 0.6; D 1.8; D + canola 0.8 AU); and tubulointerstitial fibrosis in the renal cortex (ND 1.2; D 2.0; D + canola 1.1) and the inner stripe of the outer medulla (ND 1.0; D 2.1 2; D + canola 1.1 AU) (Garman et al. 2009). Diabetic rats fed a high n-6 (omega-6) PUFA corn diet (D + corn), also exerted renoprotection, but not to the same degree as D + canola (urine albumin excretion, D + corn 33.8 mg/day; systolic blood pressure, D + corn 177 mmHg; glomerulosclerosis, D + corn 1.2 AU; cortical tubulointerstitial fibrosis, D + corn 1.6 AU; medullary tubulointerstitial fibrosis, D + corn 1.5 AU). In addition, D + canola attenuated diabetic-associated increase in collagen type I and type IV, IL-6, MCP-1(monocyte chemotactic protein-1), transforming growth factor-beta, and CD68 expression. These observations indicated a beneficial effect of high

dietary intake of n-3 PUFA canola in reducing diabetic renal disease.

Canola Oil and Omega-3 and Omega-6 Fatty Acids

Animal Studies

Results from a long-term feeding study of Sprague-Dawley rats showed that a diet containing transgenically modified canola oil was well-tolerated, and had similar biological effects, i.e., growth characteristics and hepatic metabolism of n-6 fatty acids, as a diet containing borage oil (BO) (Palombo et al. 2000). There were no adverse effects of either diet on the general health or appearance of the rats, or on the morphology of the major organs. There was no significant difference between the diet groups for total percentage of n-6 polyunsaturated fatty acids present in either the total or individual phospholipid fractions of liver or plasma. The relative percentage of gamma-linolenic acid and its main metabolite, arachidonic acid, in each phospholipid fraction of liver or plasma were also similar between groups. The percentage of 18:2n-6 in liver phosphatidylethanolamine and phosphatidylinositol/serine was higher and 22:5n-6 was lower in the high GLA canola oil (HGCO) group than the borage group. In another long-term (12-week) rat feeding study, diets containing up to 15% HGCO resulted in no adverse effects on growth, organ weight, haematology and serum biochemistry as compared to the diet containing 15% BO (Liu et al. 2004). Lower final body weights and higher tissue levels of GLA, dihomo-gamma-linolenic acid (20:3n-6) and arachidonic acid (20:4n-6) were found in the 15% HGCO dietary group as compared with the 15% BO dietary group suggesting that HGCO may be a safe alternative.

Tso et al. (2002) reported the development of a new canola strain capable of producing >30% gamma-linolenic acid [GLA, 18:3(n-6)] in the seed oil. Their study showed that the digestion, uptake and lymphatic transport of this high GLA content canola oil (HGCO) and the normal physiologic changes associated with fat absorption were similar in the HGCO-and GLA-rich borage oil-fed Sprague Dawley rats, indicating that HGCO was absorbed and transported into lymph similarly to borage oil (BO). In a subsequent study they compared the effects of borage oil (BO: 23% GLA), HGCO diluted to 23% GLA (GLA-23) with those of undiluted HGCO containing 36% GLA (GLA-36) on reproduction, pup development, and pup brain fatty acid composition in mice (Wainwright et al. 2003). Their findings showed that despite equivalent levels of GLA, GLA-23 differed from BO in that it reduced pup body weight and was associated with a slight increase in neonatal pup attrition, but there were no significant effects on pup behavioral development or on performance in the plus maze. An increase in dietary GLA resulted in an increase in brain 20:4n-6 and 22:4n-6, with a corresponding decrease in 22:6n-3. Again, despite their similar levels of GLA, these effects tended to be larger in GLA-23 than in BO. In comparison with GLA-23, GLA-36 had larger effects on growth and brain fatty acid composition but no differences with respect to effects on reproduction and behavioral development. They concluded that the high gamma-linolenic acid-content canola oil could be used as an alternative source of gamma-linolenic acid.

Clinical Studies

A 42-day cross-over design study of canola oil versus sunflower oil diet in eight normolipidemic men found that consumption of canola oil diet resulted in higher n-3 fatty acid levels and lower n-6 fatty acid levels in plasma phospholipids than consumption of the sunflower oil diet (Corner et al. 1990). In another 18-day cross-over design study of volunteers, they found that consumption of canola oil containing linolenic acid (18:3n-3) moderately increased eicosapentaenoic acid (EPA) (20:5n-3) concentrations and altered the concentrations of other n-6 and n-3 fatty acids in human platelet phospholipids (Weaver et al. 1990). EPA and 22:5n-3 were significantly higher in alkenylacyl ethanolamine phosphoglyceride (PPE) and EPA in total phosphatidylcholine (PC) after canola consumption compared with mixed fat diet(Pre-exp) and sunflower-oil-based diet rich in linoleic acid

(18:2n-6). Lower concentrations of 20:4n-6 and 22:4n-6 were observed with canola in PC and lower concentrations of 22:4n-6 in PPE.

In a 2×6 weeks' randomized dietary intervention, blind cross-over design study 40 healthy unconfined women and men (age 20–46 years), were administered two fish restricted diets, namely low erucic acid rapeseed oil (RO) diet and Trisun-sunflower oil (TSO) diet, with similar proportions of saturated : monounsaturated : polyunsaturated fatty acids (11.5:17.5:8.5% of total energy, En%), but differing in their alpha-linolenic acid (ALA) content (2.2 and 0.3 En%) and n-6 : n-3-ratio (3 : 1 and 23 : 1, respectively) (Valsta et al. 1996). The proportion of triglycerides and cholesterol esters ALA decreased on the TSO diet (from 1.6 to 0.9% and from 0.9 to 0.4%, respectively) and increased on the RO diet (from 1.7 to 3.4% and from 0.9 to 1.3%, respectively) compared to the baseline level. The proportion of eicosapentaenoic acid (EPA) in all three plasma fractions decreased on the TSO diet but not on the RO diet. The proportions of docosa-hexaenoic acid (DHA) decreased on both experimental diets and there was no difference in cholesterol esters DHA between the diets. Phospholipid docosapentaenoic acid (DPA) and phospholipid DHA remained at a higher level on the RO diet compared to the TSO diet.

Egert et al. (2007) compare the effects of three rapeseed oil-rich diets, fortified with alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA) on low-density lipoprotein (LDL) fatty acid composition, ex-vivo LDL oxidizability and tocopherol requirement. They employed a randomised control parallel design study with three dietary groups of 48 healthy young subjects (13 males, 35 females) who completed the study. They found that the content of the three n-3 polyunsaturated fatty acid differentially increased in the LDL: on the ALA diet, the ALA content increased by 89%; on the EPA diet, the EPA content increased by 809%; and on the DHA diet, the DHA content increased by 200%. In addition, the EPA content also enhanced (without dietary intake) in the ALA group (+35%) and in the DHA group (+284%). In the context of a monounsaturated fatty acid-rich diet, ALA enrichment did not enhance LDL oxidizability, whereas the effects of EPA and DHA on ex-vivo LDL oxidation were inconsistent, possibly in part due to further changes in LDL fatty acid composition. Tocopherol concentrations in LDL decreased in the ALA group (−13.5%) and DHA group (−7.3%). Plasma contents of tocopherol equivalents significantly decreased in all three experimental groups (ALA group:−5.0%, EPA group:−5.7%, DHA group:−12.8%).

Using 24-h food recall data of adult participants aged > or = 20 years (n = 8,983) from the 1999–2002 National Health and Nutrition Examination Survey (NHANES) Johnson et al. (2007) calculate the effect of substituting canola oil for dietary corn, cottonseed, safflower, soybean, and vegetable oils described as "not further specified" and of canola oil-based margarine for other spreads at 25, 50, and 100% replacement levels. They found that substitution of canola oil and canola oil-based margarine for most other vegetable oils and spreads increases compliance with dietary recommendations for saturated fatty acid, monounsaturated fatty acid, and alpha-linolenic acid, but not for linoleic acid, among US adults.

Anticancer/Antimutagenic Activities

Hardman (2007) found that dietary canola oil suppressed growth of implanted MDA-MB 231 human breast tumours in nude mice. Compared to mice that consumed the corn oil containing diet, the mice that consumed the canola oil containing diet had significantly more eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) in both tumours and livers, and the mean tumour growth rate and cell proliferation in the tumour were significantly slower. In vivo, alpha linolenic acid (ALA, 18:3n-3) can be converted to EPA or DHA. About 25 days after diet change, mice that consumed the corn oil diet stopped gaining weight, whereas the mice that consumed the canola oil diet continued normal weight gain. Ion et al. (2010) found that maternal consumption of canola oil suppressed mammary gland tumori-

genesis in C3(1) TAg mice offspring. Compared to offspring of mothers fed the corn oil diet (CO/CO group), offspring of mothers fed the canola oil diet (CA/CO group) had significantly fewer mammary glands with tumours. At 130 days of age, the CA/CO group had significantly fewer tumours per mouse (multiplicity); the tumour incidence (fraction of mice with any tumour) and the total tumour weight (per mouse that developed tumour) was less than one half that of the CO/CO group. At 170 days of age, the total tumour weight per mouse was significantly less in the CA/CO group and if a tumour developed the rate of tumour growth rate was half that of CO/CO group. These results indicate that maternal consumption of canola oil was associated with delayed appearance of mammary gland tumours and slowed growth of the tumours that developed.

In in-vitro studies, human breast cancer T47D and MCF-7 cells treated with canola oil showed reduced cancer cell growth and increased expression of caspase-3 and p53 (Cho et al. 2010). Canola showed synergistic cancer cell growth inhibition effects with two chemotherapeutic drugs, tamoxifen and cerulenin. In a subsequent live animal experiment, female Sprague-Dawley rats with mammary tumours chemically induced by N-nitroso-N-methylurea fed canola oil diet had reduced tumour volumes and showed an increased survival rate as compared to corn oil-fed rats. The results suggested that canola oil may have inhibitory effects on breast cancer cell growth.

Wan et al. (2011) demonstrated that in human cervical carcinoma cell (Hela cells) BnRCH, the protein product from a novel gene isolated from *Brassica napus* with E3 ubiquitin-protein ligase activity, inhibited the cell growth of Hela cells and increased their sensitivity to the anti-cancer chemotherapeutic drug cisplatin. The inhibitory effect of BnRCH in Hela cells was attributed to G2 phase cell cycle arrest with the transcriptional up-regulation of p21 (waf1/cip1), rather than apoptosis. The data suggested BnRCH to have potential use in cancer therapy.

The detrimental glucosinolate progoitrin was reduced by 65%, and the beneficial glucosinolate glucoraphanin (a precursor of sulforaphane, a potent anti-carcinogen) was increased to a relatively high concentration (42.6 μmol/g) in seeds of *B. napus* transgenic plants through silencing of the GSL-ALK gene family using RNA interference (Liu et al. 2012). They demonstrated the potential application of the new germplasm with reduced detrimental glucosinolates and increased beneficial glucosinolates for producing improved brassica vegetables

Canolol was found to be one of the most potent antimutagenic compounds when *Salmonella typhimurium* TA102 was used in the modified Ames test (Kuwahara et al. 2004). Its potency was higher than that of flavonoids (e.g., rutin) and alpha-tocopherol and was equivalent to that of ebselen. Canolol suppressed the endogenous mutagen peroxynitrite ONOO(-)-induced bactericidal action. It also reduced intracellular oxidative stress and apoptosis in human cancer SW480 cells when used at a concentration below 20 μM under hydrogen peroxide induced oxidative stress. In addition, canolol suppressed plasmid DNA (pUC19) strand breakage induced by peroxynitrite, as revealed by agarose gel electrophoresis. Cao et al. (2008) indicated canolol to be effective for suppressing inflammation, gastric epithelial cell proliferation and gastric carcinogenesis in *Helicobacter pylori* -infected Mongolian gerbils. *H. pylori*-induced gastritis, 5′-bromo-2′-deoxyuridine (BrdU) labelling and scores for cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) immunohistochemistry were attenuated in the canolol-treated groups. Expression of inflammatory cytokines interleukin-1 beta (IL-1 beta), tumour necrosis factor-alpha (TNF-alpha), COX-2 and iNOS mRNA in the gastric mucosa, and serum 8-hydroxy-2′-deoxyguanosine (8-OHdG), anti-*H. pylori* IgG and gastrin levels were also significantly lower in canolol-treated groups. In addition, the incidence of gastric adenocarcinoma was drastically reduced in the *Helicobacter pylori* + MNU + canolol-treated group [15.0% (6/40)] compared to the control group. Interestingly, the viable *Helicobacter pylori* count was not changed by the canolol containing diet.

Animal studies showed that dietary canola oil may be chemopreventive for colon tumour development in Fischer rats; dietary canola oil significantly decreased colonic tumour incidence and tumour multiplicity as compared to dietary corn oil (Bhatia et al. 2011). Canola oil increased ω-3 fatty acid levels and decreasing COX-2 levels in the colon and serum compared to the corn oil group.

Immunomodulatory Activity

In a study of 41 trauma patients, aged 18–47 years, an experimental diet supplemented with arginine and canola oil, a source of omega-3 fatty acids, was found to be efficient in enhancing the function of the immune system (Mendez et al. 1996). Subjects fed this supplemented diet showed a return to normal immune function levels faster than those patients on the standard diet. Procoagulant activity (PCA) in patients on the experimental diet was normal after 6 days, however patients on the standard diet did not see a return in normal PCA until day 10. PGE2 production by monocytes was observed to increase in patients on the experimental diet and decrease in patients on the standard diet. The lymphocyte response level to mitogens was initially decreased in both groups of injured patients compared to the healthy control, but patients on the experimental diet achieved the same level of responsiveness as the healthy controls by day 8.

Anticlastogenic Activity

Evangelista et al. (2004) found that pretreatment with a single dose of olive, extra virgin olive and canola oils caused a statistically significant decrease in the total of chromosomal aberrations and abnormal metaphases induced by cisplatin when compared with the groups treated with cisplatin alone. The anticlastogenic effects observed in the pretreatment with olive, extra virgin olive and canola oils was ascribed to the oil contents, probably their antioxidant property.

Antimicrobial Activity

Among the phenolic compounds isolated from rapeseeds, phenolic acids, and especially sinapic acid exhibited the most active bactericidal activity (Nowak et al. 1992).

Effect on Bone Quality

Results of animal studies suggested that the amount and source of fat used in the diet after weaning increase body growth and fat depots and affect insulin resistance and, consequently, bone health (Costa et al. 2011). After 60 days feeding, weaning rats fed a high-fat diet containing soybean oil or a high-fat diet of canola oil showed more energy intake, body density growth and intra-abdominal fat mass. However, the soybean group had a higher area (200%) and a lower number (44%) of adipocytes, while the control-diet and canola groups did not differ. The serum concentrations of glucose and insulin and the insulin resistance index were significantly increased in the canola group (15, 56, and 78%, respectively) compared to the control group. Bone measurements of the soybean and canola groups showed a higher femur mass (25%) and a higher lumbar vertebrae mass (11%) and length (5%). Computed tomography analysis revealed more radio density in the proximal femoral epiphysis and lumbar vertebrae of canola group compared to the soybean and control groups. Costa et al. (2012) reported that after 60 days feeding, weaning rats fed canola oil diet showed the following: lower liver (−12%) and intra-abdominal fat mass (−19%) area of adipocyte (−60%), cholesterol (−33%), insulin (−22%), lower total body (−9%) and spine (−33%) bone mineral content and bone area (−7 and−24%, respectively), femur mass (−9%), width of the diaphysis (−6%), femur (−10%) and lumbar vertebrae bone mineral density (−9%), and radio density of femoral head (−8%). The lower intra-abdominal adiposity could have more beneficial effects in a short term, since it can be associated with a better insulin sensitivity and lipid profile, than the small reduction in femur and lumbar vertebra density.

Negative Effects

On the downside, concerns have been raised on the possible health risks of rapeseed oil/canola oil based on animal studies: growth retardation, myocardial lesions, myocardial lipidosis, decrease in platelet count and increase in platelet size, induction of vitamin E deficiency, hypertension (high blood pressure), and shortening of life span (Hulan et al. 1977; Hung et al. 1977; Sauer et al. 1997; Innis and Dyer 1999; Naito et al. 2000a, b, c, d, 2003; Ohara et al. 2008, 2009; Okuyama et al. 2010; Papazzo et al. 2011). Also, recent animal studies had demonstrated that erucic acid (22:1n-9) had the ability to cross the blood brain barrier and enter the brain (Golovko and Murphy 2006). Erucic acid can negatively affect cell membrane structure and function, which is critical in nerve cells. Vles and Cottenbos (1989) stated that animal studies had shown that erucic acid in "large amounts retards growth and causes changes in various organs". The heart appears to be the principal target organ for toxic effects following short-term exposure to edible oils containing erucic acid (FSANZ 2003). The most common observed effect, among rats, pigs and monkeys, is myocardial lipidosis. Studies in rats and young pigs demonstrated a dose relationship between the level of erucic acid in the diet and severity of myocardial lipidosis. Increased myocardial lipidosis was reported with doses of erucic acid at 1,500 mg/kg bw/day in rats, although in nursling pigs this occurred at 900 mg/kg bw/day. In addition, other studies detected traces of other toxic substances not listed in the ingredients, but which were found in the oil as byproducts of the extensive processing. For example, a Florida study found up to 4.6% trans fats in commercial canola oil as a byproduct of the necessary deodorization processing of canola oil (O'Keefe et al. 1994). They measured the concentrations of trans isomers of 18:2w6 and 18:3w3 in soybean and canola oils purchased in the U. S. Isomers identified included 18:2ct, 18:2tc, 18:3tct + ctt, 18:3cct, 18:3ctc, and 18:3tcc. The degree of isomerizations of 18:2w6 and 18:3w3 ranged from 0.3 to 3.3% and 6.6 to 37.1%, respectively. The trans contents were between 0.56 and 4.2% of the total fatty acids.

Studies indicated that castration did not influence cardiac fatty acid composition in Sprague-Dawley rats (Hulan et al. 1977). The incidence of myocardial lesions in entire and castrated females and in castrated males was similar while significantly more entire males developed lesions. Rats fed a diet containing 20% *Brassica napus* var. Zephyr rapeseed oil showed a significantly higher incidence of heart lesions than did rats fed diets containing 5 or 20% corn oil. Similarly, significantly more rats fed the 20% corn oil diet had lesions than rats fed the 5% corn oil diet. The involvement of androgens in the formation of myocardial lesions was suggested, since castration significantly lowered the incidence in males but not in females. A much higher incidence of focal myocardial necrosis was found in animals receiving high-erucate rapeseed oil relative to animals given the corn oil (Hung et al. 1977). The incidence in rats fed diets containing very low-erucate rapeseed oil was intermediate between these latter two extremes. Triglyceride concentrations in the hearts of animals given the high-erucate oils were 7–12 times greater than all other groups. The level of triglycerides in the hearts of rats fed the very low-erucate oils was not significantly different from the corn oil group. The level of total fatty acids in tissue phospholipids was the same regardless of dietary treatment. High-erucate rapeseed oil gave growth rates which were significantly less than all other groups.

Sauer et al. (1997) reported that neonatal piglets raised on canola oil based milk replacer diets supplemented according to NRC regulations, and with an α-tocopherol (mg) to PUFA (g) ratio of 0.49:1, had low α-tocopherol levels in their tissues. The piglets exhibited signs of vitamin E deficiency which ranged from acute, with high mortality, to mild, with only microscopic evidence of hepatocyte dissociation. Piglets raised on a soybean oil based milk replacer diet, supplemented with the same amount of α-tocopherol, and with a ratio of α-tocopherol to PUFA of 0.21:1, showed no signs of vitamin E deficiency and had significantly higher tissue levels of

vitamin E than the piglets raised with the canola oil milk replacer.

Dietary canola oil was found to alter haematological indices and blood lipids in neonatal piglets fed formula (Innis and Dyer 1999). Piglets fed formulas with 100% canola oil had lower platelet counts than piglets fed formula soybean oil or the canola oil mimic. Platelet counts were lower, and platelet distribution width and volume were higher, when formulas with 100% canola or soybean rather than the blended oil formulas were fed. The results showed that formula fat composition influenced the developing haematological system and that canola oil suppressed the normal developmental increase in platelet count in piglets. In another study in stroke-prone spontaneously hypertensive rats (SHRSP), Naito et al. (2000c) found that after 4-week feeding, activated partial thromboplastin time in the canola oil group was significantly shorter than that in the soybean oil group, though there were no between-group differences in plasma Ca(2+), platelet density and platelet aggregation. Erythrocytes from the canola oil group were less tolerant to low osmotic pressure than those from soybean oil group. They concluded that the canola oil-induced shortening of blood coagulation time and increased fragility in erythrocyte membranes may have relevance to the promotion of strokes in SHRSP rats.

Studies demonstrated that canola oil intake as the only dietary fat elevated blood pressure of spontaneously hypertensive rats (SHR) and Wistar Kyoto (WKY) rats provided with drinking water containing 1% NaCl (Naito et al. 2000d). The elevation in blood pressure was mediated through mechanisms other than blunt dilating response of the blood vessel due to dysfunction of the endothelium or vascular smooth muscle, the augmented response to norepinephrine in the arteries and the increased amount of norepinephrine in the sympathetic nerve endings. The lesions in the heart and kidney in SHR rat observed may be related to a strain-specific peripheral vascular deterioration which was disclosed by the extremely high blood pressure in the canola oil group. In another study comparing dietary intake of rapeseed oil or soybean oil as the only dietary fat In WKY rats, they found that from week 5 of feeding, systolic blood pressure of the canola oil group became higher than that of the soybean oil group (Naito et al. 2000a). They postulated that the elevation in blood pressure may be mediated through an increase in body fluid via activation of Na(+) pump or Na(+), K(+)-ATPase and/or a blunt endothelium-dependent vasodilation by increased superoxide. The 13-week canola oil intake increased plasma levels of Na(+) and lipids, and decreased the level of K(+) compared to those in the soybean oil group. The canola oil group also exhibited a high density of neutrophils and a low density of platelets compared to the soybean oil group. The activities of catalase and superoxide dismutase in the hepatic cytosol were reduced in the canola oil group. The increased plasma lipids and the changes in the densities of platelets and neutrophils appeared not to be critical in WKY rats. However, these would tend to promote peripheral vascular lesions in spontaneously hypertensive rats and stroke-prone spontaneously hypertensive rats, prone to atheroscrelotic vascular injury. This was confirmed in another study where canola oil intake as the sole dietary fat for 4 weeks increased systolic blood pressure of stroke-prone spontaneously hypertensive rats (Naito et al. 2000b). The elevation in blood pressure was attributed to altered Na+, K+-ATPase activity. They found that changes in vascular responsiveness to vasoconstrictors and production of prostanoids were unlikely to have relevance to the elevation of blood pressure in SHR rats.

In another study with SHRSP rats they reported that after the 4-week administration, mean systolic blood pressure in the canola oil group and the soybean oil group were 233 and 223 mmHg, respectively (Naito et al. 2003). Phytosterol levels in both plasma and erythrocyte membranes reflected those contained in the oils ingested. Na(+), K(+)-ATPase activities in the brain, heart and kidney were enhanced in the canola oil group. They concluded that enhancement of hypertension-related deterioration in

organs was likely to have relevance to the short life span in the canola oil group and that enhanced Na(+), K(+)-ATPase activity by phytosterols in the oil ingested may play a role in these changes. In a 26-week dietary intake of rapeseed oil and soybean oil in SHR rats, they found that dietary canola oil induced hyperlipidemic condition, in which glucose-6-phosphate dehydrogenase (G6PD) may serve as an NADPH provider, and aggravates genetic diseases in SHR rats (Ohara et al. 2008). The increased cyclooxygenase-2 (COX-2) expression indicated a role of renin-angiotensin-aldosterone system activation in the increased vascular lesions, whereas the effects of oxidative stress remained unclear. In another 13 week study, WKY rats were used to avoid the difficulty in evaluating the results in SHRSP due to irregular deterioration in conditions by stroke (Ohara et al. 2009). They found that compared to a to a standard diet, both diets containing canola oil or ICOM (an interesterified canola oil mimic) similarly elevated blood pressure, increased plasma lipids, activated hepatic glucose-6-phosphate dehydrogenase, decreased platelets, shortened blood coagulation times and induced abnormalities in the kidney. Thus, canola oil specific fatty acid composition appeared to affect the pathophysiology of the rat and produce consequent aggravation of pathological status, especially in SHRSP rats. In a recent study of SHRSP rats they found that the testosterone levels in the serum and the testes were found to be significantly lower in the canola oil group than in the soybean oil group, while no significant differences were detected in the corticosterone and estradiol levels in tissues (Okuyama et al. 2010). They also found that that hydrogenated soybean oil, with a survival-shortening activity comparable to that of canola oil, also decreased the testosterone level in testes to a similar degree. They concluded that the testosterone-lowering activity of canola and hydrogenated soybean oil observed in SHRSP in relation to other causative factors may also possibly affect the physiology of SHRSP rats.

In a recent study on SHRSP rats, ingestion of canola oil for 25 days caused a reduction in antioxidant status and elevated plasma lipids, all risk factors for cardiovascular disease (Papazzo et al. 2011). However, canola oil in combination with salt intake increased malondialdehyde (MDA), a marker of lipid peroxidation and decreased LDL cholesterol level, NAPDH oxidase subunits and aortic superoxide dismutase gene expression.

Goitrogenic Effect

Glucosinolates in *Brassica* crops had been reported to have a deleterious effect on domesticated livestock (ruminants, swine, poultry) when consumed at high concentrations (Bell and Belzile 1965; Iwarsson et al. 1973; Fenwick et al. 1983; Griffiths et al. 1998). This was mainly attributable to the presence of presence of progoitrin, which accumulated in the seeds of oilseed rape (Griffiths et al. 1998). However, there is no evidence for any goitrogenic effect on humans from *Brassica* consumption (Mithen 2001). Commercial oil seed rape cultivars grown have been developed with low seed glucosinolate content (canola type) by breeding and selection (Rosa et al. 2010).

Allergy Problem

Pollen from oilseed rape (OSR), *Brassica napus* had been recognized as a potential cause of allergic sensitization. Focke et al. (1998) identified two low-molecular-weight allergens of 6/8 kD and 14 kD and a high molecular-weight cluster (27–69 kD) comprising six cross-reactive peptides. The three allergens were recognized by 50, 34 and 80% of patients, respectively. The identified allergens represented cross-reacting homologues of well-known pollen allergens, i.e. calcium-binding proteins, profilins, and high-molecular-weight glycoproteins. Via cross-reactivity, exposure to OSR pollen may be a prolonging and aggravating factor in underlying birch and grass pollen allergy. A polygalacturonase

(pectinase) was identified as a new rapeseed allergen (Chardin et al. 2003).

Traditional Medicinal Uses

The root is regarded as emollient and diuretic. The root extract has been used as a remedy for bronchial catarrh and chronic coughs. The pulverised seed with salt has been used to treat cancer. The powdered seed with camphor has been used to treat stiff joints and rheumatism and used as eardrop to relieve earache.

Other Uses

After oil is extracted from the seed, the remaining by-product, canola seed meal is used as a high protein (40%) animal feed. Canola seed meal is mainly used for cattle and to a lesser extent for pigs and poultry. In some organic farms, sheep or cattle are allowed to graze on the plants. Rapeseed "oil cake" is also used as a fertilizer in China. After harvesting the stubble is ploughed back into the soil as green manure or used as bedding. The seed husks have been reported to be used in plastering house walls.

Biodiesel is produced from canola oil through a refinery process called transesterification. This process is a reaction of the oil with an alcohol to remove the glycerin, which is a byproduct of biodiesel production. Pure, 100% biodiesel – called B100 – can be blended in any proportion with petroleum diesel for use in diesel engines that run heavy equipment, long haul trucks, farm machinery, municipal fleets and generators.

Seventeen samples of Canadian rapeseed oil containing low up to 4.1% erucic acid (LEAR oil) gave Crismer value of 68.45C with a range of 67–69.29 and those with high 20–45% erucic acid oil (HEAR oil) gave Crismer values ranging from 76 to 82% (Sahasrabudhe 1977). Crismer value measures the miscibility of an oil in a standard solvent mixture. HEAR oil is used in lubricants, especially where high heat stability is required. Its high polarity, uniform molecule size, and long carbon chains endows it with greater affinity to metal surfaces and better lubricity than mineral oils. In the oleo-chemical industry, HEAR oil is used as a source of erucic acid to produce a slipping and anti-blocking agent used in plastic foils, foaming agents used for instance in mining industry, emulsifying agents, surfactants and many other chemicals for both food and non-food industries. The long chain length of erucic acid makes it a unique raw material in the oleochemical industry. Rapeseed oil is also used as an illuminant, and in the production of resins, soaps, polyamide fibres and as a vegetable wax substitute. Rape oil is used in massage and oil baths.

Oilseed rape (*B. napus*) straw was found to be feasible raw materials for either biogas or ethanol production; however, improvement of biogas productivity or ethanol yield was necessary before an economical process could be achieved (Petersson et al. 2007). Polyurethane (PUR) plastic sheets with excellent mechanical properties can be prepared by reacting polyols synthesized from canola oil with aromatic diphenylmethane diisocyanate (Kong and Narine 2007).

Comments

In accordance with Codex Standard for Named Vegetable Oils (Codex Alimetarius 1999), rapeseed oil (turnip rape oil; colza oil; ravison oil; sarson oil: toria oil) refers to oil produced from seeds of *Brassica napus*, *Brassica rapa*, *Brassica juncea* and *Brassica tournefortii* species. Rapeseed oil – low erucic acid (low erucic acid turnip rape oil; low erucic acid colza oil; canola oil) refers to oil produced from low erucic acid oil-bearing seeds of varieties derived from the *Brassica napus*, *Brassica rapa* and *Brassica juncea*, species. Also low-erucic acid rapeseed oil must not contain >2% erucic acid (as % of total fatty acids). International industry standards require canola meal to be low in glucosinolates (total glucosinolates of 30 μmol/g) in toasted oil free meal (OECD 2001). Food Standards Australia New Zealand (FSANZ), formerly called Australia New Zealand Food Authority (ANZFA),

does not consider canola meal as a food fraction suitable for humans due to the presence of glucosinolates (ANZFA 2001).

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Brassica nigra

Scientific Name

Brassica nigra (L.) W.D.J. Koch

Synonyms

Brassica brachycarpa P. Candargy, *Brassica bracteolata* Fisch. & C.A. Mey., *Brassica elongata* var. *longipedicellata* Halácsy ex Formánek, *Brassica nigra* f. *breviflora* Zapal., *Brassica nigra* f. *condensata* Hausskn., *Brassica nigra* f. *dentifera* Zapal., *Brassica nigra* f. *glabrata* Zapal., *Brassica nigra* f. *hispida* O.E. Schulz, *Brassica nigra* subsp. *hispida* (O.E. Schulz) Gladis, *Brassica nigra* subsp. *nigra* (L.) W.D.J. Koch, *Brassica nigra* var. *abyssinica* Alexander Br., *Brassica nigra* var. *bracteolata* (Fisch. & C.A. Mey.) Spach ex Coss., *Brassica nigra* var. *carneodentata* Kuntze, *Brassica nigra* var. *japonica* (Thunb.) O.E. Schulz, *Brassica nigra* var. *nigra* W.D.J. Koch, *Brassica nigra* var. *subglabra* Kuntze, *Brassica nigra* var. *tortuosa* (Pers.) Alef., *Brassica nigra* var. *torulosa* (Pers.) Alef., *Brassica nigra* var. *turgida* (Pers.) Alef., *Brassica persoonii* Rouy & Foucaud, *Brassica sinapioides* Roth ex Mert. & W.D.J. Koch, *Brassica sinapioides* Roth, *Brassica sinapis* Noulet, *Brassica turgida* Rouy & Foucaud [Illeg.], *Crucifera sinapis* (L.) E.H.L. Krause, *Melanosinapis communis* K.F. Schimp. & Spenn., *Melanosinapis nigra* (L.) Calest., *Mutarda nigra* (L.) Bernh., *Raphanus sinapis-officinalis* Crantz, *Sinapis bracteolata* G. Don, *Sinapis erysimoides* Roxb., *Sinapis japonica* Thunb., *Sinapis nigra* L., *Sinapis persoonii* (Rouy & Foucaud) A. Chev., *Sinapis tetraedra* J. Presl & C. Presl, *Sinapis torulosa* Pers., *Sisymbrium nigrum* (L.) Prantl.

Family

Brassicaceae

Common/English Names

Abyssinian Mustard, Black Mustard, Brown Mustard, Cadlock, Indian Mustard, Scurvy, Senvil, Shortpod Mustard, True Mustard, Warlock.

Vernacular Names

Albanian: Djegëz, Sinapi I Zi;
Amharic: Tikur Senafitch;
Arabic: Habet El-Baraka, Khardal, Khardal Aswad;
Armenian: Mananekh, Mananex;
Azeri: Xardal;
Basque: Ziape;

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Belarusian: Čornaja Harčyca. Muštarda;
Bhutan: Payga Tsen, Pega (Dzongkha);
Brazil: Mostarda Preta;
Breton: Sezv-Du;
Burmese: Moan-Ñhing: Nak;
Catalan: Mostassa Negra;
Chinese: Hei Jie, Hei Jie Zi;
Coptic: Shlequm;
Croatian: Crna Gorušica, Crna Vrzina;
Czech: Brukev Černá, Černohořčice Seta, Hořčice Černá;
Danish: Sort Sennep;
Dominican Republic: Mostaza;
Dutch: Bruine Mosterd, Junceamosterd, Sareptamosterd, Zwarte Mosterd;
Eastonian: Must Kapsasrohi;
Esperanto: Mustardo Nigra, Nigra Sinapo;
Ethiopia: Senafitch;
Farsi: Khardel, Khardel Siyah;
Finnish: Mustasinappi;
French: Moutarde Brune, Moutarde Noire, Moutarde De Chine, Moutarde De l'Inde;
Frisian: Moster;
Gaelic : Praiseach Dhubh;
Georgian: Mdogvi ;
German: Braunsenf, Brauner Senf, Französchischer Senf, Gartensenf, Grüner Senf, Holländischer Senf, Mostardkorn, Mpstert, Roter, Schwarz-Senf, Schwarzer Senf, Senf, Senfkohl, Senfkraut ;
Greek: Napy, Sinapi, Sinapi Mauro, Sinaposporos (Seeds);
Hawaiian: Mākeke;
Huasa: Mastad;
Hebrew: Hardal Shahor, Kruv Shahor;
Hmar: Anthrammu;
Hungarian: Barna Mustármag, Fekete Mustár, Fekete Mustármag, Francia Mustár, Vörös Mustár;
Icelandic: Mustarðskorn;
India: Behar, Horiyah, Xoriyah (Assamese), Besar (Bodo), Kalo Sorse, Rai Sorse, Sorsa (Bengali), Kalhurevi (Dhivehi), Rai (Gujarati), Banarasi Rai, Kali Rai, Kali Sarson, Lal Sarson, Rai, Sarson (Hindu), Sasive (Kannada), Rai (Maithili), Kafu, Kadugu (Malayalam), Hangam (Manipuri), Kali Mohair, Mohair (Marathi), Antram (Mizoram), Gakrie (Naga- Angami), Ozowoo (Naga –Mao), Ganang (Naga-Rongmei), Kayānghan (Naga –Tankhul), Sorissa (Oriya), Rai (Punjabi), Krishnika, Krishnasarshapa, Rajakshavak (Sanskrit), Kadugu (Tamil), Avalu (Telugu), Dasemi (Tulu), Rai, Sarson (Urdu);
Indonesian: Sesawi Hitam, Biji Sesawi Hitam, Sesawi Coklat, Biji Sesawi Coklat;
Italian: Cavalo Senape Nera, Mostarda, Senape, Senape Nera, Senevra;
Japanese: Burakku-Masutado, Kuro-Garashi;
Kashmiri: Ausur, Assour;
Kazakh: Qisi, Qisa;
Khasi: Tyrso;
Korean: Hukkyeoja, Hukkyoja, Meosutadu, Mosutadu; Kas, Gas, Yanggyeoja;
Laotian: Matsatat;
Latvian: Melnā Sinepes;
Lithuanian: Juodasis Bastutis, Juodosios Garstyčios;
Macedonian: Crn Sinap;
Malaysia: Saw, Biji Sawi;
Mongolian: Har Gich;
Nepal: Tori, Rai (Nepali), Rayo, Paka, Tu (Newari);
Norwegian: Sort Sennep, Svartsennep;
Pahlavi: Spandaan;
Philippines: Mustasa (Tagalog);
Polish: Czarna Gorczyca, Gorczyca Czarna, Kapusta Czarna, Kapusta Gorczyca, ;
Portuguese: Mostarda Negra, Mostarda Preta;
Romanian: Muştar Negru;
Russian: Francuzskaja Gorčica, Gorchitsa Chërnyi, Gorchitsa Chyornaya;
Serbian: Crna Slačica, Gorčica Crna;
Slovašcina: Črna Gorčica, Črna Ogrščica, Ogrščica Črna;
Slovencina: Horčicové Semená, Horčica Čierna, Kapusta Čierna;
Spanish: Ajenape, Aleza, Jeben, Jenape Ajenabo, Laparda, Lujarda, Mostaza Negra, Mostaza De Indias, Ziape;
Sri Lanka: Aba (Sinhala);
Swahili: Haradali;
Swedish: Brunsenap, Svartsenap;
Thai: Mastar;
Tigrinya: Senafech Tselim;

Turkish: Chordal, Hardal, Kara Hardal, Siyah Hardal;
Turkmen: Gara Gorçitsa;
Ukrainian: Hirchytsya Chorna;
Uzbek: Qora Xantal, Qora Gorchitsa;
Vietnamese: Cải Đen, Hắc Giới;
Welsh: Mwstart Du;
Yiddish: Shvartse Gortshitse, Shvartse Mustarde, Shvartser Zeneft;

Origin/Distribution

The plant is widespread in Central and Southern Europe and most regions with a temperate climate. The original home of the species is unknown, but it has been suggested (Vavilov 1949; Rakow 2004) that the plant belongs to a Mediterranean center with a secondary center in the Near East (Vaughan and Hemingway 1995).

Agroecology

Black mustard is adaptable to a temperate and subtropical climatic regime with an annual temperature range of 6–27 °C. It is unsuitable for the lowlands of the hot, wet tropics. It tolerates annual rainfall of 300–1,700 mm and is grown as a rainfed crop in areas of low or moderate rainfall.

It is adaptable to a wide range of soils with pH 4.9–8.2. It thrives best on light sandy loams with pH 5–8 or deep rich fertile soils. It abhors heavy clay soils.

Edible Plant Parts and Uses

Black mustard seed is used primarily as a spice and condiment. Finely ground seeds of black and white mustard are mixed together to form the mustard meal or powder, when mixed with vinegar forms the condiment "Continental mustard", "French mustard" or "Dijon mustard"; and when mixed in water and salt forms "English mustard". Mustard is incorporated in various food products such as salad creams, mayonnaise, sauces, pickles, piccalilli (chopped pickled vegetables and spices), and curries. Mustard acts as a preservative against the action of yeasts and moulds and as an efficient emulsifying agent in creams and mayonnaise.

Black mustard seed is commonly used as a spice in Indian cuisine, for example in curries. The seeds are usually thrown into hot oil or ghee, after which they pop, releasing a characteristic nutty flavour. Black mustard seeds are also a component in the Bengali five spice mixture *panch phoron* (mixture of fenugreek, nigella, cumin, fennel and black mustard seeds in equal portion) and the South Indian mixture *sambar podi* (blend of roasted coriander seeds, black mustard seed, fenugreek seeds, yellow lentils and Bengal gram). The seeds have a significant amount of fatty oil and is often used as a cooking oil in India. Mustard oil is also used for flavouring by dribbling the oil over boiled vegetables and also used as salad oil. It is also used in pickled raw vegetables (achar), where it contributes pungency and acts as a preservative.

Black mustard is deemed as "generally recognised as safe" (GRAS 2760) in the United States of America.

In Ethiopia the plant is cultivated as a vegetable and spice. The leafy young shoots and leaves are consumed cooked as vegetables. They are more pungent than white mustard and are also used in salads.

Botany

An erect, branched, aromatic, fast-growing, sparsely pubescent annual herb, 0.3–2 (–3) m tall, sparsely pubescent basally and with taproot. Lower leaves are lyrate-pinnatisect, 6–30 × 1–10 cm, with 1–3 pairs of lateral lobes and larger terminal lobe, glaucous and hispid

on both surfaces (Plates 1–2); upper leaves linear (Plates 3–4) or linear-oblong, 5 × 1.5 cm, entire or sinuate, glabrous, rarely dentate, glaucous below, dark green above all leaves petiolate. Flowers in elongate terminal racemes, pedicels 1–4 mm long in flower to 13 mm long in fruit (Plates 3–4). Sepals oblong ascending, petals regular, yellow, ovate with rounded apices, 7–9 mm long, stamens 6 with greenish-yellow , glabrous filaments and yellow oblong anthers, ovary green terete and glabrous. Fruit a silique, long slender beaked pod, 1.0–2.0 cm long, smooth cylindrical, 1.5–2 mm wide with 10–12 seeds, beak seedless, on 6–13 cm long pedicels, ascending usually parallel to stem axis. Seeds dark reddish-brown to black, oval to spherical (Plate 5), about 1–1.3 mm in diameter, more or less covered with white pellicle, taste pungent.

Plate 1 Mustard seedling

Plate 2 Close-up lyrate mustard leaf

Plate 3 Mustard grown in cabbage patch for pest control

Plate 4 Mustard pods, flower and linear, entire upper leaves

Plate 5 Black mustard seeds

Nutritive/Medicinal Properties

The nutrient value of black mustard seed per 100 g edible portion had been reported by Toxopeus and Utomo (1999) as: water 8 g, protein 29 g, carbohydrates 19 g, fibre 11 g, ash 5 g, Ca 0.4 g, P 0.6 g, Fe 21 mg, β-carotene equivalent 0.6 g, thiamine 0.4 mg, riboflavin 0.31 mg and niacin 7.3 mg. Fatty acid composition (% weight) of the parental variety *B. nigra* var. *Junius* was reported as C16:0 (plamitic acid) 5%, C 18:0 (stearic acid) 1.4%, C18:1 (oleic acid) 10.9%, C 18:2 (linoleic acid) 23.8%, C18:3 (linolenic acid) 17.0%, C 20:1 (eicosenoic acid) 7.2% and C22:1 (erucic acid) 31.2% (Chevre et al. 1991). Much higher levels of linoleic and linolenic acids and much lower levels of eicosenoic and erucic acids were found in progenies derived from some disomic addition lines.

Black mustard seed also contain sinigrin (prop-2-enylglucosinolate). Sinigrin concentration varied from 0.4 to 4.5% DM over 3 years in the seeds of *B. nigra* and *B. juncea* (Halva et al. 1986). *B. nigra* and *B. juncea* var. *rugosa* (mustard greens) were found to have high concentrations of sinigrin in the seed and seedling (Rangkadilok et al. 2002a). Glucoraphanin was absent in both species. A sinigrin purity of 98.01–99.11% and an efficiency of 82.85–83.62%, were obtained from black mustard (*Brassica nigra*) seeds and horseradish (*Armoracia rusticana*) roots by ionic exchange chromatography (DEAE Sephadex A-50) (Stoin et al. 2007).

Sinigrin concentration in *B. nigra* decreased from seedling to early flowering stage, increased in the late flowering stage and then decreased again during seed maturation (Rangkadilok et al. 2002b). Glucosinolate levels of up to 120 ìmol/g DM were found in *B. nigra* and *B. juncea*, while *B. rapa* did not show values over 25 ìmol/g DM at any stage of the investigated plant life cycles (leaf, bud, flower and seed (Bellostas et al. 2004)). Total glucosinolate concentration increased in reproductive organs towards the end of the growth, and in the last growth stage (green seeds in the pod) values as high as 98 ìmol/g DM were found in pods of *B. nigra*. At the last growth stage studied, aliphatic glucosinolates (e.g. sinigrin) were present in greatest concentration in all vegetative parts in *B. nigra*, constituting 50% of total glucosinolates in roots (4 imol/g), 100% of total glucosinolates in stem (14 imol/g) and leaves (5 imol/g) and 98% of total glucosinolates in pods (98 imol/g) while aromatic glucosinolate phenethylglucosinolate 3 imol/g (about 40% of total glucosinolates) and indol-3-methyl glucosinolate (10% of total glucosinolates) were found in the roots, and indol-3-methyl glucosinolate (2 imol/g) in the pods. Sinigrin concentration also increased in maturing seeds while the concentration in pods decreased.

B. nigra flowers contained levels of glucosinolates up to five times higher than those of leaves (Smallegange et al. 2007). Five glucosinolates were identified: the aliphatic sinigrin, the aromatic phenylethylglucosinolate, and three indole glucosinolates: glucobrassicin, 4-methoxyglucobrassicin, and 4-hydroxyglucobrassicin. Sinigrin was by far the most abundant compound in all three *B. nigra* genotypes. Sinigrin, 4-hydroxyglucobrassicin, and phenylethylglucosinolate were present at significantly higher levels in flowers than in leaves.

Volatiles found in the green tissues of *B. nigra* predominated by allyl isothiocynanate, followed by 2-phenylethyl- isothiocyanate and other compound *cis*-3-hexen-l-yl acetate (Olivier et al. 1999). AITC release varied more across genotypes of *B. nigra* (0.4–3.5 mg AITC/g tissue) than *B.juncea* (0–2.6 mg AITC/g tissue). Volatile compounds identified from *B. nigra* plant exposed to leaf and root herbivory included: α-farnese, α-humulene, α-muurolene, α-pinene, α-ylangene, benzene, benzonitrile, aromadendrene, β-cubebene, β-farnesene, 2-β-pinene, 3-butenenitrile, cadinene, camphene, δ-3-carene, dimethyl disulfide, dimethyl tridisulfide, dimethylnonatriene, junipene, limonene, linalool, *m*-cymeme, methyl thiocyanate, thujone, *trans*-caryophyllene, trimethyl tridecatetraene (Soler et al. 2007). Dimethyl sulfide, dimethyl disulfide, sothiocyanate, and methanethiol emissions increased from *B. nigra* and *B. juncea* roots after *Delia radicum* larval damage (van Dam et al. 2012). Sinigrin was also detected in the roots.

Young leaves of black mustard were found to contain high levels of sinigrin (>10 mMol) in the phloem sap, and nutrients 216 mMol amino acids, 26% sugars, in contrast mature, pre-senescent leaves contained lower nutrient contents, 77–83 mM amino acids, 19–20% sugars and lower sinigrin contents 1–2 mM (Merritt 1996). Flavonoids found in *B. nigra* leaves were all flavonol glycosides of kaempferol, quercetin and isorhamnetin: kaempferol 3-glucoside, kaempferol 7-glucoside, kaempferol 3-sophoroside, keampferol 3-feruloyl-sophoroside, kaempferol 3-sinapoyl-sophoroside, kaempferol 3,7-diglucoside, kaempferol 3-sophoroside 7-glucoside, quercetin 3-glucoside, quercetin 7-glucoside, quereetin 3-sophoroside, quercetin 3,7-diglucoside, quercetin 3-sophoroside 7-glucoside, isorhamnetin 3-glucoside, isorhamnetin 7-glucoside, isorhamnetin 3-sophoroside, isorhamnetin 3,7-diglucoside, and isorhamnetin 3-sophroside 7-glucoside (Aguinagalde 1988). *B. nigra* was characterized by the presence of isorhamnetin 3-sophoroside. The predominant phenolic compounds found in *B. nigra* leaves were gallic acid, followed by quercetin, ferulic acid, caffeic acid and rutin (Rajamurugan et al. 2011).

Antioxidant Activity

Brassica nigra varieties exhibited potent hydroxyl radical-scavenging activity above 90% at a concentration of 1 μg/mL extract (Chung et al. 1997). The active principle was identified as 3,5-dimethoxy-4-hydroxycinnamic acid methyl ester. The methanol extract of *B. nigra* leaf exhibited antioxidant activity in a dose dependent manner from 10 to 500 μg/mL (Rajamurugan et al. 2011). Total phenol content was found to be 171.73 gallic acid equivalents and the total flavonoid content 7.45 quercetin equivalents. In another study, total antioxidant capacity of *B. nigra* leaf ethanolic extract was found to be 97.08 mg/g of ascorbic acid (Alam et al. 2011). *Brassica nigra* showed IC_{50} value of 63.09 μg/mL whereas the standard antioxidant showed IC_{50} value 14.45 μg/mL in DPPH method. The standard antioxidants ascorbic acid, galic acid and quercetin showed e reducing power 485.75, 736.30 and 763.01%, respectively whereas *Brassica nigra* extract showed the value 263.69%. IC_{50} value in NO scavenging activity of the extract was found to be 118.21 μg/mL whereas ascorbic acid showed the value 5.47 μg/mL and quercetin had the value 15.24 μg/mL. Phytochemical screening showed the presence of alkaloids, flavonoids, glycosides and carbohydrates in the extract. Total phenol content in the plant was 6.67 mg/g of galic acid. *Brassica nigra* was found to contain 2.04 mg/g of quercetin in flavonoid assay.

Anticancer Activity

Allyl isothiocyanate (AITC) and phenyl isothiocyanate (PITC) significantly inhibited human umbilical vein endothelial cells (HUVECs) cell migration, invasion, and tube formation (Thejass and Kuttan 2007). Both compounds were highly potent in the downregulation of vascular endothelial growth factor (VEGF) and proinflammatory cytokines such as interleukin (IL)-1β, IL-6, granulocyte macrophage colony-stimulating factor (GM-CSF), and tumor necrosis factor α (TNF-α). Treatment with these compounds showed an elevation in the levels of antiangiogenic factors IL-2 and tissue inhibitor of metalloproteinases (TIMP)-1. Furthermore both compounds, significantly reduced VEGF mRNA expression in B16F-10 melanoma cells. The findings suggested that AITC and PITC acted as angiogenesis inhibitors through the downregulation of VEGF and proinflammatory cytokines such as IL-1β, IL-6, GM-CSF, and TNF-α and upregulation of IL-2 and TIMP. Angiogenesis is a crucial step in the growth and metastasis of cancers. Allyl isothiocyanate (AITC) at 10 μM inhibited proliferation of Ehrlich ascites tumor (EAT) cells (Kumar et al. 2009). It significantly reduced ascites secretion and tumor cell proliferation by about 80% and inhibited vascular endothelial growth factor expression in tumor-bearing mice in-vivo. It also reduced vessel sprouting and exhibited potent antiangiogenic activity in the chorioallantoic membrane and

cornea of the rat. AITC arrested the growth of EAT cells by inducing apoptosis and effectively arrested cell cycle progression at the G1 phase.

Antimutagenic Activity

Polasa et al. (1994) demonstrated that *Brassica nigra* exhibited antimutagenic effect and could be a potent antagonist of the adverse biological effects of the ultimate metabolites of benzo[o] pyrene (B[a]P.), a ubiquitous environmental genotoxicant. There was a significant reduction in reversion frequency of the TA98 and TA100 strains of *Salmonella typhimurium* in mustard-fed rats.

Antidiabetic Activity

Streptozotocin induced diabetic rats treated aqueous extract of *B. nigra* seed gave the lowest serum glucose value (29 mg/dL) increase between 0 and 1 h of glucose tolerance test (GTT) compared to 54, 44 and 44 mg/day with chloroform, acetone and ethanol extracts respectively (Anand et al. 2007). Administration of 200 mg/kg body weight of aqueous extract to diabetic animals daily once for 1 month lowered fasting serum glucose (FSG) levels while in the untreated group FSG remained at a higher value. In *B. nigra* treated animals the increase in glycosylated hemoglobin (HbA1c) and serum lipids was much less when compared with the levels in untreated diabetic controls. In diabetic rats treated with the aqueous extract for 2 months, decrease of serum glucose, increase of serum insulin and release of insulin from pancreas along with the restoration of key regulatory enzyme activities of carbohydrate metabolism and glycogen content were observed (Anand et al. 2009). The therapeutic role of the aqueous extract could be attributed to the release of insulin from pancreas and change of glucose metabolizing enzyme activities to normal levels, thus stabilizing glucose homeostasis in the liver and kidney. The LD_{50} was found to be more than 15 times the effective dose (ED) implying higher margin of safety for the extract.

Antiinflammatory Activity

In-vivo anti inflammatory test using carrageenan induced rat paw edema, the ethanolic extract of *Brassica nigra* leaf (500 mg/kg) gave 17.9% inhibition whereas standard phenylbutazone (100 mg/kg) gave 39.38% (Alam et al. 2011). In-vitro anti inflammatory test of *B. nigra* by protease inhibition method also gave 42.57% inhibition of trypsin at dose 250 μg/mL.

Antimicrobial Activity

Allyl glucosinolate (sinigrin), generally converted to the volatile allyl isothiocyanate (AITC), was the predominant glucosinolate produced in cultivars of *B. nigra* and *B. juncea* (Daxenbichler et al. 1991); it had been reported to be one of the most potent antimicrobial compounds formed by *Brassica* spp. (Fenwick and Heaney 1983; Mari et al. 1993; Kirkegaard et al. 1996;). Only AITC completely inhibited mycelial growth and germination of five postharvest fruit pathogens in a study including a number of sulphur compounds (Mari et al. 1993). Of six *Brassica* species assayed, only cultivars of *B. nigra* and *B. juncea* suppressed radial growth of *Fusarium sambucinum* (>50% inhibition of control) (Mayton et al. 1996). Allyl isothiocyanate (AITC) was detected in the leaf tissues and *B. nigra* cultivars had the highest levels of AITC among all the *Brassica* assayed.

Volatiles from all accessions of *B. juncea* and *B. nigra* significantly reduced radial growth of both *Verticillium dahliae* and *Helminthosporium solani* compared to the control (Olivier et al. 1999). *B. nigra* accessions released allyl isothiocyanate (AITC) in concentrations greater than 1.2 mg/g, and completely prevented fungal growth and spore germination. *B. nigra* oil exhibited inhibitory effect on the in-vitro growth of two fresh hospital isolates of *Staphylococcus aureus* and *Escherischia coli* (Obi et al. 2009).

Anthelmintic Activity

Crude aqueous and methanolic extracts of *Brassica nigra* (seeds) showed in-vitro anthelmintic effects against Eritrean adult earthworm *Pheretima posthuma* (Basha et al. 2011). The paralysis and death time of worms in all extracts was found to be dose dependent and higher anthelmintic activity was observed in aqueous extracts in comparison to methanolic extracts.

Protease Inhibitory Activity

B. nigra seed was found to contain a thermostable protein inhibitor of trypsin and subtilisin, called BN with molecular weight of 15,500 Da and composed of two disulfide-linked polypeptide chains, consisting of 39 and 90 residues, respectively (Genov et al. 1997).

Allergy

A case of allergic contact dermatitis to mustard (*Brassica nigra*) in a salad maker was reported by Dannaker and White (1987). The sources of skin contact included a commercial salad cream, a vinegrette, and various members of the mustard family, Cruciferae. Morisset et al. (2003) conducted a prospective study with double-blind placebo-controlled food challenge trials in 30 subjects aged 3–20 years presenting positive prick tests to ground mustard seeds (*Brassica nigra*), mustard flour (*B. juncea*), metabisulfite-free strong mustard seasoning (*B. juncea*) and a commercialized allergenic extract (*B. nigra*). They found that about 23.3% of the sensitized subjects were allergic to a routine dose of mustard and that positive prick tests and the presence of specific IgE were not predictive.

Traditional Medicinal Uses

Black mustard has been used in traditional herbal medicine (Grieve 1971; Vaughan and Hemingway 1995; Bown 1995; Foster and Duke 1998). Mustard seed is taken as a tonic, digestive, emetic, and appetite stimulant. When swallowed whole with molasses it acts as a laxative. Seed decoction is taken as a therapy for liver and spleen indurations and also to treat carcinoma, tumours and abscesses. Hot water containing bruised mustard seeds makes an invigorating foot bath and is also good for colds and headaches. Pulverised mustard seeds are mixed with flour and water to from a cataplasm with paste that is applied to the skin to treat rheumatism, and to reduce congestion in internal organs. They are also used externally as poultices. Applied externally, mustard relieves congestion by drawing the blood to the surface as in head afflictions, neuralgia and spasms. Old herbals recommended mustard for treating alopecia, epilepsy, snakebite, and toothache. Mustard is also recommended as an aperient ingredient of tea, useful in hiccup. Mustard oil is said to stimulate hair growth and useful in pleurisy and pneumonia. Mustard flour is considered antiseptic.

Other Uses

The plant is often grown as a green manure, it is very fast, producing a bulk suitable for digging into the soil in about 8 weeks.

B. nigra fixed oil is used as a lubricant, illuminant, and in soap-making. Mustard has been used in the wine industry in France and Spain to remove mustiness in wine and wine barrels. It has also been used to prevent secondary fermentation in wine which would lead to bad flavour. Mustard oil (allyl isothiocyanate) is used in commercial cat and dog repellent mixtures. The seed residues left after oil extraction can be used as fertilisers but is unsuitable as stock feed because of the presence of allyl isothiocyanate in the residues.

B. nigra and related *Brassica* species that contain glucosinolates can be employed in biofumgation to suppress soil borne pests and pathogens. *B. nigra* oil at a dose of 4% significantly reduced total haemolymph and fat body protein in *Spodoptera littoralis* larvae (Khatter and Abduldahb 2010).

Comments

Brassica nigra (BB – 2n = 16) together with *B. rapa* (AA – 2n = 20) and *Brassica oleracea* (CC – 2n = 18) represent three important ancestral parental genomes from which many other *Brassica* species (hybrids) have been created by interspecific breeding as outlined in the Triangle of U, a theory about the evolution and relationships between members of the plant genus *Brassica* proposed in 1935 by Woo Jang-choon a Korean-Japanese botanist who was working in Japan (where his name was transliterated as "Nagaharu U" (Nagaharu 1935)). These hybrids are said to be allotetraploids as they contain four genomes, derived from two different ancestral species or more specifically, amphidiploid as they contain one diplod genome from each of the ancestral *Brassica* species. Examples are *Brassica juncea* (brown mustard) with AABB – 2n = 36, *B. napus* (rapeseed) with AACC – 2n = 38 and *B. carinata* (Ethiopian mustard) with BBCC – 2n = 34 genomes. Data from molecular studies indicated that the three diploid species are themselves paleopolyploids (Lysak et al. 2007).

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Chenopodium quinoa

Scientific Name

***Chenopodium quinoa* Willd.**

Common/English Names

Quinoa, Quinua.

Synonyms

Chenopodium album subsp. *quinoa* (Willd.) Kuntze, *Chenopodium album* var. *quinoa* (Willd.) Kuntze, *Chenopodium album* f. *subspontaneum* Kuntze, *Chenopodium ccoyto* Toro Torrico, *Chenopodium ccuchi-huila* Toro Torrico, *Chenopodium chilense* Pers. (inval.), *Chenopodium guinoa* Krock., *Chenopodium hircinum* f. *laciniatum* (Moq.) Aellen, *Chenopodium hircinum* var. *quinoa* (Willd.) Aellen, *Chenopodium hircinum* f. *rubescens* (Moq.) Aellen, *Chenopodium hircinum* f. *viridescens* (Moq.) Aellen, *Chenopodium nuttalliae* Saff., *Chenopodium purpurascens* var. *punctulatum* Moq., *Chenopodium quinoa* var. *laciniatum* Moq., *Chenopodium quinoa* var. *lutescens* Hunz., *Chenopodium quinoa* var. *melanospermum* Hunz., *Chenopodium quinoa* subsp. *milleanum* Aellen, *Chenopodium quinoa* var. *orbicans* Murr, *Chenopodium quinoa* f. *purpureum* Aellen, *Chenopodium quinoa* var. *rubescens* Moq., *Chenopodium quinoa* var. *viridescens* Moq..

Vernacular Names

Argentina: Dawe, Sawe (Mapuche);
Bolivia: Supha, Jopa, Jupha, Juira, Ära, Qallapi, Vocali (Amyara), Ayara, Kiuna, Kuchikinwa, Achita, Kinua, Kinoa, Chisaya Mama (Quechua);
Brazil: Quinoa;
Bulgarian: Nemerizliva Laikuchka;
Chile: Dawe, Quinhua;
Columbia: Suba, Pasca (Chibchan);
Czech: Merlík Čilský;
Danish: Kvinoa, Quinoa, Rismælde;
Dutch: Gierstmelde, Quinoa;
Eastonian: Tšiili Hanemalts;
Ecuador: Ayara, Kiuna, Kuchikinwa, Achita, Kinua, Kinoa, Chisaya Mama (Quechua);
Finnish: Kinua, Kvinoa;
French: Quinoa, Petit Riz, Riz Du Pérou;
German: Quinoa, Reismelde;
Hungarian: Libatop, Mirhafű;
Icelandic: Frumbyggjanjóli, Inkanjóli;
Italian: Farinello;
Latvian: Kvinoja;
Norwegian: Perumelde, Quinoa;
Peru: Ayara, Kiuna, Kuchikinwa, Achita, Kinua, Kinoa, Chisaya Mama (Quechua);
Polish: Komosa Ryżowa;

Family

Chenopodiaceae

T.K. Lim, *Edible Medicinal and Non-Medicinal Plants: Volume 5, Fruits*,
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Portuguese: Arroz-Miúdo-Do-Perú, Espinafre-Do-Perú, Quinoa;
Spanish: Arroz Del Peru, Qunigua, Quina, Quinoa;
Swedish: Mjölmålla, Quinoa.

Origin/Distribution

Quinoa originated in the Andean region of South America. It has been successfully domesticated 3,000–4,000 years ago for human consumption.

Agroecology

Quinoa is a cool climate crop with optimal growing conditions from −3°C at night to 30°C during the day, and with annual precipitation from 1,500 mm to over 2,500 mm. Its traditional cultivation area is from latitude 8°N to 30°S. It is grown from sea level to 3,800 m altitude (Bhargava et al. 2006).

Quinoa prefers semi-deep, well-drained, sandy soil but will also grow in clayey soils. It will grow in pH range of 4.5–8 depending on ecotypes. Its tolerance to cold, drought conditions is dependent on ecotypes.

The plant shows tolerance to frost, salinity and drought, and has the ability to grow on marginal, low fertility soils (Galwey 1992; Bhargava et al. 2006). For such reasons, quinoa may be of value in Europe as a break between cereal crops and after potato crops (Galwey 1992). Quinoa's ability to produce high-protein grains under ecologically extreme conditions makes it important for the diversification of future agricultural systems, especially in high-altitude areas of the Himalayas and North Indian Plains (Bhargava et al. 2006). When grown in the areas to which it is best adapted, it should be able to compete with cereals in both human diets and animal feeds.

Edible Plant Parts and Uses

The grain (seed), young leaves and young ears are used as human food. All these parts are usually thoroughly soaked in water and rinsed to remove the bitter saponins.

Quinoa grains are traditionally toasted or ground into flour. Quinoa can be cooked in the same way as rice in a rice cooker. Quinoa can be ground into powder and used as porridge. They can also be boiled, added to soups, made into breakfast foods like flakes, cereals or pastas, pancakes and bread. Some recipes of quinoa include *tamales*, *huancaína* sauce, and casseroles, stews, *torrejas*, vegetable *pilafs*, pastries, biscuits, sweets and desserts. Quinoa is also made into soft and fermented, hot and cold beverages and beer. A lightly fermented quinoa drink, *chicha*, is revered as the "Drink of the Incas". A high content protein beverage from the mixture of liquid extracts of quinoa and two legumes: mesquite (*Prosopis chilensis*) and lupine (*Lupinus albus*) and flavoured with raspberry pulp was developed to feed children with nutritional deficiencies (Cerezal Mezquita et al. 2012).

When cooked, they have a nutlike flavour, and they remain separate, fluffy, and chewy. Quinoa can be used as a high protein breakfast mixed with honey, almonds or berries. In Peru and Bolivia, quinoa flours, flakes, tortillas, pancakes, and puffed grains are produced commercially.

Quinoa is gluten-free and has demonstrated value as a partial wheat-flour substitute for enriching unleavened bread, cakes, and cookies or in gluten free food products. Blends of wheat flour containing up to 30% quinoa flour produce fully acceptable loaf breads. Mixing quinoa with corn, wheat, barley, or potatoes produces foods that are both filling and nutritious. In Peru and Bolivia, malnourished children have been reported to be fed such quinoa-fortified foods with good results.

Quinoa is considered pseudocereal or pseudograin, and has been recognized as a complete food due to its remarkable protein quality and exceptional balance between oil, protein and fat (Abugoch James 2009; Vega-Gálvez et al. 2010). For millions in the Andes it is a major source of protein. Quinoa provides an excellent and high quality protein profile (15%) containing a balanced set of essential amino acids for humans like oats and unlike wheat or rice which are deficient in lysine. quinoa is an excellent example of 'functional food' that aims at lowering the risk of various

diseases (Vega-Gálvez et al. 2010). Functional properties are imparted also by its minerals, vitamins, fatty acids and antioxidants like polyphenols, phytosterols, and flavonoids that provide nutraceutical benefits to human nutrition, particularly to protect cell membranes, with proven good results in brain neuronal functions. Its minerals function as cofactors in antioxidant enzymes, adding higher value to its rich proteins. Quinoa is a rich source of dietary fibre and phosphorus and is high in magnesium and iron, and being gluten free is easily digested. Quinoa also contains phytohormones, which offer an advantage over other plant foods for human nutrition. Quinoa possesses some functional (technological) properties like solubility, water-holding capacity (WHC), gelation, emulsifying, and foaming that accord diversified uses (Abugoch James 2009). It is also considered an oil crop, with an interesting content of omega-6 and pronounced vitamin E content. Quinoa starch has physicochemical properties (such as viscosity, freeze stability) which bestow it with functional properties with novel uses. Because of these traits quinoa has recently been used as a novel functional food (Abugoch James 2009; Vega-Gálvez et al. 2010) and was recommended as a candidate food crop in NASA's Controlled Ecological Life Support System for long-duration manned spaceflights (Schlick and Bubenheim 1996).

Quinoa can be germinated and the sprouts used as salads. Quinoa ears and young leaves are also used as vegetables. The ears are used to make pickles, and the leaves are eaten fresh in salads or cooked like spinach.

Protein isolates were prepared from quinoa seed by alkaline solubilisation at pH 9 called Q9, and at pH 11, called Q11 (Abugoch et al. 2008). Q9 and Q11 had high levels of essential amino acids, with high levels of lysine. Some differences were found that could be attributed to the extreme pH treatments in protein isolates and the nature of quinoa proteins. Q9 and Q11 may be used as a valuable source of nutrition for infants and children. Q9 may be used as an ingredient in nutritive beverages, and Q11 may be used as an ingredient in sauces, sausages, and soups.

Gluten free food products viz. pancakes, scones, precooked pizza and bread were formulated for people with celiac disease (gluten intolerance disease) based on quinoa, rice and corn flours and starches (Del Castillo et al. 2009). Significant differences were found in protein, fat moisture, ash and fibre content and in most of the texture parameters studied in formulated and commercial food groups. An increase of protein of 88 and 198% was found for formulated pancakes and scones respectively, while formulated prepizza and bread showed lower contents (8 and 22%) in comparison to the commercial products, however all formulated products had Chemical Scores above 100. The formulated products most acceptable (values over 80%) were scones and pancakes. Overall, the formulated products provided good quality proteins, exhibited good textural characteristics and adequate percentages of acceptability to be used in the feeding of celiac patients. Studies also found that 100% of celiac people tested were disposed to buy cookies formulated from gluten free defatted hazelnut and quinoa flours (Villarroel et al. 2009). Desirable characteristics highlighted besides the low prolamine content of 1.5 ppm (CODEX limit for classification as gluten free is 20 ppm) included protein (8.9%), fibre (12.7%) and good shelf life against rancidity. Improved functional properties of gluten-free pasta could be obtained by combination amaranth, quinoa and buckwheat into one flour blend (Schoenlechner et al. 2010). Dough matrix for gluten-free pasta was improved by combining 60% buckwheat, 20% amaranth and 20% quinoa. After decreasing dough moisture to 30%, addition of an increased amount of egg white powder of 6% and addition of 1.2% emulsifier (distilled monoglycerides) texture firmness as well as cooking quality of gluten-free pasta produced from such a flour blend reached acceptable values comparable to wheat pasta.

Botany

C. quinoa is an annual herbaceous plant, growing 0.20–3 m tall, with angular, ribbed stem with longitudinal green or red streaks and branched taproot. Leaves are alternate, simple, lower leaves on longer petioles, lamina ovate-rhomboid to deltoid, irregularly and coarsely toothed or incised, upper leaves elliptic-oblong to lanceolate, with toothed

margins and shorter petioles. Inflorescence large, axillary and terminal leafy panicle consisting of clusters of flowers in glomerules, reddish, purplish to golden (Plates 1–3). Flowers bisexual, regular, small, sessile, pentamerous, tepals connate at base, stamens with short filaments and basifixed anthers opposite tepals, ovary superior depressed globose and1 celled, and style short with two feathery stigmas. Fruit an indehiscent achene, protected by the perigonium (incurved tepals), thin-walled and one-seeded. Seeds are 1–2.6 mm, lenticular, smooth, white, yellow, red, purple, brown or black (depending on variety) (Plates 4–5) with thin leathery testa and endospermous.

Nutritive/Medicinal Properties

Nutrient value of quinoa per 100 g edible portion has been reported by USDA (2012) as: water 13.28 g, energy 368 kcal (1,539 kJ), protein 14.12 g, fat 6.07 g, ash 2.38 g, carbohydrate 64.16 g, total dietary fibre 7.0 g, starch 52.22 g, Ca 47 mg, Fe 5.47 mg, Mg 197 mg, P 457 mg, K 563 mg, Na 5 mg, Zn 3.10 mg, Cu 0.590 mg, Mn 2.033 mg, Se 8.5 µg, thiamine 0.360 mg, riboflavin 0.318 mg, niacin 1.520 mg, pantothenic acid 0.772 mg, vitamin B-6 0.487 mg, total folate 184 µg, choline 70.2 mg, betaine 630.4 mg, vitamin A 14 IU, vitamin A, 1 µg RAE, β-carotene 8 µg, β-cryptoxanthin 1 µg lutein + zeaxanthin 163 µg, vitamin E (α-tocopherol) 2.44 mg, β-tocopherol 0.08 mg, γ-tocopherol 4.55 mg, δ-tocopherol 0.35 mg, total saturated fatty acids 0.706 g, 16:0 (palmitic) 0.6 g, 18:0 (stearic) 0.037 g, 20:0 0.030 g, 22:0 0.030 g, 24:0 0.010 g, total monounsaturated fatty acids 1.613 g, 18:1 undifferentiated (linoleic) 1.420 g, 20:1 0.093 g, 22:1 undifferentiated 0.083 g, 24:1c 0.017 g; total polyunsaturated fatty acids 3.292 g, 18:2 undifferentiated 2.977 g,18:3 undifferentiated 0.260 g, 22:6 n-3 (DHA) 0.047 g; tryptophan 0.167 g, threonine 0.421 g, isoleucine 0.5 04 g, leucine 0.840 g, lysine 0.766 g, methionine 0.309 g, cystine 0.203 g, phenylalanine 0.593 g, tyrosine 0.267 g, valine 0.594 g, arginine 1.091 g, histidine 0.407 g, alanine 0.588 g, aspartic acid 1.134 g, glutamic acid 1.865 g, glycine 0.694 g, proline 0.773 g and serine 0.567 g.

Plate 1 Flowering quinoa plants (International Potato Center, Lima, Peru)

Plate 2 Maturing quinoa flower heads (L & H Damen, Kindred Organics)

Quinoa was found to be a good source of thiamine (0.4mg/100g), folic acid (78.1 mg/100 g),

Plate 3 Close-up of quinoa flower heads (L & H Damen, Kindred Organics)

Plate 4 Brown quinoa grains

and vitamin C (16.4 mg/100 g). The seeds contain twice as much γ-tocopherol (5.3 mg/100 g) as α-tocopherol (2.6 mg/100 g) and larger amounts of calcium (874 mg/kg), phosphorus (5.3 g/kg), magnesium (26 mg/kg), iron (81 mg/kg), zinc (36 mg/kg), potassium (12 g/kg), and copper (10 mg/kg) than most of the common cereal grains (Ruales and Nair 1993a). The amounts of mercury, lead, and cadmium were low in relation to the values of tolerable intake for these elements. All values are expressed on a dry-weight basis. The fat content of raw quinoa seeds was 9.7% on a dry-weight basis with high amounts of oleic acid (24.8%) and linoleic acid (52.3%). The level of linolenic acid was 3.9%. The process of removing saponins from the seeds reduces the vitamin and mineral contents to some extent. The loss was significant in the case of potassium, and considerable also in the case of iron and manganese.

Plate 5 White quinoa grains

Studies showed that the quinoa flour contained 11.2% moisture, 13.5% crude protein, 6.3% ether extract, 9.5% crude fibre, 1.2% total ash, 58.3% carbohydrate and per 100 g sample 120 mg D-xylose, 101 mg maltose, 19 mg glucose and 19.6 mg fructose (Ogungbenle 2003). The high proportion of maltose suggesting that it would be useful in malted drink formulations. The values for the chemical properties of the oil extracted were: acid value, 0.50%; iodine value, 54.0%; peroxide value, 2.44%; and saponification value, 192.0%. Quinoa has a high water absorption capacity (147.0%) and low foaming capacity and stability (9.0, 2.0%). The flour has a least gelation concentration of 16% w/v. Protein solubility of the flour was also evaluated and found to be pH dependent, with minimum solubility at about pH 6.0.

Protein contents of ten quinoa cultivars from the Andean highlands (Bolivia/Argentina site) and Argentinean Northwest (Encalilla site) ranged from 91.5 to 155.3 and from 96.2 to 154.6 g/kg dry mass for Encalilla and Bolivia/Argentina seeds respectively, while essential amino acid concentrations ranged from 179.9 to 357.2 and from 233.7 to 374.5 g/kg protein respectively (Gonzalez et al. 2012). Grain yields of five cultivars growing at Encalilla were higher, and four were lower, compared with data from the Bolivia/Argentina site. Both environmental and climatic factors were found to influence the nutritional composition of quinoa cultivars growing in different agroecological regions.

Quinoa was found to have a higher protein content and a better balanced protein profile than do cereals, supplying high levels of lysine, histidine and methionine + cystine (Galwey 1992). Quinoa starch comprised much smaller granules than do cereal starches, with a lower amylose level and more viscous. These differences should make it suitable for some specialised industrial uses, including manufacture of a carbohydrate-based cream substitute. The grain of most varieties were found to contain saponins, bitter compounds which have to be removed by washing or abrasion before consumption. Seeds of quinoa (*Chenopodium quinoa*), kiwicha (*Amaranthus caudatus*) and kañiwa (*Chenopodium pallidicaule*) were found to be good sources of phenolic compounds (Repo-Carrasco-Valencia et al. 2010). Their calcium, zinc and iron contents were higher than in common cereals. In general, roasting did not significantly affect mineral dialyzability. Conversely, in boiled grains there was an increase in dialyzability of zinc and, in the case of kañiwa, also in iron and calcium dialyzability.

The amino acid composition of the protein in raw quinoa and washed quinoa exhibited similar profiles (Ruales and Nair 1992). The first limiting amino acids were the aromatic amino acids thyrosine + phenylalanine giving a chemical score of 86 for protein in raw quinoa and 85 for protein in washed quinoa. Threonine was the next limiting amino acid followed by lysine. The lysine and sulfur amino acids (methionine + cystine) contents were relatively high. In general, the content of essential amino acids in quinoa was higher than in common cereals. The animal experiments showed NPU (Net protein utilisation) values of 75.7, BV (Biological value) of 82.6 and TD (true digestibility) value of 91.7 for the protein in raw quinoa. The digestibility of the protein in quinoa was comparable to that of other high quality food proteins. Saponins did not exert any negative effect on the nutritive quality of the protein.

Studies showed that the amount of soluble proteins was higher than the standard value for wheat and maize and was very close to that of barley's (González et al. 1989). The yield of free sugars like glucose (4.55%), fructose (2.41%) and sucrose (2.39%) were also significant. Iron and calcium levels were higher than the reported values for maize and barley; similarly for the caloric value (435.5 kcal/100 g). Protein content and proteic tryptophan of quinoa were similar to that of wheat and spelt, but higher than in other cereals (Comai et al. 2007). Free tryptophan in quinoa flour showed values similar to those of wheat, oats and sorghum Kalblank, lower than those of barley, spelt and pearl millet, but higher than in rice, maize, rye, sorghum DK 34 – Alabama hybrid. Further, nonproteic tryptophan appeared bound both to water soluble proteins and to proteins soluble at pH 8.9. The non-protein tryptophan fraction, was reported to be the only fraction able to enter the brain, and more easily absorbed, thus guaranteeing a greater amount available for uptake by the central nervous system.

The fatty acid composition of whole quinoa seeds was found to be similar to that reported for other cereal grains, with linoleic, oleic and palmitic acids as the major acids (Przybylski et al. 1994). Quinoa seed lipids contained the largest amount of neutral lipids among all the seed fractions analysed. A very high content of free fatty acids was determined in whole quinoa seed and hulls, accounting for 18.9 and 15.4% of total lipids, respectively. Triglycerides were the major fraction present comprising over 50% of the neutral lipids. Diglycerides contributed 20% of the neutral lipid fraction. Of the phospholipids, lysophosphatidyl ethanolamine, was the most

abundant comprising 45% of the total polar lipids. Phosphatidyl choline was the second major phospholipid component and contributed 12% of whole seed phospholipids. Considerable variation in phospholipids was evident between the different fractions.

Scanning electron microscopy of the starch in raw quinoa seeds showed polygonal granules (0.6–2.0 μm diameter) to be present both singly and as spherical aggregates (Ruales and Nair 1994). The gelatinisation temperature of the starch was 67°C. Cooked samples manifested the highest degree of gelatinisation (97%), followed by the drum-dried (96%) and autoclaved (27%) samples. Cooking and autoclaving modified the viscosity of the paste. The drum-dried sample manifested a higher initial viscosity at 25°C. The in-vitro digestibility of raw quinoa starch was 22%, while that of autoclaved, cooked and drum-dried samples was 32, 45 and 73%, respectively. Saponins did not affect the digestibility of the starch, though they tended to increase the amylograph viscosity. The total dietary fibre content in the cooked sample (11.0%) was significantly lower than that in the autoclaved (13.2%), drum-dried (13.3%) or raw samples (13.3%), while the insoluble dietary fibre fraction in the samples did not change with heat treatment. However, as compared with that of raw quinoa, the soluble dietary fibre fraction was lowered significantly both by cooking (0.9%) and by autoclaving (1.0%).

The hydrolysed quinoa extract obtained by enzymatic hydrolysis of quinoa seed was found to be rich in essential amino acids especially leucine, isoleucine, and valine (Meneguetti et al. 2011). Supplementation studies with the hydrolysed extract showed no hepatic and renal toxicity in wistar rats. Decreased food intake, body weight, fat deposition, and blood triacylglycerol level were observed in rats of the supplemented groups (sedentary and exercised supplemented groups). The results suggested a potential use of hydrolysed quinoa in human nutrition.

The β-carotene, calcium, iron and zinc content in the leaves of 46 accessions of three *Chenopodium* species viz. *Chenopodium album*, *C. album* ssp. *amaranticolor* and *Chenopodium quinoa* exhibited a wide range of variability (in mg/100 g fresh weight), inter-specific as well as varietal, for the β-carotene (0.19–5.91 mg), calcium (358.35–960.10 mg), iron (0.56–7.90 mg) and zinc content (0.07–4.26 mg) (Sharma et al. 2012). Between the two methods used to cook leaves, stir-frying showed better retention of micronutrients than pressure cooking.

Other Phytochemicals

On the basis of its saponin content, quinoa was categorised as "sweet" being saponin free on with <0.11% saponin on a fresh weight basis or "bitter" with >0.11% saponins (Koziol 1990). Saponins were reported as the major anti-nutritional factor found in quinoa grain (Koziol 1992). Most of the saponins were found concentrated in the outer layers of the grain (perianth, pericarp, seed coat, and a cuticle-like layer) which facilitated their removal industrially by abrasive dehulling (Reichert et al. 1986) or traditionally by soaking and washing the grains with water. Quinoa protein was found to be of exceptional quality. Animal feeding studies showed that raw quinoa (both sweet and bitter) exhibited protein efficiency ratio (PER) values from 44 to 93% and cooked quinoa PER values from 102 to 105%. In contrast, raw and cooked wheat exhibited PER values from 23 to 32% of the casein control (Koziol 1992).

Triterpenoid Saponins and Sapogenins

Nine trimethylsilylated pentacyclic triterpenes were isolated from quinoa seeds: β-amyrin, α-amyrin, erythrodiol, oleanolic acid, ursolic acid, echinocystic acid, hederagenin, gypsogenin and queretaroic acid (Burnouf-Radosevich et al. 1985). Oleanolic acid and hederagenin were confirmed to be major triterpenes of *Chenopodium quinoa* seed saponins. From brans of quinoa grains, five new saponins were isolated and their structures were elucidated as 28-*O*-β-glucopyranosyl esters of hederagenin 3-*O*-β-glucopyranosyl-(1→3)-α-arabinopyranoside and 3-*O*-β-glucopyranosyl-(1→3)-β-galactopyranoside,

and 28-*O*-β-glucopyranosyl esters of phytolaccagenic acid 3-*O*-α-arabinopyranoside, 3-*O*-β-glucopyranosyl-(1 → 3)-α-arabinopyranoside and 3-*O*-β-glucopyranosyl-(1 → 3)-β-galactopyranoside (Mizui et al. 1988). Four saponins were isolated from quinoa seeds and identified as glycosides of oleanolic acid. Saponin 4, 3-*O*-[(β-D-xylopyranosyl)(1 → 3)]-[β-D-glucuronopyranosyl-6-*O*-methyl ester]-oleanolic acid was a new natural compound (Ma et al. 1989).

From the brans of quinoa grains, oleanolic acid and chikusetsusaponin IVa together with five other new saponins, designated as quinoa-saponins-6-10 (Mizui et al. 1990). The toxic/biter principles in quinoa seeds were found to be a mixture of saponins whose acidic hydrolysis gave oleanolic acid and hederagenin (3:1) as the only detectable saponin aglycons (Meyer et al. 1990). One of these saponins (quinoside A) was identified as a tetraglycoside of hederagenin named olean-12-ene-28-oic acid, 3,23-bis(*O*-β-*D*-glucopyranosyloxy)-*O*-β-D-glucopyranosyl-(l-3)-*O*-α-L-arabinopyranosyl ester (3β,4α). The major aglycone in the quinoa saponin mixture was identified as phytolaccagenic acid (>40% total), with hederagenin (~25%) and oleanolic acid (30%) aglycones also being present (Ridout et al. 1991).

Two main types of saponins were found in quinoa bran (Ruales and Nair 1993b). The amount of saponin A (β-d-glucopyranosyl-[β-d-glucopyranosyl-(1 → 3)-α-l-arabino-pyranosyl-(1 → 3)]-3-β-23-dihydroxy-12-en-28-oate methyl ester) was 0.7% of the dry weight and that of the saponin B (β-d-glucopyranosyl-[β-d-glucopyranosyl-(1 → 3)-α-l-arabino-pyranosyl-(1 → 3)]-3-β-23-dihydroxyolcan-12-en-28-oate) was 0.2% of the dry weight. After scrubbing and washing, the level of saponin-A remaining in the seeds decreased to 0.31% of the dry weight, and saponin-B was completely removed by this process. The content of phytic acid in the quinoa seeds was about 1% of the dry matter, and scrubbing and washing reduced the phytic acid content of the seeds by about 30%. Neither protease inhibitor nor tannins were detected in the quinoa seeds.

The sapogenin content in seeds of sweet genotypes of quinoa varied from 0.2 to 0.4 g/kg dry matter and in seeds of bitter genotypes from 4.7 to 11.3 g/kg dry matter (Mastebroek et al. 2000). The difference in sapogenin content between leaves and seeds was much higher in bitter genotypes than in sweet genotypes. Hederagenin was the major sapogenin found in leaves, and oleanolic acid in seeds. Dini et al., (2001a) isolated six triterpenoid saponins from the edible grain quinoa: phytolaccagenic acid 3-*O*-[α-L-arabinopyranosyl-(1″ → 3′)-β-D-glucuronopyranosyl]-28-*O*-β-D-glucopyranoside (1); spergulagenic acid 3-*O*-[β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 3)-α-L-arabinopyranosyl]-28-*O*-β-D-glucopyranoside (2); hederagenin 3-*O*-[β-D-glucopyranosyl-(1 → 3)-α-L-arabinopyranosyl]-28-*O*-β-D-glucopyranoside (3); phytolaccagenic acid 3-*O*-[β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl]-28-*O*-β-D-glucopyranoside (4); hederagenin 3-*O*-[β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl]-28-*O*-β-D-glucopyranoside (5); and spergulagenic acid 3-*O*-[α-L-arabinopyranosyl-(1″→3′)-β-D-glucuronopyranosyl]-28-*O*-β-D-glucopyranoside (6). Saponins 5 and 6 are new. Dini et al., (2001b) isolated six triterpenoid saponins from the edible grain quinoa: phytolaccagenic acid 3-*O*-[α-L-arabinopyranosyl-(1″→3′)-β-D-glucuronopyranosyl]-28-*O*-β-D-glucopyranoside (1); spergulagenic acid 3-*O*-[β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 3)-α-L-arabinopyranosyl]-28-*O*-β-D-glucopyranoside (2); hederagenin 3-*O*-[β-D-glucopyranosyl-(1 → 3)-α-L-arabinopyranosyl]-28-*O*-β-D-glucopyranoside (3); phytolaccagenic acid 3-*O*-[β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl]-28-*O*-β-D-glucopyranoside (4); hederagenin 3-*O*-[β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl]-28-*O*-β-D-glucopyranoside (5); and spergulagenic acid 3-*O*-[α-L-arabinopyranosyl-(1″→3′)-β-D-glucuronopyranosyl]-28-*O*-β-D-glucopyranoside (6). The oleanane-type saponins (5, 6) were isolated for the first time in this plant, two of the

phytolaccagenane (1, 3) were new compounds and two (2, 4) were previously found in quinoa.

Seven triterpenoid saponins were isolated from the seeds of "kancolla", a sweet variety of *Chenopodium quinoa (*Dini et al. 2002). Their structures were phytolaccagenic acid 3-*O*-[α-L-arabinopyranosyl-(1″→3′)-β-D-glucurono pyranosyl]-28-*O*-β-D-glucopyranoside, oleanolic acid 3-*O*-[β-D-glucopyranosyl-(1″→3′)-α-L-arab inopyranosyl]-28-*O*-β-D-glucopyranoside, hederagenin 3-*O*-[β-D-glucopyranosyl-(1″→3′)-α-L-arabinopyranosyl]-28-*O*-β-D-glucopyranoside, phytolaccagenic acid 3-*O*-[β-D-glucopyranosyl-(1″→3′)-α-L-arabinopyranosyl]-28-*O*-β-D-glucopyranoside, oleanolic acid 3-*O*-[β-D-glucurono pyranosyl]-28-*O*-β-D-glucopyranoside, oleanolic acid 3-*O*-[α-L-arabinopyranosyl-(1″→3′)-β-D-glucuronopyranosyl]-28-*O*-β-D-glucopyranoside, and the new compound serjanic acid 3-*O*-[β-D-glucopyranosyl-(1″→3′)-α-L-arabinopyranosyl]-28-*O*-β-D-glucopyranoside. Twelve triterpene saponins were isolated from the debittered seeds of quinoa (Zhu et al. 2002). Among them, three compounds, including 3-*O*-β-D-glucuropyranosyl oleanolic acid (1), 3-*O*-β-D-glucopyranosyl-(1→3) -α-L-arabinopyranosyl hederagenin (2), and the newcompound3-*O*-β-D-glucopyranosyl-(1→3)-α-L-arabinopyranosyl-30-*O*-methyl spergulagenate 28-*O*-β-D-glucopyranosyl ester (3), were identified for the first time from quinoa seeds. The other isolated saponins had been previously reported in quinoa.

At least 16 saponins were detected in the seeds of *Chenopodium quinoa* (Woldemichael and Wink 2001). The five previously isolated major saponins, 3-*O*-β-D-glucuronopyranosyl oleanolic acid 28-*O*-β-D-glucopyranosyl ester, 3-*O*-α-L-arabinopyranosyl hederagenin 28-*O*-β-D-glucopyranosyl ester, 3-*O*-β-D-glucopyranosyl-(1→3)-α-L-arabinopyranosyl hederagenin 28 -*O*-β-D-glucopyranosyl ester, 3-*O*-α-L-arabino pyranosyl phytolaccagenic acid 28-*O*-β-D-glucopyranosyl ester, 3-*O*-β-D-glucopyranosyl -(1→3)-α-L-arabinopyranosyl phytolaccagenic acid 28-*O*-β-D-glucopyranosyl ester, and the new saponin 3-*O*-β-D-glucopyranosyl-(1→3)-α-L-arabinopyranosyl phytolaccagenic acid were isolated and characterized.

Twenty triterpene saponins (1–20) were isolated from different parts of *Chenopodium quinoa* (flowers, fruits, seed coats, and seeds) (Kuljanabhagavad et al. 2008). Four compounds (1–4) were identified: 3β-[(*O*-β-d-glucopyranosyl-(1→3)-α-l-arabinopyranosyl)oxy]-23-oxo-olean-12-en-28-oic acid β-d-glucopyranoside (1), 3β-[(*O*-β-d-glucopyranosyl-(1→3)-α-l-arabinopyranosyl)oxy]-27-oxo-olean-12-en-28-oic acid β-d-glucopyranoside (2), 3-*O*-α-l-arabinopyranosyl serjanic acid 28-*O*-β-d-glucopyranosyl ester (3), and 3-*O*-β-d-glucuro nopyranosylserjanicacid28-*O*-β-d-glucopyranosyl ester (4). The following known compounds have not previously been reported as saponin constituents from the flowers and the fruits of this plant: two bidesmosides of serjanic acid (5, 6), four bidesmosides of oleanolic acid (7–10), five bidesmosides of phytolaccagenic acid (11–15), four bidesmosides of hederagenin (16–19), and one bidesmoside of 3β,23,30-trihydroxy olean-12-en-28-oic acid (20).

Phenol Derivatives-Alcohols, Aldehydes and Glycosides

Gorinstein et al. (2007) reported that the total phenolic content of quinoa was 600 μg GAE/g of grain dw, 96.4 mg/100 g cyanidin-3-glucoside dw, and 102 mg/100 g (+) catechin dw. Quercetin and isorhamnetin were detected in the fruit (seeds) of quinoa (Bahrman et al. 1985). Two new flavonol glycosides: kaempferol 3-apiofuranosyl (1‴→2″) rhamnopyranosyl (1‴→6″) galactoside and kaempferol 3-apiofuranosyl (1‴→2″) rhamnopyranosyl (1‴→6″) galactoside together kaempferol 3-(2,6-dirhamnopyranosyl) galactoside, the main flavonoid glycoside, were isolated from quinoa seeds (De Simone et al. 1990). Six flavonol glycosides were isolated from quinoa seeds and their structures established as kaempferol 3-*O*-[β-D-apiofuranosyl(1′–2″)]-β-D-galactopyranoside (1), kaempferol 3-*O*-[α-L-rhamnopyranosyl(1″–2″)]-β-D-galactopyranoside (2), kaempferol 3-*O*-[β-D-apiofuranosyl (1′–2″)-α-L-rhamnopyranosyl(1″–6″)]-β-D-galactopyranoside (3), kaempferol 3-*O*-(2,6-di-α-L-rhamnopyranosyl)-β-D-galactopyranoside (4), quercetin 3-*O*-[β-D-apiofuranosyl

(1′–2″)-α-L-rhamnopyranosyl(1″–6″)]-β-D-galactopyranoside (5) and quercetin 3-O-(2,6-di-α-L-rhamnopyranosyl)-β-D-galactopyranoside (6) (Zhu et al. 2001b).

Polyphenols isolated from quinoa seeds were dominated by kaempferol and quercetin glycosides; also isolated was a glucoside of vanillic acid (Dini et al. 2004). The compounds were: quercetin 3-*O*-β-D-apiofuranosyl-(1‴ → ~2″)-*O*-[α-L-rhamnopyranosyl-(1‴ → 6″)]-β-D-galactopyranoside-3′,4′-dimethyl ether (1); kaempferol 3-*O*-(2,6-di-α-L-rhamnopyranosyl)-β-D-galactopyranoside (mauritianin) (2); kaempferol 3-*O*-β-D-apiofuranosyl(1‴ → 2″)-*O*-[α-L-rhamnopyranosyl(1‴ → 6″)]-β-D-galactopyranoside(3);quercetin3-*O*-(2,6-di-α-L-rhamnopyranosyl)-β-D-galactopyranoside (4); kaempferol 3-*O*-β-D-glucuronic acid (4) and vanillic acid glucosyl ester (6).

The main phenolic acid found in quinoa seeds and sprouts was gallic acid (Paśko et al. 2008). *p*-hydroxybenzoic acid, vanillic acid, and *p*-coumaric acid, caffeic acid, and cinnamic acid were also found in the seeds and *p*-coumaric acid, syringic acid, and ferulic acid in the sprouts. The main flavonoid found in the sprouts was rutin. Vitexin, isovitexin, and morin were also detected in the sprouts, and orientin, vitexin, isovitexin, morin, and traces of hesperidin and neohesperidin in the seeds. Although sprouting conditions (daylight or darkness) had no effect on gallic acid content, light caused an increase in the amount of rutin and darkness resulted in increased amounts of isovitexin and vitexin.

Free phenolic compounds were found to be in the range of 2.746–3.803 g/kg of quinoa, while the content of bound phenolic compounds varied from 0.139 to 0.164 g/kg (Gómez-Caravaca et al. 2011). Twenty-five compounds were tentatively identified and quantified in the free polar fraction, and five compounds in the bound polar fraction. 1-*O*-galloyl-β-D-glucoside, acacetin, protocatechuic acid 4-*O*-glucoside, penstebioside, ethyl-*m*-digallate, (epi)-gallocatechin, and canthoside were tentatively identified for the first time in quinoa. The content of saponins ranged from 5.6 to 7.5% of the total composition of whole quinoa flour.

Alkaloids

Pyridine derivatives comprising five betaines were isolated from quinoa seeds: glycine betaine, trigonelline, trigonelline methylester, trigonelline glucosylester and 3-carboxy-1-(2-sulfoethyl)-pyridinium, the last two of which had not previously been reported in the literature (Dini et al. 2006).

Ecdysteroids

Five ecdysteroids were isolated from quinoa seeds: ecdysterone, makisterone A, 24-epimakisterone A, 24(28)-dehydromakisterone A, and 20,26-dihydroxyecdysone (Zhu et al. 2001a). Ecdysteroids were reported to be moulting hormones in insects. Three new phytoecdysteroids have been isolated from the seeds of *Chenopodium quinoa* and structurally identified as 20,26-dihydroxy, 28-methyl ecdysone, 20,26-dihydroxy, 24(28)-dehydro ecdysone, and 20-hydroxyecdysone 22-glycolate (Nsimba et al. 2008b).

Monoterpenoids – Hydrocarbons and Aromatic Monoterpenoids, Alcohols, Ketones, Acetates, Hydroperoxides, Peroxides, Pinene and Camphene Derivatives

The following monoterpenoid volatile compounds were detected in the essential oil of quinoa (Dembitsky et al. 2008): β-pinene, ρ-mentha-1(7),8diene, α-terpene, ρ-cymene, *trans*-ρ-menth-2-en-1-ol, γ-terpinene, camphor, pinocarvone, terpin-1-ol, *trans*-carveol, *cis*-acaridole, *cis*-isoascaridole, α-terpinyl acetate and E-caryophyllene.

Phytate

The phytate, IP6 (inositol hexaphosphate) + IP5 (inositol pentaphosphate) content in quinoa flour was reduced 4–8%, by cooking, 35–39% by germination, 61–76% by soaking, and 82–98% by fermentation (using *Lactobacillus plantarum*) (Valencia et al. 1999). The highest reduction, about 98%, was obtained after fermentation of the germinated flour. Cooking had no effect on the amount of soluble iron. Iron solubility increased, however, two to four times after soaking and germination, three to five times after fermentation

and five to eight times after fermentation of the germinated flour samples and was highly correlated to the reduction of IP6 + IP5. There was no difference between the quinoa varieties with regard to phytate reduction and iron solubility. The pH in fermented samples was reduced from 6.5 to about 3.5, due to lactic acid formation.

Some of the reported pharmacological properties of quinoa are elaborated below.

Antioxidant Activity

Six flavonol glycosides isolated from *C. quinoa* seeds exhibited antioxidant activity in DPPH assay (Zhu et al. 2001b). Two quercetine 3-glycosides exhibited much stronger activity compared to that of kaempferol 3-glycosides. The results confirmed that compounds with 3′,4′-dihydroxy substituents in the B ring had much stronger antioxidative activities than those without ortho-dihydroxy substitution in the B ring and suggested that quinoa seeds serve as a good source of free radical scavenging agents. Gorinstein et al. (2007) reported the antioxidant activity of polyphenol dry matter methanol extract of quinoa in the DPPH assay to be 30%, in the β-carotene linoleate model system to be 34% and 1.71 μM TE/g TEAC (trolox equivalent coefficient).

The antioxidant activity of quinoa extracts was found to be less correlated to the phenolics content suggesting that non-phenolic compounds may play a major role in its free radical scavenging activity (Nsimba et al. 2008a). Three new phytoecdysteroids 20,26-dihydroxy, 28-methyl ecdysone, 20,26-dihydroxy, 24(28)-dehydro ecdysone, and 20-hydroxyecdysone 22-glycolate, isolated from the seeds of *C. quinoa* exhibited DPPH scavenging ability (Nsimba et al. 2008b). Jung et al. (2006) determined the antioxidant activity of the seeds and sprouts of *C. quinoa* by using a new rapid antioxidative power method, electron spin resonance (ESR) spectroscopy. Storage time and temperature (25–55°C) had significant effects on the oxidative stability of free fatty acids, conjugated diene hydroperoxides, and hexanal used as indicators of lipid oxidation of ground quinoa (Ng et al. 2007). The interaction between storage time and temperature was not significant for conjugated diene hydroperoxides produced. The results from these tests suggested that quinoa lipids were stable for the period of time studied (30 days). With vitamin E as a naturally antioxidant occurring abundantly in quinoa, the potential for quinoa to be a new oilseed could be enhanced. Quinoa whole grain was found to have total phenolic content of 39.4 mg GAE/100 g grain and oxygen radical absorbance capacity (ORAC) of 1,641 μmol TE/100 g grain (Okarter 2012). Quinoa also contained 35.5 μmol/100 g grain ferulic acid, 13.1 μmol/100 g grain *p*-coumaric acid, 15.2 μmol/100 g grain *p*-hydroxybenzoic acid and 19.2 μmol/100 g grain vanillic acid in the insoluble bound fraction. Flavonoids (quercetin, kaempferol, catechin, and rutin) were not detected in the insoluble-bound fraction of quinoa grain. None of the phenolic compounds had any cellular antioxidant activity, most likely because these phenolic compounds did not have the structure necessary to impart cellular antioxidant activity. The data suggested that the potential health benefit of whole grain consumption in the lower gastrointestinal tract was independent of the cellular antioxidant activity of the phenolic compounds found in the insoluble-bound fraction of whole grains.

The antioxidant activity of bitter quinoa seeds as evaluated by DPPH (1, 1-diphenyl-2-picrilhydrazyl) and FRAP (ferric reducing/antioxidant power) assays was higher than that of sweet quinoa seeds. This activity principally depended on phenols and flavonoids in bitter quinoa seeds, while it was mainly due to phenol, flavonoid and carotenoid compounds in sweet quinoa seeds (Dini et al. 2010). Additionally, boiling caused a significant loss of antioxidant capacity in water.

Ten thermally processed Peruvian Andean grains (five cereals, three pseudocereals, and two legumes) were evaluated for potential type 2 diabetes-relevant antihyperglycemia and antihypertension activity (Ranilla et al. 2009). Pseudocereals such as quinoa (*Chenopodium quinoa*) and kañiwa (*Chenopodium pallidicaule*) were found to be rich in quercetin derivatives (1,131 and 943.5 μg [expressed as quercetin aglycone]/g of

sample weight, respectively) and had the highest antioxidant activity (86 and 75%, respectively). None of the Andean cereals exhibited any α-amylase inhibitory activity.

Studies demonstrated that quinoa seeds could act as a moderate protective agent against potential of fructose-induced changes in rats by reducing lipid peroxidation and by enhancing the antioxidant capacity of blood (plasma) and heart, kidney, testis, lung and pancreas (Pasko et al. 2010). Fructose administration (310 g/kg fodder for 5 weeks) to rats caused oxidative stress that was manifested by the increase in plasma malondialdehyde (MDA), and by the non-significant changes in the enzymatic antioxidant potential in plasma and most tissues. Co-administration of quinoa seeds (310 g/kg fodder) restored normal activities of some enzymes. It also influenced the oxidative stress as was evidenced by decreasing MDA in plasma, and increasing the activities of antioxidant enzymes (erythrocyte superoxide dismutase – eSOD, catalase plasma glutathione peroxidase).

Letelier et al. (2011) found that a quinoa seed coats hydroalcoholic extract, possessed thiol compounds in addition to polyphenols, recognized antioxidants. Accordingly, it inhibited microsomal lipid peroxidation and the loss of microsomal thiol content, both oxidative conditions promoted by Cu2+/ascorbate. In a study comparing fresh with the corresponding dehydrated quinoa samples, it was found that the drying operation led to reductions of 10% in proteins, 12% in fat and 27% in both fibres and ashes (Miranda et al. 2010). In fresh quinoa, potassium and copper were found to be the most and least abundant minerals, respectively. Sucrose was the predominant sugar, followed by fructose and glucose. Overall antioxidant activity was affected by drying temperatures. Thermal degradation, especially at 60, 70 and 80°C, resulted in a marked reduction in total phenol content. However, vitamin E showed an important increase at 70 and 80°C. The antioxidant capacity presented similar values at 40, 50 and 80°C due to temperature/drying time equivalent processes.

Quinoa tempeh produced by fermentation with *Rhizopus oligoporeus* was found to exhibit potent antioxidant activity (Matsuo 2005). The 80% methanol extract from quinoa-tempeh increased both activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) in the liver, and accelerated the production of 12-hydroxyeicosatetraenoic acid (12-HETE) in the lungs of rats. In rats fed vitamin E-free diets with 80% methanol extract of quinoa-tempeh, the α-tocopherol concentration, thiobarbituric acid-reactive substance (TBARS) value, and activities of GSH-Px and SOD in serum showed a similar concentration to those of the control rats fed a vitamin E-supplemented diet. However, the hepatic GSH-Px and SOD activities were higher than those in the control rats. In contrast, in rats fed a vitamin E-free diet with the 80% methanol extract of quinoa, the serum α-tocopherol level was lower, and both TBARS values of serum and liver were higher than those in the control rats.

Cytotoxicity Activity

Saponins and their aglycones from quinoa was tested for cytotoxicity in HeLa cells (Kuljanabhagavad et al. 2008). Induction of apoptosis in Caco-2 cells by four bidesmosidic saponins 1–4, and their aglycones I–III was determined by flow cytometric DNA analysis. The four compounds were: 3β-[(*O*-β-d-glucopyranosyl-(1→)-α-l-arabinopyranosyl)oxy]-23-oxo-olean-12-en-28-oicacidβ-d-glucopyranoside (1), 3β-[(*O*-β-d-glucopyranosyl-(1→3)-α-l-arabinopyranosyl)oxy]-27-oxo-olean-12-en-28-oic acid β-d-glucopyranoside (2), 3-*O*-α-l-arabino pyranosyl serjanic acid 28-*O*-β-d-glucopyranosyl ester (3), and 3-*O*-β-d-glucuronopyranosyl serjanic acid 28-*O*-β-d-glucopyranosyl ester (4). The saponins with an aldehyde group were most active.

Anti-Skin Aging Activity

Three new phytoecdysteroids, 20,26-dihydroxy, 28-methyl ecdysone, 20,26-dihydroxy, 24(28)-dehydro ecdysone, and 20-hydroxyecdysone 22-glycolate isolated from quinoa seeds demonstrated inhibitory effect on calf skin collagenase,

the enzyme involved in aging skin diseases (Nsimba et al. 2008b). All three compounds demonstrated a higher potency to inhibit this matrix metalloproteinase and to chelate the iron ion, both with respect to the number of carbonyl groups bearing their carbon skeleton, suggesting that their mechanism of action involves their ability to coordinate both ions (either the zinc ion of the catalytic domain of collagenase or the iron ion), acting as an electron donor. The results suggested that ecdysteroids might be considered as potent chemical agents to prevent or delay both collagenase-related skin damages and oxidative stress.

Antiobesity Activity

Studies by Foucault et al. (2012) demonstrated that quinoa possessed antiobesity activity in-vivo and could be used as a nutritional supplement for the prevention and treatment of obesity and obesity-associated disorders. Supplementation with quinoa reduced adipose tissue development in high-fat diet (HF) mice without modification of their body weight gain. This was associated with reduced adipocyte size and a decrease in the expression of several genes involved in lipid storage, including lipoprotein lipase and phosphoenolpyruvate carboxykinase. Additionally, quinoa markedly attenuated mRNA levels of several inflammation markers (monocyte chemotactic protein-1, CD68) and insulin resistance (osteopontin, plasminogen activator inhibitor-1 (PAI-1)) as compared to HF mice. Quinoa supplementation also reversed the effects of HF-induced down regulation of the uncoupling protein(s) (UCP(s)) mRNA levels in muscle.

Haemolytic Activity

Both bidesmosides and derived monodesmosides showed little or no antifungal activity, whereas a comparatively higher degree of hemolytic activity could be determined for monodesmosides. The haemolytic activities of triterpenoid saponins from *C. quinoa* were investigated. Results of the hemolysis test showed that the only bidesmoside to be active, chikusetsusaponin IVa 257, showed activity at 260 μg/mL, which can only be described as week. The most active saponin was its monodesmoside form. Hederagenin monodesmosides also showed strong activity (Woldemichael and Wink 2001).

Immunoadjuvant Activity

Chenopodium quinoa saponins were found to have immunoadjuvant activity (Verza et al. 2012). Two quinoa saponin fractions, FQ70 and FQ90, were found to enhance significantly the production of humoral and cellular immune responses of mice subcutaneously immunized with ovalbumin. FQ70 and FQ90 significantly enhanced the amount of anti-OVA-specific antibodies in serum (IgG, IgG1, and IgG2b) in immunized mice. The adjuvant effect of FQ70 was significantly greater than that of FQ90. Also, FQ90 significantly enhanced concanavalin A-induced splenocyte proliferation.

Anthelmintic And Anticancer Activities

Cis-acaridole and *cis*-isoascaridole had been reported as constituents of quinoa essential oil (Dembitsky et al. 2008). Ascaridole, also known as ascarisin (1,4-epidioxy-*p*-menth-2-ene), had been used as a major anthelmintic against *Ascaris* roundworm and hookworm infestations in humans, cats, dogs, horses, and pigs since the early 1900s (Duviau 1953). Ascaridole had been reported to have sedative and pain-relieving properties as well as antifungal activity (Pare et al. 1993). Ascaridole was also found to be a potent inhibitor in-vitro development of *Plasmodium falciparum* (Pollack et al. 1990), *Trypanosoma cruzi* (Kiuchi et al. 2002), and *Leishmania amazonensis* (Monzote et al. 2006). Ascaridole also showed in-vitro inhibitory activity against different tumour cell lines CCRF-CEM (human caucasian acute lymphoblastic leukaemia), HL60 (human promyelocytic leukemia cells),

MDA-MB-231 (human breast carcinoma). The findings suggested that ascaridole may be an interesting novel candidate drug for cancer treatment (Efferth et al. 2002).

Traditional Medicinal Uses

The leaves, stems and grain of quinoa have been used medicinally for wound healing, as an analgesic against toothace, disinfectant of the urinary tract and anti-inflammatory. Quinoa is also used in the case of fractures, internal haemorrhaging and as an insect repellent.

Other Uses

The whole plant is used as green fodder. Harvest residues, leaves and stalks are also used to feed cattle, sheep, pigs, llamas, alpacas, donkeys, guinea pigs, horses and poultry.

Quinoa saponins have many uses which includes detergent for clothing, washing and as an antiseptic for skin injuries. Studies showed that quinoa starch could be used as biodegradable fillers in low density polyethylene (LDPE) films (Ahamed et al. 1996).

Comments

Quinoa is easily propagated from seeds and can also be propagated using stem cuttings.

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Davidsonia pruriens

Scientific Name

***Davidsonia pruriens* F. Muell**.

Synonyms

Davidsonia pungens auct

Family

Cunoniaceae also placed in Davidsoniaceae

Common/English Names

Davidson plum, Davidson's Plum, Davidsonia Plum, Queensland Davidson plum

Vernacular Names

Australia: Do-rog, Ooray (Aboriginal);

Origin/Distribution

The fruit is native to Australia, endemic to north-eastern Queensland from Cardwell area to Cooktown and inland to near Atherton.

Agroecology

Its natural habitat is in the tropical rainforest of north-east Queensland, from near sea level to 1,000 m altitude. The plant thrives under shade or partial shade in the humid rainforest surrounds.

Edible Plant Parts and Uses

The fruits, while edible, are not particularly palatable. Its aroma has been described as earthy, like fresh beetroot with slight pickled notes. Its taste is sour with some astringency and slight bitterness.

The fruits make excellent jams, sauces, cordial and a full-flavoured, dry red wine. The fruit is also utilised as natural food colourant in sauces, ice cream and drinks.

Studies showed that Davidson plum extract was suitable as a source of anthocyanin-based food colorant and extract from Tasmania pepper leaf can be used as a co-pigment for Davidson's plum anthocyanins (Jensen et al. 2011).

Botany

A small slender tree 6–8 (–12)m high, with a bole not exceeding 30 cm and with brown to dark grey, flaky bark and indumentum on all aerial parts

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Plate 1 Sapling of Davidson plum

Plate 2 Pinnate leaf with dentate leaflets

during the tenth leaf sapling stage (Plate 1). Leaves alternate, pinnate with (7) 9–19 leaflets, petiole 10–30 cm long, stipules persistent and conspicuous, hirsute, cordate to suborbicular, green, margin dentate, rachis toothed, juvenile leaves winged (Plates 2 and 3). Leaflets (12–) 18–35(–46) cm long, (6–)8–12(–16) cm wide,

Plate 3 Leaf with toothed rachis

apex acute to acuminate, base cuneate to obtuse, margin secondarily dentate, veins 15–27 pairs, upper surface green slightly glossy, hirsute on both surface, petiolules 0–5 mm. Terminal leaflet obovate and largest, lateral leaflets lanceolate to oblong or to oblong-ovate or oblong-obovate, basal leaflet pair broad –ovate to ovate. Inflorescences mostly cauliflorous, pendent, open, paniculate, usually more than 30 cm long with 2–24 lateral spikes, amplexicaul bracts and small sessile bracteoles. Flowers 4- or 5-merous, dark pink; sepals 5.0–8.0 mm long, recurved, connate basally, pink, outer surface hirsute, inner surface pubescent, persistent; stamens with 3.5–4.6 mm long filaments, oblong, yellow anthers; ovary densely hirsute; styles 2 (or 3), divided almost to base, glabrous. Fruit obovoid or ellipsoid, laterally compressed, 3.8–6.0 cm long by 3.0–5.3 cm wide, purple-black to blue-black, glaucous, mesocarp dark red (Plate 4), with a distinct dorsal crest, usually containing two laterally compressed pyrenes with fimbriate or laciniate margins. Each pyrene contains an ovate to broadly ovate seed.

Nutritive/Medicinal Properties

Food value of ripe Davidson plum flesh was reported as: energy 264 kJ, moisture 78.2 g, protein 1 g, N 0.16 g, fat 0.2 g, ash 1.1 g, fructose 2.5 g, glucose 1.3 g, total sugars 3.9 g, starch 10.4 g, available carbohydrates 14.3 g, Ca 16 mg,

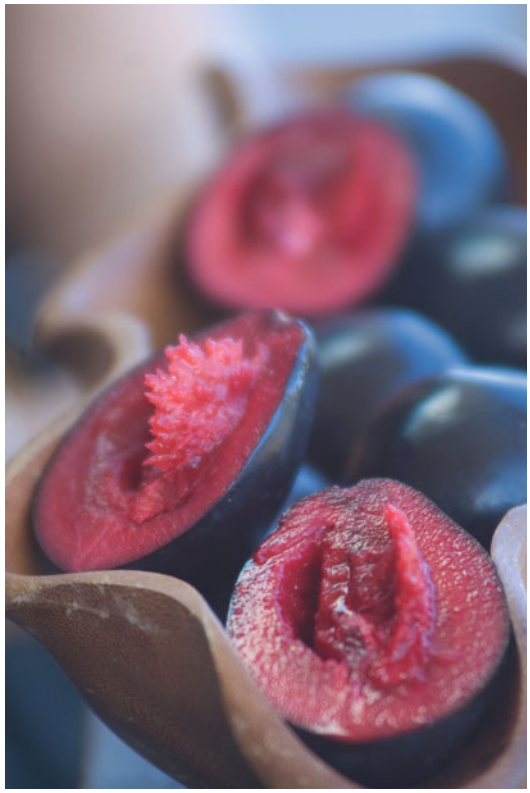

Plate 4 Ripe Davidson plum halved to show the red flesh (G Mcguire)

Mg 27 mg, P 18 mg, K 364 mg, Na 45 mg, niacin equivalents 0.17 mg, vitamin C 30 mg, total folates 29 μg, α-carotene 16 μg, β-carotene 65 μg, cryptoxanthin 14 μg, β-carotene equivalents 80 μg, retinol equivalents 13 μg (Arcot 2006). Other analyses conducted by Konczak et al. (2009, 2010) reported the following nutrient values for Davidson's plum: dry matter 7.1 g; minerals (mg/100 g DW) – Zn 0.426 mg, Mg 138.1 mg, Ca 217.35 mg, Fe 1.24 mg, P 94.45 mg, Na 1.77 mg, K 1465.5 mg, Mn 19.55 mg, Cu 0.638 mg, Mo 11.0 mg, K:Na ratio 828.0; vitamins (mg/100gDW) – α-tocopherol 0.52 mg, β-tocopherol 0.38 mg, γ-tocopherol 0.26 mg, vitamin E 1.16 mg and total folate 40 μg/100 g DW; lutein 1.15 mg/100 g DW, chlorophyll b 1.96 mg/100 g DW, total phenolics 48.60 mg Gallic Acid Equivalent/g DW and total anthocyanin 47.80 mg C-3 G (cyaniding 3-glucoside) Eq/g DW. Major phenolic compounds (mg/g DW) detected in the fruit include: delphinidin sambubiose 22.70 mg, cyaniding sambubiose 2.08 mg, peonidin sambubiose 7.07 mg, pelargonidin sambubiose traces, malvinidin sambubiose traces and possibly myricetin, rutin and quercetin hexoside.

Safety analysis carried out by Hegarty et al. (2001) reported Davidson plum fruit to contain virtually no oxalic acid, cyanogens nor saponins, the results were all below the limit of detection of 0.08 g/100 g for oxalic acid, 0.1 mg/100 g for cyanogens, and 0.6 mg/100 g for saponins.

Antioxidant Activity

The total reducing capacity of five Australian fruits including Davidson plum was 3.5–5.4-fold higher than that of blueberry as assayed ferric reducing antioxidant power, and the radical scavenging activities as evaluated by 2,2-diphenyl-1-picrylhydrazyl assay of was also higher (Netzel et al. 2006). The total phenolic level by Folin-Ciocalteu assay highly correlated with the antioxidant activity. Furtheranalyses revealed simple anthocyanin profiles of one to four individual pigments, with cyanidin as the dominating type.

Davidson plum was found to have high antioxidant and reducing power activity (Konczak et al. 2009, 2010). It exhibited high total Oxygen Radical Absorbance Capacity (ORAC) expressed in μmol TE (Trolox equivalent/g DW) of 1192.65 μmol, ORAC-H(hrophilic) of 982.41 μmol, ORAC-L (lipophilic) of 210.38 μmol and total reducing activity of 670.7 μmol Fe^{+2}/g DW assayed by ferric reducing antioxidant power (FRAP). Its ORAC value was 2.7 fold higher than blueberry, contribution of compounds present in the hydrophilic fractions was 82.4%. Relatively high antioxidant activity 17.6% was detected in the lipophilic fraction. Lipophilic compounds like vitamin E, lutein, carotenoids and chlorophyll were possible sources of this activity. High positive correlation was found between the phenolic compounds and antioxidant capacity of the hydrophilic extract

Other Uses

Its decorative foliage has made it a popular ornamental plant for a large container and it will tolerate extended periods indoors.

Comments

The plant is usually propagated from fresh seed but cuttings are also successful.

Davidsonia is found to comprise three species; *D. pruriens* F. Muell., the type species, from north-eastern Queensland; *D. jerseyana* (F. Muell. ex F.M. Bailey) G. Harden & J.B. Williams, a known variety from north-eastern New South Wales here elevated to specific rank; and *D. johnsonii* J.B. Williams & G. Harden, a well-known but hitherto undescribed species from north-eastern New South Wales and south-east Queensland (Harden and Williams 2000).

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Punica granatum

Scientific Name

***Punica granatum* L.**

Synonyms

Granatum punicum St.-Lag., *Punica florida* Salisb., *Punica grandiflora* hort. ex Steud., *Punica multiflora* hort. ex Siebold & Voss, *Punica nana* L., *Punica spinosa* Lam.

Family

Lythraceae, also placed in Punicaceae.

Common/English Name

Pomegranate

Vernacular Names

Afghanistan: Poste-Anar;
Albanian: Shegë;
Arabic: Darabhte-Naiy, Gulnar, Julnar, Rana, Roman, Rumman Shajratur Rumman;
Armenian: Noor, Nur;
Azerbaijan: Hap, Nar;
Brazil: Roma, Romeira, Romazeira;
Burmese: Talebin, Thale, Salebin;
Catalan: Magraner;
Chinese: An Shih Hu, Shi Liu, Shi Liu Pi;
Croatian: Nar, Šipak;
Czech: Granátové Jablko, Granátovník, Granátovník Obecný, Granátovník Punský, Marhaník;
Danish: Granatæble;
Dutch: Granaatappel, Granaatboom;
Eastonian: Granaatõun, Harilik Granaadipuu;
Esperanto: Granato, Granatujo;
Finnish: Granaattiomena;
French: Balaustier, Grenade, Grenadier, Grenadier Commun, Grenadier D'europe, Pommier De Carthage;
Georgian: Broceuli;
German: Echte Granate, Granatbaum, Granatapfel, Granatapfelbaum, Granatapfelstrauch, Grenadine;
Greek: Rodi, Ródi, Rodia, Rodiá;
Guatemala: Granad;
Hebrew: Rimmon, Rimon;
Hungarian: Gránátalma, Közönséges Gránátalma, Pomagránát, Termesztett Gránátalma;
Icelandic: Granatepli, Kjarnepli;
India: Dalim (Assamese), Dalim, Dalimgachh (Bengali), Dadim, Danoi, Daroona, Darooni (Dogri), Dadam, Dadamna Bee (Gujarati), Amar, Anaar, Anar, Anar-Ka-Per, Anar-Ke-Per, Anardana, Auar, Dalimo, Dalimu, Dalmiya, Daram, Daran, Darim, Darimu, Daroo, Daru, Dhalim, Dharimb, Dharu, Doran, Gulnar-Ka-Per, Nirgal, Ringal, (Hindu), Daadima, Daalimbe, Daalimbe Mara, Dalimba, Dadima, Dadimbe, Dalimabay, Dalimba, Dalimbare, Dalimbe, Dalimbe-Gida, Dalimbuhannu, Dhalimbe, Huli

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Daalimbe Mara, Hulidalimbe, Hushidalimbe, Husidalimbe (Kannada), Dalimb (Konkani), Dadimam, Dadiman, Madala, Matalam, Matalam-Cheti, Matalanarakam, Pumatalam, Raktabijam, Talimadalam, Talimatalam, Urumampalam, Urumampazham, Uruyampalam (Malayalam), Kaphoi, Kamphoi (Manipuri), Anārdānā, Anardana, Daalimb, Dalimb, Dalimba, ḍāḷīmb, ḍāḷīmbāce Dāṇe (Marathi), Theibuhfai (Mizoram), Dalimba, Nagarata, Theibuhfai (Oriya), Anar (Punjabi), Bijapura, Dadima, Dadima-Phalam, Dadimah, Dadimam, Dadimaphalam, Dadimasara, Dadimavrikshaha, Dadimba, Dalika, Dantabijaka, Darimba, Ija, Karaka, Kuchaphala, Kuttima, Lohitapushpaka, Lohitapuspaka, Madhubija, Milapatra, Milapatraka, Mukhavallabha, Nagarata, Parvarut, Phalamla, Phalashadava, Pindapushpa, Pindira, Raktabija, Raktapushpa, Shukadana, Shukavallabha, Sunila, Suphala, Svadvamla, Valkaphala, Vrittaphala (Sanskrit), Arocakana-cani, Arulmaram, Arumaram, Atalai, Catimataki, Catipancu, Cerukkam, Cikappumatalai, Civappuccantanikacceti, Civappuccantanikam, Civappumatalai, Cukacanam, Cukatanam, Cukavallam, Cukkilestam, Ekamuli, Inippu Matalai, Inippumatalai, Inippumatulai, Irattapittapicakam, Irattavicam, Irattavitacceti, Irucakam, Irucukam, Kalkapalam, Kalumal Madalai, Karkapalacceti, Karkapalam, Kavaiyal, Kovarttanam, Kucapalam, Kucapalamaram, Kukarumulimpam, Kurucattam, Kuttinam, Maathulai, Madalai, Madalai-Ch-Chedi, Madalai-P-Pazham, Madalam, Madalangkai, Madalum Vayr, Madhalai, Madhulam, Madhulami, Madulai, Madulam, Madulungam, Magilam Palam, Malaki, Mandulai, Manimatari, Manipicam, Manipicamaram, Manivicam, Maniviciramam, Maniviciramaram, Maralam, Maralam, Maralamaram, Marayam, Matalaimacaki, Matalaimacakimaram, Matalam, Matalampu, Matalunkam, Mathalai, Mathulai, Matulai, Matulainkam, Matulam, Matulankam, Matulankam, Matulankamaram, Matulunkam, Matulunkamaram, Matuvicam, Nallamatulai, Narumatulam, Narumatulam, Nattumatalai, Palacatavam, Palacatavamaram, Palacavatam, Palapuracceti, Palapurakam, Palapurakamaram, Picapuram, Picapuram, Pintirakacceti, Pintirakam, Pintiram, Piraputam, Pu-Madalai, Pulimadalai, Pulippumatulai, Pumadalai, Rumman, Tacanapicam, Tadimadalai, Tadimam, Talimpamayati, Tantapicakam, Tantapicam, Tantapijakam, Tatimakkani, Tatimam, Tatimatulai, Tittippumatulaimaram, Tittippuppalai, Tucakamatulai, Tucakatitam, Tucakatitamaram, Tuccam, Tuccam, Tusagam, Urucakam, Urumamapalam, Uruntanirpputpi, Utirapantam, Varaimatalacci, Varaiyutakam, Vinnarakam, Vinnarakamaram, Vintapurakam, Viraiyotakam, Virotam, Viruttapalam (Tamil), Daadimamu, Daadimba, Daalimba Chettu, Daalimma, Daanimma, Dadima, Dadima-Chetu, Dadimamu, Dadimba, Dadima Pandu, Dadimma, Dalimba, Dalimba-Chettu, Dalimma, Dalunimma, Danima, Danimma, Danimmapandu, Danimma-Chettu, Dhanimmapandu, Karakamu, Pulladaanimma, Pulladanimma, Puvvudaanimma, Puvvudanimma, Thiyyadaanimma, Tiyyadanimma (Telugu), Aab-E-Amar, Amardana, Anaar, Anar, Anar Dana, Anar Dona, Anar Shirin, Anardana, Anaspal, Goolnar, Gul Amar, Gul Anar, Gul-I-Anar, Gulnar, Gulnar (Gulnar Farsi), Hab-I-Qilqil, Naspal, Poast Anar, Rub Amar Shirin, Rub Anar, Rub Anar Shirin, Rub Anar Tursh, Rub-I-Anar Shirin, Sharbat Anarshirin, Tub-I-Anar Shirin (Urdu);

Indonesia: Delima, Gangsalan;

Iran: Ìgolnar-E-Farsiî;

Italian: Granato, Melagrano, Melogranato, Melograno, Melograno Bonsai, Melograno Da Fiore, Pomo Granato, Pomo Punico;

Japanese: Sekiryu, Zakuro;

Kazakh: Anar, Anar Ağaşı, Anar Ağašy, Ahap;

Khmer: Totum;

Korean: Seok Ryu, Seongnyu, Sokryunann, Songnyu;

Kurdish: Henar;

Laotian: Kok Mak Phi La,Ph'iilaa;

Luganda: Nkomawawanga;

Malaysia: Buah Delima;

Maltese: Rummiena;

Nepal: Anaar, Daariim, Darmi;

Norwegian: Granateple;

Pakistan: Anar;

Papiamento: Granatapel;

Persian: Anaar, Darakhte-Gulnar, Darakhte-Nar, Dulim, Dulima, Gulnar, Gulnar (Flowers), Nar;

Philippines: Delima, Granada (Tagalog);
Polish: Granat, Granatowiec Właściwy;
Portuguese: Romã, Romãnzeira, Romãnzeira-De-Jardim, Romeira;
Romanian: Rodie;
Russian: Granat, Granatnik;
Samoan: Limoni;
Sardinian: Melagranada;
Serbian: Hap;
Slovak: Granátové Jablko, Granátové Semená, Granátovník Púnsky;
Slovenia: Granatno Jabolko;
Spanish: Granada, Granado, Grenada, Grenadier, Mangraner, Mangrano;
Swedish: Granatäpple;
Swahili: Komamanga, Kudhumani;
Syrian: Ruman;
Thai: Ma Ko, Thap Thim (Central), Phila (Nong Khai), Bakoh (Northern);
Tongan: Pomikanite;
Turkish: Rumman, Nar, Nar Cğacı;
Ukrainian: Granat;
Vietnamese: Cây Lựu, Lựu, Thap Lựu;
Yiddish: Milgraym.

Origin/Distribution

The pomegranate tree is native from the Middle east to the Himalayas in northern India. It has been cultivated and naturalised since ancient times throughout the Mediterranean region of Asia, Caucasus, northern Africa and Europe. The fruit has manifold uses as it is today and was featured in Egyptian mythology and art, in the Old Testament of the Bible and in the Babylonian Talmud. From its native range, it was introduced to central and southern India and southeast Asia. It was reported growing in Indonesia in 1416. It was introduced into Latin America and California by the Spanish in 1796, it is now grown in California and Arizona. It has been widely cultivated throughout India and drier parts of southeast Asia and tropical Africa. The most important growing regions are Egypt, China, Afghanistan, Turkey, Syria, Pakistan, Bangladesh, Iran, Iraq, India, Myanmar and Saudi Arabia. There are some commercial orchards in Israel on the coastal plain and in the Jordan Valley.

Agroecology

Pomegranate is primarily mild-temperate to subtropical and naturally adapted to regions with cool winters and hot summers, but can also be grown in warm tropical areas, such as in southern India, southeast Asia and various islands in the Caribbean. Areas with mean annual temperature of 20–24°C is ideal. It suffers severe, irrecoverable injuries at temperatures below –11.0°C. The plant thrives in a semi-arid condition with mean annual rainfall of 500 to 1,000 mm and is extremely drought-tolerant. It does not flower and fruit well in very humid and wet climates. It is cultivated up to altitudes of 2,000 m as occur throughout the western range (Baluchistan, N. & S. Waziristan, NWFP, Kurram, Dir, Chitral) in Pakistan. The species is adaptable to a wide range of soil types including soils on which other fruit species will not grow. It thrives on calcareous soil, alkaline soil, gravelly soil and on deep, acidic loams. For commercial cultivation well-drained, heavy, light and medium soils are preferred although it can withstand seasonal waterlogging. Irrigation is required to sustain high yields in drier areas.

Edible Plant Parts and Uses

The fruit is relished fresh, out of hand by quartering the fruit and lifting out the rind to exposed the juice-laden arils around the seeds, both of which are eaten. The fruit is also consumed as juice which is the basis for lemonades or a beverage similar to wine. In the Middle east, Caucasus and India, pomegranate juice is a very popular beverage. For beverage purposes, the juice is usually sweetened. Pomegranate juice is widely made into grenadine syrup for use in mixed drinks, cocktails and often processed into wine. In Saudi Arabia, the juice sacs may be frozen intact or the extracted juice may be concentrated and frozen, for future use. The juice can be processed into jellies by the addition of pectin and sugar.

Pomegranate is also used in food and as a spice condiment. Fresh pomegranate arils are used in preparation of curd rice *Dadhojanam* (Telugu) in Andhra Pradesh in India. In northern India, the

reduced juice is used for desserts and for marinating and tenderising meat due to its proteolytic enzymes. Dried pomegranate arils are used in various cuisines such as trail mix, granola bars, or as toppings for ice-cream, yogurt and salads. Dried whole arils are commonly sold in ethnic Indian subcontinent markets. They impart a subtle, sweet-sour and tart flavour popular in Punjab and Gujarat. Dried pomegranate seeds, '*anardana*', has culinary importance as spice for vegetable and legume dishes in Northern India and in Pakistani cuisine. These dried seeds are used as an acidic condiment for chutney and curry preparation. The dried seeds can also be ground and used, which results in a deeper flavoring in dishes and prevents the seeds from getting stuck in teeth. Seeds of the wild pomegranate variety known as *daru* from the Himalayas are renown as quality sources for this spice. In Turkey, pomegranate seeds are also used in salads and sometimes as garnish for desserts such as *güllaç*. In Greece and Cyprus, pomegranate is used to make *kolliva*, a mixture of pomegranate seeds and sugar.

Pomegranate juice can also be processed into a concentrate, syrup and sauces for juice in food dishes and desserts. In Iran, a traditional recipe *fesenjan* is made from a thick pomegranate sauce and ground walnuts used for duck and poultry or in a popular pomegranate soup *ash-e nar*. In Azerbaijan, pomegranate sauce *narsharab*, made from pomegranate juice, is served with fish or *tika kabab* (grilled, roasted or stewed meat). In Turkey, pomegranate sauce called *nar ekşisi* is used as a salad dressing, to marinate meat, or simply to drink straight. Pomegranate syrup used in *muhammara*, a roasted red pepper, walnut, and garlic spread popular in Syria and Turkey. Pomegranate is also popular in Greek cuisine such as *kollivozoum*i, a creamy broth made from boiled wheat, pomegranates and raisins, legume salad with wheat and pomegranate, traditional Middle Eastern lamb kebabs with pomegranate glaze, pomegranate eggplant relish, and avocado-pomegranate dip. Pomegranate is also processed into a liqueur and fruit confectionery used as ice-cream toppings or mixed with yogurt and jam on toast.

Plate 1 Foliage of pomegranate shrub

Botany

A deciduous, much-branched, small tree or shrub 1.5–6 m high with a smooth, dark grey bark (Plate 1). Branches are terete, opposite and branchlets usually ending in spines. Leaves are opposite, glabrous, coriaceous, glossy green, entire, simple, oblong-lanceolate (Plates 1, 2 and 3) to obovate or elliptic, 19–35(−50) × 8–12 (−15) mm, subpetiolate, apex sub-actue to obtuse. Flowers are large, showy, scarlet red or white, bisexual, to 4 cm across, solitary or clustered at the shoot apex (Plates 2 and 3). Calyx campanulate, reddish or purplish with six triangular, persistent lobes, Petals 6, broadly obovate, wrinkled, alternating with the sepal lobes, stamens numerous, multiseriate, persistent, inserted on flower tube, Ovary subglobose, inferior with three cells in two-series, style one thick, reddish, stigma simple slightly bilobed. Fruit globose to subglobose, 6–8 cm in diameter, pale red to scarlet to purple or brownish,; the rind thick and coriaceous (Plates 4, 5, 6 and 7). Internally, the fruit is partitioned by thin leathery yellow septa into compartments filled with transparent sacs (arils) filled with tart, flavourful, fleshy, juicy, red, pink or whitish pulp (Plates 7 and 8). In each sac, there is one white, pink or red, angular, soft or hard seed 10–13 mm long.

Plate 2 Pomegranate flowers and leaves

Plate 4 Maturing pomegranate fruits

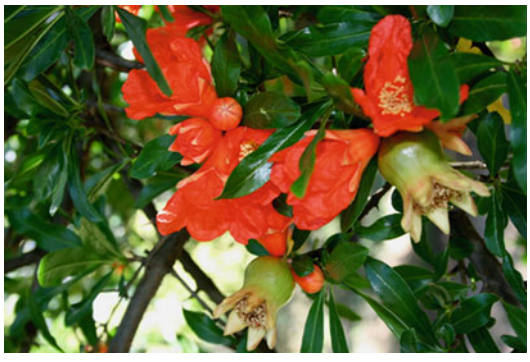

Plate 3 Close-up flowers, leaves and young fruits

Plate 5 Graded harvested pomegranate on sale in a supermarket

Nutritive/Medicinal Properties

Fruit Nutrients

Food value of raw, pomegranate fruit (refuse 44% skin and membrane) per 100 g edible portion based on the California Wonderful variety is as follows (USDA 2012): water 77.93 g, energy 83 kcal (346 kJ), protein 1.67 g, total lipid (fat) 1.17 g, ash 0.53 g, carbohydrate 18.70 g; fibre (total dietary) 4 g, total sugars 13.67 g, minerals – calcium 10 mg, iron 0.30 mg, magnesium 12 mg, phosphorus

Plate 6 Bruised, ungraded pomegranate fruit on sale in local market

Plate 7 Whole ripe fruit and halved to show the edible aril sacs

Plate 8 Close up view to show the aril sacs

36 mg, potassium 236 mg, sodium 3 mg, zinc 0.35 mg, copper 0.158 mg, manganese 0.119 mg, selenium 0.5 µg; vitamins – vitamin C (total ascorbic acid) 10.2 mg, thiamin 0.067 mg, riboflavin 0.053 mg, niacin 0.293 mg, pantothenic acid 0.377 mg, vitamin B-6 0.075 mg, folate (total) 38 µg, total choline 7.6 mg, vitamin E (α-tocopherol) 0.60 mg, vitamin K (phylloquinone) 16.4 µg, lipids – fatty acids (total saturated) 0.120 g, 12:0 (lauric acid) 0.006 g, 14:0 (myristic acid) 0.006 g, 16:0 (palmitic acid) 0.070 g, 18:0 (stearic acid) 0.038 g; fatty acids (total monounsaturated) 0.093 g, 16:1 undifferentiated (palmitoleic acid) 0.012 g, 18:1 undifferentiated (oleic acid) 0.077 g, 20:1 (gadoleic acid) 0.004 g; fatty acids (total polyunsaturated) 0.079 g, 18:2 undifferentiated (linoleic acid) 0.079 g, total *trans* fatty acids 0.009 g, campesterol 1 mg and β-sitosterol 4 mg.

Nutrient value of bottled pomegranate juice per 110 g edible portion (USDA 2012) is water 85.95 g, energy 54 kcal(228 kJ), protein 0.15 g, total lipid 0.29 g, carbohydrate 13.13 g, total dietary fibre 0.1 g, total sugars 12.65 g, glucose 6.28 g, fructose 6.37 g, ash 0.49 g, calcium 11 mg, iron 0.10 mg, magnesium 7 mg, phosphorus 11 mg, potassium 214 mg, sodium 9 mg, zinc 0.09 mg, copper 0.021 mg, manganese 0.095 mg, selenium 0.3 µg; vitamins – vitamin C (total ascorbic acid) 0.1 mg, thiamin 0.015 mg, riboflavin 0.015 mg, niacin 0.233 mg, pantothenic acid 0.285 mg, vitamin B-6 0.040 mg, folate (total) 24 µg, total choline 4.8 mg, vitamin E (α-tocopherol) 0.38 mg, vitamin K (phylloquinone) 10.4 µg. fatty acids (total saturated) 0.077 g, 12:0 (lauric acid) 0.004 g, 14:0 (myristic acid) 0.004 g, 16:0 (palmitic acid) 0.0744 g, 18:0 (stearic acid) 0.024 g; fatty acids (total monounsaturated) 0.050 g, 16:1 undifferentiated (palmitoleic acid) 0.008 g, 18:1 undifferentiated (oleic acid) 0.049 g, 20:1 (gadoleic acid) 0.003 g; fatty acids (total polyunsaturated) 0.050 g, 18:2 undifferentiated (linoleic acid) 0.050 g. The edible portion of pomegranate fruit constituted 52% of the total fruit weight, comprising 78% juice and 22% seeds (El-Nemr et al. 1990). The fresh juice contained 85.4% moisture, 10.67% total sugars, 1.4% pectin, 0.1 g/100 mL total acidity (as citric acid), 0.7 mg/100 mL ascorbic acid, 19.6 mg/100 mL free amino nitrogen and 0.05 g/100 mL ash. The seeds were a rich source of total lipids (27.2%), protein (13.2%), crude fibre (35.3%) and ash (2.0%), and also contained 6.0% pectin and 4.7% total sugars. The iron, copper, sodium, magnesium and zinc contents of the juice were lower than

those of seeds, except potassium which was 49.2 ppm in the juice. The seed lipids had a refractive index of 1.518, melting point 13.0°C, iodine value 74.2, acid number 1.1, unsaponifiable matter 0.7%, saponification value 188.9, ester value 187.8 and glycerol content 10.3%. The lipids contained 11 fatty acids, with caprylic (36.3%), the predominant acid, followed by stearic acid (22.5%); linoleic acid (10.3%) and oleic acid (5.1%). The saturated fatty acids of the seed lipids constituted 83.6% of the total fatty acids content.

Vitamin C content in 20 different Turkish cultivars of pomegranate had a range of 312–1.050 mg/100 g, oil content a range of 2.41–3.73%, sterol content a range of 5.78–8.43%, anthocyanin content a range of 2,100–4,400 mg/L, potassium a range of 250–1,200 ppm, calcium a range of 35–326 ppm, magnesium a range of 176–427 ppm, iron a range of 21–46 ppm, sodium a range of 35–76 ppm, and phosphorus a range of 12–43 ppm (Dumlu and Gürkan 2007). Elfalleh et al. (2009) found total sugars of pomegranate juice comprised about 7 g/100 mL fructose and about 8 g/100 mL glucose, soluble proteins about 7 g/L, 9.46 mg/100 mL of phosphorus, and 271.94 mg/100 mL of potassium. The peel contained 9.43 and 210.86 mg/100 g of phosphorus and potassium respectively. The sodium contents were nearly 7 mg/100 mL in both peel and juice.

Nutrient composition of the juice for most components was comparable to the whole fruit. Protein and fat values were higher in the whole fruit compared to the juice due to the seeds, which are 10% of the aril (juice sac) weight (Thomas and Gebhardt 2008). Pomegranate aril juice was reported to provide about 16% of an adult's daily vitamin C requirement per 100 mL serving, and to be a good source of vitamin B5 (pantothenic acid), potassium and antioxidant polyphenols. The tocopherol (α-tocopherol, γ-tocopherol, and δ-tocopherol) contents were, respectively, 165.77, 107.38, and 27.29 mg/100 g from dry pomegranate seed (Elfalleh et al. 2011a, b).

A total of 18 compounds were found in pomegranate aroma profiles, including monoterpenes, aldehydes, alcohols, monoterpenoids and linear hydrocarbons (Calín-Sánchez et al. 2011). The most abundant compounds were *trans*–2-hexenal, 3-carene, α-terpinene and α-terpineol. The total concentration of volatiles ranged from 1.7 to 10.9 g/kg. Overall consumer preference of pomegranate juices was associated with the presence of monoterpenes such as α-pinene, β-pinene, β-myrcene, limonene and γ-terpinene. The presence of aldehydes such as hexanol, hexanal and *cis*-3-hexenol was correlated with poor overall consumer liking. High overall consumer liking was associated with intense and acceptable fresh pomegranate odour and flavour (high scores of satisfaction degree), medium intensity of red colour and low sourness.

Other Fruit Phytochemicals

Pomegranate is a fruit rich in polyphenols that include flavonoids, tannins and hydrolyzable tannins (Gil et al. 2000; Seeram et al. 2005a, b). Pomegranate contain a complex mixture of gallotannins, ellagitannins, ellagic acid and anthocyanins (Madrigal-Carballo et al. 2009). Pomegranate juice was found to be rich in tannins, anthocyanins, ellagic acid derivatives, and hydrolyzable tannins (Gil et al. 2000). The predominant organic acid in pomegranate was citric acid followed by malic acid (Pande and Akoh 2009). The peel fraction had the highest total hydrolyzable tannins content (4,792.3–6,894.8 mg/100 g of FW).

A total of 35 dimers of flavanol-anthocyanin adducts were detected, consisting of mono- and disubstituted hexoside derivatives of the adducts between the flavan-3-ols (epi)gallocatechin, (epi)catechin and (epi)afzelechin and the anthocyanidins delphinidin, cyanidin and pelargonidin in pomegranate juice (Sentandreu et al. 2010). Anthocyanidins found in pomegranate fruit included: delphinidin, cyanidin, and pelargonidin (Noda et al. 2002). Pomegranate fruit was reported to contain ellagic acid, gallagic acid, punicalins and punicalagins (Reddy et al. 2007); ellagic acid, caffeic acid, luteolin and punicic acid (Lansky et al. 2005a, b); pelargonidin-3-galactose, cyanidin-3-glucose, gallic acid, quercetin, and myricetin (Naz et al. 2007); gallic

acid, methyl gallate, ellagic acid, (+) catechin, isoquerecitrin, D-mannitol, ursolic acid, oleanolic acid, β-sitosterol and daucosterol (Rena et al. 2009). Pomegranate fruit was found to have a low level of indolamines (8–12 μg/g serotonin, 4–9 μg/g tryptamine, and 13–29 ng/100 g melatonin) (Badria 2002). Gözlekçi et al. (2011) found that in all the Turkish pomegranate cultivars the highest levels of total phenolic content were obtained from the peel extracts. The total phenolic content ranged from 1,775.4 to 3,547.8 mg gallic acid equivalent (GAE)/L among the cultivars. However, the total phenolic content of pomegranate juice and seed extract ranged from 784.4 to 1,551.5 mg GAE/L and 117.0–177.4 mg GAE/L, respectively. Four phenolic compounds were identified and quantified in pomegranate peel and pulp: 2 hydroxybenzoic acids (gallic and ellagic acids) and 2 hydroxycinnamic acids (caffeic and *p*-coumaric acids) (Elfalleh et al. 2011a).

Ellagitannins isolated from pomegranate pericarp included: inhibitors punicalin, punicalagin, granatin B, gallagyldilactone, casuarinin, pedunculagin, tellimagrandin I, gallic acid, granatin A, corilagin and ellagic acid (Satomi et al. 1993). Pomegranate fruit peel had been reported to be a rich source of hydrolyzable tannins called ellagitannins (ETs); pomegranate ETs were found to show potent antioxidant, antiatherosclerotic and anticancer activities (Seeram et al. 2005b). The major fruit peel ETs were punicalagin (80–85% w/w) and ellagic acid (EA; 1.3% w/w) and unquantified amounts of punicalin and ellagitannin-glycosides (hexoside, rhamnoside and pentoside). Pomegrante fruit peel is currently an underutilized food by-product with potential to develop phytoceuticals with potential health benefits or to develop products for use in the cosmetic and food biopreservative industries (Seeram et al. 2005b). Prodelphinidins and gallocatechins including gallocatechin, gallocatechin-(4–8)-catechin, gallocatechin-(4–8)-gallocatechin and catechin-(4–8)-gallocatechin were identified from pomegranate peels (Plumb et al. 2002). Luteolin, luteolin 7-*O*-glucoside, kaempferol, kaempferol-3-*O*-glucoside, kaempferol-3-*O*-rhamnoglycoside and quercetin were found in the fruit peel (van Elswijk et al. 2004). Of the ellagitannins isolated from pomegranate pericarp, seven namely punicalin, punicalagin, granatin B, gallagyldilactone, casuarinin, pedunculagin and tellimagrandin I were found to be active carbonic anhydrase inhibitors and four namely gallic acid, granatin A, corilagin and ellagic acid to be weakly active inhibitors. The type of inhibition by three and seven punicalagin and gallagyldilactone was found to be noncompetitive. A new antifungal peptide designated as pomegranin with a molecular mass of 11 kDa, was isolated from fresh pomegranate peels (Guo et al. 2009). Epicatechin, epigallocatechin 3-gallate, flavan-3-ol, catechin were found in the fruit peel and juice (de Pascual-Teresa et al. 2000). Pomegranate fruit and juice were found to contain the following lignans: isolariciresinol, medioresinol, matairesinol, pinoresinol, secoisolariciresinol and syringaresinol (Bonzanini et al. 2009). Total lignin contents in the seeds was determined as 36.1 μg/g, in wood knots 17.8 μg/g, in fruit pulp 11.2 μg/g and in the endocarp.3.3 μg/g. Syringaresinol was most abundant in the seed (23.5 μg/g), pinoresinol in knots (8.9 μg/g), pulp (7.4 μg/g) endocarp (3.3 μg/g) and juice (2.1 μg/g). Lignans were also found in two concentrated juices and three pomegranate beverages at levels of 0.4–4.4 μg/g. In addition to the peel, mesocarp, and twigs, lignans were detected in two juices obtained from entire pomegranate fruits, four commercial juices, and three encapsulated pomegranate extracts (Fischer et al. 2012). Isolariciresinol was the predominant lignan with contents of 5.0, 10.5, and 45.8 mg/kg dry matter in processed pomegranate mesocarp, peel, and twigs, respectively.

Six anthocyanin pigments identified as delphinidin 3-glucoside, delphinidin 3,5-diglucoside, cyanidin 3-glucoside, cyanidin 3,5-diglucoside, pelargonidin 3-glucoside and pelargonidin 3,5-diglucoside were found to be responsible for the red colour of pomegranate juice (cv 'Mollar') (Gil et al. 1995). The fruit skin contained only the cyanidin and pelargonidin derivatives. Generally, there was an increase in juice pigmentation with fruit ripening. The concentration of pigments in juice obtained from mature pomegranates ranged between 50 and 100 μg of anthocyanin per gram

fresh weight of arils. Six anthocyanin pigments delphinidin 3-glucoside and 3,5-diglucoside, cyanidin 3-glucoside and 3,5-diglucoside and pelargonidin 3-glucoside and 3,5-diglucoside were found to be responsible for the red color of pomegranate juice (Hernández et al. 1999). Generally, juice pigmentation increased as the fruit ripened. In the early fruit-ripening stages, delphinidin 3,5-diglucoside was the major pigment, followed by cyanidin 3,5-diglucoside, while in the later stages, the monoglucoside derivatives cyanidin 3-glucoside and delphinidin 3-glucoside increased considerably. The pelargonidin derivatives were always present in small amounts. RP-HPLC analysis of pomegranate arils' anthocyanins revealed mono- and diglucosylated delphinidins and cyanidins as the major anthocyanins and pelargonidins as minor components (Borochov-Neori et al. 2011). Anthocyanin accumulation changed inversely to the season's temperatures. Cyanidins were generally more abundant but delphinidin accumulation was enhanced in cooler season. Monoglucosylated anthocyanins prevailed at cooler temperatures and subsided during seasonal warming with a concomitant rise in diglucoside proportion.

The major anthocyanins detected in the 15 Iranian pomegranate varieties were as follows: delphinidin 3-glucoside (2.19–16.29 mg/L), delphinidin 3,5-diglucoside (2.36–63.07 mg/L), pelargonidin 3-glucoside (0.26–1.36 mg/L), pelargonidin 3,5-diglucoside (0.01–8.11 mg/L), cyanidin 3-glucoside (5.78–30.38 mg/L), and cyanidin 3,5-diglucoside (4.39–166.32 mg/L) (Alighourchi et al. 2008). The major anthocyanins in the juice of 6 Iranian pomegranate cultivars were delphinidin 3,5-diglucoside (372–5,301 mg/L), cyanidin 3,5-diglucoside (242–2,361 mg/L), delphinidin 3-glucoside (49–1,042 mg/L) and pelargonidin 3,5-diglucoside (7–90 mg/L) (Mousavinejad et al. 2009). The cultivar, Saveh Black Leather had the highest level of ellagic acid (160 mg/L). Pomegranate juices obtained from six Iranian pomegranate cultivars were found to have 15.77–19.56 total soluble solids content (Brix), pH values of 3.06–3.74, titrable acidity concentration from 0.51 to 1.35 g/100 g, total sugars content from 16. to 22.76 g/100 g (Faroogh), total anthocyanins 7.93–27.73 mg/100 g, ascorbic acid 8.68–15.07 mg/100, total phenolics content 526.40–797.49 mg tannic acid/100 g, The total tannins level 18.77–38.21 mg tannic acid/100 g, condensed tannins from 12.14 mg to 12.57 catechin/100 g, antioxidant activity from 46.51 to 52.71% (Zarei et al. 2010). Phenolics, flavonoids, anthocyanins, and tannins of pomegranate juices, obtained from nine Tunisian ecotypes were quantified by El Kar et al. (2011). Phenolics ranged from 1,570 to 3,299 mg gallic acid equivalents/L and flavonoids from 135 to 156 mg quercetin equivalent/L of juice. Highest anthocyanin content was 156 mg cyanidin–3-glucoside equivalent/L and highest tannin content was 2,550 mg catechin equivalent/L of juice. Tartaric and quinic acids were confirmed in pomegranate juice at concentrations of 1–5 and ~ 1 mg/L, respectively (Ehling and Cole 2011).

Twenty-one volatile compounds were found in fresh pomegranate juices from nine Spanish cultivars, including aldehydes, monoterpenes, and alcohols (Melgarejo et al. 2011). The most abundant compounds were hexanal, limonene, *trans*-2-hexenal, and *cis*-3-hexenol. The presence of monoterpenes (α-terpineol) was correlated with overall consumer preference of pomegranate juice while high aldehydes (*trans*-2-hexenal) concentrations were correlated with poor overall consumer liking. 5-Hydroxymethyl furfural was determined to be at a significant level in traditional sour concentrate of pomegranate juice (Orak 2009). Pomegranate was known to contain estrogens (estradiol, estrone, and estriol) (Mori-Okamoto et al. 2004). Polysaccharide (PSP001) was isolated from pomegranate rind (Joseph et al. 2012).

Phytochemicals in Seeds

Pomegranate seed oil was found to have 8% saturated fatty acids, 10% monounsaturated, 10% diunsaturated and approximately 70% conjugated acid, most probably punicic acid (El-Shaarawy and Nahpetian 1983). Pomegranate seed was found to have high contents of α-tocopherol (161.2–170.1 mg/100 g) and γ-tocopherol (80.2–92.8 mg/100 g). The seeds of *Punica granatum*

also contained ursolic acid and β-sitosterol along with a long straightchain hydrocarbon – nonacosene (Ahmed et al. 1995). Presence of estrogens and glycosides were also detected. Estrone, an estrogen, was identified in pomegranate seeds (Heftmann et al. 1966). Cold pressed pomegranate seed oil was found to contain punicic acid (65.3%), palmitic acid (4.8%), stearic acid (2.3%), oleic acid (6.3%), linoleic acid (6.6%) and three unidentified peaks from which two (14.2%) were probably isomers of punicic acid (Schubert et al. 1999). Pomegranate seed had an average lipid content of 19.2% with punicic acid as the predominant fatty acid (Pande and Akoh 2009). Pomegranate seed oil was found to be rich in 1-*O*-*trans*,*cis*,*trans*-9,11,13-octadecatrienoyl glycerol and also to have small amounts of 1-*O*-isopentyl-3-*O*-octadec-2-enoyl glycerol and the known *cis*-9-octadecenoic, octadecanoic and eicosanoic acids (Fatope et al. 2002). Pomegranate seed oil (PGO) was reported to be rich in 70% *cis*(c)9,*trans*(t)11,c13-18:3 as conjugated linolenic acids (CLA) (Kohno et al. 2004). A triglyceride, di-*O*-punicyl-*O*-octadeca-8*Z*,11*Z*,13*E*-trienylglycerol, was isolated and characterized from the seeds of *Punica granatum* from India and Iran (Yusuph and Mann 1997). Four compound were isolated from pomegranate seeds namely coniferyl 9-*O*-[β-d-apiofuranosyl(1 → 6)]-*O*-β-d-glucopyranoside (1) and sinapyl 9-*O*-[β-d-apiofuranosyl(1 → 6)]-*O*-β-d-glucopyranoside (2), 3,3′-di-*O*-methylellagic acid (3), 3,3′,4′-tri-*O*-methylellagic acid (4) (Wang et al. 2004). Pomegranate seed oil from 21 pomegranate cultivars was found to have mainly unsaturated fatty acids (about 88%) (El Kar et al. 2011). The predominant fatty acid was linolenic acid (44.51–86.14%), followed by linoleic acid (3.57–13.92%), oleic acid (3.03–12.88%), palmitic acid (3.13–11.82%), stearic acid (1.68–15.64%), gadoleic acid (0.50–4.91%), lignoceric acid (<2.53%), arachidic acid (<1.70%) and myristic acid (<0.85%). Pomegranate seed linolenic acid isomers, punicic acid and α-eleostearic acid were found in pomegranate seeds (Tran et al. 2010).

A high yield (3.1–4.2%) of unsaponifiable matter containing tocopherol, aliphatic alcohol (including policosanol), squalene, phytosterols and triterpene was obtained from pomegranate seed oil (Caligiani et al. 2010). The levels of squalene (up to 800 mg/kg), policosanol (118–185 mg/kg), β-sitosterol (up to 8,069 mg/kg) and cycloartenol (5,916–7,766 mg/kg) were found while β- and δ-tocopherol were the most abundant vitamin E forms. The seed oil of *P. granatum* may be an interesting alimentary source of substances of nutraceutical value involved in the modulation of cholesterol metabolism. Linolenic acid isomers like punicic acid and α-eleostearic acid were reported from pomegranate seeds (Tran et al. 2010). Qualitatively, the pomegranate fatty acid composition of 21 pomegranate cultivars (15 Tunisian and 6 Chinese) seed oil was identical comprising mainly unsaturated about 88% (Elfalleh et al. 2011b). The predominant fatty acid was linolenic acid (44.51-86.14%), followed by linoleic acid (3.57-13.92%), oleic acid (3.03-12.88%), palmitic acid (3.13-11.82%), stearic acid (1.68-15.64%), gadoleic acid (0.50-4.91%), lignoceric acid (< 2.53%), arachidic acid (< 1.70%) and myristic acid (< 0.85%). (Wang et al. 2004) isolated the following bioactive compounds from pomegranate seeds: coniferyl 9-*O*-[β-d-apiofuranosyl(1 → 6)]-*O*-β-d-glucopyranoside; sinapyl 9-*O*-[β-d-apiofuranosyl (1 → 6)] -*O*-β-d-glucopyranoside; 3,3′-di-*O*-methylellagic acid; 3,3′,4′-tri-*O*-methylellagic acid; phenethyl rutinoside; icariside D1 and daucosterol. A new class III chitinase (pomegranate seed chitinase) with a molecular weight of approximately 30 kDa was isolated and purified from pomegranate seeds (Yang et al. 2011). This chitinase was found to naturally bind calcium ions with high capacity and low affinity, suggesting it to be a calcium storage protein. This enzyme was found to be widely distributed in the stroma of amyloplasts of the embryonic cells, suggesting that amyloplasts in seeds could serve as an alternative plastid for calcium storage.

Phytochemicals in Flowers

Two new β-sitosterol esters elucidated as stigmast-5-en-3β-ol-3β-dodecanoate (β-sitosterol laurate) and stigmast-5-en-3β-ol-3β-tetradecanoate (β-sitosterol

myristate) along with the known compounds n-tricosane, n-heptacosanyl n-hexanoate olean-5,12-dien-3β-ol-28-oic acid and olean-12-en-3β-ol-28-oic acid were isolated from pomegranate flowers (Bagri et al. 2009b). A new polyphenol compound named pomegranatate, together with, ellagic acid, 3,3′,4′-tri-*O*-methylellagic acid, ethyl brevifolincarboxylate, urolic and maslinic acids, and daucosterol were isolated from the ethanolic extract of the flowers of *Punica granatum* (Wang et al. 2006). Maslinic acid exhibited antioxidant activity as evaluated by measurement of LDL susceptibility to oxidation. A taraxastane-type triterpene, punicanolic acid; two galloyl glucoses, 1,2,6-tri-*O*-galloyl β-D-glucopyranoside, 1,2-di-*O*-galloyl-4,6-*O*-(S)-hexahydroxydiphenoyl β-D-glucopyranoside; flavones, luteolin; triterpnenes oleanolic acid, maslinic acid; and β-sitosterol were isolated from pomegranate flowers (Xie et al. 2008).

Phytochemicals in Leaves

An alkaloid 2-(2-propenyl)-Δ1-piperideine was isolated from pomegranate leaves (Roberts et al. 1967).

Pomegranate leaves were found to contain tannins granatin A, granatin B, corilagin, strictinin, 1,2,4,6- tetra-*O*-galloyl—β-D-glucose and 1,2,3,4,6 –penta-*O*-galloyl-β-D-glucose and an ellagitannin, punicafolin elucidated as 1, 2, 4-tri-*O*-galloyl-3, 6-(R)-hexahydroxydiphenoyl-β-D-glucose (Tanaka et al. 1985, 1990). Pomegranate leaves were found to be rich in polyphenols: brevifolin carboxylic acid, brevifolin, corilagin, 3,6-(*R*)-hexahydroxydiphenoyl-(α/β)-$^{1}C_{4}$-glucopyranose, 1,2,6-tri-*O*-galloyl-β-$^{4}C_{1}$-glucopyranose, 1,4,6-tri-*O*-galloyl-β-$^{4}C_{1}$-glucopyranose, ellagic acid, 3,4,8,9,10-pentahydroxydibenzo[*b,d*]pyran-6-one, granatin-B and punicafolin (Nawwar et al. 1994b); N-(2′,5′-dihydroxyphenyl) pyridinium chloride, as well as the known flavone glycosides, apigenin 4′-*O*-β-glucopyranoside, luteolin 4′-*O*-*P*-glucopyranoside, luteolin 3′-*O*-β-glucopyranoside and luteolin 3′-*O*-β-xylopyranoside (Nawwar et al. 1994a); ellagitannin, punicafolin, tannins, granatins A and B, corilagin, strictinin, 1,2,4,6-tetra-*O*-galloyl-β-D-glucose and 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (Tanaka et al. 1985); gallotannins, 1,2,4-tri-*O*-galloyl-β-glucopyranose and 1,3,4-tri-*O*-galloyl-β-glucopyranose together with the hitherto unknown ellagitannins, 1,4-di-*O*-galloyl-3,6-(*R*)-hexahydroxydiphenyl-β-glucopyranose and brevifolin carboxylic acid 10-monopotassium sulphate (Hussein et al. 1997). A hydroquinone pyridinium alkaloid in the form a mixture of a conjugated and a cross-conjugated heterocyclic mesomeric betaine was isolated from the leaves of *Punica granatum* (Schmidt et al. 2005). Balwani et al. (2011) isolated a novel compound, 2-methyl-pyran-4-one-3-*O*-β-d-glucopyranoside from pomegranate leaves.

Phytochemicals in Stem Bark/Root

These alkaloid isopelletierine, methylisopelletierine, pelletierine, pseudopelletierine were isolated from pomegranate bark (Chilton and Partridge 1950; Wibaut et al. 1954) and roots (Chilton and Partridge 1950); isopelletierine, methylisopelletierine and ψ pelleterine from bark (Wibaut and Hollstein 1957); and n-acetyl-sedridine from bark and root (Neuhöfer 1990). The bark is rich in punicotannic acid (about 22%) and also contains gallic acid, mannite and four alkaloids isopelletierine, methylisopelletierine, pelletierine, pseudopelletierine (Grieve 1971). The following alkaloids were isolated from pomegranate bark and roots: pelletierine, methylisopelletierine, pseudopelletierine and from roots norpseudopelletierine, sedridine, 2-(2′-hydroxypropyl) Δ1-piperidine; 2-(2′-propenyl)Δ1-piperidine, hygrine and norhygrine (Neuhöfer et al. 1993). Tannins and related compound were isolated from pomegranate bark and included punicalin and punicalagin elucidated as to 4, 6-(S, S)-gallagyl-D-glucose (1) and 2,3-(S)-hexahydroxy-diphenoyl-4,6-(S, S)-gallagyl-D-glucose (2), respectively and a hydrolyzable tannin, 2-*O*-galloyl-4,6-(S,S)-gallagyl-D-glucose (Tanaka et al. 1986a); ellagitannins, punicacorteins A, B, C and D, punigluconin, casuariin and casuarinin (Tanaka et al. 1986b). Punicacorteins

A, B, C and D were established as novel C-glycosideic ellagitannins, the former two possessing a unique tetraphenyl (gallagyl) ester group, and the latter two containing a galloyl group in place of the gallagyl group, while punigluconin was elucidated as 2,3-di-*O*-galloyl-4,6-(S)-hexahydroxydiphenoyl gluconic acid. A flavonoid diglycoside, quercetin-3,4′-dimethyl ether-7-*O*-α-L-arabinofuranosyl (1→6)-β-D-glucopyranoside, quercetin, pelargonidine-3,5-diglucoside and ellagic acid were isolated from pomegranate bark (Chauhan and Chauhan 2001). The heartwood of *Punica grantum* was found to contain ellagitannins: diellagic acid rhamnosyl (1→4) glucopyranoside and 5-*O*-galloylpunicac ortein D, tannin metabolites, punicacortein D, punicalin, punicalagin and 2-*O*-galloylpunicalin (El-Toumy and Rauwald 2002); ellagic acid rhamnosides: 3-*O*-methylellagic acid 4-*O*-α-L-rhamnopyranoside and 3,4′-*O*-dimethylellagic acid 4-*O*-α-L-rhamnopyranoside together with brevifolincarboxylic acid, 3-*O*-methylellagic acid and 4,4′-*O*-dimethylellagic acid (El-Toumy and Rauwald 2003); 3′-*O*-methyl-3,4-methylenedioxyellagic acid, as well as eight known ellagitannins and gallotannins (El-Toumy et al. 2001). A new dimeric gallic acid glycoside named humarain was isolated from stem bark of *Punica granatum* (Tantray et al. 2009).

Punica granatum is a unique medicinal plant with a long and extensive ethnomedicinal uses since ancient times. Various parts of the plant viz. seed, aril, fruit juice, peel, leaf, flower, bark, and roots have been reported to contain bioactive phytochemicals with interesting medicinal values and pharmacological activities. The phytochemistry and pharmacological properties of pomegranate plant parts suggest a wide range of clinical applications for the treatment and prevention of ailments such as cancer as well as other diseases where chronic inflammation is believed to play an essential etiologic role (Lansky and Newman 2007). The synergistic action of the pomegranate constituents appears to be superior to that of single constituents. In the past two decade, numerous in-vitro, in-vivo and preclinical studies on the antioxidant, anticarcinogenic, and anti-inflammatory properties of pomegranate constituents have been published, focusing on treatment and prevention of cancer, cardiovascular disease, diabetes, dental conditions, erectile dysfunction, bacterial infections and antibiotic resistance, and ultraviolet radiation-induced skin damage (Jurenka 2008). Other potential applications include infant brain ischemia, male infertility, Alzheimer's disease, arthritis, and obesity.

Antioxidant Activity

Aqueous and ethyl acetate extracts of pomegranate arils, juice and peels exhibited good antioxidant activity (Ricci et al. 2006). Pomegranate juice, peel, and seed oil antioxidants were confirmed by ferric reducing antioxidant power (FRAP) and oxygen radical absorbance capacity (ORAC) methods (Elfalleh et al. 2011). The highest values were recorded in peels with 25.63 mmol trolox equivalent/100 g and 22.08 mmol TE/100 g for FRAP and ORAC assay, respectively. The tocopherol (α-tocopherol, γ-tocopherol, and δ-tocopherol) contents were, respectively, 165.77, 107.38, and 27.29 mg/100 g from dry pomegranate seed. Four phenolic compounds were identified and quantified in pomegranate peel and pulp: 2 hydroxybenzoic acids (gallic and ellagic acids) and 2 hydroxycinnamic acids (caffeic and *p*-coumaric acids). Results showed that the antioxidant potency of pomegranate extracts was correlated with their phenolic compound content. In particular, the highest correlation was reported in peels. High correlations were also found between peel hydroxybenzoic acids and FRAP ORAC antioxidant capacities. Identified tocopherols appeared to contribute in major part to the antioxidant activity of pomegranate seed oil.

Gil et al. (2000) found that the antioxidant activity of commercial pomegranate juices (18–20 TEAC) was three times higher than those of red wine and green tea (6–8 TEAC). Commercial juices extracted from whole pomegranates showed higher antioxidant activity than in experimental juices obtained from the arils only (12–14 TEAC). Further, they found that commercial juices contained the pomegranate abundant tannin

punicalagin (1,500–1,900 mg/L) while only traces were detected in the experimental juice obtained from arils showing that pomegranate industrial processing extracts some of the hydrolyzable tannins present in the fruit rind. Also, anthocyanins, ellagic acid derivatives, and hydrolyzable tannins were found in the pomegranate juices. The results of studies by Tzulker et al. (2007) showed that the antioxidant activity in pomegranate aril juice correlated significantly to the total polyphenol and anthocyanin contents. However, the homogenates prepared from the whole fruit exhibited an approximately 20-fold higher antioxidant activity than the level found in the aril juice. Unlike the arils, the antioxidant level in the homogenates correlated significantly to the content of the four hydrolyzable tannins in which punicalagin was predominant, while no correlation was found to the level of anthocyanins.

Pomegranate juice was found to be a potent inhibitor of superoxide anion-mediated disappearance of nitric oxide (Ignarro et al. 2006). It was much more potent than Concord grape juice, blueberry juice, red wine, ascorbic acid, and DL-α-tocopherol. As little as three μl of a six-fold dilution of pomegranate juice, in a reaction volume of 5,000 μl, produced a marked antioxidant effect, whereas 300 μl of undiluted blueberry juice or nearly 1,000 μl of undiluted Concord grape juice were required to produce similar effects. pomegranate juice and other antioxidant-containing products were found to augment the anti-proliferative action of nitric oxide (DETA/NO) on vascular smooth muscle cell (rat aorta) proliferation. and other antioxidant-containing products were found to augment the anti-proliferative action of NO on vascular smooth muscle cell (rat aorta) proliferation. Pomegranate juice was much more effective than the other products tested and elicited no effects when tested alone in the absence of added NO. Pomegranate juice elicited no effects on eNOS protein expression or catalytic activity and did not enhance promoter activity in the eNOS gene. The observations indicated that pomegranate juice possessed potent antioxidant activity that resulted in marked protection of nitric oxide against oxidative destruction

Pande and Akoh (2009) in their study found the highest antioxidant capacity to be in pomegranate leaves followed by peel, pulp, and seed. The tannin rich mixtures from pomegranate by-product exhibited IC_{50} values against reactive oxygen species (ROS) generation at 0.8–19 μg/mL. The antioxidant capacity (ORAC) of pomegranate juice was 2,860 μmol TE/100 g pomegranate juice which was comparable to blueberry and grape juice (Thomas and Gebhardt 2008). Oral administration of flavonoid rich fractions from pomegranate fruits to rats at a dose of 10 mg/kg/day exhibited potential antiperoxidative activity (Sudeesh and Vijayalakshmi 2005). Malondialdehyde, hydroperoxides and conjugated dienes levels in the liver were significantly decreased antioxidative enzymes catalase, superoxide dismutase (SOD), glutathione peroxidase and glutathione reductase were significantly elevated. Glutathione content in the tissues were also increased. Pomegranate fermented juice and cold pressed seed oil exhibited potent antioxidant activity almost equivalent to butylated hydroxyanisole (BHA) and green tea (*Thea sinensis*), but significantly higher than that of red wine (*Vitis vitifera*) (Schubert et al. 1999). Flavonoids extracted from cold pressed pomegranate seed oil exhibited 31–44% inhibition of sheep cyclooxygenase and 69–81% inhibition of soybean lipoxygenase. Flavonoids extracted from pomegranate fermented juice displayed 21–30% inhibition of soybean lipoxygenase but showed no significant inhibition of sheep cyclooxygenase. Total polyphenols in cold pressed pomegranate seed oil showed a concentration by weight of approximately 0.015%. Fatty acid composition in cold pressed pomegranate seed oil showed punicic acid (65.3%) along with palmitic acid (4.8%), stearic acid (2.3%), oleic acid (6.3%), linoleic acid (6.6%) and three unidentified peaks from which two (14.2%) are probably isomers of punicic acid.

Acetone extract (70%) of pomegranate fruit displayed scavenging activity against hydroxyl (·OH) and superoxide (O2·-) radicals (Noda et al. 2002). Its three major anthocyanindins, delphinidin, cyanidin, and pelargonidin, scavenged O2·- in a dose-dependent fashion with ID_{50} values of

2.4, 22, and 456 μM, respectively but did not effectively scavenge nitric oxide. The anthocyanidins inhibited a Fenton reagent ·OH generating system. Further, the anthocyanidins inhibited hydrogen peroxide-induced lipid peroxidation in the rat brain homogenates with ID_{50} values 0.7, 3.5, and 85 μM, respectively for delphinidin, cyanidin, and pelargonidin (Noda et al. 2002). In another study, pomegranate elagitannins – ellagic acid, gallagic acid, punicalins and punicalagins from pomegranate fruit showed IC_{50} values of 1.1, 3.2, 2.3 and 1.4 μM, respectively, against reactive oxygen species (ROS) generation and no toxicity up to 31.25 μg/mL against HL-60 cells (Reddy et al. 2007). The good antioxidant action of punicalagin a high molecular weight polyphenol isolated from pomegranate fruit pith and carpellary membrane was expressed not only through its scavenging reactions but also by its ability to form metal chelates (Kulkarni et al. 2007). Binding of punicalagin with bovine serum albumin and metal ions such as iron and copper revealed different binding affinities, whereas its binding with DNA was very weak and non-specific. In-vitro cytotoxic studies against three cell lines, namely, Vero (normal African green monkey kidney cell line), Hep-2 (human larynx epithelial cancer cell line), and A-549 (human small cell lung carcinoma cell line) showed that punicalagin, was toxic only at higher concentration.

Studies found that pomegranate peel had the highest antioxidant activity among the peel, pulp and seed fractions of 28 kinds of fruits commonly consumed in China as determined by FRAP (ferric reducing antioxidant power) assay (Guo et al. 2003). In a subsequent study (Li et al. 2006) pomegranate peel extract was shown to have markedly higher antioxidant capacity than the pulp extract in scavenging or preventive capacity against superoxide anion, hydroxyl and peroxyl radicals as well as inhibiting CuSO4-induced LDL oxidation. The contents of total phenolics, flavonoids and proathocyanidins were also higher in peel extract than in pulp extract. The large amount of phenolics contained in peel extract may cause its strong antioxidant ability. The authors concluded that pomegranate peel extract appeared to have more potential as a health supplement rich in natural antioxidants than the pulp extract. Separate studies showed pomegranate peel extracts to have both antioxidant and antimutagenic properties and may be exploited as biopreservatives in food applications and neutraceuticals (Negi et al. 2003). All the pomegranate peel extracts (ethyl acetate, acetone, methanol and water) exhibited marked antioxidant capacity, but the water extract was the lowest. The order of antioxidant capacity varied because of differential responses at four concentrations (25, 50, 75 and 100 μg/mL) in each solvent (Negi et al. 2003). Studies in male rats showed that pomegranate fruit peel extract decreased lipid peroxidation in hepatic, cardiac, and renal tissues and serum glucose concentration (Parmar and Kar 2008). Pomegranate peels were found to contain potent antioxidant contents, as evidenced by free radical DPPH scavenging value of 3.58 μg/mL and ABTS scavenging value of 7.364 mM Trolox equivalent antioxidant capacity/100 g dry weight (Elfalleh et al. 2009). Aqueous and alcoholic extracts of pomegranate rind showed good antioxidant effect with IC_{50} ranging from 34.78 to 135.27/mL for aqueous and 40.03–105.93 μg/mL for alcoholic extracts (Rajan et al. 2011). Phenolic compounds, tannins and flavonoids were the major phytochemicals present in both the extracts. The aqueous and alcoholic extract yielded 122.33 and 176 mg/g gallic acid equivalent phenolic content, 135.33snf 81.33 mg/g quercetin equivalent flavonoid and 81.66 and 114.23 mg/g tannic acid equivalent tannins respectively.

Plumb et al. (2002) found that the prodelphinidin dimers from pomegranate peels were potent antioxidants in the aqueous phase, being much more effective than the gallocatechin monomer in scavenging of the radical cation of 2,2-azinobis (3-ethyl-benzothiazoline-6-sulphonate, ABTS) relative to the water-soluble vitamin E analogue Trolox C (expressed as Trolox C equivalent antioxidant capacity, TEAC). In the lipid phase, only one of the dimers (gallocatechin-(4–8)-catechin) was significantly more effective than the monomer in the inhibition of lipid peroxidation of phosphatidylcholine vesicles. The water, methanol, acetone and ethyl acetate (EtOAc) extracts of

pomegranate peel phenolics showed enhanced inhibitory effect on lard peroxidation as the phenolic concentrations increased (Zhang et al. 2007). Acetone extract exhibited the highest antiliperoxidant activity followed by water, methanol and EtOAc extracts. Acetone extract at 0.1% (w/w) and water extract at 0.2% (w/w) exhibited an antiliperoxidant effect close to that of tea polyphenols (0.02%, w/w) and higher than that of BHT (butylated hydroxytoluene) (0.02%, w/w). At 0.2% (w/w), acetone extract exerted a higher inhibitory activity on lard oxidation than that of tea polyphenols and BHT. Studies by Guo et al. (2007) showed that showed that red pomegranate peel extract had the best effect on the scavenging ability of superoxide anion with lowest IC_{50} value (4.01 μg/mL) among all pomegranate extracts (peel, juice, and seed of three varieties). The peel extract of white pomegranate had the best scavenging ability on hydrogen peroxide with the lowest IC_{50} value (0.032 μg/mL) of the nine extracts. The seed extract of white pomegranate could scavenge hydroxide radical most effectively of the nine extracts (the IC_{50} value 1.69 μg/mL). The seed extract of white pomegranate (the IC_{50} value was 3.67 μg/mL) was the most powerful on the DNA damage-preventing effect of the extracts. The results of studies by Xu et al. (2008) indicated that pomegranate peel extracts exerted protective effects on oxidative stress in mice loaded with restraint stress which may be attributed to its free radical scavenging activity and lipid peroxidation inhibitory effect. The extract decreased alanine aminotransferase and malondialdehyde levels and increased antioxidant capacity in the liver and glutathione levels in plasma as compared with restraint stress control mice. The methanol fraction of pomegranate peel showed highest antioxidant activity by all the four in vitro assays viz. DPPH free radical scavenging, phosphomolybdenum, FRAP (Fe(3+) reducing power) and CUPRAC (cupric ions (Cu(2+)) reducing ability) comparable to ascorbic acid and butylated hydroxy toluene (BHT) followed by activity in ethanol, acetone, and ethyl acetate fractions (Zahin et al. 2010a).

In cell free-systems, preparations from various parts of pomegranate displayed displayed good antioxidant capacity as assayed by 1,1-diphenyl-2-picrylhydrazyl (DPPH), chemiluminescence luminol/xanthine/xanthine oxidase and lipoxygenase assays, with relative potency sequence of rind extract > pomegranate juice > aril juice (Sestili et al. 2007). However, only the rind extract was capable of preventing the deleterious effects – cytotoxicity, DNA damage and depletion of non-protein sulphydrils (NPSH) pool, caused by treatment of cells with hydroxide peroxide, tert-butylhydroperoxide or oxidized lipoproteins (Ox-LDL) via a mechanism which was postulated to involve both direct scavenging of radical species and iron chelation. The results suggested that the aril juice the major and tasty part of pomegranate fruit, did not contain ellagic acid and punicalagin (i.e. the polyphenols highly represented in the rind which appeared to be responsible for the antioxidant capacity) in amounts sufficient to exert cytoprotection in oxidatively injured, living cells. Based on these results, the authors advocated that development and evaluation of rinds-only based derivatives of pomegranate for antiatherogenic preventive purposes in humans should be encouraged.

The antioxidant activity (percentage of inhibition of on peroxidation in linoleic acid system) of CPJ (traditional sour concentrate of pomegranate juice) was determined to be higher (85.91%) than that of PJ (pomegranate juice) (79.06%) (Orak 2009). During the concentration process, the reducing sugars, glucose and fructose level of CPJ showed an increase to 46.46, 23.89, and 22.53%, respectively. In CPJ the amounts of sodium, iron, zinc, copper and lead were found lower than those of PJ. In contrast, potassium and magnesium mineral contents increased during concentration. The total phenolics were also found to be 3,246 and 9,870 μg/mL in PJ and CPJ, respectively. The total anthocyanin content of PJ was found to be 492.9 mg/L but it was not determined in CPJ. 5-Hydroxymethyl furfural was determined to be at a significant level in CPJ as a result of the heat process.

Sezer et al. (2007) found that pomegranate and red wines decreased low-density lipoprotein (LDL) diene levels following a 30-min incubation period compared with controls. However, pure pomegranate wine demonstrated a greater antioxidant effect on diene level (110 μmol/mg of LDL protein)

than pure red wine (124 μmol/mg of LDL protein). The phenol levels of pomegranate and red wines (4,850 mg/L gallic acid equivalents and 815 mg/L gallic acid equivalents, respectively) were in accordance with their total antioxidant activity (39.5 and 33.7%, respectively).

Four compound from pomegranate seeds namely coniferyl 9-*O*-[β-d-apiofuranosyl (1→6)]-*O*-β-d-glucopyranoside (1) and sinapyl 9-*O*-[β-d-apiofuranosyl(1 → 6)]-*O*-β-d-glucopyranoside (2), 3,3′-di-*O*-methylellagic acid (3), 3,3′,4′-tri-*O*-methylellagic acid (4) displayed antioxidant activity, which was evaluated by measurement of low-density lipoprotein (LDL) susceptibility to oxidation and by in-vitro determination of malondialdehyde (MDA) levels in the rat's brain (Wang et al. 2004).

Ethanolic extract of pomegranate flowers was found to contain a large amount of polyphenols and to exhibit potent reducing ability, both indicative of potent antioxidant ability (Kaur et al. 2006). The extract showed 81.6% antioxidant activity in DPPH model system. The flower extract was found to significantly scavenge superoxide (O^{2-}) (by up to 53.3%), hydrogen peroxide (H2O2) (by up to 30%), hydroxyl radicals ($^{-}$OH) (by up to 37%) and nitric oxide (NO) (by up to 74.5%). The extract also inhibited ($^{-}$OH) induced oxidation of lipids and proteins in vitro. These results indicated pomegranate flower extract to exert a significant antioxidant activity in-vitro.

Daily consumption of pomegranate juices was found to be potentially better than apple juice in improving antioxidant function in the elderly (Guo et al. 2008). As the plasma ascorbic acid, vitamin E, and reduced glutathione contents did not differ significantly between the apple and pomegranate groups in the study, the phenolics may be the functional components contained in pomegranate juice that accounted for the observations.

Anticancer Activity

Recent in-vitro studies and preclinical animal studies have shown that pomegranate extracts selectively inhibit the growth of breast, prostate, colon and lung cancer cells (Adhami et al. 2009). An initial phase II clinical trial of pomegranate juice in patients with prostate cancer reported significant prolongation of prostate specific antigen doubling time. Some of these researches are further elaborated herein.

Various parts of the pomegranate fruit e.g. seed oil, juice, fermented juice and peel extract, had been shown to exert suppressive effects on human breast cancer cells in-vitro and in this context, three estrogenic compounds, i.e. luteolin, quercetin and kaempferol, were detected in the fruit peel extract (van Elswijk et al. 2004). Studies showed pomegranate fruit possessed chemopreventive and adjuvant therapeutic potential for human breast cancer (Kim et al. 2002). Polyphenols from fermented pomegranate juice, pericarp, and oil inhibited aromatase activity by 60–80% indicating its ability to effect a blockade of endogenous active estrogen biosynthesis. Fermented juice and pericarp polyphenols, and whole seed oil, inhibited 17-β-hydroxysteroid dehydrogenase Type 1 from 34 to 79%, at concentrations ranging from 100 to 1,000 μg/mL in the sequence seed oil >>fermented juice polyphenols>pericarp polyphenols. Lyophilized fresh pomegranate juice elicited a 55% inhibition of the estrogenic activity of 17-β-estradiol; whereas the lyophilized juice by itself displayed only minimal estrogenic action. Inhibition of cell lines by fermented juice and pericarp polyphenols was according to estrogen-dependent (MCF-7) >>estrogen-independent (MB-MDA-231)>normal human breast epithelial cells (MCF-10A). In both MCF-7 and MB-MDA-231 cells, fermented pomegranate juice polyphenols consistently displayed about twice the anti-proliferative effect as fresh pomegranate juice polyphenols. Pomegranate seed oil elicited 90% inhibition of proliferation of MCF-7 at 100 μg/mL medium, 75% inhibition of invasion of MCF-7 across a Matrigel membrane at 10 μg/mL, and 54% apoptosis in MDA-MB-435 estrogen receptor negative metastatic human breast cancer cells at 50 μg/mL. In a murine mammary gland organ culture, fermented juice polyphenols effected 47% inhibition of cancerous lesion formation induced by the carcinogen 7,12-dimethylbenz[a] anthracene (DMBA). Pomegranate seed oil and fermented pomegranate juice polyphenols were found to have anti-angiogenic activity (Toi et al.

2003). In-vitro studies showed that these pomegranate fractions strongly suppressed vascular endothelial growth factor in normal human breast epithelial cells (MCF-10A) and in estrogen sensitive (MCF-7) human breast cancer cells, but upregulated migration inhibitory factor in estrogen resistant (MDA-MB-231) human breast cancer cells. An anti-proliferative effect on angiogenic cells was shown in human umbilical vein endothelial cell (HUVEC) and in myometrial and amniotic fluid fibroblasts, and inhibition of HUVEC tubule formation was also demonstrated in an in-vitro model employing glass carrier beads. Additionally, they showed a significant reduction in new blood vessel formation using the chicken chorioallantoic membrane (CAM) model in-vivo. In another study, pretreatment of mouse mammary organ culture with pomegranate fermented juice polyphenols (W), a high-performance liquid chromatographic (HPLC) peak separated from W (peak B), or pomegranate seed oil prior to exposure to the to the carcinogen 7,12-dimethylbenz[a] anthracene (DMBA) resulted in a 42% reduction in the number of lesions for W compared with control, peak B and pomegranate seed oil each effected an 87% reduction (Mehta and Lansky 2004). Both pomegranate extracts and genistein inhibit the growth of MCF-7 breast cancer cells through induction of apoptosis, with combination treatment being more efficacious than single treatments (Jeune et al. 2005). More recent studies demonstrated that pomegranate fruit extract dose-dependently inhibited NF-kB-dependent reporter gene expression associated with proliferation, invasion, and motility in aggressive breast cancer phenotypes while suppressing RhoC and RhoA protein expression (Khan et al. 2009). The bioactive components of the fruit extract comprised mainly ellagitannins and phenolic acids in the aqueous fruit extract and conjugated octadecatrienoic acids in the lipid fruit extract derived from seeds. The results suggested a role of pomegranate fruit extract in lowering the metastatic potential of aggressive breast cancer species. Pomegranate extract inhibited the proliferation and viability of MMTV-Wnt-1 mouse mammary cancer stem cells in-vitro in a time- and concentration-dependent manner (Dai et al. 2010). Its constituents ellagic ursolic acid and luteolin also caused a time- and concentration-dependent reduction of cell proliferation and viability, suggesting that they contribute to the inhibitory effect of the extract, while caffeic acid had no effect. The methanolic pomegranate fruit peel extract was found to reduce cell proliferation and induce apoptosis on MCF-7 breast cancer cells (Dikmen et al. 2011). In addition, expression of the pro-apoptotic gene Bax was increased, and that of the anti-apoptotic gene Bcl-2 was decreased after pomegranate extract treatment. The extract exhibited high antioxidant activity and yielded total phenolic content of 331.28 mg of gallic acid equivalents/g of extract with ellagic acid as the most abundant constituent.

Among the ten pomegranate ellagitannin-derived compounds (namely ellagic acid, gallagic acid, urolithins A and B and their acetylated, methylated, and sulfated analogues), urolithin B (UB) was shown to most effectively inhibit aromatase activity in a live breast cancer cell assay (Adams et al. 2010). UB significantly inhibited testosterone-induced MCF-7aro cell proliferation. The remaining test compounds also exhibited antiproliferative activity, but to a lesser degree than UB. The results suggested pomegranate ET-derived compounds to have potential for the prevention of estrogen-responsive breast cancers. Pomegranate seed linolenic acid isomers, punicic acid and α-eleostearic acid were found to be selective estrogen receptor modulators (SERMs) in-vitro (Tran et al. 2010). Punicic acid inhibited (IC_{50}) estrogen receptor (ER) α at 7.2 μM, estrogen receptor β at 8.8 μM. α-eleostearic acid (AEA) inhibited ERα/ERβ at 6.5/7.8 μM. Punicic acid agonized ERα/ERβ (EC_{50}) at 1.8/2 μM, antagonizing at 101/80 μM. α-eleostearic acid antagonized ERα/ERβ at 150/140 μM. Both isomers induced ERα and ERβ mRNA expression in MCF-7 breast cancer cells, but not in MDA-MB-231 breast cancer cells. Punicic acid, an omega-5 fatty acid in pomegranate seed oil, was found capable of inhibiting breast cancer proliferation (Grossmann et al. 2010). Proliferation was inhibited 92 and 96% for MDA-MB-231 and MDA-ERα7 cells,

respectively. Further punicic acid induced apoptosis in the MDA-MB-231 and MDA-ERα7 cells by 86 and 91%, respectively compared to untreated control cells and disrupted cellular mitochondrial membrane potential. The results suggested the breast cancer inhibitor properties of punicic acid were dependent on lipid peroxidation and the protein kinase C signalling pathway.

Treatment of human lung carcinoma A549 cells with pomegranate fruit extract resulted in a decrease in the viability of A549 cells and dose-dependent arrest of cells in G0-G1 phase of the cell cycle (Khan et al. 2007a, b). Treatment of cells with pomegranate fruit extract inhibited (i) phosphorylation of MAPK proteins, (ii) PI3K, (iii) phosphorylation of Akt at Thr308, (iv) NF-kappaB and IKKα, (v) degradation and phosphorylation of IkappaBα, and (vi) Ki-67 and PCNA. Oral administration of pomegranate fruit extract (0.1 and 0.2%, wt/vol) to athymic nude mice implanted with A549 cells resulted in a significant inhibition in tumour growth. Treatment of mice with pomegranate juice prior to exposure to carcinogens benzo(a)pyrene (B(a)P) and N-nitroso-tris-chloroethylurea (NTCU), resulted in statistically significant lower lung tumour multiplicities than mice treated with carcinogens only (Khan et al. 2007a). Treatment of cells with pomegranate fruit extract caused inhibition of (a) activation of nuclear factor-kappaB and IkappaBα kinase, (b) degradation and phosphorylation of IkappaBα, (c) phosphorylation of mitogen-activated protein kinases (extracellular signal-regulated kinase 1/2, c-Jun NH(2)-terminal kinase 1/2, and p38), (d) phosphatidylinositol 3-kinase (p85 and p110), (e) phosphorylation of Akt at Thr(308), (f) activation of mammalian target of rapamycin signaling, (g) phosphorylation of c-met, and (h) markers of cell proliferation (Ki-67 and proliferating cell nuclear antigen) and angiogenesis (inducible nitric oxide synthase, CD31, and vascular endothelial growth factor) in lungs of B(a)P- and NTCU-treated mice. Overall, the results suggested that pomegranate fruit extract could be a useful chemopreventive/chemotherapeutic agent against human lung cancer.

Flavonoid-rich polyphenol fractions from the pomegranate fruit had been reported to exert anti-proliferative, anti-invasive, anti-eicosanoid, and pro-apoptotic actions in breast and prostate cancer cells and anti-angiogenic activities in-vitro and in-vivo (Kawaii and Lansky 2004). They found that various fruit extracts had proportional inhibitory effects on human HL-60 promyelocytic leukemia cell proliferation. Fermented pomegranate juice and aqueous extract of pomegranate pericarps were found to be strong promoters of differentiation in all settings, while fresh juice extract showed only a relatively mild differentiation-promoting effect. Li et al. (2011) found that pomegranate ellagitannins bound with gelatin to form self-assembled nanoparticles. Ellagitannins encapsulated in nanoparticles were less effective in inducing the early stage of apoptosis on human promyelocytic leukemia cells HL-60. But they had similar effects in inducing late stage of apoptosis and necrosis. Differentiation refers to the ability of cancer cells to revert to their normal counterparts, and its induction represents an important noncytotoxic therapy for leukemia, and also breast, prostate, and other solid malignancies (Kawaii and Lansky 2004).

Pomegranate emulsion treatment (1 or 10 g/kg) to rats, started 4 weeks prior to the dietary carcinogen diethylnitrosamine (DENA) challenge and continued for 18 weeks thereafter, showed striking chemopreventive activity demonstrated by reduced incidence, number, multiplicity, size and volume of hepatic nodules, precursors of hepatocellular carcinoma (Bishayee et al. 2011). Both doses of the emulsion significantly attenuated the number and area of γ-glutamyl transpeptidase-positive hepatic foci compared with the DENA control. The emulsion also attenuated DENA-induced hepatic lipid peroxidation and protein oxidation and elevated protein and messenger RNA expression of the hepatic nuclear factor E2-related factor 2 (Nrf2).

The methanolic extract of *Punica granatum* flowers was exhibited inhibitory effect on tumour necrosis factor-α (TNF-α, 1 ng/mL)-induced cytotoxicity in L929 (murine fibroblast) cells (Xie et al. 2008). A new taraxastane-type triterpene, punicanolic acid (1), was isolated from

the active fraction (ethyl acetate-soluble fraction) together with four triterpenes (2–5), two galloyl glucoses (6, 7), two flavones (8, 9), and β-sitosterol. Among the constituents, 1, oleanolic acid (2), maslinic acid (4), 1,2,6-tri-*O*-galloyl β-D-glucopyranoside (6), 1,2-di-*O*-galloyl-4,6-*O*-(S)-hexahydroxydiphenoyl β-D-glucopyranoside (7), and luteolin (8) significantly inhibited TNF-α-induced cytotoxicity in L929 cells at 30 μM.

Four pure chemicals, ellagic acid (E), caffeic acid (C), luteolin (L) and punicic acid (P), all important components of the aqueous compartments or oily compartment of pomegranate fruit exhibited anticancerous activities by inhibiting human PC-3 prostate cancer cell invasion of Matrigel artificial membranes (Lansky et al. 2005a). All compounds significantly inhibited invasion when employed individually. When C, P, and L were equally combined at the same gross dosage (4 μg/mL) as when the compounds were tested individually, a supra-additive inhibition of invasion was observed. Pomegranate cold-pressed seed oil, fermented juice polyphenols (W), and pericarp polyphenols (P) each acutely inhibited in-vitro proliferation of human prostate cancer, LNCaP, PC-3, and DU 145 human cancer cell lines (Albrecht et al. 2004). These effects were mediated by changes in both cell cycle distribution and induction of apoptosis. For example, the androgen-independent cell line DU 145 showed a significant increase from 11 to 22% in G(2)/M cells by treatment with pomegranate oil (35 μg/mL) with a modest induction of apoptosis. In other cell lines/treatments, the apoptotic response predominated, for example, in PC-3 cells treated with pomegranate pericarp polyphenols, at least partially through a caspase 3-mediated pathway. All agents potently suppressed PC-3 invasion through Matrigel, and furthermore pomegranate pericarp polyphenols and seed oil demonstrated potent inhibition of PC-3 xenograft growth in athymic mice. Overall, the study demonstrated significant antitumour activity of pomegranate-derived materials against human prostate cancer. In another study, combinations of the anatomically discrete pomegranate fractions: fermented pomegranate juice polyphenols (W), pomegranate pericarp (peel) polyphenols (P) or pomegranate seed oil (Oil) exhibited synergistic prostate cancer suppression (Lansky et al. 2005b). Supra-additive, complementary and synergistic effects were proven in all models. Proliferation effects were additionally evaluated with CompuSyn software median effect analysis and showed a concentration index CI < 1, confirming synergy.

Pomegranate fruit extract (PFE) exhibited antiproliferative and proapoptotic activities against human prostate cancer cells (Malik et al. 2005; Malik and Mukhtar 2006). PFE (10–100 μg/mL; 48 h) treatment of highly aggressive human prostate cancer PC3 cells resulted in a dose-dependent inhibition of cell growth/cell viability and induction of apoptosis. Immunoblot analysis revealed that PFE treatment of PC3 cells resulted in (i) induction of Bax and Bak (proapoptotic); (ii) down-regulation of Bcl-X(L) and Bcl-2 (anti-apoptotic); (iii) induction of WAF1/p21 and KIP1/p27; (iv) a decrease in cyclins D1, D2, and E; and (v) a decrease in cyclin-dependent kinase (cdk) 2, cdk4, and cdk6 expression. Findings established the involvement of the cyclin kinase inhibitor-cyclin-cdk network during the antiproliferative effects of PFE. Oral administration of PFE (0.1 and 0.2%, wt/vol) to athymic nude mice implanted with androgen-sensitive CWR22Rnu1 cells resulted in a significant inhibition in tumour growth concomitant with a significant decrease in serum prostate-specific antigen levels. The results suggested that pomegranate juice may have cancer-chemopreventive as well as cancer-chemotherapeutic effects against prostate cancer in humans. In a phase II, Simon two-stage clinical trial for men with a rising prostate-specific antigen (PSA), daily consumption of pomegranate juice was found to have a positive effect following surgery or radiation for prostate cancer (Pantuck et al. 2006). There were no serious adverse events reported and the treatment was well tolerated. Mean PSA doubling time significantly increased with treatment from a mean of 15 months at baseline to 54 months post-treatment. In-vitro assays comparing pretreatment and posttreatment patient serum on the growth of human prostate cancer LNCaP showed a 12% decrease in cell proliferation and a 17%

increase in apoptosis, a 23% increase in serum nitric oxide, and significant reductions in oxidative state and sensitivity to oxidation of serum lipids after versus before pomegranate juice consumption. In further studies, a standardized ellagitannins (ETs)-enriched pomegranate extract (PE), significantly inhibited LAPC-4 xenograft growth in severe combined immunodeficient (SCID) mice as compared to vehicle control Seeram et al. 2007). Ellagic acid and several synthesized urolithins were shown to inhibit the growth of human prostate cancer CaP cells in-vitro. The chemopreventive potential of pomegranate ETs and localization of their bioactive metabolites in mouse prostate tissue suggested that pomegranate may play a role in CaP treatment and chemoprevention.

The results of studies demonstrated that an ellagitannin-rich pomegranate extract could inhibit tumour-associated angiogenesis as one of several potential mechanisms for slowing the growth of prostate cancer in chemopreventive applications (Sartippour et al. 2008). A pomegranate extract standardized to ellagitannin content (POMx) inhibited the proliferation of LNCaP and HUVEC cells significantly under both normoxic and hypoxic conditions. HIF-1α (hypoxia-inducible factor-1α) and VEGF (vascular endothelial growth factor) protein levels were also reduced by POMx under hypoxic conditions. POMx decreased prostate cancer xenograft size, tumour vessel density, vascular endothelial growth factor (VEGF) peptide levels and HIF-1α expression after 4 weeks of treatment in severe combined immunodeficient (SCID) mice. Studies showed that pomegranate extract inhibited androgen-independent prostate cancer growth through a nuclear factor-kappaB-dependent mechanism (Rettig et al. 2008). Pomegranate extract (PE) inhibited NF-kappaB and cell viability of prostate cancer cell lines in a dose-dependent fashion in vitro. Maximal PE-induced apoptosis was dependent on PE-mediated NF-kappaB blockade. In the LAPC4 xenograft model, PE delayed the emergence of LAPC4 androgen-independent xenografts in castrated mice through an inhibition of proliferation and induction of apoptosis. The scientist also showed that Pomegranate polyphenols inhibited gene expression and androgen receptor (AR) most consistently in the human prostate cancer LNCaP-AR cell line (Hong et al. 2008). Therefore, inhibition by pomegranate polyphenols of gene expression involved in androgen-synthesizing enzymes and the AR may be of particular importance in androgen-independent prostate cancer cells and the subset of human prostate cancers where AR is up-regulated. Koyama et al. (2010) demonstrated that pomegranate extract derived from rind and arils (minus seeds) inhibited cell proliferation and induced apoptosis in human LAPC4 prostate cancer cells by modulation of the IGF-IGFBP (insulin growth factor – insulin growth factor binding proteins) axis. Pomegranate extract treatment also decreased IGF-1 mRNA expression in a dose-dependent manner indicating that its actions also involved tumour-specific suppression of IGF-1.

Pomegranate peel extracts increased the levels of oxygen radical absorbance capacity (ORAC) in plasma and the density of lecithin and the levels of Zn in prostatitic rats (Kuang et al. 2009). It decreased the levels of malondialdehyde of prostate and the activity of acid phosphatase and the number of white blood cell and adjusted the levels of NO in plasma compared with the prostatitis model group. The results indicated that pomegranate peel extracts could markedly improve the protective function of oxidation resistance. Pomegranate ellagitannins/microbial metabolites were found to have CYP1B1 (a target in prostate cancer chemoprevention) inhibitory activity in prostate cancer cells (Kasimsetty et al. 2009). Urolithin A, a microbial metabolite, was the most potent uncompetitive inhibitor of CYP1B1-mediated ethoxyresorufin-*O*-deethylase (EROD) activity, exhibiting two-fold selectivity over CYP1A1, while urolithin B was a noncompetitive inhibitor with three-fold selectivity. The punicalins and punicalagins exhibited potent CYP1A1 inhibition with 5–10-fold selectivity over CYP1B1. Cellular uptake experiments demonstrated a five-fold increase in urolithin uptake by 22Rv1 cells. Western blots of the CYP1B1 protein indicated that the urolithins interfered with the expression of CYP1B1 protein. Thus,

urolithins were found to display a dual mode mechanism by decreasing CYP1B1 activity and expression. Wang et al. (2011) showed that in addition to causing cell death of hormone-refractory prostate cancer cells, pomegranate juice also increased cell adhesion and decreased cell migration of the unkilled cells. Pomegranate juice was found to upregulate genes involved in cell adhesion such as E-cadherin, intercellular adhesion molecule 1 (ICAM-1) and down-regulated genes involved in cell migration such as hyaluranan-mediated motility receptor (HMMR) and type I collagen. In addition, pomegranate juice significantly decreased the level of secreted pro-inflammatory cytokines/chemokines such as IL-6, IL-12p40, IL-1β and RANTES, thereby having the potential to decrease inflammation and its impact. Pomegrante juice also inhibited the ability of the chemokine SDF1α to chemoattract these cancer cells. Faria et al. (2007) found that pomegranate juice consumption decreased total hepatic cytochrome P450 (CYP) content as well as the expression of CYP1A2 and CYP3A in male mice. Prevention of procarcinogen activation through CYP activity/expression inhibition may be involved in pomegranate juice's effect on tumour initiation, promotion, and progression

Pomegranate juice showed greatest antiproliferative activity against all cell lines namely human oral (KB, CAL27), colon (HT-29, HCT116, SW480, SW620) and prostate (RWPE-1, 22Rv1) tumour cells by inhibiting proliferation from 30 to 100% (Seeram et al. 2005a). At 100 μg/mL, pomegranate juice, ellagic acid, punicalagin and a standardized total pomegranate tannin (TPT) extract induced apoptosis in HT-29 colon cells. However, in the HCT116 colon cells, ellagic acid, punicalagin and TPT but not pomegranate juice induced apoptosis. The trend in antioxidant activity was pomegranate juice > TPT > punicalagin > ellagic acid. Their data indicated the superior bioactivity of pomegranate juice compared to its purified individual polyphenolic active ingredients illustrating the multifactorial effects and chemical synergy of the action of multiple compounds. In further studies, they (Adams et al. 2006) found that pomegranate juice significantly suppressed TNF-α-induced COX-2 protein expression by 79%, total pomegranate tannin extract (TPT) 55%, and punicalagin 48% in HT-29 colcon cells. In addition, pomegranate juice reduced phosphorylation of the p65 subunit and binding to the NFkappaB response element 6.4-fold, TPT suppressed NFkappaB binding ten-fold, punicalagin 3.6-fold, whereas ellagic acid was ineffective. Pomegranate juice also abolished TNFα-induced AKT activation, needed for NFkappaB activity. Pomegranate fruit rich in ellagitannins may have beneficial effects against colon cancer. In the stomach and gut, ellagitannins were reported to be hydrolyzed to release ellagic acid (EA) and were converted by gut microbiota to urolithin A (3,8-dihydroxy-6H-dibenzopyran-6-one) type metabolites (Sharma et al. 2010). They reported that pomegranate ellagitannin extract, ellagic acid, and their colonic metabolite, urolithin A inhibited Wnt signaling, which plays a pivotal role in human colon carcinogenesis, suggesting that ET-rich foods may have potential against colon carcinogenesis and that urolithins were relevant bioactive constituents in the colon. Studies by González-Sarrías et al. (2009) showed that elagic acid and its colonic metabolites, urolithin-A (3,8-dihydroxy-6H-dibenzo[b,d] pyran-6-one) and urolithin-B (3-hydroxy-6H-dibenzo[b,d]pyran-6-one), modulated phase I and phase II detoxifying enzymes in colon cancer Caco-2 cells. Ellagic acid and urolithins may exert some blocking chemopreventive effects in the colon but this effect may be critically affected by interfering factors, such as the food matrix nature. Saruwatari et al. (2008) found that pomegranate juice potently inhibited the sulfoconjugation of 1-naphthol in Caco-2 human colon carcinoma cells. The inhibition was both dose- and culture time-dependent, with a 50% inhibitory concentration (IC_{50}) value of 2.7% (vol/vol). Punicalagin, the most abundant antioxidant polyphenol in pomegranate juice, was also found to strongly inhibit sulfoconjugation in Caco-2 cells with an IC_{50} of 45 μM. additionally pomegranate juice and punicalagin both inhibited phenol sulfotransferase activity in Caco-2 cells. The data also suggested that constituents of pomegranate

juice, most probably punicalagin, impaired the enteric functions of sulfoconjugation and that this may have effects upon the bioavailability of drugs and other compounds and may be related to the anticarcinogenic properties of pomegranate juice. Pomegranate seed oil (PGO) rich in 70% *cis*(c)9,*trans*(t)11,c13-18:3 as conjugated linolenic acids (CLA) could suppress by azoxymethane -induced colon carcinogenesis, and the inhibition was associated in part with the increased content of CLA in the colon and liver and/or increased expression of peroxisome proliferator-activated receptor (PPAR) γ protein in the colon mucosa (Kohno et al. 2004). Pomegranate extract was found to induce cell cycle arrest and alter cellular phenotype of human pancreatic cancer cells PANC-1 and AsPC-1 (Nair et al. 2011)

Studies by Weisburg et al. (2010) showed that pomegranate extract exerted greater antiproliferative effects towards cancer (such as HSC-2 carcinoma), than to normal, cells, isolated from the human oral cavity. The antiproliferative mechanism of pomegranate extract was, in part, by induction of oxidative stress. The mode of cell death was by apoptosis, as activation of caspase-3, and cleavage of PARP. Reduction of caspase-3 activation and of PARP cleavage in cells co-treated with pomegranate extract and either cobalt or pyruvate, respectively, as compared to pomegranate extract alone, indicated that apoptosis was through the prooxidant nature of pomegranate extract.

Pomegranate seed oil (5%) significantly decreased mice skin tumour incidence, multiplicity, and 12-*O*-tetradecanoylphorbol 13-acetate (TPA)-induced ornithine decarboxylase activity, an important event in skin cancer promotion (Hora et al. 2003). The results suggested the potential of pomegranate seed oil as a safe and effective chemopreventive agent against skin cancer. Afaq et al. (2005a, b) demonstrated that topical application of pomegranate fruit extract (PFE) prior to 12-*O*-tetradecanoylphorbol-13-acetate (TPA) application on mouse skin afforded significant time-dependent inhibition, against TPA-mediated increase in skin edema and hyperplasia, epidermal ornithine decarboxylase (ODC) activity and protein expression of ODC and cyclooxygenase-2. Also, application of PFE resulted in inhibition of TPA-induced phosphorylation of ERK1/2, p38 and JNK1/2, as well as activation of NF-kappaB and IKKα and phosphorylation and degradation of IkappaBα. Pretreatment of PFE on TPA-induced skin tumour promotion in 7,12-dimethylbenz(a)anthracene-initiated CD-1 mouse substantially reduced tumour incidence and lower tumour body burden when assessed as total number of tumours per group, percent of mice with tumours and number of tumours per animal as compared to animals that did not receive PFE. Skin application of PFE prior to TPA application also resulted in a significant delay in latency period from 9 to 14 weeks and afforded protection when tumour data were considered in terms of tumour incidence and tumour multiplicity. Studies by George et al. (2011) suggested that pomegranate fruit extract (PFE) and diallyl sulfide (DAS) in combination afforded better suppressive activity of mouse skin tumours than either of these agents alone. PFE and DAS alone delayed onset and tumour incidence by ~55 and ~45%, respectively, while their combination at low doses synergistically decreased tumour incidence more potentially (~84%,). Further, regression in tumour volume was seen with continuous combinatorial treatment. The inhibition was associated with decreased expression of phosphorylated ERK1/2, JNK1 and activated NF-κB/p65, IKKα, IκBα phosphorylation and degradation in skin tissue/tumour.

Polysaccharide (PSP001) isolated from pomegranate rind was found to have antioxidant, antitumour and immunomodulatory properties (Joseph et al. 2012). PSP001 exhibited a dose-dependent enhancement in antioxidant activity using concentrations from 10 to 1,000 μg/mL when evaluated using various assays such as, ferric reducing antioxidant power assay, linoleic acid emulsion thiocyanate assay, and superoxide, hydroxyl and nitric oxide radical scavenging assays except for the DPPH assay for which the highest activity was obtained at 200 μg/mL. PSP001 exhibited anticancer activity with IC_{50} values of 97.21 and 52.8 μg/-mL following 72 h incubation for MCF-7 (breast cancer), and K562(leukemia) cells, respectively.

Antimutagenic Activity

All the pomegranate peel extracts (ethyl acetate (EtOAc), acetone, methanol and water) decreased sodium azide mutagènicity in *Salmonella typhimurium* strains (TA100 and TA1535), either weakly or strongly (Negi et al. 2003). At 2,500 μg/plate all the extracts showed strong antimutagenicity. The antimutagenicity of the water extract was followed by acetone, EtOAc and methanol extracts. The methanol pomegranate peel fraction with promising antioxidant activity showed antimutagenic activity against sodium azide and methyl methane sulphonate with percent inhibition of mutagenicity ranging from 66.76 to 91.86% in a concentration-dependent manner using the Ames Salmonella/microsome assay (Zahin et al. 2010a). Similar trend of inhibition of mutagenicity (81.2–88.58%) against indirect mutagens (2-aminofluorene and benzo(a)pyrene) was also recorded. Phytochemical analysis by HPLC, LC-MS of total phenolic content revealed high content of ellagitannins which might be responsible for promising antioxidant and antimutagenic activities of *P. granatum* peel extract.

Methanol extract of *Punica granatum* flowers (15 mg/plate) showed the highest antimutagenic activity in *Salmonella typhimurium* TA 98 and TA 100, respectively (Wongwattanasathien et al. 2010). The protective effects of these flower extracts might be due to the presence of antimutagenic components that were supposed to be flavonoids.

Antiviral Activity

Studies demonstrated that tannin from the pericarp of *Punica granatum* was an effective agent against genital herpes simplex virus (HSV-2) (Zhang et al. 1995). The tannin not only inhibited HSV-2 replication, but also showed stronger effects of killing virus and blocking its absorption to cells. *Punica granatum* extract showed anti- human herpes simplex virus type 1 (HSV-1) activity, which was possibly contributed by the polyphenolic compounds in the herbal extract (Li et al. 2004). Studies by Neurath et al. (2005) indicated that HIV-1 entry inhibitors from pomegranate juice adsorbed onto corn starch and the resulting complex blocked virus binding to CD4 and CXCR4/CCR5 and inhibited infection by primary virus clades A to G and group O. Their results suggested the possibility of producing an anti-HIV-1 microbicide from inexpensive, widely available sources. Pomegranate juice containing polyphenols, β-sitosterol, sugars and ellagic acid) was reported to inactivate HIV and further shown to inactivate influenza, herpes viruses and poxviruses (Kotwal 2008). A formulation consisting of fulvic acid, a complex mixture of compounds was previously reported to render vaccinia virus, HIV and SARS virus non-infectious. Recently, both fulvic acid and pomegranate juice were shown to inactivate genetically diverse strains of influenza including H5N1, further confirming the broad spectrum nature of these agents. Sundararajan et al. (2010) found that the acidity of pomegranate juice and concentrated liquid extract contributed to rapid anti-influenza activity, but this was not a factor with pomegranate polyphenols powder (93%) extract. Studies using pomegranate powder extract showed that 5 min treatment at room temperature with 800 μg/mL pomegranate polyphenols resulted in at least a 3log reduction in the titers of influenza viruses PR8 (H1N1), X31 (H3N2), and a reassortant H5N1 virus derived from a human isolate. However, the antiviral activity was less against a coronavirus and reassortant H5N1 influenza viruses derived from avian isolates. Electron microscopic analysis indicated that viral inactivation by pomegranate polyphenols was primarily a consequence of virion structural damage.

Pomegranate polyphenol extract was shown to have anti-influenza virus properties (Haidari et al. 2009). Of four major polyphenols in pomegranate polyphenol extract (PPE) (ellagic acid, caffeic acid, luteolin, and punicalagin) punicalagin was the effective, anti-influenza component. Punicalagin blocked replication of the virus RNA, inhibited agglutination of chicken RBC's by the virus and had virucidal effects. Further, the combination of PPE and oseltamivir synergistically increased the anti-influenza

effect of oseltamivir. The data showed PPE inhibited the replication of human influenza A/Hong Kong (H3N2) virus in-vitro. Exposure of foodborne virus surrogates feline calicivirus (FCV-F9), murine norovirus (MNV-1), and MS2 (ssRNA) bacteriophage to pomegranate juice and pomegranate polyphenols resulted in titer reductions after one hour at room temperature, suggesting promise for use in hurdle technologies and/or for therapeutic or preventive use (Su et al. 2010).

Antimicrobial Activity

Ethanolic extracts of *Garcinia mangostana*, *Punica granatum* and *Quercus infectoria* were found to have good antimicrobial activity of nine Thai medicinal plants with MICs for methicillin-resistant *Staphylococcus aureus* (MRSA) isolates of 0.05–0.4, 0.2–0.4 and 0.2–0.4 mg/mL, respectively, and for *S. aureus* ATCC 25923 of 0.1, 0.2 and 0.1 mg/mL, respectively (Voravuthikunchai and d Kitpipit 2005). MBCs for MRSA isolates were 0.1–0.4, 1.6–3.2 and 0.4–1.6 mg/mL, and for *S. aureus* ATCC 25923 were 0.4, 3.2 and 1.6 mg/mL, respectively. *Punica granatum* was found to have anti-quorum-sensing activity and may be useful in combating pathogenic bacteria and reduce the development of antibiotic resistance (Koh and Tham 2011; Zahin et al. 2010b). In another study the ethanolic extract of *P. granatum* exhibited bacteriostatic and bactericidal activities against two enterohemorrhagic *Escherichia coli* strains (Voravuthikunchai and Limsuwan 2006). The ethanolic extract of *P. granatum* had MICs of 0.49–1.95 mg/mL and MBCs of 1.95–3.91 mg/mL. The extract also demonstrated ability to modulate hydrophobicity characteristics of the bacteria. Pomegranate aril extracts exhibited antimicrobial effect on seven bacteria: (*Bacillus megaterium*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Corynebacterium xerosis*, *Escherichia coli*, *Enterococcus faecalis*, *Micrococcus luteus*), and three fungi (*Kluvyeromyces marxianus*, *Rhodotorula rubra*, *Candida albicans*) (Duman et al. 2009). The MIC values for active pomegranate extracts ranged between 30 and >90 μg/mL.

Powdered pomegranate peel, fennel, cumin and acacia bark all showed antifungal activity with pomegranate showing the highest inhibition of *Candida albicans* (Pai et al. 2010). Ethanol extract of *P. granatum* exhibited strong antibacterial activity against *Escherichia coli* (Sharma et al. 2009).

Studies showed that *Punica granatum* (pomegranate) methanolic extract (PGME) dramatically enhanced the activity of all antibiotics tested (Braga et al. 2005a). Synergic activity was detected between PGME and the five antibiotics tested, chloramphenicol, gentamicin, ampicillin, tetracycline, and oxacillin, ranging from 38 to 73%. Using PGME (0.1 × MIC) in combination with ampicillin (0.5 × MIC), cell viability was reduced by 99.9 and 72.5% in methicillin-sensitive *Staphylococcus aureus* (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) populations, respectively. PGME increased the post-antibiotic effect (PAE) of ampicillin from 3 to 7 h. Pomegranate extract inhibited *Staphylococcus aureus* growth and subsequent enterotoxin production (Braga et al. 2005b). Of several Thai medicinal plants, the ethanol extract of *P. granatum* fruit rind displayed the most outstanding in-vitro antibacterial activity with MIC of 0.39 and 12.5 mg/mL and MBC of 1.56 and 12.5 mg/mL against *Staphylococcus aureus* and *Escherichia coli* respectively (Chansakaow et al. 2005). The extract was found to contain both hydrolysable and condensed tannins. The methanol pomegranate pericarp extract exhibited maximum antibacterial activity against *Salmonella typhimurium*, *Salmonella typhi* and *Shigella dysenteriae* Serotype 1 (Pradeep et al. 2008). Studies showed that the antibacterial activity of pomegranate rind can be enhanced by the addition of metal salts and vitamin C (McCarrell et al. 2008). Pomegranate rind extracts (PRE) exhibited activity against the Gram positive organisms at 24 h were inactive against Gram negative bacteria. Addition of Cu^{2+} salts to PRE solutions extended the activities resulting in no detectable growth being observed for the PRE/Cu^{2+} combination against *Escherichia coli*, *Pseudomonas*

aeruginosa and *Proteus mirabilis*. Minimal antimicrobial activity was observed following incubation with Fe^{2+}, Mn^{2+} or Zn^{2+} salts alone or in combination with PRE against any of the organisms in the test panel. The addition of vitamin C markedly enhanced the activities of both PRE/Fe^{2+} and PRE/Cu^{2+} combinations against *Staphylococcus aureus*.

Pelargonidin-3-galactose, cyanidin-3-glucose, gallic acid, quercetin, and myricetin isolated from the methanolic extract of pomegranate fruit exhibited appreciable activity against species of *Corynebacteria*, *Staphylococcus*, *Streptococcus*, *Shigella*, *Salmonella*, *Bacillus subtilis*, *Vibrio cholera*, and *Escherichia coli* (Naz et al. 2007). However, all these compounds were more inhibitory against Gram-positive species. Gallic acid exerted the highest inhibitory activity against all the tested bacteria. Various tannin-rich fractions from pomegranate byproduct and the ellagitannins, ellagic acid (1), gallagic acid (2), punicalins (3), and punicalagins (4) displayed antimicrobial activity when assayed against *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans*, *Cryptococcus neoformans*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Aspergillus fumigatus* and *Mycobacterium intracellulare* (Reddy et al. 2007). Compounds 2 and 4 showed activity against *P. aeruginosa*, *C. neoformans*, and MRSA. A new antifungal peptide designated as pomegranin, isolated from fresh pomegranate peels, was found to inhibit mycelial growth of the fungi *Botrytis cinerea* and *Fusarium oxysporum* with an IC_{50} of 2 and 6.1 μM, respectively (Guo et al. 2009).

Lyophilized pomegranate juice (LPJ) exhibited antilisterial activity in-vitro and in ground beef (Lucas and Were 2009). Against five *Listeria monocytogenes* strains, LPJ had a MIC of 1.50–1.75% (wt/vol). The LPJ (0, 30, 60, and 120 min of heating) significantly inhibited growth of all five *L. monocytogenes* strains in refrigerated ground cooked beef by 1.80–4.61 log CFU/g at day 21. Heating did not negatively impact LPJ antilisterial activity.

Ethanol peel extract of pomegranate exhibited in-vitro and in-vivo antimicrobial activity against *Salmonella typhimurium* (Choi et al. 2011). The minimal inhibitory concentrations of their extract were in the range of 62.5–1,000 μg/mL. in a *S. typhimurium* infection mouse model. The extract was found to have significant effects on mortality and the numbers of viable *S. typhimurium* recovered from faeces. Although clinical signs and histological damage were rarely observed in the treated mice, the untreated controls showed signs of lethargy and histological damage in the liver and spleen. The results of this study indicated that the peel extract had the potential to provide an effective treatment for salmonellosis.

Studies on patients with denture stomatitis showed that gel extract of *P. granatum* may be used as a topical antifungal agent for the treatment of candidosis associated with denture stomatitis (Vasconcelos et al. 2003). In subsequent studies, *Punica granatum* phytotherapeutic gel and miconazole (Daktarin oral gel) exhibited antimicrobial effect against three standard streptococci strains (*Streptococcus mutans*, *Streptococcus sanguis* and *Streptococcus mitis*), *S. mutans* clinically isolated *and Candida albicans* either alone or in association (Vasconcelos et al. 2006). The minimum inhibitory concentrations of adherence of *Punica granatum* gel against the test organisms were: 1:16 for *S. mutans* (ATCC), *S. mutans* (CI) and *S. sanguis*; 1:128 for *S. mitis* and 1:64 for *C. albicans*. The minimum inhibitory concentrations of adherence of miconazole against the same organisms were: 1:512, 1:64, 1:4, 1:128 and 1:16, respectively. In experiments with three and four associated microorganisms, the *Punica granatum* gel had greater efficiency in inhibiting microbial adherence than the miconazole. The results of this study suggest that this phytotherapeutic agent might be used in the control of adherence of different microorganisms in the oral cavity. Studies showed that the hydroalcoholic extract from *Punica granatu*m fruits was very effective against dental plaque microorganisms, decreasing the colony forming units per milliliter (CFU/mL) by 84% (Menezes et al. 2006). While similar values were observed with chlorhexidine, used as standard and positive control (79% inhibition). However, another study found that the gel containing 10% *Punica granatum* extract was not efficient in preventing supragingival dental plaque formation and

gingivitis (Salgado et al. 2006). Methanolic extract of pomegranate peel exhibited antibacterial activity against oral pathogens: *Staphylococcus aureus* and *S. epidermidis* (Abdollahzadeh et al. 2011). Only at concentration of 8 mg/mL and 12 mg/mL the extract was effective against *Lactobacillus acidophilus*, *Streptococcus mutans* and *Streptococcus salivarius*. The extract did not inhibit *Actinomyces viscosus* and *Candida albicans*.

Pomegranate rind extract (PRE) singularly showed limited efficacy against methicillin-sensitive and -resistant *Staphylococcus aureus* (MSSA, MRSA) respectively but in combination with Cu(II) ions (cupric sulphate), it exhibited moderate antimicrobial effects against clinical isolates of MSSA, MRSA and Panton-Valentine Leukocidin positive community acquired MSSA (PVL positive CA-MSSA) isolates. (Gould et al. 2009).

Anti-gingivitis/Amtiplaque Activity

Sastravaha et al. (2005) showed that adjunctive local delivery of extracts from *Centella asiatica* in combination with *P. granatum* significantly improved clinical signs of chronic periodontitis such probing pocket depth, attachment level, gingival index at 3 and 6 months and of bleeding index at 6 months in the test group as compared to control. No significant differences in plaque index were found between the two treatment modalities. The test group also showed statistically greater reduction of interleukin IL-1β at both 3 and 6 months and lower IL-6 concentration. A study of young adults showed that 4 weeks of thrice daily mouth rinsing with the extract improved salivary measures relevant to oral health including gingivitis (DiSilvestro et al. 2009). Salivary changes observed included a reduction in total protein (associated with plaque forming bacteria readings), activities of aspartate aminotransferase (an indicator of cell injury) and α-glucosidase activity (a sucrose degrading enzyme). The changes also included increased activities of the antioxidant enzyme ceruloplasmin and radical scavenging capacity.

Pomegranate mouth-rinse was found to have an antiplaque effect (Bhadbhade et al. 2011). Pomegranate extract was efficacious against *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Prevotella intermedia* strains in-vitro. Pomegranate mouth-rinse could be explored as a long-term antiplaque rinse with prophylactic benefits.

Probiotication Activity

Probiotication improved the antioxidant activity of sweet pomegranate aril juice from 74.4 to 91.82%, and sour pomegranate juice from 82.64 to 97.8% (Fazeli et al. 2011). Based on the ferric reducing antioxidant power (FRAP) value, the reducing power of the probioticated pomegranate juices was also much stronger than the nonprobioticated juices. The FRAP values for sweet and sour probioticated pomegranate juices were 97.34 and 120.7 mmol/L, respectively, which were notably higher than 85.87 and 93.4 mmol/L for sweet and sour nonprobioticated juices. Total counts of *Lactobacillus casei* GG increased by about three log in sweet and two log in sour juices after 48 h incubation. Both fermentated and nonfermentated juices exhibited a potent and wide-spectrum antibacterial effect, with the highest activity against *Pseudomonas aeruginosa* with the sweet juice showing wider zones of growth inhibition. The results showed that probiotication of sweet and sour pomegranate juices could add to their beneficial antioxidant activities. Pomegranate byproducts and punicalagins inhibited the growth of pathogenic clostridia and *Staphylococcus aureus* (Bialonska et al. 2009b). The growth of probiotic lactobacilli and bifidobacteria were generally not affected by ellagitannins. The effect of pomegranate ellagitannins on bifidobacteria was species- and tannin-dependent. The growth of *Bifidobacterium animalis* ssp. *lactis* was slightly inhibited by punicalagins, punicalins, and ellagic acid. Pomegranate ellagitannin-enriched polyphenol extract (POMx) supplementation significantly enhanced the growth of *Bifidobacterium breve* and *Bifidobacterium infantis.*

Bialonska et al. (2009a) found that products of the intestinal microbial transformation of pomegranate ellagitannins may account for systemic

antioxidant effects. While moving through the intestines, pomegranate ellagitannins namely ellagic acid and punicalagins are metabolized by gut bacteria into urolithins that readily enter systemic circulation. Their study found that the antioxidant activity of urolithins was correlated with the number of hydroxy groups as well as the lipophilicity of the molecule. The most potent antioxidants were urolithins C and D with IC_{50} values of 0.16 and 0.33 μM, respectively, when compared to IC_{50} values of 1.1 and 1.4 μM of the parent ellagic acid and punicalagins, respectively. The dihydroxylated urolithin A showed weaker antioxidant activity, with an IC_{50} value 13.6 μM, however, the potency was within the range of urolithin A plasma concentrations.

Antiatherogenic Activity

Numerous laboratory research, animal and human pilot studies had reported on the effectiveness of pomegranate fruit, pomegranate juice and pomegranate fruit polypehnols in reducing heart disease risk factors LDL oxidation, blood pressure, serum angiotensin converting enzyme (ACE) activity, cholesterol esterification, macrophage oxidative status, and macrophage foam cell formation, all of which are steps in atherosclerosis and cardiovascular disease (Aviram et al. 2000, 2002, 2004, 2008; Aviram and Dornfeld 2001; Kaplan et al. 2001; Esmaillzadeh et al. 2004; Fuhrman et al. 2005; de Nigris et al. 2005; Rosenblat et al. 2006a, b; Fuhrman and Aviram 2007; Bagri et al. 2009). In healthy humans, pomegranate juice consumption decreased LDL susceptibility to aggregation and retention and increased the activity of serum paraoxonase by 20% (Aviram et al. 2000). Paraoxanase an HDL-associated esterase, could protect against lipid peroxidation. In apolipoprotein E-deficient E^o mice, oxidation of LDL by peritoneal macrophages was reduced by up to 90% after pomegranate juice consumption and this effect was associated with reduced cellular lipid peroxidation and superoxide release. The uptake of oxidized LDL and native LDL by mouse peritoneal macrophages obtained after pomegranate juice administration was reduced by 20%. Further, pomegranate juice supplementation of E^o mice reduced the size of their atherosclerotic lesions by 44% and also the number of foam cells compared with control E^o mice supplemented with water. The potent antiatherogenic effects in healthy humans and in atherosclerotic mice may be attributable to its antioxidative properties. Anti-atherosclerotic properties was attributed to pomegranate potent anti-oxidative characteristics. After consumption of pomegranate juice, a 36% reduction in serum angiotensin converting enzyme (ACE) activity and a 5% reduction in systolic blood pressure were noted in hypertensive patients (Aviram and Dornfeld 2001). Similar dose-dependent inhibitory effect (31%) of pomegranate juice on serum ACE activity was observed also in-vitro. Additional studies showed that pomegranate juice supplementation to atherosclerotic mice reduced macrophage lipid peroxidation, cellular cholesterol accumulation and development of atherosclerosis (Kaplan et al. 2001). Pomegranate juice supplementation reduced each of the proatherogenic variables. It significantly induced serum paraoxonase activity and reduced mouse peritoneal macrophage (MPM) lipid peroxide content compared with placebo-treated mice and control mice. Pomegranate juice administration to apolipoprotein E-deficient E^o mice significantly reduced the oxidized (Ox)-LDL MPM uptake by 31% and MPM cholesterol esterification and increased macrophage cholesterol efflux by 39% compared with age-matched, placebo-treated mice. Pomegranate juice consumption reduced macrophage Ox-LDL uptake and cholesterol esterification to levels lower than those in 4-month-old, unsupplemented controls. Pomegranate juice supplementation to E^o mice with advanced atherosclerosis reduced the lesion size by 17% compared with placebo-treated mice. In a separate study, supplementation of young (2-month-old) E^o mice for 2 months with a tannin fraction isolated from pomegranate juice reduced their atherosclerotic lesion size, paralleled by reduced plasma lipid peroxidation and decreased Ox-LDL MPM uptake. Studies indicated that the proatherogenic effects induced by perturbed shear stress in cultured human coronary artery endothelial cells could be reversed by

chronic administration of pomegranate juice (de Nigris et al. 2005, 2007). Pomegranate juice concentrate and pomegranate fruit extract rich in punicalagin reduced the activation of redox-sensitive genes ELK-1, p-JUN, p-CREB, and increased eNOS expression (which was decreased by perturbed shear stress) in cultured endothelial cells and in atherosclerosis-prone areas of hypercholesterolemic mice. Furthermore, oral administration of pomegranate juice to hypercholesterolemic mice at various stages of disease reduced significantly the progression of atherosclerosis and isoprostane levels and increased nitrates. de Nigris et al. (2006) found that pomegranate juice reverted the potent down-regulation of the expression of endothelial nitric-oxide synthase (NOSIII) induced by oxidized low-density lipoprotein (oxLDL) in human coronary endothelial cells. Their data suggested that pomegranate juice could exert beneficial effects on the evolution of clinical vascular complications, coronary heart disease, and atherogenesis in humans by enhancing the nitric-oxide synthase bioactivity.

Aviram et al. (2002) reported that pomegranate polyphenols protected low-density lipoprotein (LDL) against cell-mediated oxidation via two pathways, including either direct interaction of the polyphenols with the lipoprotein and/or an indirect effect through accumulation of polyphenols in arterial macrophages (Aviram et al. 2002). Pomegranate polyphenols were shown to reduce the capacity of macrophages to oxidatively modify LDL, due to their interaction with LDL to inhibit its oxidation by scavenging reactive oxygen species and reactive nitrogen species and also due to accumulation of polyphenols in arterial macrophages; hence, the inhibition of macrophage lipid peroxidation and the formation of lipid peroxide-rich macrophages. Additionally, pomegranate polyphenols increased serum paraoxonase activity, resulting in the hydrolysis of lipid peroxides in oxidized lipoproteins and in atherosclerotic lesions. These antioxidative and antiatherogenic effects of pomegranate polyphenols were demonstrated in-vitro, as well as in-vivo in humans and in atherosclerotic apolipoprotein E deficient mice. Dietary supplementation of polyphenol-rich pomegranate juice to atherosclerotic mice significantly inhibited the development of atherosclerotic lesions and this may be attributed to the protection of LDL against oxidation.

Subsequent studies indicated that that pomegranate juice consumption by patients with carotid artery stenosis CAS decreased carotid carotid intima-media thickness (IMT) and systolic blood pressure and these effects could be related to the potent antioxidant characteristics of pomegranate juice polyphenols (Aviram et al. 2004). For all studied parameters, the maximal effects were observed after 1 year of pomegranate juice consumption. Further consumption of pomegranate juice, for up to 3 years, had no additional beneficial effects on IMT and serum paraoxonase 1 (PON 1) activity, whereas serum lipid peroxidation was further reduced by up to 16% after 3 years of pomegranate juice consumption. The antiatherogenic properties of pomegranate juice (PJ) were attributed to its antioxidant potency and to its capacity to decrease macrophage oxidative stress, the hallmark of early atherogeneis (Rosenberg et al. 2006). Pomegranate juice polyphenols and sugar-containing polyphenolic anthocyanins were shown to confer PJ its antioxidant capacity. Their study showed that PJ sugar consumption by diabetic mice for 10 days resulted in a small but significant decrement in their peritoneal macrophage total peroxide levels and an increment in cellular glutathione content, compared to mouse peritoneal macrophages harvested from control diabetic mice administrated with water. These antioxidant/antiatherogenic effects could be due to the presence of unique complex sugars and/or phenolic sugars in PJ. They further showed the anti-oxidative characteristics of PJ unique phenolics punicalagin and gallic acid could be related, at least in part, to their stimulatory effect on macrophage paraoxonase 2 (PON2) expression, a phenomenon which was shown to be associated with activation of the transcription factors PAPR γ and AP-1 (Shiner et al. 2007). Similar results were obtained by pomegranate byproduct (which includes the whole pomegranate fruit left after juice preparation) (17 or 51.5 μg of gallic acid equiv/kg/day) administration to apolipoprotein e-deficient mice that resulted in attenuation

of atherosclerosis development as a result of decreased macrophage oxidative stress and reduced cellular uptake of oxidized low-density lipoprotein (Rosenblat et al. 2006). In-vitro studies showed that preincubation of J774.A1 macrophages with pomegranate juice resulted in a significant reduction in Ox-LDL degradation by 40% (Fuhrman et al. 2005). Macrophage cholesterol biosynthesis was inhibited by 50% after cell incubation with pomegranate juice. This inhibition, however, was not mediated at the 3-hydroxy-3 methylglutaryl coenzyme A reductase level along the biosynthetic pathway. It was concluded that pomegranate juice-mediated suppression of Ox-LDL degradation and of cholesterol biosynthesis in macrophages could lead to reduced cellular cholesterol accumulation and foam cell formation.

Studies in Iran reported that consumption of concentrated pomegranate juice may modify heart disease risk factors in hyperlipidemic (cholesterol ≥ 5.2 mmol/L or triacylglycerol ≥ 2.3 mmol/L) patients (Esmaillzadeh et al. 2004, 2006). After consumption of concentrated pomegranate juice, significant reductions were seen in total cholesterol, low-density lipoprotein (LDL)-cholesterol, LDL-cholesterol/high-density lipoprotein (HDL)-cholesterol, and total cholesterol/HDL-cholesterol. But, there were no significant changes in serum triacylglycerol and HDL-cholesterol concentrations. Anthropometric indices, physical activity, kind and doses of oral hypoglycemic agents, and the intakes of nutrients and flavonoid-rich foods showed no change during the concentrated pomegranate juice consumption period. Rosenblat et al. (2006) reported that pomegranate juice consumption by diabetic patients did not affect serum glucose, cholesterol and triglyceride levels, but it resulted in a significant reduction in serum lipid peroxides and TBARS (thiobarbituric acid reactive substance) levels by 56 and 28%, whereas serum SH (sulfhydryl) groups and paraoxonase 1 (PON1) activity significantly increased by 12 and 24%, respectively. In the patients versus controls monocytes-derived macrophages (HMDM), they observed increased level of cellular peroxides (by 36%), and decreased glutathione content (by 64%). Pomegranate juice consumption significantly reduced cellular peroxides (by 71%), and increased glutathione levels (by 141%) in the patients' HMDM. The patients' versus control HMDM took up oxidized LDL (Ox-LDL) at enhanced rate (by 37%) and pomegranate juice consumption significantly decreased the extent of Ox-LDL cellular uptake (by 39%). They thus concluded that pomegranate juice consumption by diabetic patients did not worsen the diabetic parameters, but rather resulted in anti-oxidative effects on serum and macrophages, which could contribute to attenuation of atherosclerosis development in these patients.

Pomegranate juice was found to have potent antiatherogenic activity (Fuhrman and Aviram 2007). In-vitro studies demonstrated a pomegranate juice dose-dependent antioxidant capability against lipid peroxidation in plasma (by 33%), in LDL (by 43%), and in HDL (by 22%). Pomegranate juice consumption by hypertensive patients reduced their systolic blood pressure (by 6%), along with inhibition (by 40%) of angiotensin converting enzyme (ACE). Pomegranate juice supplementation to atherosclerotic apolipoprotein E-deficient (E°) mice reduced their atherosclerotic lesion size by 44% and the number of foam cells in their lesion. Consumption of pomegranate juice by ten patients with carotid artery stenosis (CAS) for 1 year reduced the patients' carotid intima-media thickness (IMT) by 32%. These effects were associated with ex-vivo reduced lipid peroxidation in plasma and in isolated lipoproteins in humans and mice. Furthermore, pomegranate juice consumption by humans increased the activity of their serum paraoxonase (PON1), an HDL-associated esterase that protects against lipid peroxidation. Macrophage atherogenicity was studied in mouse peritoneal macrophages (MPM) harvested from E° mice. Following pomegranate juice consumption, uptake of oxidized LDL and cell-mediated oxidation of LDL by macrophages was reduced by 88 and by 20%, respectively, in association with reduced cellular lipid peroxidation, reduced superoxide anion release due to decreased NADPH-oxidase activation, and elevated glutathione content. In-vitro studies demonstrated that

pomegranate juice reduced macrophage Ox-LDL degradation by 40%, and macrophage cholesterol biosynthesis by 50%. Overall, the results of the above studies demonstrated that pomegranate juice consumption had very potent antiatherogenic properties, which could be associated mainly with pomegranate juice hydrolysable tannin antioxidative properties.

In a recent study (Aviram et al. 2008) pomegranate juice (PJ), fruit peels (POMxl, POMxp), arils (POMa), seeds (POMo), and flowers (POMf), extracts all were found to possess antioxidative properties in-vitro. After consumption of pomegranate juice, fruit peel, aril and flower extracts the atherosclerotic lesion area in atherosclerotic apolipoprotein e-deficient (E 0) mice was significantly decreased by 44, 38, 39, 6, or 70%, respectively, as compared to placebo-treated group, while pomegranate seed oil had no effect. Pomegrante flower consumption reduced serum lipids, and glucose levels by 18–25%. Consumption of the extracts except for the seed oil resulted in a significant decrement, by 53, 42, 35, 27, or 13%, respectively, in MPM (mouse peritoneal macrophage) total peroxides content, and increased cellular paraoxonase 2 (PON2) activity, as compared to placebo-treated mice. The uptake rates of oxidized-LDL by E (0)-MPM were significantly reduced by approximately 15% after consumption of juice and the two fruit peel extracts. Similar results were obtained on using J774A.1 macrophage cell line. Finally, pomegranate phenolics (punicalagin, punicalin, gallic acid, and ellagic acid), as well as pomegranate unique complexed sugars, could mimic the antiatherogenic effects of the pomegranate extracts. Rock et al. (2008) reported that after 4 weeks of pomegranate juice consumption by male patients, basal serum oxidative stress was significantly decreased by 35%, whereas serum concentrations of thiol groups significantly increased by 25%. Moreover, HDL-associated paraoxonase 1(PON1), arylesterase, paraoxonase, and lactonase activities increased significantly after pomegranate juice consumption by 34–45%, as compared to the baseline levels. PON1 protein binding to HDL was significantly increased by 30% following pomegranate juice consumption, and the enzyme became more stable. In male patients that consumed pomegranate polyphenol extract and in female patients that consumed pomegranate juice, a similar pattern was observed, although to a lesser extent. These beneficial effects of pomegranate consumption on serum PON1 stability and activity could lead to retardation of atherosclerosis development in diabetic patients.

Results of a randomized, double-blind, parallel trial involving men (45–74 years old) and women (55–74 years old) with moderate coronary heart disease risk suggested that in subjects at moderate coronary heart disease risk, pomegranate juice consumption had no significant effect on overall carotid intima-media thickness progression rate but may have slowed carotid intima-media thickness progression in subjects with increased oxidative stress and disturbances in the triglycerides-rich lipoprotein/high-density lipoprotein axis (Davidson et al. 2009).

Antihyperlipidemic/Antiobesity Activity

Lei et al. (2007) reported that the pomegranate leaf extract could inhibit the development of obesity and hyperlipidemia in high-fat diet induced obese mice. Mice treated with the extract presented a significant decrease in body weight, energy intake and various adipose pad weight percents and serum, serum total cholesterol (TC), triglyceride (TG), glucose levels and TC/high-density lipoprotein cholesterol (HDL-C) ratio after 5 weeks treatment. Further, the extract significantly attenuated the raising of the serum TG level and inhibited the intestinal fat absorption in mice given a fat emulsion orally. The effects were postulated to be partly mediated by inhibiting the pancreatic lipase activity and suppressing energy intake. Yamasaki et al. (2006) found that mice fed dietary pomegranate seed oil (PSO) high in levels of punicic acid showed significant increases in serum triacylglycerol and phospholipid levels but not in total cholesterol. Punicic acid could be detected in serum, liver, and adipose tissues in mice fed the 0.12 or 1.2% PSO diet. Oral administration of streptozotocin-induced diabetic Wistar rats with of 250 and 500 mg/kg

of aqueous pomegranate flower extract for 21 days resulted in a significant fall in fasting blood glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, very low density lipoprotein, lipid peroxidation level (Bagri et al. 2009). Pomegrante extract elevated levels of high density lipoprotein cholesterol (HDL-C), reduced glutathione (GSH) and the antioxidative enzymes, glutathione peroxidase (GPx), glutathione reductase (GR), glutathione-S-transferase (GST), superoxide dismutase (SOD) and catalase (CAT). McFarlin et al. (2009) found that weight gain in high fat diet mice was associated with an increase in biomarkers of cholesterol profile, glucose sensitivity, adipose tissue accumulation and systemic low-grade inflammation. despite a similar level of energy intake, high-fate diet mice had a greater concentration of leptin and a lower concentration of adiponectin compared to high fat + pomegranate seed oil diet mice. Pomegranate seed oil, a rich source of 9-*cis*, 11-*trans* conjugate linolenic acid, only altered body weight accumulation, final body weight, leptin, adiponectin and insulin. Pomegranate seed oil intake was associated with an improvement in insulin sensitivity, suggesting that risk of developing type two diabetes may have been reduced; however, CVD risk did not change. Lan et al. (2009) demonstrated that ellagic acid in pomegranate leaf tannins could be transported into HepG2 cells and this correlated with total cholesterol alteration in the cells.

Vroegrijk et al. (2011) found that pomegranate seed oil, a rich source of punicic acid, ameliorated high-fat diet induced obesity and insulin resistance in mice, independent of changes in food intake or energy expenditure. compared to high fat diet mice, its intake resulted in a lower body weight and improved peripheral insulin sensitivity but did not affect liver insulin sensitivity. In a randomized, double-blind, placebo-controlled clinical trial of 20 obese adult volunteer, pomegranate juice administration for 1 month did not modify insulin secretion and sensitivity in the obese patients, however, the natural evolution to increased weight and adiposity was halted (González-Ortiz et al. 2011).

Rosenblat and Aviram (2011) found that the inhibitory effect of pomegranate juice on triglyceride biosynthesis could be attributed to a direct effect of pomegranate juice on the activity of diacylglycerol acyltransferase 1 (DGAT1) the rate-limiting enzyme in triglyceride biosynthesis. Pomegranate juice and its constituent punicalagin significantly and dose-dependently decreased the triglyceride content and triglyceride biosynthesis rate in J774A.1 macrophages or in C57BL/6 mouse peritoneal macrophages. Both pomegranate juice and punicalagin increased (1.7-fold) mouse peritoneal macrophages paraoxonase 2 (PON2) mRNA expression, and PON2 was previously shown to inhibit DGAT1 activity. However, the addition of PJ or punicalagin (50 μM) to microsomes from PON2-deficient mouse peritoneal macrophages still resulted in a significant reduction (50–58%) in DGAT1 activity.

Antihypertensive Activity

In a randomised block design study of student volunteers, supplementation of pomegranate juice caused a fall in diastolic blood pressure and this could be related to ROS scavenging activity rather than to angiotensin-converting enzyme inhibitors (Wright and Pipkin 2008)

Oral administration of pomegranate juice extract (100 and 300 mg/kg) to angiotensin-II treated rats for 4 weeks significantly reduced the mean arterial blood pressure and vascular reactivity changes to various catecholamines (Waghulde et al. 2010). Pomegranate juice administration significantly decreased the serum levels of ACE (angiotensin converting enzyme) and the levels of thiobarbituric acid reactive substances (TBARS); while enzyme activity of superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GSH) in kidney tissue showed a significant elevation in pomegranate juice treated angiotensin-II induced hypertensive rats. The results suggested that pomegranate juice extract could prevent the development of high blood pressure induced by angiotensin-II probably by combating the oxidative stress and antagonizing the physiological actions of angiotensin-II. Chronic administration of pomegranate fruit juice (PJ) extract (100 and 300 mg/kg; p.o.

for 4 weeks) reduced the mean arterial blood pressure and vascular reactivity changes to various catecholamines and also reversed the biochemical changes induced by diabetes and angiotensin II (Ang II) (Mohan et al. 2010b). Acute subcutaneous administration of Angiotensin II causes a rise in blood pressure in streptozotocin-induced diabetic Wistar rats. PJ treatment also caused a significant decrease in levels of thiobarbituric acid reactive substances (TBARS) in the kidney and pancreas while activities of enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione reductase (GSH) showed significant elevation. PJ treatment prevented the tubular degenerative changes induced by diabetes. The results suggested that the PJ extract could prevent the development of high blood pressure induced by Ang II in diabetic rats probably by combating the oxidative stress induced by diabetes and Ang II and by inhibiting ACE activity.

Antidiabetic Activity

Pomegranate in particular its flowers, seeds, and juice have been employed for the treatment of various diseases in traditional Unani and Ayurvedic systems of medicine in India but only the flower has been prescribed for the treatment of diabetic disorders (Li et al. 2008; Katz et al. 2007). The mechanisms for it hypoglycaemic effects are largely unknown, though recent research suggested pomegranate flowers and juice may prevent diabetic sequelae via peroxisome proliferator-activated receptor (PPAR) α/γ binding and nitric oxide production (Katz et al. 2007; Huang et al. 2005a, b; Li et al. 2008; Xu et al. 2009). Pomegranate compounds associated with such effects include oleanolic, ursolic, and gallic acids (Katz et al. 2007). Another study suggested that *Punica granatum* flower (PGF) extract inhibited increased cardiac fatty acid uptake and oxidation in the diabetic condition (Huang et al. 2005b). PGF extract and its component oleanolic acid enhanced peroxisome proliferator-activated receptor (PPAR)-α luciferase reporter gene activity in human embryonic kidney 293 cells. This effect was completely suppressed by a selective PPAR-α antagonist MK-886, consistent with the presence of PPAR-α activator activity in the extract and this component. The findings suggested that PGF extract improved abnormal cardiac lipid metabolism in Zucker diabetic fatty rats by activating PPAR-α and thereby lowering circulating lipid and inhibiting its cardiac uptake. Excess triglyceride (TG) accumulation and increased fatty acid (FA) oxidation in the diabetic heart contribute to cardiac dysfunction. In subsequent in-vitro studies, the scientists (Huang et al. 2005a) demonstrated that 6-week oral administration of methanol extract from PGF (500 mg/kg, daily) inhibited glucose loading-induced increase of plasma glucose levels in Zucker diabetic fatty rats (ZDF), a genetic animal model for type two diabetes, whereas it did not inhibit the increase in Zucker lean rats (ZL). The treatment did not lower the plasma glucose levels in fasted ZDF and ZL rats. Further, RT-PCR results demonstrated that the PGF extract treatment in ZDF rats enhanced cardiac PPAR-γ mRNA expression and restored the down-regulated cardiac glucose transporter (GLUT)-4 (the insulin-dependent isoform of GLUTs) mRNA. These results suggest that the anti-diabetic activity of PGF extract may result from improved sensitivity of the insulin receptor. From the in-vitro studies, it was demonstrated that the PGF extract enhanced PPAR-γ mRNA and protein expression and increased PPAR-γ-dependent mRNA expression and activity of lipoprotein lipase in human THP-1-differentiated macrophage cells. Phytochemical investigation demonstrated that gallic acid in PGF extract was mostly responsible for this activity. Further in-vitro studies showed that *Punica granatum* flower extract and its components oleanolic acid, ursolic acid, and gallic acid inhibited lipopolysaccharide-induced NF-kappaB activation in macrophages. The findings indicated that *Punica granatum* flower extract reduced cardiac fibrosis in Zucker diabetic fatty rats, at least in part, by modulating cardiac ET-1 and NF-kappaB signalling. Recent studies suggested that pomegranate flower (PGF) medicine ameliorated diabetes and obesity-associated fatty liver, at least in part, by activating hepatic expression of genes responsible for fatty acid oxidation (Xu et al. 2009). PGF-treated ZDF

rats showed reduced ratio of liver weight to tibia length, hepatic triglyceride contents and lipid droplets. These effects were accompanied by enhanced hepatic gene expression of peroxisome proliferator-activated receptor (PPAR)-α, carnitine palmitoyltransferase-1 and acyl-CoA oxidase (ACO), and reduced stearoyl-CoA desaturase-1. In contrast, PGF showed minimal effects on expression of genes responsible for synthesis, hydrolysis or uptake of fatty acid and triglycerides.

PGF treatment also increased PPAR-α and ACO mRNA levels in HepG2 cells. Li et al. (2008) reviewed the dual PPAR-α/-γ activator properties of pomegranate flower and its potential treatment of diabetes and its associated complications. PPARs are nuclear transcription factors and are the major regulators of lipid and glucose metabolism. PPAR-α is involved in the regulation of fatty acid (FA) uptake and oxidation, inflammation and vascular function, while PPAR-γ participates in FA uptake and storage, glucose homeostasis and inflammation. Synthetic PPAR-α or PPAR-γ agonists have been widely used in the treatment of dyslipidaemia, hyperglycaemia and their complications. However, they are associated with an incidence of adverse events. Given the favourable metabolic effects of both PPAR-α and PPAR-γ activators, as well as their potential to modulate vascular disease, combined PPAR-α/-γ activation has recently emerged as a promising concept, leading to the development of mixed PPAR-α/-γ activators.

Hontecillas et al. (2009) demonstrated that punicic acid (PUA), a conjugated linolenic acid isomer found in pomegranate, caused a dose-dependent increase PPAR α and γ reporter activity in 3 T3-L1 pre-adipocyte cells and bound although weakly to the ligand-binding domain of human PPAR γ. Dietary PUA decreased fasting plasma glucose concentrations, improved the glucose-normalizing ability, suppressed NF-kappaB activation, TNF-α expression and upregulated PPAR α- and γ-responsive genes in skeletal muscle and adipose tissue. PUA improved glucose homeostasis and suppress obesity-related inflammation

Studies in India showed that pomegranate seed extract (150, 300 and 600 mg/kg) administered orally to streptozotocin (STZ)-induced diabetic rats caused a significant reduction of blood glucose levels by 47 and 52%, respectively, at the end of 12 h (Das et al. 2001). Kim et al. (2011) found that administration of pomegranate extract to streptozotocin (STZ)-induced diabetic mice for 4 weeks improved postprandial glucose regulation. Further elevated Na(+)-dependent glucose uptake by brush border membrane vesicles isolated from STZ mice was normalized by pomegranate treatment. The results suggested that pomegranate extract could play a role in controlling the dietary glucose absorption at the intestinal tract by decreasing sodium-coupled glucose transporter SGLT1 expression, and may contribute to blood glucose homeostasis in the diabetic condition.

Oral administration of pomegranate flower (PGF) extract markedly lowered plasma glucose levels in non-fasted Zucker diabetic fatty rats (a genetic model of obesity and type two diabetes), whereas it had little effect in the fasted animals, suggesting it affected postprandial hyperglycemia in type two diabetes (Li et al. 2005). The extract was found to markedly inhibit the increase of plasma glucose levels after sucrose loading, but not after glucose loading in mice, and it had no effect on glucose levels in normal mice. In-vitro, PGF extract demonstrated a potent inhibitory effect on α-glucosidase activity (IC_{50}: 1.8 μg/mL). These findings strongly suggested that PGF extract improved postprandial hyperglycemia in type two diabetes and obesity, at least in part, by inhibiting intestinal α-glucosidase activity. Postprandial hyperglycemia plays an important role in the development of type two diabetes and has been proposed as an independent risk factor for cardiovascular diseases. In a recent paper, Bagri et al. (2009a) reported that oral administration of pomegranate aqueous extract at doses of 250 and 500 mg/kg for 21 days to STZ-induced diabetic rats resulted in a significant reduction in fasting blood glucose, total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), very low density lipoprotein (VLDL), and tissue lipid peroxidation

levels coupled with elevation of high density lipoprotein cholesterol (HDL-C), glutathione (GSH) content and antioxidant enzymes in comparison with diabetic control group. The results suggested that PG could be used, as a dietary supplement, in the treatment of chronic diseases characterized by atherogenous lipoprotein profile, aggravated antioxidant status and impaired glucose metabolism and also in their prevention.

In-vitro studies showed that pomegranate juice polyphenols increased recombinant paraoxonase-1 binding to high-density lipoprotein (HDL) beyond their antioxidative effect (Fuhrman et al. 2010). Further recombinant paraoxonase-1 was found to be associated more efficiently with HDLs isolated from diabetic patients after pomegranate juice consumption versus HDLs isolated before pomegranate juice consumption.

Antiinflammatory and Antiarthritic Activity

Studies by Ahmed et al. (2005) showed that pomegranate fruit extract or compounds derived from it may inhibit cartilage degradation in osteoarthritis and may also be a useful nutritive supplement for maintaining joint integrity and function. The extract inhibited interleukin (IL)-1β induced expression of matrix metalloproteinases by suppressing the activation of mitogen-activated protein kinases and nuclear factor-kappaB in human chondrocytes in-vitro. Pomegranate methanol extract was found to dose-dependently inhibit tumour necrosis factor α (TNF-α) production in lipopolysaccharide (LPS) stimulated cells (Jung et al. 2006). The data suggested that the extract may suppress LPS-stimulated TNF production through inhibition of Nfkappab in BV2 microglia cells.

Shukla et al. (2008b) reported that consumption of hydrolyzable tannins-rich pomegranate extract potently delayed the onset and reduced the incidence and severity of collagen-induced arthritis in mice. Pomegranate extract -fed mice had reduced joint infiltration by the inflammatory cells, and the destruction of bone and cartilage were alleviated. Levels of interleukin IL-6 were significantly decreased in the joints of pomegranate-fed mice with collagen-induced arthritis. In mouse macrophages, pomegranate extract abolished multiple signal transduction pathways and downstream mediators implicated in the pathogenesis of rheumatoid arthritis. In another study, rabbit plasma samples collected after oral ingestion of polyphenol rich pomegranate fruit extract were found to inhibit the IL-1β-induced PGE2 and NO production in chondrocytes (Shukla et al. 2008a). These same plasma samples also inhibited both COX-1 and COX-2 enzyme activity ex-vivo but the effect was more pronounced on the enzyme activity of COX-2 enzyme. The studies suggested that pomegranate fruit extract-derived bioavailable compounds may exert an anti - inflammatory effect by inhibiting the inflammatory cytokine-induced production of PGE2 and NO in-vivo. Pomegranate extract rich in polyphenols was found to inhibit the interleukin-1β-induced activation of MKK-3, p38α-MAPK and transcription factor RUNX-2 in human osteoarthritis chondrocytes (Rasheed et al. 2010). This pharmacological actions of pomegranate extract suggest that the extract or its derived compounds may be developed as MKK and p38-MAPK inhibitors for the treatment of osteoarthritis and other degenerative/inflammatory diseases. In a pilot12 week open-labelled study, pomegranate consumption reduced the composite Disease Activity Index (DAS28) and tender joint count in rheumatoid arthritis patients, and this effect could be related to the antioxidative property of pomegranates (Balbir-Gurman et al. 2011). The results suggested dietary supplementation with pomegranates may be a useful complementary strategy to attenuate clinical symptoms in rheumatoid arthritis patients.

Supplementation of obese Zucker rats with pomegranate fruit extract (PFE) or pomegranate juice (PJ) significantly decreased the expression of vascular inflammation markers, thrombospondin (TSP), and cytokine TGFβ1, whereas seed oil supplementation had a significant effect only

on TSP-1 expression (de Nigris et al. 2007a). Plasma nitrate and nitrite (NO(x)) levels were significantly increased by PFE and PJ. In addition, the effect of PFE in increasing endothelial NO synthase (eNOS) expression was comparable to that of PJ. The data suggested possible clinical applications of PFE in metabolic syndrome (clinical conditions such as obesity, hypertension, dislipidemia, and diabetes).

In-vivo studies revealed that aqueous pomegranate peel extract inhibited neutrophil myeloperoxidase activity and attenuated lipopolysaccharide-induced lung inflammation in mice (Bachoual et al. 2011). Inhibition of myeloperoxidase activity by pomegranate extract could explain its antiinflammatory action.

Balwani et al. (2011) demonstrated that 2-methyl-pyran-4-one-3-*O*-β-d-glucopyranoside (MPG) isolated from pomegranate leaves, inhibited TNFα-induced cell adhesion molecules expression by blocking nuclear transcription factor-κB (NF-κB) translocation and activation. The results suggested that MPG could be useful as a novel lead molecule for developing future antiinflammatory agents. Oral pomegranate extract decreased reactive oxygen species concentration and acute inflammation in the tympanic membrane in rats after myringotomy (Kahya et al. 2011). The density of inflammatory cells was significantly less in rats treated with the extract and the lamina propria thickness and vessel density were also significantly reduced.

Hepatoprotective Activity

Pretreatment of Wistar rats with a methanolic extract of pomegranate peel followed by carbon tetrachloride treatment retained catalase, peroxidase, and superoxide dismutase to values comparable with control values, whereas lipid peroxidation was reduced by 54% as compared to control (Chidambara Murthy et al. 2002). Histopathological studies of the liver supported the hepatoprotective effects exhibited by the extract by restoring the normal hepatic architecture. Kaur et al. (2006) demonstrated that pre-treatment of mice with pomegranate flower extract at a dose regimen of 50–150 mg/kg body weight for a week significantly and dose dependently protected against ferric nitrilotriacetate (Fe-NTA)-induced oxidative stress as well as hepatic injury. The extract conferred up to 60% protection against hepatic lipid peroxidation and preserved glutathione (GSH) levels and activities of antioxidant enzymes viz., catalase (CAT), glutathione peroxidase (GPX) glutathione reductase (GR) and glutathione-S-transferase (GST) by up to 36, 28.5, 28.7, 40.2 and 42.5% respectively. A protection against Fe-NTA induced liver injury was apparent as inhibition in the modulation of liver markers viz., aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubin and albumin in serum. The histopathological changes produced by Fe-NTA, such as ballooning degeneration, fatty changes, necrosis were also alleviated by the extract. The flower extract was found to significantly scavenge superoxide radicals by up to 53.3%, hydrogen peroxide by up to 30%, hydroxyl radicals by up to 37% and nitric oxide by up to 74.5%. The extract also inhibited (.)OH induced oxidation of lipids and proteins in vitro. The potent antioxidant property of the flower extract was postulated to be responsible for its hepatoprotective effects. In another study, pomegranate flower infusion was found to exhibit hepatoprotective and antioxidant effect against trichloroacetic acid (TCA)-exposed rats (Celik et al. 2009). The infusion significantly decreased levels of aspartate aminotransferase and alanine aminotransferase; increased significantly glutathione S-transferase activity in the liver, brain and spleen and maintained superoxide dismustase level in the liver.

Intake of pomegranate juice by mice for weeks was found to confer hepatic protection against protein and DNA oxidation (Faria et al. 2007b). There was also a significant decrease in GSH (reduced glutathione) and GSSG (oxidized glutathione), without change in the GSH/GSSG ratio. All studied enzymatic activities (superoxide dismutase (SOD), glutathione peroxidase (GPX), glutathione S-transferase (GST) and glutathione

reductase (GR) and catalase) were found to be decreased by pomegranate juice treatment. Also, glutathione S-transferase and glutathione synthetase transcription were also decreased in this group. Chronic pomegranate peel extract administration to rats alleviated the bile duct ligation (BDL)-induced oxidative injury of the liver and improved the hepatic structure and function (Toklu et al. 2007). Plasma antioxidant capacity and hepatic glutathione levels were significantly depressed by BDL but were increased back to control levels in the pomegranate extract-treated BDL group. Increases in tissue malondialdehyde levels and myeloperoxidase activity due to BDL were reduced back to control levels by pomegranate extract treatment. Similarly, increased hepatic collagen content in the BDL rats was reduced to the level of the control group with extract treatment.

Cardioprotective Activity

Sumner et al. (2005) showed that daily consumption of pomegranate juice may improve stress-induced myocardial ischemia in patients who have coronary heart disease in a randomized, placebo-controlled, double-blind study. After 3 months, the extent of stress-induced ischemia decreased in the pomegranate group (SDS −0.8 ± 2.7) but increased in the control group (SDS 1.2 ± 3.1). This benefit was observed without changes in cardiac medications, blood sugar, hemoglobin A1c, weight, or blood pressure in either group. Mohan et al. (2010a) demonstrated that pre-treatment of male Wistar rats with pomegranate juice (100 and 300 mg/kg, p.o.) and its butanolic extract(100 mg/kg., p.o.) for a period of 21 days significantly inhibited the effects of isoproterenol-induced myocardial infarction such as heart rate, pressure rate index, ECG patterns, levels of lactate dehydrogenase, creatine kinase, superoxide dismutase and catalase in the serum and vascular reactivity changes. Treatment with PJ and B-PJ (100 mg/kg., p.o.) alone did not alter any of the parameters as compared to vehicle-treated Wistar rats. Hassanpour et al. (2011) found that pomegranate fruit extract displayed cardioprotective doxorubicin (Dox)-induced cardiotoxicity in rats. Rats administered the extract showed decreased QT and increase in heart rate compared to the Dox group Significant decrease in creatine kinase-MB isoenzyme, lactate dehydrogenase and no such significant decrease in aspartate aminotransferase were observed as compared to the Dox group. There was significant increase in the level of reduced glutathione, whereas inhibition of lipid peroxidation and increase in superoxide dismutase concentration was not significant in the extract treated group compared to the Dox group. Histopathological study of the extract -treated group showed slight protection against myocardial toxicity induced by Dox.

Gastroprotective/Antiulcerative Activities

P. granatum fruit peel extract elicited 100% precipitation of ovine haemoglobin in-vitro and when orally administered to ethanol-induced gastric-damaged rats produced a significant decrease in gastric lesions (Gharzouli et al. 1999). The acid content of the stomach was significantly increased by pomegranate (368%) suggesting that monomeric and polymeric polyphenols could strengthen the gastric mucosal barrier. Administration of 70% methanolic pomegranate rind extract inhibited aspirin- and ethanol-induced gastric ulceration (Ajaikumar et al. 2005). Treated animals showed increased antioxidant levels of superoxide dismutase (SOD), catalase, glutathione (GSH) and glutathione peroxidase (GPx) and decreased level of tissue lipid peroxidation. No erosion of gastric mucosa, sub-mucosal edema and neutrophil infiltration was observed in treated animals. Pomegranate tannins (500, 150, 50 mg/kg) significantly inhibited ulcerative formation induced by both water immersion stress and pylorus ligation, and decreased the gastric mucosa damages induced by intragastric absolute ethanol, in dose-dependent manner in rats (Lai et al. 2009). Its antiulcer effect was found to be due to increasing secretion of adherent mucus and free mucus from the stomach wall, which may inhibit

generation of oxygen-derived free radicals, and decrease the consumption glutathione peroxidase (GSH-PX) and superoxide dismutase (SOD), decrease absolute alcohol-induced elevation of malondialdehyde and maintain content of NO at normal level. *Punica granatum* peel extract (PPE) supplementation of irradiated rats reduced oxidative damage in the ileal tissues and protected against ionizing radiation-induced enteritis and leukocyte apoptosis in rats, probably by a mechanism associated with the decreased production of reactive oxygen metabolites and enhancement of antioxidant mechanisms (Toklu et al. 2009). PPE treatment reversed all these biochemical indices induced by irradiations such as the decrease in glutathione and total antioxidant capacity associated with increases in malondialdehyde levels, myeloperoxidase activity, collagen content of the tissue with a concomitant increase 8-hydroxy-2′-deoxyguanosine (an index of oxidative DNA damage) and increases in pro-inflammatory cytokines (TNF-α, IL-1β and IL-6) and lactate dehydrogenase. histopathological alterations and the increase in leukocyte apoptosis and cell death induced by irradiation was also reversed by PPE.

Oral administration of aqueous methanolic extract of pomegranate (490 and 980 mg/kg bw) significantly reduced the ulcer lesion index produced by alcohol, indomethacin, and aspirin, at both doses in rats (Alam et al. 2010). In pylorus-ligated rats the extract significantly reduced the ulcer lesions, gastric volume, and total acidity and prevented the ulceration by increasing the pH and mucus secretion.

Oral administration of pomegranate extract and its ellagic acid rich fraction (100 and 200 mg/kg) significantly attenuated dextran sulfate sodium -induced colonic inflammation in mice along with attenuation of histamine, myeloperoxidase and oxidative stress (Singh et al. 2009). The antiulcerative effect was comparable to sulphasalazine (100 mg/kg, p.o.) and sodium cromoglycate (40 mg/kg i.p). The authors stated that the antiulcerative effects may be attributed to mast cell stabilizing, antiinflammatory and antioxidant actions. Pomegrante peel extracts exhibited remarkable in-vitro anti-*Helicobacter pylori* activity against the clinical isolates of *H. pylori* (mean of inhibition zone diameter ranging from 16 to 40 mm/50 μg disc). *Helicobacter pylori* infection causes lifelong chronic gastritis, which can lead to peptic ulcer, mucosa-associated lymphoid tissue (MALT) lymphoma and gastric cancer.

Nephroprotective Activity

Pretreatment of rats with hydroalcoholic extract of pomegranate flowers (125 and 250 mg/kg p.o. twice daily for 3 days) significantly attenuated hypertonic glycerol-induced myoglobinuric renal dysfunction in a dose-dependent manner (Singh et al. 2011). The mechanism of renoprotective effects of *Punica granatum* was found to involve activation of PPAR-γ and nitric oxide-dependent signalling pathway.

Immunomodulatory Activity

Pomegranate fruit rind powder at the dose of 100 mg/kg orally as aqueous suspension was found to stimulate the cell-mediated and humoral components of the immune system in rabbits (Gracious Ross et al. 2001). The pomegranate powder elicited an increase in antibody titer to typhoid-H antigen. It also enhanced the inhibition of leucocyte migration in Leucocyte Migration Inhibition test and induration of skin in delayed hypersensitivity test with Purified Protein Derivative (PPD) confirming its stimulatory effect on cell-mediated immune response. Punicalagin isolated from pomegranate fruit was found to be a potent immune suppressant, based on its inhibitory action on the activation of the nuclear factor of activated T cells (NFAT). Punicalagin downregulated the mRNA and soluble protein expression of interleukin-2 from anti-CD3/anti-CD28-stimulated murine splenic CD4+ T cells and suppressed mixed leukocytes reaction (MLR) without exhibiting cytotoxicity to the cells. In vivo, the punicalagin treatment inhibited phorbol 12-myristate 13-acetate (PMA)-induced chronic ear edema in mice and decreased CD3+ T cell infiltration of the inflamed tissue. The results suggested that punicalagin could be a potential candidate for the therapeutics of various

immune pathologies. Yamasaki et al. (2006) found that dietary pomegranate seed oil (PSO) high in levels of punicic acid (9c, 11 t, 13c-octadecatrienoic acid), may enhance B-cell function in mice. Splenocytes isolated from mice fed 0.12 or 1.2% PSO produced larger amounts of immunoglobulins G and M but not immunoglobulin A irrespective of stimulation with or without phorbol 12-myristate 13-acetate and the calcium ionophore A23187. Dietary PSO did not affect the percentages of B cells or CD4-positive or CD8-positive T cells in splenocytes. A polysaccharide (PSP001) isolated from pomegranate rind was found to have immunomodulatory activity (Joseph et al. 2012). PSP001 showed in-vitro growth stimulatory effect on isolated normal lymphocytes, and a proliferative index of 1.21 at a concentration of 1,000 μg/-mL was obtained, indicating immunomodulatory activity.

Wound Healing Activity

Wistar rats with excision wounds treated with 5% water-soluble gel formulated from the methanolic extract of dried pomegranate rind, showed good complete wound healing after 10 days (Chidambara Murthy et al. 2004). In comparison in rats treated with 2.5% gel, healing was observed on day 12, and in the positive control animals receiving the blank gel took 16–18 days for complete healing. Collagen content in terms of hydroxyproline level increased by two-fold in the group treated with 5.0% gel. The gel extract was found to contain gallic acid and catechin as major components. Aslam et al. (2006) found that pomegranate seed oil, but not aqueous extracts of fermented juice, peel or seed cake, stimulated human keratinocyte proliferation in monolayer culture. Contrariwise, pomegranate peel aqueous extract (and to a lesser extent, both the fermented juice and seed cake extracts) stimulated type I procollagen synthesis and inhibited matrix metalloproteinase-1 (MMP-1; interstitial collagenase) production by dermal fibroblasts, but had no growth-supporting effect on keratinocytes. The results suggested that pomegranate peel aqueous extract could promote regeneration of dermis and pomegranate seed oil could promote regeneration of epidermis. Pomegranate peel methanol extract-based ointment significantly enhanced wound contraction and the period of epithelialization as assessed by the mechanical (contraction rate, tensile strength), the biochemical (increasing of collagen, DNA and proteins synthesis) and the histopathological characteristics in guinea pigs (Hayouni et al. 2011). The extract displayed antioxidant activity as potent as natural and synthetic compounds (Trolox, Butylated hydroxyanisole, Quercetin). In addition, the extract exhibited significant antibacterial and antifungal activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella anatum*, *Salmonella typhimurium*, *Streptococcus pneumoniae*, and fungi *Candida albicans*, *Candida glabrata*, *Trichopyton rubrum* and *Aspergillus niger*. The results suggested that the pomegranate formulated ointment may be used as skin repair agent without hazard to human health. The ethanol extract of *P. granatum* flowers showed significant wound healing activity when topically administered in rats (Pirbalouti et al. 2010). The extract significantly increased the rate of wound contraction and collagen turnover.

Photoprotective Activity

In-vitro studies using normal human epidermal keratinocytes, showed that pre-treatment with pomegranate fruit extract rich in anthocyannins and hydrolyzable tannins protected against the adverse effects of UV-B radiation by inhibiting UV-B-induced modulations of nuclear factor kappa B (NF-kappaB) and mitogen-activated protein kinases (MAPK) pathways (Afaq et al. 2005a, b). Similarly, they reported pomegranate fruit extract to be an effective agent for ameliorating UVA-mediated skin damages by modulating cellular pathways in-vitro (Syed et al. 2006). UVA-mediated cellular damage occurs primarily through the release of reactive oxygen species and is responsible for immunosuppression, photodermatoses, photoaging and photocarcinogenesis. Pretreatment of normal human epidermal keratinocytes with the extract (60–100 μg/mL) for 24 h before exposure to UVA resulted in

a dose-dependent inhibition of UVA-mediated phosphorylation of signal transducers and activators of transcription 3 (STAT3), protein kinase B/AKT and mitogen activated protein kinases (MAPKs) viz. extracellular signal-regulated kinase (ERK1/2). The extract pretreatment also inhibited UVA exposure-mediated increases in Ki-67 antigen and PCNA (proliferating cell nuclear antigen) and increased the cell-cycle arrest induced by UVA in the G1 phase and the expression of Bax and Bad (proapoptotic proteins), while suppressing Bcl-X(L) antiapoptotic protein expression. Studies by Zaid et al. (2007) showed that pretreatment of human immortalized HaCaT keratinocytes with polyphenol-rich pomegranate fruit extract inhibited UVB-mediated decrease in cell viability, decrease in intracellular glutathione content and increase in lipid peroxidation. immunoblot analysis showed that pretreatment of HaCaT cells with pomegranate fruit extract inhibited UVB-induced (1) upregulation of MMP-1, -2, -7 and -9, (2) decrease in TIMP-1, (3) phosphorylation of MAPKs and (iv) phosphorylation of c-jun, whereas no effect was observed on UVB-induced c-fos protein levels. The results suggested that pomegranate fruit protected HaCaT cells against UVB-induced oxidative stress and markers of photoaging and could be a useful supplement in skin care products.

Pomegranate fruit extract (5–60 mg/L) was effective at protecting human skin fibroblasts from cell death following UV irradiation (Pacheco-Palencia et al. 2008). This photoprotective effect was postulated to be related to a reduced activation of the pro-inflammatory transcription factor NF-kappaB, suppression of proapoptotic caspase-3, and an increased G0/G1 phase, associated with DNA repair. Higher polyphenolic concentrations (500–10,000 mg/L) were required to achieve a significant reduction in UV-induced reactive oxygen species levels and increased intracellular antioxidant capacity. Pretreatment of reconstituted human skin "Epiderm" with pomegranate-derived products POMx juice, POMx extract and pomegranate oil inhibited UVB-induced cyclobutane pyrimidine dimers (CPD), 8-dihydro-2′-deoxyguanosine (8-OHdG), protein oxidation and proliferating cell nuclear antigen (PCNA) protein expression (Afaq et al. 2009). Further, pretreatment of Epiderm with pomegranate-derived products resulted in inhibition of UVB-induced collagenase (MMP-1), gelatinase (MMP-2, MMP-9), stromelysin (MMP-3), marilysin (MMP-7), elastase (MMP-12), and tropoelastin. MMP-2 and MMP-9 activities were also inhibited. Overall, the results suggested that all three pomegranate-derived products may be useful against UVB-induced damage to human skin. Park et al. (2010) using cultured human skin fibroblasts, demonstrated that pomegranate fruit rind extract rich in polyphenols catechin, quercetin, kaempferol, and equol significantly protected against UVB-induced skin damage. The synthesis of collagen was increased and the expression of MMP-1 was decreased.

Oral feeding of pomegranate fruit extract to mice provided substantial protection from the adverse effects of UVB radiation via modulation in early biomarkers of photocarcinogenesis (Afaq et al. 2010). The extract inhibited UVB-induced: skin edema; hyperplasia; infiltration of leukocytes; lipid peroxidation; hydrogen peroxide generation; ornithine decarboxylase (ODC) activity; and ODC, cyclooxygenase-2 and proliferating cell nuclear antigen protein expression. The extract enhanced repair of UVB-mediated formation of cyclobutane pyrimidine dimers (CPDs) and 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxodG). The extract inhibited UVB-mediated nuclear translocation of NF-κB; activation of IKKα; and phosphorylation and degradation of IκBα. Additionally, the extract further enhanced UVB-mediated increase in tumour suppressor p53 and cyclin kinase inhibitor p21. In further studies, Khan et al. (2012) reported that oral feeding of pomegranate fruit extract to SKH-1 hairless mice inhibited UVB-induced epidermal hyperplasia, infiltration of leukocytes, protein oxidation and lipid peroxidation. Immunoblot analysis demonstrated that oral feeding of pomegranate fruit extract to mice inhibited UVB-induced (1) nuclear translocation and phosphorylation of nuclear factor kappa B/p65, (2) phosphorylation and degradation of IκBα, (3) activation of IKKα/IKKβ and (4) phosphorylation of mitogen-activated protein kinase proteins and c-Jun. Pomegranate fruit extract consumption also inhibited UVB-induced protein expression

of (1) COX-2 and iNOS, (2) PCNA and cyclin D1 and (3) matrix metalloproteinases-2,-3 and -9 in mouse skin. Overall, the data showed that pomegranate fruit extract consumption afforded protection to mouse skin against the adverse effects of UVB radiation by modulating UVB-induced signalling pathways.

In a double-blind, placebo-controlled trial involving female subjects age 20–40s, Kasai et al. (2006) found that oral administration of an ellagic acid-rich pomegranate extract had an inhibitory effect on a slight pigmentation (stains and freckles, brightness of face) in the human skin caused by UV irradiation.

Skin Whitening Activity

Methanolic pomegranate extract showed 53.4% in-vitro mushroom tyrosinase inhibitory activity (Adhikari et al. 2008). A pomegranate rind extract was found to have skin whitening activity (Yoshimura et al. 2005). The extract exhibited inhibitory activity against mushroom tyrosinase in-vitro comparable to that of the skin whitening agent, arbutin. When taken orally the extract inhibited UV-induced skin pigmentation on the back of brownish guinea pig. The results suggested the skin-whitening effect of the extract was probably due to inhibition of the proliferation of melanocytes and melanin synthesis by tyrosinase in melanocytes. A pomegranate polysaccharide fraction inhibited the formation of advanced glycation end-products (AGEs) by 28% and also inhibited the formation of fructosamine in the BSA/Glucose system (Rout and Banerjee 2007). The fraction inhibit 1,1-diphenyl-2-picrylhydrazyl (DPPH) and 2,2′-Azinobis[3-ethylbenzothiazoline-6-sulfonate] ABTS(+) radical activities by 69 and 88%, respectively with 4 μg/mL concentration It also inhibited mushroom tyrosinase by 43% at 10 μg/mL concentration suggesting its efficacy as a potential skin whitener.

Anti-hyperoxaluria Activity

Pomegrante juice was shown to have a protective effect against ethylene glycol-induced nephrolithiasis in rats (Tugcu et al. 2008). Ethylene glycol caused hyperoxaluria characterised by severe crystalization in renal tubules and granulovacuolar epithelial cell degeneration, marked elevation in malondialdehyde and nitric oxide levels and decrease of reduced glutathione (GSH) in rats There was no crystal formation in the rats treated with ethylene glycol and pomegranate juice. Administration of pomegranate juice at medium and high dosage to rats was found to have inhibitory effects on renal tubular cell injury and oxidative stress caused by oxalate crystal deposition by reducing ROS, iNOS, p38-MAPK, and NF-kB expression (Ilbey et al. 2009).

Antidiarrhoeal Activity

Rats treated with methanol pomegranate seed extract exhibited significant inhibitory activity against castor-oil induced diarrhoea and PGE2 induced enteropooling (Das et al. 1999). The extract also displayed a significant reduction in gastrointestinal motility in charcoal meal test in rats.

Antiplatelet Aggregation Activity

Pomegranate juice and polyphenol-rich pomegranate fruit extract reduced platelet aggregation, calcium mobilization, thromboxane A(2) production, and hydrogen peroxide formation, induced by collagen and arachidonic acid (Mattiello et al. 2009). The polyphenol – rich fruit extract was more potent in reducing platelet activation. Studies showed that pomegranate fruit components (mainly ellagic acid) modulated human thrombin amidolytic activity (Cuccioloni et al. 2009).

Antiosteoporotic Activity

Pomegranate fruit ethanol extract was found to significantly increase the growth of osteoblastic MC3T3-E1 cells and caused a significant elevation of alkaline phosphatase (ALP) activity and collagen content in the cells (Kim and Choi 2009). Treatment the extract decreased the TNF-α-induced production of interleukin IL-6 and nitric oxide in osteoblasts.

Uterine Contractile Activity

Promprom et al. (2010) found pomegranate seed extract to be a potent stimulator of phasic activity in rat uterus. Pomegranate seed extract and β-sitosterol, the main constituent of the extract (16%), increased spontaneous contractions of the rat uterus in a concentration-dependent manner. Their data suggested that the uterotonic effect was due to nonestrogenic effects of β-sitosterol acting to inhibit K channels and sarcoplasmic reticulum calcium ATPase and thereby increasing contraction via calcium entry on L-type calcium channels and myosin light chain kinase.

Antidementia and Central Nervous System Activities

Two β-secretase (BACE1) inhibitors (anti-dementia agents) were isolated from pomegranate rind and identified as ellagic acid and punicalagin with IC_{50} values of 3.9×10^{-6} and 4.1×10^{-7} M (Kwak et al. 2005). Ellagic acid and punicalagin were less inhibitory to α-secretase (TACE) and other serine proteases such as chymotrypsin, trypsin, and elastase, thus indicating that they were relatively specific inhibitors of BACE1. β-Secretase is an aspartic-acid protease involved in the pathogenesis of Alzheimer's disease

Studies showed that ethanolic extract of *P. granatum* seeds significantly exhibited the anxiolytic activity animal models of elevated plus maze test, barbiturate-induced sleeping time, tail suspension test, hot-plate and tail-flick tests (Kumar et al. 2008). The extract (250 and 500 mg/kg) significantly increased the sleeping latency and reduced the sleeping time. Tail suspension test showed that the extract (250 and 500 mg/kg) was able to induce a significant decrease in the immobility time, similar to imipramine, a recognized antidepressant drug. Tail-flick and hot-plate tests exhibited antinociceptive property of pomegranate extract, similar to morphine, a recognized antinociceptive agent. Phytochemical screening and measurement of reducing power revealed the central nervous system (CNS) activity of ethanol extract of pomegranate seeds may be due to its antioxidative profile.

Supplementation of pomegranate flowers led to improvements in learning and memory performances of streptozotocin-induced diabetic rats (Cambay et al. 2011). Supplementation of pomegranate flowers restored the elevated levels of lipid peroxidation and decreased level of glutathione towards their control values. Daily pomegranate flower supplementation to diabetic rats reduced the increase in glial-fibrilar acidic protein (GFAP) contents induced by diabetes in the hippocampus. The observations suggested that pomegranate flower supplementation decreased oxidative stress and amelioratedimpairment in learning and memory performances in diabetic rats and may be clinically useful in treating neuronal deficit in diabetic patients.

Neuroprotective Activity

Loren et al. (2005) found that maternal dietary supplementation with pomegranate juice was neuroprotective in an animal model of neonatal hypoxic-ischemic brain injury. Dietary supplementation with pomegranate juice resulted in markedly decreased brain tissue loss (>60%) in all three brain regions assessed, with the highest pomegranate juice dose having greatest significance Pomegranate juice also diminished caspase-3 activation by 84% in the hippocampus and 64% in the cortex. In further studies, the scientists showed that pomegranate polyphenols and resveratrol reduced caspase-3 activation following neonatal hypoxic-ischemic injury (West et al. 2007). In separate study, transgenic mice (APP(sw)/Tg2576) treated with pomegranate juice had significantly less (approximately 50%) accumulation of soluble Aβ42 and amyloid deposition in the hippocampus as compared to control mice (Hartman et al. 2006). Mice administered pomegranate juice learned water maze tasks more quickly and swam faster than controls. The results suggest that pomegranate juice may be useful in Alzheimer's disease and warrant further studies. Choi et al. (2011b) found that the ethanol pomegranate extract mitigated H_2O_2-induced oxidative stress in PC12 cells. Additionally, the extract inhibited neuronal cell

death caused by Aβ-induced oxidative stress and Aβ-induced learning and memory deficiency in mice.

Embryo and Sperm Protective Activity

Studies showed that pomegranate fruit extract exhibited embryo protective effect against adriamycin-induced oxidative stress in chick embryos (Kishore et al. 2009). Pre-administration of pomegranate fruit extract significantly ameliorated to normal, embryo gross morphological deformities and significant changes in the levels of biochemical parameters in amniotic fluid observed in the adriamycin-treated group.

Pomegranate juice consumption by healthy male rats provided an increase in epididymal sperm concentration, sperm motility, spermatogenic cell density and diameter of seminiferous tubules and germinal cell layer thickness and antioxidant activity, and it decreased abnormal sperm rate when compared to the control group (Türk et al. 2008). A significant decrease in malondialdehyde level and marked increases in glutathione, glutathione peroxidase and catalase activities, and vitamin C level were observed in rats treated with different doses of pomegranate juice. Studies showed that ethanolic extract of pomegranate could be useful for the treatment of the deleterious effect of lead acetate administration on sperm production in rats (Leiva et al. 2011). The extract exhibited antioxidant activity similar to that of ascorbic acid and prevented lead acetate -induced spermatogenic disruption in rats. Its antioxidant activity could explain its capacity to reverse the damage produced by lead acetate on spermatogenesis.

Amelioration of Erectile Dysfunction Activity

In a randomized, placebo-controlled, double-blind, crossover study involving male patients with mild to moderate erectile dysfunction, of the 42 subjects who demonstrated improvement in Global Assessment Questionnaires (GAQ) scores after beverage consumption, 25 reported improvement in erectile function after drinking pomegranate juice (Forest et al. 2007). Subjects were more likely to have improved scores when pomegranate juice was consumed. Although overall statistical significance was not achieved, this pilot study suggested the possibility that larger cohorts and longer treatment periods may achieve statistical significance. Studies in rabbits with atherosclerosis-induced erectile dysfunction showed that pomegranate extract significantly improved intracavernosal blood flow, erectile activity, smooth muscle relaxation and fibrosis of the atherosclerotic group in comparison with the atherosclerotic group receiving placebo, but did not normalize them to the age-matched control levels (Zhang et al. 2011). Pomegranate extract appeared more effective in diminishing oxidative products, preventing superoxide dismutase and aldose reductase gene upregulation, and protecting mitochondrial, endothelial and caveolae structural integrity of the atherosclerotic group. The study showed that dietary antioxidants could improve arteriogenic erectile dysfunction.

Estrogenic Activity

Pomegranate known to contain estrogens (estradiol, estrone, and estriol) exhibited estrogenic activities in mice (Mori-Okamoto et al. 2004). Administration of pomegranate extract (juice and seed extract) for 2 weeks to ovariectomized mice prevented the loss of uterus weight and shortened the immobility time compared with 5% glucose-dosed mice (control). Further, ovariectomy-induced decrease of bone mineral density was normalized by administration of the pomegranate extract. The bone volume and the trabecular number were significantly increased and the trabecular separation was decreased in the pomegranate-dosed group compared with the control group. Some histological bone formation/resorption parameters were significantly increased by ovariectomy but were normalized by administration of the pomegranate extract. These changes suggested that the pomegranate extract inhibited

ovariectomy-stimulated bone turnover. The authors concluded that pomegranate may be clinically effective on a depressive state and bone loss in menopausal syndrome in women.

Cytochrome P450-3A (Drug-Drug Interaction) Activity

Studies in human volunteers, found that in human liver microsomes, the mean 50% inhibitory concentrations (IC_{50}) for pomegranate juice (PJ) and grapefruit juice (GFJ) versus CYP3A (triazolam α-hydroxylation) were 0.61 and 0.55%, (v/v) respectively without preincubation of inhibitor with microsomes (Farkas et al. 2007). After preincubation, the IC_{50} for PJ increased to 0.97% whereas the IC_{50} for GFJ decreased to 0.41% suggesting mechanism-based inhibition by GFJ but not PJ. Administration of PJ also did not affect C(max), total area under the curve (AUC), or clearance of oral midazolam. However, GFJ increased midazolam C(max) and AUC by a factor of 1.3 and 1.5, respectively, and reduced oral clearance to 72% of control values. The results suggested PJ did not alter clearance of intravenous or oral midazolam, whereas GFJ impaired clearance and elevated plasma levels of oral midazolam. Jarvis et al. (2010) reported a potential interaction between pomegranate juice and warfarin as laboratory studies hade shown that pomegranate juice inhibited cytochrome P450 enzymes involved in warfarin metabolism. In a an open-label, randomized, single-center, two-period crossover study in healthy Japanese volunteers, a single subtherapeutic doses of midazolam following 2 weeks consumption of pomegranate juice did not significantly alter the pharmacokinetic profile of midazolam compared with that of the control (Misaka et al. 2011).

Effect on Chronic Obstructive Pulmonary Disease

Results of a 5-week randomized, double-blind, placebo-controlled study involving 30 patients suggested that polyphenol-rich pomegranate juice (PJ) supplementation added no benefit to the current standard therapy in patients with stable chronic obstructive pulmonary disease (Cerdá et al. 2006). The high TEAC (Trolox Equivalent Antioxidant Capacity) of PJ could not be extrapolated in-vivo probably due to the metabolism of its polyphenols by colonic microflora. The understanding of the different bioavailability of dietary polyphenols was thus critical before claiming any antioxidant-related health benefit.

Ergogenic Activity

Elbow flexion strength was significantly higher during the 2- to 168-h period post-exercise with pomegranate juice compared with that of placebo (Trombold et al. 2011). Elbow flexor muscle soreness was also significantly reduced with pomegranate juice compared with that of placebo and at 48 and 72 h post-exercise. Isometric strength and muscle soreness in the knee extensors were not significantly different with pomegranate juice compared with those using placebo. The results indicated a mild, acute ergogenic effect of pomegranate juice in the elbow flexor muscles of resistance trained individuals after eccentric exercise.

Carbonic Anhydrase Inhibition Activity

Seven highly active ellagitannin inhibitors against carbonic anhydrase, punicalin (2), punicalagin (3), granatin B (5), gallagyldilactone (7), casuarinin (8), pedunculagin (9) and tellimagrandin I (10), and four weakly active ellagitannin inhibitors, gallic acid (1), granatin A (4), corilagin (6) and ellagic acid (11), were isolated from pomegranate pericarps (Satomi et al. 1993). The type of inhibition by compounds (3) and (7) using *p*-nitrophenyl acetate as a substrate, was noncompetitive. Carbonic anhydrase inhibitors are used as antiglaucoma drugs, and many potent carbonic anhydrase inhibitors have also been shown to inhibit the growth of several tumour cell lines in-vitro and in-vivo providing interesting leads for developing novel antitumour therapies (Supuran et al. 2004)

Analgesic Activity

Using the hot plate method in mice, pomegranate flower extracts showed significant analgesic activity at a dose of 50 mg/kg body weight (Chakraborthy 2008). Maximum analgesic activity was observed at 60 min after drug administration, which was equivalent to the standard drug used morphine sulphate.

Antiplasmodial/Anti-protrozoal Activities

Two milliliters of aqueous extract of pomegranate roots exhibited higher activity on cultures from *Entamoeba histolytica* than from *Entamoeba invadens* strains, producing growth inhibitions of about 100 and 40% respectively (Segura et al. 1990). Alkaloid concentrations of 1 mg/mL had no amoebicide activity, however tannins at concentrations of 10 μg/mL for *E. histolytica*, and 100 μg/mL for *E. invadens* were sufficient to produce an growth inhibition about 100%. Tannic acid was also tested on the cultures of *E. histolytica* producing a high inhibitory activity on growth, this effect was produced at 0.01 mg/mL similar to that observed with the tannin mixture.

The methanolic extract of pomegranate was reported to in-vitro inhibit the growth of the malarial parasite, *Plasmodium berghei* (Dell'Agli et al. 2009). In another study, gallagic acid and punicalagin from pomegranate by-product exhibited antiplasmodial activity against *Plasmodium falciparum* D6 and W2 clones with IC_{50} values of 10.9, 10.6, 7.5 and 8.8 μM, respectively (Reddy et al. 2007). Pomegranate extract exhibited strong antimalarial activity against *Plasmodium falciparum* (Valdés et al. 2010).

P. grantum plant extract also exhibited in-vitro activity against the vaginal parasite, *Trichomonas vaginalis* (El-Sherbini et al. 2009).

Hydroalcoholic pomegranate extract inhibited the growth of intracellular amastigotes of *Leishmania amazonensis* with IC_{50} value of 69.6 μg/mL (García et al. 2010). Additionally, a low toxicity on macrophage from BALB/c mice was observed.

Anthelminthic Activity

Wibaut and Hollstein (1957) found that the anthelminthic activity of pomegranate bark extract was mainly due to isopelletierine, methylisopelletierine while ψ pelleterine was less active

Molluscicidal Activity

The molluscicidal activity of *P. granatum* bark and *Canna indica* root against the snail, *Lymnaea acuminata* was found to be both time and dose dependent (Tripathi and Singh 2000). The toxicity of *P. granatum* bark was more pronounced than that of *C. indica*. The 24 h LC_{50} of the *C. indica* was 6.54 mg/L whereas that of the bark of *P. granatum* was 4.39 mg/L. The ethanol extract of *P. granatum* (24 h LC_{50}: 22.42 mg/L) was more effective than the ethanol extract of *C. indica* (24 h LC_{50}: 55.65 mg/L) in killing the test animals. *P. granatum* and *C. indica* may be used as potent molluscicides since the concentrations used to kill the snails were not toxic to the fish *Colisa fasciatus*, sharing the same habitat with the snail. In a subsequent study, Tripathi et al. (2004) reported that sub-lethal 24 h exposure to active fraction of pomegranate bark separately or in combination with Canna roots significantly inhibited the activity of acetylcholinesterase, acid/alkaline phosphatase, Na(+)K(+)ATPase and lactic dehydrogenase in the nervous tissue of *Lymnaea acuminata.*

Pharmacokinetics/Bioavailability of Pomegranate Phytochemicals

Lei et al. (2003) found that ellagic acid, the principal bioactive component of pomegranate leaf extract, had poor absorption and rapid elimination after oral administration pomegranate leaf extract, and part of it was absorbed from stomach. Studies in rats showed that only 3–6% of the ingested punicalagin was detected as such or as metabolites in urine and faeces (Cerdá et al. 2003b). Only traces of punicalagin metabolites

being detected in liver or kidney. The transformation of ellagic acid derivatives to 6H-dibenzo[b,d] pyran-6-one derivatives in the rat was confirmed. Studies of Cerdá et al. (2004) found that the potential systemic biological effects of pomegranate juice ingestion should be attributed to the colonic microflora metabolites rather than to the polyphenols present in the juice. Neither the potent antioxidant punicalagin nor ellagic acid present in pomegranate juice were detected in both plasma and urine on ingestion of pomegranate juice. Three microbial ellagitannin-derived metabolites were detected: 3,8-dihydroxy-6H-dibenzo[b,d]pyran-6-one glucuronide, an unidentified aglycone (tentatively, trihydroxy-6H-dibenzo[b,d]pyran-6-one) and hydroxy-6-H-dibenzo[b,d]pyran-6-one glucuronide in the plasma and urine. The metabolites did not show significant antioxidant activity compared to punicalagin from pomegranate juice. In separate studies, ellagic acid was detected in human plasma at a maximum concentration (31.9 ng/mL) after 1 h post-ingestion of pomegranate juice but was rapidly eliminated by 4 h (Seeram et al. 2004). Six hours post-ingestion of pomegranate juice, ellagic acid (EA) was detected in plasma of all healthy human volunteers with a maximum concentration of 0.06 μmol/L, area under concentration time curve of 0.17 (μmol × h) × L(-1), time of maximum concentration of 0.98 h, and elimination half-life of 0.71 h (Seeram et al. 2006). Ellagic acid metabolites, including dimethylellagic acid glucuronide (DMEAG) and hydroxy-6H-benzopyran-6-one derivatives (urolithins), were also detected in plasma and urine in conjugated and free forms. DMEAG was found in the urine obtained from 15 of 18 subjects on day 0, but was not detected on d −1 (day before) or +1 (day after), demonstrating its potential as a biomarker of intake. Urolithin A-glucuronide was found in urine samples from 11 subjects on d 0 and in the urine from 16 subjects on d +1. Urolithin B-glucuronide was found in the urine of three subjects on d 0 and in the urine of five subjects on d+1. The scientists asserted that urolithins, formed by intestinal bacteria, may contribute to the biological effects of pomegranate juice as they may persist in plasma and tissues and account for some of the health benefits noted after chronic juice consumption. Studies by Seeram et al. (2008) found that pomegranate juice, pomegranate polyphenol liquid extract and pomegranate polyphenol powder extract provide similar levels of plasma and urinary ellagitannin metabolites such as urolithin A, in human subjects. There was a delay in time of maximum concentration of pomegranate powder extract compared to pomegranate juice and pomegranate polyphenol liquid. Mertens-Talcott et al. (2006) found ellagic acid from pomegranate extract to be bioavailable at 1 h after consumption by healthy volunteers. Its metabolites urolithin A, urolithin B, hydroxyl-urolithin A, urolithin A-glucuronide, and dimethyl ellagic acid-glucuronide were found in the plasma. The antioxidant capacity measured with the oxygen radical absorbance capacity (ORAC) assay was increased with a maximum effect of 32% after 0.5 h, whereas the generation of reactive oxygen species (ROS) was not affected.

Toxicological/Safety Studies

Vidal et al. (2003) found that in chick embryo model doses of hydroalcoholic pomegranate fruit extract of less than 0.1 mg per embryo were not toxic. The LD_{50} of the extract, determined in OF-1 mice of both sexes after intraperitoneal administration, was 731 mg/kg. Confidence limits were 565–945 mg/kg. At the doses of 0.4 and 1.2 mg/kg of extract, the repeated intranasal administration to Wistar rats produced no toxic effects in terms of food intake, weight gain, behavioural or biochemical parameters, or results of histopathological studies. Cerdá et al. (2003a) found that repeated oral administration of high doses of the pomegranate ellagitannin punicalagin to rats for 37 days was not toxic. Punicalagin and related metabolites were identified in plasma, liver, and kidney. Five punicalagin-related metabolites were detected in liver and kidney, that is, two ellagic acid derivatives, gallagic acid, 3,8-dihydroxy-6H-dibenzo[b,d] pyran-6-one glucuronide, and 3,8,10-trihydroxy-6H-dibenzo[b,d]pyran-6-one. Feedstuff intake,

food utility index, and growth rate were lower in punicalagin treated rats during the first 15 days without significant adverse effects, which could be due to the lower nutritional value of the punicalagin-enriched diet together with a decrease in its palatability (lower food intake). No significant differences were found in punicalagin treated rats in any blood parameter analyzed (including the antioxidant enzymes glutathione peroxidase and superoxide dismutase) with the exception of urea and triglycerides, which remained at low values throughout the study. Clinical studies by Heber et al. (2007) demonstrated the safety of a pomegranate ellagitannin-enriched polyphenol dietary supplement in overweight individuals with increased waist size and provided evidence of antioxidant activity in humans reflected by a significant reduction in thiobarbituric acid reactive substances (TBARS) linked with cardiovascular disease risk. Patel et al. (2008) found that the no observed-adverse-effect level (NOAEL) for a standardized pomegranate fruit extract was determined as 600 mg/kg body weight/day, the highest dose tested in rats. Compared to the control group, administration of the extract did not result in any toxicologically significant treatment-related changes in clinical observations, ophthalmic examinations, body weights, body weight gains, feed consumption, clinical pathology evaluations and organ weights.

Toxicological evaluation of pomegranate seed oil (PSO) showed that the no observable adverse effect level (NOAEL) was 50,000 ppm PSO (=4.3 g PSO/kg body weight/day) (Meerts et al. 2009). No mutagenicity of PSO was observed in the absence and presence of metabolic activation up to precipitating concentrations of 5,000 μg/plate (Ames test) or 333 μg/mL (chromosome aberration test). The acute oral toxicity study revealed no significant findings at 2,000 mg PSO/kg body weight.

Results from reversion and gene-conversion test in microorganisms, sister chromatid exchanges, micronuclei and sperm-shape abnormality assays in mice, clearly showed that the hydroalcoholic extract of pomegranate whole fruit was genotoxic when tested both in-vitro and in-vivo (Sánchez-Lamar et al. 2008).

Traditional Medicinal Uses

The bark of the roots, the flowers, the rind of pomegranate fruit and the seeds, are official in many pharmacopoeias. Various parts of the pomegranate plant have been extensively used for thousands of years in traditional medicine in the Middle East, Ancient Greece and Asia (Burkill 1966; Grieve 1971; Stuart 2012); and in India such as in the Ayurveda and Unani systems of medicine (Nadkarni and Nadkarni. 1982; Sharma et al. 2002; Kapoor 2000; Pradeep et al. 2008). The fruit rind and stem bark have been used as a traditional remedy for diarrhoea, dysentery and intestinal parasites. Pomegranate pericarp has been commonly employed as a crude drug in Indian traditional medicine for the treatment of diarrhoea as well as for use as an astringent, antihelminthic, asphrodisacs, laxative, diuretic, stomachic, cardiotonic and refrigerant. The seeds and juice are considered as bitter and astringent and employed as a tonic for hear and throat ailments. The astringent qualities of the flower sap, fruit rind and tree bark are considered useful remedies for nose bleeds and gum bleeds, toning skin, (after mixing with mustard oil) firming-up sagging breasts and treating haemorrhoids. A syrup prepared from the fruit is useful in all bilious complaints. The juice of the fresh fruit is much esteemed in dyspepsia and as a cooling, thirst-quenching beverage in fever and sickness. The fruit juice is also found beneficial in leprosy. Pomegranate fruit juice has been used as eye-drops to treat cataracts.

Dried, pulverized flower buds are employed as a remedy for bronchitis. Pomegranate has been reported as a remedy for diabetes in the Unani system of medicine practiced in the Middle East and India. The ancient Greeks and Egyptians used the fruit rind, flowers and root bark as astringents and the last as vermicide for treating tapeworms. In Malaysia, the root bark is used as vermifuge and powdered root bark is administered to children for stomach pains. The root is also used for diarrhoea and tits sap used for treating sore-eyes. Leaves are used in jamu preparations with a raft of other herbal ingredients for many medicinal complaints. Pounded leaves are

used in a complex bolus for stomach ache and the fruit juice is recommended for coughs. In Singapore, the root bark has been used in as a component in a compound infusion or decoction taken by women for 40 days after childbirth. Other traditional uses of the fruit rind and root include as a treatment for snakebite (Jain and Puri 1984), diabetes (Singh 1986), burns (Siang 1983), leprosy and assorted gynecological problems (Singh et al. 1980). In Sri Lanka, the fresh fruit has been used as a refrigerant to lower fever (Arseculeratne et al. 1985).

In the Philippines, a decoction of the tender leaves is used as a gargle for affections of the buccal cavity. The rind of the fruit is used internally in decoction as anthelmintic and taenifuge. In Mexico, a decoction of the flowers is gargled to relieve oral and throat inflammation. In Korea, traditional uses of the fruit and rind include as an anthelminthic and for phlegm, cholethiasis, tineapedis and laryngitis.

Other Uses

Punica granatum is a drought tolerant tree suitable for arid and semi-arid zone afforestation. Pomegranate has deep rooting system and is used for erosion control, planted along rivers to stabilize banks. An ideal suitable ornamental plant for gardens and amenity parks. Pomegranate grows along well as intercrop with grapes in Mediterranean countries. The tree is sometimes used for fencing and planted as boundary plants. Pomegranate leaf litter decomposes slowly and is suitable for mulching. The leaves are foraged by domesticated stock. Ink can be made by steeping the leaves in vinegar. Both the fruit rind and the flowers yield dyes for textiles. The light-coloured wood is hard and durable, mostly used in making farm implements, walking-sticks and in woodcrafts as it is only available in small dimension. Tree branches are used as firewood. The bark is used in tanning and dyeing providing the yellow hue for Moroccan leather. Root bark yields a black ink rich in tannins. In Japan, an insecticide is derived from the bark.

Studies revealed that pomegranate peel can prepared as an adsorbent in treating industrial effluents containing phenols and safely disposed of by stabilizing into cement (Bhatnagar and Minocha 2009). Studies showed that that pomegranate peel waste can be used as adsorbent beneficially for nickel removal from aqueous solution (Bhatnagar and Minocha 2010). Pomegranate husk when converted into activated carbon exhibited its ability to remove hexavalent chromium from wastewater (Nemr 2009).

Studies showed that the nutritive value and the antioxidant capacity of pomegranate peel could be enhanced by ensiling into a favorable health-promoting constituent of feedlot beef cattle diet (Shabtay et al. 2008). Dietary supplementation with fresh peels promoted significant increases in feed intake and α-tocopherol concentration in the plasma, with positive tendency toward increased weight gain of bull calves.

The pomegranate fruit is steeped in religious and cultural significance in Judaism, Christianity, Islam, Hinduism religions, Persian, Armenian, Azerbaijani and Chinese cultures (Wikipedia 2012).

Comments

Pomegrante germinates readily from seeds and are established from seedlings, rooted hardwood cuttings, from air layering and suckers.

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Trapa natans

Scientific Name

***Trapa natans* L.**

Synonyms

Trapa acornis Nakano, *Trapa amurensis* Flerow, *Trapa amurensis* var. *komarovii* Skvortsov, *Trapa arcuata* S.H. Li & Y.L. Chang, *Trapa bicornis* Osbeck, *Trapa bicornis* var. *acornis* (Nakano) Z.T. Xiong, *Trapa bicornis* var. *bispinosa* (Roxb.) Nakano, *Trapa bicornis* var. *cochinchinensis* (Lour.) Steenis, *Trapa bicornis* var. *quadrispinosa* (Roxb.) Z.T. Xiong, *Trapa bicornis* var. *taiwanensis* (Nakai) Z.T. Xiong, *Trapa bispinosa* Roxb., *Trapa bispinosa* var. *iinumae* Nakano, *Trapa chinensis* Lour., *Trapa cochinchinensis* Lour., *Trapa dimorphocarpa* Z.S. Diao, *Trapa japonica* Flerow, *Trapa japonica* var. *jeholensis* (Nakai) Kitag., *Trapa japonica* var. *longicollum* Z.T. Xiong, *Trapa japonica* var. *magnicorona* Z.T. Xiong, *Trapa japonica* var. *tuberculifera* (V.N. Vassil.) Tzvelev, *Trapa jeholensis* Nakai, *Trapa korshinskyi* V.N. Vassil., *Trapa litwinowii* V.N. Vassil., *Trapa litwinowii* var. *chihuensis* S.F. Guan & Q. Lang, *Trapa manshurica* Flerow, *Trapa manshurica* fo. *komarovi* (Skvortsov) S.H. Li & Y.L. Chang, *Trapa manshurica* var. *bispinosa* Flerow, *Trapa natans* fo. *quadrispinosa* (Roxb.) Makino, *Trapa natans* var. *amurensis* (Flerow) Kom., *Trapa natans* var. *bicornis* (Osbeck) Makino, *Trapa natans* var. *bispinosa* (Roxb.) Makino, *Trapa natans* var. *japonica* Nakai, *Trapa natans* var. *pumila* Nakano ex Verdc., *Trapa natans* var. *quadrispinosa* (Roxb.) Makino *Trapa potaninii* V.N. Vassil., *Trapa pseudoincisa* Nakai, *Trapa pseudoincisa* var. *aspinosa* Z.T. Xiong, *Trapa pseudoincisa* var. *complana* Z.T. Xiong, *Trapa pseudoincisa* var. *nanchangensis* W.H. Wan, *Trapa pseudoincisa* var. *potaninii* (V.N. Vassil.) Tzvelev, *Trapa quadrispinosa* Roxb., *Trapa quadrispinosa* var. *yongxiuensis* W.H. Wan, *Trapa saissanica* (Flerow) V.N. Vassil., *Trapa sibirica* Flerow, *Trapa sibirica* var. *saissanica* Flerow, *Trapa sibirica* var. *ussuriensis* Flerow, *Trapa taiwanensis* Nakai, *Trapa tranzschelii* V.N. Vassil., *Trapa tuberculifera* V.N. Vassil.

Family

Lythraceae also placed in Trapaceae.

Common/English Names

Bat Nut, Bull Nut, European Water Chestnut, Horn Nut, Jesuit's Nut, Jesuits' Nut, Ling Nut, Singhara Nut, Water Caltrop, Water Chestnut, Water Nut.

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Vernacular Names

Canada: Corniche, Trape D'Eau (French);
Chinese: Ci Ling, Língjiǎo, Ou Ling, Si Jiao Ling,Ye Ling, Ling Kok;
Czech: Kotvice Plovoucí;
Danish: Flydende Hornnød; Hornnød, Vandkastanje;
Dutch: Waternoot, Waterkastanje;
Eastonian: Vesipähkel;
Finnish: Vesipähkinä;
French: Châtaigne D'Eau, Châtaigne D'Eau À Quatre Cornes, Châtaigne D'Eau Européenne, Châtaigne D'Eau Tetracorne, Cornelle, Cornue, Mâcre Commune, Macre Nageante, Marron D'Eau, Noix Aquatique, Trape;
German: Chinesische Wassernuss; Singharanuß, Wasserkastanie, Wassernuß;
Hungarian: Sulyom, Sulyomfélék;
India: Paniphal (Bengali), Simghada, Simghara, Singhara, Singada, Hingada (Hindu), Singara, Mullu Kombu Balli, Mullu Kombu Beeja, Neeru Acrotu (Kannada), Karimpolam, Vankottakkaya (Malayalam), Heikak (Manipuri), Shingada, Singhaada (Marathi), Jalakantaka, Jalaphala, Jalaphalam, Jalashaya, Jalasuchi, Jalavalli, Kshirashukla, Sanghatica, Shringakanda, Shringamula, Shringaruha, Shringata, Shrni, Shukladugdha, Sringataka, Srngata, Srngatah, Srngataka, Srngatakah, Srngatakam, Trika, Trikonaphala,Trikota,Varikantaka,Varikubshaka, Ingataka (Sanskrit), Cimkhara (Tamil), Kubjakamu (Telugu);
Italian: Castagna D'acqua, Trapa, Tribolo Acquatico;
Japanese: Oni Bishi, Ko Oni Bishi, Akami-Bisi, Hishi, Tou Bishi;
Malaysia: Ling Kok (Cantonese);
Nepal: Singada;
Norwegian: Vassnøtt;
Polish: Kotewka Orzech Wodny;
Portuguese: Castanha D'água;
Romanian: Cornaci;
Russian: Orech Vodianoi, Orech Vodjanoj, Vodianoi Orekh Plavaiushchii;
Slovencina: Kotvica Plávajúca;
Spanish: Abrojo De Agua, Castaña De Agua;
Sri Lanka: Ikiliya, Singhara (Sinhalese);
Swedish: Sjönöt;
Thai: Kra Chom, Krachab, Ma Ngaeng.

Origin/Distribution

Water caltrop native to warm temperate parts of Eurasia and Africa. It is widely cultivated in tropical and subtropical Asia; naturalized in Australia and North America. It is cultivated in China: (Anhui, Fujian, Guangdong, Guangxi, Guizhou, Hainan, Hebei, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Jilin, Liaoning, Nei Mongol, Shaanxi, Shandong, Sichuan, Xinjiang, Xizang, Yunnan, Zhejiang), Taiwan, India, Indonesia, Japan, Korea, Laos, Malaysia, Pakistan, Philippines, Russia, Thailand, Vietnam; Africa (Nigeria), SW Asia (Iran) and some countries in Europe. It is common in almost all states of Northern India but is extensively grown in Uttar Pradesh, Madhya Pradesh, Bihar and Orissa. In past centuries it was much cultivated for the fruits in Europe to E Asia and India.

Agroecology

Trapa natans is an aquatic species, occurring in lakes, ponds, streams, ditches, canals, and slow running water from near sea level to 2,700 elevation. The plant prefers a sunny position and slightly acidic, nutrient rich water with a pH range of 6.7–8.2 and alkalinity of 12–128 mg/L of calcium carbonate. *Trapa natans* rapid and profuse growth out-competes native vegetation and spreads either by the rosettes detaching from their stems and floating to another area, or more often by the nuts being swept by currents or waves to other parts of the lake or river. It is often planted in artificial water dams and ponds.

Edible Plant Parts and Uses

The kernel of the fruit (nut) is usually cooked before eating. The highly nutritious kernel is ground into flour and used for various food preparations.

In Southern China, the nut is boiled and sold as an occasional street-side snack. In Peninsular Malaysia, The boiled nut is popularly consumed during the moon cake-lantern festival in August by the Chinese inhabitants. A pleasant herbal tea is made from the rind in Kampuchea. The kernel is also available in cans. In India, the fruit when dried is ground to a flour called *singhare ka atta* which is used in many religious rituals and can be consumed as a *phalahar* diet on the Hindu fasting days, the *navratas*.

Botany

An annual, rooted aquatic plant with a leafy rosette stem that floats on the surface. Lower adventitious roots are unbranched and thread-like and anchored the plant into the mud, while upper roots are sparsely branched and fibrous. The submersed stem is thin and limp and about 3.5–5 m long. Leaves from this plant are both surfaced and submerged. Surface floating leaves are triangular, diamond-shaped, or oval, 2–5 cm long, dentate margin, glossy abaxially and dull, finely pubescent adaxially on hairy, 10–15 cm long petioles (Plates 1 and 2). The petioles have an inflated spongy region (air bladder) in the middle (Plates 1 and 2). Submersed leaves are long and narrow, finely divided, feather-like and opposite in arrangement. Flower solitary, in leaf axils, small, 8 mm long, with four white or purplish-white petals on short, thick stalks that float among the upper leaves. Fruit a hard, woody or bony nut large, 2.5–3 cm across, variously-shaped, swollen at the middle and have 2–4 sharp barbs that resemble horns (Plates 1, 2, and 3). Each nut contains a single, fleshy seed. The nuts ripen approximately a month after flowering.

Nutritive/Medicinal Properties

The nutrient composition of the raw fruit per 100 g edible portion is: energy 117 kcal, moisture 66.4 g, protein 4.1 g, fat 0.4 g, total carbohydrate 27.8 g, fibre 0.8 g, ash 1.3 g, Ca 54 mg, P 114 mg, Fe 1.2 mg, Na 21 mg, K 452 mg, β-carotene

Plate 1 Rosette of leaves with swollen bladder in the middle of the petiole

Plate 2 Close-up of plant with young fruit and diamond-shaped leaves

Plate 3 Dried mature fruit with two horns

traces, thiamin 0.13 mg, riboflavin 0.06 mg, niacin 2.0 mg and ascorbic acid 7 mg (Leung et al. 1972).

The fruit is also rich in starch and manganese and contains more calcium, iron and phosphorous than rice.

Proximate composition of the fruit kernel was reported as per 100g: moisture 7.6%, organic matter 87%, crude protein (N×6.25) 11.4%, crude lipid 8.0%, ash 13.3%, total carbohydrate (nitrogen free extract+crude fibre) 67.3%, crude fibre 4.2% gross energy 347 kcal/100 g, vitamin E 61.3 mg/100 g, vitamin C 3 mg/100 g, carotenoid 0.2 mg/100 g, Zn 1.4 mg/dL, Mg 25.1 mg/dL, Cu 0.1 mg/dL, Ca 20 ppm, Na 5 mg/dL, K 27.7 mg/dL, P 0.9 g/kg (Kalita et al. 2007). The fruit of *Trapa natans* was found to possess the following minerals in mg/100 g: Cu 0.74–1.84 mg, Fe 28.52–72.00 mg, Mn- 3.78–11.00 mg, and Zn 3.86–8.20 mg in the peel; and Cu 0.68–1.24 mg, Fe- 11.76–16.10 mg, Mn 0.66–1.80 mg and Zn 3.86–8.22.54–5.40 mg in the kernel (Babu et al. 2011).

Proximate nutrient composition of water chestnut (*Trapa natans* var. *bispinosa*) was reported by Singh et al. (2010) as moisture 81.12%, crude lipid 0.36%, crude fibre 0.72%, crude ash 1.33%, crude protein 1.87%, total sugars 5.635, reducing sugars 1.27% and non-reducing sugars 4.36%. Total soluble solids was 7.2 Brix and titratable acidity was 0.142%. The phytochemical study of aqueous washings of *Trapa natans* showed the presence of non reducing polysaccharide, calcium, chlorides, bromides, vitamin K and pyridoxine (Rao et al. 2011). Glycosides, alkaloids, steroids, proteins and tannins were absent.

The Brabender amylogram (6% concentration) of water chestnut (*Trapa natans* var. *bispinosa*) starch showed that its pasting temperature was 71°C and its viscosity was low and remained constant during heating and increased slightly on cooling (Hizukuri et al. 1988). The amylose of the starch was composed of three components differing in molecular size and the number of chains. The amylopectin contained 44 ppm of phosphorus, and its number- and weight-average chain lengths were 22 and 26, respectively. The starch granules of *T. bispinosa* were either oval or round in shape with small horn(s) protruding from the surface (Tulyathan et al. 2005). Amylose content of the starch was 29.62% (dry weight basis). The pasting temperatures of 6–8% starch suspension were 81–83°C. Brabender amylogram showed no peak viscosity and very low breakdown, indicating high heat and shear stability of the starch suspension. The starch pastes were highly retrograded and formed an opaque gel. The X-ray diffraction patterns of the starch revealed a C-type crystallite. The starch granules were more resistant to acid hydrolysis (2.2 N HCl) at ambient temperature.

Antinutrients and Heavy Metals

Antinutrients found in the fruit kernel were: trypsin inhibitor 1.53 g%, calcium oxalate 0.9 g%, tannin 0.5 g% and phytate 0.004 g% (Kalita et al. 2007). *Trapa natans* growing in water contaminated by metals Cr, Pb and Fe in much higher than recommended permissible limits of WHO was analysed for these elements (Rai and Sinha 2001). Despite varying levels of metals found in various fruit parts of *T. natans*, the metal accumulation in the kernel was alarming. However, metal content decreased significantly in various parts after boiling the fruit.

Antioxidant Activity

Three dibenzo-.ALPHA.-pyrones, 3-hydroxy-6 H-dibenzo[b,d]pyran-6-one (1), 3,8-dihydroxy-6 H-dibenzo[b,d]pyran-6-one (2), 3,9-dihydroxy-6 H-dibenzo[b,d]-pyran-6-one (3) isolated from *Trapa natans* fruits inhibited lipid peroxidation which was induced by interaction of hemoglobin and hydrogen peroxide in-vitro (Shirataki and Toda 2001). While compound 2 and 3 exhibited antioxidative effects, inhibitory effect of 3 was stronger than those of 2 and methyl gallate and gallic acid. Antioxidative effect of compound 1 was weak. Studies showed that aqueous extract of *Trapa natans* fruit rind had significant antioxidant activity against free radicals (Malviya et al. 2010). The extract was found to contain a large amount of polyphenols and also exhibited an

immense reducing ability. The total content of phenolic, flavonoid and tannin compounds was estimated as 63.81 mg of gallic acid equivalents/g of dry material, 21.34 mg of rutin equivalents/g of dry material and 17.11 mg of total tannin equivalent/g of dry material, respectively. IC_{50} values for different antioxidant model were calculated as 128.86 μg/mL for DPPH radicals, 97.65 μg/mL for $O_2^{\bullet-}$, 148.32 μg/mL for H_2O_2 and 123.01 μg/mL for NO, respectively.

Antimicrobial Activity

The rind of the nut had been reported to have antimicrobial activity (Parekh and Chanda 2007). Maximum antibacterial activity was seen against Gram negative bacteria. *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Pseudomonas pseudoalcaligenes* were completely resistant while best antibacterial activity was shown against *Pseudomonas putida* followed by *Pseudomonas testosteroni* and *Proteus morganii* respectively while *Proteus mirabilis* was inhibited by four of the solvents only. Amongst *Klebsiella* species, *Klebsiella pneumoniae* showed high susceptibility with all the solvents while *Klebsiella aerogenes* showed slightly less susceptibility. The resistant strains were *Citrobacter fruendii*, *Enterobacter aerogenes*, *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and *Salmonella typhimurium*. Amongst Gram positive bacteria, *Micrococcus flavus* was the most susceptible bacteria and *Bacillus subtilis* was the most resistant. All other bacteria showed intermediate effects. Antifungal activity was greater against the moulds than yeast. Maximum activity was shown against *Aspergillus candidus* followed by *Mucor hiemalis*. Except *Trichosporon beigelii*, all the yeast *Candida* spp. and *Cryptococcus* spp. were resistant to all the solvents. *Aspergillus niger* was the most resistant fungal strain. Amongst the seven solvents (petroleum ether, 1, 4 dioxan, chloroform, acetone, dimethylformamide, ethanol, water) employed, water and petroleum ether extracts showed minimum activity, most of the microbial strains being resistant. The antimicrobial activity increased as the polarity of the solvents increased. Maximum antibacterial and antifungal activity was with 1, 4-dioxan extract.

A novel antifungal plant peptide named Tn-AFP1, with molecular mass of 1,230 Da was purified from fruits of *Trapa natans* (Mandal et al. 2011). It contained 11 amino acid residues: LMCTHPLDCSN. Purified Tn-AFP1 showed the inhibition of *Candida tropicalis* growth in vitro and disrupted the biofilm formation in a concentration dependent manner. It also showed downregulation of MDR1 and ERG11 gene expression. Characterization of Tn-AFP1 could contribute in designing novel derivative(s) of this peptide for the development of more effective antimycotic compounds.

Antiviral Activity

Trapa natans in herbal mixture with other plants was found to have antiviral activity (Hijikata et al. 2005, 2007). Clinical studies carried out in Japan reported that the treatment with the herbal mixture WTTCGE comprising *Wisteria floribunda*, *Trapa natans*, *Terminalia chebulae*, *Coix lachryma-jobi*, *Ganoderma lucidum*, and *Elfuinga applanata*, provided fast, effective relief from the symptoms of recurrent herpes genitalis in all 15 patients and herpes labialis in all 13 patients. The mean duration before relief from herpes genitalis occurred was 10.9 days without WTTCGE treatment and 4.9 days with it. Similarly, the time required to obtain relief from herpes labialis was 7.8 days without WTTCGE treatment and 4.0 days with it. The scientists also found that a herbal formula WTMCGEPP containing (*Wisteria floribunda* 0.38, *Trapa natans* 0.38, *Myristica fragrans* 0.38, *Coix lachryma-jobi* 0.75, cultivated *Ganoderma lucidum* 0.75, *Elfuinga applanata* 0.38, tissue cultured *Panax ginseng* 0.3, and *Punica granatum* 0.38: numerals designate dry weight gram/dose), decreased herpes zoster pain for five Japanese patients suffering from shingles. Pain relief started within a few days of intake and was almost complete within 10 days. Two acute herpes zoster with manifestations including trigeminal nerve ophthalmia (both 74 years old), lower body zoster (70 years old), herpes zoster

oticus (17 years old), and leg herpes (28 years old), responded quickly to treatment and no patient developed post-herpetic neuralgia (PHN) after more than 1 year of follow-up.

Analgesic Activity

T. bispinosa root methanolic extract was found to produce significant analgesic activity in mice (Agrahari et al. 2010a). In tail flick method, the extract at 200 mg/kg showed significant activity after 45 min but in tail immersion method, the extract showed significant activity at all tested dose levels after 30 min interval.

Antiinflammatory Activity

Aqueous extract of the fruit pericarp and seed showed anti-inflammatory activity by decreasing mean paw volume induced by carrageenan in rat's paw (Patel et al. 2011). The pericarp showed more potent activity than the seed. The findings supported traditional use of the fruit for its anti-inflammatory activity.

Drug Formulation Activity

Studies showed that *Trapa natans* starch could be used as an excipient in various oral tablet dosage formulations (Rao et al. 2011). The physico-chemical properties and the granulating and release properties of the *Trapa natans* starch compared well with a standard starch in a tablet formulations using Diclofenac as model drug. The drug release from tablets prepared by *Trapa natans* starch was more than 99.7% in 1 h.

Traditional Medicinal Uses

In China, the flowers have been reported as astringent in fluxes, the fruit is used in the treatment of fever, drunkenness and sunstroke and the plant to be anticancer, antipyretic and tonic. In Kampuchea a tea of the rind is taken as a tonic in fever. In Ayurvedic traditional medicine the fruit is deemed as aphrodisiac, appetiser, astringent, coolant, diuretic, tonic, antipyretic and is used for bronchitis, burns, diarrhoea, dysentery, dyspepsia, fatigue, fever, haemorrhage, inflammation, leprosy and pharyngitis. *T. bispinosa* is used in indigenous system of medicine as nutrient, appetizer, aphrodisiac with miscellaneous use and is useful in the disease of nervous system (Agrahari et al. 2010b).

Other Uses

The fruit is an important worship food as prayer offering during worship in the Chinese Chou dynasty.

Comments

The aquatic plant is extremely polymorphous based on leaf and fruit characters and sometimes split into approximately 40 taxa at species and/or subspecific level with very narrow distribution areas. The species has been introduced into North America and has become an invasive species in eastern areas of Canada and the United States. It is also deemed a noxious weed in Australia.

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Papaver somniferum

Scientific Name

***Papaver somniferum* L.**

Synonyms

No synonyms recorded

Family

Papavaraceae

Common/English Names

Breadseed Poppy, Edible-Seeded Poppy, Garden Poppy, Gear, Maw Seed, Medicinal Poppy, Oilseed Poppy, Opium Poppy, Poppy Seeds, Scag, Smack, Small Opium Poppy, White Poppy.

Vernacular Names

Afrikaans: Opium papaver;
Albanian: Lulëkuqe;
Amharic: Papi;
Arabic: Abou En Noum, Abunom, Afiun, Bazrul-Khash-Khash, Bizrul Khashkhash, Bizrul-Khashkhash, Khashkhash, Khashkhash Aswad, Khashkhashul Baiza, Nabatul-Khash-Khash, Qishr-Ul-Khashkhash, Qishrul Khashkhash, Qishrul-Khash-Khash, Qishrul-Khashkhash, Ude Saleeb;
Aramaic: Maikon;
Argentina: Amapola;
Armenian: Megon, Mekon; Megoni Good, Mekoni Kut;
Azeri: Xaş-Xaş;
Basque: Lobelarr;
Belarusian: Mak, Opiumny Mak;
Brazil: Papoula (Portuguese);
Burmese: Bhainzi;
Catalan: Cascall, Herba Dormidora, Pintacoques;
Chinese: Ying Suhk Hohk (Cantonese), Ya Pian, Ying Su, Ying Su Qioa (Mandarin);
Coptic: Khaulan, Neman;
Croatian: Vrtni Mak';
Czech: Mák Sety;
Danish: Birkes, Opiumvalmue (Plant), Valmue Frø (Seeds);
Dutch: Blauwmaanzaad, Maankop, Maanzaad, Slaapbol, Slaappapaver;
Egypt: Abu El Noom;
Finnish: Oopiumiunikko, Pioniunikko, Uniko
French: Oeillette, Pavot Officinal, Pavot Somnifère, Pavot À Opium, Pavot De Jardin;
Gaelic: Codalion, Paipin;
Galician: Adormideira, Durmideira, Mapoula, Sementes De Mapoula;
Georgian: Khoshkhoshi, Q'aq'acho, Qaqacho; Q'aq'achos Tesli, Qaqachos Tesli (Seeds), Xoshxoshi;
German: Gartenmohn, Mohn, Ölmohn, Opiummohn, Schlafmohn;
Greek: Aphioni, Mekon;

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Hebrew: Parag Tarbuti, Pereg;
Hungarian: Kerti Mák, Mák;
Icelandic: Birki, Valmúafræ;
India: Aphu Guti (Assamese), Pasto, Post, Posto Dana (Bengali), Aping Bipang (Garo), Afeem, Afim, Afin, Afyun, Amal, Aphim, Aphim posta, Doda, Kahs-Khasa, Kas-Kas, Kashkash, Khash--Khash-Ke-Khash, Khash-Khash, Khash-Khash-Ka-Per, Khash-Khash-Ke-Bonde, Post, Posta, Sufeed Srah (Hindu), Abini, Afeemu Gida, Afirm, Aphimu, Biligasagase, Biligasgase, Gasagase, Kasakase, Kasakathi Gida, Khasa-Khasi-Gida, Khasakhasi, Khuskhus (Kannada), Afium, Avin, Karappu, Kasakasa, Kasha-Kashach-Chedi, Kashakasha, Kaskasu (Malayalam), Afeem, Afu, Aphu, Khas Khas, Khaskhashinche Baend, Khuskhus, Posta (Marathi), Aphima, Posta, Postak (Oriya), Khaskhas, Post (Punjabi), Aaphuka, Ahifen, Ahiphena, Ahiphenam, Aphukam, Chosa, Kakasha, Kasabijam, Khakasa, Khas-Khas, Khasa, Khaskhasa, Nagaphena, Phaniphena, Post, Postubejam, Postuvrikshaha, Ullasata (Sanskrit), Abhini, Abini, Acarankam, Apenam, Apin, Apini, Apinicetti, Atilam, Cacavinmayirttali, Casa Casa, Cettanti, Cukkumatantulam, Gasha-Gasha, Gasha-Gasha-Chedi, Gasha-Gasha-Tol, Gashagasha, Iracanatikam, Kacakaca, Kacakacacceti, Kacavanipam, Kannatayacceti, Kasa-Kasa, Kasakasa, Parunkam, Postaka, Postaka-Chedi, Postakai, Postakkaycceti, Posthakkai, Posttakkai, Postukkaycceti, Vellai Postakay (Tamil), Abhini, Gasagasala, Gasagasala-Chettu, Gasagasalu, Gasalu, Gasugasalu, Kasakasa, Nallamandu, Nallamanthu, Posta-Katol, Postakaya-Chettu (Telugu), gasugase (Tulu), Afiun, Afyun, Kaknar Nim Kofta, Khashkhash, Khashkhash Safaid, Khashkhashsufaid, Khashkhassh (Safaid/Siyah), Khaskhash, Kokinar, Koknar Nim Kofta, Opium, Poast Khahkhash, Poast Khashkash, Poast Khashkhash, Poast-I-Khashkhash, Post-E-Khashkhash, Tukhm Khashkash, Tukhm Khashkhas Safaid, Tukhm Khashkhash, Tukhm Khashkhash Safaid, Tukhm-I-Khashkhash, Tukhm-I-Khaskhash Safaid (Urdu);
Irish: Poipin;
Italian: Papavero;
Japanese: Keshi, Papi;
Kashmiri: Khash-Khash;
Kazakh: Köknär;
Khasi: Aphim;
Korean: Apyeon, Apyon, Popi, Yanggwibi;
Laotian: Fin, Ya Yang, Za Zang;
Latvian: Magone;
Lithuanian: Aguonos, Daržinė Aguona;
Macedonian: Afion, Bulka, Mak;
Malaysia: Kas Kas;
Maltese: Peprina;
Mongolian: Namuu;
Nepali: Aphim;
Norwegian: Opiumsvalmue, Valmue;
Persian: Afiun, Khash-Khash, Khashkhash, Khashkhash Sufaid, Koknar, Post-E-Koknar, Post-Koknar, Poste Koknar, Poste-Khash-Khash, Postekoknar, Tukhme-Koknar, Tukme Koknar;
Polish: Mak Lekarski;
Portuguese: Dormideira, Papoila;
Romanian: Mac, Mac De Gradină, Mac Somnifer;
Russian: Mak Snotvornyj, Opijnyj Mak
Serbian: Mak;
Slovaščina: Vrtni Mak;
Slovencina: Mak, Mak Siaty;
Spanish: Ababa, Adormidera (Soporifera), Amapola, Amapola Real, Semillas De Amapola;
Swedish: Opievallmo, Opiumvallmo, Pionvallmo, Vallmo;
Thai: Fin Ton Fin;
Turkish: Gelincik Çiçeği, Haşhaş; Haşhaş Tohumu;
Turkmen: Läbik, Läle;
Ukrainian: Mak Snodijnyj;
Uzbek: Lolaqizg'aldoq;
Vietnamese: Á Phiện, Anh Túc, Chù Gia Đình (H'Mong), Co Khoản Nheng (Thai), Lão Phèn (Tay), Á Phù Dung, Cây Thẩu, Cây Thuốc Phiện, Vây Anh Túc;
Welsh: Pabi;
Yiddish: Mon, Mon Mondl, Mondl.

Origin/Distribution

Opium poppy is generally believed to have originated from Asia Minor but its exact place is unknown. Opium poppy is probably one of the earliest plants cultivated by men in Europe since

the Neolithic era and represent one of mankind's oldest medicinal plant. The plant has been domesticated by the Sumerians, Sumerian, Assyrians, Egyptians, Minoans, Greeks, Romans, Persians and Arabs. Over the centuries, however, it has been taken extensively into the Far East including India, Northern Burma and Thailand and China.

Agroecology

Opium poppy is generally a cool climate crop. Studies showed that the optimum temperature for growth and development of poppy appeared to be between 16 and 20°C, with no serious reduction in growth rate from thermoperiods of 13.5 to 21.5°C and little delay in development from thermoperiods 17.5°C or above (Acock et al. 1997). However, poppy development rate was found to be partly controlled by photoperiod and development rate affects partitioning, which in turn affected growth rate. Earlier studies by Gentner et al. (1975) reported opium poppy to be a long-day plant with a critical day length for flowering of 14–16 h. Flowering was found to be induced by two or more long photoperiods or by a single period of light longer than 24 h. Wang et al. (1997) divided the development period up to flowering into four photoperiod phases from emergence to anthesis which marked changes in its sensitivity to photoperiod: a photoperiod-insensitive juvenile phase (JP), a photoperiod-sensitive inductive phase (PSP), a photoperiod-sensitive post-inductive phase (PSPP) and a photoperiod-insensitive post-inductive phase (PIPP). They found PSPP to be the only phase that clearly exhibited sensitivity to temperature.

Opium poppy has been reported to tolerate annual rainfall from 300 to 17,300 mm and it does poorly in the humid tropics.

Opium poppy thrives in rich, well-drained soils and tolerates moderately acidic to alkaline soils. Studies showed soil pH to be one of the principal factors considered required for maximum yield (Temple-Smith et al. 1983). They reported that capsule and morphine yield increased more than two-fold as the pH in the surface soil (0–150 mm) increased from 5.6 to 6.1, and by 30-fold where the pH increased from 5.1 to 6. Poppy yield responses to liming were attributed primarily to alleviation of aluminium toxicity but the effects on yield of reductions in soluble aluminium and increases in available calcium were confounded by application of ground limestone.

Edible Plant Parts and Uses

Poppy seeds of *Papaver somniferum* are an important food item providing poppy seed spice and the healthful edible poppy seed oil. Poppy seeds contain low levels of opiates (not psychoactive at amounts used in cooking) (Erowid 2003) and the oil extracted from them contains even less. Opium poppy seeds are widely used in cuisines from many cultures for cooking, confectionery, bakery and desserts. Poppy seeds are popularly used in food items such as bagels (ring-shaped bread), bialys (Yiddish bread roll), pretzels, muffins, and cakes. Poppy seeds are used as filling ingredients for homnetash (Yiddish pastry) and strudel pastries. Poppy seeds can be dry roasted and ground to be used in wet curry (curry paste) or dry curry used in chapatis and in chutneys. They impart a creamy and nut like flavor, and when used with ground coconut, poppy seeds provide a unique and flavour-rich curry base. Poppy seeds fried in butter can added to noodles or pasta. Poppy seeds can be added to vegetable sauces such as asparagus and root sauces; they can be sprinkled on to coleslaw. They can be used to top creamed potatoes and au gratin dishes, and used in fish dishes. Poppy seed oil known as *oillete* by the French, can be used to substitute olive oil for culinary purposes. The oil is used locally in making sweets in some parts of Asia. Some native tribes in southeast Asia consume the young leaves as vegetables.

Botany

A robust annual, glabrous, glaucous, lactiferous herb or small shrub to 150 cm high, rarely branched with erect tap root. Leaves alternate; lamina ovate or oblong, 7–25 cm, both surfaces

glabrous, glaucous and rather waxy, veins distinct, slightly raised, base cordate, margin irregularly undulate-serrate, apex acuminate to obtuse; lower leaves shortly petiolate but upper leaves sessile and amplexicaul. Flower buds ovoid-oblong, glabrous, 1–3.5 cm long. Flowers large, showy, 5–12 cm across, strongly cupulate, white, pinkish or reddish, rarely pale violet, with or without a basal dark blotch. Sepals 2 green caducous, 2–3.5 cm. Petals 4 twice as large as sepals, obovate-orbicular, with margin usually wavy or variously cut, caduceus. Stamens numerous with white filaments and yellowish, oblong-linear anthers. Ovary green, superior, spherical, 1–2 cm across, glabrous with 4–18 parietal placentas and many ovules and with 5–12 (−18) stigmas united into a compressed disk with deeply crenulate lobes. Capsules stipitate, subglobose to oblong–ellipsoid, not ribbed, to 5–9 by 4–5 cm, glaucous pale green (Plates 1 and 2) becoming brown when mature crowned by stigmatic disk. Seeds many, globose to reinform, small, reticulate, deep gray to black (Plate 3).

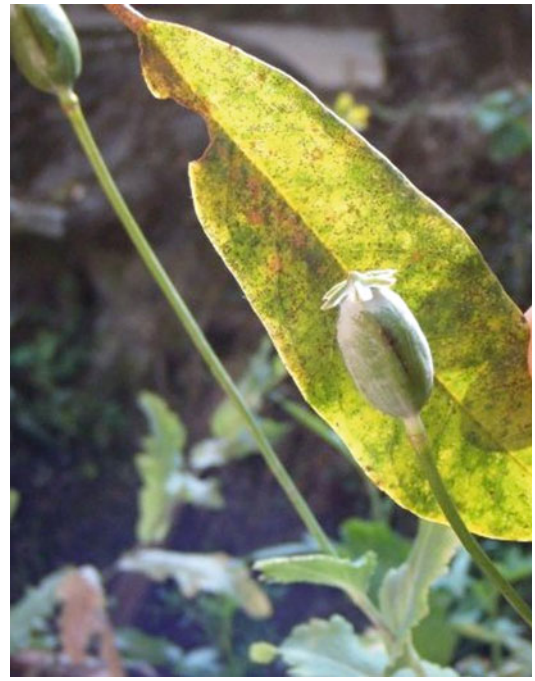

Plate 1 Opium poppy capsule

Nutritive/Medicinal Properties

Proximate nutrient composition per 100 g edible portion of poppy seed (*Papaver somniferum*) spice was reported as: water 5.95 g, energy 525 kcal(2,196 kJ), protein 17.99 g, total lipid 41.56 g, ash 6.37 g, carbohydrate 28.13 g, total dietary fibre 19.5 g, total sugars 2.99 g, sucrose 2.33 g, glucose 0.37 g, fructose 0.29 g, Ca 1,438 mg, Fe 9.76 mg, Mg 347 mg, P 870 mg, K 719 mg, Na 26 mg, Zn 7.90 mg, Cu 1.627 mg, Mn 6.707 mg, Se 13.5 μg, vitamin C 1 mg, thiamine 0.854 mg, riboflavin 0.1 mg, niacin 0.896 mg, pantothenic acid 0.324 mg, vitamin B-6 0.247 mg, total folate 82 μg, total choline 8.8 mg, betaine 0.9 mg, vitamin E (α-tocopherol) 1.77 mg, β-tocopherol 8.30 mg, γ-tocopherol 8.82 mg, δ-tocopherol 0.23 mg, total saturated fatty acids 4.517 g, 6:0 0.037 g, 14:0 0.077 g, 16:0 3.581 g, 18:0 0.782 g, 20:0 0.039 g, total monounsaturated fatty acids 5.982 g, 16:1 0.039 g, 18:1 5.864 g, 20:1 0.078 g, total polyunsaturated fatty acids 28.569 g, 18:2 28.295 g,

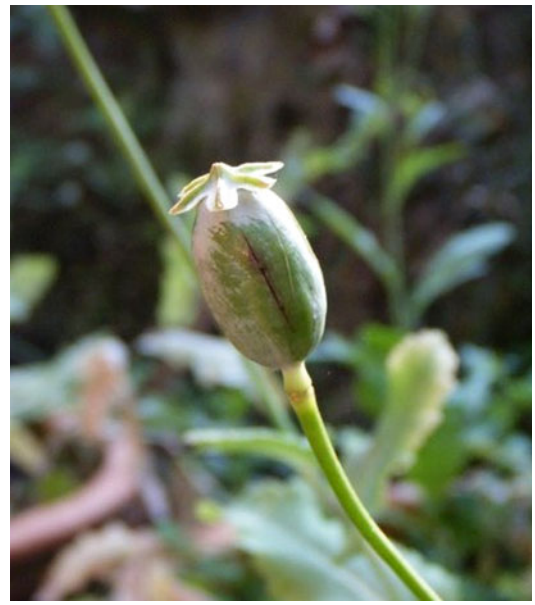

Plate 2 Close up of capsule showing the lobed stigmatic disc

Plate 3 Small, reinform-shaped opium poppy seeds

18:3 0.273 g, 18:3 n-3 c,c,c (ALA) 0.273 g, stigmasterol 7 mg, campesterol 29 mg, β-sitosterol 109 mg, tryptophan 0.184 g, threonine 0.686 g, isoleucine 0.819 g, leucine 1.321 g, lysine 0.952 g, methionine 0.502 g, cystine 0.297 g, phenylalanine 0.758 g, tyrosine 0.727 g, valine 1.095 g, arginine 1.945 g, histidine 0.471 g, alanine 0.839 g, aspartic acid 2.365 g, glutamic acid 4.299 g, glycine 0.952 g, proline 2.754 g, and serine 0.952 g (USDA 2012). Opium poppy seed was found to have a high lipid content (50% of the seed dry weight) (Luthra and Singh 1989). The non-polar lipids, particularly triacylglycerols, constituted a major portion (86%) of the total lipids. The relative percentages of polar lipids (phospho- and glycolipids), sterols and free fatty acids in the oil declined with seed maturation. Palmitic, oleic and linoleic were the major fatty acids at all the stages of the seed development, with a clear predominance of linoleic acid. The proportion of linoleic acid increased tremendously with the deposition of triacylglycerols and was negatively correlated with linoleic acid.

Proximate nutrient composition per 100 g edible portion of poppy seed oil was reported as: energy 884 kcal (3,699 kJ), total lipid 100 g, vitamin E (α-tocopherol) 11.40 mg, total saturated fatty acids 13.50 g, 16:0 10.60 g, 18:0 2.90 g, total monounsaturated fatty acids 19.70 g, 18:1 19.70 g, total polyunsaturated fatty acids 62.40 g, 18:2 62.40 g and phytosterols 276 mg (USDA 2011). Poppy seed oil was reported to contain palmitic (12%), stearic (3%), oleic (20%) and linoleic acid (65%) Sengupta and Mazumder (1976). Lipolysis with pancreatic lipase indicated the following glyceride composition: S3 (3 saturated fatty acids) (trace), S2U (2 saturated and 1 unsaturated fatty acid) (5%), SU2 (34%) and U3 (3 unsaturated fatty acids) (61%) or saturated dilinolein (19%), oleo-dilinolein (25%), and trilinolein (27%).

Srinivas and Narasinga Rao (1981) reported 46.2–49.4% oil, 21.5–23.5% crude protein, 14–15% crude fibre in poppy seed. The proximate analysis of poppy seeds showed the following composition (g/kg): lipids 440 g, protein 211 g, moisture 50 g, ash 63 g, crude fibre 62 g and total carbohydrates 236 g (Nergiz and Ötles 1994). Potassium and calcium were the predominant elements. Linoleic acid was the major unsaturated fatty acid (750 g/kg total fatty acids) while palmitic acid was the main saturated 1 (86–4 g kg). The amounts of α-, β- and δ-tocopherols found in poppy seed oil were 220, 40 and 20 μg/g respectively. Among the water-soluble vitamins determined, pantothenic acid was found at the highest level followed by niacin and thiamin. The oil content in *P. somniferum* was 47.8 and 38.0% in *P. setigerum* while C18 fatty acids were quite comparable (Singh et al. 1998). The F8 genotypes of their cross had higher oil contents (>40%) and fatty acid concentrations than the parental species. Linoleic acid ranged between 68 and 74.4% and oleic acid varied between 13.6 and 20.3%. High oleic desaturation ratio (ODR, >0.79) and C18 polyunsaturated fatty acid (>87%) with very low C18: 3 (0.37) indicate the possibility of using poppy oil for the edible oil industry. Oleic (18:1) acid was not correlated with the other fatty acids, except for significant negative correlation with linoleic (C18: 2) acid. The major fatty acid in poppy oil was linoleic acid comprising 74.5% of total fatty acids (Bozan 2008). Poppy seed oil contained 11.0 mg/100 g poppy total tocols and was especially rich in gamm-tocopherol 30.9 mg/100 g oil and also contained alpha-tocopherol. Oxidative stability

of poppy oil (5.56 h) was most stabile oil compared to safflower oil (2.87 h) and flax oil (1.57 h).

The major volatile compounds of opium poppy seed oil were identified as 1-pentanol (3.3–4.9%), 1-hexanal (10.9–30.9%), 1-hexanol (5.3–33.7%), 2-pentylfuran (7.2–10.0%), and caproic acid (2.9–11.5%) (Krist et al. 2005). The predominant triglyceride components were found to be composed of linoleic, oleic, and palmitic acid, comprising approximately 70% of the oils. TAG patterns of the different poppy varieties were found to be very homogeneous.

Oil contents of poppy seeds of 18 Turkish poppy varieties ranged from 35.38 to 47.95% (Rahimi et al. 2011). The major fatty acid was linoleic acid (18:2) 68.76–74.22%, followed by oleic acid (C18:1) 13.30–17.80%, palmitic acid (C16:0) 7.96–10.19%, stearic acid (C18:0) 1.84–2.40%, linolenic acid (C18:3) 0.55–0.75%, palmitoleic (C16:1) 0.11–0.25%, heptadecenoic (C17:1) 0.02–0.04% and gadoleic acid (C20:1) 0.04–0.06%. Meconic acid was isolated from *P. somniferum* by F. W. Sertürner and from opium gum (Ayyangar and Bhide 1988).

Özcan and Atalay (2006) reported the following proximate nutrient values for seeds of 7 Turkish opium poppy varieties 3.39–4.76% water, 11.94–13.58% crude protein, 4.92–6.25% crude ash, 22.63–30.08% crude fibre, 0.72–1.68% HCl-insoluble ash, 6367.0–6740.5 kcal/100 g crude energy and 32.43–45.52% crude oil content. Mineral contents of poppy seeds (ppm) of 7 Turkish varieties were: aluminium 12.6–41.3 ppm, boron 18.5–69.4 ppm, calcium 8756.8–10712.4 ppm, cadmium 0.2–0.3 ppm, chromium 2.3–5.2 ppm, copper 9.6–27.3 ppm, iron 64.1–104.5 ppm, potassium 6012.1–10535.7 ppm, lithium 6.5–6.7 ppm, magnesium 3406.8–3872.2 ppm, manganese 60.9–78.0 ppm, sodium 522.2–1365.3 ppm, nickel 1.6–4.0 ppm, phosphorus 9081.4–12760.0 ppm, lead 0.3–1.6 ppm, strontium 86.0–184.3 ppm, vanadium 25.2–26.8 ppm, and zinc 21.3–45.2 ppm. The physical and chemical properties of poppy oils from the seven varieties were: free fatty acids (% oleic acid) 1.0–3.2, iodine value 122.0–129.5, refractive index n20 1.4773, unsaponifiable matter % 1.06–2.40%, saponification value 199.5–206 and pH 3.7–4.2. Fatty acid composition of the poppy oils comprised palmitic % 12.85–18.70, stearic 2.40–4.30%, oleic 13.11–24.13%, linoleic 52.60–71.50%, and linolenic 0.16–0.5%. Tocopherol content of poppy oils comprised α-tocopherol 26.8–37.2 ppm, β-tocopherol 343.7–567.3 ppm, δ-tocopherol 6.1–18.6 ppm, total tocopherols 348.8–623.1 ppm.

Opium was reported to contain besides alkaloids approximately 5–20% water, about 20% various sugars, and several simple organic acids, including fumaric acid, lactic acid, oxaloacetic acid, and meconic acid (Schiff 2002).

Opiate Alkaloids

Opium poppy, *Papaver somniferum*, today is the commercial source of the narcotic analgesics morphine and codeine. Along with these 2 morphinans, opium poppy produces approximately 80 alkaloids belonging to various tetrahydrobenz ylisoquinoline-derived classes (Weid et al. 2004). Six major alkaloids of opium poppy were discovered over a century ago – morphine by F.W. Sertürner in 1805, codeine by P.J. Robiquet in 1817, thebaine by Thiboumèry in 1835, noscapine by Derosne in 1803, narceine by Pelletier in 1832 and papaverine by Merck in 1848 (Preininger 1986). Only five of these alkaloids account for virtually all of the quantitative alkaloid content in opium, including: the morphinans morphine (8–17%), codeine (0.7–5%), and thebaine (0.1–2.5%t); the benzylisoquinoline papaverine (0.5–1.5%t); and the phthalideisoquinoline noscapine (narcotine) (1–10%) (Kapoor 1995; Paul et al. 1996). The other minor alkaloids occur in trace amounts and are represented by the following alkaloid classes: aporphines, protoberberines and tetrahydroprotoberberines, tetrahydroisoquinolines benzophenanthridines, and rhoeadines (Kapoor 1995). In opium, the alkaloids occur as salts of organic acids, such as meconic or lactic acid. Opium also contains mucilage, sugars, salts (e.g. sulphates), free organic acids such as meconic,

lactic, fumaric and oxalacetic acid, meconiasin, caoutchouc, albuminous substances, colouring matters and water; and sulphuric acid has been found in the ash (Grieve 1971). Most of the world legal opium production is used to obtain morphine, codeine and noscapine.

The alkaloids reported in opium poppy and opium include: hydroxycodeine from opium (Dobbie and Lauder 1911); neopine from opium (Dobbie and Lauder 1911; Homeyer and Shilling 1947); narceine from opium (Addinall and Major 1933) and from poppy capsules (Gorecki and Bognár 1968; Tulecki and Gorecki 1969); morphine from opium poppy capsules (Pfeifer and Weiss 1955; Pfeifer 1956) and from opium (Brochmann-Hanssen 1972); narcotoline from opium (Pfeifer 1957a, b) and from poppy capsule (Baumgarten and Christ 1950; Bognár et al. 1967a; Tulecki and Gorecki 1969); porphyroxine from opium poppy and opium (Awe and Winkler 1958); S-(+)-laudanosine from opium (Kleinschmidt 1959; Machovicova et al. 1977); protopine from opium (Kleinschmidt 1959; Bessonova et al. 1970; Battersby et al. 1975); laudanidine from opium (Kleinschmidt 1959; Brochmann-Hanssen and Furuya 1964b; Brochmann-Hanssen et al. 1965); berberine from opium poppy (Ose et al. 1960); coptisine from opium (Hakim et al. 1961); papaverine, papaveraldine (xanthaline), thebaine, and cryptopine (Ramanathan 1963); pseudomorphine from opium (Froemming et al. 1963); (±)-reticuline and (+)-reticuline from opium (Brochmann-Hanssen and Furuya 1964a, b; Brochmann-Hanssen and Nielsen 1965a, b); glaudin from opium (Pfeifer 1964, 1965b); magnoflorine and corytuberine from opium (Nijland 1965); (−)-isocorypalmin from opium (Pfeifer 1965a); 6-methylcodeine from opium (Brochmann-Hanssen and Nielsen 1965a); codamine and (+)-laudanosine (Brochmann-Hanssen et al. 1965); papaverrubine B (*O*-methylporphyroxine) from opium (Hughes and Farmilo 1965; Pfeifer 1965a, 1966); papaverrubine C (epiporphyroxine) (Pfeifer 1965a, b; Hughes et al. 1967); α-allocryptopine from opium (Brochmann-Hanssen and Nielsen 1966a); porphyroxine (papaverrubin D) from opium (Pfeifer 1966); scoulerin from opium (Brochmann-Hanssen and Nielsen 1966b); isocorypalmine from opium (Pfeifer 1965a) and ripe opium poppy (Proksa et al. 1979; Proksa and Cerny 1981); isoboldine an aporphine alkaloid from opium (Brochmann-Hanssen et al. 1967); porphyroxine from opium (Brochmann-Hanssen and Hirai 1967); theibane, papaverin, narcotolin from poppy capsule (Bognár et al. 1967b); narcotoline, cryptopine, papaverine and narceine palaudine, a benzylisoquinoline alkaloid from opium (Brochmann-Hanssen and Hirai 1968); N-methyl-14-O-desmethylepiporphyroxine, a member of papaverrubine alkaloids and their N-methyl derivatives from opium (Brochmann-Hanssen et al. 1968); salutaridine and 13-oxycryptopine from opium (Brochmann-Hanssen et al. 1970); canadine from Kirghiz opium (Bessonova et al. 1970) and from opium poppy (Battersby et al. 1975); norreticuline, norlaudanosoline, (+)-laudanosine, (+)-laudanidine, (+)-codamine, (+)-reticuline, 1,2,3,4-tetrahydropapaverine, papaveroline 6,3′,4′-trimethyl ether (pacodine) from opium (Brochmann-Hanssen et al. 1971a); aporphine alkaloids – reticuline, corytuberine, isoboldine, proporphine and magnoflorine from opium poppy (Brochmann-Hanssen et al. 1971b); coreximine, a tetrahydro-ψ-berberine, reticuline, scoulerine, isocorypalmine from opium poppy (Brochmann-Hanssen et al. 1971c); theibaine from opium poppy capsule (Bognár et al. 1967b; Hodková et al. 1972); morphine and dihydroprotopine from opium poppy (Stefanov et al. 1972); 16-hydroxythebaine (Brochmann-Hanssen et al. 1972); cryptopine, β-allocryptopine and papaveraldine from dried poppy capsule (Hodková et al. 1972); noscapine, papaverine, atropine and scopolamine (Ono et al. 1972); sanguinarine, norsanguinarine, dihydrosanguinarine, oxysanguinarine, protopine, cryptopine, magnoflourine and choline from opium poppy callus tissues (Furuya et al. 1972; Ikuta et al. 1974) and sanguinarin from opium poppy suspension culture (Forche and Frautz 1981; Songstad et al. 1989); orientaline, an aporphine alkaloid, norlaudanosoline, orientaline, isoboldine, norprotosinomenine,

magnoflorine from opium poppy (Brochmann-Hanssen et al. 1973); stepholidine, a protoberberine alkaloid from opium poppy (Brochmann-Hanssen and Richter 1975); (−)-tetrahydropapaverine, (−)-nor-reticuline, (−)-norori-entaline, norprotosinomenine, papaverine, papaveroline, tetrahydropapaverine, noriso-orientaline from opium (Brochmann-Hanssen et al. 1975); morphine, codeine, cryptopine, thebaine, papaverine, and narcotine from opium (Ziegler et al. 1975); codamine from poppy capsules (Mamochkina et al. 1976); laudanidine from green poppy, salutaridine from ripe poppy (Proksa et al. 1979); five major alkaloids narcotine, papaverine, thebaine, codeine, and morphine and minor alkaloids salutaridine, oripavine, laudanosine, isothebaine, cryptopine, alpinigenine, narceine, protopine, and gnoscopine (Vincent and Engelke 1979); thebaine and cryptopine from opium (Ramanathan and Chandra 1980); narceine imide, both E and Z isomers of narceine imide from poppy (Proksa and Voticky 1980); narcotine and papaverine from opium (Ramanathan and Chandra 1981); oripavine from dried opium poppy capsule (Nielsen et al. 1983); five principal alkaloids (morphine, codeine, thebaine, noscapine and papaverine), three minor alkaloids (laudanosine, cryptopine and narceine) from opium gum (Ayyangar and Bhide 1988); somniferine from opium (Dragar and Bick 1988); narceine and a secophthalideisoquinoline alkaloid, narceinone from dried capsule (Chaudhuri and Thakur 1989); sanguinarine from opium poppy cell cultures (Songstad et al. 1989); 5′- O -demethylnarcotine (Répási et al. 1993); sanguinarine and sanguinarine analogues, oxysanguinarine, norsanguinarine and dihydrosanguinarine, and the protopine-type alkaloids, protopine and cryptopine (Williams and Ellis 1993); morphine, codeine, thebaine, noscapine and papaverine from crude opium (Bjørnsdottir and Hansen 1995); morphine, codeine, thebaine, oripavine, papaverine, narcotine, narceine, cryptopine and salutaridine from poppy straw and opium (Trenerry et al. 1995); morphine 14.45–15.95%, codeine 2.0–3.45%, thebaine 1.32–2.73%, papavarine 0.92–2.37%, narcotine 3.85–5.77 from opium gum (Reddy et al. 2003); tetrahydrobenzylisoquinolines: reticuline, protosinomenine, norprotosinomenine, isoorientaline, and norcoclaurine (Ounaroon et al. 2003); protoberberine alkaloids stylopine, canadine, tetrahydropalmatine, tetrahydroxyberbine and scoulerine, quaternary ammonium alkaloid, (S)-*cis*-N-methylstylopine, simple isoquinoline, benzylisoquinoline, and pavine alkaloids (Liscombe and Facchini 2007).

Together with bismorphine A, a new compound bismorphine B was identified in the wounded capsules of *Papaver somniferum* (Morimoto et al. 2003). Bismorphine B was determined as a novel morphinan alkaloid, in which two morphine units were coupled through a biphenyl ether bond. This alkaloid was found to more effectively cross-link cell wall polysaccharide pectins than bismorphine A leading to resistance against hydrolysis by pectinase. Both transformed and untransformed cell suspension cultures derived from *Agrobacterium rhizogenes*-transformed *Papaver somniferum* accumulated high quantities of benzylisoquinoline alkaloids, of which the major species was sanguinarine (Williams and Ellis 1993). These cell lines also produced a variety of minor alkaloids, including the sanguinarine analogues, oxysanguinarine, norsanguinarine and dihydrosanguinarine, and the protopine-type alkaloids, protopine and cryptopine.

Morphinan, tetrahydrobenzylisoquinoline, benzo[c]phenanthridine, and phthalideisoquinoline alkaloids were determined in tissues of the Tasmanian *Papaver somniferum* elite cultivar C048-6-14-64 and compared with that from the low-morphine cultivar “Marianne” (Frick et al. 2005). In the elite cultivar, 91.2% of the latex alkaloids consisted of the three pharmaceutically most valuable alkaloids: morphine, codeine, and thebaine. In the root system, the major alkaloids were sanguinarine/10-hydroxysanguinarine and dihydrosanguinarine/10-hydroxydihydrosanguinarine. In the stems and leaves of, the same alkaloids were determined as in the latex. In the condiment cultivar, 80.5% of the alkaloids of the latex consisted of the 2 phthalideisoquinoline

alkaloids narcotoline and noscapine. Only 18.8% of the relative total alkaloid content were morphinan alkaloids. In contrast to the narcotic cultivar, in which the benzo[c]phenanthridines in roots dominated over the morphinan and tetrahydrobenzylisoquinoline alkaloids, the concentration of benzo[c]phenanthridines in "Marianne" was similar to that of morphinan and tetrahydrobenzylisoquinoline alkaloids. These data suggested a differential alkaloid regulation in each cultivar of *P. somniferum*. Highest concentration of morphinan and phthalidoneisoquinoline was observed in 30 day root tissue of *P. somniferum* where morphine reach and narcotoline reached levels of 313 and 490 μg/g fresh weight (Williams and Ellis 1989)

Opium poppy is a chief source of diverse physiologically active alkaloids, required by the pharmaceutical industry. Most renown of the benzylisoquinoline-derived alkaloids are the narcotic analgesic phenanthrene alkaloids morphine and codeine. Other important alkaloids are the antitussive phthalidisoquinoline noscapine, the vasodilator papaverine and the antimicrobial benzo(c)phenenthridine sanguinarine. Thebaine is used to manufacture semi-synthetic morphine analogues i.e. oxycodone, oxymorphine, buprenorphine etc.

The concentrations of codeine, morphine, thebaine, papaverine, and narcotine were 44, 167, 41, 67, and 230 μg/g in Indian poppy seeds, and were 1.8, 39, 1.0, 0.17, 0.84 μg/g in Netherlands poppy seeds, respectively (Paul et al. 1996). Shukla et al. (2010) reported the following variations in the content of 5 alkaloids in the opium of 122 accessions of opium poppy: morphine range 9.20–20.86%, mean 15.41%; codeine range 1.57–6.76%, mean 3.21%; thebaine range 0.61–8.36%, mean 2.05%; narcotine range 2.27–17.92%, mean 8.18%; and papaverine range 0–6.,40%, mean 1.25%.

Keto acids, involved in the biosynthesis of alkaloids in opium poppy plant were reported to include pyruvic acid, α-ketoglutaric acid, oxaloacetic acid, phenylpyruvic and *p*-hydroxphenylpyruvic acid (Jindra et al. 1964). The following carbohydrates were isolated form opium poppy capsule: glucose, fructose, sucrose, sedoheptulose, mannoheptulose, plus a complex polysaccharide (Ottestad et al. 1959). Acid hydrolysis of the polysaccharide products yielded monosaccharides, arabinose, xylose, rhamnose, glucose, galactose, uronic acid, and an unidentified component.

Flavonols (kaempferol and quercetin) were present in all flower organs at all stages of floral morphogenesis in *Papaver somniferum* (Beliaeva and Evdokimova 2004). In the plants with normal flower structure, the contents of flavonols (kaempferol + quercetin) sharply increased with the beginning of differentiation of flower organs, to reach a maximum in the open flower, when gametogenesis was terminated and fertilization occurred. The level of flavonol contents in the petals (upper part) and stamen was at a maximum at all stages of flower development, while that in the gynaecium was at a minimum. The relationship between degradation of flavonols (kaempferol, quercetin, and myricetin) and biosynthesis of anthocyanins in poppy flowers were reported by Rat'kin et al. (2003). The highest flavonol-degrading activity was found in white flower mutants towards all substrates, particularly, quercetin. The flavonol-degrading activity increased considerably with the content of cyanidin. A similar relationship was found in the mutants synthesizing both cyanidin and pelargonidin. The plants accumulating considerable quantities of pelargonidin in their petals had accordingly higher flavonol-degrading activity and predominantly hydrolyzed kaempferol. Calmodulins with molecular weight 17,000 were isolated and characterized from *Papaver somniferum* (Thompson et al. 1989). Amino acid compositions were similar with those of known calomundins, with regard to the presence of trimethyllysine and the ratio of phenylalanine to tyrosine. Opium poppy calmondin stimulated calmodin dependent cAMP phosphodiesterase with K(a) of 1.09 nanomolar.

Latex from the opium poppy was found to contain two latex specific protein bands which were designated major latex proteins (MLPs) (Nessler et al. 1985). MLPs were found to be concentrated in the latex cytosol and not in alkaloidal vesicles. Analysis of latex proteins indicated the two MLP bands to compose of several distinct polypeptides with similar relative molecular

weights. Latex from the opium poppy (*Papaver somniferum*) was found to contain an abundant group of laticifer-specific, low-molecular-weight polypeptides called the major latex proteins (MLPs) (1994). MLPs are encoded by a family of 9 genes which can be divided into two distinct subfamilies based on DNA. The organization of the MLP family is consistent with the triploid-hybrid origin of the opium poppy. Decker et al. (2000) characterised the soluble proteins present in the latex of opium poppy. Of the two main fractions of the latex, the sedimented faction was found to be rich in alkaloids and the cytosolic serum to be rich in proteins. Of the serum, representing the protein-rich part of the latex, 75 spots were analysed; for 69 proteins a function could be assigned due to homology to known proteins. Further, codeinone reductase, a representative of the specific enzyme system in morphine biosynthesis, could be detected within the cytosolic serum fraction. In the vesicle-containing pellet, 23 protein spots were analysed. Along with the 2 morphinans, morphine and codeine, opium poppy produces approximately 80 alkaloids belonging to various tetrahydrobenzylisoquinoline-derived classes (Weid et al. 2004). It has been known for over a century that morphinan alkaloids accumulate in the latex of opium poppy. In their study, they reported the immunolocalization of 5 enzymes of alkaloid formation in opium poppy: (R,S)-3′-hydroxy-N-methylcoclaurine 4′-*O*-methyltransferase central to the biosynthesis of tetrahydroisoquinoline-derived alkaloids, the berberine bridge enzyme of the sanguinarine pathway, (R,S)-reticuline 7-*O*-methyltransferase specific to laudanosine formation, and salutaridinol 7-*O*-acetyltransferase and codeinone reductase, which lead to morphine. In capsule and stem, both *O*-methyltransferases and the *O*-acetyltransferase were found predominantly in parenchyma cells within the vascular bundle, and codeinone reductase was localized to laticifers, the site of morphinan alkaloid accumulation. In developing root tip, both *O*-methyltransferases and the *O*-acetyltransferase were found in the pericycle of the stele, and the berberine bridge enzyme was localized to parenchyma cells of the root cortex. Laticifers were not found in developing root tip, and, likewise, codeinone reductase was not detected.

Antitumour Activity

The alkaloid noscapine, from opium poppy, is used as an antitussive drug and has low toxicity in humans and mice. Ye et al. (1998) demonstrated that noscapine bound stoichiometrically to tubulin, altered its conformation, affected microtubule assembly, and arrested mammalian cells in mitosis. Further, noscapine caused apoptosis in many cell types with potent antitumour activity against solid murine lymphoid tumours (even when the drug was administered orally) and against human breast and bladder tumours implanted in nude mice. Newcomb et al. (2008) showed that noscapine potently suppressed prolierfation and induced apoptosis in human glioma cell lines. Induction of apoptosis was associated with activation of the c-jun N-terminal kinase signaling pathway concomitant with inactivation of the extracellular signal regulated kinase signaling pathway and phosphorylation of the anti-apoptotic protein Bcl-2. Noscapine-induced apoptosis was associated with the release of mitochondrial proteins apoptosis-inducing factor (AIF) and/or cytochrome c. Their results suggested the potential importance of noscapine as a novel agent for use in patients with glioblastoma owing to its low toxicity profile and its potent anticancer activity.

Analgesic/Antinoceptive Activity

Morphine, from *Papaver somniferum*, is the most widely used compound among narcotic analgesics and remains the gold standard among analgesic drugs employed in clinical practice today (Calixto et al. 2000). The most characteristic effect of morphine is the modulation of pain perception resulting in an increase in the threshold of noxious stimuli (Benyhe 1994). Antinociception induced by morphine was found to be mediated via opioid receptors. Recently, the primary receptor for

morphine-type drugs called the mu-opioid receptor was cloned from rat brain. Studies by Yamada et al. (2006) demonstrated that morphine produced a dose-dependent antinociceptive effect in the tail flick test in the knockout mice, although higher doses were needed to produce antinociception than in wild type mice. The thermal antinociception was found to be via the kappa opioid receptor in the spinal cord in the absence of the mu opioid receptor.

Poppy Seed Consumption and Detection of Alkaloids Post-Ingestion

Bjerver et al. (1982) found the morphine concentration in poppy seed of different brands to vary from 9.4 to 374 μmol/kg, in poppy seed paste 290 μmol/kg, in urine 0.3 and 0.67 μmol/l sampled 3 and 15 h after ingestion of poppy seed cake respectively. ElSohly et al. (1990) found in their study of subjects ingesting poppy seed rolls, the total opiates level was less than 150 ng/mL 24 h after ingestion. In one subject who subjects ingested a poppy seed cake containing 15 g seed analysed to contain 169 μg morphine/g seed, urinary levels of total morphine exceeded 300 ng/mL for approximately 24 h with the highest levels of 2,010 ng/mL morphine and 78 ng/mL codeine 9 h after ingestion.

Papaver somniferum seeds were found to contain total morphine (free and bound) in the range 58.4–62.2 μg/g seeds and total codeine (free and bound) in the range 28.4–54.1 μg/g seeds (Lo and Chua 1992). Soaking seeds in water was found to remove 45.6% of the free morphine and 48.4% of the free codeine. In ingesting a curry meal or two containing various amounts of washed seeds (morphine intake: 200.4–1,002 μg; codeine intake: 95.9–479.5 μg), the urinary morphine levels were found to be in the range 0.12–1.27 μg/mL urine and urinary codeine levels in the range 0.04–0.73 μg/mL urine. Opium poppy seed alkaloids may be urinary products after poppy seed consumption, the lowest detectable concentrations of codeine, morphine, thebaine, papaverine, and narcotine in urine were found to be 4, 4, 5, 0.4, and 4 ng/mL, respectively (Paul et al. 1996). The detection of urinary narcotine, papaverine, or thebaine may be utilized to differentiate poppy seed consumption from illicit codeine, morphine, or heroin use. *Papaver somniferum* alkaloids were rapidly detected within 2 min in process streams using monolithic column high-performance liquid chromatography with chemiluminescence detection (Costin et al. 2007). Limits of detection were 1×10^{-10}, 5×10^{-10}, 5×10^{-10} and 1×10^{-10} M, for morphine, codeine, oripavine and thebaine, respectively.

The universally accepted 300 ng/mL cut-off limit for opiate assays stated to be mandatory for all drug screening laboratories by the Substance Abuse and Mental Health Services Administration, had been questioned recently due to positive results being obtained following the ingestion of poppy seed containing food products. Meadway et al. (1998) in their study found that after consumption of 2 poppy seed roll, one subject tested opiate positive up to 6 h post ingestion with maximum urinary morphine and codeine concentrations of 832.0 ng/mL (@ 2–4 h post ingestion) and 47.9 ng/mL (@ 0–2 h post ingestion) respectively. Following the ingestion of poppy seed cake containing an average of 4.69 g of seed per slice by 4 individuals, opiate positive screening results were obtained for up to 24 h. In one subject (dose equivalent to 0.07 g poppy seed/kg body weight) maximum urinary morphine and codeine concentrations of 302.1 ng/mL (@ 0–2 h) and 83.8 ng/mL (@ 2–4 h) respectively were recorded. Their findings demonstrated that the poppy seed defence could be used as an argument in medico-legal and employment medical cases.

Allergy to Opium Poppy (P. somniferum)

Six of twenty-eight workers of a pharmaceutical factory producing morphine and other alkaloids extracted from shells of *Papaver somniferum* showed clinical symptoms of sensitization to this allergen and positive skin tests (Moneo et al. 1993). Specific IgE could be found on the six sensitized patients by an ELISA and a RAST test using an aqueous extract of *P. somniferum*. An SDS-PAGE of the extract revealed a major protein band with an estimated mol wt of 52,000 Da.

This band had the highest IgE-binding capacity as shown by immunoblotting. The results suggested *P. somniferum* allergy to be mediated by an IgE mediated mechanism and not by a pharmacological or toxic effect of the alkaloids or polyphenols.

Traditional Medicinal Uses

The plant, capsule, seeds and opium have been used in traditional folkloric medicine in different cultures in Europe, the Middle East and Asia (Burkill 1966; Hartwell 1967–1971; Grieve 1971; Duke 1973; Duke 1983; Do et al. 2004). Opium poppy is regarded as astringent, analgesic, anodyne, expectorant, aphrodisiac, antispasmodic, diaphoretic, bactericidal, calmative, carminative, demulcent, emollient, expectorant, hypotensive, hypnotic, narcotic, nervine, sedative, sudorific and tonic. Poppy plant has been used in folkloric medicine for asthma, bladder, bruises, cancer, catarrh, cold, colic, conjunctivitis, cough, diarrhea, dysentery, dysmenorrhea, enteritis, enterorrhagia, fever, flux, headache, hemicrania, hypertension, hypochondria, hysteria, inflammation, insomnia, leucorrhea, malaria, mania, melancholy, nausea, neuralgia, otitis, pertussis, prolapse, proctitis, rheumatism, snakebite, spasm, spermatorrhea, sprain, stomachache, swelling, toothache, tumour, ulcers, and warts.

Poppy plant, boiled in oil, is claimed to aid indurations and tumours of the liver. The tincture of the plant is said to cure cancerous ulcers. In Ayurvedic medicine the plant is considered aphrodisiac, astringent, fattening, stimulant, tonic, and good for the complexion. The dried capsules without the seeds are used to treat cough and diarrhoea in Vietnam. Dried capsules have also been used to treat cough in Europe and diarrhoea and cough in China. The capsule decoction and an injection of the seed decoction are claimed to help uterine cancer. in Unani medicine, the fruit is recommended for anemia, chest pains, dysentery, fever. In Ayurvedic medicine, the capsule is regarded as antitussive, cooling, deliriant, excitant, and intoxicant, and anaphrodisiac if freely consumed. When the Roman soldiers at Golgotha took pity on their prisoner on the cross, they added this poppy juice to the potion of sour wine.

In Ayurvedic medicine, the seeds are considered aphrodisiac, constipating, and tonic. Iranians use the seed for epistaxis; a paste made from Linum, Malva, and Papaver is applied to boils. The Chinese in Peninsular Malaysia have used the seed medicinally in the treatment of nausea, vomiting, fluxes and fevers.

Opium has been reported to be used as a remedy for such cancerous conditions as cancer of the skin, stomach, tongue, uterus, carcinoma of the breast, polyps of the ear, nose, and vagina; scleroses of the liver, spleen, and uterus; and tumours of the abdomen, bladder, eyes, fauces, liver, spleen, and uvula. Opium is unexcelled as a hypnotic and sedative and is frequently administered to relieve pain and calm excitement. As astringent, it is administered for diarrhoea and dysentery. For its expectorant, antitussive, diaphoretic, analgesic and antispasmodic properties it is used to treat certain types of cough, etc. Externally, opium has been applied for haemorrhoids, for leprosy and in wound of the eyes. Opium has been used in Lebanon to quieten excitable people, to relieve toothache, headache, incurable pain, and for boils, coughs, dysentery, and itches. Algerians pack opium into tooth cavities to relive pain.

Opium although is still listed in official pharmacopoeias of some countries, the use of opium or opium preparations has largely been displaced by its purified, extracted alkaloids, mainly morphine, codeine and noscapine (narcotine).

Other Uses

Opium poppy plant also has valuable ornamental uses as a garden flowering plant, and its flowers and dried pods are used in various floral arrangement. Poppy seeds are use as bird feed. Poppy seed oil is a source of drying oil used for the manufacture of paints, varnishes, and soaps. In Turkey, poppy seed are almost exclusively used for the extraction of oil. The nutritious poppy-seed cake or meal left after extraction of the oil is used alone or mixed with other feeds, suitable as food for cattle and other animals.

Comments

Tasmania is the world's largest producer of opium alkaloids for the pharmaceutical market, producing about 50% of the world's concentrated poppy straw (CPS) for morphine and related opiates from merely 10.7% of the production area (Dicker 2001). Other major producers are Turkey with 23% of morphine CPS, France with 21% morphine CPS and Spain with 4%. India, by contrast, produces traditional opium from which the United States extracts opium alkaloids.

The legal production of opium is restricted to India, but extensive illegal opium production is found in the 'Golden Triangle' (the border region of Thailand, Burma (Myanmar) and Laos), the 'Golden Crescent' (Pakistan, Afghanistan, Iran), Lebanon and Mexico.

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Avena sativa

Scientific Name

***Avena sativa* L.**

Synonyms

Avena agraria var. *mutica* Brot., *Avena algeriensis* Trab., *Avena anglica* Roem. & Schult. pro syn., *Avena byzantina* var. *thellungiana* (Malzev) Tab. Morais, *Avena cinerea* Roem. & Schult. pro syn., *Avena dispermis* Mill. nom. superfl., *Avena distans* Schur, *Avena fatua* f. *brachytricha* Thell., *Avena fatua* f. *glaberrima* Thell., *Avena fatua* f. *macrathera* Thell., *Avena sterilis* f. *pseudosativa* Thell., *Avena fatua* f. *setulosa* Thell., *Avena fatua* subsp. *macrantha* (Hack.) Malzev, *Avena fatua* subsp. *nodipilosa* Malzev, *Avena fatua* subsp. *praegravis* (E.L. Krause) Malzev, *Avena fatua* subsp. *sativa* (L.) Thell., *Avena fatua* var. *contracta* (Neilr.) Thell., *Avena fatua* var. *glaberrima* (Thell.) Malzev, *Avena fatua* var. *macrotricha* Malzev, *Avena fatua* var. *microtricha* Malzev, *Avena fatua* var. *pilifera* Malzev, *Avena fatua* var. *pilosa* (Koeler) Malzev nom. illeg., *Avena fatua* var. *sativa* (L.) Hausskn., *Avena fatua* var. *subuniflora* Trab., *Avena flava* Roem. & Schult. pro syn., *Avena fusca* Schur nom. illeg., *Avena fuscoflora* Schur pro syn., *Avena georgiana* Roem. & Schult. pro syn., *Avena glabrata* Hausm., *Avena grandis* Nevski, *Avena heteromalla* Haller, *Avena hungarica* Lucá nom. nud., *Avena macrantha* (Hack.) Nevski, *Avena mutica* Krock., *Avena* × *mutata* Samp., *Avena nodipilosa* (Malzev) Malzev, *Avena orientalis* Schreb., *Avena orientalis* f. *flavescens* Peterm., *Avena pendula* Gilib., *Avena persarum* Nevski, *Avena podolica* Pascal ex Zuccagni pro syn., *Avena polonica* Schwägr. ex Schmalh., *Avena ponderosa* L. ex B.D. Jacks. nom. nud., *Avena praecocioides* Litv., *Avena praecoqua* Litv., *Avena praegravis* (E.L. Krause) Roshev., *Avena pseudosativa* (Thell.) Herter, *Avena racemosa* Thuill., *Avena sativa* convar. *nodipilosa* (Malzev) Tzvelev, *Avena sativa* prol. *grandiuscula* Malzev, *Avena sativa* subsp. *chinensis* (Fisch. ex Roem. & Schult.) Holub, *Avena sativa* subsp. *contracta* (Neilr.) Celak., *Avena sativa* subsp. *macrantha* (Hack.) Rocha Afonso, *Avena sativa* subsp. *nodipilosa* (Malzev) Vasc., *Avena sativa* subsp. *orientalis* (Schreb.) Asch. & Graebn., *Avena sativa* subsp. *praegravis* (E.L. Krause) Cif. & Giacom., *Avena sativa* subsp. *praegravis* (E.L. Krause) Tab. Morais, *Avena sativa* subvar. *pilosa* Koeler, *Avena sativa* var. *brachytricha* (Thell.) Tzvelev, *Avena sativa* var. *chinensis* Döll, *Avena sativa* var. *contracta* Neilr., *Avena sativa* var. *flavescens* (Peterm.) Soó, *Avena sativa* var. *fuscoatra* (Peterm.) Soó, *Avena sativa* var. *glaberrima* (Thell.) Maire & Weiller, *Avena sativa* var. *macrantha* Hack., *Avena sativa* var. *macrathera* (Thell.) Parodi, *Avena sativa* var. *macrotricha* (Malzev) Tzvelev, *Avena sativa* var. *microtricha* (Malzev) Tzvelev, *Avena sativa* var. *nigra* E. Krause, *Avena sativa* var. *orientalis* (Schreb.) Alef., *Avena sativa* var. *pilifera* (Malzev) Tzvelev, *Avena sativa* var. *pilosa* (Koeler) Tab. Morais, *Avena sativa* var. *praegravis* E. Krause, *Avena sativa* var. *secunda* Alph. Wood, *Avena sativa* var. *setulosa* (Thell.) Parodi, *Avena sativa* var.

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subuniflora (Trab.) Tzvelev, *Avena sexflora* Larrañaga, *Avena shatilowiana* Litv., *Avena sterilis* var. *thellungiana* Malzev, *Avena tatarica* Ard., *Avena thellungii* Nevski, *Avena trabutiana* Thell., *Avena trisperma* Roem. & Schult., *Avena unilateralis* Brouss. ex Roem. & Schult. pro syn., *Avena verna* Heuze,

Family

Poaceae

Common/English Names

Common Oat, Cultivated Oat, Oats, Red Oat, Side Oat, Tree Oat

Vernacular Names

Afrikaans: Hawer, Hawermeel;
Arabic: Hartamân, Shûfân, Shaeer Uryan, Sult, Zîwân, Zummayr;
Brazil: Aveia;
Bulgarian: Obec;
China: Yan Mai Shu;
Croatian: Zob;
Czech: Oves setý;
Danish: Almindelig havre, havre, Saedhavre;
Dutch: Haver;
Eastonian: Harilik Kaer, Kaer;
Finnish: Kaura, Peltokuara;
French: avoine, avoine byzantine, Avoine commune, Avoine cultivée;
Gaelic: Coirce;
German: Echter Hafe, Futterhafer, Gemeiner Hafer, Hafer, Mittelmeerhafer, Rispen-Hafer, Saat-Hafer;
Greek: Vromi i imeros, Vromi i kalliergoumeni;
Hawaiian: ‘Oka;
Hungarian: Abrakzab, Zab;
Icelandic: Akurhafrar, Hafrar;
India: Gandal, Ganer, Jai, Jayee (Hindu), Atiyav, Mundyav (Sanskrit);
Indonesian: Gandum;
Italian: Avena, Avena Commune, Biada, Gramigna montana;
Japanese: Enbaku, Ma Karasu Mugi, Ooto, Ooto Mugi;
Latvian: Auzas;
Lithuanian: Avižos;
Malaysia: Oat;
Norwegian: Havre;
Polish: Owies, Owies zwyczajny;
Portuguese: aveia, aveia-amarela;
Russian: Oves kul’tivirovannyi, Oves posevnoi;
Serbian: Ovas;
Slovaščina: Oves, Oves navadni;
Slovencina: Ovos siaty;
Spanish: Avena, avena común, avena roja;
Swedish: havre, vanlig havre;
Thai: Khao ot;
Turkish: Kültür Yulafi, Sifali Yulaf, Yulaf;
Ukranian: Obec;
Vietnamese: Yến Mạch.

Origin/Distribution

The common cultivated oat (*Avena sativa*) and its closely related minor crop, *Avena byzantina* are both hexaploid and classified as secondary crop, i.e., derived from weeds of the primary cereal domesticates in the Fertile Crescent of the Near East (Zhou et al. 1999). *Avena sterilis* L., the oldest hexaploid oat, is the putative progenitor of all cultivated and wild hexaploid oat species. Genetic evidence based on random amplified polymorphic DNA (RAPD) marker variation and the distribution of the 7C-17 intergenomic chromosomal translocation, revealed that all cultivated hexaploids are derived from progenitor, *A. sterilis* germplasm from Southwest Asia, present-day Iran, Iraq, and Turkey. At least two paths of domestication occurred: one from *A. sterilis* with the translocation to *A. sativa* and one from *A. sterilis* without the translocation to *A. byzantina*.

Agroecology

Oats are widely grown as annual crop in the temperate zone and also in the sub-tropics and in the high altitude tropics (1,600–2,800 m). Oats are cold-tolerant and are unaffected by late frosts or snow. Oats have a lower summer heat

requirement and greater tolerance of rain than wheat, rye, secale and barley. In the temperate zone, oat is usually sown in Spring or early summer, in sub-tropical and Mediterranean conditions it is grown in the cool season, late summer or early fall.

Oats can be successfully grown on a wide range of soil types although medium textured soils are preferred to sandy soils because of their greater water holding capacity. With adequate fertilisation and irrigation, oats can be successfully grown in sandy soils. Deep well-drained soils are ideal for oats. Soils with acidity, prone to water-logging and salt problems can adversely affect the desired yield and the quality of oats.

Edible Plant Parts and Uses

Oats are used in various ways in food as whole grains, rolled oats, crushed into oatmeal or ground into oat flour. Oats used as cereal, is better known as a breakfast cereal, used whole or as rolled oats in cold cereals such as muesli or granola. Oat meal is mainly used in porridge or in an array of baked products such as oatcake, oatmeal cookies and oat bread. Oats are now popularly use raw in cookies. Oats are also widely used as a thickener in soups. Oat flour is used in making biscuits, sourdough etc. It is not really suitable for making bread as it lacks gluten. Oat flour is used as an antioxidant in food products and some vegetable oils as it inhibits rancidity and increases the length of shelf-stability of fatty foods and vegetable oils. An edible oil obtained from the grains, is used in the manufacture of breakfast cereals. In Scotland, the oat starch that remains after milling, is fermented for several days and the liquid portion is poured away and drunk and the remaining starch residue is boiled and thickened with water and salt to make the Scottish dish *sowan* which is served with butter or dipped into milk.

Roasted oat grains is also used as a substitute for coffee. Oats are also one of the cereals used as a basic ingredient for brewing beer and whisky. In Britain, oat malt stout used to be produced, and oatmeal stout is brewed using a portion of oats for the wort. Oatmeal caudle, made of ale and oatmeal with spices, used to be a traditional British drink. In Latin America, a cold, sweet drink made of ground oats and milk is a popular beverage.

Botany

Avena sativa is an herbaceous annual, 50–180 cm tall, robust with erect unbranched culms (Plate 1). Leaf sheaths are glabrous with overlapping margins, ligules are blunt and membranous. Leaves are linear, 12–30 cm long by 5–10 (–15) mm wide, glabrous, non-auriculate with scaberulous margins. Inflorescence in diffuse or contracted nodding panicles, 15–40 cm (Plates 2, 3 and 4). Spikelets with 2–3 florets, all bisexual or the distal one or two may be reduced and male or sterile; rachilla glabrous or sparsely hirsute, not readily disarticulating above glumes and between florets; glumes lanceolate to elliptic, subequal or shorter than spikelet, 7–11 veined, smooth; lemmas lanceolate-oblong, usually leathery, occasionally papery, 5–9-veined,

Plate 1 Oat crop ready for harvesting

Plate 2 Ripe nodding panicles

Plate 3 Close-up of nodding ripened spikelets

Plate 4 Oat spikelets with glumes

glabrous to hispid, apex entire to shallowly bilobed, callus naked or sparsely bearded, awn weakly geniculate, rudimentary or absent; palea shorter than lemma, keels ciliate. Caryopsis pale brown, ellipsoid, 10 mm long by 2.5 mm wide, with long linear hilum, adherent to lemma and palea at maturity.

Nutritive/Medicinal Properties

The proximate nutrient composition of oats (*Avena sativa*) per 100 g edible portion was reported as: water 8.22 g, energy 389 kcal (1,628 kJ), protein 16.89 g, total lipid 6.90 g, ash 1.72 g, carbohydrate 66.27 g, total dietary fibre 10.6 g, Ca 54 mg, Fe 4.72 mg, Mg 177 mg, P 523 mg, K 429 mg, Na 2 mg, Zn 3.97 mg, Cu 0.626 mg, Mn 4.916 mg, thiamin 0.763 mg, riboflavin 0.139 mg, niacin 0.961 mg, pantothenic acid 1.349 mg, vitamin B-6 0.119 mg, total folate 56 µg, total saturated fatty acids 1.217 g, 12:0 (lauric) 0.024 g, 14:0 (myristic) 0.015 g, 16:0 (palmitic) 1.034 g, 18:0 (stearic) 0.065 g, total monounsaturated fatty acids 2.178 g, 16:1 undifferentiated (palmitoleic) 0.013 g, 18:1 undifferentiated (oleic) 2.165 g, total polyunsaturated fatty acids 2.535 g, 18:2 undifferentiated (linoleic) 2.424 g, 18:3 undifferentiated (linolenic) 0.111 g, tryptophan 0.234 g, threonine 0.575 g, isoleucine 0.694 g, leucine 1.284 g, lysine 0.701 g, methionine 0.312 g, cystine 0.408 g, phenylalanine 0.895 g, tyrosine 0.573 g, valine 0.937 g, arginine 1.192 g, histidine 0.405 g, alanine 0.881 g, aspartic acid 1.448 g, glutamic acid 3.712 g, glycine 0.841 g, proline 0.934 g and serine 0.750 g (USDA 2012).

The proximate nutrient composition of oat bran (the outer casing of oats, *Avena sativa*) per 100 g edible portion was reported as: water 6.55 g, energy 246 kcal (1,029 kJ), protein 17.30 g, total lipid 7.03 g, ash 2.89 g, carbohydrate 66.22 g, total dietary fibre 15.4 g, total sugars 1.45 g, Ca 58 mg, Fe 5.41 mg, Mg 235 mg, P 734 mg, K 566 mg, Na 4 mg, Zn 3.11 mg, Cu 0.403 mg, Mn 5.630 mg, thiamin 1.170 mg, riboflavin 0.220 mg, niacin 0.934 mg, pantothenic acid 1.494 mg, vitamin B-6 0.165 mg, total folate 52 µg, total choline 32.2 mg, betaine 19.6 mg, lutein + zeaxanthine 180 µg, vitamin E (α-tocopherol) 1.01 mg, β-tocopherol 0.08 mg, δ-tocopherol 0.10 mg, phylloquinone (vitamin K) 3.2 µg, total saturated fatty acids 1.328 g, 12:0 (lauric) 0.026 g, 14:0 (myristic) 0.016 g, 16:0 (palmitic) 1.128 g, 18:0 (stearic) 0.071 g, total monounsaturated fatty acids 2.376 g, 16:1 undifferentiated (palmitoleic) 0.014 g, 18:1 undifferentiated (oleic) 2.362 g, total polyunsaturated fatty acids 2.766 g, 18:2 undifferentiated (linoleic) 2.645 g, 18:3 undifferentiated (linolenic) 0.121 g, tryptophan 0.335 g, threonine 0.502 g, isoleucine 0.668 g, leucine 1.374 g, lysine 0.760 g, methionine 0.335 g, cystine 0.576 g, phenylalanine 0.908 g, tyrosine 0.668 g, valine 0.964 g, arginine 1.279 g, histidine 0.410 g,

alanine 0.872 g, aspartic acid 1.576 g, glutamic acid 3.748 g, glycine 0.947 g, proline 0.982 g and serine 0.890 g (USDA 2012).

Cultivated oat was found to have 5.9% total oil content (% dry weight seed) that can be separated into eight classes comprising two major ones polar lipids (phospholipids and glycolipids) 16% and triacylglycerols (TAG) 74.2%; and six minor ones: 1,2 diacylglycerols 1.1%; 1.3 diacylglycerols 2.3%; unknown lipid 1.4%; free fatty acids 2.5%; TAG 1 1.4%; TAG2 1.1% (Leonov et al. 2008). Fatty acid composition of different lipid classes in cultivated oat oil was as follows:

Polar lipids: 16:0 19.3%, 18:0 1.3%, 18:1 n-9 18.6%, 18:1 n-11 1.2%, 18:2 46%, 18:3 2.1%, 20:1 0.3%, 7-OH-16:0 0%, 15-OH 18–2$^{\Delta 9,12}$ (avenoleic acid) 9.8%, expoxygenated fatty acids (9,10 epoxy-18:0, 9,10-epoxy-18:1$^{\Delta 12}$, and 12,13-epoxy-18:1$^{\Delta 9}$) 0.4%.

1, 2 diacylglycerols: 16:0 13.7%, 18:0 1.7%, 18:1 n-9 30.6%, 18:1 n-11 1.0%, 18:2 36.3%, 18:3 1.3%, 20:1 0.6%, 7-OH-16:0 3.9%, 15-OH 18–2 $^{\Delta 9,12}$ (avenoleic acid) 0%, expoxygenated fatty acids (9,10 epoxy-18:0, 9,10-epoxy-18:1$^{\Delta 12}$, and 12,13-epoxy-18:1$^{\Delta 9}$) 5.4%.

1,3 diacylglycerols: 16:0 17.6%, 18:0 1.9%, 18:1 n-9 31.1%, 18:1 n-11 1.1%, 18:2 37.4%, 18:3 1.1%, 20:1 0.9%, 7-OH-16:0 0%, 15-OH 18–2 $^{\Delta 9,12}$ (avenoleic acid) 1%, expoxygenated fatty acids (9,10 epoxy-18:0, 9,10-epoxy-18:1$^{\Delta 12}$, and 12,13-epoxy-18:1$^{\Delta 9}$) 5.3%.

Unknown lipids: 16:0 14.8%, 18:0 2.0%, 18:1 n-9 26.2%, 18:1 n-11 0.9%, 18:2 36.1%, 18:3 2.3%, 20:1 0.9%, 7-OH-16:0 0%, 15-OH 18–2 $^{\Delta 9,12}$ (avenoleic acid) 2%, expoxygeanted fatty acids (9,10 epoxy-18:0, 9,10-epoxy-18:1$^{\Delta 12}$, and 12,13-epoxy-18:1$^{\Delta 9}$) 10%.

Free fatty acids: 16:0 25.7%, 18:0 2.3%, 18:1 n-9 20.4%, 18:1 n-11 1.1%, 18:2 43.5%, 18:3 0.7%, 20:1 0.7%, 7-OH-16:0 0%, 15-OH 18–2 $^{\Delta 9,12}$ (avenoleic acid) 0.1%, expoxygenated fatty acids (9,10 epoxy-18:0, 9,10-epoxy-18:1$^{\Delta 12}$, and 12,13-epoxy-18:1$^{\Delta 9}$) 4.7%.

TAG (triacylglycerols): 16:0 15.1%, 18:0 1.4%, 18:1 n-9 39.7%, 18:1 n-11 1.2%, 18:2 38.6%, 18:3 1.41%, 20:1 0.9%, 7-OH-16:0 0%, 15-OH 18–2 $^{\Delta 9,12}$ (avenoleic acid) 0.1%, expoxygenated fatty acids (9,10 epoxy-18:0, 9,10-epoxy-18:1$^{\Delta 12}$, and 12,13-epoxy-18:1$^{\Delta 9}$) 0.8%.

TAG1: 16:0 10.1%, 18:0 1.2%, 18:1 n-9 27.9%, 18:1 n-11 0.8%, 18:2 30.2%, 18:3 0.9%, 20:1 0.4%, 7-OH-16:0 0%, 15-OH 18–2 $^{\Delta 9,12}$ (avenoleic acid) 0.4%, expoxygenated fatty acids (9,10 epoxy-18:0,9,10-epoxy-18:1$^{\Delta 12}$,and12,13-epoxy-18:1$^{\Delta 9}$) 27.4%.

TAG2: 16:0 15.3%, 18:0 2.5%, 18:1 n-9 28.3%, 18:1 n-11 1.1%, 18:2 22.4%, 18:3 0.3%, 20:1 1.0%, 7-OH-16:0 0%, 15-OH 18–2 $^{\Delta 9,12}$ (avenoleic acid) 0.4%, expoxygenated fatty acids (9,10 epoxy-18:0, 9,10-epoxy-18:1$^{\Delta 12}$, and 12,13-epoxy-18:1$^{\Delta 9}$) 28%.

Two additional hydroxylated FAs, 13-hydroxy 18:2 $^{\Delta 9,11}$ and 9-hydroxy 18:2 $^{\Delta 10,12}$, were found also in the oat oil. Wild oat species tended to have higher oil and 18:1 fatty acid contents and lower amounts of 18:2 and 18:3 fatty acids as compared to cultivated oats (Leonova et al. 2008). Minor amounts of several hydroxy and epoxy fatty acids were also present in the oat oil and mainly confined to specific lipid classes. These unusual fatty acids included the previously reported 15-hydroxy 18:2 (δ 9,12) (avenoleic acid) mostly found among polar lipids and a novel 7-hydroxy-hexadecanoic acid located to 1,2-diacylglycerol. Oats were found to be enriched in the omega 3 (ω-3) fatty acid 18:3.

Oat oil was found to have β-sitosterol and Δ5-avenasterol (White and Armstrong 1986). The majority of lipids (86–90%) were found in the endosperm of the oat grain (Banas et al. 2007). Up to 84% of the lipids were deposited during the first half of seed development, when seeds where still green with a milky endosperm. Microscopy studies revealed that whereas oil bodies of the embryo and scutellum still contained a discrete shape upon grain maturation, oil bodies of the endosperms fused upon maturation and formed smears of oil. Comparative study of five small grain cereals namely barley, oats, rice, sorghum, and wheat found that the in whole or dehulled grains the oil content ranged from 2.18% of a wheat variety to 6.38% of an oat line (Liu 2011). Compared with barley and wheat, rice, oat, and sorghum had higher relative % of C18:1 (31.60–36.64 compared with 12.15–15.61) and lower %

of C18:2 (35.69–45.44 compared with 50.79–61.50). For all the grains, from seed surface to inner core, C16:0 and C18:0 increased, C18:1 and C18:3 decreased, and C18:2 changed slightly, providing a new reason for improved oxidative stability for pearled kernels.

Unlike the major cereals, in which prolamine storage proteins form about half of the total grain nitrogen, the major storage protein in oats and rice are 11S globulin-like proteins and prolamins occur at low levels (<5–10%) of the total grain protein (Shewry et al. 1995). In oats, the major globulin-like storage protein is avenalin, constituting 80% and the minor prolamine protein is avenin. Oat protein is nearly equivalent in quality to soy protein, which had been shown by the World Health Organization to be equal to meat, milk, and egg protein (Lasztity 1999). The protein content of the hull-less oat kernel (groat) was found to range from 12 to 24%, the highest among cereals.

Oats and oat bran are rich in vitamin B complex, essential elements, proteins and dietary fibre. The main component of soluble and viscous dietary fibre of oats called (1→3), (1→4)-β-D-glucan is also referred to as β-glucan (Wood 1990, 1994b; Anttila et al. 2004; Kim et al. 2006). Oat β-glucan, present in oat bran in greater concentrations than in the whole oat groat, was found to mainly compose of β-(1→3)-linked cellotriosyl and cellotetraosyl units, present at 52 and 34% by weight of the molecule, respectively (Wood et al. 1991; Wood 1994b). The remaining structure consist of β-(1→3)-linked blocks composed of four or more consecutive β-(1→4)-linked D-glucopyranosyl units. Size-exclusion chromatography indicated a molecular weight for oat β-glucan of $2–3 \times 10^6$. In general, the cereal β-glucans were similar, but the ratio of (1–3)-linked cellotriosyl to (1–3)-linked cellotetraosyl units, which constituted approximately 90% of the polysaccharides, was lower for oats (2.1–2.4) than it was for barley and rye (2.8–3.3) (Wood et al. 1994b). Cereal mixed-linkage (1→3), (1→4)-β-D-glucan is a linear polysaccharide made up entirely from glucose. Sequences of (1→4)-linked D-glucopyranosyl units are separated by single (1→3)-β-linked units. The solubility of β-glucan is enhanced by the (1→3)-linkages compared to cellulose which only has (1→4)-linkages. Aspinall and Carpenter (1984) using methylation and specific analysis showed that the soluble β-glucan extracted from oat bran contained linear chains linear chains with (1→3) and (1→4) linkages in the proportions 1:2.6. Compositional and linkage analysis studies on the water-insoluble residue revealed the presence of further β-D-glucan (5%) and arabinoxylan (3%), but only traces of cellulose (<0.5%). β-glucans from the oat cultivars and brans had the highest molecular weights (3.00×10^6), and commerically milled samples were similar (2.70×10^6), followed by barley (2.14×10^6), malts (1.22×10^6), and rye (1.13×10^6) (Wood et al. 1991). β-glucan was isolated from oat bran in a highly purified form (Johansson et al. 2000). Two types of β-glucan were obtained with different solubilities. Their molar masses were 1.6 million for the less soluble and 1.1 million for the more readily soluble type. No structural differences were found. The isolated β-glucan showed the glucose units ot be joined with 1,3- and 1,4-linkages only. The oligosaccharides produced by the action of a specific enzyme, lichenase, afforded the following major products: 32-β-D-glucosyl cellobiose (trisaccharide) and 33-β-D-glucosyl cellotriose (tetrasaccharide), which accounted for 95% of the whole. Also, 34-β-D-glucosyl cellotetraose (pentasaccharide) and other oligosaccharides with degree of polymerization (DP) higher than five were detected as minor components. Oat grains were found to have water-insoluble, non-starchy, cellulosic and non-cellulosic polysaccharides (Virkki et al. 2005).

Whole grain oats were found to have 5.8% pentosan (DW basis) and oats endosperm 0.7% whilst whole grain oats contained 3.9% β-glucan while the endosperm contained 1.8% β-glucan (Henry 1987). (1→3), (1→4)-β-D-glucan was found mainly in the endosperm cell walls and in the subaleurone layer of oats and barley (Miller and Fulcher 1994, 1995). β-glucans from the oat cultivars and brans had the highest molecular weights (Wood et al. 1994b). Bhatty (1992) found 19 genotypes of Canadian oats to have extract-viscosity (AEV) values ranging from 3.4 to 14.4 centiStokes (cS), total β-glucan 1.8–2.8%,

pentosans 2.4–4.5% and starch 49.0–75.2%. Saastamoinen et al. (1992) reported that the mean β-glucan contents of Finnish oats varied from 3.1 to 4.5% in total grain and from 4.0 to 6.3% in groats in normal oat material. In naked oats the mean β-glucan contents of varied from 3.8 to 4.9%. β-glucan content in total grain including groats and hulls of 12 oat varieties varied from 2.78% in Pol variety to 4.68% in Stil variety. β-glucan content was found to be influenced by genotype and environmental factors (Saastamoinen et al. 1992, 2004; Miller et al. 1993) but not cultivation method (traditional versus organic cultivation) and nitrogen fertilisation (Saastamoinen et al. 2004). Water-soluble and water-insoluble (1 → 3), (1 → 4)-β-D-glucans were isolated from whole-grain oats and barley and digested with lichenase (Johansson et al. 2004). Analyses of the ratio of oligosaccharides with degrees of polymerisation 3 and 4 (DP3:DP4) showed small structural differences between oats and barley and between the water-soluble and water-insoluble β-glucans. The molar masses were 500,000 g/mol for the soluble β-glucans of both oats and barley and < 200,000 g/mol for the insoluble β-glucans. Gajdosova et al. (2007) reported the content of water-soluble and water-insoluble β-D-glucans in selected oats and barley varieties followed the following sequence: barley (3.75 –7.96/100 g of dry mass) ≥ slanted naked oats (3.91 –7.47/100 g of dry mass) > hulled oats (1.97 –4.09/100 g of dry mass), whereas the content of insoluble glucans decreased in the order: hulled oats (33.73 –13.79/100 g of dry mass) > barley (10.89 –21.70/100 g of dry mass) > naked oats (5.15 –10.80/100 g of dry mass). When comparing the content of insoluble β-glucan in whole flour, bran and flour it was found that the content decreases from the outer coat to the endosperm.

Oat β-D-glucan is a valuable functional ingredient having numerous industrial, nutritional and health benefits (Ahmad et al. 2010). The water binding capacity of the β-D-glucan ranged between 3.14 and 4.52 g/g of sample. β-D-glucan exhibited ideal foaming stability when appropriate extraction technique was used. The viscosity of β-D-glucan gum ranged between 35.6 and 56.16 cp. The color analysis showed L* value of β-D-glucan gum pellet ranged between 72.18 and 83.54. Phosphorus, potassium and calcium appeared as major minerals in β-D-glucan gum whereas iron, manganese and copper appeared as minor minerals. FTIR spectroscopy also confirmed the presence of β-D-glucan, protein and other components in extracted β-D-glucan gum pellets. Overall, extracted β-D-glucan showed a good potential for industrial usage.

Soluble and viscous dietary fibres, including the β-glucan present in oats are associated with two major health promoting effects, i.e. the attenuation of postprandial plasma glucose and insulin levels and the control of cholesterol (Anttila et al. 2004). Increased viscosity in the intestine delays absorption of glucose and suppresses absorption of cholesterol and reabsorption of bile acids. Viscosity of β-glucan in foods and in the food digest depends on solubility, concentration and molecular weight. Numereous studies had reported examined the efficacy of β-glucan in terms of the lipid lowering effects, blood sugar reduction, weight reduction, immune modulator, and anticarcinogenic effect (Kim et al. 2006). Profusion of scientific studies had indicated β -glucans to promote health in a number of important ways. B-glucans have been studied for their hypocholesterolemic effects; these mechanisms include: reducing the intestinal absorption of cholesterol and bile acids by binding to β-glucans; shifting the liver from cholesterol syntheses to bile acid production; and fermentation by intestinal bacteria to short-chain fatty acids, which are absorbed and inhibit hepatic cholesterol syntheses (Rondanelli et al. 2009). Several studies had also shown that oat β-glucans blunt the glycemic and insulin response. Moreover, β-1,3-glucans had been reported to improve the body's immune system defense against foreign invaders by enhancing the ability of macrophages, neutrophils and natural killer cells to respond to and fight a wide range of challenges such as bacteria, viruses, fungi, and parasites. Also, there is renewed interest in the potential usefulness of β-glucan as a radioprotective drug for chemotherapy, radiation therapy and nuclear emergencies, particularly because glucan can be

used not only as a treatment, but also as a prophylactic (Rondanelli et al. 2009). Oat β-glucans are found in various breakfast cereals and snacks (Bell et al. 1999). Usually, several servings of these products are required to meet the Food and Drug Administration's claim of reducing the risk of heart disease.

In addition their high β-glucan content, oats contain more than 20 unique polyphenols, avenanthramides low molecular weight soluble phenolic compounds (Collins and Mullin 1988; Collins 1989) which are not present in other cereal grains. Oats groats (kernels) were found to contain more than 25 distinct aventhramides, substituted N-cinnamoylanthranilate alkaloids, while the hull extracts contained about 20 (Collins 1989). Some 15 were common to both groat and hull. A new group of phenolic acids was found in aqueous alcoholic extracts of both oat groats and hulls (Collins et al. 1991). These acids occurred as conjugates covalently linked to the amine function of several different orthoaminobenzoic acids. Mass spectral studies revealed an acid composed of C11H10O3 and a molecular weight of 190. Structural analysis (1 H-, 13C-nuclear magnetic resonance, ultraviolet, etc.) allowed formulation of the acid as 5-(4′-hydroxyphenyl)-penta-2,4-dienoic acid (i.e., 4′-hydroxycinnamylidene-acetic acid), for which the trivial name avenalumic acid was proposed. Two additional derivatives of avenalumic acid were also detected: the 3′-hydroxy- and 3′-methoxy analogues. These acids, which are the ethylenic homologues of the well- known *p*-coumaric, ferulic, and caffeic acids, may be widely distributed in cereal grains. The avenanthramides had shown strong antioxidant activity in-vitro and in-vivo and also shown to exhibit antiinflammatory, antiproliferative, and anti-itching activity, which may provide additional protection against coronary heart disease, colon cancer, and skin irritation (Meydani 2009). Oat phytoalexins, avenanthramides, were found to occur as constitutive components in seeds (Matsukawa et al. 2000). The composition of avenanthramides in dry seeds was different from that in elicitor-treated leaves. In seeds, avenanthramide C was most abundant with an amount two times larger than that of avenanthramide A or B. Conversely, avenanthramide A was the major component in elicitor-treated leaves. The hydroxycinnamoyl-CoA:hydroxyanthranilate N-hydroxycinnamoyltransferase (HHT) activity, which is responsible for the final condensation step in the avenanthramide biosynthesis, was detected in dry seeds. HHT consisted of at least two isoforms. Oat phytoalexins, avenanthramides, are a series of substituted hydroxycinnamic acid amides with anthranilate (Matsukawa et al. 2002). The anthranilate in avenanthramides is biosynthesized by anthranilate synthase. Induction of anthranilate synthase activity was investigated in oat leaves treated with oligo-N-acetylchitooligosaccharide elicitors. The total levels of tocols, phenolic acids, and avenanthramides varied by over two-fold between oat cultivars, but less variation occurred in total sterols and total folates (Shewry et al. 2008). The concentration of phenolic compounds avenanthramides (AVAs), and hydroxycinnamic acids (HCAs), a sucrose-linked truxinic acid (TASE) in oats were influenced by cultivar and year (Dimberg et al. 2005). AVAs were negatively affected by higher nitrogen rates and not affected by cropping systems (organic vs conventional) whereas HCAs were not influenced by N rates or the cropping system. The avenanthramide-rich extract (ARE) from oat bran were found to contain 6.07% N-(3′,4′-dihydroxycinnamoyl)-5-hydroxyanthranilic acid, 4.37% N-(4′-hydroxycinnamoyl)-5-hydroxyanthranilic acid, and 5.36% N-(4′-hydroxy-3′-methoxycinnamoyl)-5-hydroxyanthranilic acid (Ren et al. 2011). In addition, ARE was also rich in vanillic acid (0.60%), caffeic acid (0.50%), syringic acid (0.54%), *p*-coumaric acid (0.16%), ferulic acid (0.08%), and sinapic acid (0.03%).

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cinnamoyl-CoA:hydroxyanthranilate N-hydroxycinnamoyltransferase (HHT) activity, which is responsible for the final condensation step in the avenanthramide biosynthesis, was detected in dry seeds. HHT consisted of at least two isoforms. The content of avenanthramides in oat flakes (26–27 mg/kg) was about double that found in oat bran (13 mg/kg) (Mattila et al. 2005). β-glucan was isolated from oat porridge, bread and both fresh and dry fermentate (Johansson et al. 2007). Processing did not affect the structure of soluble β-glucan. Cooking increased the amount of soluble β-glucan but baking decreased it. They found cooking to be the most favourable process with regards to health effects.

Alkaline hydrolysis of the mixed antioxidants in oats yielded caffeic acid 29%, ferulic acid 10% (both calculated as % acyl groups), glycerol 4.5%, and long-chain hydroxyfatty acid 50% (Daniels et al. 1963). Other antioxidants identified included cosanoic acid, 6 hexacosyl caffeate and 8 hexacosane-1,26-diol diferulate. Of 24 phenolic antioxidants in oats including phospholipids and tocopherols (Daniels and Martin 1961), two were isolated and characterized (Daniels and Martin 1967). One consisted of the homologues, n-hexacosyl caffeate and n-octacosyl caffeate and the other, 26-*O*-caffeoyl-26-hydroxy-hexacosanoic acid with 28-*O*-caffeoyl-28-hydroxyoctacosanoic acid. Of the antioxidants extracted from oats, one of the antioxidant on hydrolysis yielded caffeic acid (2 mol), ferulic acid (1 mol), glycerol (1 mol) and long-chain ω-hydroxyacid (1 mol) (Daniels and Martin 1968). The ω-hydroxyacid fraction contained the homologues, C_{22} (5%), C_{26} (64%), and C_{28} (31%). Dehydrodiferulic acids (DFA) (8-5′- DFA, 8-8′-DFA, 5-5′-DFA, 8-*O*-4′-DFA could be identified in both insoluble dietary fibre (IDF) and soluble dietary fibre (SDF) of oat grains (Beunzel et al. 2001). Total dehydrodiferulic acid in IDF of oats was quantified as 3,599 μg/g, in SDF 38 μg/g. In oats, amounts of 8-5′-DFA reached up to 45% in IDF and 44.7% in SDF; 8-8′-DFA 18.8% in IDF and 32.8% in SDF; 5-5′-DFA 12.9% in IDF and 11.2% in SDF; 8-*O*-4′-DFA 21.2% in IDF and 11.4% in SDF; 4-*O*-5′ DFA was not detected in both IDF and SDF.

Spring oat whole grain extract from various locations in Finland, was found to contain seven dietary lignans, i.e., 7-hydroxymatairesinol, secoisolariciresinol, matairesinol, lariciresinol, pinoresinol, medioresinol, and syringaresinol; total lignin content varied from 820 to 2,550 μg/100 g (Smeds et al. 2009).

Antioxidant Activity

Peterson (2001) reported oats to be abundantly rich in antioxidants such as vitamin E (tocopherols), phytic acid, phenolic compounds, and avenanthramides; including the presence of flavonoids and sterols. These antioxidants were found concentrated in the outer layers of thekernel. Studies had shown that oat-containing diet boosted the antioxidant capacity of serum or meat in animals. Antioxidants have also been reported in assisting to maintain the stability of processed oat products, and oat could stabilise oils and fats against rancidity.

Free phytochemicals of oat grains had highest antioxidant activity of 31.07 μmol vitamin C equivalent/g of grain compared to wheat, rice, and corn (Adom and Liu 2002). Antioxidant activity of bound phytochemicals was 43.60 μmol and total antioxidant activity was 74.67 μmol. Ferulic acid content of oat grains (% contribution of fraction to the total μmol ferulic acid/100 g of grain) comprised total ferulic acid 184.66 μmol, free ferilic acid 0.65 μmol (0.4%), soluble ferulic acid conjugate 3.4 μmol (1.84%), bound ferulic acid 180.61 μmol (97.8%). Total phenol content in oat grains was determined as 6.53 μmol gallic acid equivalent/g of grain, bound phenols 4.76 μmol, free phenols 1.77 μmol. Total flavonoid content in oats grains was 1.16 μmol catechin equivalent per g of grain, free flavonoids 0.45 μmol, bound flavonoids 0.71 μmol. Oat whole grain was found to have total phenolic content of 79.5 mg GAE/100 g grain and oxygen radical absorbance capacity (ORAC) of 2,891 μmol TE/100 g grain (Okarter 2012). Oats contained 70.2 μmol/100 g grain of ferulic acid, and 26.4 μmol/100 g grain of *p*-coumaric acid in the insoluble bound fraction but contained no

flavonoids (qurecetin, kaempferol, catechin, and rutin) in the insoluble-bound fraction of the grain. None of the phenolic compounds had any cellular antioxidant activity, most likely because these phenolic compounds did not have the structure necessary to impart cellular antioxidant activity. The data suggested that the potential health benefit of whole grain consumption in the lower gastrointestinal tract was independent of the cellular antioxidant activity of the phenolic compounds found in the insoluble-bound fraction of whole grains.

The antioxidant capacity of the oat fractions, milled oat groat pearlings, trichomes, flour, and bran, was generally consistent with a potency rank of pearlings (2.89–8.58 TE/g) > flour (1.00–3.54 TE/g) > trichome (1.74 TE/g) = bran (1.02–1.62 TE/g) in both low-density lipoprotein (LDL) and oxygen radical absorbance capacity (ORAC) assays regardless of the free radical generator employed (Handelman et al. 1999). Of eight solvent systems used, the most potent antioxidant activities were obtained with methanolic antioxidant extracts derived from Noble and Ogle oats and hulls (Duve and White 1991). These extracts were added to soybean oil (SBO) and their effectiveness was compared with that of butylated hydroxytoluene (BHT), tertiary butyl hydroquinone (TBHQ) and a control (no additives) at 32, 60 and 180°C. Peroxide values (PV) for oils with added antioxidants during storage at 32 and 60°C showed that the Ogle oat extract was more effective than the other oat and hull extracts or the control. At 180°C all oils with added oat and hull extracts had significantly lower conjugated dienoic acid values and significantly higher 18:2/16:0 than oils with added BHT, TBHQ or the control during 14 days at frying temperature. Phenolic and ortho- and para-hydroxy-phenolic antioxidant compounds, caffeoyl and feruloyl esters, acids (ferulic and caffeic), alcohols, sugar mercaptals, glycerides n-acylamino sugars or polysaccharides, uronic acid, ketohexoses, tocopherol and derivatives of cinnamic and benzoic acids were identified in the oat and hull extracts. The contribution of oat tocols from the fractions accounted for <5% of the measured antioxidant capacity most of which was likely derived from polar phenolic compounds in the oat aleurone. In another study, the following antioxidant components of methanolic extract of groats and hulls from Ogle oats were identified and quantified (mg/kg): ferulic acid 147.2 mg, *p*-coumaric 44.9 mg, caffeic acid 16.8 mg, vanillic acid 16.1 mg, vanillin 3.4 mg, *p*-hydroxybenzoic acid 3.5 mg, 4-hydroxyphenylacetic acid 0.6 mg and catechol traces, in ground groats (Xing and White 1997). In ground hulls, the following antioxidants were quantified, caffeic acid 9142.3 mg, *p*-courmaric acid 59.7 mg, vanillic acid 24.3 mg, *p*-hydroxybenzoic acid 50 mg, 4-hydroxyphenylacetic 4.6 mg, vanillin 54.2 mg, catechol 0.1 mg, *o*-coumaric acid 6.9 mg, sinapic acid 5.6 mg, and salicylic acid 3.1 mg. Antioxidant activities of both oat extracts when added to soybean oil increased with increased concentration. During 20 days of storage, the groat extract (0.3%) was not significantly different from tertiary butylhydroquinone (TBHQ) after day 16, and hull extracts (0.2 and 0.3%) were not significantly different from TBHQ on day 20. Oils containing pure phenolics at the same concentrations measured in the oat groat and hull extracts oxidized more quickly than did oils containing the extracts. Gray et al. (2000) reported that oats (cv. Gerald) from a variety of sources when dehulled, milled and fractionated yielded a bran-rich fraction (>420 μm) and a starch-rich fraction (<420 μm). The bran-rich fractions had significantly higher antioxidant activity than the corresponding starch-rich fraction and appeared to have a more potent population of phenolic antioxidant compounds.

Two avenanthramides belonging to a group of about 40 cinnamoyl anthranilic acid derivatives in oat grains were isolated: N-(4′-hydroxy-3′methoxy-(E)-cinnamoyl)-5-hydroxyanthranilic acid (A1) and N-(4′-hydroxy-3′methoxy-(E)-cinnamoyl)-5-hydroxy-4-methoxyanthranilic acid (A2) (Dimburg et al. 1993). Using the linoleic acid system, A1 showed about 20% antioxidant activity exerted by α-tocopherol and A2 showed about 60%. A1 was mainly located in the outer part of the oat grain. A comparison of ten different oat cultivars revealed A1 contents to range from 40 to 132 μg/g of grain. The amount

of A2 was ten times lower. Optimal parameters for extraction of avenanthramides from oat bran were found to be ethanol/water/acetic acid in the ratio of 80/19.9/0.1, temperature 60°C, solid–liquid ratio of 1:8 and extraction time of 2 h (Ren et al. 2008). Under such conditions, the yield of avenanthramides was 5.29%, the content of avenanthramides could be increased up to 19.2% after being purified by AB-8 macroporous resin. It also shown that the purified avenanthramides extract had strong capacity of scavenging OH, O2-and DPPH free radical, the scavenging capacity were 79.4, 82.2 and 78.0% that of α-tocopherol respectively. Studies in mice demonstrated that avenanthramide-rich extract (ARE) from oat bran possessed the antioxidant activity and was effective against D-galactose-induced oxidative stress (Ren et al. 2011). Administration of D-galactose markedly lowered not only the activity of superoxide dismutase (SOD) and glutathione peroxidase (GPx) but also the gene expression of manganese superoxide dismutase (SOD), copper-zinc SOD, glutathione peroxidase (GPx), and lipoprotein lipase (LPL) mRNA in mice. Administration of ARE significantly reversed the D-galactose-induced oxidative stress by increasing the activity of the antioxidant enzymes and upregulating their gene expression. This was accompanied by a significant decrease in the malondialdehyde (MDA) level in mice given ARE compared to the control.

The three most abundant avenanthramide constituents of oats (*Avena sativa* L.) grain, N-(4′-hydroxy-3′-methoxycinnamoyl)-5-hydroxyanthranilic acid (Bf), N-(4′-hydroxycinnamoyl)-5-hydroxyanthranilic acid (Bp), and N-(3′,4′-dihydroxycinnamoyl)-5-hydroxyanthranilic acid (Bc), were synthesized and purified (Peterson et al. 2002). Each avenanthramide displayed antioxidant activity in both systems inhibition of β-carotene bleaching and reaction with the free radical 2,2-diphenyl-1-picrylhydrazyl (DPPH). Bc had greater activity than Bp and Bf. Bc was nearly as active as the standard synthetic antioxidant, butylated hydroxytoluene (BHT) in the β-carotene system. In the DPPH system, Bc and Bf were more active than 6-hydroxy-2,5,7,8-tetramethylchromane-2-carboxylicacid(Trolox®). Eight avenanthramides, amides of anthranilic acid (1) and 5-hydroxyanthranilic acid (2), respectively, and the four cinnamic acids *p*-coumaric (p), caffeic (c), ferulic (f), and sinapic (s) acid, were synthesized for identification in oat extracts and three compounds (2p, 2c, and 2f) were found in oat extracts (Bratt et al. 2003). As assessed by the reactivity toward 1,1-diphenyl-2-picrylhydrazyl (DPPH), all avenanthramides except 1p showed antixodant activity. Initially, the antioxidant activity of the avenanthramides decreased in a similar order as for the corresponding cinnamic acids, that is: sinapic > caffeic > ferulic > *p*-coumaric acid. The avenanthramides derived from two were usually slightly more active than those derived from one. All avenanthramides inhibited azo-initiated peroxidation of linoleic acid; 1c and 1 s were initially the most effective compounds.

Studies showed that oat phenolics, including avenanthramides, were bioavailable in hamsters and interact synergistically with vitamin C to protect LDL during oxidation (Chen et al. 2004). Peak plasma concentrations of avenanthramides A and B, *p*-coumaric, *p*-hydroxybenzoic, vanillic, ferulic, sinapic, and syringic acids appeared at 40 min after gavage treatment with oat bran phenol-rich powder. Oat phenolics from 0.52 to 1.95 μmol/L increased the lag time to LDL oxidation in a dose-dependent manner. Combining the oat phenolics with 5 μmol/L ascorbic acid extended the lag time in a synergistic fashion. In a randomized, placebo-controlled, 3-way crossover trial with 1-week washout periods, healthy older adults were given 360 mL skim milk alone (placebo) or containing 0.5 or 1 g avenanthramide-enriched mixture (AEM) extracted from oats (Chen et al. 2007). Concentrations of avenanthramide-A, avenanthramide-B, and avenanthramide-C in the AEM were 154, 109, and 111 μmol/g, respectively. Maximum plasma concentrations of avenanthramide (free + conjugated) after consumption of 0.5 and 1 g AEM were 112.9 and 374.6 nmol/L for avenanthramide-A, 13.2 and 96.0 nmol/L for avenanthramide-B, and 41.4 and 89.0 nmol/L for avenanthramide-C, respectively. The bioavailability of avenanthramide-A was four-fold larger than that of avenanthramide-B at the 0.5 g AEM dose. After consumption

of 1 g AEM, plasma reduced glutathione was elevated by 21% at 15 min and by 14% at 10 h. The results indicated oat avenanthramides to be bioavailable and increased antioxidant capacity in healthy older adults. Studies by Koenig et al. (2011) concluded that oat avenanthramides were bioavailable to the blood circulation following oral ingestion in the rat and reach peripheral tissues where they can be taken up by various organs (liver, heart, and gastrocnemius) differentially. With avenanthramides remaining in the organs for up to 12 h, it appeared possible to maintain an increased level of avenanthramides in the rat via repeated feedings.

Of all the alkaloid phenolic compounds unique to oats tested, N-(3′,4′-dihydroxy-(E)-cinnamoyl)-5-hydroxyanthranilic acid (2c), an abundant oat avenanthramide, generally had the highest antioxidant activity in DPPH (2,2-diphenyl-1-picrylhydrazyl) and FRAP (ferric reducing antioxidant potential) assay sand in antigenotoxicity using the Comet assay with stressed human adenocarcinoma colon cells (Lee-Manion et al. 2009). The drug Tranilast showed antigenotoxic effects, but not antioxidant activity, suggesting that antigenotoxicity was not dependent on antioxidant effects. The results showed that avenanthramides exerted antioxidant and antigenotoxic activities that were comparable to those of ascorbic acid and to have the potential to exert beneficial physiological effects.

Methanolic extracts of pearling oat fractions, flour and aspirations from flaking, and trichomes were found to have high, intermediate, and low antioxidant activities, respectively, evaluated by the β-carotene bleaching method (Emmons et al. 1999). Pearling fractions were also highest in total phenolics and tocols. *p*-hydroxybenzoic acid, vanillic acid, caffeic acid, vanillin, *p*-coumaric acid, and ferulic acid were identified and three avenanthramides and an unidentified ferulate derivative were also detected. Total phenolic content was significantly correlated with antioxidant activity. Antioxidant activity, evaluated by β-carotene bleaching, was correlated with measures of oxygen radical absorbance capacity and low-density lipoprotein oxidation. The data indicated a potential for oat products, especially those enriched in outer layers of the groat, to contribute to dietary intakes of antioxidant phytonutrients. Pearling of oat groats for 5–190 seconds removed <1–15% of the weight (Peterson et al. 2001). The material obtained from short pearling times was mostly bran. Longer pearling times increased the amount of starchy endosperm in the pearlings. Antioxidant activity of 80% ethanol extracts, measured by β-carotene bleaching and by reduction of the free radical, 2,2-diphenyl-1-picrylhydrazyl, was highest in the short-pearling-time fractions and decreased as more endosperm tissue was included. Likewise, there was a decreasing concentration of total phenolics, as more material was pearled from the groats. In contrast, concentrations of avenanthramides were not correlated with pearling time, indicating that they were more uniformly distributed in the groats.

Different commercial processing was found to impact on the levels of antioxidants in oats (Bryngelsson et al. 2002). Steaming and flaking of dehulled oat groats caused moderate losses of tocotrienols, caffeic acid, and the avenanthramide Bp (N-(4′-hydroxy)-(E)-cinnamoyl-5-hydroxyanthranilic acid), while ferulic acid and vanillin increased. The tocopherols and the avenanthramides Bc (N-(3′,4′-dihydroxy)-(E)-cinnamoyl-5-hydroxy-anthranilicacid)andBf(N-(4′-hydroxy-3′-methoxy)-(E)-cinnamoyl-5-hydroxy-anthranilic acid) were not affected by steaming. Autoclaving of grains (including the hulls) raised levels of all tocopherols and tocotrienols investigated except β-tocotrienol, which was not affected. Vanillin and ferulic and *p*-coumaric acids also increased, whereas the avenanthramides decreased, and caffeic acid was almost completely eliminated. Autoclaving of grains (including the hulls) caused increased levels of all tocopherols and tocotrienols analyzed except β-tocotrienol, which was not affected. Vanillin and ferulic and *p*-coumaric acids also increased, whereas the avenanthramides decreased, and caffeic acid was almost completely eliminated.

Antidiabetic Activity

Oat gum and guar gum significantly and similarly decreased postprandial glucose rise as indicated by the glycemic index in healthy subjects (Wood

et al. 1990). Results of more studies established that consumption of the more palatable oat gum (80% β-glucan) lowered postprandial plasma glucose and insulin concentrations in humans and may be comparable with or of greater benefit than guar gum (Braaten et al. 1991). Braaten et al. (1994a) further showed that consumption of oat bran and wheat farina plus oat gum meals reduced the postprandial plasma glucose excursions and insulin levels when compared with the control wheat farina meal in both control and Type 2 diabetic subjects. The results suggested that a rich in β-glucan may therefore be of benefit in the regulation of postprandial plasma glucose levels in subjects with Type 2 diabetes

Separate studies showed that increasing the dose of oat gum successively reduced the plasma glucose and insulin responses relative to a control without gum (Wood et al. 1994a). Reduction of the viscosity of oat gum by acid hydrolysis reduced or eliminated the capacity to decrease postprandial glucose and insulin levels. The ability of oat gum to modify glycemic response was unchanged following agglomeration in the presence of maltodextrin. The relationship showed that 79–96% of the changes in plasma glucose and insulin were attributable to viscosity, and that changes occurred at relatively low doses and viscosities. The effectiveness of oat β-glucan was proportional to the logarithm of the viscosity of the solution fed.

Uusitupa et al. (1992) in a randomized 8-week study of 36 subjects with mild to moderate hypercholesterolemia given oat bran (10.3 g β-glucan/day) or wheat bran, found that serum total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) significantly declined in the oat bran group during the first 4 weeks, but at 8 weeks the values were not significantly different from baseline. Changes in serum TC were mainly confined to those who ate at least two-thirds of the planned daily dose of oat bran. In wheat bran group no changes were observed in serum TC or LDL-C levels. Apolipoprotein A1 and B did not change significantly in either group. Only subjects with apolipoprotein E 3/3 phenotype (n = 12) had hypocholesterolemic response to oat bran at 4 weeks, but no change was found in those with apolipoprotein E 4/4 or 4/3 (n = 7). A 5-weeks crossover design study of six women and seven men (aged 38–61 years) with moderately high cholesterol concentrations showed that modest oat extracts (15 or 10%) incorporated into normal diets could have beneficial effects on glucose tolerance factors (Hallfrisch et al. 1995). Glucose responses were lowered by both extracts in both men and women; however, in women, responses to the 10% extract were lowest. Insulin responses did not differ between men and women, but were lower after oat extracts. Glucagon responses were higher initially in men and were reduced after oat consumption in men but not in women.

Tappy et al. (1996) found that the maximum increases observed in plasma glucose after ingestion of 35 g breakfast cereal were 67, 42 and 38% with 4.0, 6.0, and 8.4 g β-glucan, respectively, compared with the continental breakfast in NIDDM (non-insulin-dependent diabetes mellitus) subjects. There was a linear inverse relationship between dose of β-glucan and plasma glucose peak or area under the glucose curve. Postprandial insulin increase was only 59–67% as high as the continental breakfast (bread, milk, cheese, ham) after all three levels of β-glucan. The 50% decrease in glycemic response that was observed after the ingestion of 35 g carbohydrate was estimated to occur with approximately 5 g β-glucan. This dose of β-glucan can easily be attained without the loss of taste by incorporating oat bran concentrate in products. A 24-week crossover study of eight men with NIDDM showed that consumption of oat bran concentrate bread products improved glycemic, insulinemic, and lipidemic responses (Pick et al. 1996). Mean total dietary fibre intake was 19 g/day in the white bread period and 34 g/day (9 g soluble fibre per day from oat bran concentrate) in the oat bran concentrate period. Body weight remained stable. Mean glycemic and insulin response areas (area under the curve) were lower for the oat bran concentrate period than the white bread period. Mean total plasma cholesterol and low-density lipoprotein cholesterol levels were lower in the oat bran concentrate period than in the white bread period. In the oat bran concentrate period, the mean ratio of low-density lipoprotein cholesterol to high-density lipoprotein cholesterol was reduced by 24%

In an open-label, randomized cross-over study with six treatment segments of 16 volunteers, the glycemic indices of the prototype β-glucan cereal (52 ± 5) and β-glucan bar (43 ± 4.1) were significantly lower than the commercial oat bran breakfast cereal (86 ± 6) and white bread (100) (Jenkins et al. 2002). Addition of β-glucan predictably reduced the glycemic index while maintaining palatability. In a 50 g carbohydrate portion each gram of β-glucan reduces the glycemic index by 4 units, making it a useful functional food component for reducing postprandial glycemia. In a randomized, controlled, repeated measures design with two test series of 12 diabetic patients, consumption of oat bran flour high in β-glucan had a low glycemic response and acted as an active ingredient decreasing postprandial glycemic response of an oral glucose load (Tapola et al. 2005). The results of a randomized cross-over study of 12 healthy subjects suggested that intake of muesli with 4 g oat β-glucan did not affect the gastric emptying rate or satiety but lowered the postprandial blood glucose response, indicating that the gastric emptying rate did not regulate the blood glucose level (Hlebowicz et al. 2008). Muesli with 4 g oat β-glucan lowered the postprandial glucose response significantly compared to the cornflakes meal. Granfeldt et al. (2008) found that muesli enriched with 4 g of β-glucans reduced postprandial glucose and insulin levels to a breakfast based on high glycemic index (wheat) products. A total of 4 g of β-glucans from oats appeared to be a critical level for a significant decrease in glucose and insulin responses in healthy subjects.

Panahi et al. (2007) in an randomized, double-blind, crossover study of 11 healthy subjects found that different processing methods of concentrating β-glucan from oats (aqueous vs. enzymatic) resulting in different level of viscosity of β-glucan induced different effect son postprandial glycemia in healthy individuals. Processing oat β-glucan through enzymatic, rather than by aqueous methods, was found to preserve the viscosity and improved postprandial glycemic control. In another study of 13 healthy volunteers, peak glucose response was lowest after the tempe meal with high-amylose/high-ss-glucan barley tempe while insulin response was lowest after the meal with high β-glucan oat tempe (Alminger and Eklund-Jonsson 2008). The mean blood glucose responses for both the barley and the oat tempe meals were significantly lower than from the reference glucose load during the first 60 min. The calculated glycemic index for barley and oat tempe were 30 and 63, respectively. Mean serum insulin responses from barley and oat tempe were significantly lower compared with the glucose load (during the first 60 min, and the calculated insulin index was lower for oat tempe (21) compared with barley tempe (55). The results suggested that by fermentation and enclosure of high-amylose and/or high-β-glucan barley and oat kernels could have beneficial influence on postprandial plasma glucose and insulin responses. A study of differently processed oat foods isocaloric crisp bread, granola, porridge, and pasta containing 4 g of β-glucan as well as control products with low β-glucan content on glycemic response in human subjects showed that porridge and granola had the highest efficacy in attenuating the peak blood glucose response (PBGR) because of their high peak molecular weight and viscosity (Regand et al. 2009). β-glucan depolymerization in bread and pasta reduced β-glucan bioactivity. Pastas, known to have low glycemic responses, showed the lowest PBGR. Analysis of data indicated that 73% of the bioactivity in reducing PBGR could be explained by peak molecular weight × concentration of β-glucan.

Antiobesity Activity

Six grams of β-glucan from oats added to the American Heart Association Step II diet and moderate physical activity improved lipid profile and caused a decrease in weight and, thus, reduced the risk of cardiovascular events in overweight male individuals with mild to moderate hypercholesterolemia (Reyna-Villasmil et al. 2007). There was a significant increase in plasma high density lipoprotein (HDL) cholesterol in the β-glucan group. The β-glucan fortified diet was

significantly more effective in lowering plasma low density lipoprotein (LDL) cholesterol, non-HDL cholesterol levels, total cholesterol/HDL cholesterol and LDL cholesterol/HDL cholesterol ratio than the diet without β-glucan. The β-glucan diet also decreased fasting plasma glucose whereas the other diet had no effect. Also, both diets reduced body weight and body mass index significantly, with β-glucan diet having a greater effect. The diet with added β-glucan was well accepted and tolerated.

Oat β-glucan was found to increase postprandial cholecystokinin levels, decrease insulin response and improve subjective satiety in overweight human subjects (Beck et al. 2009b). They found a dose-dependent increase in β-glucan resulted in higher levels of plasma peptide Y-Y (Beck et al. 2009a). There was a significant dose response, with a positive correlation between the grams of β-glucan and peptide Y-Y area under the curve. The optimal dose of β-glucan appeared to lie between 4 and 6 g, with the effects on peptide Y-Y mediated by viscosity and concentration. In a 3 month randomised parallel study of 66 mildly overweight women, they found that addition of oat β-glucan did not enhance the effect of energy restriction on weight loss, although wide variations in observed results suggested that individual responsiveness may be an issue (Beck et al. 2010). No significant differences were noted between the groups (including control) for all outcome values, except peptide Y-Y levels. After 3 months, all groups lost weight and showed a reduced waist circumference. The study sample also showed reductions in total cholesterol, LDL, HDL, leptin, PYY, glucagon-like peptide-1 values and an increase in cholecystokinin levels. Juvonen et al. (2009) reported that oat bran beverage with low viscosity induced a greater postprandial increase in satiety and plasma glucose, insulin, cholecystokinin, glucagon-like peptide 1, and peptide YY and a greater decrease in postprandial ghrelin than the beverage with high-viscosity oat bran. Gastric emptying as measured by paracetamol absorption was also faster after low-viscosity oat bran beverage consumption. The authors concluded that viscosity differences in oat β-glucan in a liquid meal with identical chemical composition strongly influenced not only glucose and insulin responses, but also short-term gut hormone responses.

Antihypercholesterolemic Activity

Results of a meta-analysis of 20 trials conducted by Ripsin et al. (1992) supported the hypothesis that incorporating oat products into the diet caused a modest reduction in blood cholesterol level. In a 4-week, randomized, cross-over design study of 20 hypercholesterolemic male and female adults, consumption of oat fibre (oat gum, 80% β-glucan) significantly reduced the total and LDL cholesterol levels of hypercholesterolemic adults without changing HDL cholesterol (Braaten et al. 1994b).

In another study involving 23 mildly hypercholesterolemic subjects, beneficial reduction of cholesterol was obtained with modest amounts of oat extract incorporated into the diet (Behall et al. 1997). A significant dose response due to β-glucan concentration in the oat extract was observed in total cholesterol levels. Total cholesterol levels after the higher β-glucan extract diet were significantly lower than those after the low β-glucan diet. In a 11-week, randomized, controlled trial of 152 Hispanic American men and women, consumption of oat bran cereal was associated with a reduction in plasma levels of both total cholesterol and LDL-C (Karmally et al. 2005). Consumption of corn cereal did not affect either total cholesterol or LDL-C.

In a randomised trial of 75 hypercholesterolemic men and women, six grams concentrated oat β-glucan per day for 6 weeks significantly reduced total and LDL cholesterol, and the LDL cholesterol reduction was greater than the change in the control group (Queenan et al. 2007). Based on a model intestinal fermentation, this oat β-glucan was fermentable, producing higher amounts of butyrate than other fibres and may improve colon health.

Maki et al. (2007) found that high-fibre oat cereal influenced postprandial triglyceride and free fatty acid levels compared with wheat cereal product (control), which may have implications

regarding cardiovascular disease risk. Peak triglyceride concentration and mean under the triglyceride curve were lower after oat versus. wheat cereal consumption. The free fatty acid area under the curve was elevated after the oat vs. the wheat products. Postprandial insulin and glucose responses over 10 h did not differ between treatments. In a randomized, parallel-arm, controlled trial of overweight and obese adults, the group that consumed whole-grain, ready-to-eat (RTE) oat cereal had lower LDL cholesterol, total cholesterol, non-high-density lipoprotein-cholesterol compared to the control (energy-matched low-fibre food) (Maki et al. 2010). High-density lipoprotein and triglyceride responses and weight loss did not differ between groups but waist circumference decreased more with whole-grain RTE oat cereal. Larger reductions in LDL, total, and non-high-density lipoprotein cholesterol levels and waist circumference were evident as early as week 4 in the whole-grain RTE oat cereal group.

Andersson et al. (2009) found that substrains of C57BL/6 mice responded differently to the effects of oats on plasma cholesterol and lipoproteins. In C57BL/6NCrl mice, inclusion of 27 and 40% oat bran reduced total plasma cholesterol by 19 and 24%, respectively, reduced the shift from HDL to LDL + VLDL and caused increased faecal cholesterol excretion. There was no effect of oat bran on plasma levels of the inflammatory markers fibrinogen, serum amyloid A or TNF-alpha. Contrariwise in C57BL/6JBomTac mice there was no sustained effect of oat bran (27 or 40%) on plasma cholesterol after 4 weeks of feeding. The present finding that two substrains of mice respond differently to oats was of practical value, as it could assist to elucidate mechanisms of the cholesterol-lowering effect of oats. In another study they found that oat bran supplemented to a Western diet lowered plasma cholesterol, reduced levels of some inflammatory markers, increases eNOS expression and suppressed atherosclerotic lesion development in the descending aorta (−77%) and aortic root (−33%) in LDLr(−/−) mice (Andersson et al. 2010). Plasma triglycerides and relative levels of plasma LDL + VLDL were reduced accompanied by increased faecal excretion of cholesterol and bile acids. Plasma levels of fibrinogen and soluble vascular cell adhesion molecule-1 (VCAM-1) were significantly lower, and immunofluorescence of aortic sections revealed a 75% lower expression of VCAM-1 in oat-fed mice. Park et al. (2009) found that when hypercholesterolemic rats were fed diets containing the oxidized oat β-glucan, the levels of triglyceride, total cholesterol, LDL-C, and VLDL-C in the rats significantly decreased, consequently improving the serum lipid profiles. Dietary supplementation with β-glucans reduced also the total cholesterol level in liver. Further, more fecal eliminations of total cholesterol and triglyceride were observed, which were favourably correlated to their reduced levels in the serum and liver. The oxidized β-glucan derivatives exhibited enhanced water solubility and improved in vitro bile acid binding capacity.

In a parallel, placebo-controlled trial was carried out in 43 healthy men and women with elevated serum cholesterol levels, a daily dose of 4 g of oat β-glucans incorporated into a healthy ready meal did not significantly lower total cholesterol and low-density-lipoprotein cholesterol in hyperlipidemic subjects compared with an equal ready meal without β-glucans (Biörklund et al. 2008). The researchers asserted that if a food product fulfils general healthy dietary recommendations it may not necessarily be a candidate for supplementation with β-glucans. In a double-blind, parallel-design, multicenter clinical trial involving subjects with LDL cholesterol ≥3.0 and ≤5.0 mmol/L, Wolever et al. (2010) found that an extruded breakfast cereal containing 3 g oat β-glucan/day with a high-molecular weight (MW) (2,210,000 g/mol) or a medium-MW (530,000 g/mol) lowered LDL cholesterol similarly by ≈ 0.2 mmol/L (5%), but efficacy was reduced by 50% when MW was reduced to 210,000 g/mol. Their results indicated that the physicochemical properties of oat β-glucan should be considered when assessing the cholesterol-lowering ability of oat-containing products. Contrariwise, the results of the study by Immerstrand et al. (2010) suggested that the

molecular weights and viscous properties of β-glucan in oat products may not be crucial parameters for their cholesterol-lowering effects. All oat bran preparations investigated significantly reduced plasma cholesterol when compared with a cellulose-containing control diet, regardless of the molecular weight of β-glucan. Moreover, the difference in viscous properties between the processed oat bran (from 0.11 to 17.7 L/g) did not appear to play a major role in the cholesterol-lowering properties. There was no correlation between the molecular weight of β-glucan and the amount of propionic acid formed in caecum. However, there was a significant correlation between the ratio of (propionic acid + butyric acid)/acetic acid and the peak molecular weight of β-glucans: the ratio increased with increasing molecular weight. A parallel, placebo-controlled, double-blinded randomised study performed in 53 type 2 diabetic subjects found that a single daily ingestion of 3.5 g β-glucan, as required by official dietary recommendations, for 8 weeks did not change the lipid profile and HbA1c (glycosylated haemoglobin) in type 2 diabetic subjects (Cugnet-Anceau et al. 2010). Triacylglyceride decreased significantly in the β-glucan group compared with the control group.

Othman et al. (2011) in their review reported that studies conducted during the past 13 years supported the suggestion that intake of oat β-glucan at daily doses of at least 3 g may reduce plasma total and low-density lipoprotein (LDL) cholesterol levels by 5–10% in normocholesterolemic or hypercholesterolemic subjects. Numerous studies had shown that, on average, oat consumption was associated with 5 and 7% reductions in total and LDL cholesterol levels, respectively and supported a relationship between oat β-glucan and blood cholesterol levels. Their findings were consistent with earlier views of the United States Food and Drug Administration (FDA) and United Kingdom Joint Health Claims Initiative (JHCI). FDA approved a health claim for β-glucan soluble fibre from oats for reducing plasma cholesterol levels and risk of heart disease in 1997. JHCI allowed a cholesterol-lowering health claim for oat β-glucanin 2004.

Antiatherogenic Activity

Results of studies by Nie et al. (2006a) suggested that the avenanthramides of oats may contribute to the prevention of atherosclerosis through inhibition of vascular smooth muscle cells proliferation and increasing nitric oxide (NO) production. Avenanthramide-2c significantly inhibited serum-induced smooth muscle cells proliferation. Treatment of human vascular smooth muscle cells C with 40, 80, and 120 μM avenanthramide-2c inhibited cell number increase by 41, 62, and 73%, respectively. In addition, avenanthramide-2c treatment significantly and dose-dependently increased NO production in both smooth muscle cells and human aortic endothelial cells. They further showed that avenanthramide-c arrested smooth muscle cells proliferation at G1 phase by upregulating the p53-p21cip1 pathway and suppressing pRB phosphorylation (Nie et al. 2006b). This inhibitory effect of avenanthramide-c on vascular smooth muscle cell proliferation provided an additional indication for the potential health benefit of oat consumption in the prevention of coronary heart disease beyond its known effect through lowering blood cholesterol.

Anticancer Activity

Guo et al. (2010) found that avenanthramides-enriched extract of oats, avenanthramide-C and methylated form of avenanthramide-C (CH3-Avn-C) significantly inhibited cell proliferation of both COX-2-positive HT29, Caco-2, and LS174T, and COX-2-negative HCT116 human colon cancer cell lines, with CH3-Avn-C being the most potent. However, all the extracts had no effect on COX-2 expression and prostaglandin E(2) (PGE(2)) production in Caco-2 and HT29 colon cancer cells. Also, avenanthramides- enriched extract of oats had no effect on COX-2 expression, but it did inhibit COX enzyme activity and PGE(2) production in lipopolysaccharide-stimulated mouse peritoneal macrophages.

Antiinflammatory Activity

Liu et al. (2004) reported that avenanthramide (Avn)s-enriched extract of oats (AvnsO) significantly suppressed interleukin (IL)-1β-stimulated secretion of proinflammatory cytokines, such as IL-6, IL-8, and MCP-1, by human aortic endothelial cells (HAEC). Subsequently they reported that avenanthramides from oats decreased the expression of endothelial proinflammatory cytokines at least in part through inhibition of NF-kappaB activation by inhibiting the phosphorylation of IKK and IkappaB, and by suppressing proteasome activity (Guo et al. 2008). These studies provided evidence for the potential antiinflammatory and antiatherogenic effects of antioxidant avenanthramides present in oats.

Sur et al. (2008) demonstrated that avenanthramides from oats to be potent antiinflammatory agents that appear to mediate the anti-irritant effects of oats. They found that avenanthramides at concentrations as low as one parts per billion inhibited the degradation of inhibitor of nuclear factor kappa B-alpha (IkappaB-alpha) in keratinocytes. Additionally, keratinocytes treated with avenanthramides showed a significant inhibition of tumour necrosis factor-alpha (TNF-alpha) induced NF-kappaB luciferase activity and subsequent reduction of interleukin-8 (IL-8) release. Further, topical application of 1–3 ppm avenanthramides mitigated inflammation in murine models of contact hypersensitivity and neurogenic inflammation and reduced pruritogen-induced scratching in a murine itch model.

In a prospective birth cohort study of infants with increased HLA-DQB1(human leucocyte antigen β-chain)-conferred risk for type 1 diabetes from 1996 to 2000, Virtanen et al. (2010) reported that out of the 1,293 children, 77 (6.0%) developed persistent asthma; and out of the 1,288 children, 185 (14.4%) developed allergic rhinitis by the age of 5 years. Early age introduction of oats was associated with a reduced risk of persistent asthma. They also found that at early age introduction of fish was dose dependently associated with a decreased risk of allergic rhinitis

Cognitive Activity

In a double-blind, randomized, placebo-controlled crossover of healthy subjects, consumption of a special oat preparation of *Avena sativa* herba (1,250 or 2,500 mg of Neuravena®) was found to have a beneficial effect in healthy subjects, resulting in a positive impact on cognitive performance (Dimpfel et al. 2011). Statistically significant differences were observed during resting (lowering of spectral δ power) and during performance of the d2-concentration test (enhancement of spectral θ power). Also, during performance of mental arithmetic, greater enhancement of θ power was observed but only at a lower error probability.

Antiviral Respiratory Infection Activity

Studies showed that daily ingestions of oat β-glucan before intranasal infection of herpes simplex virus type 1 (HSV-)1 prevented increase in morbidity and mortality induced by exercise stress in mice (Davis et al. 2004b). Exercise stress was associated with a decrease in macrophage antiviral resistance which was blocked by ingestion of oat β-glucan. They also reported that both moderate exercise and oat β-glucan could increase innate immune function of macrophages and decrease risk of upper respiratory tract infection caused by HSV-1 in mice (Davis et al. 2004a). Their data suggested that daily ingestion of oat β-glucan may offset the increased risk of upper respiratory tract infection associated with exercise stress, which may be mediated, at least in part, by an increase in macrophage antiviral resistance. Murphy et al. (2008) further found that depletion of lung macrophages negated the beneficial effects of oat β-glucan on reducing susceptibility to viral respiratory infection following exercise stress, as evidenced by an increase in morbidity and symptom severity. Their result suggested that lung macrophages were partially responsible for mediating the beneficial effects of oat β-glucan on susceptibility to viral respiratory infection following exercise stress. They also

found that feeding with oat β-glucan, sucrose and their combination reduced morbidity and increased macrophage antiviral resistance while only sucrose and oat β-glucan reduced mortality (Murphy et al. 2009). Their data further highlighted the benefits of oat β-glucan and sucrose feedings having similar positive effects on susceptibility to respiratory infection and macrophage antiviral resistance in both resting controls and following exercise stress.

Antifungal Activity

Oat (*Avena sativa*) seed extracts exhibited a high degree of antifungal activity and could be used directly on rye bread to prevent colony formation of *Penicillium roqueforti,* a major contaminating species in industrial food processing (Sørensen et al. 2010). Antifungal candidates identified included thaumatin-like proteins, 1,3-β-glucanase, permatin precursor, pathogenesis-related protein type 1, and class I and II chitinases. Class I chitinase could be specifically removed from the oat extracts and was found to be indispensable for 50% of the *P. roqueforti* inhibiting activity. The purified class I chitinase had a molecular weight of approximately 34 kDa, optimal chitinase activity at pH 7, and existed as at least two basic isoforms (pI values of 7.6 and 8.0). Class I chitinase isoforms had a primary structure with high similarity to class I chitinases of wheat, barley and rye. Class I chitinase was at least ten times more abundant than the wheat, barley, and rye homologs and the oat seed extracts were highly active toward *P. roqueforti* as opposed to extracts of other cereal grains.

Oats Consumption and Celiac Disease

Celiac disease is an immune-mediated disease, triggered in genetically susceptible individuals by ingested gluten from wheat, rye, barley, and other closely related cereal grains (Pulido et al. 2009). Coeliac disease is triggered by an abnormal reaction to gluten (Comino et al. 2011). Peptides resulting from partially digested gluten of wheat, barley or rye cause inflammation of the small intestinal mucosa. The only treatment for celiac disease is a strict gluten-free diet for life. Finnish celiac disease and dermatitis herpetiformis patients had been using oat-containing gluten-free diets since 1997 (Peräaho et al. 2004). Peräaho et al. (2004) found that of 1,000 randomly selected members of the Celiac Society, 710 patients responded: 423 (73%) with celiac disease and 70 (55%) with dermatitis herpetiformis consumed oats. Patients appreciated the taste, the ease of use, and the low costs; 94% believed that oats diversified the gluten-free diet; 15% of celiac disease and 28% of dermatitis herpetiformis patients had stopped eating oats. The most common reasons for avoiding oats were fear of adverse effects or contamination. Hallert et al. (1999) reported that a study of adolescents found oats to be safe and well tolerated by adults with coeliac disease and dermatitis herpetiformis. They added that the risk of wheat contamination of commercial oat products remained a cause of concern and that no such studies had been made in small children. They added that the inclusion of oats, known to be a fibre-rich, naturally gluten-free food, would broaden the range of foodstuffs tolerable to coeliac patients, though for safety reasons they should be used only by adults. In 1995, the largest and most scientifically rigorous study on the safety of oats was published with the conclusion that the consumption of oats was safe for adults with celiac disease (Thompson 2003). Since 1995, several additional studies published found no adverse effects associated with the regular consumption of moderate amounts of oats. However concerns still prevailed among some authorities on celiac disease that even if oats themselves were safe, they nonetheless may be contaminated with wheat, rye, or barley.

In a randomized trial of adults with celiac disease, Janatuinen et al. (1995) found that moderate amounts of oats could be included in a gluten-free diet for most adult patients with celiac disease without adverse effects. They further found no significant differences between controls and those patients consuming oats with respect to duodenal villous architecture, inflammatory cell infiltration of the duodenal mucosa, or antibody

titres after 5 years of follow up (Janatuinen et al. 2002). In both groups histological and histomorphometric indexes improved equally with time. Their study provided evidence of the long term safety of oats as part of a coeliac diet in adult patients with coeliac disease. They also found that the majority of coeliac patients preferred oats in their diet. Srinivasan et al. (2006) reported that detailed immunohistological studies of biopsies from patients ingesting oats for 3 months did not reveal evidence of immune activation further strengthening the view that oats could be included safely in the diet of gluten sensitive patients. The distribution of intestinal HLA-DR expression was not affected by oats ingestion. In the pre-oats biopsies, the percentage of Ki-67 positive enterocytes, did not differ significantly from that found in post-oats biopsies. Moreover, oats ingestion did not alter the number of CD25 positive and tryptase positive cells.

The Canadian Celiac Association, in consultation with Health Canada, Agriculture & Agri-Food Canada and the Canadian Food Inspection Agency, had established requirements for growing, processing, and purity testing and labelling of pure oats (Rashid et al. 2007). These strategies had led to the production of pure, uncontaminated oats for the first time in Canada. Oats and oat products that are safe for consumption by individuals with celiac disease and dermatitis herpetiformis are now commercially available in Canada. For adults, up to 70 g (1/2–3/4 cup) of oats per day and for children, up to 25 g (1/4 cup) per day are safe to consume. These oats and oat products must fulfill the standards for a gluten-free diet set by the Canadian Food Inspection Agency and Health Canada. Some evidence had, however, emerged in the past few years that a small number of gluten-sensitive patients displayed a specific small intestinal T cell response to oat peptides that could not be explained by contamination with other cereals (Ellis and Ciclitira 2008). Oats could form a potentially useful part of a gluten-free diet, but patients require careful advice and monitoring, backed by robust gluten-assay techniques. Pulido et al. (2009) also reported that some evidence suggested that a small number of individuals with celiac disease may be intolerant to pure oats and some evidence from in-vitro studies suggested that an immunological response to oat avenins could occur in the absence of clinical manifestations of celiac disease as well as suggesting that oat cultivars may vary in toxicity. Despite the limitations, Health Canada and the Canadian Celiac Association (CCA) concluded that the majority of people with celiac disease could tolerate moderate amounts of pure oats. They added that incorporation of oats into a gluten-free diet could provide high fibre and vitamin B content, increased palatability, and beneficial effects on cardiovascular health. However, they recommended that individuals with celiac disease should have both initial and long-term assessments by a health professional when introducing pure oats into a gluten-free diet. Fric et al. (2011) reported that some clinical and experimental studies supported the view that a subgroup of celiac patients may be intolerant to pure oats. They proposed that in order to produce oats that are safe for all celiac patients, the following topics should be addressed: selection of oat cultivars with low avenin content, research on such recombinant varieties of oats, development of assay methods to detect avenins in oat products, guidelines for the agricultural processing of oats and the manufacture of oat products, as well as guidelines for following up with celiac patients who consume oats.

Comino et al. (2011) found that in patients with celiac disease, monoclonal antibodies (moAbs) against the main immunotoxic 33-mer peptide (A1 and G12) reacted strongly against wheat, barley and rye but showed less reactivity against oats. Results of their study showed that the reactivity of the moAb G12 was proportional to the potential immunotoxicity of the cereal cultivar. These differences may explain the different clinical responses observed in patients suffering from celiac disease and provide a means to identify immunologically safe oat cultivars, which could be used to enrich a gluten-free diet.

Traditional Medicinal Uses

Oats are cultivated chiefly for food and has been used in traditional medicine for various ailments (Chevallier 1996; Grieve 1971; Duke 1983; Chiej

1984; Bown 1995). Oats are nutritious, antispasmodic, diuretic, emollient, nervine, demulcent, refrigerant, stimulant and tonic. Oats have been taken to restore vigour after debilitating illness. Oat gruel or porridge is useful in inflammatory phlegmons, diarrhoea, dysentery, cough, hoarseness, ulceration of the throat, fevers and after parturition. A tincture of the pulverised grains in alcohol is used as a nervine, uterine tonic and to treat opium addiction. A poultice made from the pulverised grains is used in the treatment of eczema and dry skin or oat decoction strained into a bath has been used to help soothe itchiness and eczema. Oat grains have bee used as a folk remedy for tumour and to lower blood cholesterol levels. Oats are believed to stimulate sufficient nervous energy to help relieve insomnia, multiple sclerosis and chronic neurological pain. In cases of dyspepsia accompanied with acidity of the stomach, oats should be avoided. Oat grass has been used to help balance the menstrual cycle, and as a remedy for dysmenorrhea, osteoporosis and urinary tract infections.

Other Uses

Oat plant provides good forage, hay and silage for animals. Oat forage, hay, straw and grain are renowned horse fodder Oats (crimped or rolled) make up a part of the daily diet of horses, about 20% of daily intake or smaller. Oats are also fed to cattle in the form of whole, rolled or coarse flour. Oats are also employed in some brands of dog food and chicken feed. Oat straw is widly used by cattle and horse owners as bedding material. Sprouted oats are commonly marketed as cat grass to cat lovers. Oat extract is used as ingredient in some cosmetic products for soothing the skin.

Comments

There are about 25 *Avena* species. *Avena* includes several species cultivated as cereal crops (oats) and is also used for fodder and fibre production. A few species have become widespread as weeds of crops in temperate and subtropical areas.

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Coix lachryma-jobi

Scientific Name

***Coix lacryma-jobi* L.**

Synonyms

Coix agrestis Lour., *Coix arundinacea* Lam., *Coix exaltata* Jacq. ex Spreng., *Coix gigantea* J. Jacq. nom. illeg., *Coix lacryma* L. nom. superfl., *Coix lacryma-jobi* var. *maxima* Makino, *Coix lacryma-jobi* var. *novoguineensis* Pilg., *Coix ouwehandii* Koord., *Coix ovata* Stokes nom. superfl., *Coix palustris* Koord., *Coix pendula* Salisb. nom. superfl., *Coix pumila* Roxb., *Coix stigmatosa* K. Koch & Bouché, *Lithagrostis lacryma-jobi* (L.) Gaertn., *Sphaerium lacryma* (L.) Kuntze nom. superfl.

Family

Poaceae

Common/English Names

Adlay, Adlay Millet, Adlay, Coix Millet, Coix Seeds, Gromwell Reed, Indian Beads, Job's Tears, Job's-Tears, Tear Grass.

Vernacular Names

Arabic: Amadrayân, Badrâng, Dam'ayûb, Damu Ayub, Damudad;
Aymara: Mullu;
Belize: Indian Beads;
Brazil: Capim-De-Contas, Capim-De-Nossa-Senhora, Capim-Rosário, Lágrima-De-Nossa-Senhora;
Chamorro: Bilen;
Chinese: Chuan Gu, Chuan Gu Gen, Hui Hui Mi, Ma Yuen, Shan Yi Mi, Ye Yi Mi, Yi Yi Ren (Kernel), Yi Yi Gen (Root) (Mandarin), Yee Yee Yun, Yi Yi Yan, San Yi Mai (Kernal), Yi Yi Gan (Root) (Cantonese);
Chuukese: Fetin Umuno;
Columbia: Lagrimas De San Pedro;
Cook Islands: Poepoe Maori;
Czech: Jobovy Slzy, Slzovka Obecná, Slzovka Porcelánová;
Danish: Jobståre, Jobstårer;
Democratic Republic of Congo: Sapele (Balese), Sapele (Efe), Mashnagu;
Dutch: Jobstranen;
Eastonian: Harilik Pisarhein;
Fijian: Sila;
Finnish: Jobinkyynelheinä;
French: Larmes De Job, Larmilles, Herbe À Chapelets;
German: Hiobsträne, Hiobstränengras, Tränengras;

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Hawaiian: Kūkaekōlea, Pūpū Kōlea, Pü'ohe'ohe;
India: Kaurimani (Assamese), Gurgur (Bengali), Kasai, Kasi (Gujarati), Baru, Dabhir, Ganduta, Garahadua, Gargaridhan, Garun, Gulbigadi, Gurlu, Jorgadi, Kaiya, Kasei, Samkru, Sankhlu (Hindu), Ashru Beeja, Jogimani, Kaage Mani, Kaash, Kalmathu Beeja, Kalmuthu, Kashige Gida, Kothi Beeja, Koti Beeja, Manjutti (Kannada), Sohriu (Khasi), Ran Jamdhlo (Konkani), Catri-Conda, Kakkappalunku, Kattugotampu (Malayalam), Chaning (Manipuri), Kasaayi, Kasai, Len-Camani, Ran Jondhala, Ran Makkai, Ran-Jamdholo, Ranjondhala, ranmakkai (Marathi), Pingpih (Mizoram), Gavedhu, Gavedhuka, Gavedhukah, Gavedu, Gaveduk, Gojihva, Gundraguttha, Jargadi (Sanskrit), Kattu Kundumani, Kattukuntumani, Kokilatcam, Kurattippaci, Nerpul, Punaccippul (Tamil), Adavi Guruginja Gorivindlu, Gorivipusa (Telugu);
Indonesia: Jali, Jali Watu, Japen, Jelen (Javanese), Anjalai, Jelai, Kenjeali, Perara, Senjeali (Sumatra), Hajeli, Hanjeli, Hanjere (Sundanese), Jali Betul, Jelai Batu, Jelai Pulut, Menjelai, Rumput Jelai;
Italian: Erba Da Corone, Lacrima Di Giobbe, Lacrime Di Gesù;
Japanese: Hatomugi, Juzudama;
Khmer: Skuöy;
Korean: Kusulyulmu, Yulmu;
Kwara'ae: Sila;
Laotian: Düay;
Malaysia: Batak, Buah Jali, Jali-Jali, Biji Bali, Jelai, Jali Batu, Jelai Pulut, Jilai, Lanchang, Melai Tiku, Menjelai, Senjelai;
Martinique: Larmes De Job;
Mauritius: Collier Cipaye, Herbe Jobe;
Nepal: Bhirkoulo, Jabe;
Nigeria: Boukon, Bonkori, Ewuruwura;
Niuean: Tagataga, Tangatanga;
Norwegian: Jobståre, Jakobs Tårefrø, Tåregras;
Palauan: Demairuuch, Tauiir;
Panama: Lagrimas De San Pedro;
Peru: Lagrima De Job;
Philippines: Bitongan, Paias (Bagobo), Barubaioko, Bintikai, Koldasan, Tigbi (Bikol), Adlai (Bisaya), Atakai, Tikaian (Bontok), Kalabugau (Bukidnon), Aglai, Damau, Katigbi, Pintaka (Cebu Bisaya), Kibaoung (Ifugao), Abukai, Agagai, Apagi (Ivatan), Agda, Katayan (Igorot), Atakai (Iloko), Balantakan (Pampangan), Alimudias, Lamudias, Paias, Palias (Panay Bisaya), Tidbi (Samar-Leyte-Bisaya), Dalai, Glias, Lias (Subanum), Tiguas (Sulu), Kudlasan, Tigbi (Tagalog), Kambot (Tinggian);
Pohnpeian: Rosario;
Polish: Łzawica Ogrodowa;
Portuguese: Erva Dos Rosaries, Lágrimas De Job, Lágrimas De Nossa Senhora,;
Quechua: Kuymi;
Samoan: Sagasaga, Sagisagi, Sanasana;
Seychelles: Herbe Collier, Herbe Job;
Shaker: Gromwell, False Gromwell;
Sierra Leone: Kali Bugi;
Slovaščina: Jobova Solza;
Spanish: Capin De Nossa, Capin Rosario, Cuenta De La Virgen, Lagrima De San Pedro, Lagrimas De Cristo, Lágrimas De Job, Lágrimas De San Pedro, Santa Juana, Santa Maria;
Swahili: Mtasubihi, Mtasbihi;
Swedish: Jobs Tårar, Job's Tårar;
Tahitian: Poepoe;
Thai: Duai, Maduai;
Tongan: Hana, Hana Tuikahoa;
Turkish: Gözyaşı Otu, Yashé Otu;
Vietnamese: Bo Bo, Cườm Gạo, Hột Bo Bo, Ý Dĩ.

Origin/Distribution

Adlay is native to tropical Asia from India to peninsular Malaysia. The greatest diversity is found in the Malay archipelago. It has been widely introduced elsewhere and has become naturalised throughout the tropics and subtropics about 22°N and S. It has been naturalized in Africa and the southern United States and the New World tropics. The cultivation of *Coix lachrma* var. *ma-yuen* began 3,000–4,000 years ago in India, 2,000 years ago in China. It was a very important crop before maize and rice became widespread staple crops. Secondary centres of diversity developed in the hilly region of S China, and, most recently, in Brazil.

Agroecology

In its native range, adlay is commonly found growing alongside streams, ditches, and water courses in grasslands, perennial crop fields, abandoned fields, along roadsides and on slopes in disturbed mesic forest, from 0 to 2,000 m altitude. The crop thrives in fertile soils with pH of 4.5–8.4, on poor soils the fruits are hollow. It is tolerant of flooding and water-logging but is intolerant of drought. Its flowering is enhanced by short days. Total crop duration is 4–6 (−8) months. When most of the seeds are ripe, the plant starts to dry. Adlay follow the C4-cycle photosynthetic pathway.

Edible Plant Parts and Uses

Adlay grains from soft-sheeld pseudofruits are reported to have a higher protein content than other cereals and do not contain gluten. The grains are generally round, with a groove on one side, and polished white in color, though in Japan unpolished brown grains called *yuuki hatomugi*, is also available. The raw grain tastes sweet and can be eaten as a snack. It is also husked and eaten out of hand like a peanut. The grains are mostly used after drying or after roasting and cooked. The grains are boiled like rice or milled and ground into flour and used for making bread, cakes, pastries and can be substituted for rice in foodstuff. Flour does not contain gluten and is therefore mixed with wheat or other flour for making dough. A good mixture for baking purposes is 70% wheat flour and 30% Adlay flour. The grains are eaten whole in soups or ground into flour and eaten as porridge or broths. The grains and flour are readily digestible and furnish good food for convalescents. The pounded grains are also made into a sweet dish by frying and coating with sugar. The kernels are also used for making starch and for extracting oil.

In southern Vietnam, a sweet, cold soup called *sâm bổ lượng* has adlay grains as one of its ingredients. This dish is similar to the southern Chinese *tong sui* called *qīng bǔ liáng*. In China, a thick drink called *yì mí shǔi* is prepared by simmering whole polished adlay grains and sweetening with sugar. A similar drink called yulma cha is made from powdered adlay grains in South Korea. The Japanese adlay variety “Ma-yeun” is brewed into tea and roasted seeds are made into a coffee-like drink. Adlay grains are also fermented and distilled into alcoholic beverages, beer, wine and vinegar. In both Korea and China, distilled liquors are made from the grain. The South Korean liquor *okroju* is made from rice and adlay grains. In Japan, aged vinegar is made from the grain. A beer made from the pounded fermented grain is popular among Indian Naga hill tribes called *zhu* or *dhu* and in the Philippines.

Botany

Robust, erect, perennial, strongly tillering grass (Plate 1), 1–2 m tall with short rhizomes, freely branching in the upper part, often cultivated as an annual. Leaves green, alternate, simple and entire, 10–100 cm long by 2–7 cm wide, broadly lanceolate, glabrous and coarse, apex acute, base subcordate, margins rough, scabrid, mid-rib prominent (Plates 1, 2 and 3); leaf sheath terete, short, glabrous with long hairs at apex, ligule short and membranous. Inflorescences in axils of upper leaves, solitary or 2–7-fascicled and arranged panicle-like, on 3–6 cm long peduncle, consisting of separate pistillate and staminate racemes. Pistillate raceme enclosed by a hollow, bony, globular to ovoid-ellipsoid cupule 5–15 mm long, shiny, green, white, pale brown, grey, bluish or black, with a sessile spikelet accompanied by two barren pedicels (Plates 4 and 5). Staminate raceme 3–5 cm long, exserted from the mouth of the cupule (Plate 4), with about ten spikelets borne in pairs or threes, one pedicelled, the other(s) sessile. Female spikelet two-flowered, with orbicular glumes, lower floret reduced to an

Plate 1 Erect, robust clumping habit with long-peduncled, axillary inflorescence heads

Plate 3 Leaf with stem clasping base

Plate 2 Long, broadly linear-lanceolate leaves

Plate 4 Green ovoid cupule bearing the female flowers with male flowers emerging from an opening at the tope of the cupule

Plate 5 Green (immature) and black cupules

Plate 6 White, bluish-gray, yellow, brown, reddish-brown and black bead-like false fruits

orbicular lemma, upper floret with membranous lemma and palea and superior ovary with two stigmas exserted from the mouth of the cupule. Male spikelet lanceolate to ellipsoid, 7–8 mm long, 1–2-flowered, lower glume winged, upper glume boat-shaped, each floret with membranous

Plate 7 Polished adlay grains (caryopsis)

lemma and palea and three stamens. Fruit a caryopsis (grain) enclosed by the cupule (shell of false fruit), broadly ellipsoid to subglobose, dark red or black in hard-shelled types, pale brown in soft-shelled types (Plates 5 and 6). Polish grains are white to whitish-blue (Plate 7).

Nutritive/Medicinal Properties

Whole grain of *Coix lachryma-jobi* was found to contain per 100 g edible portion: water 8.9 g, energy 1,394 kJ (333 kcal) protein 10.4 g, fat 5.3 g, carbohydrate 66.5 g and fibre 10.5 g. The hulled grain was found to contain per 100 g edible portion: water 11.6 g, energy 1,511 kJ (361 kcal), protein 14.8 g, fat 4.9 g, carbohydrate 66.9 g, fibre 0.5 g, Ca 47 mg, P 254 mg, Fe 6.0 mg, β-carotene 0 mg, thiamin 0.26 mg, riboflavin 0.19 mg and niacin 4.7 mg (Leung et al. 1968). The content of essential amino acids per 100 g protein (16 g N) was: tryptophan 0.5 g, lysine 1.9 g, methionine 2.6 g, phenylalanine 4.9 g, threonine 3.0 g, valine 5.7 g, leucine 13.6 g and isoleucine 3.9 g (Busson 1965).

The endosperm of adlay seed was found to contain ca. 20% protein distributed between fraction 1 (albumins and globulins), fraction 2 (prolamins), and fraction 3 (residual proteins) extracts (Ottoboni et al. 1990). The major component was found to be prolamin, known as coixin, the amount of which ranged from 8.4 to 78.7% of the total endosperm protein. coixin into five components with molecular weights of 27 K (C1), 25 K (C2), 22 K (C3), 17.5 K (C4), and

15 K (C5). The predominant fraction, coixin, was rich in proline and leucine and poor in lysine. In subsequent studies they grouped coixins, the coixprolamins, into two distinct classes namely α-coixin and γ-coixin (Targon et al. 1992). Alpha-coixins were constituted by four size classes, while γ-coixins comprised only one molecular weight class. α-coixins were found to be synthesized in the endosperm at earlier seed developmental stages than γ-coixin. Protein bodies isolated from immature endosperm contained all coixin components. The protein bodies were localized in the starchy endosperm cells filling the spaces left by the starch granules.

Ten seed storage proteins in the prolamin family, including 8 α-coixin isoforms, 1 δ-coixin, and 1 γ-coixin, were identified in adlay grains (Lin et al. 2009). All ten coixins were found to be rich in glutamine (>20% in α-coixin isoforms, 13.3% in δ-coixin, and 31.2% in γ-coixin). The eight α-coixin isoforms were low in methionine, cysteine, and lysine (on average, 0.8, 0.6, and 0.1%, respectively). However, the δ-coixin was found to be a sulfur-rich protein (18.2% methionine and 9.1% cysteine), and the γ-coixin, a nutritive protein was composed of 2.0% methionine, 6.6% cysteine, 2.6% lysine, and 8.9% histidine. The presence of δ-coixin and γ-coixin with α-coixin isoforms was found to enhance the nutritional value of alday grain for human consumption.

Oil bodies were observed in cells of both embryo and aleurone layers of mature adlay grains (Lu et al. 2010). The contents stored in the adlay oil bodies comprised mainly neutral lipids (>90% triacylglycerols and about 5% diacylglycerols). Two oleosin isoforms (termed oleosin-H and oleosin-L) and one caleosin were present in the adlay oil bodies.

Nonstarch polysaccharides were not found in the water extract but were present in the alkali extract of adlay seeds, dark and white husk types (Apirattananusorn et al. 2008). The major components of the alkali extract from both Job's tears were protein, ash, and nonstarch polysaccharides, mainly arabinoxylans. The average molecular weight (MW) of arabinoxylans of the dark and white husk types were 741,000 Da (Pd 1.5) and 1,449,000 Da (Pd 2.6), respectively. The alkali extractable arabinoxylans were elucidated to have a (1,4)-linked β-D-xylan main chain highly substituted with single arabinose units. The results showed that the alpha- l-arabinofuranosyl residues (Ara f) were attached to the main chain mostly at O-3, followed by both O-2 and O-3 of xylopyranosyl residues (Xyl p).

Two lignans, three phenyl propanoids and 4-hydroxybenzaldehyde were isolated from the fruits of *Coix lacryma-jobi* (Katakawa et al. 2000). Their structures were elucidated be 4-ketopinoresinol (1), 1-C-(4-hydroxyphenyl)-glycerol (2), 1,2-bis-(4-hydroxy-3-methoxyphenyl)-1,3-propanediol (3), dehydrodiconiferyl alcohol (4), 4-hydroxycinnamic acid (5), and 4-hydroxybenzaldehyde.

Analogs of 2(3)-benzoxazolinone, 6-methoxy-2(3)-benzoxazolinone and 6,7-dimethoxy-2(3)-benzoxazolinone were found in the leaves of Job's tears (Tang et al. 1975).

The following benzoxazinones, 2-*O*-β-D-glucopyranosyl-7-methoxy-1,4(2 H)-benzoxazin-3-one and three congeners isolated from *Coix lachryma-jobi* var. *ma-yuen* (Nagao et al. 1985). The coixol content of *Coix lachryma-jobi* var. *mayuen* Dongbuk variety was determined as 0.846 mg/g (Choi et al. 1999). Coixol (6-methoxybenzoxazolone) was found in the root (16.1235 mg/g) leaf (10.626 mg/g) and root (5.666 mg/g) of *Coix lacryma-jobi* L.var. *mayuen* (Li et al. 2009). The contents of coixol in different parts of *Coix lacryma-jobi*. var. *ma-yuen* were as follows: root > testa > stem (Zhang et al. 2010). Four phenolic compounds and adenosine were isolated from the roots of *Coix lachryma-jobi* var. *ma-yuen* (Otsuka et al. 1989). The structures of three were determined to be 4-ketopinoresinol, and threo-1-C-syringylglycerol and erythro-1-C-syringylglycerol. The aglycone moiety of a new glucoside, 2,6-dimethoxy-*p*-hydroquinone 1-*O*-β-D-glucopyranoside, was also determined.

Antioxidant Activity

The 1-butanol-soluble fraction of adlay hulls exhibited greater capacity to scavenge 2,2′-diphenyl-1-picrylhydrazyl (DPPH) radicals when compared

with fractions soluble in water, ethyl acetate, and hexane phases (Kuo et al. 2002). Six compounds showing strong antioxidant activity in the butanol fraction were identified to be coniferyl alcohol (1), syringic acid (2), ferulic acid (3), syringaresinol (4), 4-ketopinoresinol (5), and a new lignan, mayuenolide (6). Studies showed that the following fractions of the ethanol extract of adlay testa namely ethyl acetate, ethyl acetate subfraction e, n-butanol, n-butanol subfraction c exhibited antiradical, antioxidative, and antiinflammatory activities with respect to the DPPH-scavenging capacity, LDL protection effect, and nitric oxide (NO) inhibitory activity (Huang et al. 2009b). All the listed fractions and subfractions modulated inflammation by downregulating the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) proteins. The following components detected in the ethyl acetate subfraction e and n-butanol subfraction c: chlorogenic acid, vanillic acid, caffeic acid, *p*-coumaric acid, ferulic acid and 2-*O*-β-glucopyranosyl-7-methoxy-4(2 H)-benzoxazin-3-one were found to be responsible for the antioxidant and antiinflammatory activities.

Anticancer Activity

Coix lachryma-jobi seed was found to have anitumour activity as assayed by an in-vivo growth inhibition test on a transplantable mouse tumour (Numata et al. 1994). Antitumour activity, was attributed to an acidic fraction which was composed of four free fatty acids: palmitic, stearic, oleic, and linoleic acids. Huang et al. (2002) reported that interventional therapy using a combination of *C. lachryma-jobi* seeds and lipiodol inhibited the growth of liver cancer tumours in hepatoma-bearing rats similar to that of mitomycin/lipiodol treatment. Tumour growth rate was reduced to 3.36% and the tumour inhibition rate was 85.03%. The combined treatment prolonged the survival period of hepatoma-bearing rats and this effect was better than that of single lipiodol, single *C. lachryma-jobi* seeds or mitomycin/lipiodol treatments.

Separate studies showed that a methanolic extract of adlay seed, but not the aqueous extract, exerted antiproliferative effect dose-dependently on human A549 lung cancer cells by inducing cell cycle arrest and apoptosis (Chang et al. 2003). In-vivo studies showed that prefeeding mice with diet containing 30% of powdered adlay seed for 8 months prior to feeding with the tobacco-specific carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-drinking water reduced the number of surface lung tumors by approximately 50% these results indicate that the components of adlay seed exert an anticancer effect in-vitro and in-vivo and may be useful for the prevention of lung tumorigenesis. The methanolic extract of adlay seed inhibited basal and TPA (12-*O*-tetradecanoylphorbol-13-acetate)-induced COX-2 expression of human lung cancer cells in a dose-dependent fashion, whereas COX-1 expression was not affected (Hung and Chang 2003). Further it was demonstrated that treatment of the methanolic extract reduced the PGE(2) level in serum and inhibited COX-2 expression of tumor tissues in nude mice. The overall results suggested that inhibition of COX-2 was one of the mechanisms by which the methanolic extract of adlay seed inhibited cancer growth and prevented lung tumorigenesis. Kanglaite injection was found to inhibit cyclooxygenase 2 activity in lung carcinoma A549 cells (Dong et al. 2005).

The ethyl acetate-soluble fraction of methanol extracts of adlay bran exhibited a stronger antiproliferative effect on human lung cancer cell A549, human colorectal carcinoma cell HT-29, and COLO 205 than other fractions (Lee et al. 2008). Five active lactams coixspirolactam A, coixspirolactam B, coixspirolactam C, coixlactam and methyl dioxindole-3-acetate were isolated from adlay bran. All the compounds showed anticancer activities against human lung cancer cell A549, HT-29 and COLO 205 cells with IC_{50} values between 28.6 and 72.6 μg/mL. Studies showed that Coix seed extract significantly and dose-dependently inhibited on fatty acid synthase activity and two active sites inhibited were β-ketoacyl reductases and enoyl reductase (Yu et al. 2008a). Further in-vivo experiments showed that Coix seed extract inhibited fatty acid synthase activity in the liver, and elevated lipid protein lipase hepatic lipase activity in the plasma,

and effected glucose-6-phosphate dehydrogenase activity. The study supported the premise of fatty acid synthase to be a novel target for anticancer activity, and provided a theoretical foundation for the wide application of Coix seed extract in traditional medicine.

Dietary dehulled adlay after 5 weeks of feeding at levels of 10, 20, or 40% significantly reduced the numbers of aberrant crypt foci (ACF) and aberrant crypts in male F344 rats injected with the carcinogen, azoxymethane (Shih et al. 2004). Dehulled adlay reduced the number of ACF of different sizes but did not affect the crypt multiplicity. Most ACF were found in the middle and distal colons; dehulled adlay significantly suppressed the formation of ACF in the middle colon. However, in a long-term experiment (52 weeks), dehulled adlay did not inhibit colon tumors in spite of a slight suppressing effect in the proximal colon. Rats fed diets containing 20% dehulled adlay had less COX-2 protein expression in both proximal and distal colon tumors. The inconsistent effects between COX-2 protein expression and tumor outcome may be due to regional differences in the colon and the malignancy of the tumors. These findings suggested that dehulled adlay suppressed early events in colon carcinogenesis but not the formation of tumours. Another study showed that adlay bran ethanolic extract suppressed dimethylhydrazin-induced preneoplastic lesions of the colon in F344 rats (Chung et al. 2010). Cyclooxygenase-2 (COX-2) protein expression was significantly suppressed in all colons receiving the extract, indicating that adlay bran extract delayed carcinogenesis by suppressing chronic inflammation. The extract comprised a considerable proportion of phenolic compounds, with ferulic acid as the major phenolic acid (5,206 μg/g extract). Adlay bran and its ethanolic extract and residue were found to dose-dependently and significantly reduce the number of preneoplastic aberrant crypt foci (ACF) and modified their mucin composition in chemically induced colon carcinogenesis in rats (Li et al. 2011). Adlay bran and its ethanolic extract suppressed small ACF (one, two or three crypts) and ACF in the distal colon, while the residue suppressed large ACF (four or more crypts).

The neutral lipid isolated from the endosperm of Job's tears was found to inhibit the growth of PaTu-8988 and SW1990 human pancreatic cancer cells via induction of apoptosis and cell cycle arrest as well as regulation of gene expression in-vitro (Bao et al. 2005).

Coix lachryma jobi var. *ma-yuan* was found to induce apoptosis of jurkat cell line in acute T lymphoblast leukemia (Yao et al. 2009). It inhibited the proliferation of Jurkat cells, and induced chromatin condensation and fragmentation (characteristic of apoptosis) and loss of mitochondrial membrane potential.

An intravenous emulsion (BCOE) formulated with 10% (w/v) *Brucea javanica* oil and *Coix* seed oil in the ratio of 3:1, lipid E 80, 0.3% (w/v) pluronic F-68 (F-68), 0.1% (w/v) sodium oleate and 2.5% (w/v) glycerin in water, was compared for in-vivo antitumour activity with *Brucea javanica* oil emulsion alone and Coix seed emulsion alone in S180 sarcoma-bearing mice (Yu et al. 2008a). BCOE was found to be more effective than the individual emulsions and also reduced the toxicity of the individual emulsions.

Coix lachryma-jobi seed extract emulsion significantly inhibited growth of MDA-MB-231 breast cancer cells (Woo et al. 2007). The extract downregulated expressions of COX-2 and matrixmetalloproteinases, genes considered to be important in neoplasia. The specific gene expression changes observed after Coix seed extract treatment were characteristic of inhibition of NFkappaB-dependent transcription. Coix extract also inhibited activity of protein kinase C, a major mediator of signal transduction and activator of NFkappaB. Two new lactams, coixspirolactam D (1) and coixspirolactam E (2), and a new spiroenone, coixspiroenone (3), together with seven known compounds, coixspirolactam A (4), coixspirolactam B (5), coixspirolactam C (6), coixlactam (7), coixol (8), ethyl dioxindole-3-acetate (9), and isoindol-1-one (10), and two neolignans, zhepiresionol (11) and ficusal (12), were isolated from the bioactive subfraction of adlay bran ethanolic extract (Chung et al. 2011b). All of the isolated compounds exhibited antiproliferative effects on breast cancer MCF-7, MDA-MB-231, and T-47D cells. Compounds

1, 3, 4, 6, and 7 at 50 μM significantly inhibited MCF-7 cell proliferation by 30.2, 19.2, 21.0, 13.5, and 32.4%, respectively; compounds 2, 4, and 7 significantly inhibited T-47D cells at 50 μM by 20.7, 24.8, and 28.9%; and compounds 1, 2, and 12 significantly inhibited MDA-MB-231 cells at 50 μM by 47.4, 25.3, and 69.3%, respectively.

Lu et al. (2008) reported that the FDA (food and drug administration) of United States had approved a phase II trial of Kanglaite to test its efficacy in treating non-small-cell lung cancer. Some studies had shown it could inhibit some anti-apoptotic gene and activate some pro-apoptotic gene, its injection solution is one of the new anticancer medicine that could significantly inhibit various kinds of tumour cells. Kang-Lai-Te extract derived from adlay seeds was found to inhibit human hepatoma carcinoma cell HepG2 growth by inducing apoptosis, which may be mediated through activation of the Fas/FasL pathway (Lu et al. 2009). Adlay seed was found to induce apoptosis in the hepatocellular carcinoma (HCC) cell line HepG2 cells in a concentration- and time-dependent manner, by regulating the expression of caspase-8 (Lu et al. 2011). Based on a meta-analysis of 16 studies conducted on the effectiveness and safety of Kanglaite for treating advanced non-small-cell lung cancer, Zhu et al. (2009) concluded that Kanglaite could enhance clinical effect of regular treatment, reduce side-effect and stabilise/improve quality of life. They asserted that the effect of Kanglaite being used in clinical settings needs to be confirmed by further large, multicentric trials.

Six antimutagenic constituents from adlay hull were identified as *p*-hydroxybenzaldehyde, vanillin, syringaldehyde, *trans*-coniferylaldehyde, sinapaldehyde, and coixol (Chen et al. 2011). Two of them, *trans*-coniferylaldehyde and sinapaldehyde, exhibited relatively potent scavenging of DPPH radicals, inhibited TPA stimulated superoxide anion generation in neutrophil-like leukocytes, and induced Nrf2/ARE-driven luciferase activity in human oral squamous carcinoma HSC-3 cells. Further, *trans*-coniferylaldehyde possessed cytoprotective efficacy against tert-butyl hydroperoxide-induced DNA double-strand breaks in cultured cells and was deemed to be a highly promising agent for cancer chemoprevention meriting further investigation.

Recent studies by Chen et al. (2012a, b) suggested 4-Ketopinoresinol (4-KPR), the (α-γ) double-cyclized type of lignan obtained from adlay to be a novel and more effective Nrf2/ARE-mediated transcription activator than the classical ARE activator tert-butylhydroquinone. It was found to activate the Nrf2/HO-1 axis, and to protect against oxidative stress-induced cell injury via activation of PI3K/AKT signalling pathway. The Nrf2/ARE pathway plays an important role in inducing phase II detoxifying enzymes and antioxidant proteins and has been considered a potential target for cancer chemoprevention because it eliminates harmful reactive oxygen species or reactive intermediates generated from carcinogens.

Gastroprotective Activity

Studies indicated that the ethanol extract of adlay endosperm and bran showed better antiproliferative activity against AGS gastric cancer cell line, and 19 compounds were purified from adlay bran (Chung et al. 2011a). Among the isolated compounds, caffeic and chlorogenic acids significantly suppressed the growth of AGS cells. Dehulled allay extract decreased the ulcer index (UI) and oxidative biomarkers in an indomethacin-induced gastric lesion model and elevated the non-protein sulfhydryl (NPSH) groups. The authors demonstrated that the antioxidative-active phenolic acids in dehulled adlay contributed partly to the gastroprotective effects.

Intestinal Microflora Modulating Activity

Studies showed that rats fed 5, 20, and 40% adlay had normal healthy intestinal walls and no pathogenic signs (Chiang et al. 2000). Both the 20 and 40% groups had lower culture counts of enterics in their feces than the 5% and control groups, whereas the culture counts of fecal lactic acid bacteria were higher in feces of rats fed with adlay

than in the control group. Cecal total short-chain fatty acid (SCFA) content and fecal SCFA were significantly higher in the 20 and 40% groups than in the control and 5% groups. All the adlay-fed rats had a higher fecal butyric acid concentration than the control rats. The authors concluded that adlay had a significant influence on the growth of intestinal bacteria and functions of the gastrointestinal tracts of rats. Recent studies by Wang et al. (2011) showed that hamsters administered *Bacillus*-fermented adlay experienced significantly reduced serum and hepatic total cholesterol (by 37–43% and 42–49% respectively) and triglyceride (by 22–27% and 30–35% respectively) levels compared with the high-cholesterol group. Lower low-density lipoprotein cholesterol/high-density lipoprotein cholesterol ratios in serum and increased cholesterol (by 47–52%) and triglyceride (by 40–47%) contents in faeces were also observed. *Bacillus*-fermented adlay lowered the levels of thiobarbituric acid-reactive substances, thus increasing total antioxidant and superoxide dismutase activities. Further, hamsters fed *Bacillus*-fermented adlay harboured greater populations of lactic acid bacteria, few coliforms and little *Clostridium perfringens*. The results showed that changes in lipid metabolism, antioxidant status and intestinal microflora can be greatly modulated by *Bacillus*-fermented adlay, suggesting potential novel approaches to the treatment of primary cardiovascular and intestinal diseases

Metabolic Syndrome Ameliorating Activity

Studies showed that the ethyl acetate fraction of an ethanol extract of *Coix lachryma-jobi* could be effective in ameliorating symptoms of metabolic syndrome (Do et al. 2010). The fraction exhibited a dose-dependent stimulation of glucose uptake in 3 T3-L1 cells and elicted a decrease in the expression levels of adipogenesis factors such as fatty acid synthase, sterol-regulatory-element-binding protein-1c, peroxisome proliferator-activated receptor γ, and CAATT/enhancer binding protein α in a dose-dependent manner. Further the fraction phosphorylated AMP-activated protein kinase (AMPK) and its downstream substrate acetyl-coenzymeA carboxylase in 3 T3-L1 cells in a time- and dose-dependent manner.

Antiosteoprosis Activity

Studies showed that adlay was capable of reversing the osteoporotic status in rats, and may be a helpful healthy food for osteoporosis prevention (Yang et al. 2008). Treatment with adlay seed water extract could reverse the decreased alkaline phosphatase activities and calcium levels and increased tartrate-resistant acidic phosphatase activities induced by parathyroid hormone in cultured metaphyseal tissues. In ovariectomized rats, the alkaline phosphatase activities and calcium levels were significantly decreased and tartrate-resistant acidic phosphatase activities were increased in femoral metaphyseal tissues as compared with sham-control. Treatment with water extract of adlay seed could counteract these effects in ovariectomized rats.

Antiobesity Activity

Adlay seeds were found to have hypolipidemic activity. Studies showed that 8 weeks treatment of adlay crude seed extract reduced expressions of leptin and TNF-alpha mRNA and reduced body weights, food intake, epididymal and peritoneal fat, white adipose tissue mass and serum hyperlipidemia (triglyceride, total-cholesterol) in obese rat fed induced by high fat diet (Kim et al. 2004). Studies in rats showed that adlay seed water extract exerted anti-obesity effects by modulating neuroendocrine activity in the brain (Kim et al. 2007). The results showed that the optical density of neuropeptid Y immunoreactivity in paraventricular nucleus of rats was 2.6 fold lower than high fat diet group. A similar trend was observed for leptin receptor mRNA expression.

Studies showed that rats fed a diet containing adlay oil showed a significant decrease in adipose tissue weight and relative adipose weight (Huang et al. 2005). Further, rats fed the adlay oil exhibited

significantly decreased low-density lipoprotein cholesterol (LDL-C), insulin, leptin and thiobarbituric acid reactive substance (TBARS) concentrations after 4 weeks of feeding. Although a significant decrease in total plasma cholesterol was observed in rats fed the 5% adlay oil diet, no significant difference was observed between the 10% adlay oil and control groups. All the three varieties of adlay namely Sang-Gang, Jo-Hyun and Yulmu-Ilho showed significant inhibitory activity on adipocyte 3 T3-L1 differentiation in-vitro (Lee et al. 2010). Adlay, however, showed little effects on adipocyte proliferation. Further studies with interval treatment demonstrated that adlay exerted inhibitory activity on adipocyte differentiation at the early stage of adipogenesis. The results suggested that adlay might be useful in the prevention of obesity.

Antiglomerulonephritic Activity

Kanglaite (aqueous microemulsion of an oil extracted from *C. lachryma-jobi* seeds) injection (KLT) inhibited proliferation and telomerase activity of mesangial cells with or without pre-stimulation with IL-1 (Hu et al. 2005). The results suggested KLT might be useful in the prevention and treatment of glomerular nephritis related to mesangial cell proliferation.

Hypolipidemic Activity

Studies in rats suggested the possibilities that coix-lard diet may have an inhibitory action on cholesterol synthesis in liver, a facilitating effect on biliary excretion of triglyceride, and an acceleratory action on phospholipid synthesis in liver (Park et al. 1988). Results of studies suggested that dehulled adlay exhibited not only a hypolipidemic effect but also displayed a hypoglycemic ability in diabetic rats, indicating that dehulled adlay may play an important role in the regulation of plasma lipid and glucose metabolisms in diabetic rats induced by streptozotocin (Yeh et al. 2006). Streptozotocin-induced diabetic rats fed a dehulled adlay diet exhibited a greater adipose tissue weight and a reduced food intake when compared with animals fed a cornstarch diet. Significantly decreased plasma glucose, total cholesterol and triglyceride levels were observed in rats fed the dehulled adlay diet. Further, the ingestion of dehulled adlay appeared to significantly decrease plasma low-density lipoprotein (LDL) plus very low-density lipoprotein (VLDL) cholesterol concentrations. Rats fed a dehulled adlay diet showed an increase in fecal weight and cholesterol contents of stools. Although a significantly decreased plasma thiobarbituric reactive substances (TBARS) value was observed in diabetic rats fed the dehulled adlay diet, no significant difference in the hepatic TBARS value was observed between the two dietary groups. Recent studies showed that adlay seed oil could reduce the abdominal fat tissue and low-density lipoprotein concentration, and increase the total antioxidant capacity in hyperlipidemic rats (Yu et al. 2011). Adlay seed oil also significantly decreased the malondialdehyde content in serum, and increased serum total superoxide dismutase activity in hyperlipidemic rats.

Antidysmenorrhea Activity

Studies showed that the ethyl acetate fraction of adlay hull methanol extract and its subfractions (175 μg/mL) inhibited uterine contractions induced by PGF(2alpha), the Ca^{2+} channel activator Bay K 8644, and high K^{+} in a concentration-dependent manner in-vitro (Hsia et al. 2008). The fraction also inhibited PGF(2alpha)-induced uterine contractions in vivo; furthermore, 375 μg/mL of the ethyl acetate inhibited the Ca^{2+}-dependent uterine contractions. They also demonstrated that naringenin and quercetin were the major pure chemical components of the they acetate fraction that inhibit PGF(2alpha)-induced uterine contractions. They postulated that the ethyl acetate fraction inhibited uterine contraction by blocking external Ca^{2+} influx, leading to a decrease in intracellular Ca^{2+} concentration indicating that adlay hull may be considered as a feasible alternative therapeutic agent for dysmenorrhea.

Antidiabetic Activity

Fractionation of the water extract of adlay seeds, led to isolation of three glycans, coixans A, B and C (Takahashi et al. 1986). These glycans elicited remarkable hypoglycemic effects in normal and hyperglycemic mice treated with alloxan. Results of studies by Kim and Cho (2000) susgested that *Coix lachrma-jobi* bran may have beneficial effects on blood lipid and glucose level in normal and diabetic rats. In normal rats, consumption of coix bran remarkably reduced body weight gain in chow or high fat diet fed rats. Additionally, consumption of coix bran reduced blood TG, TC and atherogenic index (26, 24 and 72%, respectively) in chow diet fed rats. Liver TG and cholesterol concentrations were reduced (43 and 49%, respectively) in high fat fed rats. In diabetic rats, fasting blood glucose level was reduced about 25% by coix bran consumption. Also, glucose challenge pattern was improved and resembled normal pattern. Elevated plasma concentrations of TG in diabetic rats and were reduced to normal level by coix bran supplementation. Elevated liver TG and cholesterol concentrations in diabetic rats were also reduced to normal level after consumption of coix bran.

Peroxisome proliferator-activated receptor gamma ligands were isolated from adlay seed (Yokoi et al. 2009). The six hydroxy unsaturated fatty acids isolated were determined as 13-hydroxy-(9E,11E)-octadecadienoic acid (13-E,E-HODE) (1), 9-hydroxy-(10E,12E)-octadecadienoic acid (9-E,E-HODE) (2), 9-hydroxy-(10E)-octadecenoic acid (3), 10-hydroxy-(8E)-octadecenoic acid (4), 8-hydroxy-(9E)-octadecenoic acid (5), 11-hydroxy-(9Z)-octadecenoic acid (6) of the isolated hydroxy unsaturated fatty acids, 9-E,E-HODE (2) exhibited the most potent PPARgamma agonist activity. 9-E,E-HODE (2) and 13-E,E-HODE (1) are the respective geometrical isomers of 9-hydroxy-(10E,12Z)-octadecadienoic acid and 13-hydroxy-(9Z, 11E)-octadecadienoic acid, both of which are likely to be natural PPARgamma agonists produced in various mammalian cells, suggesting that 9-E,E-HODE may also act as PPARgamma agonist. PPAR-gamma agonists have been used in the treatment of dyslipidaemia and hyperglycemia (Li et al. 2008).

Antiinflammatory Activity

Several (7 out of 11) benzoxazinoids isolated from roots of *Coix lachryma-jobi* var. *ma-yuen* showed antiinflammatory activity as evidenced by their inhibition of histamine release from rat mast cells stimulated with concanavalin A (Con A) and sensitized with immunoglobulin E (Otsuka et al. 1988). The results showed the free hydroxyl group at the two-position in the benzoxazinone skeleton to be important for the expression of inhibitory activity. Results of in-vitro studies by Seo et al. (2000) demonstrated that the methanol extract of adlay seeds exhibited antiinflammatory properties which may, in part, involve an inhibition of NO and O^{2-} production by activated macrophages. Three subfractions of the ethyl acetate fraction of the ethanol extract of adlay seed hull were found to have antiinflammatory activities (Huang et al. 2009a). The subfractions counteracted the increased cellular production of nitric oxide and prostaglandin E2 induced by lipopolysaccharide by down-regulating inducible nitric oxide synthase and cyclooxygenase 2 expression. Eriodictyol (1), the ceramide (2S,3S,4R)-2-[(2′R)-2′-hydroxytetracosanoyl-amino]-1,3,4-octadecanetriol (2), and *p*-coumaric acid (3) were found in the subfractions, and the first two compounds appeared to be primarily responsible for the antiinflammatory activity.

Ethanolic extract of adlay testa was found to have inhibitory effect on allergic response via the ERK signaling transduction in the rat basophilic leukemia (RBL)-2 H3 cells (Chen et al. 2010). The 20–80% ethyl acetate/hexane subfractions of the ethanol extract significantly inhibited histamine release with a IC_{50} of 75–100 μg/mL. In addition, the ethanol extract subfractions suppressed interleukin (IL)-4, IL-6, and tumour necrosis factor-alpha secretion in RBL-2 H3 cells, indicating that adlay testa were able to inhibit cytokine secretion. Two major active compounds, 4-hydroxyacetophenone and *p*-coumaric acid, were isolated from the ethanol adlay testa extract subfractions.

Anti-photoaging Activity

Recent studies by Shan et al. (2012) demonstrated that Kanglaite inhibited UVB-induced aquaporin-3 down-regulation of cultured human skin keratinocytes and to have potential as an anti-photoaging agent. One major characteristic of photoaging is the dehydration of the skin and the process involves membrane-inserted water channels (aquaporins). Kanglaite, a mixture consisting of extracts from adlay seeds had been reported to be an effective anti-neoplastic agent and to inhibit the activities of protein kinase C and NF-κB.

Antiviral Activity

Results of studies in healthy volunteers who ingested six tablets of Coix seeds three times a day (a typical dose) for 4 weeks indicated that Coix seeds increased peripheral cytotoxic lymphocytes and may be effective against viral skin infections through the enhancement of cytotoxic activity (Hidaka et al. 1992; Kaneda et al. 1992). The level of CD3+CD56+ (MHC-non restricted cytotoxic T cells) markedly increased at 4 weeks. The level of CD16+CD57− (the mature, most active natural killer cells) increased at 3 weeks. The level of CD16+CD57+ (the variable active natural killer cells) decreased at 1 week and returned to normal level thereafter. Coix seeds, a Chinese medicine have been used in Japan and reported to be effective in patients with verruca vulgaris and verrucae planae juveniles.

Reproductive Modulating Activity

In the in-vivo endocrine system study, methanolic extracts of adlay hull (AHM) decreased plasma progesterone and estradiol levels after an intravenous injection of AHM (2 mg/mL/kg) (Hsia et al. 2006, 2007). In the in-vitro studies, AHM decreased progesterone and estradiol via inhibition of (i) the cAMP-PKA signal transduction pathway, (ii) cAMP accumulation, (iii) cytochrome P450 side chain cleavage enzyme and 3β-HSD enzyme activities, (iv) protein kinase A, cytochrome P450 side chain cleavage enzyme and steroidogenic acute regulatory protein (StAR) expressions and StAR mRNA expression, and (v) aromatase activity in rat granulosa cells. These results suggest that AHM decreased the production of progesterone via mechanisms involving the inhibition of the cAMP pathway, enzyme activities, and the protein expressions of P450scc and StAR in rat granulosa cells.

Results of studies by Chang et al. (2006) showed that crude adlay hull acetone extract acted directly upon rat adrenal zona fasciculata-reticularis cells to diminish corticosterone release. The data also indicated that the inhibitory mechanism of adlay extract was mediated through an inhibition of the activities of the post-cAMP corticosterone synthesis enzymes, i.e. 3β-HSD, 21-hydroxylase, 11β-hydroxylase, and inhibition of StAR protein expression.

In-vitro studies showed that methanol extracts of adlay hull decreased testosterone release via the inhibition of (1) the PKA and PKC signal transduction pathways, (2) 17β-HSD enzyme activity in the rat Leydig cells (Hsia et al. 2009). The extract also decreased luteinizing hormone secretion induced by gonadotropin-releasing hormone in the rat's anterior pituitary (AP) gland.

Ovulatory Stimulating Activity

Ovulatory-active substances were isolated from adlay plant (Kondo et al. 1988). These compounds were determined as a 9:1 mixture of *trans*-feruloyl stigmastanol and *trans*-feruloyl campestanol (1), and a 9:1 mixture of their geometrical isomers (2). Compound 1 and a synthetic *trans*-feruloyl stigmastanol at 200 μg/day showed induction of ovulation and stimulation of ovarian follicular growth in female golden hamsters.

Drug Metabolising Enzyme Activity

Studies by Yao et al. (2011) found that feeding rats with ethanolic extract of adlay bran may suppress microsomal cytochrome P-450 (CYP)

enzyme activities and cytochrome P-450 (CYP) protein expression in the liver and lungs of rats. Furthermore, rats fed the 10% adlay diet had a higher glutathione content and glutathione peroxidase, glutathione reductase, and glutathione S-transferase activities in the lungs, but such an increase was not noted in the liver.

Antiallergic Activity

Hsu et al. (2003) found that oral administration of dehulled adlay to mice suppressed the production of IgE against ovalbumin (OVA) antigen. Serum anti-OVA IgG(2a) antibody levels were significantly increased in mice after oral administration of dehulled adlay. Further, the production of IL-2 by OVA-stimulated splenocytes was augmented in dehulled adlay-fed mice. Hydrothermal processes, including steaming and extrusion cooking, did not change the capacity of dehulled adlay to suppress IgE production. The methanolic extract of dehulled adlay exhibited the greatest capacity to reduce anti-ovalbumin (OVA) IgE production in mice. The results suggested that dehulled adlay had a modulating ability to shift the balance from Th2 to Th1 dominance in the T cell mediated immune system and may be beneficial for the treatment of allergic disorders. In-vitro studies showed that Adlay bran extract reduced the release of histamines and cytokines and suppressed the production of Akt (Chen et al. 2012a, b). These combined effects influenced the signal transduction in RBL-2 H3 cells, thereby revealing the mechanisms of the anti-allergic effects of adlay. In addition, six phenolic acids and one flavone were isolated. Of these compounds, luteolin showed the most potent inhibitory activity ($IC_{50} = 1.5$ μg/mL).

Acetylcholinesterase Inhibitory Activity

An antidementia acetylcholinesterase inhibitor isolated from Job's tears, showed high acetylcholinesterase (AChE) inhibitory activity (55.1%) (Seo et al. 2009). The IC_{50} obtained was 0.608 μg. The partial purified AChE inhibitor was soluble in methanol and hexane, and insoluble in water and was stable in the range of 30 and 70°C and pH 4.0–8.0 for 1 h.

Abortifacient Activity

Tzeng et al. (2005) reported that the water extracts of adlay seeds were capable of inducing embryotoxicity and enhancing uterine contractility during pregnancy. They found that the enhanced activities of protein kinase C-alpha, extracellular signal-regulated protein kinase (ERK) 1/2 phosphorylation, and cyclooxygenase-2 (COX-2) protein expression may contribute to these responses.

Anticonvulsant Activity

Coixol (6-methoxybenzoxazolone) found in *Coix lachryma-jobi* var. *ma-yuen*, when administered at 50–100 mg/kg i.p. decreased locomotor activities of mice and rats and produced hypothermia in rats (Gomita et al. 1981). Coixol was approximately twice as potent as chlorzoxazone in potentiating thiopental-induced sleep. It attenuated the writhing syndrome induced by 1% acetic acid and increased the threshold to jumping response induced by foot shock, to the same degree as seen with chlorzoxazone. Coixol was equipotent to chlorzoxazone in preventing convulsions induced by maximal electro-shock, while it was about 1.5 times more potent than chlorzoxazone in suppressing pentylenetetrazol-induced convulsion. Coixol 20–100 mg/kg inhibited the lever pressing response of hypothalamic self-stimulation in rats. In rats with chronically implanted electrodes, coixol 50–100 mg/kg induced drowsy patterns on the spontaneous EEG. These results indicated that coixol had pharmacological properties qualitatively similar to chlorzoxazone and acted as a central muscle relaxant with an anticonvulsant effect.

Trypsin Inhibitory Activity

A heat stable trypsin inhibitor with molecular weight of 12,000 was found in the bran of soft-shelled job's-tears (*Coix lacrymajobi*. var.

ma-yuen) seeds (Ohtsubo et al. 1985). This inhibitor contained many cysteine or cystine residues in the molecule inhibited bovine trypsin at the molar ratio of 1–2, showing that it was double-headed. Two groups of proteases (A, those with molecular weights of 55–70 kDa; and B, those with molecular weights greater than 94 kDa) and a trypsin inhibitor (JBTI) were found in developing Job'stear seeds (Ohtsubo et al. 1989). Protease A was observed only in the early stage of development (until 9 DAF (days after flowering)), protease B2 persisted during all stages, while proteases B1and B3 were present only during early and late stages, respectively. The group A proteases and one of the group B proteases (probably B1) were inhibited by diisopropyl-fluorophosphate, by trypsin inhibitors from soybean and rice, and by JBTI. The proteases that were present in the seeds of Job's tears at a late stage seemed to be localized in the germ.

Traditional Medicinal Uses

The fruits, seeds, leaves and roots of *Coix lacrima-jobi* have been used as a remedy for many ailments in traditional folkloric medicine (Watt and Breyer-Brandwijk 1962; Hartwell 1971; Burkill 1966; Adjanohoun et al. 1988; Gurib-Fakim et al. 1997; Chifundera 1998; National Institute of Materia Medica 1999; Duke et al. 2002; Jansen 2006; Stuart 2010; Chung et al. 2011a).

The kernels are used in folk therapies for various kinds of tumours such as abdominal, esophageal, gastrointestinal, and lung cancers, as well as excrescences, warts, and whitlows. Adlay is also used as folk medicine for abscess, soothing pain, anthrax, appendicitis, arthritis, beriberi, bronchitis, catarrh, diabetes, dysentery, dysuria, edema, fever, goiter, halitosis, headache, hydrothorax, pleurisy, pneumonia, post-partum, pulmonary tuberculosis, rheumatism, small-pox, splenitis, strangury, tenesmus, and intestinal worms. In Vietnam, the dried kernels are used alone or in combination with other herbal drugs for treating oedema, dysentery, oliguria, arthritis, chronic diarrhoea, lung abscess, acute appendicitis and verruca plana. The kernels are also used as general tonic. The seeds are considered by the Chinese to be nutritious, demulcent, cooling, pectoral and anthelmintic and to be especially useful in urinary affections, probably of the bladder, bronchitis and chest congestion, dyspepsia, low energy, and joint pain. The seeds have long been used to treat warts, chapped skin, rheumatism, and neuralgia in traditional Chinese medicine. A tincture or decoction of the seed is used in Europe for catarrhal affections of the air passages. The decoction of the root of the plant is said to be an excellent anthelmintic. A decoction of the root is given as a vermifuge to children in Peninsular Malaysia and also as a diuretic. In the Philippines, the root decoction is used to cure gonorrhoea. The root is used in India for menstrual disorders and the seeds for urine retion and as general tonic. In Africa, the leaf decoction is administered for headache, rheumatism and diabetes. Sap of the stem is applied against insect bites. A root decoction is employed a vermifuge and to treat dysentery, gonorrhoea and menstrual disorders. In Mauritius, the roots are used with roots of other plants and guava leaves in a decoction for diarrhoea. In Liberia, the sap from the stem is squeezed into the eye to relieve irritation due to injury.

Other Uses

Adlay is a very useful and productive grass increasingly viewed as a potential energy source. The plant is a very palatable green fodder especially for cattle and horses, and is suitable for silage. In India, the leaves are used as fodder for elephants. The shoots and leaves are also used for thatching and as material for paper. The whole inflorescence is sometimes used in dried flower arrangements. Adlay grains are much esteemed as poultry feed. The whole grain and the bran are fed to poultry and the flour can replace maize flour in poultry feed. The fruits are used for making rosaries, jewellery (bead necklaces, earrings, bracelets), seed dolls, bags, trays and strung into curtains and used in musical instruments. In Africa, hollow gourds are covered with a loose net strung with hundreds of Job's tears and when shaken create a sound which is amplified by the hollow gourd.

Comments

Job's Tears is also commonly, but misleadingly sold as Chinese pearl barley in Asian supermarkets in many western countries, despite the fact that *C. lacryma-jobi* is not of the same genus as barley (*Hordeum vulgare*).

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Echinochloa frumentacea

Scientific Name

***Echinochloa frumentacea* Link.**

Synonyms

Echinochloa colona var. *frumentacea* (Roxb.) Ridl., *Echinochloa crus-galli* subsp. *edulis* (Hitchc.) Honda nom. superfl., *Echinochloa crus-galli* var. *edulis* Hitchc. nom. superfl., *Echinochloa crus-galli* var. *frumentacea* (Link) E.G. Camus & A. Camus nom. illeg., *Echinochloa crusgalli* var. *frumentacea* (Link) W.F. Wright, *Echinochloa crus-galli* var. *frumentacea* (Link) Ridley, *Oplismenus frumentaceus* (Link) Kunth, *Panicum crus-galli* var. *edule* (Hitchc.) Makino & Nemoto nom. superfl., *Panicum crus-galli* var. *frumentacea* (Link) Trimen, *Panicum frumentaceum* Roxb. nom. illeg.

Family

Poaceae

Common/English Names

Billion-Dollar Grass, Cockspur Grass, Indian Barnyard Millet, Japanese Millet, Japanese Barnyard Millet, Sanwa Millet, Sawa Millet, Shama Millet, Siberian Millet, White Millet, White Panic, White Panicum.

Vernacular Names

Chinese: Hu Nan Bai Zi, Hu Nan Ji Zi,;
Czech: Ježatka Obilní;
Danish: Bleg Hanespore, Japanhirse;
Dutch: Japanse Gierst;
Eastonian: Söödav Kukehirss;
Finnish: Japaninhirssi;
French: Millet Japonais, Pied De Coq Cultivé;
German: Japanhirse, Japanische Hirse, Schamahirse, Sawahirse, Weizenhirse;
India: Kutki, Sama (Hindu);
Italian: Miglio Giapponese;
Japanese: Hie;
Russian: Ežovnik Chlebnyj;
Spanish: Mijo Japonés;
Swedish: Amerikansk Hönshirs, Blek Hönshirs;
Vietnamese: Cỏ Kê; Cỏ Núc; Cỏ Lồng Vực Hạt.

Origin/Distribution

Its native habitat is unknown and is believed to be in Asia – Himalaya to West Malaysia. It is considered to be a cultivated derivative of *Echinochloa colona* that arose in India and perhaps Africa. It is cultivated as a fodder grass and cereal in tropical Asia, Africa, Australia, western United

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States and Canada and in China- Anhui, Guangxi, Guizhou, Heilongjiang, Henan, Nei Mongol, Ningxia, Sichuan, Yunnan and Taiwan.

Agroecology

Japanese barnyard millet is grown in areas with mean annual temperatures of 25–30°C and annual rainfall regime of 500–750 mm with a summer dominance from sea level to 1,500 m altitude. They are drought tolerant but frost intolerant. They thrives in moist, fertile soils with pH of 4.7–7.4 but is often cultivated on marginal lands where rice and other crops will not grow well.

Edible Plant Parts and Uses

The grain is cooked and used as a millet. The grain can be cooked whole in water, like rice, or boiled with milk and sugar and eaten as porridge or can be ground into a flour. The grains can be fermented to make beer.

Botany

An annual, 1–1.2 m high with robust erect, tufted culms. Leaf sheaths are smooth and glabrous and leaf are linear, soft, 15–40 cm long by 1–2.5 cm wide, glabrous, with wavy margins and without ligules (Plate 1). Panicles 15–20 cm long, erect to slightly drooping at maturity (Plate 1). Spikelets greenish plump, ovate-elliptic to rotund, 2.5–3.5 mm, pubescent to hispid, awnless, mostly 2 or 3 florets together on scabrous pedicels. Lower glume 30–40% of spikelet length, shortly acute, mostly 3-nerved; upper slightly shorter than spikelet, shortly acute, 5–7-nerved. Lower lemma sterile. Fertile lemma ovate to elliptic, 2.5–3 mm long, with a short, herbaceous tip, smooth, shining, obscurely 5-nerved. Caryopsis ovate, about 2.1 mm long, turgid, whitish.

Plate 1 Flowering tufted clump with linear foliage

Nutritive/Medicinal Properties

Total protein in Japanese barnyard millet (*Echinochloa frumentacea*) varieties was found to compose of albumin/globulin, prolamin and glutelin fractions (Monteiro et al. 1988). Total protein of the varieties ranged from 110.5 to 139.3 mg/g of which 11.3–17.2% was albumin/globulins, 6.8–9.3% prolamins, 7.5–11.6% prolamin–like, 5.9–9.1% glutelin-like and 39.3–54.4% true glutelins. Electrophoretic analysis showed that the albumin/globulin fraction contained three or four components; the prolamin and glutelin fractions each had five components. The glutelin fraction had higher molecular weight components than the other two fractions. The proximate composition of Japanese barnyard millet (JBN) millet resembled that of other millets/cereals (Suman et al. 1992). The protein content had a mean value of 36.7 g/kg. Solubility fractionation showed glutelins to be the major

storage protein (60.8%). Contents of phenolics and tannins were estimated and found to be low. The protein digestibility of JBN flours was high (84%). The digestibilities of the different protein fractions varied from 50.9 to 68.4% with pepsin and from 26.6 to 55.8 mg/g with trypsin.

The nutrient composition (%) of barnyard millet on a dry weight basis by Ugare (2008) as: moisture 8.66%, protein 10.52%, fat 3.56%, total carbohydrates 68.76%, total minerals 2.02%, energy 398 kcal, dietary fibre 12.60% (soluble 4.24%, insoluble 8.36%), minerals (mg/100 g) Fe 11.60 mg, Cu 0.55 mg, Zn 1.50 mg, Mg 86.22 mg, Mn 0.66 mg, tannins 62.50 mg, total free phenols 51 mg and phytic acid 96 mg. Among 13 Korean barnyard millet varieties, IT153600 exhibited the highest total protein (14.75%), lipid (6.92%), and amino acids contents (137.10 mg/g) (Kim et al. 2011). For fatty acid composition, the highest linoleic acid (67.6%) content was found in K141285 which also had the highest amylose content. The highest mineral content was found in IT153604. K141285 exhibited good antioxidant effects using DPPH and ABTS. The 80% methanol extract of K141285 showed significantly high total phenolic (38.45) and flavonoid (28.71) contents.

Japanese millet was found to contain prolamins. Polypeptides of prolamins from Italian, common and Japanese millet cultivars appeared to be primarily composed of two major common subunit complexes with respective molecular masses ranging from 19 to 23 kDa and from 13 to 14 kDa (groups A and B, respectively), although a few minor variations due to varietal differences were seen (Takumi et al. 1996). Group A clearly contained one neutral subunit (21 kDa) and one basic one (22 kDa), while group B had one basic 14 kDa subunit.

Polishing can reduce the nutritive value of barnyard millet. At 8% moisture level, barnyard millet was more resistant to polishing and yielded 18.86% of bran after 6 min of milling, while at 14% moisture it was 19.21% (Lohani et al. 2012). The amount of bran removed increased significantly with time of milling. The milling time caused a reduction in the proximate composition. The maximum loss in protein, fat, ash and fibre occurred at 14% moisture content followed by 12, 10 and 8% moisture levels. Protein, fat, ash and fibre were negatively and linearly correlated with degree of polishing.

Gelatinised sample of *Echinochloa frumentacea* (var. K2) showed minimal hydrolysis of starch by porcine pancreatic alpha-amylase (Krishnakumari and Thayumanavan 1995). Gelatinised starch was highly susceptible to enzymic digestion when compared to ungelatinised starch. The extent of starch degradation varied from 71 to 85% in gelatinised samples and starch degradation in ungelatinised sample varied from 10 to 18%.

Eight compounds isolated from Indian barnyard millet were identified as L-malic acid, trans-aconitic acid, (+)-isocitric acid, 5-*O*-caffeoylquinic acid, 4-*O*-caffeoylquinic acid, isocarlinoside, 2″-*O*-rhamnosylisoorientin, and 7-*O*-(2″-*O*-glucuronosyl)glucuronosyltricin (Kim et al. 2008).

Antidiabetic Activity

The glycemic index of unprocessed dehulled grain (50.00) and dehulled, heat treated grain meals (41.71) indicated barnyard millet grain to be categorized under low GI foods (Ugare et al. 2011). The feeding intervention of processed millet for 28 days revealed significant reductions in blood glucose (139.2–131.1 mg/dL), LDL-C (from 167.7 to 162.9 mg/dL), VLDL-C (from 24.0 to 23.2 mg/dL), ratio of TC: HDL (from 4.7 to 4.6) and LDL: HDL (from 3.2 to 3.1) in the experimental diabetic volunteers. Similar, but marginal changes were observed in experimental non diabetics. The millet had 10.5% protein, 3.6% fat, 68.8% carbohydrate and 398 kcal/100 g energy. The total dietary fibre content was high (12.6%) including soluble (4.2%) and insoluble (8.4%) fractions. The study indicated that the dehulled and heat treated barnyard millet is beneficial for type-II diabetics. Studies by Anju and Sarita (2010) showed that the foxtail millet and

barnyard millet flour and biscuits had higher content of crude fibre, total ash and total dietary fibre than refined wheat flour and biscuits. Biscuits from foxtail millet flour had the lowest GI of 50.8 compared to 68 for biscuits from barnyard millet flour and refined wheat flour. Thus, besides its traditional use in making chapatti and porridge, millet can be exploited for the development of low GI therapeutic food products like biscuits.

Antimutagenic Activity

All three plant extracts including Japanese millet (*Echinochloa frumentacea*) extract showed similar antimutagenicity against 3-(5-nitro-2-furyl) acrylic acid (5NFAA) for *Salmonella typhimurium* strain TA100 and no antimutagenicity against 2-nitrofluorene (2NF) for strain TA98 (Mosovská et al. 2010). The number of revertants induced by hydrogen peroxide extract was inhibited in order amaranth > Japanese millet > sorghum. All extracts were effective in the inhibition of mutagenic activity of aflatoxin B(1).

Allergenic Activity

Rice protein 16-kilodalton (RP16KD) was shown to be one of major allergens in rice grain extracts and responsible for cross-allergenicity among the five cereal grains namely rice, wheat, corn, Japanese millet (*Panicum crus-galli* L. var. *frumentaceum* Trin.) and Italian millet (*Setaria italica* Beauv. var. *germanica* Schrad.) examined (Urisu et al. 1991). RP16KD inhibited IgE binding to all these cereal discs in a dose-dependent manner. Similarly, all of the five cereal grain extracts showed an effective decrease in IgE binding to the RP16KD disc.

Traditional Medicinal Uses

The plant is useful in the treatment of biliousness and constipation (Chopra et al. 1986).

Other Uses

This millet is cultivated for forage and grain, also sometimes as a soil stabilizer. It is frequently planted for temporary control of erosion in newly cleared and ploughed sandy soils because they grow rapidly and seed is cheap.

Eight compounds isolated from Indian barnyard millet were identified as L-malic acid, trans-aconiticacid,(+)-isocitricacid,5-*O*-caffeoylquinic acid, 4-*O*-caffeoylquinic acid, isocarlinoside, 2″-*O*-rhamnosylisoorientin, and 7-*O*-(2″-*O*-glucuronosyl)glucuronosyltricin (Kim et al. 2008). These compounds showed high antifeeding activity against brown planthopper, Nilaparvata lugens (Stål) only when they were combined.

Comments

Barnyard millet propagates readily from seeds.

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Hordeum vulgare

Scientific Name

***Hordeum vulgare* L.**

Synonyms

Frumentum hordeum E.H.L. Krause nom. superfl., *Frumentum sativum* E.H.L. Krause, *Hordeum aestivum* R.E. Regel nom. nud., *Hordeum americanum* R.E. Regel nom. nud., *Hordeum bifarium* Roth, *Hordeum brachyatherum* R.E. Regel nom. nud., *Hordeum caspicum* R.E. Regel nom. nud., *Hordeum coeleste* (L.) P. Beauv., *Hordeum daghestanicum* R.E. Regel nom. nud., *Hordeum defectoides* R.E. Regel nom. nud., *Hordeum durum* R.E. Regel nom. nud., *Hordeum elongatum* R.E. Regel nom. nud., *Hordeum gymnodistichum* Duthie, *Hordeum heterostychon* P. Beauv. orth. var., *Hordeum hexastichon* L., *Hordeum hibernaculum* R.E. Regel nom. nud., *Hordeum hibernans* R.E. Regel nom. nud., *Hordeum himalayense* Schult., *Hordeum hirtiusculum* R.E. Regel nom. nud., *Hordeum horsfordianum* R.E. Regel nom. nud., *Hordeum ircutianum* R.E. Regel nom. nud., *Hordeum jarenskianum* R.E. Regel nom. nud., *Hordeum juliae* R.E. Regel nom. nud., *Hordeum kalugense* R.E. Regel nom. nud., *Hordeum karzinianum* R.E. Regel nom. nud., *Hordeum kiarchanum* R.E. Regel nom. nud., *Hordeum laevipaleatum* R.E. Regel nom. nud., *Hordeum lapponicum* R.E. Regel nom. nud., *Hordeum leptostachys* Griff., *Hordeum macrolepis* A. Braun, *Hordeum mandshuricum* R.E. Regel nom. nud., *Hordeum mandshuroides* R.E. Regel nom. nud., *Hordeum michalkowii* R.E. Regel nom. nud., *Hordeum nekludowii* R.E. Regel nom. nud., *Hordeum nigrum* Willd., *Hordeum pamiricum* Vavilov nom. nud., *Hordeum parvum* R.E. Regel nom. nud., *Hordeum pensanum* R.E. Regel nom. nud., *Hordeum polystichon* Haller, *Hordeum polystichon* var. *hackelii* Chiov., *Hordeum polystichon* var. *vulgare* (L.) Döll, *Hordeum praecox* R.E. Regel nom. nud., *Hordeum pyramidatum* R.E. Regel nom. nud., *Hordeum revelatum* (Körn.) A. Schulz, *Hordeum sativum* Jess. nom. superfl., *Hordeum sativum* Pers. pro syn., *Hordeum sativum* subsp. *hexastichon* (L.) K. Richt., *Hordeum sativum* subsp. *vulgare* (L.) K. Richt., *Hordeum sativum* var. *trifurcatum* Schltdl. ex Orlov & Åberg, *Hordeum scabriusculum* R.E. Regel nom. nud., *Hordeum septentrionale* R.E. Regel nom. nud., *Hordeum stassewitschii* R.E. Regel nom. nud., *Hordeum strobelense* Chiov., *Hordeum taganrocense* R.E. Regel nom. nud., *Hordeum tanaiticum* R.E. Regel nom. nud., *Hordeum tetrastichum* Stokes, *Hordeum transcaucasicum* R.E. Regel nom. nud., *Hordeum violaceum* R.E. Regel nom. nud., *Hordeum vulgare* convar. *revelatum* (Körn.) Tzvelev, *Hordeum vulgare* f. *hexastichon* (L.) M. Hiroe *Hordeum vulgare* subsp. *antasiaticum* Bachteev nom. inval., *Hordeum vulgare* subsp. *hexastichon* (L.) Celak., *Hordeum vulgare* subsp. *medioasiaticum* Bachteev, *Hordeum vulgare* subsp. *spontaneum* (K. Koch) Asch. & Graebn., *Hordeum vulgare* subsp. *tetrastichum* (Stokes) Celak., *Hordeum*

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vulgare subvar. *brachyurum* Alef., *Hordeum vulgare* var. *abdulbasirovii* Omarov, *Hordeum vulgare* var. *bachteevii* Omarov, *Hordeum vulgare* var. *brachyurum* (Alef.) Körn., *Hordeum vulgare* var. *chungense* Åberg, *Hordeum vulgare* var. *coeleste* L., *Hordeum vulgare* var. *glabriviride* Trofim, *Hordeum vulgare* var. *hexastichon* (L.) Asch., *Hordeum vulgare* var. *ismailii* Omarov, *Hordeum vulgare* var. *lukyanovae* Omarov, *Hordeum vulgare* var. *lvovii* Omarov, *Hordeum vulgare* var. *multispiculum* Trofim., *Hordeum vulgare* var. *pallidum* Ser., *Hordeum vulgare* var. *patimatae* Omarov, *Hordeum vulgare* var. *revelatum* Körn., *Hordeum vulgare* var. *saidii* Omarov, *Hordeum vulgare* var. *sikangense* Åberg, *Hordeum vulgare* var. *trofimovskajae* Omarov, *Hordeum vulgare* var. *valentinae* Omarov, *Hordeum vulgare* var. *zuleichatae* Omarov, *Hordeum walpersii* R.E. Regel nom. nud., *Secale orientale* Schreb. ex Roth pro syn.

Family

Poaceae

Common/English Names

Barley, Barley Flakes, Barley Grass, Barley Grits, Barleycorn, Common Barley, Cultivated Barley, Four-Rowed Barley, Hooded Barley, Malting Barley, Naked Barley, Pearl Barley, Pot Barley, Scotch Barley, Six-Rowed Barley, Two-Row Barley.

Vernacular Names

Amharic: Gebs;
Arabic: Sha' Îr;
Brazil: Cevada;
Chinese: Da Mai, Mai Ya;
Czech: Ječmen Obecný, Ječmen Víceřadý;
Danish: Almindelig Byg, Byg;
Dutch: Gerst, Gerstegras, Gewone Gerst;
Eastonian: Harilik Oder, Mitmerealine Oder;
Finnish: Monitahoohra, Ohra.
French: Orge, Orge À Quatre Rangs;
German: Gerste, Mehrzeilige Gerste, Saat-Gerste, Sechszeilige Gerste;
Greek: Krthari, Krithe;
Hebrew: Se'orah Tarbutit;
Hungarian: Árpa, Négysoros Árpa, Takarmányárpa;
Icelandic: Bygg;
India: Job (Bengali), Jau (Gujarati), Jau (Hindu), Barli (Kannada), Yavam (Malayalam), Jau (Marathi), Barli Arisi (Tamil), Barli Biyyam (Telugu), Jau (Urdu);
Italian: Orzo, Orzo Coltivato;
Japanese: Õ-Mugi, Oo Mugi;
Korean: Pori, Taemaek;
Malaysia: Barli;
Nepali: Jhao;
Norwegian: Bygg, Seksradsbygg;
Polish: Jęczmień Zwyczajny;
Portuguese: Cevada;
Russian: Iachmen' Obyknovennyi, Iachmen' Posevnoi;
Slovašcina: Ječmen Navadni;
Slovencina: Jačmeň Siaty;
Spanish: Alcacer, Cebada, Cebada Común, Cebada Cultivada, Cebada Cuadrada, Cebada De Cuatro Carreras, Hordio;
Swahili: Shayiri;
Swedish: Korn;
Thai: Bale, Khao Bale;
Turkish: Arpa;
Vietnamese: Lúa Mạch;
Zulu: Ubhali.

Origin/Distribution

Barley was first domesticated about 10,000 years ago from its wild relative, *Hordeum vulgare* ssp. *spontaneum* in the area of the Middle East known as Fertile crescent (Badr et al. 2000). The fertile crescent also called the 'Cradle of civilization' encompasses ancient civilisations of Phoenicia, Assyria and Mesopotamia. *H. vulgare* ssp. *spontaneum* can still be found in both natural and disturbed sites such as abandoned fields and roadsides in the Middle East and adjacent areas

of Egypt. Over the past 100 years, landraces have been mostly displaced in agriculture by pure line varieties with reduced genetic diversity (Nevo 1992). Extensive cultivation, intensive breeding and selection have generated thousands of commercial varieties of barley. For commercial purpose, barley is classified into broad classes used as a basis for world trade. Major factors used to differentiate barley varieties are: feed or malting barley, winter or spring growth habit, starch amylase/pectin ratio, hulled or hulless barley, and six-rowed or two-rowed varieties. Two-rowed barley with non-shattering spikes is classified as *Hordeum distichum* L., six-rowed barley with non-shattering spikes as *H. vulgare* L. (or *H. hexastichum* L.), and six-rowed with shattering spikes as *H. agriocrithon* Åberg.

Today barley is grown in many non-tropical countries and in the montane areas of the tropics. The top dozen barley producing countries in terms of production quantity (tons) in 2010 is as follows: Germany (10,412,100), France (10,102,000), Ukraine (8,484,900), Russian Federation (8,350,020), Spain (8,156,500), Canada (7,605,300), Australia (7,294,000), Turkey (7,240,000), USA (3,924,870), Iran (3,209,590), Argentina (2,983,050) and Denmark (29,813,000) (FAO 2010).

Agroecology

Barley has a wider ecological range than any other cereals and can be grown in a wide range of environments including extremes of latitude and longitude. Cultivated barley is grown in a range of environments from subArtic to sub-tropical with greater concentration in the temperate areas and high altitudes of the subtropics and tropics. Barley is rarely grown in the tropics as it is not suited to warm humid climates (Nevo 1992). Barley has a shorter growing season than wheat or oats and can be grown at higher latitudes.

In general, barley is a cool climate crop and grows best in temperatures of 15–30°C, but it can tolerate annual temperatures of 4.3–30°C and high temperature if humidity is low (Nevo 1992). High temperatures post-anthesis, however, can reduce grain weight and change malting performance (Van gool and Vernon 2006). Barley is not as cold hardy as wheat and is grown as spring crop in temperate areas; it is more susceptible than wheat is to frost at the early seedling stage (Gomez-Macpherson 2001). In areas with comparative mild winters as the Mediterranean and India, it is grown as a winter crop. Barley tolerates annual precipitation of 190–1,760 mm; in Australia barley is grown in wheat production areas receiving 750 to <325 mm annual rainfall (Van gool and Vernon 2006). Compared to other cereals barley is better adapted to drought through water use efficiency, nevertheless drought is an important abiotic stress for barley. Water-logging is also an important constraint production for barley and is the limiting factortor in high rainfall areas (Van gool and Vernon 2006). Like other cereals barley is susceptible to water logging between germination and emergence.

Barley thrives on soils which are too light and coarse-textured or otherwise unsuitable for wheat cultivation; it does best on light or sandy loam soil. Highest grades of barley are grown on fertile, well-drained, deep loamy soils with pH of 7–8. Compared to other cereals barley is particularly sensitive to soil acidity which can be a major constraint to plant growth. Barley is also sensitive to aluminium toxicity which is associated with acid soils and boron toxicity (van Gool and Vernon 2006). Soils lower than pH 6 may induce aluminium toxicity. Barley is most tolerant to soil salinity and alkalinity of all the cereals hence it can be grown in sodic soils. For malting barleys, soils should not contain too much nitrogen.

Edible Plant Parts and Uses

Covered barley is the barley grain with intact inedible hull which must be removed before the grain is suitable for consumption. Hulled barley is covered barley which has been minimally processed with most of the bran, endosperm and germ present and is also regarded as whole grain. Hull-less barley is a type of barley with loose hull and requires minimal processing (cleaning) after it is harvested as most of the bran, endosperm and

germ occur intact. Hull-less barley is also called whole grain and naked barley. Pearled barley is covered barley that has been processed to remove the tough inedible outer hull and then pearled or polished further by an abrasive scouring process. As some of the bran, endosperm and germ may be removed by abrasive processing, pearled barley is not deemed as whole grain. Hulled barley, hull-less barley and pearled barley are available as kernels (berries), flakes, grits (cuts or bits) and flour (ground or meal).

About 85% of the world's barley production is utilised for animal feed, and the remainder used for malt production, food consumption and seed production. The dominance of barley as a traditional food grain has been diminished by wheat, rice and corn in many countries. Nonetheless, barley grain is still an important food crop in the semi-arid regions of Africa (Morocco, Algeria, Libya and Tunisia), Middle East (Saudi Arabia, Iran, Iraq and Syria), highlands of Nepal, Ethiopia and Tibet, Andean countries of South America (Peru and Chile) and in some Asian countries (China, North Korea and Himalaya) (OECD 2004; Akar et al. 2004). For instance, barley is the staple food in Tibet since 5th AD and widely used in soups, stews and bread. *Tsampa*, a Tibetan staple food stuff is made from roasted barley flour mixed with salty Tibetan butter tea. Morocco is the leading consumer of food barley grain which is made into with a diverse array of food, including soups, bread, and couscous (Grando 2005). Barley accounts for over 60% of the food consumed in the highlands of Ethiopia, where it is used in various dishes such as porridge, soups, stews, and flatbread that have deep roots in culture and tradition. Barley is the preferred grain, after teff (*Eragrostis tef*), for making Ethiopian traditional bread called *Injera*. Barley is used in a large range of traditional Arabic, Assyrian, Israelite, Kurdish and Persian cuisines such as *Kashkak*, *kashk*, *murri*, and *cholent* or *hamin*, a traditional Jewish stew. In Yemen, barley grain is consumed in various dishes and local drinks. *Maloog* bread is made from a blend of barley flour and bread wheat flour and *Matany* from barley flour and lentil flour. Nakia is a local Yemeni drink made from boiled barley grains. In Eastern Europe, barley is used in soups and stews. Barley-meal, a wholemeal barley flour, is used in porridge and gruel in Scotland, and also for gruel called *Sawiq* in the Arabic countries. In Scotland, the six-row barley grain is used to make *beremeal*, which is used locally in bread, biscuits, and the traditional beremeal *bannock*. In the Andean countries of Colombia, Ecuador, Peru and Bolivia, barley is the staple food of farmers at altitudes between 2,200 and 4,000 m above sea level. In this region barley is roasted and finely ground into *Machica* or *Pito*; barley rice, coarsely cracked barley, used for soups; and barley flakes, a relatively recent product, are eaten for breakfast. Hull-less barley is preferred, and earns a higher price than regular barley.

Use of barley in human food in developed countries is rather meagre less than 5% of the total production. However, barley is increasing in popularity as a food grain in developed societies and is being used as components of various health food products, flours for bread making, biscuits, desserts, specialty baby food, thickeners, extenders or binders. Interest in Hull-less barley (HB) utilization in the food industry has developed rapidly due to its high β-glucan content, particularly in the waxy cultivars. The soluble dietary fibres β-glucans (from barley, oat, and other cereals) has great potential as important functional ingredients for both cereal and dairy-based food systems as numerous studies have shown them to have beneficial effects on the glycaemic, insulin, and cholesterol responses to foods (Brennan and Cleary 2005). Bread-making with a composite flour (CF) consisting of 60% wheat flour (WF) and 40% hull-less barley flour, increased the total and soluble $(1\rightarrow3,1\rightarrow4)$-β-D-glucan and total arabinoxylan (AX) contents of dough and bread samples, but decreased the specific bread loaf volume (Trogh et al. 2004). Xylanase addition not only markedly improved loaf volume of CF bread, but also increased the soluble AX content of the WF and CF dough and bread samples. The results clearly showed that the combined use of hull-less barley flour and a xylanase active during bread making, led to palatable breads with high total and soluble AX and $(1\rightarrow3,1\rightarrow4)$-β-D-glucan contents. Hull-less barley may also be used for the preparation of food malt with low or high

enzyme activities, and for brewer's and distiller's malts (Bhatty 1999). The zero amylose HB starch has low syneresis or a high freeze-thaw stability suitable for use in frozen foods. Single-modified or double-modified waxy HB starch may replace corn starch in some food applications.

There is appreciable demand for high quality barley for production of *Shochu*, a Japanese distilled alcoholic spirit in Japan. Barley is also made into wine, whisky besides beer. Distilled from green beer, whisky has been made primarily from barley in Ireland. Scotland barley wine is a kind of strong beer from traditional brewing. All Scotch whisky was originally made from malted barley. Single malt Scotch whisky refers to Scotch whiskey made from malted barley and water; single grain Scotch whishky refers to Scotch whiskey made from water, malted barley and whole grains of other malted or unmalted cereals. Barley is also made into non-alcoholic beverages like barley water and barley tea. Barley water is a popular traditional soft drink in Britain. Roasted barley tea is a caffeine-free, roasted-grain-based tisane made from barley, which is popular in Japan, China and Korea. Roasted barley tea is called *mugicha* in Japan, *maicha* or *daimacha* in China and *boricha* in Korea. Roasted barley is also used as a caffeine-free coffee substitute in America and is prepared as espresso coffee substitue called *caffe d'orzo* in Italy.

Among cereal grains, barley represents the most widely and commonly used starch source for brewing beer. Barley is preferred because of its fibrous husk, which is important not only in the sparging stage of brewing (in which water is washed over the mashed barley grains to form the wort) but also as a rich source of amylase enzyme that converts starch into sugars. Both two-row and six-row barleys are used for brewing beer. Two-row barley has a lower enzyme content, less protein, more starch and thinner husk whilst six-row barley has higher enzyme content, more proteins, less starch and thicker husk (Goldammer 2008). European brewers prefer two-row barley a it has a higher starch/husk ratio and its malty flavour. American brewers prefer six-row barley because of the higher levels of diastatic enzymes and proteins which facilatites the conversion of adjunct starches during mashing. The basic essential ingredients for beer are water, starch source such as malted barley that is fermented to produce alcohol, brewer's yeast for fermentation and a flavouring such as hops. The brewing process encompasses malting, milling, mashing, lautering, boiling, fermenting, conditioning, filtering, and packaging. During malting insoluble starch is converted to soluble starch, complex proteins are degraded, nutrients are generated for yeast development and enzymes are developed. Malting comprises three steps: steeping, germination and kilning (drying).

Barley malt can be processed into non-brewing consumer food products, mainly in the form of sweetener extracts. Sweeteners include malt extract (liquid and dry) and malt syrup/sugar (liquid and dry) and diastatic malt flour which are mostly used in the confectionary and baking industries. Barley malt syrup is a dark brown, thick and sticky sweetener with a strong disitinctive flavour produced from sprouted, or malted barley, containing approximately 65% maltose, 30% complex carbohydrate, 3% protein. Consumer food products include malt drinks (milo, horlicks, ovaltine), malt chocolate confectionary (Mars maltesers using malt as sweetener) and various bakery items. Cookies are made from barley flour and malt sugar.

Botany

Annual tufted grass, 60–120 cm tall, with 2–5 tillers and, with 3–9 seminal (primary) and adventitious (nodal) root systems. Stem erect, hairy with solid nodes and 5–7 hollow, cylindrical internodes. Leaves 5–10 borne alternately at the nodes, sheath glabrous enveloping the stem (Plate 1), auricles overlapping and ligules membranaceous, hyaline and ciliolate. Leaf lamina linear-lanceolate, 5–40 cm by 0.5–1.5 cm, scaberulous. Inflorescence terminal cylindrical compressed spike, 5–12 cm long excluding the awns, densely flowered; spikelets sessile, arranged in threes on two sides of a flattened rachis, in two-rowed barley, only the central spiklet is fertile, the lateral spiklets are sterile (Plates 3 and 4), in six-rowed barley all three spikelets are fertile (Plates 1 and 2); glumes 2, narrow, small, short-awned, enclosing three

Plate 1 Six-row barley plant

Plate 2 Close-up six row barley

Plate 3 Two row barley ready for harvest

spikelets; lemma lanceolate, five-ribbed, tapering into a long straight or recurved awn; palea slightly smaller than the lemma with margins inflexed; floret with two lodicules, three stamens and ovary with two feathery stigma. Fruit caryopsis ellipsoid, about 0.9 cm long, short-pointed, grooved on inner face (Plate 5), hairy at the apex, smooth, free or adherent to palea, or both lemma and palea. Each spike may carry 25–60 kernels in six-row barley or 15–30 kernels in two-rowed barley.

Plate 4 Close-up two row barley

Nutritive/Medicinal Properties

Proximate nutrient composition of hulled barley per 100 g edible portion was reported as follows: water 9.44 g, energy 354 kcal (1,481 kJ), protein 12.48 g, total lipid 2.30 g, ash 2.29 g, carbohydrate 73.48 g, total dietary fibre 17.3 g, total sugars 0.80 g, Ca 33 mg, Fe 3.60 mg, Mg 133 mg, P 264 mg, K 452 mg, Na 12 mg, Zn 2.77 mg, Cu 0.498 mg, Mn 1.943 mg, Se 37.7 μg, thiamin 0.646 mg, riboflavin 0.285 mg, niacin 4.604 mg, pantothenic acid 0.282 mg, vitamin B-6 0.318 mg, total folate 19 μg, vitamin A 22 IU, vitamin A 1 μg RAE, vitamin E (α-tocopherol) 0.57 mg, vitamin K (phylloquinone) 2.2 μg, β-carotene 13 μg, lutein + zeaxanthin 160 μg, total saturated

Plate 5 Barley grains

fatty acids 0.482 g, 12:0 (lauric) 0.006 g, 14:0 (myristic) 0.011 g, 16:0 (palmitic) 0.411 g, 18:0 (stearic) 0.017 g, total monounsaturated fatty acids 0.295 g, 16:1 undifferentiated (palmitoleic) 0.006 g, 18:1 undifferentiated (oleic) 0.241 g, total polyunsaturated fatty acids 1.108 g, 18:2 undifferentiated (linoleic) 0.999 g, 18:3 undifferentiated (linolenic) 0.110 g, tryptophan 0.208 g, threonine 0.424 g, isoleucine 0.456 g, leucine 0.848 g, lysine 0.465 g, methionine 0.240 g, cystine 0.276 g, phenylalanine 0.700 g, tyrosine 0.358 g, valine 0.612 g, arginine 0.625 g, histidine 0.281 g, alanine 0.486 g, aspartic acid 0.779 g, glutamic acid 3.261 g, glycine 0.452 g, proline 1.484 g and serine 0.527 g (USDA 2012).

Proximate nutrient composition of raw pearled barley per 100 g edible portion was reported as follows: water 10.04 g, energy 352 kcal (1,473 kJ), protein 9.91 g, total lipid 1.16 g, ash 1.11 g, carbohydrate 77.72 g, total dietary fibre 15.6 g, total sugars 0.80 g, Ca 29 mg, Fe 2.50 mg, Mg 79 mg, P 221 mg, K 280 mg, Na 9 mg, Zn 2.13 mg, Cu 0.420 mg, Mn 1.322 mg, Se 37.7 μg, thiamin 0.191 mg, riboflavin 0.114 mg, niacin 4.604 mg, pantothenic acid 0.282 mg, vitamin B-6 0.260 mg, total folate 23 μg, total choline 37.8 mg, vitamin A 22 IU, vitamin A 1 μg RAE, vitamin E (α-tocopherol) 0.02 mg, vitamin K (phylloquinone) 2.2 μg, β-carotene 13 μg, lutein + zeaxanthin 160 μg, total saturated fatty acids 0.224 g, 12:0 (lauric) 0.003 g, 14:0 (myristic) 0.006 g, 16:0 (palmitic) 0.208 g, 18:0 (stearic) 0.008 g, total monounsaturated fatty acids 0.149 g, 16:1 undifferentiated (palmitoleic) 0.003 g, 18:1 undifferentiated (oleic) 0.122 g, total polyunsaturated fatty acids 0.560 g, 18:2 undifferentiated (linoleic) 0.505 g, 18:3 undifferentiated (linolenic) 0.055 g, tryptophan 0.165 g, threonine 0.337 g, isoleucine 0.362 g, leucine 0.673 g, lysine 0.369 g, methionine 0.190 g, cystine 0.219 g, phenylalanine 0.556 g, tyrosine 0.284 g, valine 0.486 g, arginine 0.496 g, histidine 0.223 g, alanine 0.386 g, aspartic acid 0.619 g, glutamic acid 2.588 g, glycine 0.359 g, proline 1.178 g and serine 0.418 g (USDA 2012).

Tocochromanols (vitamin E) and lipids accumulated in parallel until 80% of the final dry weight of barley kernels was reached (Falk et al. 2004). Subsequently, the tocochromanol content did not change while the lipid content decreased. Generally, only about 13% of the tocochromanols were found in the germ fraction, whereas the pericarp fraction contained about 50% and the endosperm fraction about 37% of the tocochromanols. Altogether, about 85% of the tocochromanols were tocotrienols in the barley cultivars. Of tocopherols about 80% were found in the germ fraction and the remaining 20% in the pericarp fraction. Tocotrienols were almost equally present in the pericarp and the endosperm fraction.

Liu and Moreau (2008) found that oil, free phytosterols, tocopherols, were concentrated in the outer layers, particularly in the germ layer of hulless barley. In whole kernels, homologues of both tocopherols and tocotrienols showed the same ranking order in concentrations as alpha > gamma > beta > delta. The percentage of tocotrienols in total tocols increased in abraded fractions with increasing endosperm tissue. Storage caused no change in oil and tocopherols but significant changes in sterols and tocotrienols. The changes were differential among tocotrienols isomers, with alpha-tocotrienol decreasing and delta-tocotrienol increasing. The degradation of alpha-tocotrienol was accelerated in fractions with more endosperm tissue. Grinding kernel samples before storage accelerated sterol degradation but had a limited effect on changes of tocotrienols.

Seed storage proteins, prolamins found in barley include the sulphur-rich prolamins β-hordein

and γ-hordein and the S-poor prolamin C-hordein (Shewry et al. 1995). The high lysine content in high-lysine barley genotypes was found to be modulated by single recessive genes via two mechanisms: either a decrease of the lysine-poor prolamins compensated for by increased amounts of free lysine and non-prolamin proteins, or specific lysine-rich proteins were increased (Tallberg 1982). An increased lysine content was found to be achieved by an interactive effect of the high-lysine genes. In these combinations the glutelin proteins contributed with the greatest proportion of total seed lysine. Rat nitrogen balance tests showed that the nutritional quality was improved to meet the essential amino acid requirement by man as well as monogastric animals. During grain development the percentage of albumin + globulin fraction decreased in NP 113 barley, while those of prolamine and glutelin remained unchanged (Joshi et al. 1988). The increase in prolamine was considerable from 24 to 31 DAA (days after anthesis). In its high lysine mutant Notch-2 barley, albumin + globulin and prolamine trend was similar as in NP 113, while the glutelin fraction showed an increase. The percent of albumin + globulin was slightly higher in Notch-2 as compared to NP 113. During grain development the prolamine content was substantially lower in the mutant than in the parent NP 113. The improvement in lysine in the mutant was primarily attributed to reduced synthesis of the prolamine fraction and not attributed to an increase in lysine in the mutant hordein fraction.

Barley at 14% moisture was milled under commercial conditions to produce the following end-products: fine- and coarse-grained flours, middlings and fine grits that differed in their average contents of β-glucans, total dietary fiber, ash and protein (Kiryluk et al. 2000). The fine-grained grit from impact milling coarse grit had the highest contents of β-glucans, total dietary fiber, ash and protein. This product, with a weight yield of 18.6%, contained 6.72% β-glucans, 25.12% total dietary fiber, 2.19% ash, and 15.83% protein. All these values were at about 50, 72, 55 and 24%, respectively higher than in dehulled barley.

Significant differences in total β-glucan were observed among four types of hulless barley, with average values of 7.49, 6.86, 6.30, and 4.38% for high amylose, waxy, zero amylose waxy, and normal barley, respectively (Izydorczyk et al. 2000). The extractability of β-glucan in high amylose barley was relatively low (20.6–29.7%) compared to that in normal (29.8–44.3%), zero amylose waxy (34.0–52. 5%), and waxy (36.7–52.7%) barley genotypes. The content of soluble β-glucans, β-glucanase activity, and molecular weight of β-glucans affected viscosity of barley flour slurries. Hydrothermal treatments (autoclaving and steaming) of barley had no effect on extractability of β-glucans, but prevented enzymic hydrolysis of β-glucans, and thereby substantially improved their molecular weight. The addition of enzymes (protease and esterase) during extraction and/or physical treatments (sonication) increased extractability of β-glucans from barley grains.

For all hull-less barley (HB) containing waxy (0–7% amylose), normal (≈25% amylose), or high amylose (≈42% amylose) starch, β-glucan and acid-extract viscosity were very low in the outermost 20% of the kernel (Zheng et al. 2000). For low β-glucan HB, β-glucan content was highest in the subaleurone region and declined slightly toward inner layers. For high β-glucan HB, however, more than 80% of grain β-glucan was distributed more evenly throughout the endosperm. Acid extract viscosity was significantly correlated with total ($R^2 = 0.75$) and soluble ($R^2 = 0.87$) β-glucan content throughout the kernel of all HB. Growing conditions, location and year, had significant effects on the concentration of protein, starch and β-glucan but not on their distribution patterns. Yalcin et al. (2007) found that environmental and genetic factors had an impact on the total β-glucan and total dietary fibre (TDF) contents of hull-less barley. There were significant differences among the barley genotypes and different locations in terms of β-glucan and TDF content. Holtekjølen et al. (2006b) found wide variation in of starch and non-starch polysaccharides contents in barley varieties of different origin. A strong positive correlation was found between the β-glucan and the amount of soluble

non-starch polysaccharides (NSP), and between β-glucans and protein contents. as a negative correlation was observed between β-glucan and arabinoxylan. varieties with high contents of β-glucans, soluble NSP, high soluble fibre, protein, and lower starch content were found and could be suitable for functional food products aimed at health benefits and cancer prevention.

The β-glucan content in 36 barley varieties ranged from 2.64 g/100 g dw (dry weight) for Vanessa to 8.05 g/100 g dw for Ludine, with an average value of 3.95 g/100 g dw and 50% of the compounds were in the range between 3.45 and 4.36 g/100 g dw (Panfili et al. 2008). The total tocol amount ranged from 50.3 mg/kg dw (Ladoga) to 88.6 mg/kg dw (Maggiodoro), with a mean value of 69.1 mg/kg dw and with most genotypes (50%) having a content between 62 and 75 mg/kg d.w. Adagio and Sabel were the best source of vitamin E activity, expressed as tocopherol equivalents. In the pearling by-products there was no enrichment of β-glucans, but, a seven and a fivefold increase was observed for tocopherols and tocotrienols, respectively.

Other Phytochemicals

Twenty-six volatiles comprising aldehydes, ketones, alcohols, and a furan were identified in barley (Cramer et al. 2005). 1-octen-3-ol, 3-methylbutanal, 2-methylbutanal, hexanal, 2-hexenal, 2-heptenal, 2-nonenal, and decanal were identified as key odorants in barley as their concentration exceeded their odor detection threshold in water. Hexanal (46–1,269 μg/l) and 1-pentanol (798–1,811 μg/l) were the major volatile compounds in barley cultivars. Hulled barley possessed higher total volatile, aldehyde, ketone, alcohol, and furan contents than hulless barley, highlighting the importance of the husk in barley grain aroma. The proanthocyanidin-free varieties generally exhibited higher total volatile and aldehyde contents than wild-type varieties, potentially due to decreased antioxidant activity by the absence of proanthocyanidins. Five phenolic compounds, *p*-hydroxyacetophenone, 5,7-dihydroxychromone, naringenin, quercetin, and isoamericanol A, were found barley tea, together with the known compounds, *p*-hydroxybenzaldehyde, 3,4-dihydroxybenzaldehyde, *p*-hydroxybenzoic acid, vanillic acid, and *p*-coumaric acid (Etoh et al. 2004).

One twenty seven lines of coloured barley was placed into seven groups using the colorimeter: hulled (black 1, black 2, black 3, and purple) and unhulled (black, blue, and purple) and their content of phenolic compounds, proanthocyanidins, and anthocyanins and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity were examined (Kim et al. 2007). The average content of phenolic compounds in unhulled barley groups (268.6 μg/g) was higher than that in hulled (207.0 μg/g). The average content of proanthocyanidins was significantly higher in purple and blue barley groups compared with black. The content of anthocyanins varied from 13.0 to 1037.8 μg/g. Purple and blue barley groups contained higher average contents of anthocyanins than black. The most common anthocyanin in the purple barley groups was cyanidin 3-glucoside, whereas delphinidin 3-glucoside was the most abundant anthocyanin in the blue and black groups. In coloured barley, DPPH radical scavenging activity had high positive correlation to the content of phenolic compounds and proanthocyanidins. HPLC analysis showed that as much as six times more anthocyanin per unit weight was present in the bran-rich fractions of yellow and purple barley (1,587 and 3,534 μg/g, respectively) than in their corresponding whole kernel flours (210 and 573 μg/g, respectively) (Bellido and Beta 2009). Delphinidin 3-glucoside, delphinidin 3-rutinoside, cyanidin 3-glucoside, petunidin 3-glucoside, and cyanidin chloride were identified in barley, with as many as 9 and 15 anthocyanins being detected in yellow and purple barley, respectively. Antioxidant activity analysis showed that the ORAC values for the bran-rich fractions were significantly higher than for the whole kernel flour.

5-n-alkylresorcinols were isolated from acetone extracts of grains from five barley cultivars (Zarnowski et al. 2002). The predominant compounds were 1,3-dihydroxy-5-n-heneicosylbenzene (C21:0), 1,3-dihydroxy-5-n-nonade-

cylbenzene (C19:0) and 1,3-dihydroxy-5-n-pentacosylbenzene (C25:0). The predominant alkylresorcinols identified in winter barley grains were 1,3-dihydroxy-5-n-heneicosylbenzene and 1,3-dihydroxy-5-n-pentacosylbenzene (Zarnowski and Suzuki 2004).

Phenolics acids, *trans*-ferulic aicd, *trans*–*p*-coumaric acid and *cis*-ferulic acid were found bound to celluar walls of germinated barley (Maillard and Berset 1995). Mattila et al. (2005) reported that the total ferulic acid content of grains ranged from 458 (whole wheat) to 129 (oats and barley) μmol/100 g grain, the total *p*-coumaric acid content ranged from 24 (barley) to 9 (buckwheat) μmol/100 g grain, and the total *p*-hydroxybenzoic acid content ranged from 80 (buckwheat) to 4 (corn) μmol/100 g grain. The high total *p*-hydroxybenzoic acid content in buckwheat is most likely due to the contribution of the free fraction.

Hydroxycinnamic acid content and ferulic acid dehydrodimer content were determined in 11 barley varieties (Hernanz et al. 2001). Ferulic acid was the most abundant hydroxycinnamate with concentrations ranging from 359 to 624 μg/g dry weight. *p*-coumaric acid concentrations ranged from 79 to 260 μg/g dry weight, and caffeic acid was present at levels of <19 μg/g dry weight. Among the ferulic acid dehydrodimers that were identified, 8-*O*-4′-diFA was the most abundant (73–118 μg/g dry weight), followed by 5,5′-diFA (26–47 μg/g dry weight), the 8,5′-diFA benzofuran form (22–45 μg/g dry weight), and the 8,5′-diFA open form (10–23 μg/g dry weight). Barley grains were mechanically fractionated into three fractions: F1, fraction consisting mainly of the husk and outer layers; F2, intermediate fraction; and F3, fraction consisting mainly of the endosperm. Fraction F1 contained the highest concentration for ferulic acid (from 77.7 to 82.3% of the total amount in barley grain), *p*-coumaric acid (from 78.0 to 86.3%), and ferulic acid dehydrodimers (from 79.2 to 86.8%). Lower contents were found in fraction F2, whereas fraction F3 exhibited the lowest percentages (from 1.2 to 1.9% for ferulic acid, from 0.9 to 1.7% for *p*-coumaric acid, and <0.02% for ferulic acid dehydrodimers). The solid barley residue from the brewing process (brewer's spent grain) was approximately five-fold richer in ferulic acid, *p*-coumaric acid, and ferulic acid dehydrodimers than unprocessed barley grains. The main flavanols found in the analyzed barley varieties consisting of hulled and hull-less types, of normal, waxy, and high amylose starch, as well as two-rowed and six-rowed types were two dimeric as well as four trimeric forms in addition to catechin (Holtekjølen et al. 2006a). The total amount of flavanols ranged from 325 to 527 μg/g of fresh weight of barley flour. The total amount of phenolic acids ranged from 604 to 1,346 μg/g of fresh weight of barley flour, with ferulic acid dominating. The amount of phenolic acids varied according to occurrence or lack of hull, with significantly higher levels in the hulled varieties.

Using a combination of sequential acid, alpha-amylase, and cellulase hydrolysis treatments and HPC, the following phenolic acids: benzoic acid (*p*-hydroxybenzoic, vanillic, and protocatechuic acids) and cinnamic acid derivatives (coumaric, caffeic, ferulic, and chlorogenic acids) were identified in 30 barley varieties (Yu et al. 2001). Phenolic acids, namely, vanillic, caffeic, *p*-coumaric, ferulic, and sinapic acids, were identified by HPLC in pearled barley fractions of two barley varieties (Falcon and AC Metcalfe) extracted with 80% methanol (Madhujith et al. 2006). Zhao et al. (2006) found that 80% acetone showed the highest extraction capacity for (+)-catechin and ferulic, caffeic, vanillic, and *p*-coumaric acids, 80% methanol for (−)-epicatechin and syringic acid, and water for protocatechuic and gallic acids from barley. Dimeric proanthocyanidins (prodelphinidin B3 and procyanidin B3), as well as the trimeric procyanidin C2 and three other trimeric prodelphinidins were isolated from barley using a semipreparative chromatographic method (McMurrough et al. 1996). Abraded grains contained 146–410 μg/g of phenolic acids (caffeic, *p*-coumaric, and ferulic) in hulled barley and 182–282 μg/g in hulless barle (Quinde-Axtell and Baik 2006). Hulled proanthocyanidin -containing and proanthocyanidin-free genotypes had comparable phenolic acid contents. Catechin (CE) and six major barley proanthocyanidins, including dimeric prodelphinidin B3 and procyandin

B3, and four trimers were quantified. The catechin content was higher in hulless (48–71 μg/g) than in hulled (32–37 μg/g) genotypes. The total proanthocyanidin content of abraded barley grains ranged from 169 to 395 μg CE/g in proanthocyanidin -containing hulled and hulless genotypes. Major proanthocyanidins were prodelphinidin B3 (39–109 μg CE/g) and procyanidin B3 (40–99 μg CE/g). The contents of trimeric proanthocyanidins including procyanidin C2 ranged from 53 to 151 g CE/g. Discoloration of barley flour dough correlated with the catechin content of abraded grains ($R^2 = -0.932$), but not with the content of individual phenolic acids and proanthocyanidins. Despite its low concentration, catechin appeared to exert the largest influence on the discoloration of barley flour dough among phenolic compounds. Dvorakova et al. (2008) reported that catechin and prodelphinidin B3 were respectively the major monomeric and dimeric flavan-3-ols in barley and malt. Five different flavanols were isolated from various barley cultivars and identified: (2R,3S)-catechin-7-O-β-D-glucopyranoside (1), prodelphinidin B3 (2), procyanidin B3 (3), (+)-catechin (4) and procyanidin B1 (5) together with four phenolic acids: ferulic acid, vanillic acid, *p*-coumaric acid and *p*-hydroxybenzoic acid (Klausen et al. 2010). Catechin was the compound that was present at the highest concentration in all varieties.

Dehydrodiferulic acids (DFA) (8-5′- DFA, 8-8′-DFA, 5-5′-DFA, 8-*O*-4′-DFA could be identified in both insoluble dietary fibre (IDF) and soluble dietary fibre (SDF) of barley grains (Beunzel et al. 2001). Total dehydrodiferulic acid in IDF of barley was quantified as 3,658 μg/g, in SDF 69 μg/g. In barley, amounts of 8-5′-DFA reached up to 50.7% in IDF and 38.8% in SDF; 8-8′-DFA 16.1% in IDF and 34.7% in SDF; 5-5′-DFA 14.9% in IDF and 16.7% in SDF; 8-*O*-4′-DFA 18.4% in IDF and 9.8% in SDF; 4-*O*-5′ DFA detected tracesin IDF and not detected in SDF.

Comparative study of five small grain cereals namely barley, oats, rice, sorghum, and wheat found that the in whole or dehulled grains the oil content ranged from 2.18% of a wheat variety to 6.38% of an oat line (Liu 2011). Compared with barley and wheat, rice, oat, and sorghum had higher relative % of C18:1 (31.60–36.64 compared with 12.15–15.61) and lower % of C18:2 (35.69–45.44 compared with 50.79–61.50). For all the grains, from seed surface to inner core, C16:0 and C18:0 increased, C18:1 and C18:3 decreased, and C18:2 changed slightly, providing a new reason for improved oxidative stability for pearled kernels.

Pearling was found to be more effective in concentrating total tocols and oil in barley flour than milling (Wang et al. 1993). Seven tocols namely α-tocotrienol (43.3 mg/kg), γ-tocotrienol (7.7 mg/kg), δ-tocotrienol (1.0 mg/kg); α-tocopherol (8.1 mg/kg), β-tocopherol (0.4 mg/kg), γ-tocopherol (10 mg/kg) and δ-tocopherol (0.4 mg/kg) were found in barley whole grains. Milling flour had 21% α-tocotrienol, 23% total tocol and 31% oil. Pearling grains had 39% α-tocotrienol, 7% total tocol and 20% oil; pearling flour had 61% α-tocotrienol, 93% total tocol and 80% oil. Pearling flour, 20% of kernel weight had the highest content of α-tocotrienol (115.8 mg/kg), α-tocopherol (35.4 mg/kg) total tocols (205.3 mg/kg) and oil (81.5 g/kg): 2.7, 4.4, 2.9 and 2.9 times greater than those in the whole grain respectively. Among six milling fractions (flour, fifth middling, red dog, reduction shorts, break shorts and bran), highest concentration of α-tocotrienol (50.2 mg/kg) and α-tocopherol (12.1 mg/kg) were found in reduction shorts and fifth middling. Fifth middling, red dog and reduction shorts were highest in total tocol concentrations. Fifth middling was highest in oil concentration. Flour and bran were lowest in total tocol and oil, but they were the highest in total quantities of those components because they were the largest mill fractions. In pearling fractions, the pearling flour contained higher oil, total tocols and α-tocotrienol than did the individual mill fractions high α-tocotrienol, total tocols and oil concentrations make pearling flour a potential ingredient for food products to enhance health.

Colgrave et al. (2012) characterised the suite of prolamin proteins present in barley flour. They provided spectral evidence for 3 previously characterized prolamins, 8 prolamins with only

transcript evidence, 19 genome-derived predicted prolamins and an additional 9 prolamins. Analyses of wort, the liquid extracted from the mashing process during beer production, and beer were undertaken and a similar suite of prolamins were identified. They confirmed that hordeins (gluten) to be present in beer. They detected no intact C-hordeins in hordein deletion beers although fragments of C-hordeins were present in wort. Hordein deletion beers were brewed from grains carrying mutations that prevented the accumulation of either B-hordeins (Risø 56) or C-hordeins (Risø 1508).

Sprouting barley was found to contain hordenine(*N*,*N*-dimethyl-4-hydroxyphenylethylamine) a phenethylamine alkaloid as the main alkaloid in the roots (Mann et al. 1963). Hordenine was metabolised by barley root homogenates into N-methyltyramine and probably tyramine (Russo et al. 1983). A total of 28 phenolic compounds were identified and quantified in the leaves, seeds, awns, and stems of barley, which included 4 phenolic acids, 6 C-glycosylflavones, and 18 *O*-glycosyl-C-glycosyl flavones, with some of them acylated (Ferreres et al. 2009). The greatest diversity of compounds was found in barley leaves (26 flavonoids and 2 phenolic acid derivatives), which also exhibited the highest concentration of phenolics. Isoorientin-7-*O*-glucoside (lutonarin) was the major compound in leaves, while, in general, the pair isovitexin-7-*O*-rutinoside plus isoscoparin-7-*O*-glucoside were the main phenolics in the other plant parts. Thus, barley leaves may constitute an important dietary source of protective compounds, which could be used, for example, to take profit from the wastes resulting from alcoholic drink production.

The principal flavonoid constituent isolated from barley leaves was saponarin which on acidic hydrolysis yielded a mixture of saponaretin and vitexin (Seikel and Geissman 1957). Another flavonoid, lutonarin was isolated from barley leaves (Seikel and Bushnell 1959). This glycoside resembled the unusual flavones vitexin and saponaretin (apigenin derivatives) that had been earlier isolated from barley leaves. Lutonarin yielded two aglycons on hydrolysis, lutonaretin and lutexin. A third glycoside present in trace amount in barley leaves was shown to be the 3′ methyether of lutonarin (Seikel et al. 1962). An arabinogalacto(4-*O*-methylglucurono)xylan with a DPn of about 96 was isolated from the leaves of barley (Buchala 1973). It was proposed that its hemicellulose consisted of a main chain of β (1→4)-linked d-xylopyranosyl residues to which were attached an average of 8·1 l-arabinofuranosyl residues, 3·8 galactopyranosyl-(1→4)-d-xylopyranosyl-(1→2)-l-arabinofuranosyl residues and 4·4 4-*O*-methyl-d-glucopyranuronosyl residues.

A new cyanogenic glycoside, 2-β-d-glucopyranosyl-oxy-3-methyl-(2R)-butyronitrile, the epimer of heterodendrin was isolated form barley seedling leaves (Erb et al. 1979).

Two isoforms of adenosine diphopshate glucose pyrophosphatase/phosphodiesterase (AGPPase) were characterized from barley leaves (*Hordeum vulgare* L.) (Rodríguez-López et al. 2001). One isoform, designated as soluble AGPPase1 (SAGPPase1), was soluble in low ionic strength buffers. The other, SAGPPase2, was extractable using cell wall hydrolytic enzymes or high salt concentration solutions, thus indicating that it was adventitiously bound to the cell wall. Both AGPPase isoforms were highly resistant to SDS (sodium dodecyl sulphate). Both SAGPPase1 and SAGPPase2 were found to be distinct oligomers of the previously designated HvGLP1 (*Hordeum vulgare* mRNA for germin-like protein), a member of the ubiquitously distributed group of proteins of unknown function designated as germin-like proteins (GLPs).

Carbohydrate (starches, sugars, non-starch polysaccharide) comprises about 80% of barley grain (Newman and Newman 1992). Most of the carbohydrate is starch which makes up 60% and provides energy for germination (OECD 2004). Starch is the major source of readily available energy for food and feed. In most barley, the predominant starch is amylopectin and the remainder is amylose (Newman and Newman 1992).

Non-starch polysaccharides collectively call dietary fibre and include β-glucans and arabinoxylans. The fibre content of barley is relatively high and has health benefits. The soluble β-glucans

can lower post-prandial blood glucose levels and blood cholesterol (McIntosh et al. 1991; OECD 2004). In contrast, arabinoxylans and β-glucans can have a deleterious effect on digestion in monogastric (OECD 2004). In addition, β-glucans are known to negatively impact poultry particularly young birds by reducing intestinal viscosity (Newman and Neman 1992). Barley also contained compounds some of which may protect against disease when ingested at thigh levels. These include simple phenolic acids, flavonoids and lignans all of which possessed good antioxidant properties (OECD 2004).

Antinutrients

Barley has been reported to contain antinutrients which can impair nutrient absorption and utilisation in animals such as protease enzyme inhibitors, lectins and phytic acid. Both protease and alpha amylase inhibitors are present in barley grains. Protease inhibitors especially trypsin inhibitors may decrease the digestibility of dietary proteins while amylase inhibitor may affect digestibility of dietary starch. However these inhibitors do not pose a serious risk to human health as they tend to be heat labile (OECD 2003) and due to their low levels in barley grains these protease inhibitors no significant influence on protein digestibility (Newman and Newman 1992). Such inhibitors found in barley include the trypsin inhibitor of 14,500 MW (Boisen 1983), chymotrypsin inhibitor 2 (CI-2), a serine protease inhibitor and a member of the potato inhibitor 1 family (Mcphalen and James 1987), Bowman-Birk inhibitors (BBIs) (Park et al. 2004), barley alpha-amylase/subtilisin inhibitor (BASI), a member of the Kunitz-type trypsin inhibitor family that inhibits the barley alpha-amylase 2 (AMY2) and subtilisin-type serine proteases (Nielsen et al. 2004), and phytocystatins and trypsin/α-amylase inhibitors that are involved in the plant defence mechanisms against pests and fungal pathogens (Carrillo et al. 2011). In barley, 13 cystatins (HvCPI-1 to 13) and the BTI-CMe trypsin inhibitor have been reported. Barley also have amylase inhibitor, alpha-amylase II inhibitor with 20,000 Da molecular weight that inhibits alpha-amylase II (Weselake et al. 1983). Barley grains also has the antinutrient, phytic acid and lower inositolphosphates, the main storage form of phosphates in barley seeds (Kvasnička et al. 2011). Lectins are glycoproteins that bind to specific carbohydrate groups on cell surfaces causing lesions to form. In the intestinal tract, these lesions can seriously impair the absorption of nutrients (OECD 2003). Lectins play a role in the plant response to biotc and abiotic stress factors and may also have biological and immunological properties. Barley also contain lectin, designated Lem3, a jacalin-related lectin like protein found in the lemma/palea and coleoptiles that is involved in systemic acquired resistance defence (Abebe et al. 2005), and barley lectin (BL) and its precursor form (proBL) (Wright et al. 1993) and a jacalin-related lectin designated horcolin (Grunwald et al. 2007). Dolma, a hull-less Indian barley cultivar was found to have high contents of protein, fat, starch, in-vitro digestibility of protein and starch, in-vitro availability of Ca, Fe and Zn (Jood and Kalra 2001). Hulled cultivar BH-331 showed higher values of phytic acid (925 mg/100 g), polyphenols (625 mg/100 g) and amylase inhibitor activity (169 AIU) which might have contributed towards poor in-vitro digestibility of Ca, Fe and Zn. They found that phytic acid and polyphenols manifested significantly negative correlation with in-vitro availability of Ca, Fe and Zn and protein digestibility. Whereas amylase inhibitor activity showed significant and negative correlation (−0.992) only with starch digestibility. Some phenolic compounds such as proanthocyanidins and catechins found in barley seed coats can form insoluble complexes with proteins inhibiting nutrient uitlisation (Newman and Newman 1992).

Antioxidant Activity

In two barley varieties (Falcon and AC Metcalfe) the outermost fraction yielded the highest phenolic content (Madhujith et al. 2006). Phenolic acids, namely, vanillic, caffeic, *p*-coumaric, ferulic,

and sinapic acids, were identified in the barley fractions. Overall, Falcon had a significantly higher total phenolic content than AC Metcalfe. A similar trend was observed for TEAC, DPPH, and superoxide radical scavenging capacities of the extracts. The contents of water-soluble antioxidants of Falcon and AC Metcalfe were 1.15–12.98 and 2.20–12.25 μmol of Trolox equiv/(g of defatted material), while the corresponding lipid-soluble counterparts varied from 1.44 to 4.70 μmol of α-tocopherol equiv/(g of defatted material). Nine free flavan–3-ols were identified in barley flours (cv. Gotic) and two resulting milling fractions (fine fraction 57% and coarse fraction 43%, w/w) (Verardo et al. 2008a). Catechins and their derivatives were found to make a substantial contribution to the antioxidant power of their extracts. The coarse fraction had larger concentrations of flavan-3-ols (221%) with respect to the fine fraction and showed the greatest antioxidant activity (1,200.1 μmol of Trolox equiv/100 g of flour) compared to the whole meal and fine fraction (1,025.9 and 761.7 μmol of Trolox equiv/100 g of flour, respectively). Flavonoids, saponarin and lutonarin isolated from young green barley leaves exhibited antioxidant activities comparable to those obtained from alpha-tocopherol and butylated hydroxy toluene (BHT) in all lipids tested (Benedet et al. 2007). The saponarin/lutonarin = 4.5/1 mixture inhibited malonaldehyde formation from cod liver oil by 76.47% at a level of 1 μmol and 85.88% at a level of 8 μmol. The mixture inhibited malonaldehyde formation from the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) by 45.60 and 69.24%, respectively, at a level of 8 μmol. The mixture inhibited malonaldehyde formation from the phospholipids lecithin I and II by 43.08 and 69.16%, respectively, at a level of 8 μmol. At the same concentration, it also inhibited malonaldehyde formation from blood plasma by 62.20%. Dvorakova et al. (2008) reported that catechin and prodelphinidin B3 were respectively the major monomeric and dimeric flavan-3-ols in barley and malt. Prodelphinidin B3 was shown to be the main contributor for the radical scavenging activity both for barley and malt.

Five phenolic compounds, *p*-hydroxyacetophenone, 5,7-dihydroxychromone, naringenin, quercetin, and iso-americanol A, were found barley tea, together with the known compounds, *p*-hydroxybenzaldehyde, 3,4-dihydroxybenzaldehyde, *p*-hydroxybenzoic acid, vanillic acid, and *p*-coumaric acid (Etoh et al. 2004). Among these compounds, 3,4-dihydroxybenzaldehyde, *p*-coumaric acid, quercetin, and isoamericanol A showed stronger activities than that of BHT (butylated hydroxytoluene) at 400 μM.

Total phenolic content of six barley cultivars, namely, Falcon, AC Metcalfe, Tercel, Tyto, Phoenix, and Peregrine as measured according to Folin-Ciocalteu's method ranged from 13.58 to 22.93 mg of ferulic acid equivalent/g of defatted material, with the highest content in Peregrine (Madhujith and Shahidi 2006). Total antioxidant activity as measured by Trolox equivalent antioxidant capacity ranged from 3.74 to 6.82 μmol/g of defatted material. Metal chelation capacity of the extracts as measured by 2,2′-bipyridyl competition assay varied from 1.1 to 2.1 μmol of ethylenediaminetetraacetic acid equiv/g of defatted material. IC_{50} values for 1,1-diphenyl-2-picrylhydrazyl radical as measured by electron paramagnetic resonance ranged from 1.51 to 3.33 mg/mL, whereas the corresponding values for hydroxyl radical ranged between 2.20 and 9.65 mg/mL. Inhibition of peroxyl radical induced supercoiled DNA scission ranged from 78.2 to 92.1% at the concentration of 4 mg/mL of extracts, whereas the corresponding values for hydroxyl radical induced DNA scission ranged from 53.1 to 65.3%. In another research, they reported that total phenolic content of aqueous methanolic extracts of whole kernels from six different barley cultivars as measured by Folin-Ciocalteu's method ranged from 0.68 to 1.19 mg of ferulic acid equiv/g of defatted material, whereas oxygen radical scavenging capacity and hydroxyl radical scavenging capacity values were 11.28–19.10 and 9.06–12.99 μmol of Trolox equiv/g of defatted material, respectively (Madhujith and Shahidi 2007). Protection factor, a measure of the effect of extracts on the prevention of oxidation of stripped corn oil as measured by Rancimat, ranged from 0.97 to 1.59. Further, the barley

extracts showed 19.64–33.93% inhibition against Cu^{2+}-induced human LDL cholesterol oxidation at a final concentration of 0.02 mg/mL.

Results of studies by (Zhao et al. 2006) showed that extraction solvent mixtures had significant impacts on antioxidant activity estimation, as well as different extraction capacity and selectivity for free phenolic compounds in barley. The highest DPPH* and ABTS* + scavenging activities and reducing power were found in 80% acetone extracts, whereas the strongest *OH scavenging activity, O2*- scavenging activity, and metal chelating activity were found in 80% ethanol, 80% methanol, and water extracts, respectively. Additionally, 80% acetone showed the highest extraction capacity for (+)-catechin and ferulic, caffeic, vanillic, and *p*-coumaric acids, 80% methanol for (−)-epicatechin and syringic acid, and water for protocatechuic and gallic acids. Further, correlations analysis revealed that total phenolic content, reducing power, DPPH* and ABTS* + scavenging activities were well positively correlated with each other. Thus, for routine screening of barley varieties with higher antioxidant activity, 80% acetone was recommended to extract free phenolic compounds from barley. DPPH* scavenging activity and ABTS* + scavenging activity or reducing power could be used to assess barley antioxidant activity.

Studies showed that malting had significant impacts on individual and total phenolic contents as well as antioxidant activities of barley varieties (Lu et al. 2007). The contents of some phenolic compounds and the antioxidant activities decreased significantly during steeping and the early stages of germination and then increased remarkably during the later stages of germination and subsequent kilning. The most phenolic compounds identified in barley were (+)-catechin and ferulic acid, which both changed significantly during malting. There were good correlations among DPPH radical scavenging activity, ABTS radical cation scavenging activity, reducing power, total phenolic content and sum of individual phenolic contents during malting.

Studies showed that fractionation of two pigmented wheat genotypes (blue and purple) and two black barley genotypes into bran and flour fractions had a significant influence on the antioxidant properties, total phenolic content, anthocyanin and carotenoid contents, and phenolic acid composition (Siebenhandl et al. 2007). Bran fractions had the greatest antioxidant activities (1.9–2.3 mmol TEAC/100 g) in all four grain genotypes and were 3.5-fold higher than the respective flour fractions (0.4–0.7 mmol TEAC/100 g). Ferulic acid was the predominant phenolic acid in wheat genotypes (bran fractions) while *p*-coumaric acid was the predominant phenolic acid in the bran fractions of barley genotypes. The presence of lutein and zeaxanthin was detected in all fractions with different distribution patterns within the genotypes. The highest contents of anthocyanins were found in the middlings of black barley genotypes or in the shorts of blue and purple wheat. Among the tested solvents used in the fractionation of antioxidants from nonisothermal autohydrolysis of barley husks, ethyl acetate allowed the highest yield, phenolic content, and antioxidant activity (Conde et al. 2008). Upon elution with methanol, products with high DPPH radical scavenging capacity ($IC_{50} = 0.22$ g/L) were obtained. The major compounds in the isolate were benzoic and cinnamic acids. Adsorption-desorption in commercial polymeric resins was carried out as an alternative strategy for BHEAE (crude ethyl acetate extract of barly husr resolved in ethanol) refining. This method is more suited for possible scale-up and provided a concentrate with a Trolox equivalent antioxidant capacity of 9 mM, which was obtained at a yield of 18 g/kg of barley husks.

Microwave roasting of barley grains was found to enhance the antioxidant activity (Omwamba and Hu 2010) The optimum condition for obtaining roasted barley with high antioxidant activity (90.5% DPPH inhibition) was found to be at 600 W microwave power, 8.5 min roasting time, and 61.5 g or two layers of grains. The acetone extract exhibited significantly high inhibition of lipid peroxidation and DPPH radical scavenging activity compared to the aqueous extract and α-tocopherol. The reducing power of acetone extracts was not significantly different from α-tocopherol. The acetone extract had twice the

amount of phenol content (notably phenol acids, amino phenols, and quinones) compared to the aqueous extract indicating its high extraction efficiency. The aqueous extract did not contain 3,4-dihydroxybenzaldehyde and 4-hydroxycinnamic acid phenol compounds reported to contribute to antioxidant activity in barley grain.

Studies by Papetti et al. (2006) showed the occurrence in natural barley of weak antioxidant components that were able to react against low reactive peroxyl radicals, but offered little protection against stable DPPH radicals deriving from peroxidation in rat liver hepatocyte microsomal lipids. Conversely, roasted barley yielded strong antioxidant components that were able to efficiently scavenge free radicals in any system used. The results showed that the barley grain roasting process induced the formation of soluble Maillard reaction products with powerful antiradical activity. From roasted barley solution (barley coffee) they isolated a brown high molecular mass melanoidinic component, resistant to acidic hydrolysis, that was responsible for most of the barley coffee antioxidant activity in the biosystem

Hydroxycinnamic acids and their derivatives were found to be the main bound phenols in barley flours (Verardo et al. 2008b). A total of 12 different hydroxycinnamic acids were identified. Ferulic acid (as a simple and glycosylated derivative) was the main phenolic acid in barley flours, representing 89–93% of total hydroxycinnamic acids. The amount of total hydroxycinnamic acid in air-classified coarse fraction was two and three times higher than those of whole meal and the air-classified fine fraction, respectively. Similarly, the coarse fraction showed higher antioxidant activity (650.03 micromol of TEAC/100 g of flour) compared to whole meal and the fine fraction (388.78 and 320.27 μmol of TEAC/100 g of flour, respectively). The replacement of 60% (w/w) refined wheat flour with barley coarse fraction increased the ash, fiber and flavan–3-ol contents significantly (Verardo et al. 2011). Biscuit samples enriched with barley coarse fraction had a significantly higher amount of fiber compared with the control sample (six times higher). The β-glucan content in enriched samples was 15 times higher than control samples. The flavan-3-ol loss in biscuits after baking was about 67%. The initial content of flavan-3-ols increased from 0.6 to 4.3 mg/100 g in biscuits formulated with barley coarse fraction and showed improved antioxidant properties. Lipid oxidation increased during the shelf-life; the enriched biscuit showed the higher lipid oxidation status, but the level reached during the shelf-life was lower than the limit of acceptance reported for bakery products and, for this reason, does not compromise the safety. Barley whole grain was found to have total phenolic content of 94.1 mg GAE/100 g grain and oxygen radical absorbance capacity (ORAC) of 7,081 μmol TE/100 g grain (Okarter 2012). Barley contained 133 μmol/100 g grain of ferulic acid, and 19.0 μmol/100 g grain of *p*-coumaric acid and also caffeic acid in the insoluble bound fraction but contained no flavonoids (qurecetin, kaempferol, catechin, and rutin) in the insoluble-bound fraction of the grain. None of the phenolic compounds had any cellular antioxidant activity, most likely because these phenolic compounds did not have the structure necessary to impart cellular antioxidant activity. The data suggested that the potential health benefit of whole grain consumption in the lower gastrointestinal tract was independent of the cellular antioxidant activity of the phenolic compounds found in the insoluble-bound fraction of whole grains.

The green mass of young plants of spring barley was found to be a significant source of vitamins C and E (Brezinová Belcredi et al. 2010). The highest average vitamin content was determined in the malting hulled variety Sebastian (vitamin C, 520 mg/100 g DM; vitamin E, 73.06 mg/kg DM) compared to the malting hulled variety, Malz (501 mg/100 g DM; 61.84 mg/kg DM) and non-malting variety AF Lucius (508 mg/100 g DM; 67.81 mg/100 g DM). The green mass of young barley plants exhibited statistically significant higher activity of superoxide dismutase (SOD) and catalase (CAT) at sampling I (in the phase of plant development DC 29) compared to the later sampling II (DC 31) (Ehrenbergerová et al. 2009). The hulled variety Sebastian provided statistically significant higher average SOD activity (486 U/g) versus the variety

Malz (416 U/g dry matter) and hulless line KM1910 (418 U/g dry matter). The major flavonoid antioxidants in young green barley leaves were found to be flavone-C-glycosides, saponarin and lutonarin (Markham and Mitchell 2003). The major "isoflavonoid" antioxidant in young green barley leaves was erroneously referred to 2″-*O*-glucosylisovitexin in literature since 1992.

Anti Hypercholesterolemic/ Antihyperlipidemic Activities

Animal Studies

Wang et al. (1993a, b) found that total plasma cholesterol concentration of the chicks fed barley oil was 34% lower than that of the chicks fed margarine. Plasma low density lipoprotein cholesterol concentration of chicks fed barley oil was 53 and 59% lower than those of chicks fed corn oil and margarine, respectively. Plasma high density lipoprotein cholesterol and triglyceride concentration of the barley oil group were similar to those of the margarine but higher than those of the corn oil group. Chicks fed the barley oil gained more body weight than those fed the corn oil and margarine. A greater weight gain of the chicks fed barley oil suggested that these chicks had normally functioning digestion and absorption. Alpha-tocotrienol and γ-tocotrienol content of the barley oil were 24 and 17 times greater, respectively, than those observed in the corn oil, while the same fractions were not detectable in the margarine. Polyunsaturated fatty acid content of the barley oil was more than threefold that of margarine. These data suggested α-tocotrienol and polyunsaturated fatty acids to be hypocholesterolemic components in barley oil.

Diets containing 25, 50, or 75% finely ground barley (high in soluble fiber and soluble β-glucans) fed to hamsters lowered blood lipids levels (Ranhotra et al. 1998). The 25% barley diet lowered total cholesterol by 16.4%; the 50% barley diet lowered total cholesterol further by only 4.1% while the 75% barley diet caused virtually no further lowering of total cholesterol suggesting that total cholesterol lowering response to barley was not a dose dependent response. The lowering pattern for serum triglycerides, however, suggested a dose dependent response. Serum total-CH: high-density-lipoprotein (HDL)-CH or low-density-lipoprotein (LDL)-CH: HDL-CH ratios were not significantly affected by barley level in the diets. Using a rabbit model of atherosclerosis, Yu et al. (2002b) found that addition of barley leaf extract to chow containing 0.5% cholesterol and 10% corn oil, gave 30% inhibition of hyperlipidemic atherosclerosis due to a decrease in plasma lipids and an increase in antioxidative abilities (as measured by an increase in T50 value of red blood cell hemolysis and lag phase of low-density lipoprotein oxidation and decrease in lucigenin-chemiluminescence. Their results suggested that the antioxidant and hypolipidemic effects of barley could be useful in the prevention of atherosclerosis. Yang et al. (2003) demonstrated that addition of refined β-glucan or waxy barley to the diet of male Sprague–Dawley rats did not affect Body weight gain and food efficiency. Beta-glucan or waxy barley decreased significantly serum levels of total cholesterol by 13.5 or 18.9%, and also decreased LDL-cholesterol 19.4 or 24.3%, respectively. Their addition to the diet also resulted in greater bile acid excretions compared to the control group. The waxy barley diet enhanced by 2. Three times and the β-glucan diet by 1.5 times the activity of cholesterol 7a-hydroxylase (CYP7A1). Hepatic CYP7A1 mRNA level paralleled the increases in enzyme activity. The results suggested that the hypocholesterolemic effects of both β-glucan and a waxy barley diet may be due to the enhancement of CYP7A1 expression resulting from increased faecal excretion of bile acids.

Another study showed that consumption of reduced and high molecular weight barley β-glucans decreased plasma total and non-HDL-cholesterol in hypercholesterolemic Syrian golden hamsters (Wilson et al. 2004). Animals fed a hypercholesterolemic diet containing cholesterol, hydrogenated coconut oil and cellulose, had higher plasma triglyceride concentrations. Further, consumption either high or reduced molecular weight β-glucan increased concentrations of

fecal total neutral sterols and coprostanol, a cholesterol derivative. Studies with male Wistar rats indicated that diet enriched with dietary fibre of barley decreased the atherogenic index and cholesterol level compared with the control diet whereas the use of the azoxymethane as colon-specific carcinogen substance induced a significant increase of liver lipid, serum LDL and triglyceride concentrations, but it caused a significant reduction of HDL (Lahouar et al. 2011).

Supplementation of hamster high-fat diet with single grain breads including whole grain wheat, barley, barley supplemented with hydroxypropyl methylcellulose (HPMC), debranned oat, and oat supplemented with HPMC breads significantly lowered plasma LDL-cholesterol concentrations compared to the control (Kim et al. 2011). Enrichment with HPMC further lowered plasma and hepatic cholesterol concentrations. Enrichment with HPMC further lowered plasma and hepatic cholesterol concentrations. Despite the reduced molecular weight of naturally occurring soluble β-glucan caused by the bread-making process, whole grain barley breads suppressed hepatic expression of CYP7A1 and HMG-CoAR genes responsible for bile acid and cholesterol synthesis, suggesting a possible role of bioactive compounds such as short-chain fatty acids and phenolic compounds from barley bread. Barley bread enriched with HPMC also inhibted expression of ABCG5 gene. The results suggested that distinctive modulation of synthesis and excretion of hepatic cholesterol and bile acid contributed to the cholesterol-lowering properties of whole grain barley breads and breads enriched with HPMC; this HPMC may provide consumers with a staple food that can assist in cholesterol management. They further found that HPMC increased the loaf volume of the breads by up to two times and decreased hardness immediately after baking and after up to 3 days of storage. Barley bread with HPMC was rated the highest in overall acceptability by sensory panelists compared to oat and wheat breads with or without HPMC (Kim and Yokoyama 2011). HPMC had also been used for decades in gluten-free breads at a level to optimize loaf volume.

Recent studies showed that C57BL/6 J mice fed a high-fat diet containing barley for 7 weeks had significantly reduced LDL cholesterol concentrations and elevated faecal cholesterol and bile acid (Hoang et al. 2011). The hypocholesterolemic effects of barley was found to be chiefly attributable to reduced dietary cholesterol uptake and bile acid resorption. It was also found that reduced expression of intestinal apical sodium-dependent bile acid transporter (ASBT) and Niemann-Pick C1-Like 1 (NPC1L1) gene may play a key role in the regulation of dietary cholesterol and bile acid metabolism in mice consuming a diet containing barley.

Clinical Studies

Studies by McIntosh et al. (1991) found that barley dietary fibre was more effective than wheat dietary fibre at lowering blood cholesterol in hypercholesterolemic men. Consumption of barley relative to wheat foods was associated with a significant fall in both plasma total cholesterol (6%) and in low-density-lipoprotein cholesterol (7%) whereas triglyceride and glucose concentrations did not change significantly. Barley contains β-glucan as a source of soluble dietary fibre (DF) whereas wheat contains the largely insoluble cellulose and hemicellulose fibre. Studies in moderately hypercholesterolemic men (28–62 years) showed that increasing soluble fibre through consumption of barley in a healthy diet significantly reduced total cholesterol and LDL cholesterol thereby reducing cardiovascular risk factors (Behall et al. 2004b). Similar results were found in another study of mildly hypercholesterolemic subjects (nine postmenopausal women, nine premenopausal women, and seven men) where the addition of barley rich in β-glucan to a healthy diet was effective in lowering total and LDL cholesterol in both men and women (Behall et al. 2004a). Yu et al. (2002a) found that daily supplementation of diabetic patients for 4 weeks with barley leaf extract may help to scavenge oxygen free radicals, increase the LDL-vitamin E content, and inhibit LDL oxidation. They found that, the addition of vitamins C and E to BL can inhibit small, dense LDL oxidation more effectively, which may protect against

vascular diseases in type 2 diabetic patients. In another study of hyperlipidemic patients, smokers and non-smokers, Yu et al. (2004) found that supplementation with young barley leaf extract or adlay (*Coix lacryma-jobi*) decreased plasma total and LDL-cholesterol (LDL-C) and inhibited LDL oxidation. Young barley leaf extract exerted stronger antioxidative effect on the prevention of LDL oxidation than adlay. The results also indicated that the antioxidative effect was less pronounced in smokers than in non-smokers. However, in a randomised single-blinded, crossover, 2×4-week study of 18 mildly hyperlipidemic men, the effect of β-glucan-enriched barley on lipid profile was highly variable between subjects, and there was no evidence of a clinically significant improvement in cardiovascular disease risk across this group of mildly hyperlipidemic men (Keogh et al. 2003). In a randomized single blinded crossover study of 14 healthy women, Keogh et al. (2007) found that inclusion of an ingredient containing increased soluble fibre and amylose (barley) did not reduce spontaneous food intake but rather was associated with higher subsequent energy intakes despite its reduced glycaemic and insulinemic effects.

Talati et al. (2009) found in their analysis of eight randomized controlled trials of 4–12 weeks' duration, the use of barley significantly lowered total cholesterol (weighted mean difference [WMD],−13.38 mg/dL; 95% CI,−18.46 to −8.31 mg/dL), low-density lipoprotein (LDL) cholesterol (WMD,−10.02 mg/dL; 95% CI,−14.03 to −6.00 mg/dL) and triglycerides (WMD, −11.83 mg/dL; 95% CI,−20.12 to −3.55 mg/dL) but did not appear to significantly alter high-density lipoprotein (HDL) cholesterol. In a meta-analysis of 11 eligible randomized clinical trials published from 1989 to 2008, consumption of barley and β-glucan isolated from barley lowered total and low-density lipoprotein (LDL) cholesterol concentrations compared with control (AbuMweis et al. 2010). There were no significant subgroup differences by type of intervention and food matrix. In an earlier randomized, double-blinded, placebo-controlled intervention study of 44 hypercholesterolemic Japanese men with a body mass index (BMI) >22 kg/m^2, consumption of pearl barley with a high β-glucan content was found to reduce not only serum LDL-C but also visceral fat area (Shimizu et al. 2008). In a 6-week randomized study of hypercholesterolemic men and women, supplementation with isolated barley β-glucans of different molecular weights did alter effects on body weight with the high-molecular weight fibre significantly decreasing body weight (Smith et al. 2008). However effects on cardiovascular disease markers were small.

The meta-analysis of 126 clinical studies from 30 research articles by Tiwari and Cummins (2011) revealed that consumption of 3 g/day of oat or barley β-glucan was sufficient to decrease blood cholesterol, low-density lipoprotein and triglyceride/triacylglycerol levels whereas the effect on blood glucose level was still inconclusive, with high heterogeneity, and required further clinical research studies with longer intervention periods. An increase in high-density lipoprotein cholesterol was found with the random-effect model.

Antidiabetic Activity

Animal Studies

Studies in Goto-Kakizaki (GK) rats demonstrated that barley enabled glycemic control and improved glucose tolerance compared with rice or alpha-corn starch (Li et al. 2003). After 3 months feeding fasting plasma glucose, plasma cholesterol and triglyceride levels in the high dietary fibre barley group were significantly lower than in the rice or corn starch groups. Glucose tolerance in the high barley group was markedly improved.

Results of a comparative study on the effects of malted barley extract (MBE) and banaba (*Lagerstroemia speciosa*, a diabetic herbal) extract on blood glucose levels in genetically diabetic mice (C57BL/KsJ(−) m (+/+) Lepr (db)) demonstrated that malted barley extract alleviated many of the symptoms of diabetes in genetically obese mice and may offer promise as a therapeutic supplement for the normalization of blood glucose levels in humans with hyperglycemia and have beneficial

effects in patients with non-insulin-dependent diabetes mellitus (Hong and Jai Maeng 2004). Fasting blood glucose was significantly lower in the MBE group compared with the control. Hemoglobin A1c content was significantly lower in the MBE group compared with either the control or banaba group. The glucose-6-phosphatase activity in kidney was significantly lower in both the MBE and banaba groups compared with the control group, but there was no significant difference between the MBE and banaba groups. There was no significant difference in the serum insulin level among groups. Studies demonstrated that diabetes onset was delayed and diabetes incidence was significantly reduced in female mice that received the wheat and barley protein-free diet throughout life (45% by age 32 weeks vs. 88% in control mice), from weaning (42%), or from 3 to 10 weeks of age only (36%), and diabetes development was not completely restored by gliadin supplementation of the wheat and barley protein-free diet (58%) (Schmid et al. 2004). Insulin autoantibodies and insulitis scores were reduced, and intra-pancreatic IL-4 mRNA increased in wheat and barley protein-deprived mice. Diabetes incidence was neither reduced by fish-oil or vitamin D3 supplementation alone, nor in mice fed a wheat and barley protein-free diet that was supplemented with fish-oil and vitamin D3. The results supported a link between dietary wheat and barley proteins and the development of autoimmune diabetes.

Clinical Studies

Shukla et al. (1991) found that the glycaemic response to barley was significantly lower than that to white bread in both healthy and non-insulin-dependent diabetes mellitus (NIDDM) subjects. But the insulinaemic response to barley was significantly lower than that to white bread only in healthy subjects. In NIDDM subjects, there was a tendency for the response to barley to be higher than that to white bread 0.5 h after ingestion. For maize, none of the variables examined was significantly different as compared to white bread. The glycaemic response to bajra (*Pennisetum typhoideum*) was significantly lower than that to white bread in healthy subjects, but the two responses were indistinguishable in NIDDM subjects. Barley, with a low glycaemic index (68.7 in healthy and 53.4 in NIDDM subjects) and a high insulinaemic index (105.2) in NIDDM subjects appeared to mobilize insulin in NIDDM making it a specially suitable cereal for diabetes mellitus.

All barley products of Glacier genotype with different amylose-amylopectin ratios (7–44% amylose) elicited lower postprandial glycemic and insulinemic responses and higher satiety scores when compared with white wheat bread in normal subjects (Granfeldt et al. 1994). The lente behavior of the boiled flours was probably attributable to the viscous properties of the β-glucans. However, the boiled flours produced higher glucose and insulin responses than did the corresponding boiled kernels. The impact of amylose: amylopectin on the metabolic responses was marginal. The high-amylose products released starch more slowly from a dialysis tubing during enzymic incubation of chewed samples compared with the corresponding products with less amylose. The in-vitro resistant starch content ranged from 0.4% in waxy to 5.6% in the high-amylose flour product (starch basis). In a study of nine healthy subjects, common oat and barley porridges produced postprandial glucose and insulin responses similar to the white wheat bread reference, suggesting that the naturally occurring dietary fibre in these whole-meal flours had no impact on the glucose tolerance (Liljeberg et al. 1996). In contrast, all high fibre barley products induced significantly lower responses than did the reference product, with the glycemic and insulin indices ranging from 57 to 72 or 42 to 72%, respectively. The results suggested that products based on a high fiber barley genotype, can be used as a potential component of diets for patients with diabetes and hyperlipidemia, and for individuals predisposed to metabolic disease.

Studies in 11 healthy men showed that carbohydrate was more slowly absorbed from the two high-fibre meals prepared from two types of barley flour: barley naturally high in β-glucan and the other a flour enriched in β-glucan during processing (Bourdon et al. 1999). Plasma glucose and insulin concentrations increased significantly after all meals but the insulin response was more

blunted after the barley-containing meals. Cholecystokinin remained elevated for a longer time after the barley-containing meals. Consumption of the barley-containing meals appeared to stimulate reverse cholesterol transport, which may contribute to the cholesterol-lowering ability of barley. The results confirmed the premise that when fibre sources containing viscous polysaccharides were included in a meal, a slower rate of carbohydrate and lipid absorption will modify the alimentary hormone and lipid responses.

In a study of ten healthy volunteers, breakfast products prepared from barley flour enriched with β-glucan exhibited favourable responses on glucose metabolism, and particularly on insulinemic responses (Casiraghi et al. 2006). In general, cookies responded better to the addition of barley fiber than crackers. Individual glycemic index values were 78, 81, 49 and 34 for whole-wheat crackers, whole-wheat cookies, barley crackers and barley cookies respectively. Insulin curves were significantly different both between type of processing and fiber source and insulin indices were different between fiber but not between processing. Retinyl-palmitate and triacylglycerol daily profiles were not significantly different between the factors studied. The results highlighted the complexity of the effect that barley fiber may exert when added to different food products in reducing postprandial metabolic responses. Another study with 15 healthy volunteers showed improved glucose tolerance (lower blood glucose response) at breakfast, following an evening meal with barley kernels appeared to emanate from suppression of plasma free fatty acid levels, mediated by colonic fermentation of the specific indigestible carbohydrates present in barley kernels, or, to the combination of the low-GI features and colonic fermentation (Nilsson et al. 2006). In a separate study of 18 lean, healthy men, supplementation of a high-carbohydrate starchy breakfast with barley β-glucan was found to improve postprandial glycaemic and insulinaemic response of the meal probably due to increased gastro-intestinal viscosity, but not when added to a high-carbohydrate beverage where rapid absorption combined with decreased β-glucan concentration and viscosity may obviate this mechanism (Poppitt et al. 2007). The high-carbohydrate breakfasts decreased total, LDL- and HDL-cholesterol from baseline to 60 min postprandially but there were no differential effects of β-glucan treatment on circulating lipids.

Rendell et al. (2005) compared Prowashonupana (Prowash), a shrunken-endosperm, short awn, waxy starch, hulless barley with low starch, high fibre, high protein, and a relatively high concentration of free sugars with oatmeal on glycemic response in diabetic and non-diabetic subjects. Following ingestion of Prowash a substantial reduction of the post-prandial glycemic peak was observed compared to LMR (a commercial liquid meal replacer) or oatmeal. In the non-diabetic subjects, the maximal rise in glucose from baseline was 26.3 mg/dL after LMR, 41.3 mg/dL after oatmeal and 6.4 mg/dL after Prowash. The maximal increase in glucose in the diabetic patients was 69.9 mg/dL after LMR, 80.8 mg/dL after oatmeal and 28.4 mg/dL after Prowash. The maximal increase in insulin post-LMR was 33.9 mIU/mL in the diabetic patients and 54.0 mIU/mL in the non-diabetic controls. Oatmeal elicited a maximal insulin increase of 29.9 mIU/mL in the control subjects and 21.4 mIU/mL in the diabetic patients. In contrast, the maximal insulin increase after Prowash was 8.6 mIU/mL in the non-diabetic controls and 6.8 mIU/mL in the diabetic patients.

In a study of 13 healthy volunteers, peak glucose response was lowest after the tempe meal with high-amylose/high-ss-glucan barley tempe while insulin response was lowest after the meal with high β-glucan oat tempe (Alminger and Eklund-Jonsson 2008). The calculated glycemic index for barley and oat tempe were 30 and 63, respectively. The calculated insulin index was lower for oat tempe (21) compared with barley tempe (55). The results suggest that cereal products with beneficial influence on postprandial plasma glucose and insulin responses can be tailored by fermentation and enclosure of high-amylose and/or high-β-glucan barley and oat kernels. In a randomized, single-blind, controlled crossover trial, eight healthy human subjects,

consumption of chapatis (unleavened Indian flatbread) containing high-molecular-weight barley β-glucan at doses of 4 and 8 g per serving significantly reduced postprandial blood glucose at 45 min (Thondre and Henry 2009). The glycemic index (GI) values of chapatis with 4 and 8 g β-glucan were 43 to 47% lower (GI, 30 and 29, respectively) compared with chapatis without β-glucan (GI, 54). In a study of the postprandial glycemic response and glycemic index (GI) of spaghetti made with semolina and the addition of two β-glucan barley concentrates, Glucagel (GG) and Barley Balance (BB), the BB concentrate was found to significantly decrease the incremental areas under the curve (IAUC) and GI of spaghetti at a dose of 10% (chillo et al. 2011). The GI of 10% BB spaghetti was 54% lower (GI = 29) than that of the control (GI = 64).

In two separate non-blind randomised crossover trials of human subjects, Thondre et al. (2012) found that the glycaemic response to both barley porridges with varying dietary fibre content was significantly lower than the reference glucose. There was no significant difference between the glucose areas under the curve or glycaemic index for the two barley porridges. They concluded that that irrespective of the difference in total fibre content or serving size of barley porridges, their glycaemic index values did not differ significantly.

Anticancer Activity

The proliferation of Caco-2 colorectal adenocarcinoma cells was significantly inhibited in a dose-dependent fashion in the presence of all aqueous methanolic barley kernel extracts tested at the end of the day 4 of incubation (Madhujith and Shahidi 2007). At the end of day 4, barley extracts rendered 29.3–51.2 and 9.3–15.9% inhibition of cell proliferation at 0.5 and 0.05 mg/mL, respectively. Jeong et al. (2009) found 3, 4-dihydroxybenzaldehyde purified from barley seeds to scavenge DPPH radical, hydroxyl radical and intracellular ROS as evaluated by DPPH radical and hydroxyl radical scavenging assay, Fe(2+) chelating assay, and intracellular ROS (reactive oxygen species) scavenging assay by DCFDA (dichlorofluorescin diacetate). In in-vitro oxidative DNA damage assay and the expression level of phospho-H2A.X, it inhibited oxidative DNA damage and its treatment decreased the expression level of phospho-H2A.X. In oxidative cell death and apoptosis assay, the treatment of 3,4-dihydroxybenzaldehyde attenuated H_2O_2-induced cell death and apoptosis. The results suggested that barley may exert the inhibitory effect on H_2O_2-induced tumour development by blocking H_2O_2-induced oxidative DNA damage, cell death and apoptosis.

Lunasin, a unique 43-amino acid peptide found in barley seeds, had been shown to be chemopreventive in mammalian cells and in a skin cancer mouse model (Jeong et al. 2010). Lunasin extracted from the kidney and liver of rats fed with lunasin-enriched barley inhibited the activities of HATs (histone acetyl transferases), yGCN5 by 20 and 18% at 100 nM, and PCAF (P300/CBP-associated factor) activity by 25 and 24% at 100 nM, confirming that the peptide was intact and bioactive. Purified barley lunasin was found localized in the nuclei of NIH 3 T3 (mouse embryonic fibroblast) cells. Barley lunasin added to NIH 3 T3 cells in the presence of the chemical carcinogen MCA (3-methylcholanthrene) activated the expression of tumor suppressors p21 and p15 by 45 and 47%, decreased cyclin D1 by 98%, and inhibited Rb hyperphosphorylation by 45% compared with the MCA treatment alone. The findings confirmed lunasin to be prevalent in barley, bioavailable, and bioactive and that consumption of barley could play an important role of cancer prevention in barley-consuming populations.

Barley-derived β-glucan with an average low molecular weight of 2 kDa (BBG-Low) appreciably induced the formation of mature dendritic cells from immature dendritic cells (Tanioka et al. 2011). The results suggested BBG-Low would be useful as a potent nontoxic immunostimulator and may be useful for preventing or even curing cancer.

Antiinflammatory Activity

Fractions obtained from a green barley extract commercialized as an antiinflammatory product under the name of "Natural SOD" were found to inhibit tumour necrosis factor alpha (TNF-alpha) production/release by an LPS-activated human monocytes line (THP–1). TNF-alpha plays an important role in inducing inflammation (Cremer et al. 1996). They demonstrated that the anti-inflammatory propery of "Natural SOD" was due to its high concentration of micromolecular substances with antioxidant and antiinflammatory properties, that were able to scavenge ROS and to suppress TNF alpha production, main inflammation mediators produced by specialised cells from peripheral blood and synovial fluid of patients with rheumatoid arthritis (Cremer et al. 1998). Giriwono et al. (2011) found that fermented barley extract (FBE) suppressed acute elevation in oxidative stress as a response to lipopolysaccharide (LPS)-induced inflammation. Rats supplemented with FBE for 10 days showed decreases in plasma interleukin (IL)-1β, IL-6, and tumour necrosis factor-α by 25, 34, and 35% respectively after LPS challenge. Liver damage was significantly reduced, as evidenced by a 44% decrease in plasma alanine aminotransferase. FBE supplementation sustained liver anti-oxidative enzymes, catalase, glutathione peroxidase, and superoxide dismutase, at transcriptional and enzymatic levels, thus suppressing oxidative stress markers such as plasma nitric oxide and 8-hydroxy-2′-deoxyguanosine, by 42 and 23% respectively. They concluded that active compounds in FBE effectively inhibited the propagation of inflammation by suppressing oxidative stress.

Hakkarainen et al. (1984) reported that full protection against nutritional encephalomalacia in chicks was obtained with a supplementation level of 7.5 mg DL-α-tocopheryl acetate/kg diet (= a total vitamin E content of 11.20 mg/kg diet) or with a supplement of 8.7 g barley oil/kg diet (= a total vitamin E content of 22.99 mg from barley oil/kg diet). This gave a biopotency factor of 0.49 for barley for prevention of nutritional encephalomalacia of the chicks, as compared to that of DL-α-tocopheryl acetate. The liver and plasma responses to the total vitamin E in the barley-oil diet compared with those of the DL-α-tocopheryl acetate reference diet gave identical values for the regression coefficients, i.e. in both liver-storage and plasma-storage assays the value for slopes of dose–response lines was 0.37. This indicated that the biopotency of the total vitamin E in barley was 37% of that of dietary DL-α-tocopheryl acetate and that barley was not as rich a source of vitamin E.

Anti-ulcerative Colitic Activity

Koh and Kim (2011) in their review of germinated barley foodstuff as prebiotics for the prevention of colitis-associated colon cancer stated that therapeutic strategies that modify intestinal microbiota, such as the use of probiotics, prebiotics, and/or synbiotics, have the potential for treating inflammatory bowel disease (IBD) patients and preventing colitis-associated colon cancer (CAC). IBD which includes Crohn′s disease and ulcerative colitis (UC) is a chronic and relapsing inflammatory disorder in the gut. They stressed that patients with long-standing IBD are at increased risk of developing colitis-associated colon cancer (CAC), and that IBD is generally accepted to be attributable to the interaction between genetic, microbial, and host immunological factors.

Kanauchi et al. (1998) found germinated barley foodstuff (GBF), derived from the aleurone and scutellum fractions of germinated barley, to be rich in glutamine and low-lignified hemicellulose, and increased mucosal protein, RNA, and DNA content in the intestine when fed to normal rats. In rats with colitis induced by dextran sulfate sodium (DSS), GBF and germinated seeds effectively prevented bloody diarrhoea and mucosal damage in colitis compared with controls and rats receiving sulfasalazine, a drug used to treat inflammatory bowel disease. However, non-germinated samples did not have a protective effect.

GBF increased mucosal protein and RNA content in the colitis model. Araki et al. (2000) demonstrated that plus *Clostridium butyricum* inhibited DSS-induced experimental colitis in rats. The combination of GBF plus *C. butyricum* most effectively prevented bloody diarrhoea and mucosal damage; and effectively increased faecal short-chain fatty acid (SCFA) levels. They found that GBF and GBF-fibre significantly attenuated the clinical signs of colitis and decreased serum alpha1-acid glycoprotein levels, with a significant increase in caecal butyrate production, while GBF-protein did not (Kanauchi et al. 2001). Also treatment with GBF alone and GBF plus salazosulfapyridine significantly accelerated colonic epithelial repair and improved clinical signs.

Germinated barley food-stuff (GBF) made from malt is an insoluble mixture of glutamine-rich protein and hemicellulose-rich dietary fibre and is also a prebiotic foodstuff as it effectively increases luminal butyrate production by stimulating the growth of protective bacteria. (Kanauchi et al. 2002). Prebiotics are "non-digestible food ingredient that beneficially affect the host by selectively stimulating the growth and/or activity of one, or a limited number of bacteria already resident in the gut, thus improving host health" (Lim et al. 2005). Prebiotics usually include such fermentable substrates as lactosucrose, fructo-oligosaccharides, inulin, and resistant starch. In contrast, probiotics are defined as "living, non-pathologic microorganism, usually *Lactobacilli* and *Bifidobacteria*, which exert a positive influence on host health and/or physiologic when digested" (O'Hara and Shanahan 2006). Kanauchi et al. (2002) showed in a 4-week multi-center open control trial with 18 patients with mildly to moderately active ulcerative colitis, GBF treatment significantly decreased clinical activity index scores compared with the control group. GBF therapy increased faecal concentrations of protective *Bifidobacterium* and *Eubacterium limosum*. The results supported the use of GBF treatment as a new adjunct therapy for ulcerative colitis.

Fukuda et al. (2002) compared the therapeutic efficacy of a prebiotic, GBF, with that of probiotics (mixture of *Lactobacillus* and *Clostridium butyricum*), and antibiotics (vancomycin, metronidazole) in an experimental colitis rat model induced by dextran sodium sulphate. They found that GBF treatment significantly reduced colonic inflammation as assessed by clinical scores with an increase in caecal butyrate levels. The probiotic treatment did not show such an effect. Both antibiotic treatments significantly attenuated clinical and pathological scores. However, in contrast to GBF, antibiotic treatment led to a significant decrease in caecal butyrate levels. The data suggested that modification of the intestinal microflora by prebiotics, including GBF, may serve as a useful adjunct in the treatment of ulcerative colitis as well as antibiotic treatment. Using an experimental model in which colitis was induced by transferring CD4 + CD54RB (High) T cells to SCID mice, GBF reduced inflammation by modulating the colonic mucosal immune system (Kanauchi et al. 2008b). Body-weight loss and occult blood were significantly reduced in the mice that had been fed with GBF. In these mice, there were also significant reductions in interferon-gamma mRNA expressions and interleukin IL-6 in the colonic mucosa, as compared with the control group. GBF also significantly ameliorated mucosal damage and mucin positive goblet cell depletion. In contrast, transforming growth factor-beta (TGF-beta) expression significantly increased in the GBF group, compared with the control group. They also showed that prebiotic treatment with GBF exhibited anti-tumorigenicity in rats with colonic cancer induced by azoxymethane (Kanauchi et al. 2008a). GBF treatment significantly decreased the number of aberrant crypt foci and beta-catenin formations in the colonic mucosa. GBF significantly increased the production of slc5a8, a tumour suppressor gene, as well as the caecal butyrate content and β-glucosidase activity. The number of heat shock protein (HSP) 25-positive cells in GBF group was higher than that in the control group.

More recently Komiyama et al. (2011) using DSS for the chronic and subacute colitis models,

found that in the chronic phase, no incidence of adenomatous dysplasia was found in GBF treated rats; the stratified squamous epithelium area of GBF was significantly lower than that of the controls. In contrast, dysplasia was confirmed only in the control group. GBF treatment significantly lowered the cecal succinate content and significantly elevated β-glucosidase activity compared to the controls. In the subacute phase, the mucosal damage score of GBF was significantly attenuated, and the proliferative cell nuclear antigen (PCNA) labeling index of the colonic mucosa in the GBF group was significantly higher than that of the control group. The results showed that GBF effectively prevented colitis-related dysplasia and inflammatory change in chronic and subacute colitis models by modulating the intestinal environment as a prebiotic and that GBF may contribute to the prevention of mucosal damage, with different proliferative effects on the epithelium in the regeneration and steady states.

Hair Growth Promoting Activity

Kamimura and Takahashi (2002) discovered intensive growth-promoting activity, about 140% relative to controls, in barley extract. From the LH-20 active aqueous methanol fraction, two major substances were identified, procyanidin B-3 and (+)-catechin. Purified procyanidin B-3 showed high hair-growing activity in the form of in-vitro hair epithelial cell growth-promoting activity and in-vivo anagen-inducing activity; however (+)-catechin showed no hair-growing activity. They found that addition of TGF-beta1 to hair epithelial cell cultures dose-dependently decreased the cell growth, and addition of procyanidin B-3 to the culture neutralized the growth-inhibiting effect of TGF-beta1. From these results, they concluded that procyanidin B-3 could directly promote hair epithelial cell growth in-vitro, possessing the potential to counteract the growth-inhibiting effect caused by TGF-beta1 in-vitro, and had potential to stimulate anagen induction in-vivo.

Antihyperuricemic Activity

In a randomized, placebo-controlled, parallel-group, double-blinded study of 111 subjects with serum uric acid levels of 6.0–7.9 mg/dl, after 12 weeks consumption of a fermented barley extract P prepared from barley-shochu distillery by-products, the serum uric acid levels changed by −0.21 mg/dl in the barley test group, showing a significant decrease in comparison to those of the placebo group (+0.02 mg/dl) (Hokazono et al. 2010). Additionally, the uric acid clearance in the barley test group showed a tendency to increase after 12 weeks more than in the placebo group. No abnormalities in the physical and clinical tests were observed, and no adverse diagnostic findings were attributed to the intake of the barley test meal. The results demonstrated the benefits and safety of the treatment to subjects with slightly high serum uric acid or mild hyperuricemia.

Antidepressant Activity

Oral administration of young green barley leaf to mice produced an antidepressant-like effect in the forced swimming test, reducing immobility duration compared to the vehicle group (Yamaura et al. 2010). Baley leaf induced a moderate decrease in the expression of mRNA for nerve growth factor, in a dose-dependent manner indicating that the antidepressant-like effects of the young green barley leaf were, at least in part, mediated by an inhibition of the increase in the hippocampus levels of nerve growth factor.

Adregenic Activity

Studies in animals (rats, dogs) showed that hordenine acted indirectly as an adregenic drug, stimulating the release of norepinephrine whilst increasing heart rate, systolic and diastolic blood pressure, peripheral blood flow volume and inhibiting gut movements (Hapke and Strathmann 1995). But it had no effect upon the psychomotorical behaviour of mice. All effects were short-lived.

Antimicrobial Activity

Papetti et al. (2007) showed that barley coffee (BC), a beverage made from roasted barley, interfered with cariogenic bacterium, *Streptococcus mutans* adsorption to hydroxyapatite. Fractionation of barley coffee yielded two fractions: <1,000 Da molecular mass (LMM) fraction, which contained polyphenols, zinc, and fluoride ions, and the >1,000 kDa MM fraction, which consisted of a potent brown antioxidant, melanoidin, both displayed antiadhesive properties. High-MM melanoidin was not detected in unroasted barley, indicating that it was formed during the roasting process. In further studies, they showed that barley coffee and its two fractions at concentrations ranging from 60 to 15 mg/mL that were devoid of antimicrobial activity, inhibited *S. mutans* biofilm formation (Stauder et al. 2010). Additionally barley coffee and its fractions exhibited anti-biofilm activity towards a variety of *S. mutans* clinical strains isolated from saliva, plaque and caries lesions of adult donors. The HMM melanoidin fraction was more active than the LMM fraction

Barley and Coeliac Disease

Anand et al. (1978) found that beside wheat gluten, barley and rye were also involved in causing coeliac disease but not maize and rice. Coeliac disease or celiac spru or gluten-sensitive enteropathy is a digestive disorder of the small intestine caused by intolerance of genetically susceptible individuals to the ingestion of gluten from wheat, barley, and rye (Ciclitira et al. 2001; Fraser and Ciclitira 2001; Fasano and Catassi 2001; Cárdenas and Kelly 2002). Gluten is a complex storage protein found in endosperm kernels of the above cereals. The sensitivity response is triggered by the prolamin fraction of the storage proteins: in wheat gliadins and glutenins, in barley the hordeins and the secalins in rye (Shewry et al. 1995; OECD 2004) which casues villous atrophy, damage to the mucosal lining of the small intestine. In celiac sufferers, the consumption of gluten can result in diarrhoea, malabsorption, steatorrhoea, anaemia, fatigue, osteopenia, nutritional and vitamin deficiencies complications of pregnancy and associated autoimmune diseases, such as insulin dependent diabetes mellitus, hypothyroidism (Fraser and Ciclitira 2001; Fasano and Catassi 2001; Cárdenas and Kelly 2002). Some sufferers may have only minimal changes in the epithelium and exhibit a milder constellation of symptoms such as abdominal discomfort, bloating, indigestion, or non-gastrointestinal symptoms (or no obvious symptoms at all).

The fundamental method of therapy gluten-sensitive celiac disease is strict lifelong adherence to a gluten-free diet (GFD) that eliminates protein cereal--gluten contained in wheat, rye and barley (Fasano and Catassi 2001; Cárdenas and Kelly 2002; Krums et al. 2011). For diarrhea and malabsorption syndrome adsorbents, astringents, enzymes, intestinal antiseptic and probiotics are used. Intravenous electrolyte mixture containing potassium, calcium and magnesium are employed for correction of metabolic disorders. To eliminate protein deficiency, drugs used solid protein mixture of pure amino acids, gluten-free mixes for enteral feeding.

Barley Allergy

Inhalation of barley flour can cause baker's asthma or barley grain dust, an occupational allergy. Occupational asthma due to barley grain dust, species *Hordeum vulgare* was reported in a man in Singapore (Yap et al. 1994). He developed immediate symptoms of sneezing, cough and dyspnoea on exposure to barley only. Bronchial provocation testing to the barley confirmed the diagnosis. A 50-year-old man developed bronchial asthma both after exposure to feeding stuffs and cereal flours and after ingestion of beverages made of cereal flours. Bronchial challenge tests with every allergen showed no response except for an immediate response to barley flour (Vidal and González-Quintela 1995). Glycosylated forms of proteins from the cereal trypsin/alpha amylase inhibitor family had been identified as major allergens associated with baker's asthma (Sanchez-Monge et al. 1992; Armentia et al. 1993).

The tetrameric alpha-amylase inhibitors CM16* (MW 16 kDa protein) from wheat and CMb* from barley were found to be the strongest allergens, and also the non-glycosylated, monomeric 14.5 kDa allergen, BMAI-1 from barley. Ingestion of barley may induce symptoms of food allergy in sensitive individuals especially children (Armentia et al. 2002). The most important allergens were wheat followed by barley and rye. Symptoms include gastrointestinal complaints, atopic dermatitis and analyphylaxis. Barley allgergens have been reported to cause atopic dermatitis in adult patients (Varjonen et al. 1994). Contact dermatitis and anaphylaxis can also be induced by barley proteins in beer. Two proteins barley protein Z(4) (45 kDa) and lipid transfer protein a (LTP1) (9 kDa) were identified as main allergens from a crude preparation of beer which gave positive sera and contact results in some sensitive individuals (Garcia-Casado et al. 2001). Barley pollen transcripts exhibted cross-reactivity with known allergen transcripts and therefore barley pollen may be a source of aeroallergenic proteins for individuals near agricultural sites (Astwood et al. 1995)

Traditional Medicinal Uses

Barley has been used as folk remedies for various ailments (Grieve 1971; Bown 1995; Chevallier 1996; Duke and Ayensu 1985). Barley grain is reported to be digestive, nutritive, febrifuge, diuretic, ecbolic, emollient, expectorant, febrifuge, and stomachic. Barley grain is demulcent and easily digestible, and used in dietary of babies, invalids and convalescents. Barley gruel is used to treat painful dyspepsia, Barley should not be administered to lactating mothers as it is antilactagogue, but is used to reduce excessive lacatation. Barley is also used as a poultice for burns and wounds. Barley is a useful folk therapy for bronchitis, coughs, burns, cancer, stomach tumours, catarrh, chilblains, cholecystosis, cholera, cough, debility, diarrhea, fever, inflammation, measles, phthisis, puerperium, sores, and urogenital ailments. Germinated seeds are demulcent, expectorant, galactofuge, lenitive, abortifacient, and stomachic and useful for infantile lacto-dyspepsia, regurgitation of milk and breast distension. Barley shoots are diuretic.

Other Uses

Globally up to 85% of barley produced is used for animal feed cattle (beef and dairy), swine and poultry (Bhatty 1999; Akar et al. 2004; OECD 2004). Barley is the principal feed grain in Canada, Europe, and in the northern United States The whole barley kernel is rolled, ground or flaked prior to being fed to improve digestibility (OECD 2004). Brewer's and distiller barley grians and sprouts from malting barley also have desirable protein content for animal diets (Akar et al. 2004). Hull-less barley may also be used as a feed for swines and poultry but not broilers (Bhatty 1999). However, arabinoxylans and beta-glucans in barley can have a deleterious effect on digestion in monogastric (OECD 2004). In addition, β-glucans are known to negatively impact poultry particularly young birds by reducing intestinal viscosity (Newman and Neman 1991).

In England, barley straw is placed in mesh bags and floated in fish ponds or water gardens to help reduce algal growth without harming pond plants and animals. A new stabilized variegated variety of *Hordeum vulgare*, called Hordeum vulgare varigate, has been introduced for cultivation as an ornamental and pot plant for pet cats to nibble on. Barley stems left after harvesting are a source of fibres for making paper, a biomass for fuel etc. and they can be shredded and used as a mulch.

Barley is also be used as a feed stock for fuel alcohol production. Studies showed that barley can be employed as a feedstock for bioethanol production and value-added products (Gibreel et al. 2009). A very high gravity (VHG) traditional fermentation approach utilizing jet-cooking fermentation revealed that both dehulled Bold and Xena barley varieties produced ethanol concentrations higher than that produced by wheat (12.3, 12.2, and 11.9%, respectively) but lower than that produced by corn (13.8%). VHG-modified Stargen-based fermentation of dehulled Bold

barley demonstrated comparable performance (14.3% ethanol) relative to corn (14.5%) and wheat (13.3%). The highest yield of phenolics was detected in dried distiller's grain with solubles (DDGS) of Xena (14.6 mg of gallic acid/g) and Bold (15.0 mg of gallic acid/g) when the hull was not removed before fermentation. The highest concentration of sterols in DDGS was found in Xena barley (3.9 mg/g) when the hull was included. The DDGS recovered from VHG jet-cooking fermentations of Fibar, dehulled Bold, and corn demonstrated similar levels of tocopherols and tocotrienols. The barley DDGS was the highest in in-vitro energy digestibility.

Comments

In barley, spikelets occur in alternating triplets along the rachis, when only the central spikelet is fertile, the two laterals ones are reduced producing two-row barley. When the two lateral and central spikelets are fertile as a result of mutation in a pair of genes, one dominant and the other recessive, six-row barley are formed.

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Oryza sativa

Scientific Name

***Oryza sativa* L.**

Synonyms

Oryza aristata Blanco nom. illeg., *Oryza communissima* Lour., *Oryza denudata* Steud. nom. nud., *Oryza elongata* Steud. nom. nud, *Oryza formosana* Masam.& Suzuki, *Oryza glutinosa* Lour., *Oryza marginata* Steud. nom. nud., *Oryza montana* Lour., *Oryza mutica* Steud. nom. nud., *Oryza nepalensis* G. Don ex Steud. nom. nud., *Oryza palustris* Salisb. nom. superfl., *Oryza parviflora* P. Beauv. nom. nud., *Oryza perennis* Moench, *Oryza plena* (Prain) N.P. Chowdhury, *Oryza praecox* Lour., *Oryza pubescens* Steud. nom. nud., *Oryza pumila* Steud. pro syn., *Oryza repens* Buch.-Ham. ex Steud. nom. nud., *Oryza rubribarbis* (Desv.) Steud., *Oryza sativa* f. *spontanea* Roshev., *Oryza sativa* subsp. *japonica* S. Kato, *Oryza sativa* var. *formosana* (Masam. & Suzuki) Yeh & Hendr., *Oryza sativa* var. *plena* Prain, *Oryza sativa* var. *rubribarbis* Desv., *Oryza sativa* var. *savannae* Körn., *Oryza segetalis* Russell ex Steud. nom. nud., *Oryza sorghoidea* Steud. nom. nud.

Family

Poaceae

Common/English Names

Asian Rice, Common Rice, Cultivated Rice, Rice, Lowland Rice, Paddy Rice, Upland Rice.

Vernacular Names

Afrikaans: Rys;
Albanian: Oriz;
Arabic: Al Ruzz, Arruzz, Arz, Barbar, Eruz, Ross, Urz;
Armenian: Brinz;
Brazil: Arroz;
Bulgarian: Oriz;
Burmese: Saba, Sabar-Bin;
China: Dao, Dao Zi (Seed), Gu Ya, Jīng Mǐ, Mi (Polished Rice), Nuo Dao Gen Xu, Shui Dao, Zhan Dao, Zhan Nian, Ya Zhou Zai Pei Dao;
Catalan: Arròs;
Croatian: Pirinač, Riža;
Czech: Rýže Seta;
Danish: Raa Ris, Ris, Uafskallet Ris;
Dutch: Padie, Rijst;
Eastonian: Harilik Riis;
Finnish: Kuorimaton Riisi, Gemeiner Reis, Paddy-Reis, Raakariisi, Reis, Riisi, Rohreis;
French: Riz, Riz Cargo, Riz Commun, Riz Cultivé, Riz Non Décortiqué, Riz De Plaine, Riz Paddy, Riz Vêtu;
German: Kultur-Reis, Reis;
Hungarian: Hántolatlan Rizs, Rizs;
Icelandic: Hrísgrjón;

T.K. Lim, *Edible Medicinal and Non-Medicinal Plants: Volume 5, Fruits*,
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India: Dhan (Assamese), Dhan (Bengali), Choka, Dangar (Gujarat), Caval, Chauval, Chaval, Dhan, Hal, Saal, Saatti, Sawal, Seal (Hindi), Akki, Batta, Battha, Bhatta, Bhattha, Nellu (Kannada), Ari, Navaranellu, Nellu (Malayalam), Phaou (Manipuri), Bhat, Pendha, Saala, Tandul, Tandula, Thandula (Marathi), Dhano (Oriya), Ahi, Bilvaja, Dhanya, Dhanyah, Garuda, Hima, Jiraka, Kacoraka, Kalama, Kalmasa, Kapinjala, Khanjarita, Magadhi, Mahasali, Nivara, Pita, Raktabhasali, Raktasali, Rukmavanti, Sali, Sastika, Saugandhi, Shali, Sukala, Tandula, Tandulam, Vara, Vilavasin, Vrihi (Sanskrit), Ari, Arici, Aricikkati, Arisee, Arishi, Arisi, Arshi, Cali, Cennel, Iyavam, Kalamam, Kalanippayir, Kalunir, Karunkuruvai Arici, Kati Nir, Nel, Nell, Nellu, Nerpori, Pacharisi, Risi Tantulam, Torai, Torai, Vai, Vari, Viriki, Viriki, Yavam (Tamil), Biyam, Biyyam, Cheni, Dhaanyamu, Dhanyamu, Errajilama, Errajilama Vadlu,Mattakaa,Mattakaaralu,Nevaridhaanyamu, Nevaridhanyamu, Pari, Urlu, Vadlu, Vari, Vudlu, Yerra Rajanaalu (Telugu), Biranj Sathi (Chawal), Chawal (Urdu);
Indonesia: Padi (General), Pari (Javanese), Pare (Sundanese);
Italian: Riso, Risone;
Japanese: Gemmai (Unpolished), Hakumai (White Polished), Ine, Raisu, Suitou,;
Khmer: Srö:W;
Korean: Bap;
Laos: Khauz;
Latvian: Risi;
Lithuanian: Ryžis (Singular), Ryžiai (Plural);
Macedonian: Oriz;
Malaysia: Padi (Unhusked Grain), Beras (Husked, Polished Grain), Nasi (Cooked Rice);
Maltese: Ross;
Nepalese: Caamal, Dhaan;
Norwegian: Ris;
Papaimento: Aros;
Papua New Guinea: Rais;
Persian: Biranj, Birinj, Darakhat-E-Shora;
Philippines: Parai (Bikol), Pagei (Bontok), Ammai (Ibanag), Pagai (Iloko), Ammai (Itogon), Pai (Sulu), Palai, Palay (Tagalog);
Polish: Ryż;
Portuguese: Arroz, Arroz Em Casca, Arroz Paddy;
Romanian: Orez;
Serbian: Pirinač;
Shona: Mupunga;
Slovašcina: Riž;
Slovencina: Ryža Siata;
Spanish: Arroz, Arroz Con Cáscara, Arroz Con Cáscara Asiático, Arroz Irrigado;
Swedish: Paddyris, Ris;
Thai: Khao Chow (Common rice), Khao Nyo (Glutinous Rice), Khao Puak (unhusked Grain), Khao San (Husked, Polished Grain);
Turkish: Pirinç;
Vietnamese: Cây Lúa, Gạo.

Origin/Distribution

A single-origin model suggested that two main subspecies of Asian rice, *Oryza sativa*, *indica* and *japonica*, were domesticated from the wild rice *Oryza rufipogon* (Oka and Morishima 1982). Results of recent studies using demographic modelling based on single nucleotide polymorphism data and a diffusion-based approach by a team from Stanford University, New York University, Washington University, and Purdue University provided conclusive evidence that domesticated rice had a single origin (Molina et al. 2011). Bayesian phylogenetic analyses implementing the multispecies coalescent and using previously published phylogenetic sequence datasets also indicated to a single origin of Asian domesticated rice. They dated the origin of rice domestication at about 8,200–13,500 years ago which was consistent with known archaeological data reported by Fuller et al. (2010) that suggested rice was first cultivated at around this time in the Yangtze Valley of China.

Today rice is cultivated in Europe, Africa, tropical and temperate Asia, Australia, and North and South America. World leading producers of paddy rice in descending order comprises: China 197,212,010MT, India, 120,620,000MT, Indonesia 66,411,500MT, Bangladesh 49,355,000 MT, Vietnam 39,988,900MT, Myanmar 33,204,500MT, Thailand 31,597,200MT, Philippines 15,771,700MT, Brazil 11,308,900Mt, USA 11, 027,000MT, Japan 10, 600,000MT and Cambodia 8,245,320MT (FAO 2012).

Agroecology

The cultivation of rice extends a as far north as 53°N in Moho, northern China and as far south as 35°S in New South Wales, Australia and from sea level to as high as 2,300 m up in the northwestern Himalayas. With the exception of cold tolerant cultivars that can withstand low temperatures of 12–15°C, rice generally is intolerant of such low temperatures. Night temperatures below 15°C have been reported to cause poor germination or death of seedlings, yellowing of leaves, low tiller number, degeneration of spikelets, high spikelet sterility, stunting, and poor panicle exsertion causing low grain yields. The optimum temperatures during the growing season range from 20 to 38°C and temperatures above 21°C are required for flower anthesis and pollination. Low soil and floodwater temperatures also affect the nutrition, growth and grain yield of rice.

Modern rice cultivars are photoperiod insensitive whilst traditional rice cultivars are generally photoperiod sensitive, and flower when day-lengths are short. Solar radiation is important during the flowering and ripening stages as such grain yields are higher during the dry season than wet season.

Water is the major limiting factor for growth of rice and rice is intolerant of desiccation. Upland rice is usually grown as rainfed crop and requires at least 750 mm rainfall during the 3–4 months growth period. Lowland rice are usually grown in flats, river and delta basins (Plate 1). Irrigated rice needs about 1,200 mm rainfall per crop or 200 mm per month.

Rice can be grown in dry soil or puddled soil and cultivated like an upland crop (Plate 4), or in inundated soils. Rice can be grown on sandy to clayey soils with 1–50% organic matter content pH 3–10, nil to 1% salt content and nutrient availability from acute deficiencies to surplus. Rice thrives best in heavy soil and optimum 1 pH of 6.5–7 in flooded soil.

Edible Plant Parts and Uses

Rice is the main staple food of 40% of the world population and the main food throughout South-East Asia. After being harvested, rice is de-husked to remove the inedible hull. The resulting grains are usually eaten as white, polished rice from which the bran has been removed. Brown rice is the whole, unpolished grain with both the bran and germ intact and with outer husk removed. Whole "brown" rice is mainly popular as a "health food" in western countries. Rice is most often consumed as whole grains, boiled or steamed in water or it can be processed into flour. Rice is eaten with other food dishes – vegetables, pulses, meat and sea food. Rice flour lacks gluten and so is usually consumed as noodles and not bread, as the absence of gluten results in poor quality bread. Rice flour is used for breakfast foods, meat products, baby foods, bread and cake mixes, and cosmetics. Rice cultivars with starch high in amylopectin and with low, negligible or no amylose, are waxy or glutinous, and are used industrially as a thickening agent for sauces and puddings, and in eastern Asia for snack foods, such as rice crackers, cakes and desserts. Glutinous rice is also called sticky rice, sweet rice, waxy rice, pearl rice, botan rice, biroin chal, mochi rice, *nuòmǐ* (Mandarin), *chi̍t-bí* (Hokkien), *kao hnyin* (Burmese), and *pulut* (Malay). Glutinous rice does not contain dietary gluten and can be used in gluten-free diets. Glutinous rice can be used either milled or unmilled. Milled glutinous rice is white in color and fully opaque (unlike non-glutinous rice varieties, which are somewhat translucent when raw), whereas the bran can give unmilled glutinous rice a purple, brownish-red or black color.

Plate 1 Ripening padi in lowland padi field

Rice is consumed in a diverse array of food products.

Sushi is a Japanese food consisting of cooked vinegared short-grained glutinous rice (*shari*) combined with other ingredients (*neta*) such as seafood (fish, tuna, shrimp, seafood stick), omelette, seaweed (*nori*), cucumber, radish, parsley, avocado, thinly sliced carrot, tofu and soy paper. The most well-known and popular type of sushi is *makizushi* or rolled sushi, a cylindrical piece, formed with the help of a bamboo mat, called a *makisu.* Other types of sushi include *futomaki*, thick rolls; *hosomaki* thin rolls, *temaki* cone-shaped hand rolls; *Oshizushi* pressed sushi and *narezushi* fermented sushi.

Rice Noodles

Rice noodles are very popular in east and southeast Asian cuisines. Rice noodles are generally made from rice flour and water as the main ingredients; they do not contain egg as such are also vegan. One well-known rice noodle is the broad 5–10 mm by 10–15 mm long opaque, white strips sliced from 2 to 3 mm sheets of rice cake called *shahe fen, he fen* in Mandarin, or *ho fen, ho fun* in Cantonese or *kway teow* in Hokkien or Teochew or *guotiao* in Pinyin; *guay tiew sen yai* in Thai, *Bánh canh* in Vietnamese, *kwetiau* in Indonesia and *da fen* in Sabah. *Kway teow* is made famous in the dish called char *Kway teow* – rice noodles fried with chicken, beef, prawns, thin slices of Chinese sausages (*lup cheong*) or with cockles, garlic, eggs and bean sprouts in thick dark soya sauce. *Kway teow* is also prepared in various rice noodle soups such as the famous Vetnamese *phở* served with beef called *phở bò*, or with chicken called *phở gà* in a tasty stock soup, garnished and eaten with bean sprouts, basil, mint and chilli. Steamed rice noodle rolls called *chee cheong fun* (literally pig intestine noodles) are very popular in southern China, Singapore and Malaysia. They are made from a broad sheet of rice cake, filled with shrimps, pork, beef, strips of mushroom or vegetable, rolled into a cylinder and steamed. Steamed rice noodle rolls are commonly served as a dish in *Dim Sum*. Another popular rice noodle is the thin (1–2 mm) strips of rice noodles called vermicelli, sold usually dried as rice sticks and hydrated before use. Rice vermicelli is used in soup dishes, laksa, stir fries noodles, or in salads. Rice vermicelli is called *mi fun* in Cantonese, *bihun* in Hokkein or Malay, *senmee* (Thai), *bún* (Vietnamese), *bihon*, *bijon*, (Tagalog) and *sevai* (Tamil). Another less common type of Chinese rice noodles is *lǎo shǔ fěn* (literally rat's noodle) or *loh shu fun* (Cantonese) or silver needle noodle or short rice noodle. This noodle is short, about 3 cm long and 3–5 mm in diameter with tapering ends and semi-transparent. This noodle type is usually eaten in noodle soups or in *kon-lon* type a semi-dry noodle dish with a marinated meat and gravy sauce. *Khanom chin* is a special Thai rice noodle made from fermented rice flour. In southern India and Sri Lanka, string rice hoppers, very thin strips of rice noodles called *Idiyappam*, *noolappam* or *noolputtu* are very popular. String hoppers are generally served as the main course at breakfast with curry or brown palm sugar or dinner together with a curry (potato, egg, fish or meat curry). In Malaysia, string hoppers are called *puttu mayam*. Pasta can be made from brown rice as an alternative to wheat flour for individuals with gluten intolerance.

Rice Cakes, Dumplings

Rice, both glutinous and non-glutinous, in the form of whole grains, ground rice or flour can be made into various types of cakes and dumplings.

Zongji is a Chinese dumpling made of glutinous rice and sweet or savoury meat or vegetarian (chopped Chinese mushrooms, and/or beans) fillings wrapped in bamboo leaves which is then steamed. Zonji is especially eaten during the Double Fifth, *Tuen Ng* (Cantonese), *Duānwǔ Jié* (Mandarin) or Dragon Boat Festival on the fifth day of the fifth month in the Lunar calendar. *nuòmǐ fàn* is steamed glutinous rice cooked with thin slices of chinese sausage (*lup cheong*), chopped shitake mushroom, chopped barbecue pork, dried shrimp or scallop and wrapped in lotus leaf. This is served as a dim-sum dish in Honk Kong, Malaysia, Singapore and in Chinese

restaurants all over the world. Another variant of the *No mai gai*, another dim sum dish of glutinous rice, chopped chinese mushroom and marinated boneless chicken pieces wrapped in lotus leaf and steamed. Yet another variation is the *Ba bao fan* or eight treasure rice', a dessert made of glutinous rice, mixed with lard and eight kinds of fruit or nuts and steamed. *Tāngyuán* (Mandarin) or *Tong yuen* (Cantonese) is small round dumpling white or red coloured balls made from glutinous rice flour eaten in a sweet, plain or savoury soup during the Lunar New year festival, Lantern festival or on auspicious occasions such as birthdays. *Nian gao* or Year cake is a Chine rice cake made from glutinous rice pounded and grounded into a paste, eaten especially during the Lunar New year festivities. *Nian gao* can also be sliced and stir fried as a savoury dish with ingredients like beef, pork, sacllions and cabbage. *Erkaui* is kind of rice cake, eaten as stir-fry with red chillies, szechuan pepper and salt, and is a common street food in the Yunnan Province in southwest China.

Mochi is a Japanese rice cake made of glutinous rice pounded into paste and moulded into the desired shape. *Mochi* is a traditional treat during the Japanese New year, but is also eaten year round. *Senbei* is a type of flat Japanese pancake cooked by baking or grill. It comes in various shapes and sizes and is often eaten with green tea. In Korea, there are different types of rice cakes, *tteok*, made from glutnous rice flour. *Tteok guk* or *tteok* soup is eaten on New Year's day and sweet *tteok* eaten on birthdaysand weddings. *Tteok* can be eaten steamed, boiled, pounded or pan-fried. There is white rice cake (*hintteok*), steamed rice cake (*sirutteok*), rice cake coated with bean (adzuki or mung bean) powder (*injeolmi*), rice cake steamed on a layer of pine needles (*songpyeon*), flower shaped rice cake, pan-fried rice cake (*juak*), rice cake with honey or Korean syrup (*ggul tteok*), small sweet pancakes made of glutinous rice flour, and flower petals of Korean azalea, chrysanthemum, or rose (*hwajeon*) and dumpling coated with bean paste (*gyeongda*n). In Vietnam, there is *bánh bèo* is a variety of small steamed rice cake or rice pancake with savoury ingredients like chopped dried or fresh shrimp, scallions, mung bean paste, crispy fried shallots, fish sauce, rice vinegar, and oil; bánh bò a sweet, chewy sponge cake made from rice flour, water, sugar, and yeast; *bánh đúc* a cake made from non-glutinous rice flour garnished with savoury ingredients or served as a dessert in the form of gelatinous blocks that are often colored green by the addition of *Pandanus amaryllifolius* leaf extract and *bánh chưng* made from glutinous rice, mung bean, pork and other ingredients.

In the Philippines, rice cakes are commonly made with coconut milk; *suman* made from glutinous rice and coconut milk steamed in banana leaves; *sapin-sapin* a layered glutinous rice and coconut dessert; *bibingka* rice cake made with rice flour and coconut milk or water and lined with banana leaves, baked in an clay pot oven or preheated charcoal; *espanol* made from rice flour cooked in coconut milk and sweetened coconut strips. In India, *pitha* is usually a thin-flat cake prepared from a batter made with soaked and ground rice; fried in oil, roasted over a slow fire or baked and rolled over a hot plate once made. *Pithas* may also have various stuffings. *Idli*, a southern cake made by steaming fermented batter of black lentils and rice; *puttu* another southern Indian dish made of firm cylinders of steamed ground rice with layers of coconut and *puto*, steamed rice cake eaten alone or with butter and/or garted coconut.

In Malaysia and Singapore steamed rice cake called *chwee kueh* made from rice flour, is eaten topped with savoury radish and chilli sauce. In Malaysia, Singapore, Indonesia and Brunei, there is the popular lontong, made of compressed rice rolled in banana leaves and cooked that is then cut into small cakes served with gado-gado, satay or curries. Also, a type of rice dumpling called ketupat, rice contained a rhomboid shaped pouch emade from young coconut palm fronds and cooked. Ketupat is always eaten with beef or chicken satay and a spicy, sweetisdh peanut sauce or beef *rendang*. It is traditionally served by Malays at open houses on festive occasions such Hari Raya (Aldi Fitri). Puffed rice cakes, popular in North America and other Western countries, are made with puffed rice. *Rijsttaart* and *Rijstevlaai* are kinds of rice pie in Dutch and

Belgian cuisine, with the filling of mixed rice, sugar, eggs and milk. Italy has *torte di riso* rice cakes sometimes eaten as a substantial dessert at the end of a meal.

Rice Porridge (Congees), Puddings

In East and south-east Asia, rice porridge is often synonymous with rice congee, made by boiling whole rice grains in water. They can be served in thick or semi-liquid consistency or as gruel (watery, light porridge). Congee is often eaten as a breakfast meal but also as supper or lunch. Congee may be eaten plain or served with side dishes that include salted fish, salted duck egg, century egg, *zhacai* or *cha tsoi* (pickled mustard) dried anchovies, pickled cucumber, dace (Chinese carp), cooked bamboo shoots, pickled fermented vegetable, fried peanuts, toufu, wheat gluten, *youtiao* (*You char kway*) or Chinese oil stick or fried bread stick, lettuce, vegetables, meat and other condiments (fried onions, pepper, sesame seed, soy sauce or sesame oil). Congee is also prepared as meat congee where small chopped meat pieces (chicken, pork, marinated pork intestines, shrimp or fish) with or without peanuts are boiled together with the rice. Culture also often dictates the way congee is cooked and eaten. Congee has different appellations in various Asian cultures, it is also called *kanji* (Tamil/Tulu), *kaÐni* (Malayalam), *pakhal bhat* (Oriya), *ganji* (Kannada/Telugu), *juk* (Cantonese, Korean), *moe* (Hokkien and Teochew), *zhou* (Mandarin), *cháo* (Vietnamese), *deythuk* (Tibetan), *chok* (Thai), *kayu* (Japanese), *lúgaw* (Filipino), *Bubur* or *kanji* (Malay) or *jaou* (Bengali). In the Nordic countries, rice porridge cooked in milk is a common breakfast, and sometimes dinner. When served, it is commonly sprinkled with cinnamon and sugar and served with milk. Cold rice porridge is mixed with whipped cream and something sweet such as strawberry, cherry or raspberry sauce and served as rice cream dessert. Other ingredients such as orange, vanilla and chopped almond are often added.

Rice pudding is a dish made from rice mixed with water coconut milk or milk (whole, condensed or evaporated) and sometimes other ingredients such as cinnamon, vanilla, lemon/orange rind, raisin, pistachio, honey brown or white sugar. Different variants are used for either desserts or dinners in different cultures. In Thailand there is *khao niao dam* (black rice pudding); banana rice pudding in Kampuchea; *pultu hitam* made from boiled black glutinous rice served with coconut milk in Malaysia, Brunei and Singapore, and called *ketan hitam* in Indonesia and tsamporado (chocolate rice pudding) in the Philippines. In Sri Lanka, there is kiribath rice pudding made with coconut milk; In India and Pakistan there is *kheer*, made with slow-boil milk. In India, *phirni/paayesh*, grounded basmati rice or parboiled rice, cardamom and pistachio, can be served hot or cold; *payasam* with slow-boiled milk, sugar/jaggery and lots of nuts and *dudhapak* with slow-boiled milk and sugar/basmati rice and lots of nuts and saffron. In the Middle east, there is the Kurdish *sorbeşîr* with saffron; Lebanese *moghli* with anise, caraway, and ginger; the Arabic *muhalibiyy*a with milk, rice flour, sugar, and rosewater and *shir-berenj*, *shoal-e-zard* (Tajik, Afghan and Iranian) rice puddings. In the United Kingdom, rice pudding is a popular, traditional dessert.

Rice Beverages

Rice is also processed into various types of non-alcoholic and alcoholic beverages. Rice water is a suspension of rice starch prepared by draining boiled rice or by boiling rice until it dissolves completely. *Hyeonmi cha*, is a Korean tisane made from roasted brown rice. In the East, there are three kinds of fermented rice beverages: beer, wine and a distilled spirit.

Rice wine is made from yeast fermentation of rice starch converted to sugars and alcohol. In Malaysia, rice wine called *beram* is made from the fermentation of glutinous rice inoculated with yeast in vats for several months. Rice wine is much used in Chinese cuisine and in other Asian cuisines. Amazke is a traditional sweet, low-alcohol or non-alcohol Japanese drink made from fermented rice. In China, there is *Ang jui*, red rice wine, popular among the Foo Chow ethnic group; *Chou jui*, a milkyglutinous rice wine popular in Xian, *Mi jui* a clear sweet rice wine from fermented glutinous rice and *Huang jui* (yellow or

brownish wine) made from fermented, non-glutinous rice. In the Philippines, there is *Kulapo*, a reddish rice wine strongly odoured and with a high alcohol content; *Tapuy*, a clear rice wine and *Pangasi* rice wine. In Korea, there is *Cheongju* and *Beopju* rice wine; gamju – a milky sweet wine and *Makgeolli* a milky traditional wine. In India there is *Sonti* rice wine, Bhutan has *Ara* rice wine, Nepal and Tibet have *Raksi* rice wine. Vietnamese rice wine, *Rượu cần* is drunk through long, thin bamboo tubes. In Myanmar, *Thi* rice wine is served in a clay pot with a straw to sip. Thailand has *Sato* rice wine, Laos has *Lao-lao*. *Brem* is a Balinese rice wine. In Malaysia, there is *Tuak*, a Dayak rice wine from Sarawak and from Sabah, *Liming*, a Kadazan rice wine and *Tapai*, a Kadazan-Dusun rice wine.

Rice beer is produce by brewing which involves steeping rice starch in water and fermenting with brewer' yeast to produce alcohol. There are several steps in the brewing process, which include malting, milling, mashing, lautering, boiling, fermenting, conditioning, filtering, and packaging. The most well known type of beer that uses rice as a main ingredient, the rice lager, also comes from Japan. The rice lagers produced by Kirin, Sapporo and Asahi are extremely popular throughout Japan, and at sushi restaurants globally. *Saké* or *saki* is a beer and not a wine as it is produced by means of a brewing process more like that of beer. In Malaysia rice beer or *badek* or *arak tapai* is made by boiling rice grains, spreading and sprinkling it with yeast and wrapping it in fresh leaves usually banana and keeping it moist. The arak tapai that drips from it is alcoholic and sweetish and the slightly fermented rice left from the making of the beer is used in food.

Rice spirit is an alcoholic beverage made from fermented rice by distillation to produce alcohol and not by brewing. They are called *arak* in Malaysia and Indonesia. *Awamor*i is an example of rice spirit produced in the southern islands of Okinawa. Thai Indica rice rather than short-grained Japonica rice are used. *Awamori* is an extremely robust drink, and can be 60% proof, with its alcohol content increasing with age. Other well known rice spirits are *baijiu* – Chinese distilled alcoholic beverage which is produced in southern China typically made from glutinous rice and from sorghum or other cereals elsewhere in China and Hmong rice spirit.

Botany

Annual grass, 50–130 cm tall, up to 5 m long in deep-water rices, forming small tufts (Plates 1, 2 and 3). Roots fibrous, arising from the base of the shoots. Stem (culm) erect to ascending, glabrous, composed of a series of nodes and internodes, the number depending on cultivar and growing season; each node with a single leaf, and sometimes also with a tiller or adventitious roots; internodes usually short at base of plant, progressively increasing towards top. Leaves in two ranks; sheaths initially enclosing each other, forming a pseudostem, later enclosing the internodes; ligule triangular to linear-lanceolate (Plates 1, 2 and 3),

Plate 2 Padi plants with ripe harvestable ears

Plate 3 Close –up of ripening padi ear

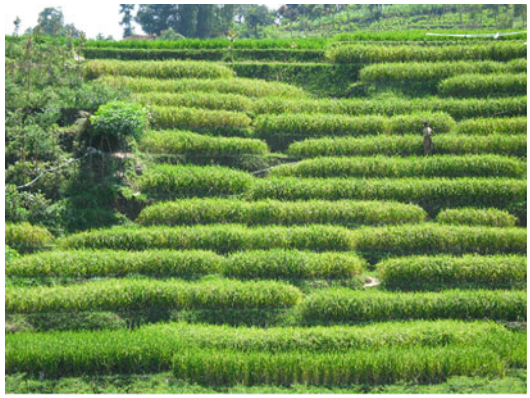

Plate 4 Terraced padi field on hill slopes

Plate 5 Harvested ripe padi ears

Plate 6 Glutinous short-grained Japonica rice variety

Plate 7 Wehani brown rice in Sabah

Plate 8 Bukit merah brown rice in Sabah

1–1.5 cm long, often split; auricles often present, falcate, 1–5 mm long, hairy; blade linear, 24–60 cm × 0.6–2.2 cm, glabrous, smooth to scabrous, often with spiny hairs on margin. Inflorescence a terminal panicle, 9–40 cm long, with 50–500 spikelets depending on the cultivar; spikelets single, borne on a short pedicel, oblong to lanceolate, 7–11 mm long, about 2–3 times longer than wide, containing a single bisexual flower, with two small glumes, a large, 6–10 mm long, boat-shaped lemma sometimes with an awn up to 15 cm long, and likewise palea with very short awn, six stamens, a broad ovary, and two plumose stigmas (Plates 1, 2, 3 and 5). Fruit (caryopsis, grain) varying in size, shape and colour, ovoid, ellipsoid or cylindrical, 5–7.5 mm × 2–3.5 mm, white, whitish-yellow, brown, reddish, fuscous or blackish-brown (Plates 6, 7, 8, 9, 10 and 11).

Nutritive/Medicinal Properties

Proximate nutrient composition of long-grained, regular, raw, unenriched white rice per 100 g edible portion had been reported as: water 11.62 g, energy 365 kcal (1,527 kJ), protein 7.13 g, total

Plate 9 Tadong brown-black rice in Sabah

Plate 10 Bukit Laun brown rice in Sabah

lipid 0.66 g, ash 0.64 g, carbohydrate79.95 g, total dietary fibre 1.3 g, total sugars 0.12 g, Ca 28 mg, Fe 0.80 mg, Mg 25 mg, P 115 mg, K 115 mg, Na 5 mg, Zn 1.09 mg, Cu 0.220 mg, Mn 1.088 mg, Se 15.1 µg, thiamin 0.070 mg, riboflavin 0.049 mg, niacin 1.600 mg, pantothenic acid 1.014 mg, vitamin B-6 0.164 mg, total folate 8 µg, total choline 5.8 mg, vitamin E (α-tocopherol) 0.11 mg, vitamin K (phylloquinone) 0.1 µg, total saturated fatty acids 0.180 g, 14:0 (myristic) 0.004 g, 16:0 (palmitic) 0.161 g, 18:0 (stearic) 0.012 g, total monounsaturated fatty acids 0.206 g, 16:1 undifferentiated (palmitoleic) 0.002 g, 18:1 undifferentiated (oleic) 0.203 g, total polyunsaturated fatty acids 0.177 g, 18:2 undifferentiated (linoleic) 0.146 g, 18:3 undifferentiated (linolenic) 0.031 g, tryptophan 0.083 g, threonine 0.255 g, isoleucine 0.308 g, leucine 0.589 g, lysine 0.258 g, methionine 0.168 g, cystine 0.146 g, phenylalanine 0.381 g, tyrosine 0.238 g, valine 0.435 g, arginine 0.594 g, histidine 0.168 g, alanine 0.413 g, aspartic acid 0.670 g, glutamic acid 1.389 g, glycine 0.325 g, proline 0.335 g, and serine 0.375 g (USDA 2012).

Plate 11 Local Sri Aman rice in Sabah

Proximate nutrient composition of short-grained, raw, unenriched white rice per 100 g edible portion had been reported as: water 13.29 g, energy 358 kcal (1,498 kJ), protein 6.50 g, total lipid 0.52 g, ash 0.54 g, carbohydrate79.15 g, Ca 3 mg, Fe 0.80 mg, Mg 23 mg, P 95 mg, K 76 mg, Na 1 mg, Zn 1.10 mg, Cu 0.210 mg, Mn 1.037 mg, thiamin 0.070 mg, riboflavin 0.048 mg, niacin 1.600 mg, pantothenic acid 1.287 mg, vitamin B-6 0.171 mg, total folate 6 µg, total saturated fatty acids 0.140 g, 14:0 (myristic) 0.003 g, 16:0 (palmitic) 0.125 g, 18:0 (stearic) 0.010 g, total monounsaturated fatty acids 0.161 g, 16:1 undifferentiated (palmitoleic) 0.002 g, 18:1 undifferentiated (oleic) 0.159 g, total polyunsaturated fatty acids 0.138 g, 18:2 undifferentiated (linoleic) 0.114 g, 18:3 undifferentiated (linolenic) 0.024 g, tryptophan 0.075 g, threonine 0.233 g, isoleucine 0.281 g, leucine 0.538 g, lysine 0.235 g, methionine 0.153 g, cystine 0.133 g, phenylalanine 0.348 g, tyrosine 0.217 g, valine 0.397 g, arginine 0.542 g, histidine 0.153 g, alanine 0.377 g, aspartic acid 0.611 g, glutamic acid 1.268 g, glycine 0.296 g, proline 0.306 g, and serine 0.342 g (USDA 2012).

Proximate nutrient composition of long-grained, raw, brown rice per 100 g edible portion had been reported as: water 10.37 g, energy

370 kcal (1,548 kJ), protein 7.94 g, total lipid 2.92 g, ash 1.53 g, carbohydrate 77.24 g, total dietary fibre 3.5 g, total sugars 0.85 g, sucrose 0.85 g, Ca 23 mg, Fe 1.47 mg, Mg 143 mg, P 333 mg, K 223 mg, Na 7 mg, Zn 2.02 mg, Cu 0.277 mg, Mn 3.743 mg, Se 23.4 μg, thiamin 0.4010 mg, riboflavin 0.093 mg, niacin 5.091 mg, pantothenic acid 1.493 mg, vitamin B-6 0.509 mg, total folate 20 μg, total choline 30.7 mg, vitamin E (α-tocopherol) 1.20 mg, vitamin K (phylloquinone) 1.9 μg, total saturated fatty acids 0.584 g, 12:0 (lauric) 0.003 g, 14:0 (myristic) 0.011 g, 16:0 (palmitic) 0.498 g, 18:0 (stearic) 0.052 g, total monounsaturated fatty acids 1.056 g, 16:1 undifferentiated (palmitoleic) 0.010 g, 18:1 undifferentiated (oleic) 1.046 g, total polyunsaturated fatty acids 1.044 g, 18:2 undifferentiated (linoleic) 1.000 g, 18:3 undifferentiated (linolenic) 0.044 g, tryptophan 0.101 g, threonine 0.291 g, isoleucine 0.336 g, leucine 0.657 g, lysine 0.303 g, methionine 0.179 g, cystine 0.096 g, phenylalanine 0.410 g, tyrosine 0.298 g, valine 0.466 g, arginine 0.602 g, histidine 0.202 g, alanine 0.463 g, aspartic acid 0.743 g, glutamic acid 1.618 g, glycine 0.391 g, proline 0.372 g, and serine 0.411 g (USDA 2012).

Sookwong et al. (2007) reported that the average of total tocotrienol content in 109 kinds of Japanese rice bran samples was 830 μg/g dry wt. Two cultivars, Kouchi-Akamai, Joushuu, and Wataribune were found as tocotrienol-rich rice bran varieties (1,350–1,430 μg T3/g dry wt). The average toctrienol:vitamin E ratio was 61 but cultivars Hirayama, Moritawase, and Kaneko ahd 80–86%.

Studies showed that the order of vitamin E, total tocopherols, total tocotrienols, and γ-oryzanol contents in 16 commercial Taiwanese rice was: rice bran > brown rice > rice husk > polished rice (Huang and Ng 2011b). γ-tocotrienol was the highest vitamin E isomer present in all rice samples, while β-tocopherol, β-tocotrienol, δ-tocopherol, and δ-tocotrienol were present in trace amounts. The Japonica varieties contained a higher total tocopherol, total tocotrienol, and γ-oryzanol than the Indica varieties. They also have a higher level of α-tocopherol and α-tocotrienol but a lower level of γ-tocopherol and γ-tocotrienol than the Indica varieties. However, no obvious difference in total tocopherol, total tocotrienol, and γ-oryzanol content was noted between black- and red-coloured rice varieties. Huang and Ng (2011a) developed an improved normal phase high performance liquid chromatographic (NP-HPLC) method for simultaneous quantification of eight vitamin E isomers (α-, β-, γ- and δ-tocopherols and α-, β-, γ- and δ-tocotrienols) and γ-oryzanol in rice. A linear correlation coefficient ($R^2 > 0.99$) and high reproducibility were obtained at concentrations ranging 0.05–10 μg/mL for vitamin E isomers and 0.5–500 μg/mL for γ-oryzanol. The contents of protein, lipid, total phenolics, total flavonoids, total anthocyanins, total proanthocyanidins, total γ-oryzanol, total tocopherols and total tocotrienols varied among red rice SA-586 and its NaN_3-induced mutants (Jeng et al. 2011). The brans of mutants M-18, M-56 and M-50 contained more proanthocyanidins, γ-oryzanol, vitamin E than that of SA-586, respectively. M-54 accumulated more Fe content (588.7 mg kg bran dry weight) than SA-586 (100.1 mg/kg bran dry weight). These mutants could be used to produce high-value phytochemicals or Fe byproducts from bran during rice grain milling or as genetic resources for rice improvement programs.

Colour measurements on flour of five raw rice cultivars with different degrees of milling (DOM) showed that red and brown pigments were concentrated in the outer rice layers, i.e. bran and outer endosperm (DOM < 15%) (Lamberts and Delcour 2008). Yellow pigments were virtually absent in the middle and core endosperm (DOM > 15%). Determinations of the carotenoid levels in raw brown rice samples indicated that carotenoid levels in raw brown rice were lower than in common non-rice cereals. The major brown rice carotenoids were β-carotene and lutein (both ca. 100 ng/g), while zeaxanthin levels were lower (ca. 30 ng/g). Tropical japonica rice, the most consumed subgroup in the United States, tended to have the lowest levels of carotenoids in the bran while temperate japonicas had the highest (Belefant-Miller and Grace 2010). Carotenoid levels were found to be stable over 10 years of storage. The major carotenoid in rice bran was lutein. Black rice cultivars had higher flavonoids and carotenoids than the red and white cultivars (Kim et al. 2010).

Zubair et al. (2012) reported on the composition and variation of fatty acids, sterols, tocopherols and γ-oryzanol among selected Pakistani rice varieties namely Basmati Super, Basmati 515, Basmati 198, Basmati 385, Basmati 2000, Basmati 370, Basmati Pak, KSK-139, KS-282 and Irri-6. Oil content extracted with n-hexane from different varieties of brown rice seed (unpolished rice) was found to range from 1.92 to 2.72%. Total fatty acid contents among rice varieties tested varied between 18,240 and 25,840 mg/kg brown rice seed. The rice tested mainly contained oleic (6,841–10,952 mg/kg) linoleic (5,453–7,874 mg/kg) and palmitic acid (3,613–5,489 mg/kg). The amounts of total phytosterols ranged from 739.4 to 1330.4 mg/kg rice seed, comprising β-sitosterol (445–656 mg/kg), campesterol (116–242 mg/kg), Δ(5)-avenasterol (89–178 mg/kg) and stigmasterol (75–180 mg/kg). The content of α-, γ- and δ-tocopherols varied from 39.0 to 76.1, 21.6–28.1 and 6.5–16.5 mg/kg rice seed, respectively. The amounts of different γ-oryzanol components identified as cycloartenyl ferulate, 24-methylene cycloartanyl ferulate, campesteryl ferulate and β-sitosteryl ferulate, were in the range of 65.5–103.6, 140.2–183.1, 29.8–45.5 and 8.6–10.4 mg/kg rice seed, respectively. Overall, the concentration of these bioactives was higher in the Basmati rice cultivars showing their functional food superiority.

The lipids of rice brans comprised mainly triacylglycerols (TAG; 84.9–86.0 wt.%), free fatty acids(4.2–4.6 wt.%), and phospholipids (PL; 6.5–6.7 wt.%), whilst other components were also detected in minor proportions (0.2–2.1 wt.%) (Yoshida et al. 2011). The PL components included phosphatidyl choline (43.3–46.8 wt.%) phosphatidyl ethanolamine (25.0–27.3 wt.%) and phosphatidyl inositol (20.2–23.2 wt.%). Fatty acid distribution of TAG was characterized as: unsaturated FA predominantly concentrated at the sn-2 position and saturated FA primarily occupying the sn-1 or sn-3 position in these lipids.

Dehydrodiferulic acids (DFA) (8-5′- DFA, 8-8′-DFA, 5-5′-DFA, 8-*O*-4′-DFA) could be identified in both insoluble dietary fibre (IDF) and traces in soluble dietary fibre (SDF) of rice grains (Beunzel et al. 2001). Total dehydrodiferulic acid in IDF of rice was quantified as 4,042 μg/g, in SDF traces (<3 μg/g). In rice, amounts of 8-5′-DFA reached up to 45.5% in IDF and traces in SDF; 8-8′-DFA 22.2% in IDF and traces in SDF; 5-5′-DFA 13.3% in IDF and trace in SDF; 8-*O*-4′-DFA 18.6% in IDF and traces in SDF; 4-*O*-5′ DFA 0.4% in IDF and not detected in SDF.

Two new tocotrienols were isolated from stabilized and heated rice bran, apart from the known α-, β-, γ-, and δ-tocopherols and tocotrienols (Qureshi et al. 2000). Their structures were elucidated as desmethyl tocotrienol [3, 4-dihydro-2-methyl-2-(4,8,12-trimethyltrideca-3′(E),7′(E), 11′-trienyl)-2 H-1-benzopyran-6-ol] and didesmethy tocotrienol [3, 4-dihydro-2-(4,8,12-trimethyltrideca-3′(E),7′(E), 11′-trienyl)-2 H-1-benzopyran-6-ol]. The level of vitamin E in rice germ was five times greater than in rice bran, but the level of γ-oryzanol in rice germ was five times lower than in rice bran (Yu et al. 2007). Also, the major vitamin E component was α-tocopherol in rice germ and γ-tocotrienol in rice bran. The data suggest both rice bran and germ to have significantly different profiles of vitamin E and γ-oryzanol components.

Juliano (1992) had categorized rice according to amylose content into four groups: waxy (0–5%), very low (5–12%), low (12–20%), intermediate (20–25%) and high (25–33%). However, commercially, rice is classified based on amylose content as either low (<20% amylose), medium (21–25% amylose) or high (25–33% amylose). In the mixed Malaysian variety of MR219 and MR220, the amylose content of germinated brown rice (21.78%) was found to be significantly lower than that of brown rice (23.83%) or white rice (25.775) (Musa et al. 2011).

Nutritionally, starch fraction in rice can be classified according to in-vitro digestibility as rapidly digestible (RDS), slowly digestible (SDS), and resistant starch (RS); the latter two classes have been reported to have significant implications on human health, particularly glucose metabolism, diabetes management, colon cancer prevention, mental performance, and satiety (Patindol et al. 2010). Their study of 16 cultivars grown in southern USA showed that cultivar, location, and cultivar-by-location interaction contributed to the variations in RDS, SDS, and RS contents. Apparent amylose content correlated positively with RS ($R^2 = 0.54$), negatively

with RDS ($R^2 = -0.29$), and insignificantly with SDS ($R^2 = 0.21$). RS and SDS were not collinear; it does not follow that a cultivar high in RS will also be high in SDS, and vice versa.

Zaima et al. (2010) employed imaging mass spectrometry with matrix-assisted laser desorption/ionization (MALDI-IMS) to study the localization and composition of metabolites in rice grain. Lysophosphatidylcholine (LPC) was found localized in the endosperm. Phosphatidylcholine (PC), γ-oryzanol and phytic acid were localized in the bran (germ and seed coat), and α-tocopherol was distributed in the germ (especially in the scutellum). In addition, MALDI-IMS revealed the LPC and PC composition of the rice samples. The LPC composition, LPC (1-acyl 16:0), LPC (1-acyl 18:2), LPC (1-acyl 18:1) and LPC (1-acyl 18:0), was 59.4, 19.6, 14.2 and 6.8% respectively. The PC composition, PC (diacyl 16:0/18:2), PC (diacyl 16:0/18:1), PC (diacyl 18:1/18:3), PC (diacyl 18:1/18:2) and PC (diacyl 18:1/18:2), was 19.6, 21.0, 15.0, 26.7 and 17.8% respectively.

Among selected cereals rice with total phenolic content of 5.56 μmol of gallic acid equiv/g of grain was lowest compared to corn the highest with 15.55 μmol of gallic acid equiv/g of grain (Adom and Liu 2002). The major portion of phenolics in grains existed in the bound form (85 in corn, 75% in oats and wheat, and 62% in rice), wheat had 13.43 μmol of gallic acid equiv/g of grain of bound phenolics and 1.9 μmol of gallic acid equiv/g of grain of free phenolics. Ferulic acid was the major phenolic compound in grains tested, with free, soluble-conjugated, and bound ferulic acids present in the ratio 0.1:1:100. Ferulic acid content of rice grains (% contribution of fraction to the total μmol ferulic acid/100 g of grain) comprised total ferulic acid 153.39 μmol, free ferulic acid 0.70 μmol (0.5%), soluble ferulic acid conjugate 9.9 μmol (6.5%), and bound ferulic acid 142.8 μmol (93%). Rice had a total flavonoid content of 0.92 μmol catechin equivalent per g of grain, made up of 0.60 μmol catechin equivalent per g of grain of bound flavonoids and 0.33 μmol catechin equivalent per g of grain of free flavonoids. Corn had the highest total antioxidant activity (181.42 μmol of vitamin C equiv/g of grain), followed by wheat (76.70 μmol of vitamin C equiv/g of grain), oats (74.67 μmol of vitamin C equiv/g of grain), and rice (55.77 μmol of vitamin C equiv/g of grain). Bound phytochemicals were the major contributors to the total antioxidant activity: 90% in wheat, 87% in corn, 71% in rice, and 58% in oats.

Gorinstein et al. (2007) reported that the total phenolic content of jasmine rice was 330 μg GAE/g of grain dw, 83 mg/100 g cyanidin-3-glucoside dw, and 38 mg/100 g (+) catechin dw; and the total phenolic content of rice bran was 920 μg GAE/g of grain dw, 132 mg/100 g cyanidin-3-glucoside dw, and 185 mg/100 g (+) catechin dw.

The yields of total phenols, oryzanols and ferulic acid from defatted rice bran extracted with methanol were 2,204, 316, and 233 ppm, respectively (Renuka Devi and Arumughan 2007b). Subsequent fractionation, resulted in three enriched fractions, viz., acetone extract (AE), acetone extract-lipophilic fraction AE-LP, enriched in oryzanols and tocols by about 65 times, and acetone extract-polar fraction AE-PP, enriched in ferulic acid by 70 times compared to their contents in defatted rice bran. Tricin and β-sitosterol were identified in the crude methanolic extracts of defatted rice bran (Renuka Devi and Arumughan 2007a).

Rice bran had ester levels of 3.4 mg/g of bran, and rice bran oil had levels of 15.7 mg/g of oil (Norton 1995). The principal esters from rice bran were cycloartenyl, 24-methylenecycloartanyl, and campesteryl ferulate Rice bran oils had low levels of 24-methylenecycloartanyl but high levels of cyclobranol esters. Ten components of γ-oryzanol present in rice bran oil were identified as δ(7)-stigmastenyl ferulate, stigmasteryl ferulate, cycloartenyl ferulate, 24-methylenecycloartanyl ferulate, δ(7)-campestenyl ferulate, campesteryl ferulate, δ(7)-sitostenyl ferulate, sitosteryl ferulate, compestanyl ferulate, and sitostanyl ferulate (Xu and Godber 1999). Three of these, cycloartenyl ferulate, 24-methylenecycloartanyl ferulate, and campesteryl ferulate, were major components of γ-oryzanol. Using high-performance liquid chromatography with tandem mass spectrometric (LC/MS/MS) detection, nine new relatively polar triterpene alcohol and sterol esters including

hydroxylated ferulate esters and caffeate esters were detected from the phytosterol γ-oryzanol in rice bran (Fang et al. 2003). Three hydroxylated triterpene alcohol ferulates, (24S)-cycloart-25-ene-3β,24-diol-3β-*trans*-ferulate (1), (24R)-cycloart-25-ene-3β, 24-diol-3β-*trans*-ferulate (2), and cycloart-23Z-ene-3β, 25-diol-3β-*trans*-ferulate (3), along with known compounds cycloartenol *trans*-ferulate (4) and 24-methylenecycloartanol *trans*-ferulate (5) were isolated from rice bran (Luo et al. 2005). The major components of γ-oryzanol in rice were found to be 24-methylenecycloartanyl ferulate, cycloartenyl ferulate, campesteryl ferulate, β-sitosteryl ferulate and campestanyl ferulate (Miller et al. 2003). Analysis of 30 brown rice samples of various cultivars, grown at different sites and in different seasons, revealed the γ-oryzanol content to range from 26 to 63 mg/100 g (Miller and Engel 2006). Cycloartenyl ferulate and 24-methylenecycloartanyl ferulate were the major components of gamma-oryzanol followed by campesteryl ferulate, campestanyl ferulate, and β-sitosteryl ferulate. The proportions of individual steryl ferulates exhibited great variability. However, the proportions of the sum of 4,4′-dimethylsteryl ferulates (cycloartenyl ferulate, 24-methylenecycloartanyl ferulate) and the sum of 4-desmethylsteryl ferulates (campesteryl ferulate, campestanyl ferulate, and β-sitosteryl ferulate) were rather uniform. The significant natural variability observed for γ-oryzanol content and composition of steryl ferulates were shown to be influenced by environmental conditions but not by the degree of maturity of rice grains.

The isolation of oryzanol from crude rice bran oil was achieved by a two-step crystallization process (Zullaikah et al. 2009). In the first crystallization, oryzanol was concentrated in the liquid phase along with free fatty acid, monoacylglycerol, squalene, tocols, and phytosterols, whereas the solid phase contained mainly triacylglycerol and steryl esters. Oryzanol-rich product obtained from the first crystallization was subjected to the second crystallization where the oryzanol-rich product was kept at room temperature (20.5°C) for 24 h. Under optimal operation conditions, oryzanol with purity and recovery of 93–95 and 59%, respectively, was obtained from rice bran oil with an initial free fatty acid content of about 5%. Oryzanol in rice bran oil could be enriched by using nonporous polymeric membranes (Manjula and Subramanian 2008). During membrane processing, oryzanol content in the refined rice bran oil increased from 2,420 to 7,340 mg/kg (approximately threefold enrichment). While processing crude oil and model oil systems, the oryzanol content in the oil improved from 17,600 to 27,300 mg/kg and 20,400 to 30,300 mg/kg, respectively.

Six feruloyl esters of triterpene alcohols and sterols, viz., two *trans*-ferulates, cycloeucalenol and 24-methylenecholesterol *trans*-ferulates, and four *cis*-ferulates, cycloartenol, 24-methyelenecycloartanol, 24-methylcholesterol, and sitosterol *cis*-ferulates, besides five known *trans*-ferulates, cycloartenol (CAR), 24-methylenecycloartanol (24-MCA), 24-methylcholesterol, sitosterol, and stigmastanol *trans*-ferulates, and one known *cis*-ferulate, stigmastanol *cis*-ferulate, were isolated from the methanol extract of edible rice bran (Akihisa et al. 2000).

Rice had lowest total phenolic content (5.56 μmol of gallic acid equiv/g of grain) while corn had the highest total phenolic content (15.55 μmol of gallic acid equiv/g of grain) of the grains tested, followed by wheat (7.99 μmol of gallic acid equiv/g of grain) and oats (6.53 μmol of gallic acid equiv/g of grain) (Adom and Liu 2002). The major portion of phenolics in grains existed in the bound form (85% in corn, 75% in oats and wheat, and 62% in rice). Rice had 3.46 μmol of gallic acid equiv/g of grain of bound phenolics and 2.1 μmol of gallic acid equiv/g of grain of free phenolics. Ferulic acid was the major phenolic compound in grains tested, with free, soluble-conjugated, and bound ferulic acids present in the ratio 0.1:1:100. Ferulic acid content of rice grains (% contribution of fraction to the total μmol ferulic acid/100 g of grain) comprised total ferulic acid 153.39 μmol, free ferulic acid 0.70 μmol (0.5%), soluble ferulic acid conjugate 9.9 μmol (6.5%), and bound ferulic acid 142.8 μmol (93%). Rice had a low total flavonoid content of 0.92 μmol catechin equivalent per g of grain, made up of 0.60 μmol catechin equivalent

per g of grain of bound flavonoids and 0.33 μmol catechin equivalent per g of grain of free flavonoids. Rice had lowest total antioxidant activity (55.77 μmol of vitamin C equiv/g of grain) while corn had the highest total antioxidant activity (181.42 μmol of vitamin C equiv/g of grain), followed by wheat (76.70 μmol of vitamin C equiv/g of grain) and oats (74.67 μmol of vitamin C equiv/g of grain). Bound phytochemicals were the major contributors to the total antioxidant activity: 90% in wheat, 87% in corn, 71% in rice, and 58% in oats. Bound phytochemicals could survive stomach and intestinal digestion to reach the colon. This may partly explain the mechanism of grain consumption in the prevention of colon cancer, other digestive cancers, breast cancer, and prostate cancer, which is supported by epidemiological studies.

The red rice bran essential oils yield was 0.031%, and its major constituents were (E)-β-ocimene (3.12%), nonanal (11.32%), (2E, 4E)-decadienal (2.54%), myristic acid (41.32%), geranyactone (2.41%) and methyl oleate (2.46%) (Chung et al. 2011). The black rice bran essential oils yield was 0.053%, and its major constituents were nonanal (8.31%), acrylic acid (3.21%), 2-hydroxy-6-methylbenzaldehyde (2.81%), pelargonic acid (4.21%) and myrisitc acid (28.07%).

Five bioactive compounds were isolated from the ethylacetate-soluble fraction of the aleurone layer of *Oryza saliva* cv. Heugjinjubyeo, a highly developed anthocyanin-pigmented rice cultivar: 4-carboethoxy-6-hydroxy-2-quinolone (1), ethyl-3, 4-dihydroxybenzoic acid (2), 4-hydroxy-3-methoxyphenylacetic acid (3), 3, 4-dihydroxybenzoic acid (4), and 4-hydroxy-3-methoxy cinnamic acid (5) (Chung and Shin 2007). Ten pigmented rice varieties contained two major anthocyanins, cyanidin 3-glucoside and peonidin 3-glucoside (Ryu et al. 1998). Total anthocyanin contents varied greatly in the range of 0–493 mg/100 g grain among varieties. Three anthocyanin pigments were identified in black and wild rice: cyanidin-3-glucoside the most abundant pigment, cyanidin-fructoside and an unidentified pigment (Kim et al. 2008b). Four different anthocyanins viz. cyanidin-3-glucoside, peonidin-3-glucoside, cyanidin-3, 5-diglucoside, cyanidin-3-rutinoside were identified in black rice (Hou et al. 2011). The free, bound, and total phenolic contents of 12 diverse varieties of black rice bran samples varied from 2,086 to 7,043, from 221.2 to 382.7, and from 2,365 to 7,367 mg of gallic acid equiv/100 g of dry weight (DW), respectively (Zhang et al. 2010a, b). The percentage contribution of free phenolics to the total ranged from 88.2 to 95.6%. The mean values of free, bound, and total phenolic contents of black rice bran were 8, 1.5, and 6 fold higher than those of white rice bran, respectively. The free, bound, and total flavonoid contents of black rice bran samples ranged from 3,462 to 12,061, from 126.7 to 386.9, and from 3,596 to 12,448 mg of catechin equiv/100 g of DW, respectively. The percentage contribution of free flavonoids to the total ranged from 96.3 to 97.6%. The mean values of free, bound, and total flavonoid contents of black rice bran were 7.4, 1.9, and 6.7 fold higher than those of white rice bran, respectively. The free, bound, and total anthocyanin contents of black rice bran samples ranged from 1,227 to 5,096, from 4.89 to 8.23, and from 1,231 to 5,101 mg of cyanidin-3-glucoside equiv/100 g of DW, respectively. The percentage contribution of free anthocyanins to the total ranged from 99.5 to 99.9%. Cyanidin-3-glucoside, cyanidin-3-rutinoside, and peonidin-3-glucoside were detected in black rice bran samples and ranged from 736.6 to 2,557, from 22.70 to 96.62, and from 100.7 to 534.2 mg/100 g of DW, respectively. India Njavara Black rice bran was found to contain tricin and two rare flavonolignans: tricin 4′-*O*-(erythro-β-guaiacylglyceryl) ether and tricin 4′-*O*-(threo-β-guaiacylglyceryl) ether (Mohanlal et al. 2011).

Studies showed that ferulic acid was the major soluble phenolic acid in rice husk at all stages, and its concentration decreased steadily during grain development (Butsat et al. 2009). The ratio of ferulic to *p*-coumaric acid was approximately 2:1 at all stages. The most abundant bound phenolic acid in all rice husk extracts was *p*-coumaric acid, followed by ferulic acid along with traces of syringic, vanilic, and *p*-hydroxybenzoic acids. The pigmented rice husk gave higher free total phenolic contents than normal rice husk (Butsat and Siriamornpun 2010). However, there was no significant difference in bound total phenolic

contents between pigmented rice and normal rice husks. Ferulic and *p*-coumaric acids were the major phenolic acids in the free fraction of pigmented rice husks, whereas vanillic acid was the dominant phenolic acid in the free fraction of normal rice husks. *p*-coumaric acid was highly found in bound form of both pigmented and normal rice husks. Rice husks lignin was found to be mainly formed by guaiacyl and *p*-hydroxyphenyl units (Salanti et al. 2010). The acidolytic extraction showed an appreciable lignin recovery and high purity, whereas the lignin sample from alkaline enzymatic extraction was found to be rich in residual polysaccharides and oxidized functionalities.

Thirty-five volatile compounds were identified in black rice, an aromatic specialty rice popular in Asia with a unique flavour (Yang et al. 2008a). Aldehydes and aromatics were quantitatively in the greatest abundance, accounting for 80.1% of total relative concentration of volatiles. The concentration of 2-acetyl-1-pyrroline (2-AP) was high, exceeded only by hexanal, nonanal, and 2-pentylfuran. 2-AP, guaiacol, indole, and *p*-xylene largely influenced the difference between the aroma in cooked black and white rice. 2-AP and guaiacol were major contributors to the unique character of black rice based on odour thresholds, relative concentrations, and olfactometry. In another study, 25 odorants with an intermediate or greater intensity (odor intensity>or=3) and deemed to be major odor-active compounds were isolated in six distinctly different rice flavor types (basmati, jasmine, two Korean japonica cultivars, black rice, and a nonaromatic rice) (Yang et al. 2008b). 2-acetyl-1-pyrroline (2-AP) had the lowest odor threshold (0.02 ng/L) followed by 11 aldehydes (ranging from 0.09 to 3.1 ng/L), guaiacol (1.5 ng/L), and 1-octen-3-ol (2.7 ng/L). Odor activity values (OAVs), for 2-AP, hexanal, (E)-2-nonenal, octanal, heptanal, and nonanal comprised >97% of the relative proportion of OAVs from each rice flavor type, even though the relative proportion varied among samples. Thirteen odor-active compounds [2-AP, hexanal, (E)-2-nonenal, octanal, heptanal, nonanal, 1-octen-3-ol, (E)-2-octenal, (E, E)-2,4-nonadienal, 2-heptanone, (E, E)-2,4-decadienal, decanal, and guaiacol] among the six flavor types were the primary compounds explaining the differences in aroma. In a more recent study, 21 and 23 odorants were detected in cooked samples of premium-quality, waxy and black-pigmented rice cultivars, respectively (Yang et al. 2010). Hexanal was the main odorant in premium-quality and waxy cultivars; however, waxy cultivars had 16 times higher hexanal odour activity values (OAVs) than premium-quality cultivars, indicating premium-quality rice had a less pronounced overall aroma. 2-Acetyl-1-pyrroline was the main contributor to overall aroma in black-pigmented rice, followed by guaiacol. Six odour-active compounds (2-acetyl-1-pyrroline, guaiacol, hexanal, (E)-2-nonenal, octanal and heptanal) contributed the most in discriminating the three types of specialty rice.

One hundred twenty-nine of volatile compounds were identified in red and black rice bran (Sukhonthara et al. 2009). Myristic acid, nonanal, (E)-β-ocimene and 6, 10, 14-trimethyl-2-pentadecanone were the main compounds in red rice bran, whereas myristic acid, nonanal, caproic acid, pentadecanal and pelargonic acid were the major compounds in black rice bran. Guaiacol, occurring in 0.81 mg/100 g in black rice bran, was responsible for the characteristic component in black rice.

Thirteen Korean specialty rice samples were evaluated for their flavor components using descriptive analysis and GC-O. Nineteen aroma attributes in cooked Korean specialty rice samples were evaluated by eight trained panelists and statistically correlated to the concentration of aroma-active compounds (Limpawattana et al. 2008). Prediction models were developed for most aroma descriptors including popcorn, cooked grain, starchy, woody, smoky, grain, corn, hay-like, barney, rancid, waxy, earthy, and sweet aroma using stepwise multiple linear regression. (E,E)-2, 4-decadienal, naphthalene, guaiacol, (E)-2-hexenal, 2-acetyl-1-pyrroline, 2-heptanone contributed most to these sensory attributes.

A greater extent and higher rate of undesirable changes in volatile compounds were found in fragrant rice samples stored under Nylon/LLDPE/ambient temperature condition (Tananuwong and Lertsiri 2010). Nevertheless, this condition is acceptable for the retail trade of organic rice

in Thailand. For samples vacuum packed in Nylon/LLDPE pouches at ambient temperature, significant increases in hexanal, 2-pentylfuran, 1-octanol and 4-vinyl guaiacol and significant decreases in 2-AP and geranyl acetone were found after the second month (Tananuwong and Lertsiri 2010). Vacuum packing in laminated oriented olypropylene/aluminum/linear low density polyethylene (OPP/Al/LLDPE) pouches or storage at 15°C better retarded the formation of volatile lipid oxidation products and greater retained desirable odorants, including 2-AP. However, accumulation of lipid oxidation products and 4-vinyl guaiacol was apparent after the sixth month under these storage conditions. Storage conditions using reduced temperature or better packaging materials may be more appropriate for exported rice or superior-grade fragrant rice to better maintain the desirable rice aroma.

All free amino acids except arginine were present in the greatest quantities in the outermost layer of the 5%-milled kernel with a decreasing concentration gradient toward the center (Saikusa et al. 1994). Water soaking of the flours generated increases in the contents of most amino acids and decreases in the glutamate and taurine contents. Glutamate, γ-aminobutyric acid (GABA), and arginine could be assumed to contribute to the taste of cooked rice. GABA content in the germ increased remarkably with soaking under a slightly acidic condition, suggesting the potential for rice germ to be included in the diet of people with hypertension.

Volatile compounds of cooked rice from scented (Aychade, Fidji) and nonscented (Ruille) cultivars grown in the Camargue area in France were compared to that of a marketed Asian scented one (Thai) (Maraval et al. 2008). Gas chromatography-olfactometry analyses of the organic extracts resulted in the perception of 40 odorous compounds. Only two compounds, oct-1-en-3-one and 2-acetyl-1-pyrroline, were almost always perceived. Sixty compounds were identified and quantified by GC-MS, including a few new odor-active components. Calculated odor-active values evidenced that the Thai sample odor differed from that of scented Camargue cultivars because of the degradation of lipids and of cinnamic acid compounds.

Phytochemicals in Rice Products

More than 60 volatile compounds were identified in rice cakes (Buttery et al. 1999). Major volatiles included 1-hydroxy-2-propanone, furfuryl alcohol, 2, 5-dimethylpyrazine, 2-methylpyrazine, pyrazine, hexanal, furfural, pentanol, 3-hydroxy-2-butanone (acetoin), and ethyl-3, 6-dimethylpyrazine. Compounds with a high probability of contributing to the aroma and flavor included 3-methylbutanal, dimethyl trisulfide, 2-ethyl-3, 5-dimethylpyrazine, 4-vinylguaiacol, hexanal, (E,E)-2,4-decadienal, 2-methylbutanal, 2-acetyl-1-pyrroline, 1-octen-3-ol, and 1-octen-3-one.

Bioactive compounds isolated from *Monascus pupureus* fermented rice included anka (Wang et al. 2000); cholestin (Lin et al. 2008) monacolin K, ankaflavin, monascin (Lin et al. 2011) and two new steroids: (22S, 23R, 24S)-20β, 23α,25α-trihydroxy-16,22-epoxy-4,6,8(14)-trienergosta-3-one (1), and (22E, 24R)-3β,5α-dihydroxyergosta-23-methyl-7,22-dien-6-one (2), as well as two known compounds (22E, 24R)-3β,5α-dihydroxyergosta-7,22-dien-6-one (3) and (22E, 24R)-6β-methoxy-ergosta-7,22-diene-3β,5α-diol (4) (Shang et al. 2011). One new tetralone, monaspurpurone (1), was isolated from the ethanol extract of a yellow mutant of the fungus *Monascus purpureus* grown on rice, along with five known compounds, β-sitosteryl palmitate (2), ergosterol (3), ankaflavin (4), monascin (5) and *p*-nitrophenol (6) (Cheng et al. 2010c).

Two enantiomeric azetidine-type amino acids isolated from the n-butanol-soluble fraction of the 70% ethanol extract of red-mold rice fermented with *Monascus pilosus* were elucidated as (+)-[1; (+)-monascumic acid] and (−)-syn-2-isobutyl-4-methylazetidine-2,4-dicarboxylic acids [2; (−)-monascumic acid] (Akihisa et al. 2004). A new sesquiterpene, monaspilosuslin, as well as seven known compounds 3β-hydroxystigmast-5-en-7-one, β-sitostenone, monascin, ankaflavin, N-*trans*-feruloyltyramine, vanillic acid and α-tocopheryl quinone, were isolated from the

n-butanol-soluble fraction of the 70% ethanolic extract of red yeast rice fermented with the fungus *Monascus pilosus.* (Cheng et al. 2010b)

Phytochemicals in Rice Straw

Eighty-nine components comprising 20 alcohols, 16 ketones, 14 aldehydes, 11 acids, 11 hydrocarbons, 5 esters, 3 lactones and 9 miscellaneous were identified in the rice samples of two ancient cultivars Onshinomai, Asamurasaki and one modern cultivar Hinohikari. Palmitic acid (77.36–102.92 μg/g straw) was the most abundant component in these samples, followed by hexahydrofarnesyl acetone (47.13–72.38 μg/g straw), and phytol (6.74–20.39 μg/g straw). Other components included myristic acid 11.76–13.07 μg/g straw, lauric acid 3.51–6.94 μg/g straw, pentadecanoic acid (6.61–19.88 μg/g straw) and farnesylacetone (1 .81–5.38 μg/g straw). The main aliphatic aldehyde was pentadecanal (2.30–5.08 μg/g straw) and hexadecanal (0.78–4.91 μg/g straw). The content of β-ionone and 5,6-epoxy-β-ionone were significantly higher in Onshinomai than the other two varieties. The contents of (Z)-dihydroapofarnesol, hexahydrofarnesol, geranyl acetone and nonanal in Hinohikari were higher than the other varieties. Hinohikari (5.63 μg/g straw) had lower content of 4-vinyl-guiacol content compared to Onshinomai 7.29 μg/g straw and Asamurasaki 6.11 μg/g straw.

Rice bran had been reported to contain important bioactive phytochemicals such as steryl ferulates including γ-oryzanol and its major components such as cycloartenyl ferulate (CAF), 24-methylenecycloartanyl ferulate (24-mCAF), β-sitosteryl ferulate (β-SF), and campesteryl ferulate (Islam et al. 2011). All these components had been intensively studied due to their crucial roles in pathological processes and have been reported to have to antioxidant, anti inflammatory, anti ulcerogenic, hypolipidemic, anti neoplastic, anti diabetic, and anti allergic properties. In- vivo and in vitro studies had elucidated that rice bran phytosteryl ferulates mediated anti inflammatory effects by down-regulating the inflammatory transcription factor, nuclear factor κB (NF-κB), which in turn reduced expression of inflammatory enzymes such as COX-2 and iNOS, and proinflammatory cytokines such as IL-1β, IL-6 and TNF-α. In addition, rice bran phytosteryl ferulates up-regulated blood adiponectin levels via indirect activation of peroxisomal proliferator-activated receptor γ (PPARγ) through NF-κB inhibition.

Antioxidant Activity

In-Vitro Antioxidant Activity in Rice Grain, Rice Bran, Husk

The aleurone layer of *Oryza sativa* cv. Heugjinmi yielded a new quinolone alkaloid, 4-carbomethoxy-6-hydroxy-2-quinolone, showing moderate antioxidative activity in a 1,1-diphenyl-2-picrylhydrazyl (DPPH) free-radical scavenging assay (Chung and Woo 2001). From the black coloured rice bran of *Oryza sativa* cv. Heugjinjubyeo, a new 2-arylbenzofuran, 2-(3,4-dihydroxyphenyl)-4,6-dihydroxybenzofuran-3-carboxylic acid methyl ester, oryzafuran was isolated (Han et al. 2004). Five bioactive compounds isolated from the ethylacetate-soluble fraction of the aleurone layer of *Oryza saliva* cv. Heugjinjubyeo, a highly developed anthocyanin-pigmented rice cultivar: 4-carboethoxy-6-hydroxy-2-quinolone (1), ethyl-3,4-dihydroxybenzoic acid (2), 4-hydroxy-3-methoxyphenylacetic acid (3), 3,4-dihydroxybenzoic acid (4), and 4-hydroxy-3-methoxy cinnamic acid (5) showed significant antioxidant activity in a concentration-dependent manner through the scavenging of DPPH radicals (Chung and Shin 2007).

Gorinstein et al. (2007) reported the antioxidant activity of polyphenol dry matter methanol extract of jasmine rice in the DPPH assay to be 20%, in the β-carotene linoleate model system to be 21.2% and 1.47 μM TE/g TEAC (trolox equivalent coefficient) and rice bran in the DPPH assay to be 79%, in the β-carotene linoleate model system to be 78% and 2.67 μM TE/g TEAC.

Most of the antioxidant activities of soluble and bound phenolic acids in rice husk extracts

were found at flowering stage (Butsat et al. 2009) and there were high correlations of antioxidant activity to levels of soluble ferulic, gallic, and *p*-coumaric acids. The antioxidant activity of rice husk extracts was positively correlated with the total free phenolics content and individual phenolic acids especially ferulic acid (Butsat and Siriamornpun 2010) thus suggesting that the rice husk could be a potential phenolic acid source and may therefore offer an effective source of natural antioxidant.

In-vitro studies showed that methanol extracts of rice hulls possessed significant ROS scavenging and metal chelating activities and protective effect against oxidative DNA damage in human lymphocytes (Jeon et al. 2006). Methanol extract of far-infrared irradiated rice hull showed higher scavenging activity than non-irradiated intact rice hull for DPPH radical scavenging. The protective effect of rice hull extract against DNA damage induced by H2O2 increased as its concentration increased from 12.5 to 50 μg/mL, as indicated by DNA strand breakage decreasing from 38 to 22% with far-infrared irradiated rice hull nd from 49 to 28% with non-irradiated intact rice hull as compared with H2O2-treated positive controls.

Dehulled red rice showed a total antioxidant capacity (TAC) more than three times greater than dehulled white rice and its high TAC was essentially characterized by the presence of proanthocyanidins (PA) and associated phenolics (Finocchiaro et al. 2007). Milling caused a significant loss of TAC, even if red rice maintained a higher TAC. Cooking caused a further loss of antioxidants, but when there was a full uptake of cooking water by the grains ("risotto") this loss was limited. Thus, the consumption of whole or partially milled rice cooked as risotto would be preferred to preserve its nutritional properties (namely tocols, γ-oryzanols, and polyphenols).

Vitamin E (α-tocopherol, α-tocotrienol, γ-tocopherol, and γ-tocotrienol) and γ-oryzanol components (cycloartenyl ferulate, 24-methylenecycloartanyl ferulate, and campesteryl ferulate) purified from rice bran, exhibited significant antioxidant activity in the inhibition of cholesterol oxidation system accelerated by 2,2′-azobis (2-methylpropionamidine) dihydrochloride (Xu et al. 2001). The highest antioxidant activity was found for 24-methylenecycloartanyl ferulate, and all three γ-oryzanol components had activities higher than that of any of the four vitamin E components. Because the quantity of γ-oryzanol was up to ten times higher than that of vitamin E in rice bran, γ-oryzanol may be a more important antioxidant of rice bran in the reduction of cholesterol oxidation than vitamin E, which had been considered to be the major antioxidant in rice bran. The antioxidant function of these components against cholesterol oxidation may contribute to the potential hypocholesterolemic property of rice bran. The ethanol-precipitable fraction of the water extract of Japanese rice bran (*Oryza sativa* japonica) showed significant antioxidant activity (Higashi-Okai et al. 2004). It also exerted antigenotoxic activity by suppressing Trp-P-1-induced umu C gene expression in *Salmonella typhimurium.* The antioxidative and antigenotoxic activity of ethanol-precipitable fraction was associated with a proteinous component with the molecular weight >30 kDa, identified possibly as a peroxidase enzyme.

Parrado et al. (2003) reported on the development of a water-soluble oryzanol enzymatic extract (WSOEE), which showed greatly increased antioxidant functionality than rice bran. The WSOEE γ-oryzanol composition profile was similar to that of rice bran (cycloartenyl, 24-methylene cycloartenyl, campesteryl, and sitosteryl ferulates), but with two major differences: WSOEE γ-oryzanol concentration was five times higher than that of rice bran, and WSOEE was water soluble. WSOEE total antioxidant capacity to trap the peroxyl radical was high, and similar to that of Trolox. The capacity to inhibit lipid peroxidation induced by cumene hydroperoxide in rat brain homogenate yielded a protection similar to that of Trolox. WSOEE also showed the capacity to protect protein from oxidation phenomena in rat brain homogenate, with a behavior similar to that of melatonin.

The hot water extract of Japanese rice bran exhibited potent DPPH radical-scavenging activity (Okai and Higashi-Okai 2006). Its ethanol-soluble (ES) fraction exhibited high radical-scavenging activity in a dose-dependent manner, but a weak radical-scavenging activity was detected in the ethanol-precipitable (EP) fraction. Their activities

were proportional to the amounts of phenolic substances in each fraction. Four major phenolic acids (ferulic, *p*-coumaric, *p*-hydroxybenzoic and vanillic acids) and four minor phenolic acids (caffeic, gentisic, protocatechuic and syringic acids) were detected in the bran fractions. Among these phenolic acids, protocatechuic, caffeic, ferulic and gentisic acids showed relatively strong radical scavenging activities (EC_{50}: 8, 9, 29 and 75 μM, respectively) compared with the control antioxidants such as ascorbic acid and α-tocopherol (EC_{50}: 93 and 134 μM). *P*-coumaric, syringic and vanillic acids exhibited weak but significant radical-scavenging activities (EC_{50}: 780, 2,640 and 3,250 μM).

The phytochemical compounds oryzanols, tocopherols, tocotrienols and ferulic acid, tricin and β-sitosterol were identified in the crude methanolic extracts (CME) of defatted rice bran (DRB) and enrichment of antioxidants in CME resulted in three enriched fractions viz. acetone extract (AE), acetone extract-lipophilic fraction (AE-LP) and acetone extract-polar fraction (AE-PP) (Renuka Devi and Arumughan 2007a). The scavenging effects of DRB extracts and their phytochemical constituents against DPPH and superoxide radicals were determined and EC_{50} (g antioxidant/kg DPPH) values of CME, AE, AE-LP, AE-PP, oryzanols, ferulic acid, tocols (Tmix), tricin, β-sitosterol, butylated hydroxytoluene (BHT) and tertiary-butylhydroquinone (TBHQ) were 1,977, 1,945, 7,985, 1,072, 972, 174, 164, 3,947, 21,416, 1,120 and 61, respectively. The DRB extracts and their phytochemical constituents when assayed by cytochrome C and NBT (nitroblue tetrazolium) methods showed positive superoxide radical scavenging effects. The order of efficacies of the extracts was AE-PP > AE > CME > AE-LP in both assays, but the activities were higher for the former method. The DPPH as well as superoxide scavenging activities of AE, AE-LP and AE-PP could largely be attributed to the levels of total phenols (TPC) and ferulic acid in it.

Rice bran methanolic extract from Njavara showed the highest antioxidant and cell cytotoxic properties compared to the other three Indian rice varieties Vasumathi, Yamini, Jyothi (Rao et al. 2010). IC_{50} values for scavenging DPPH and nitric oxide were in the range of 30.85–87.72 μg/mL and 52.25–107.18 μg/mL respectively. Total antioxidant activity and reducing power were increased with increasing amounts of the extract. Total phenolic and flavonoid contents were in the range of 3.2–12.4 mg gallic acid-equivalent (GAE)/g bran and 1.68–8.5 mg quercetin-equivalent/g bran respectively. IC_{50} values of cytotoxic assay (MTT assay) were 17.53–57.78 μg/mL. Njavara extracts also showed highest reducing power activity, anti-proliferative property in C6 glioma cells. Correlation coefficient and regression analysis of phenolic content with DPPH and NO scavenging, MTT (−[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide) assay, total antioxidant assay and reducing power showed a highly significant correlation coefficient values (96–99%) and regression values (91–98%).

In-Vitro Antioxidant Activity in Coloured Rice

Pigmented rice and rice bran had been reported to be rich sources of phenolic compounds and to have potent antioxidant and reducing activities.

The extracts from white-, black-, and red-hulled rice prepared with highly polar solvents, methanol and deionized water, exhibited higher DPPH* and tert-butyl hydroperoxyl radical scavenging activities (Oki et al. 2002). Moreover, the acetone extract from red-hulled rice exhibited a high DPPH* and tert-butyl hydroperoxyl radical scavenging activity, while no such activity was detected for the acetone extracts from white- and black-hulled rice. The major components responsible for the radical scavenging in the acetone extract from red-hulled rice were identified as procyanidins. Chiang et al. (2006) found that in HepG2 cells black rice extract significantly suppressed superoxide anions (O2*-) and reactive oxygen species and significantly increase superoxide dismutase (SOD) and catalase (CAT) activities by 161.6 and 73.4%, respectively. The major components responsible for the free-radical-scavenging and antioxidative properties were attributed to cyanidin-3-*O*-glucoside chloride and peonidin-3-*O*-glucuside chloride.

Water extracts of brown rice (unpolished rice) and rice bran of Sangyod, a red pigmented rice

variety exhibited significantly higher antioxidant activity than those of Dawk Mali 105, a commercial white-coloured rice which exhibited only moderate to low activity (Srisawat et al. 2010). High levels of antioxidant activity of the water extracts of Sangyod were highly correlated to their flavonoid and phenolic contents, which were approximately 2.5 and 3 times higher, respectively, than those of Dawk Mali 105. Red unpolished Thai rice was found to be a rich source of phenolic compounds, had good antioxidant ability (good DPPH scavenging and ferric reducing power) and may play a crucial role in oxidative stress prevention (Rattanachitthawat et al. 2010).

The diethyl ether fraction of methanolic extract of Njavara Black rice bran yielded three important compounds namely, tricin and two rare flavonolignans- tricin 4′-*O*-(erythro-β-guaiacylglyceryl) ether and tricin 4′-*O*-(threo-β-guaiacylglyceryl) ether (Mohanlal et al. 2011). The EC_{50} values of these compounds in DPPH system were 90.39, 352.04 and 208.1 μg/mL, respectively. Quantification of the compounds in Njavara Black and staple, non-medicinal rice varieties Sujatha and Palakkadan Matta showed that tricin was present 39.64 and 16.12 fold higher in Njavara Black, compared to Sujatha and Palakkadan Matta respectively.

The lipophilic extract from the outer bran fraction (OBF) of purple rice bran had a lower content of total tocols and γ-tocols, compared with the inner bran fraction (IBF), while the contents of γ-oryzanol in both fractions were not different (Jang and Xu 2009). However, the lipophilic phenolic content and free radial scavenging activity of the OBF were 6.0 μg catechin equivalent (CE)/g and 5.6 μmol trolox equivalent (TE)/g and higher than those of the IBF, respectively. For the hydrophilic extracts, the level of anthocyanins in the IBF (29.0 mg/g) was eight fold higher than that in the OBF. Further, the hydrophilic phenolic content and free radical scavenging activity of the IBF were 489.1 μg CE/g and 433.6 μmol TE/g, respectively, while they were 113.9 μg CE/g and 78.2 μmol TE/g in the OBF. Both hydrophilic extracts showed significantly higher phenolic content and free radical scavenging activity than any lipophilic extract. The results indicated that the activity of purple rice bran hydrophilic antioxidants was much greater than that of its lipophilic antioxidants and anthocyanins and γ-tocols largely located in the inner portion of purple rice bran.

Semsang et al. (2011) reported that a purple mutant variety designated BKOS of the aromatic, robust and highly nutritious Thai jasmine rice cv. KDML105, had higher phenolic content and enhanced antioxidant activity. The BKOS extracts showed the highest total phenol content (0.140 and 0.096 mg of gallic acid equivalent (GAE)/g dry extract from uncooked and cooked rice, respectively). The BKOS extracts also had enhanced antioxidant activities, determined using three standard methods: 2,2′-diphenyl-1-picrylhdrazyl (DPPH) free radical scavenging, ABTS radical cation (ABTS•(+)) decolourisation and ferric-reducing antioxidant power assays. BKOS extracts showed 2–2.5-fold increased levels for each method. Suwannalert and Rattanachitthawat (2011) found that unpolished Thai rice strain of Leum Phua, had high levels of monomeric anthocyanin pigment 36.96 mg/L equivalent, total phenolic content 1.36 mg GA/g sample, and antioxidant activities namely DPPH (36.94 mg vitamin C/g sample), ABTS (5.54 mg trolox/g sample) and FRAP 18.20(μmol Fe2+/g sample) compared to other cultivars Klam, Hawm Nil and Black Rose. Muntana and Prasong (2010) reported that the total phenolic content of Thai white, red and black rice bran extract were in the range of 0.8931–0.9884, 1.0103–1.0494 and 1.0810–1.2239 mg gallic acid equivalent (GAE/mg), respectively. With thiocyanate antioxidant method, percentage inhibition were in the range of 10.15–20.68, 30.64–38.80 and 25.52–26.28 for white, red and black rice bran extract, respectively. With DPPH radical-scavenging assay, methanolic extract of 5,718 showed the highest (IC_{50} = 0.0057 mg/mL) while cv. Homchaiya showed the lowest (IC_{50} = 0.2582 mg/mL) activities. All of extracts showed lower activity than BHA (IC_{50} = 0.0012 mg/mL). However, the antioxidant activity of all rice bran extracts indicated high antioxidant efficiency in the following order: red > black > white colour rice brans.

Pigmented rice bran extract was found to have greater reducing power than a normal rice bran extract from a long grain white rice (Laokuldilok et al. 2011). All bran extracts were highly effective

in inhibiting linoleic acid peroxidation (60–85%). γ-oryzanol (39–63%) and phenolic acids (33–43%) were the major antioxidants in all bran samples, and black rice bran also contained anthocyanins 18–26%. Pigmented rice bran was also rich in anthocyanin cyanidin-3-glucoside (58–95%). Ferulic acid was the dominant phenolic acid in the rice bran samples. Black rice bran contained higher levels of gallic, hydroxybenzoic, and protocatechuic acids than red rice bran and normal rice bran. In addition, the incorporation of 5% black rice bran to wheat flour used for making bread produced a marked increase in the free radical scavenging and antioxidant activity compared to a control bread. In a separate study, the concentrations of lipophilic antioxidants of vitamin E (tocopherol and tocotrienols) and γ-oryzanols in rice brans of various colours white, light brown, brown, purple, and red were 319.67–443.73 and 3861.93–5911.12 μg/g bran dry weight (DW), respectively, and were not associated with bran colour (Min et al. 2011). The total phenolic, total flavonoid, and antioxidant capacities of ORAC (oxygen radical absorbance capacity), DPPH radical scavenging, and iron-chelating in the free fraction were correlated with the intensity of bran colour, while variations of these in the bound fraction were less than those in the free fraction among brans. Compounds in the bound fraction had higher antioxidant capacity of ORAC than DPPH, relative to those in the free fraction. The bound fraction of light-colour brans contributed as much to its total ORAC as the free fraction. Total anthocyanin was highest in purple bran while total proanthocyanidin concentration was the highest in red rice bran. The predominant anthocyanin was cyanidin-3-glucoside. Red and purple brans had several fold higher total phenolics and flavonoids as well as ORAC and DPPH, from both free and bound fractions, than freeze-dried blueberry and broccoli. The results indicated rice brans to be natural sources of hydrophilic and lipophilic phytochemicals for use in quality control of various food systems as well as for nutraceutical and functional food application.

A standardized extract of black rice pigmented fraction (BRE) containing known proportions of cyanidin 3-glucoside and peonidin 3-glucoside displayed remarkable antioxidant activities and free radical scavenging capacities in a battery of in-vitro model systems (Hu et al. 2003). Significant prevention of supercoiled DNA strand scission induced by reactive oxygen species (specifically, peroxyl radical and hydroxyl radicals) and suppression of the oxidative modification of human low-density lipoprotein was obtained with the fraction. Moreover, the fraction reduced the formation of nitric oxide by suppressing inducible nitric oxide synthase expression in murine macrophage RAW264.7 cells, without introducing cell toxicity. The results suggested that black rice contained anthocyanin pigments with notable antioxidant and anti-inflammatory properties with potential use in nutraceutical or functional food formulations. The free, bound, and total antioxidant activities of 12 diverse varieties of black rice bran samples ranged from 476.9 to 180, from 47.91 to 79.48, and from 537.5 to 1,876 μmol of Trolox equiv/g of DW, respectively (Zhang et al. 2010a). The percentage contribution of free antioxidant activity to the total ranged from 88.7 to 96.0%. The average values of free, bound, and total antioxidant activity of black rice bran were more than 8, 1.5, and 6 times higher than those of white rice bran, respectively. The total antioxidant activity of black rice bran was correlated to the content of total phenolics, total flavonoids, and total anthocyanins and also was significantly correlated to the contents of cyanidin-3-glucoside, cyanidin-3-rutinoside, and peonidin-3-glucoside. These results indicated significant differences in phytochemical content and antioxidant activity among the different black rice varieties. Black rice bran was found to have higher content of phenolics, flavonoids, and anthocyanins and higher antioxidant activity when compared to white rice bran. The phenolics, flavonoids, and anthocyanins of black rice bran being mainly present in free form. The most abundant anthocyanin was cyanidin 3-glucoside in black and red rices (Abdel-Aal et al. 2006).

The essential oils of rice bran showed inhibitory activity against complement system with 50% inhibitory concentrations (IC_{50}) values of 246 ppm (red rice bran) and 193 ppm (black rice bran) (Chung et al. 2011). Also, myristic acid, nonanal, (E)-β-ocimene and pelargonic acid were tested against complement system. Pelargonic acid was shown to moderate activity (50% inhibitory concentration = 132 μM).

An evaluation of DPPH radical scavenging activity of three types of coloured rice bran viz. forbidden rice, red rice and green rice, obtained from rice in which the pigment layer had been removed at milling yields of 90–100% and 80–90% revealed that rice bran obtained from forbidden rice at milling yields of 90–100% and 80–90% and rice bran obtained from red rice at milling yields of 90–100% showed favourable antioxidant activity (Fujita et al. 2010). The antioxidant components responsible for the antioxidant activity of the three types of colored rice bran were confirmed to be 3,4-dihydroxy methyl benzoate and *p*-methoxyphenol.

Animal Studies

Studies by Toyokuni et al. (2002) showed that unpolished coloured (black or red) rice instead of white rice ameliorated oxidative renal tubular damage in rats induced by ferric nitrilotriacetate. Renal lipid peroxidation was exacerbated in white rice-fed group in comparison with standard chow group, this exacerbation was not observed in red or black rice-fed groups. Serum protocatechuic acid and renal catalase activity were significantly increased after black rice diet, partly elucidating the antioxidative effect. Further, coloured rice were rich in proteins. In in-vivo C57BL/6 mice studies, plasma HDL-cholesterol was significantly higher, and thiobarbituric, acid-reactive substances were significantly lower in the black rice extract group (Chiang et al. 2006). Increased hepatic superoxide dismutase (SOD) and catalase (CAT) activities were observed in black rice extract -treated mice as compared to the control mice.

In another study, rats fed with Thai brown rice was found to high levels of 25-hydroxyvitamin D3[25(OH)D3] and α-tocopherol and low level of oxidative stress marker, malondialdehyde (MDA) through both radical and non radical antioxidant defences (Suwannalert et al. 2010). MDA levels were strongly inversely related to 25-hydroxyvitamin D3 and α-tocopherol levels. Brown rice whole grain was found to have total phenolic content of 65.8 mg GAE/100 g grain and oxygen radical absorbance capacity (ORAC) of 2,516 μmol TE/100 g grain (Okarter 2012). Brown rice contained 88.6 μmol/100 g grain of ferulic acid, and 32.7 μmol/100 g grain of *p*-coumaric acid in the insoluble bound fraction but contained no flavonoids (qurecetin, kaempferol, catechin, and rutin) in the insoluble-bound fraction of the grain. None of the phenolic compounds had any cellular antioxidant activity, most likely because these phenolic compounds did not have the structure necessary to impart cellular antioxidant activity. The data suggested that the potential health benefit of whole grain consumption in the lower gastrointestinal tract was independent of the cellular antioxidant activity of the phenolic compounds found in the insoluble-bound fraction of whole grains.

Antioxidant Activity in Rice By-Products

In the DPPH assay, the antioxidant activities of the Korean rice wine concentrates, including Maesilju (MSJ), Kookhwaju-1 (KHJ-1), Kookhwaju-2 (KHJ-2), Gugijaju (GGJ), Sasamju (SSJ), and Sogokju (SGJ), were 40, 66, 64, 35, 35, and 63%, respectively (Jeong et al. 2011). Additionally, the concentrates inhibited the formation of malonaldehyde (MA) from cod liver oil by 49, 83, 75, 82, 89, and 90%, respectively. The volatile extracts of Korean rice wine concentrates MSJ, KHJ-1, KHJ-2, GGJ, SSJ, and SGJ inhibited the oxidation of hexanal by 97, 99, 90, 90, 50, and 51%, respectively. Among the nonvolatile extracts of KRWs, KHJ-2 showed the highest inhibitory effect on MA formation.

An ethyl acetate extract of Kurosu (EK), a vinegar made from unpolished rice, exhibited the highest antioxidative activity in both thiobarbituric acid (TBA) method and the 1,1-diphenyl-2-picrylhydrazyl radical systems (Nishidai et al. 2000). Further, EK significantly suppressed double TPA application-induced H2O2 generation (53%) and lipid peroxidation determined by the TBA-reacting substance level (95%).

Antidiabetic Activity

Animal Studies

Administration of a pre-germinated brown rice diet to streptozotocin-induced diabetic rats ameliorated the elevation of blood glucose and

PAI-1 concentrations significantly, and tended to decrease the plasma lipid peroxide concentrations in comparison with rats fed a white rice diet (Hagiwara et al. 2004). Studies in Sprague–Dawley streptozotocin-induced diabetic rats fed diet containing resistant starch from corn or rice showed that resistant starch from corn and rice significantly lowered plasma total lipid and cholesterol concentrations compared to the diabetic control (Kim et al. 2003). The total liver cholesterol lowering effect was observed with resistant starch from rice. Neither immunoglobulin G nor C(3) were influenced by resistant starch. Izumi et al. (2007) demonstrated that 3% milled-rice exerted beneficial effects on blood glucose level and serum lipid concentrations in spontaneously non-insulin-dependent diabetic rats (Otsuka Long-Evans Tokushima Fatty rats (OLETF)). During the feeding period of 140 days, body weight of the OLETF rats receiving the 3% milled rice was significantly lower than that of the rats fed on the diet containing polished rice. The liver weight, the level of total lipids in liver, and the concentrations of triglyceride and total cholesterol in liver and serum of the OLETF rats on the 140th day were significantly lower in the 3% MRD than the polished rice group. The fasting blood glucose levels and incremental areas under the curve of blood glucose concentrations were significantly lower in the OLETF rats. Separate studies in OLETF diabetic rats, showed that ingestion of pre-germinated brown rice (PR) instead of white rice ameliorated both insulin resistance and imbalance of the levels of plasma adipocytokines leading to diabetic complications (Torimitsu et al. 2010). Ingestion of PR decreased elevated levels of HbA(1c) (glycated haemoglobin), TNF-α (tumour necrosis factor- a) and PAI-1 (plasminogen activator inhibitor-1) in OLETF rats. The decrease in adiponectin level of OLETF rats was ameliorated by PR-feeding. The size of adipocytes in PR-fed OLETF rats was smaller than that in white-rice-fed OLETF rats. In earlier studies in Wistar rats, they found that the high content of insoluble fibre was the major constituent responsible for lowering the postprandial blood glucose concentration in the pregerminated brown rice (Seki et al. 2005).

Jung et al. (2007) showed that administration of the ethyl acetate fraction of rice phenolic acids and it component, ferulic acid to C57BL/KsJ db/db mice significantly decreased blood glucose levels and increased plasma insulin levels hepatic glycogen synthesis and glucokinase activity compared with the control group. They significantly decreased plasma total cholesterol and low density lipoprotein (LDL) cholesterol concentrations. The results suggested that the phenolic acid fraction of rice bran and ferulic acid may be beneficial for treatment of type 2 diabetes because they regulate blood glucose levels by elevating glucokinase activity and production of glycogen in the liver.

Xie et al. (2008) reported that the novel fusion of a recombinant human-insulin-like growth factor (rhIGF-1) with a rice binding protein was found to accumulate abundantly in transgenic rice seeds. The unprocessed transgenic seeds could significantly increase plasma rhIGF-1 level and reduce blood glucose of diabetic mice via oral delivery. Also, the transgenic rice seeds reduced blood glucose of diabetic mice by enhancing islet cells survival and increasing insulin secretion rather than increasing insulin sensitivity. In subsequent studies, they found that rice-derived rhIGF-I was effective in inducing membrane ruffling and glucose uptake on rat skeletal muscle cells (Cheung et al. 2011). Oral meal test with rice-containing rhIGF-I acutely reduced blood glucose levels in streptozotocin-induced and Zucker diabetic rats, whereas it had no effect in normal rats. They also reported that only glutelin signal peptide could lead to successful expression of hIGF-I and one gram of hIGF-I rice grain possessed the maximum activity level equivalent to 3.2 μmolar of commercial rhIGF-I.

Clinical Studies

Glycemic index responses of two Thai cooked rices and six types of cooked noodles consumed by eight noninsulin-dependent diabetics correlated positively with in-vitro starch digestibility of food slurry and negatively with amylose content of the food (Juliano et al. 1989). Glutinous (waxy) rice had the highest values, and mung bean noodles the lowest.

Larsen et al. (1996) compared the effects meals of white bread, cooked polished rice with high (27%) and low amylose content (12%) with different gelatinisation temperature and as non-parboiled and parboiled in 12 non-insulin-dependent diabetic (NIDDM) subjects. The results showed that the glycaemic indices (GI) of all rice varieties were lower than that of white bread. GI of parboiled rice with a high amylose content was lower than that of parboiled rice with a low amylose content indicating glycaemic response to be independent of parboiling and physico-chemical characteristics. The study showed that the amylose content, but not the gelatinisation temperature, may be an useful criterion in selection of low GI rices also after parboiling. They also studied the influence of parboiling and the severity of the process on glycaemic and insulinaemic responses to rice in nine type 2 diabetic subjects (Larsen et al. 2000). Rice samples elicited lower postprandial plasma glucose response than white bread. There was no effect of traditional parboiled on glycaemic index, whereas severely pressure parboiled reduced the glycaemic index by almost 30% compared to non-parboiled

The glycaemic response of different varieties of rice grown in Sri Lanka were studied in 22 fibre mill workers aged between 25 and 50 years (Hettiarachchi et al. 2001). The glycaemic indices of varieties of red raw rice varied between 56 and 73 and the variety Bg 350 had the lowest glycaemic index. There was no significant difference between mean glycaemic index of varieties of white raw and some varieties of red raw rice. Parboiled varieties of red raw rice had a significantly lower glycaemic index than white raw rice and some of the red raw rice.

The influence of three kinds of processed rice food, garaeduk, bagsulgi, and cooked rice on the enzymatic hydrolysis of rice starch in-vitro and on the postprandial glucose and insulin responses in ten patients with type 2 diabetes mellitus were assessed (Kim et al. 2004). The postprandial serum glucose and insulin levels at 90 min after ingesting bagsulgi and cooked rice were less than those at 60 min while the levels at 90 min after ingesting garaeduk were higher than those at 60 min. Garaeduk also significantly decreased the incremental responses of glucose and insulin when compared with bagsulgi and cooked rice. The results suggested that garaeduk would be the most unlikely to increase the postprandial serum glucose and insulin levels among the three rice foods. They concluded that food form, which eventually differentiated each food by its specific surface area with the same degree of maceration because of the characteristic physical strength, affected the rate of rice starch hydrolysis both in-vitro and in-vivo.

In a week-long study of 11 diabetic patients, daily administration of a diet enriched with 40 g fibre (30.6% insoluble and 11.7% soluble components) from rice bran, significantly reduced mean fasting and postprandial serum glucose levels (Rodrigues Silva et al. 2005). For all patients, the high-fibre diet increased faecal weight. This increase was due to the fibre excreted, rather than water retained. There was no relationship between the increase in fibre intake and its faecal excretion. Sucrose and raffinose were found in the bran, but not in the faeces. Lactose was present in the stools of the patients receiving enriched diet.

In a randomised crossover study of brown rice administration involving ten healthy and nine type 2 diabetic volunteers, the glycemic area and glycemic index were, respectively, 19.8 and 12.1% lower in brown rice than milled rice in healthy volunteers, while in diabetics, the respective values were 35.2 and 35.6% lower (Panlasigui and Thompson 2006). The effect was partly due to the higher amounts of phytic acid, polyphenols, dietary fibre and oil in brown compared to milled rice and the difference in some physico-chemical properties of the rice samples such as minimum cooking time and degree of gelatinisation. Also total sugar released in vitro was 23.7% lower in brown rice than in milled rice. In a randomized, controlled, crossover study design with a washout period of 6 weeks between the two phases of 11 healthy, non-obese and 10 obese subjects given a modified diet of equal proportions of fibre-rich Goami No. 2 rice and standard rice, body weight was significantly lower in both the non-obese and obese subjects (Lee et al. 2006). The BMI (body mass

index) was significantly lower in obese subjects. The modified diet was associated with lower serum triacylglycerol, total cholesterol, low-density lipoprotein cholesterol and C-peptide concentrations in the obese subjects.

Effects of pre-germinated brown rice (PGBR) on postprandial blood glucose and insulin concentrations were compared with brown rice (BR) and white rice (WR) in two studies of 19 and 13 healthy young subjects (Ito et al. 2005). They found that the incremental areas under the curve (IAUC) of blood glucose concentrations after the administration of PGBR and BR were lower than those after WR but were not different between BR and PGBR (Study 1). The higher the ratio of PGBR/WR, the lower the glycemic index became (Study 2). The results suggested that intake of pre-germinated brown rice instead of white rice was effective for the control of postprandial blood glucose concentration without increasing the insulin secretion.

A 12-week study involving 28 diabetic volunteers demonstrated that stabilized rice bran could lower the level of glycated hemoglobin (HbA1c) and blood lipids and raise blood adiponectin concentrations in type 2 diabetic subjects (Cheng et al. 2010a). Postprandial glucose and the area under the glucose curve of the rice bran group were significantly lower than baseline levels by 14.4 and 15.7%, respectively. The HbA1c values in the rice bran group were also significantly lower compared to baseline. Serum total cholesterol, LDL cholesterol and plasma free fatty acid concentrations in the rice bran group were 9.2, 13.7 and 20% lower, respectively, and adiponectin concentration 40% higher than in the placebo group.

The results of a cross-over study of 11 subjects with impaired fasting glucose (IFG) or type 2 diabetes suggested that diets including pre-germinated brown rice may be useful to control blood glucose level (Hsu et al. 2008). Blood concentrations of fasting blood glucose, fructosamine, serum total cholesterol and triacylglycerol levels were favourably improved on the pre-germinated brown rice, but not on the white rice diet. White rice is made by polishing brown rice and has lost various nutrients.

Epidemiological Studies

Sun et al. (2010) using diet, lifestyle practices, and disease status data of 39,765 men and 157,463 women in the Health Professionals Follow-up Study and the Nurses' Health Study I and II prospectively examined the effect of white and brown rice consumption in relation to type 2 diabetes. They found that higher intake of white rice was associated with a higher risk of type 2 diabetes. In contrast, high brown rice intake was associated with a lower risk of type 2 diabetes. Their findings supported the recommendation that most carbohydrate intake should come from whole grains rather than refined grains to help prevent type 2 diabetes. Using data from 25,666 men and 33,622 women aged 45–75 years who participated in the second survey of the Japan Public Health Center-based Prospective Study, Nanri et al. (2010) found that elevated intake of white rice was associated with an increased risk of type 2 diabetes in Japanese women. In men, the association was unclear, although there was a suggestion of a positive association in persons who were not engaged in strenuous physical activity.

Hypocholesteromic/ Antihypertriglyceridemic Activity

In-Vitro Studies

Gamma-oryzanol, a mixture of ferulic acid esters of sterol and triterpene alcohols, was found to occur in rice bran oil at a level of 1–2%, where it serves as natural antioxidant (Scavariello and Arellano 1998). Recent research showed that gamma-oryzanol could lower the cholesterol levels in the blood, lowering the risk of coronary heart disease, besides that, it also has been used in Japan like natural antioxidant in foods, beverages and cosmetics. Results of in-vitro studies suggested that the hypocholesterolemic activity of γ- oryzanol was due in part to decreased apical uptake of cholesterol into enterocytes and perhaps a decrease in 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase activity (Mäkynen et al. 2012).

Animal Studies

Seetharamaiah and Chandrasekhara (1989) reported that the serum total, free esterified and (LDL + VLDL)-cholesterol levels of rats maintained on a 10% refined rice bran oil diet were significantly lower than those on a 10% groundnut oil diet and HDL-cholesterol were higher. Addition of oryzanol at 0.5% level to the diet containing rice bran oil showed a further significant decrease in serum total cholesterol. Liver lipids of rats fed bran oil were also markedly lower than their groundnut oil fed counterparts. The cholesterol lowering ability of rice bran oil appeared to be due to oryzanol and to some other components of the unsaponifiable matter. In an 18-week study, wistar rats fed 20% rice bran oil or peanut oil, gained more weight than groups fed 5% oil (Purushothama et al. 1995). The animals which received rice bran oil in their diet had, in general, comparatively lower levels of cholesterol, triglycerides and phospholipids. In contrast, rats receiving 20% rice bran oil in their diet, showed an increase of 20% in high density lipoproteins (HDL-C), compared to the animals fed with peanut oil. Similarly, low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) were lower in rice bran oil-fed groups, than in the peanut oil-fed groups. There was, however, no significant differences in the cholesterol/phospholipid (C/P) ratio of the two groups.

Two new tocotrienols, desmethyl tocotrienol [3, 4-dihydro-2-methyl-2-(4,8,12-trimethyltrideca-3′(E),7′(E), 11′-trienyl)-2 H-1-benzopyran-6-ol] and didesmethy tocotrienol [3, 4-dihydro-2-(4,8,12-trimethyltrideca-3′(E),7′(E), 11′-trienyl)-2 H-1-benzopyran-6-ol], isolated from rice bran, significantly lowered serum total and LDL cholesterol levels and inhibited HMG-CoA reductase activity in chickens (Qureshi et al. 2000).

Animal studies showed that rice bran extract (Ricetrienol) containing α-tocopherol, tocotrienol and phytosterol prevented the elevation of plasma peroxylipid in obese diabetic KKAy mice (Kanaya et al. 2004). Ricetrienol administration did not affect hyperglycemia, body weight or hyperlipidemia. Plasma malonedialdehyde, urine 8-isoprostane and 8-OHdG in the normal diet diabetic KKAy mice were significantly increased compared with the non-diabetic mice and the elevation of plasma malonedialdehyde was significantly suppressed by 0.1% Ricetrienol. glutathione peroxidase mRNA expression was significantly increased in the Ricetrienol group when compared with the non-diabetic mice. Plasma α-tocopherol in the Ricetrienol group was significantly higher than that in the normal diet diabetic KKAy mice.

Studies showed that rice bran oil (RBO) and oryzanol in the diets reduced plasma lipid and lipoprotein cholesterol concentrations and aortic cholesterol ester accumulation to a greater extent than ferulic acid in hypercholesterolemic hamsters (Wilson et al. 2007). After 10 weeks on the diets, plasma total cholesterol (TC) and non-high-density lipoprotein cholesterol (HDL-C) (very low- and low-density lipoprotein) concentrations were significantly lower in the RBO (−64 and −70%, respectively), the ferulic acid (−22 and −24%, respectively) and the oryzanol (−70 and −77%, respectively) diets compared to control. Plasma TC and non-HDL-C concentrations were also significantly lower in the RBO (−53 and −61%, respectively) and oryzanol (−61 and −70%, respectively) diets compared to the ferulic acid. Hamsters fed the control and ferulic acid diets had significantly higher plasma vitamin E concentrations compared to the RBO (201 and 161%, respectively) and oryzanol (548 and 462%, respectively) diets; the ferulic acid and oryzanol diets had significantly lower plasma lipid hydroperoxide levels than the control (−57 and −46%, respectively) diet. The study suggested that at equal dietary levels, oryzanol had a greater effect on lowering plasma non-HDL-C levels and raising plasma HDL-C than ferulic acid, possibly through a greater extent to increase faecal excretion of cholesterol and its metabolites such as coprostenol. However, ferulic acid may have a greater antioxidant capacity via its ability to maintain serum vitamin E levels compared to RBO and oryzanol. Thus, both oryzanol and ferulic acid may exert similar antiatherogenic effect.

Lee et al. (2007a, b, c) found that rats fed germinated giant embryonic rice (GGED) for 5 weeks had higher HDL-cholesterol compared to those fed giant embryonic rice (GED), or conventional brown rice. there were no differences in the plasma

total cholesterol and triglyceride concentrations between the groups. The atherogenic indices of both giant embryonic rice groups were higher than brown rice. While superoxide dismutase and catalase were significantly activated in rats fed both GGE-D and GE-D, glutathione peroxidase was significantly and most effectively activated in those fed GGE-D. The results indicated consumption of germinated giant embryonic rice to be effective in lowering atherosclerosis cardiovascular disease risk. Studies in Sprague–Dawley male rats showed that hypercholesterolaemia and elevation of LDL-cholesterol were successfully ameliorated by the experimental diets containing brown rice (BR) and pre-germinated brown rice (PGBR) (24 and 48 h pre-germination) (Roohinejad et al. 2010). It was also found that the significantly better effect on lipid profile of hypercholesterolaemic rats was observed by prolonging the pre-germination time. As compared to non-germinated brown rice, the germinated brown rice showed the higher cardio-protective effect on hypercholesterolaemic Sprague–Dawley male rats. The study suggested that PGBR could be used instead of BR and polished rice in the human diet although both brown rice and pre-germinated brown rice contained various functional compounds such as γ-oryzanol, dietary fibre and γ-aminobutyric acid (GABA). Mohd Esa et al. (2011) found that rabbits fed a germinated brown rice (GBR) diet demonstrated significantly lower levels of total cholesterol (TC), low-density lipoprotein (LDL), LDL/HDL, and atherogenic index (AI) and a higher level of high-density lipoprotein (HDL) compared to brown and white rice. Results from atherosclerotic plaque assessment further supported the findings. The level of malondialdehyde (MDA), an indicator for oxidative stress, was also reduced by GBR diet. The positive change in lipid profile in the rabbits fed germinated brown rice for 10 weeks appeared to correspond with the higher amounts of γ-oryzanol, tocopherol, and monounsaturated fatty acid (MUFA) content.

Clinical Studies

In two studies, a parallel-arm design (26 volunteers) and randomized cross-over (14 volunteers) studies rice bran oil, not fibre, lowered cholesterol in healthy, moderately hypercholesterolemic adults (Most et al. 2005). There were no substantial differences in the fatty acid composition of the diets; therefore, the reduction of cholesterol was due to other components present in the rice bran oil, such as unsaponifiable compounds.

In a randomised study of 202 middle-aged adults with diabetes or a high risk for diabetes substituting white rice (WR) with brown rice (BR) for 16 weeks did not substantially affect metabolic risk factors (BMI, waist circumference, blood pressure, glycated hemoglobin, and serum lipid, glucose, and insulin concentrations) (Zhang et al. 2011). Over the course of the intervention, no between-group differences were found for any markers except the serum LDL cholesterol concentration, which decreased more in the white rice group compared to the brown rice group and this was found only in patients with diabetes. The reversion rate of reduced serum HDL cholesterol was marginally higher in the BR group (14.9%) than in the WR group (6.9%). Among diabetic patients, a greater reduction in diastolic blood pressure was observed in the BR group compared to the WR group.

Red Yeast Rice and Antihyperchlosterolemic Activity

Red yeast rice, a *Monoacus* rice product, has been used for centuries in China as both a food and a medicinal product (Ma et al. 2000; Wang and Lin 2007). Red yeast rice is also known as red mould rice, red Chinese rice; and in China and Taiwan as *Hong Qu*, *Hon-Chi*, *Anka* or *Ang-kak*, and in Japan as *Beni Koji* or red Koji. Red yeast rice is made by solid state fermentation of moist rice by a yeast *Monascus purpureus*. In Chinese medicine, red yeast rice is used to lower cholesterol, improve blood circulation, and aid digestive problems. It has been found to contain monacolin family of polyketides, the major bioactive compounds and other substances such as flavonoids, polyunsaturated fats, phytosterols, pyrrolinic compounds, and trace elements (Ma et al. 2000; Wang and Lin 2007). Fourteen monacolin compounds namely monacolin K (mevinolin), monacolin J, monacolin L, monacolin M, monacolin X, and their hydroxy

acid form, monacolin K hydroxyacid (MKA), monacolin J hydroxy acid (MJA), monacolin X hydroxy acid (MXA), monacolin L hydroxy acid (MLA), monacolin M hydroxy acid (MMA) as well as dehydromonacolin K; dihydromonacolin L; compactin; 3α-hydroxy-3,5-dihydromonacolin L were identified in red yeast rice (Li et al. 2004). The most important bioactive compound isolated from *Monascus* is monacolin K, which is identical to the potent cholesterol-lowering, antiatherosclerotic drug lovastatin, a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor that prevent the reduction of HMG-CoA to mevalonic acid and the formation of cholesterol. Red yeast rice had been reported to lower blood-lipid levels (Wang et al. 1997; Li et al. 1998, 2004; Qin et al. 1999; Heber et al. 1999; Ma et al. 2000; Heber et al. 2001; Huang et al. 2007; Venero et al. 2010). In food, red yeast rice is used as an additive for the colouring, flavouring and preservation of foods, which may be permitted in some Asian countries but not in Europe. The European Food Safety Authority (EFSA) has reported on the Scientific Opinion on the substantiation of health claims related to monacolin K from red yeast rice and maintenance of normal blood LDL-cholesterol concentrations (EFSA 2011) but has not classified such products as food or medicine, thus the EFSA's opinion should not be interpreted as an approval of red yeast rice for food or medicinal use.

Studies of nine proprietary products of red rice yeast showed wide variation in the content and profile of monacolins and some also contained citrinin a toxic fermentation byproduct (Heber et al. 2001). Total monacolin content varied from 0 to 0.58% w/w and only 1 of 9 preparations had the full complement of 10 monacolin compounds. Citrinin was found at measurable concentrations in seven of the nine preparations. They recommended that standardized manufacturing practices should be established for Chinese red yeast rice sold as a dietary supplement in order ensure equivalence of content of active ingredients in preparations being sold to the public and to limit the production of unwanted byproducts of fermentation such as citrinin. Citrin had been reported to be hepatotoxic and nephrotoxic (Lee et al. 2007a, b, c). Citrinin was detected in samples of commercial *Monascus* fermentation products at concentrations varying between 0.2 and 17.1 μg/g (Sabater-Vilar et al. 1999). Citrinin and two *Monascus* extracts induced a positive dose-dependant mutagenic response in the *Salmonella*-hepatocyte-assay using strain TA-98. However, no mutagenicity could be detected in the *Salmonella*-microsome assay, neither with nor without S9-mix, for citrinin and *Monascus* extracts, applying TA-98, TA-100, TA-1535, TA-1538 and TA-97. Gordon et al. (2010) found marked variability in monacolin content in 12 proprietary red yeast rice (RYR) products and the presence of citrinin in one-third of the formulations tested. There was marked variability in the 12 RYR products in total monacolins (0.31–11.15 mg/capsule), monacolin K (lovastatin) (0.10–10.09 mg/capsule), and monacolin KA (0.00–2.30 mg/capsule). Four products had elevated levels of citrinin. Chen and Hu (2005) reported the development of a mutant strain of *Monacus* sp. M12-69 that could be used to produce red fermented rice with high concentration of monacolin K (2.52 mg/g) and low concentration of citrinin (0.13 ng/g).

Red yeast rice has been reported to have adverse effects attributable to its constituent monacolin K (lovastatin), including an increased risk of myopathy, acute rhabdomyolysis, symptomatic hepatitis and anaphylactic reactions. Prasad et al. (2002) reported a case of an herbal preparation-induced rhabdomyolysis in a stable renal-transplant recipient, attributed to the presence of red yeast rice (*Monascus purpureus*) within the mixture. Rhabdomyolysis is a breakdown of muscle fibres that leads to the release of muscle fibre content (myoglobin) into the bloodstream and is a known complication of hepatic 3-methylglutaryl coenzyme A reductase (HMG-CoA) inhibitor (statin) therapy for post-transplant hyperlipidemia. Smith and Olive (2003) reported a case of a middle-aged man presented with joint pain and muscle weakness who had ingested the herbal preparation Chinese red rice 3 months earlier. that had begun

2 months before presentation. Three months before presentation, he had begun to take the herbal preparation Chinese red rice. Laboratory testing revealed a moderately elevated creatine phosphokinase which rose again when he resumed the product 8 months later. A butcher preparing sausages containing red yeast rice was presented with severe anaphylactic reaction developing sneezing, rhinitis, conjunctivitis, generalised pruritus, followed by widespread urticaria (Wigger-Alberti et al. 2002). *Monascus purpureus* could be shown as allergic agent by means of prick-to-prick test, cellular antigen stimulation test (CAST) and different immunoblots. A case of a women developing hepatitis was reported after taking red yeast rice, however, no cause-effect relationship was established as the women was also taking two other medications (Roselle et al. 2008).

Animal Studies

Li et al. (1998) demonstrated that *Monascus purpureus* (red yeast rice) significantly reduced serum total cholesterol and triglycerides in rabbits and quail with experimental hyperlipidemia and suppressed atherosclerosis by an atherogenic diet. The aorta and lipidosis in the livers of red yeast rice-treated rabbits were less severe than those of the control model rabbits. In another study in hypertriglyceridemic rats anka, a fermented rice product of *Monascus* sp., exhibited hypotriglyceridemic effect (Wang et al. 2000). After 6 months, the concentrations of serum triglycerides, total cholesterol, VLDL-C, and LDL-C had significantly decreased, whereas that of HDL-C had slightly increased in 30% fructose-Anka-fed rats as compared with the 30% fructose-fed rats, but hepatic lipase activity had increased in the Anka-fed groups. The ratio of lipoprotein lipase/hepatic lipase was not significantly different between 30% fructose-Anka-fed rats and 30% fructose-fed rats. The dietary intake and weight of these two groups were approximately the same. Similar results were obtained in non-induced hypertriglyceridemic rats. The concentrations of triglycerides and cholesterol did not significantly differ in the liver.

Clinical Studies

Wang et al. (1997) conducted a in a multicenter, single-masked clinical trial of 446 hyperlipidemic patients, randomly assigned to two groups: a group of 324 patients received a M. *purpureus* (red yeast) rice (RYR) preparation, and a positive control group of 122 patients administered another Chinese herbal medicine, Jiaogulan (*Gynostemma pentaphylla*). After 8 weeks, serum total cholesterol decreased significantly by 22.7% and low-density lipoprotein cholesterol by 30.9% in the patients treated with RYR preparation, and patients in the positive control group showed 7.0 and 8.3% reductions, respectively. RYR treatment also significantly increased high-density lipoprotein (HDL) cholesterol by 19.9%, which was a significantly larger increase than the 8.4% increase observed in the positive control group. Importantly, RYR preparation significantly lowered serum triglycerides by 34.1% after 8 weeks, which was a significantly greater decrease than the reduction of 12.8% observed in the positive control group. Some patients experienced a few mild side effects (heartburn, flatulence, and dizziness) during the 8-week treatment with RYR preparation. They concluded that the traditional Chinese rice preparation used as a dietary supplement was extremely effective and well tolerated in reducing elevated serum cholesterol and triglycerides. In a double-blind, placebo-controlled, prospectively randomized 12-week controlled trial involving 83 healthy subjects (46 men and 37 women aged 34–78 years) with hyperlipidemia and not being treated with lipid-lowering drugs, red yeast rice was found to significantly reduce total cholesterol, LDL cholesterol, and total triacylglycerol concentrations compared with placebo (Heber et al. 1999). HDL cholesterol did not change significantly. In a double-blind, placebo-controlled clinical trial involving 70 elderly hyperlipidemic patients, red yeast rice (RYR) preparation was found to be effective in managing elevated serum cholesterol and triacylglycerols and to be safe (Qin et al.1999). RYR preparation (1.2 g/day) significantly reduced serum total cholesterol by 25.9% and LDL-cholesterol by 32.8%, whereas the control group (1.2 g/day placebo) showed 6.5 and 7.9% reductions, respectively. Notably this RYR preparation,

after 8 weeks lowered serum triacylglycerols by 19.9% this was significant from the 2.3% increase observed in controls. 91.2% of patients in the treatment group showed a significant improvement in their lipid profile.

In a study of 79 hypercholesterolemic patients (aged 23–65 years), Huang et al. (2007) found that 8-week treatment with red yeast rice (twice daily dose) showed significantly greater reduction than placebo treatment in low-density lipoprotein cholesterol levels, total cholesterol/high-density lipoprotein cholesterol, low-density lipoprotein cholesterol/high-density lipoprotein cholesterol and apolipoprotein B/apolipoprotein A-I ratios. In a randomized, controlled trial study involving 62 patients with dyslipidemia and myalgias caused by intolerance to statins, red yeast rice and therapeutic lifestyle change decreased LDL cholesterol level without increasing creatinine phosphokinase (CPK) or pain levels and may be a treatment option for dyslipidemic patients who cannot tolerate statin therapy (Becker et al. 2009). In the red yeast rice group, LDL cholesterol decreased by 1.11 mmol/L (43 mg/dL) from baseline at week 12 and by 0.90 mmol/L (35 mg/dL) at week 24. In the placebo group, LDL cholesterol decreased by 0.28 mmol/L (11 mg/dL) at week 12 and by 0.39 mmol/L (15 mg/dL) at week 24. Low-density lipoprotein cholesterol level was significantly lower in the red yeast rice group than in the placebo group at both weeks 12 and 24. In another study, of 43 adults with dyslipidemia and history of statin discontinuation because of myalgia, two treatments were compared red yeast rice 2,400 mg twice daily versus pravastatin 20 mg twice daily for 12 week (Halbert et al. 2010). The low-density lipoprotein cholesterol level decreased 30% in the red yeast rice group and 27% in the pravastatin group. The mean pain severity did not differ significantly between the two groups. No difference was found in muscle strength between the two groups at week 4, week, or week 12. The authors concluded that red yeast rice was tolerated as well as pravastatin and achieved a comparable reduction of low-density lipoprotein cholesterol in a population previously intolerant to statins.

In a multicenter study of nearly 5,000 Chinese patients with previous myocardial infarction and average low-density lipoprotein cholesterol levels at baseline were randomly assigned to either to placebo or to Xuezhikang (XZK), a partially purified extract of red yeast rice, daily for an average of 4.5 years (Lu 2008). Frequencies of Frequencies of the primary end point (nonfatal myocardial infarction and death from coronary heart disease) were 10.4% in the placebo group and 5.7% in the XZK-treated group, with absolute and relative decreases of 4.7 and 45%, respectively. Treatment with XZK also significantly decreased cardiovascular events and total mortality by 30 and 33%, the need for coronary revascularization by 1/3, and lowered total and low-density lipoprotein cholesterol and triglycerides, but raised high-density lipoprotein cholesterol levels. The study concluded that long-term therapy with XZK significantly decreased the recurrence of coronary events and the occurrence of new cardiovascular events and deaths, improved lipoprotein regulation, and was safe and well tolerated. In another randomised, study of 1,530 elderly hypertensive patients (> or = 65-years-old) with previous myocardial infarction in the Chinese Coronary Secondary Prevention Study were assigned either to placebo (n = 758) or to Xuezhikang (n = 772) (Li et al. 2009). There were 68 cases of coronary events (8.8%) detected in the Xuezhikang group and 108 cases (14.3%) in the placebo group (38.2% risk reduction by Xuezhikang therapy). Death from coronary heart disease (CHD) totalled 49 cases in the Xuezhikang group (6.4%) and 68 cases in the placebo group (9.0%), indicating that Xuezhikang significantly decreased the risk of CHD death by 29.2%. Their study demonstrated that Xuezhikang therapy could effectively and safely reduce cardiovascular events and all-cause death in Chinese elderly hypertensive patients with previous myocardial infarction.

Venero et al. (2010) found that red yeast rice modestly decreased total and LDL cholesterol, was well-tolerated, and was an acceptable alternative in 25 patients intolerant to lipid-lowering medications. These patients had experienced myalgias (68%), gastrointestinal intolerance (16%), and/or elevated alanine aminotransferase levels (8%) with previous use of other lipid-lowering agents. The total cholesterol decreased 15%

and LDL cholesterol decreased 21% during 74 ± 39 days of treatment. Most (92%) patients tolerated the treatment, and many (56%) achieved their LDL cholesterol goal. In statin-intolerant patients, the total cholesterol level decreased 13% and LDL cholesterol decreased 19%.

In a meta-analysis conducted by Liu et al. (2006) 93 randomized trials (9,625 participants) published in PubMed, CBMdisk, TCMLARS, the Cochrane Library, and AMED up to December 2004 were included and three red yeast rice (RYR) preparations (Cholestin, Xuezhikang and Zhibituo) were tested. The combined results showed significant reduction of serum total cholesterol levels, triglycerides levels and LDL-cholesterol levels and increase of HDL-cholesterol levels by RYR treatment compared with placebo. The lipid modification effects appeared to be similar to pravastatin, simvastatin, lovastatin, atorvastatin, or fluvastatin. Compared with non-statin lipid lowering agents, RYR preparations appeared superior to nicotinate and fish oils, but equal to or less effective than fenofibrate and gemfibrozil. No significant difference in lipid profile was found between Xuezhikang and Zhibituo. RYR preparations were associated with non-serious adverse effects such as dizziness and gastrointestinal discomfort.

Anti-hypoadiponectinemia/Metabolic Syndrome Amelioration Activity

Low circulating levels of adiponectin are related to metabolic syndrome, a cluster of risk factors including insulin resistance and type 2 diabetes and is found to associate partly with chronic stress at work in human (Ohara et al. 2011). They found that γ-aminobutyric acid (GABA) and γ-oryzanol abundantly contained in germinated brown rice significantly increased the relative low molecular weight (LMW) and high molecular weight (HMW) adiponectin levels under immobilization stress. Additionally, the co-administration of GABA and γ-oryzanol also increased both relative LMW and HMW adiponectin levels respectively and was effective in an earlier phase from 30 to 54 h. The results indicate that the co-administration of GABA and γ-oryzanol might be effective in preventing stress-induced hypoadiponectinemia in mice and be also a promising tool for improving metabolic syndrome aggravated by chronic stress. Studies in mice had demonstrated that γ-oryzanol from rice bran suppressed NF-κB activation and increased adiponectin secretion from adipocyte (Ohara et al. 2009; Nagasaka et al. 2011). In a subsequent study, they found that oral administrations of beef tallow and palmitate significantly suppressed serum adiponectin levels into around half of the initial level from 48 to 96 h after administration compared with the case of corn oil (Nagasaka et al. 2011). Co-administration of γ-oryzanol successfully remedied mouse hypoadiponectinemia induced by ingestion of beef tallow and the relative adiponectin levels attained to 1.66 at 96 h after administration.

Rice bran fractions, Driselase (DE) and ethanol fractions (DF) appeared to have a beneficial dietary component that improved hypertension, hyperlipidemia, and hyperglycemia in stroke-prone spontaneously hypertensive rats (SHRSP) (Ardiansyah et al. 2006). After 8 weeks feeding, blood pressure decreased in the DF and EF groups in comparison with the control group. Plasma ACE inhibitory activity, BUN (blood urea nitrogen), BUN/creatinine ratio, albumin, triglyceride, and glucose levels were lower in the DF and EF groups than in the control group. Plasma nitric oxide and urinary 8-hydroxy-2′-deoxyguanosine levels were lower in the DF and EF groups than in the control group. In a subsequent study DF and ferulic acid diets significantly improved hypertension as well as glucose tolerance, plasma nitric oxide (NOx), urinary 8-hydroxy-2′-deoxyguanosine and other parameters in SHRSP rats (Ardiansyah et al. 2007). In particular, compared to the ferulic acid diet, the DF diet produced a significant improvement in urinary NOx, hepatic triacylglycerol and several mRNA expressions of metabolic parameters involved in glucose and lipid metabolisms. The results of the metabolic syndrome-related parameters obtained suggest that the Driselase diet was more effective than the ferulic acid diet. In another study, hypertension and plasma lipid, nitric oxide, insulin, leptin, adiponectin levels, and glucose metabolism were significantly improved in

SHRSP rats administered adenosine, an active component from the Driselase-treated fraction from rice bran (Ardiansyah et al. 2009). The mRNA expression levels of genes involved in lipid and glucose metabolism were altered in the adenosine group. Single oral administration of adenosine (10 mg/kg body weight) improved hypertension and plasma triglyceride, glucose, and nitric oxide levels 2 h after administration. The results indicated that oral acute and chronic administration of adenosine were beneficial and improved the metabolic syndrome-related disease parameters. In a 12-week randomized, double-blind, placebo-controlled study of 30 subjects, consumption of brown lees (a fermentation by-product from Korean rice wine production) was compared with a mixed-grain dietary product (Kim et al. 2011). Consumption of rice brown lees resulted in greater reduction in waist circumference and levels of aspartate transaminase and alanine transaminase compared to the mixed grain group, suggesting improvement in metabolic parameters in diabetic patients.

Anticancer Activity

In-Vitro-Studies

In-vitro studies showed that the transformation of umbilical blood B lymphocytes stimulated by Epstein-Barr virus and expression of Epstein-Barr virus-early antigen in Raji cells may be significantly inhibited by selenium-rich rice extract, suggesting that selenium-rich rice could be used for preventing nasopharyngeal carcinoma (Jian et al. 2003). Studies showed that addition of selenium-enriched rice or selenite significantly inhibited the incidence of cyclophosphamide-induced micronuclei and mitomycin C -induced chromosomal aberration in mice and the effect was dose-dependent (Hu et al. 2005). Regular rice did not alter the occurrence of chemical-induced mutation. Providing selenite or selenium-enriched rice also significantly increased the activity of glutathione peroxidase in liver and the selenium concentration in blood compared to regular rice.

The ethanol-water bran extracts of five pigmented rice cultivars demonstrated anti-tumour-promoting activity by inhibition of Epstein-Barr virus early-antigen activation (EBV-EA) induced by the tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate (Nam et al. 2005a). Compared to non-pigmented white cooking rice extract, the pigmented bran extracts strongly inhibited phorbol ester-induced tumour promotion in marmoset lymphoblastoid cells B95-8 in-vitro. Nam et al. (2005b) also reported that ethanol-water extracts of two blackish-purple pigmented exhibited higher activities than no-pigmented brown rice variety in the following tests: inhibition of xanthine oxidase activity; chelation of ferrous ions; reduction of potassium ferricyanide; scavenging of superoxide anions, hydroxyl radicals, and intracellular peroxides; inhibition of 4-nitroquinoline N-oxide-induced mutagenesis; and inhibition of phorbol ester-induced tumour promotion, in mammalian cells (human leukemia HL-60, marmoset B lymphoblastoid B95-8, and Chinese hamster V79 lung cells)

Hydroxylated triterpene alcohol ferulates from rice bran namely 24R-cycloart-25-ene-3β,24-diol-3β-*trans*-ferulate (2), and cycloart-23Z-ene-3β,25-diol-3β-*trans*-ferulate(3),cycloartenol *trans*-ferulate (4) and 24-methylenecycloartanol *trans*-ferulate (5) showed moderate cytotoxicity against MCF-7 breast cancer cells (Luo et al. 2005).

Two bioactive anthocyanin compounds, peonidin 3-glucoside and cyanidin 3-glucoside, isolated from black rice strongly inhibited growth of HS578T human breast cancer cells via G2/M arrest (Chen et al. 2005). Peonidin 3-glucoside treatment suppressed protein levels of cyclin-dependent kinase (CDK)-1, CDK-2, cyclin B1, and cyclin E, whereas cyanidin 3-glucoside decreased the protein levels of CDK-1, CDK-2, cyclin B1, and cyclin D1. Furthermore, cyanidin 3-glucoside or peonidin 3-glucoside also induced caspase-3 activation, chromatin condensation, and apoptosis. The rice anthocyanins also inhibited the growth of Lewis lung carcinoma cells in-vivo. Both anthocyanins also exhibited the anti-metastatic effects by strongly inhibiting the invasion and motility of SKHep-1 cells. (Chen et al. 2006). This effect was associated with a reduced expression of matrix metalloproteinase (MMP)-9 and urokinase-type plasminogen activator (u-PA).

Peonidin 3-glucoside and cyanidin 3-glucoside also exerted an inhibitory effect on the DNA binding activity and the nuclear translocation of AP-1. Both compounds also exerted an inhibitory effect of cell invasion on various cancer cells (SCC-4, Huh-7, and HeLa). In further studies, they found that peonidin 3-glucoside inhibited metastasis of Lewis lung carcinoma cells by downregulation of proteinases activities and MAPK (nitrogen-activated protein kinase) pathway (Ho et al. 2010).

Two new tocotrienols, desmethyl tocotrienol [3, 4-dihydro-2-methyl-2-(4,8,12-trimethyltrideca-3′(E),7′(E), 11′-trienyl)-2 H-1-benzopyran-6-ol] and didesmethy tocotrienol [3, 4-dihydro-2-(4,8,12-trimethyltrideca-3′(E),7′(E), 11′-trienyl)-2 H-1-benzopyran-6-ol], isolated from rice bran, exhibited greater in-vitro antioxidant activities and greater suppression of B16 melanoma cell proliferation than α-tocopherol and known tocotrienols (Qureshi et al. 2000). Treatment of human mesothelioma H28 cells with γ-tocotrienol-rich fraction (TRF) from rice bran elicited a marked reduction in the viability of H28 cells in a dose-dependent manner, while cisplatin treatment had no effect on the cells, indicating that H28 cells are resistant to cisplatin (Nakashima et al. 2010). A significant increase in cytotoxicity was observed in H28 cells treated with TRF, and this effect was enhanced by the combination treatment with cisplatin. The cytotoxic effect was closely related to the inhibition of phosphatidylinositol 3-kinase (PI3K)-AKT signalling.

Steroids isolated from *Monascus purpureus*-fermented rice: (22S, 23R, 24S)-20β,23α, 25α-trihydroxy-16,22-epoxy-4,6,8(14)-trienergosta-3-one (1), and (22E, 24R)-3β,5α-dihydroxyergosta-23-methyl-7,22-dien-6-one (2), (22E, 24R)-3β,5α-dihydroxyergosta-7,22-dien-6-one (3) and (22E, 24R)-6β-methoxyergosta-7,22-diene-3β,5α-diol exhibited cytotoxic activity against the lung adenocarcinoma (A549) with IC_{50} values of 0.08, 0.94, 12.6 and 13.5 μM, respectively (Shang et al. 2011). Further, compounds 1 and 2 exhibited moderate activities against human ovarian cancer (A2780), with IC_{50} values of 2.8 and 5.1 μM.

Purple rice bran extract (PRE) and its constituents, and its constituents exhibited protective effect against angiogenesis induced by vascular endothelial growth factor (VEGF) (Tanaka et al. 2012). PRE significantly suppressed VEGF-induced tube formation, proliferation and migration in human umbilical vein endothelial cells (HUVECs) and human retinal microvascular endothelial cells (HRMECs) as well as phosphorylation of extracellular signal-regulated kinase (ERK) and p38. Cyanidin and peonidin also suppressed the proliferation and migration induced by VEGF.

Animal Studies

Kawabata et al. (1999) demonstrated that gamma-aminobutyric acid (GABA)-enriched defatted rice-germ and rice germ (2.5% in the diet) significantly inhibited aberrant crypt foci formation in male F344 rats. In a subsequent 30 week study, dietary exposure to rice-germ during the initiation phase significantly reduced the incidence of colonic adenocarcinoma (71 versus 29%) induced by azoxymethane. GABA-enriched defatted rice-germ or rice-germ during the post-initiation phase also decreased the frequency of colonic adenocarcinoma. Ferulic acid, a major constituent of rice bran or germ exhibited chemopreventive effects against 4-nitroquinoline-1-oxide (4NQO)-induced oral carcinogenesis in male rats (Mori et al. 1999; 2000). The incidences of tongue carcinomas and preneoplastic lesions (severe dysplasia) in rats of the group given ferulic acid in the diet at a dose of 500 ppm after exposure to 4NQO for 5 weeks in drinking water at a dose of 20 ppm, was significantly lower on termination of the experiment (32 weeks). They also examined the effect of rice germ on azoxymethane (AOM)-induced formation of aberrant crypt foci (ACF) in male F344 rats and found that Exposure to defatted rice germ or rice germ during the initiation phase or the post-initiation phase also decreased incidences of AOM-induced large bowel neoplasms.

In a two-stage carcinogenesis experiment with dimethylbenz[a]anthracene/TPA, EK, an ethyl acetate extract of Kurosu, a vinegar made from unpolished rice, significantly reduced the number of tumours per mouse by 36% at 15 weeks after promotion (Nishidai et al. 2000).

Antiinflammatory Activity

Isovitexin, isolated from hull of *Oryza sativa* inhibited the release of TNF-alpha, a proinflammatory cytokine, upon lipopolysaccharide activation with a 50% inhibitory concentration (IC_{50}) of 78.6 μM (Huang et al. 2005). Isovitexin markedly reduced lipopolysaccharide -stimulated prostaglandin E2 production in a concentration-dependent manner, with an IC_{50} of 80.0 μM. The expression of cyclooxygenase-2 was also inhibited by isovitexin treatment. The results suggested that suppression of ROS-mediated COX-2 expression by isovitexin was beneficial in reducing inflammation and carcinogenesis. Rice bran extracts were found to have inhibitory properties against three key pro-inflammatory enzymes (cyclooxygenase [COX] 1, COX2, and 5-lipoxygenase [5-LOX]) (Roschek et al. 2009) One extract (SRB-AI) exhibited significant COX1 and COX2 inhibitory activities with 50% inhibitory concentration (IC_{50}) values for COX1 and COX2 of 305 and 29 μg/mL, respectively, but no 5-LOX inhibition. The second extract (SRB-AII) inhibited COX1, COX2, and 5-LOX with IC_{50} values of 310, 19, and 396 μg/mL, respectively. The third extract (SRB-AIII), a blend of SRB-AI and SRB-AIII, inhibited COX1, COX2, and 5-LOX with respective IC_{50}values of 48, 11, and 197 μg/mL. SRB-AI, SRB-AII, and SRB-AIII extracts contained over 620, 770, and 810 compounds, respectively. Of these, 17 were identified as key bioactives for cyclooxygenase and/or lipoxygenase inhibition.

Methanol extract of rice bran and γ-oryzanol inhibited 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice (Yasukawa et al. 1998). The active components of rice bran, sitosterol ferulate, 24-methylcholesterol ferulate, cycloartenol ferulate and 24-methylenecycloartanol ferulate also inhibited markedly TPA-induced inflammation in mice. The ID_{50} of these compounds for TPA-induced inflammation was 0.2–0.3 mg/ear. Further, cycloartenol ferulate markedly inhibited the tumour-promoting effect of TPA in 7,12-dimethylbenz[a]anthracene-initiated mice. Treatment of ovalbumin-treated BALB/c mice with ethanolic extract of black rice (DA-9201) resulted in significant reductions in the accumulation of eosinophils in peribronchial areas, chronic pulmonary inflammation and progression of airway remodelling (Lee et al. 2006). In addition, DA-9201 significantly reduced total serum and BALF IgE levels and Th2 cytokines. The results indicated that DA-9201 may play an important role in attenuating the progressing of airway inflammation and remodeling and suggest the potential benefits of DA-9201 in prevention or treatment of asthma.

Six feruloyl esters of triterpene alcohols and sterols, viz., two *trans*-ferulates, cycloeucalenol and 24-methylenecholesterol *trans*-ferulates, and four *cis*-ferulates, cycloartenol, 24-methyelenecycloartanol, 24-methylcholesterol, and sitosterol *cis*-ferulates, besides five known *trans*-ferulates, cycloartenol (CAR), 24-methylenecycloartanol (24-MCA), 24-methylcholesterol, sitosterol, and stigmastanol *trans*-ferulates, and one known *cis*-ferulate, stigmastanol *cis*-ferulate, were isolated from the methanol extract of edible rice bran (Akihisa et al. 2000). All of the ferulates showed marked inhibitory activity against 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice and their 50% inhibitory dose (ID_{50}) was 0. 1–0.8 mg per ear. Further, two free triterpene alcohols, CAR and 24-MCA, showed strong inhibition (ID_{50} 0.2–0.3 mg/ear), eight free sterols examined showed weaker activity (ID_{50} 0.7–2.7 mg/ear) than their corresponding ferulates. An ethyl acetate extract of Kurosu, a vinegar made from unpolished rice, inhibited 12-*O*-tetradecanoyl phorbol-13-acetate (TPA)-induced edema formation (14%) and myeloperoxidase activity (52%) in female ICR mouse skin (Nishidai et al. 2000).

In-vivo studies using a model of dextran sulphate sodium (DSS)-induced colitis in mice, showed that gamma-oryzanol and its component cycloartenyl ferulate markedly inhibited tissue myeloperoxidase activity, mRNA expressions of pro-inflammatory cytokines and COX-2, NF-kappaB p65 nuclear translocation and inhibitory protein of nuclear factor-kappaB-alpha degradation levels that were significantly increased by DSS (Islam et al. 2008) . In-vitro assay demonstrated that γ-oryzanol and cycloartenyl ferulate had strong antioxidant effects comparable to those of α-tocopherol. Of tricin and two rare flavonolignans- tricin in Njavara Black rice bran,

tricin and tricin 4′-*O*-(threo-β-guaiacylglyceryl) ether showed antiinflammatory effect of >65% after 5 h, at 2 mg/kg, in carrageenan-induced, paw edema experiments in rats (Mohanlal et al. 2011). Treatment of human peripheral blood mononuclear cells with the flavonoid, tricin from Njavara rice, resulted in significant down-regulation of LPS-elicited production of TNF-α, IL-6, PGE(2) and NO. Tricin was found to be a potential blocker of the expression of isoforms of nitric oxide synthase, cyclooxygenase and matrix metalloproteinases. Modulation of the cascade of molecular events in lipopolysaccharide signalling also included inhibition of transcription factor NF-κB. Modulation of the expression of different inflammatory mediators and the inhibitory effects on cell signalling pathways were suggested to be responsible for tricin antiinflammatory activity.

Anti atherosclerotic Activity

Chen et al. (2000) found that that black and red rice might be effective in reducing atherosclerotic plaques on the aorta of rabbits fed a cholesterol-enriched diet. Aorta plaque area (% of total surface) in the black and red rice groups was significantly lower than that in the white rice group. The concentrations of HDL-C and ApoAI were significantly higher in the black and red rice groups than those in the white groups. No significant difference was found between the black and red rice groups. Studies in rabbits showed that red or black rice consumption reduced or retarded the progression of atherosclerotic plaque development induced by dietary cholesterol (Ling et al. 2001). Compared with the high cholesterol and white rice rabbit groups, serum HDL cholesterol and apolipoprotein (apo) A-I concentration were greater in the red and black rice rabbit groups. Also, liver reactive oxygen species (ROS) and aortic malondialdehyde (MDA) were significantly lower, and the liver total antioxidative capacity and erythrocyte superoxide dismutase (SOD) activity were significantly higher in the red and black rice groups. The enhanced serum HDL cholesterol and apo A-I concentrations, and the increased antioxidant and decreased oxidative status may be mechanisms of the antiatherogenic effect of red or black rice. Similar results were obtained with supplementation of black rice outer layer fraction to rabbits which decreased atherosclerotic plaque formation and increased antioxidant status compared to white rice outer layer fraction (Ling et al. 2002).

Supplementation of diets with the black rice pigment fraction was found to attenuate atherosclerotic plaque formation in apolipoprotein e deficient mice (Xia et al. 2003). The apoE-deficient mice fed the black rice pigment fraction diet had 48% less atherosclerotic lesion area compared with apoE-deficient mice fed only the AIN-93 G diet and 46% less lesion area compared with mice fed the white rice outer layer fraction diet. This was paralleled with significantly lower total serum cholesterol, lower liver and aorta cholesterol and higher HDL cholesterol concentrations and lower antioxidized LDL antibody titer in apoE-deficient mice fed the black rice pigment fraction diet compared with the other groups. Moreover, mice fed the black rice pigment fraction diet also had lower CD4(+) T lymphocyte expression and weaker inducible nitric oxide synthase expression compared with mice fed the AIN-93 G diet and the white rice outer layer fraction diet, respectively. The authors concluded that the inhibition of atherosclerotic lesions of the black rice pigment fraction was attributed to the improvement in cholesterol accumulation and reduction in oxidative stress and inflammation. Yang et al. (2011) demonstrated that thromboxane A_2, the thrombogenic ratio of thromboxane A_2 and prostacyclin, serum calmodulin, and soluble *P*-selectin were significantly decreased in dyslipidemic rats fed a high fat diet supplemented with anthocyanin extract from black rice. The extract supplementation also markedly reduced serum triglyceride and raised hepatic CPT-1 mRNA expression. The findings suggested that dietary intake of AEBR reduced platelet hyperactivity, hypertriglyceridemia, and body weight gain, and facilitated maintenance of optimal platelet function in dyslipidemic rats induced by high fat diets.

In a recent study, dietary rice protein isolate (RPI) was found to attenuate atherosclerosis in apoE-deficient mice by upregulating antioxidant enzymes (Burris et al. 2010). Reduced atherosclerotic lesions were observed in aortic sinus

and enface analyses of the descending aorta RPI-fed apoE–/– mice compared with casein-fed mice. Plasma oxLDL and anti-oxLDL IgG levels were significantly decreased in RPI-fed compared to casein-fed animals. Plasma and aortic tissue GSH levels and GSH: GSSG ratio were higher in RPI-fed mice compared to casein-fed group. The reduction in atherosclerotic lesions in mice was suggested to be mediated in part by inhibiting oxidative stress and subsequent oxLDL generation that could result in reduced foam cell formation, an early event during atherogenesis.

Cholestin (from *Monascus purpureus*-fermented rice), was found to reduce homocysteine -stimulated endothelial adhesiveness as well as suppressing intracellular ROS (reactive oxygen species) formation, nuclear factor NF-kappaB activation, and vascular cell adhesion molecule-1 (VCAM-1) expression in treated human aortic endothelial cells (HAECs) (Lin et al. 2008). The results suggest that the natural compound cholestin may have potential implications in clinical atherosclerosis disease. Similarly in a subsequent study *Monascus purpureus*-fermented rice metabolites, monacolin K, ankaflavin, and monascin were found to reduce TNF-α-stimulated endothelial adhesiveness as well as downregulating intracellular ROS formation, NF-κB activation, and VCAM-1/E-selectin expression in HAECs, supporting the notion that the various metabolites from *Monascus-purpureus* fermented rice might have potential implications in clinical atherosclerosis disease (Lin et al. 2011).

Cardioprotective Activity

Animal study demonstrated that brown and black rice had cardioprotective effects (Kim et al. 2006). High-density lipoprotein cholesterol was significantly higher in rats fed diets of black rice and white rice (WHBL) or mixture of black rice and brown rice (BRBL) compared with diets of white rice (WH) or mixture of white rice with brown rice (WHBR). Plasma triglyceride, total cholesterol and low-density lipoprotein cholesterol in rats fed the white rice diet were higher than in other groups. The level of thiobarbituric acid reactive substances in liver was shown to be higher in rats in the order of those fed WH, WHBR, WHBL and BRBL. While superoxide dismutase and chloramphenicol acetyltransferase did not differ among the four groups, glutathione and glutathione peroxidase in WH were significantly lower than in other groups

In a randomised 6-month study of 60 patients with coronary heart disease (CHD) aged 45–75 years, dietary supplementation of black rice pigment fraction (BRF) was found to exert cardioprotective effects by improving plasma antioxidant status and inhibiting inflammatory factors (Wang et al. 2007). Compared to white rice fraction supplementation, BRF supplementation greatly enhanced plasma total antioxidant capacity, significantly reduce plasma levels of soluble vascular cell adhesion molecule-1 (sVCAM-1) soluble CD40 ligand and high sensitive C-reactive protein (hs-CRP) in the test group. No significant changes were observed in plasma total superoxide dismutase activity, lipids level and carotid artery intima-media thickness between two groups. In a randomised 6-week study involving 40 women aged 20 and 35 years, consumption of a mixture of brown rice and black rice (BRBL) caused a significant reduction in weight, body mass index, and body fat than white rice (WR) (Kim et al. 2008a). The levels of total cholesterol and triacylglycerols decreased gradually and significantly after intervention in both groups, with no significant difference between groups. Superoxide dismutase activity was not affected by dietary intervention, but glutathione peroxidase activity in the BRBL group was higher than in the WR group, and the level of thiobarbituric acid-reactive substance was lower in the BRBL group compared to the WR group. They concluded that meal replacement with mixed rice was superior to replacement with white rice in weight control, improving antioxidant enzyme activity.

Hepatoprotective Activity

Hou et al. (2010) showed that the anthocyanin-rich extract from black rice exhibited

hepatoprotective effect on chronically alcohol-induced liver damage in rats. Administration of ethanol (3.7 g/kg/day) to Wistar rats for 45 days induced liver damage with a significant increase in aspartate transaminase (AST), alanine transaminase (ALT), gamma glutamyl transferase (GGT) in the serum and the hepatic malondialdehyde (MDA) level. In contrast, administration of the black rice extract (500 mg/kg) along with alcohol significantly decreased the activities of liver enzymes (AST, ALT and GGT) in serum, the MDA levels and the concentrations of serum and hepatic triglyceride (TG) and total cholesterol (TCH). Rats treated with the extract displayed a better profile of the antioxidant system with normal glutathione peroxidase (GSH-Px), superoxide dismutase (SOD) and glutathione S-transferase (GST) activities.

Immunomodulatory Activity

In-vivo studies showed that after a month feeding, compared to high oleic-sunflower oil, rice bran oil (rich in linoleic acid and gamma-oryzanol) modulated the immune system by significantly enhancing B-lymphocyte proliferation and TH1-type cytokines such as interleukin IL-2 or TNF-alpha in 4 week-old Balb/C mice (Sierra et al. 2005). The reduction in found in the TH2 cytokine IL-4 and IgE (56.9 vs. 42.4 ng/mL; HOSO vs. RBO, n = 10 per group) levels suggested ice bran oil may have antiallergenic properties. The results suggested that although γ-oryzanol may modulate the immune system, it was not responsible for the overall immunostimulation effect seen for rice bran oil.

Antiaging/Skin Care Activity

Manosroi et al. (2012b) demonstrated that niosomes composed of Tween 61 and cholesterol at 1:1 molar ratio could be entrapped with the mixture of the three semi-purified rice bran bioactive compounds ferulic acid (F), γ-oryzanol (O), and phytic acid (P). They found that the highest cumulative amount in viable epidermis and dermis of F, O, and P were from Gel niosome, Cream niosome, and Mixed FOP at 1.564, 15.972, and 25.857 ng/cm^2, respectively. Niosomes enhanced the transdermal absorption of the hydrophobic compound O, while retarding the hydrophilic compounds F and P indicating the less systemic risk of F and P than O when entrapped in niosomes. Thus, transdermal absorption of F, O, and P appeared to depend on niosomal size, lipophilicity of the bioactive compounds, and types of formulations. Subsequent studies showed that gel and cream formulations containing niosomes entrapped with the rice bran bioactive compounds ferulic acid, γ-oryzanol and phytic acid gave superior clinical anti-aging activity which can be applied as a novel skin product (Manosroi et al. 2012a). Gel and cream containing the semi-purified rice bran extracts entrapped in niosomes gave no sign of erythema and edema detected within 72 h on the shaved rabbit skin. These formulations also demonstrated higher hydration enhancement and improvement of skin lightening, thickness, roughness, and elasticity on the skin of 30 human volunteers within the 28-day treatment not more than 9, 27, 7, 3, and 3 times, respectively.

Bioactive compounds ferulic acid, gamma-oryzanol and phytic acid in rice bran have been widely used as antioxidants in skin care products. Manosroi et al. (2011) reported that gel and cream containing the rice bran bioactive compounds entrapped in niosomes showed higher antioxidant activity (ORAC value) at 20–28 μmol of Trolox equivalents (TE) per gram of the sample than the placebo gel and cream which gave 16–18 μmolTE/g. Human sebum treated with these formulations showed more lipid peroxidation inhibition activity than with no treatment of about 1.5 times. The three different independent techniques including corneometer, vapometer and confocal Raman microspectroscopy (CRM) indicated the same trend in human skin hydration enhancement of the gel or cream formulations containing the rice bran extracts entrapped in niosomes of about 20, 3 and 30%, respectively.

Rice extracts, such as starch and oil, are used in a range of cosmetic and hygiene products. Rice starch can be mixed with honey to nourish the skin and can be used in cosmetics to reduce facial 'shine'. The oil is used in sun-care products to absorb UV-rays, as well as in conditioners for hair-care and in shower and shampoo products. It is also reported to have moisturising and anti-ageing properties. Extracts containing rice protein are added to hair products to give a feeling of volume and thickness to the hair.

Photoprotective Activity

A water-soluble enzymatic extract from rice bran was found to have photoprotective activity and to have promising applications in the field of dermatology (Santa-Maria et al. 2010). At a concentration of 10 μg/mL, the extract protected human keratinocyte monolayers from irradiation by decreasing lipid peroxidation by 33%. In reconstructed human epidermis, 100 μg/mL decreased lipid peroxidation process by 44% comparable to that of vitamin E at 600 μg/mL. The extract did not induce cytotoxic effect for concentrations up to 100 μg/mL.

CNS, Autonomic Nervous System and Neuroprotective Activity

Hiraga et al. (1993) showed that cycloartenol ferulic acid ester, a component of γ-oryzanol a phytosterol derived from rice bran had a suppressant effect on the central nervous system. Additionally, its efficacy in several models of cerebral dysfunction was demonstrated. Since no clear effects could be obtained under the treatments with γ-oryzanol, cycloartenol ferulic acid ester appeared to be more useful than γ-oryzanol.

In a study of lead-exposed weaning rats, administration of a pre-germinated brown rice decreased the accumulation of lead and decreased Pb-induced learning and memory deficits (Zhang et al. 2010b) compared to other diets of white rice, brown rice and control group. The protective effect was postulated to be related to the antioxidative effects and large amount of gamma-aminobutyric acid in pre-germinated brown rice.

In-vitro studies in PC12 cells, showed that ethanol extract of *Monascus*-fermented red mold rice (RMR), provided stronger neuroprotection in rescuing cell viability as well as repressing inflammatory response and oxidative stress (Lee et al. 2007a, b, c). Dietary administration of RMR to rats with Alzheimer's disease infused with Abeta40 into the cerebral ventricle, potently reversed the memory deficit in the memory task. Abeta40 infusion increased acetylcholinesterase activity, reactive oxygen species, and lipid peroxidation and decreased total antioxidant status and superoxide dismutase activity in the brain, but these damages were potently reversed by RMR administration, and the protection was more significant than that with lovastatin administration. They also reported that *Monascus purpureus*-fermented red mold rice (RMR) repressed amyloid beta peptide-induced neurotoxicity via potent synergism of anti-inflammatory and antioxidative effect (Lee et al. 2008). Monacolin K, a metabolite of ethanol extract of RMR repressed Abeta40 neurotoxicity via repressing small G-protein-mediated inflammation, and other metabolites of RMR ethanol extract also exhibited potent antioxidative ability against Abeta-induced oxidative stress. Importantly, stronger effects on repressing the Abeta40-induced cell death, inflammation, and oxidative stress were performed by RMR ethanol extract than that by the equal levels of lovastatin, which resulted from a potent synergism made up of monacolin K, antioxidants, and anti-inflammatory agents. The results suggest the potential to develop RMR as a novel functional food for the prophylaxis of Alzheimer's disease pathogenesis. Lee et al. (2009) found that RMR promoted antioxidase activity against oxidative injury and improved the memory ability of zinc-deficient rats. Decreases of antioxidant enzyme activities in the hippocampus and cortex were observed, and the levels of Ca, Fe, and Mg were increased in the hippocampus and cortex of Zn-deficient rats, leading to memory and learning ability injury. However, the administration of RMR (1- or 5-fold dosage) and with or without Zn significantly improved the antioxidase and neural activity to maintain cortex and hippocampus functions. Lee et al. (2010) also found that the ethanol extract of RMR suppressed cholesterol-raised

β-secretase activity and further resulted in the increase of neuroprotective soluble APP alpha-fragment (sAPPalpha) secretion in cholesterol-treated human neuroblastoma IMR32 cell. In the animal test, RMR potently reversed the memory deficit in the water maze and passive avoidance tasks. The neuroprotection provided by RMR downregulated Abeta40 formation and deposition by suppressing the cholesterol-raised β-secretase activity and apolipoprotein E expression, as well as mediated the proteolytic process of amyloid precursor protein toward neuroprotective sAPPalpha secretion in the hippocampus.

Okada et al. (2000) examined the usefulness of defatted rice germ enriched with γ-aminobutyric acid (GABA) as a functional food with tranquilizer effects, particularly on sleeplessness, depression and autonomic disorder observed during the menopausal or presenile period in 20 female patients. The most common mental symptoms during the menopausal and presenile period such as sleeplessness and depression were improved in more than 65% of the patients. Overall improvement was observed in 75% of the patients

Anti hypercalciuric Activity

Rice bran treatment was found to be efficacious in hypercalciuric patients with urinary calculous disease (Ohkawa et al. 1983). After the administration of defatted rice bran at a dosage of 20 g daily for 4 weeks, urinary calcium excretion was reduced significantly from 402 mg to 291 per 24 h. In six patients who showed a reduction of urinary calcium excretion an increase in urinary calcium excretion was observed 4 weeks after stopping the rice bran administration. In a clinical study of 70 patients with hypercalciuria rice bran treatment (10 g twice daily) for 1 month to 3 years, a significant decrease in urinary calcium excretion, which was maintained during treatment. Evidence of stones decreased clearly among patients treated with rice bran for 1–3 years (Ohkawa et al. 1984). Rice-bran therapy was found to be particularly useful in patients with hyperabsorptive hypercalciuria and it was effective in the prevention of recurrent urinary stone disease (Ebisuno et al. 1986). Urinary calcium excretion was considerably reduced, while urinary phosphate and oxalate were slightly increased Urinary magnesium, uric acid, serum calcium, phosphate, magnesium and uric acid were not affected. There were no changes in serum iron, copper and zinc even when patients were treated for long periods. The treatment was tolerated well and there were no serious side effects. In a long term rice bran treatment of 182 patients with idiopathic hypercalciuria, the frequency of new stone formation was drastically reduced in 49 patients who underwent treatment for more than 3 years (Ebisuno et al. 1991). During treatment, 61.2% of patients remained in remission. Rice bran was well tolerated in almost all cases and there were no serious side effects

Administration of rice bran to 10 patients with recurrent nephrolithiasis and hypercalciuria for 60 days elicited an of 40% reduction of hypercalciuria in all patients (Noronha et al. 1989). Urinary magnesium was reduced in 28% and oxalate excretion was increased in 28%. The rate of decrease of urinary calcium was 65% in the absorptive type and 33% in the renal type of hypercalciuria.

Antimicrobial Activity

Two antimicrobial substances in rice hull were isolated and identified as 4-hydroxybenzoic acid and *trans* 4-hydroxycinnamic acid (Cho et al. 1998). Most of the Gram-positive and some Gram-negative bacteria were sensitive to *trans* 4-hydroxycinnamic acid and 4-hydroxybenzoic acid at IC_{50} concentrations of 100–170 and 160 μg/mL, respectively. Crude protein extracts from *Escherichia coli* expressing rice cDNAs exhibited in-vitro antibacterial activities against the Gram-positive bacteria (*Bacillus pumilus*, *B. subtilis*, *Staphylococcus aureus*, and *Sarcina lutea*) (Zhai et al. 2011). However, rice dehydrins purified by immunoaffinity chromatography were not active against the bacteria. Of the truncated rice dehydrins containing either K- or S-segment, K-segment peptides, and not S-segment, were found to be responsible for the antibacterial activities against Gram-positive bacteria. Antibacterial assay with synthetic K-segments indicated that the peptides inhibited growth of *B. pumilus* with minimum inhibition

concentration and minimum bactericidal concentration of 130 and 400 μg/mL, respectively.

Antianaphylactic/Antiallergic Activity

Ethanol-water (70% v/v) extracts from five pigmented black rice brans were found to be more effective than an extract from a non-pigmented rice cultivar in suppressing the release of histamine and β-hexosaminidase from basophilic RBL-2H3 cells stimulated with both Ionophore A23187 and immunoglobulin E (IgE)-antigen complexes (Choi et al. 2007). Suppression was also obtained with A23187-stimulated rat peritoneal mast cells. The inhibition of the immune process by the pigmented brans was confirmed by the observed modulation of the proinflammatory cytokine gene expressions and cytokine release, as indicated by the reduction in tumour necrosis factor (TNF)-alpha, interleukin (IL)-1beta, IL-4, and IL-6 mRNA expressions determined with the reverse transcription-polymerase chain reaction (RT-PCR). Rice bran from the LK1-3-6-12-1-1 cultivar was the most effective inhibitor in all assays suggesting it to protect against allergic diseases such as hay fever and asthma.

Methanol extract of *Oryza sativa* (Dong-Jin) dose-dependently inhibited systemic anaphylaxis induced by compound 48/80 in rats (Kim et al. 1999). The extract dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 and also inhibited local anaphylaxis activated by anti-dinitrophenyl (DNP) IgE. The results indicated the extract to possess antianaphylactic activity by inhibition of histamine release from mast cells in-vivo and in-vitro.

Studies demonstrated that cycloartenyl ferulate (cycloartenol ferulic acid ester; CAF), a natural product from rice bran oil-derived gamma-oryzanol, when intradermally with anti-DNP IgE into the dorsal skin of rats, attenuated the passive cutaneous anaphylaxis reaction induced by DNP-HSA (dintrophenyl- human serum albumin) (Oka et al. 2010). CAF and gamma-oryzanol also inhibited the degranulation of DNP-IgE sensitized RBL-2H3 mast cells stimulated with anti-DNP-HSA. The study demonstrated CAF captured IgE, prevented it from binding to FcepsilonRI, and attenuated mast cell degranulation.

Prebiotic Activity

Nemoto et al. (2011) reported that brown rice fermented by *Aspergillus oryzae* may have potential as a prebiotic. Incubation of fecal slurries with fermented brown rice resulted in increased organic acids and fecal bifidobacteria numbers in-vitro. However, they could not detect its effects on the intestinal environment in-vivo.

Allergy

Yet unidentified high-molecular-weight allergens from rice grains, predominantly a 56-kDa glycoprotein, appeared to be responsible for anaphylaxis after consumption of rice in a German patient (Trcka et al. 2011). Prick-to-prick tests were positive to raw and cooked rice (basmati rice and long-grain rice) and preparations of different rice extracts.

Traditional Medicinal Uses

Burkhill (1966) has documented many traditional uses of rice in southeast Asia. In Malaysia, powdered rice is used unscented (*bedak*), or scented (*pupur*) in various ways such as the use of small pieces of the fragrant pandan leaf as cosmetic powder to apply to the face for a clear complexion; neck and body parts for rashes. Rice cosmetic powder is also prescribed with crushed pepper for rubbing on hands and feet for gouty twinges. Sprouted rice grains i.e. malted rice is employed as a peptic, tonic and carminative medicine. Hot boiling water is poured over rice grains and is drank for diarrhoea. The drink is called *air kerak nasi* or a rice gruel boiled to a mush is prescribed for diarrhoea. The top part of the rice that has been best boiled is used as eye lotion. Boiled rice is mashed into a paste or moulded into balls and applied to carbuncles,

boils, swellings and skin blemishes. Other medicinal herbs e.g. *Euphorbia* extract are sometimes added to the rice balls to increase their medicinal effects and such medicament preparations are often dried and stock for later use. Sticky glutinous rice is taken to treat stomach upsets, indigestion and heart-burn. Brown rice extracts have been used to treat breast and stomach cancer and warts, and also been used to treat indigestion, nausea and diarrhoea. Polishing from rice mill is sometimes used to treat beriberi. In Kampuchea, the hulls are employed for treating dysentery, while the hulls of a 3-month old rice plant are used as a diuretic. An infusion of burnt rice straw is used as ingredient in a mixture for supraemia. Lye made from burnt straw ash is used in Java for washing hair and is also taken internally as an abortifacient. Njavara is an important medicinal rice variety of Kerala, India, widely used in Ayurveda as a 'health food' and in the treatment of rheumatoid arthritis, paralysis, neurodegenerative diseases and in rejuvenation therapy (Mohanlal et al. 2011). Rice water is prescribed in the Pharmacopoeia of India as an ointment to treat inflamed surface.

Other Uses

The growing rice plant makes nutritious fodder. The husk or hull is used as fuel, bedding, absorbent, building board, and carrier for vitamins, drugs, toxicants, etc. The charred rice hull is used for filtration of impurities in water, medium for hydroponics and manufacture of charcoal briquettes. Chaff left after milling is used as fuel for the mill and charred husks is used to ameliorate soils and used as compost. The rice bran or meal obtained in pearling and polishing is a valuable livestock and poultry food. It consists of the pericarp, the aleurone layer, the embryo and some of the endosperm. The bran contains 14–17% oil. Crude rice bran oils are used for producing solidified oil, stearic and oleic acids, glycerine and soap. Processed bran oil is used for cooking, antirust and anticorrosive agents, textile and leather finishers, and in medicine. China, India, Japan, Vietnam and Thailand are the main producers of rice-bran oil. Starch is made from broken rice, and used as laundry starch, in foods, and textile manufacture. Rice straw is used for animal feed and bedding, but is nutritionally inferior to other cereal straws unless ensiled. It is used for the manufacture of straw boards and pulp for paper, mat- and hat-making, for mushroom growing medium, for the production of organic manure, for mulching crops such as onions, garlic and cucurbits, and only rarely for rope and roof thatch.

Ferulic acid, a potential cancer chemopreventive agents could be synthesized using organic synthetic methods from rice bran pitch, a blackish brown waste oil with high viscosity, discharged in the process of the rice bran oil production (Taniguchi et al. 1999).

Comments

Oryza sativa contains two major subspecies: the sticky, short grained *japonica* or *sinica* variety, and the non-sticky, long-grained *indica* variety. *Japonica* are usually cultivated in dry fields, in temperate East Asia, upland areas of Southeast Asia and high elevations in South Asia, while *indica* are mainly lowland rices, grown mostly submerged, throughout tropical Asia. Rice is known to come in a variety of colors, including: white, brown, black, purple, and red.

The amended final report published in the International Journal of Toxicology (2006) on the safety assessment of cosmetic ingredients derived from rice covers the following products: Rice Bran Oil, *Oryza sativa* (Rice) Germ Oil, Rice Bran Acid, *Oryza Sativa* (Rice) Bran Wax, Hydrogenated Rice Bran Wax, *Oryza Sativa* (Rice) Bran Extract, *Oryza Sativa* (Rice) Extract, *Oryza Sativa* (Rice) Germ Powder, *Oryza Sativa* (Rice) Starch, *Oryza Sativa* (Rice) Bran, Hydrolyzed Rice Bran Extract, Hydrolyzed Rice Bran Protein, Hydrolyzed Rice Extract, And Hydrolyzed Rice Protein (Anonymous 2006). The Cosmetics Ingredient Panel (CIP) concluded that these rice-derived ingredients are safe as cosmetic ingredients in the practices of use and concentrations as described in this safety assessment.

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Setaria italica

Scientific Name

***Setaria italica* (L.) P. Beauv.**

Synonyms

Alopecurus caudatus Thunb., *Chaetochloa germanica* (Mill.) Smyth, *Chaetochloa italica* (L.) Scribn., *Chaetochloa italica* var. *germanica* (Mill.) Scribn *Chamaeraphis italica* (L.) Kuntze, *Chamaeraphis italica* var. *germanica* (Mill.) Kuntze, *Echinochloa erythrosperma* Roem. & Schult., *Echinochloa intermedia* Roem. & Schult., *Ixophorus italicus* (L.) Nash, *Oplismenus intermedius* (Hornem.) Kunth, *Panicum aegyptiacum* Roem. & Schult. pro syn., *Panicum asiaticum* Schult. & Schult.f. pro syn., *Panicum chinense* Trin., *Panicum compactum* Kit. pro syn., *Panicum erythrospermum* Vahl ex Hornem., *Panicum italicum* L., *Panicum italicum* convar. *moharicum* Alef., *Panicum italicum* var. *californicum* (Kellog) Körn., *Panicum italicum* var. *erythrospermum* Körn., *Panicum italicum* var. *germanicum* (Mill.) Koeler, *Panicum italicum* var. *inerme* Döll, *Panicum italicum* var. *longisetum* Döll, *Panicum italicum* var. *nigrum* Körn., *Panicum elongatum* Salisb. nom. superfl., *Panicum germanicum* Mill., *Panicum germanicum* Willd. nom. illeg., *Panicum globulare* (J. Presl) Steud., *Panicum glomeratum* Moench nom. superfl., *Panicum intermedium* Vahl ex Hornem., *Panicum itieri* (Delile) Steud., *Panicum macrochaetum* (Jacq.) Link, *Panicum maritimum* Lam., *Panicum melfrugum* Schult. & Schult.f. nom. nud., *Panicum miliaceum* Blanco nom. illeg., *Panicum moharicum* (Alef.) E.H.L. Krause, *Panicum panis* (Jess.) Jess., *Panicum pumilum* Link nom. illeg., *Panicum serotinum* Trin. pro syn., *Panicum setaceum* Trin. pro syn., *Panicum setosum* Trin. pro syn., *Panicum sibiricum* Roem. & Schult. pro syn., *Panicum verticillatum* var. *majus* Thunb., *Panicum viride* subsp. *italicum* (L.) Asch. & Graebn., *Panicum viride* var. *italicum* (L.) Backer, *Panicum vulgare* Wallr. nom. superfl., *Paspalum germanicum* (Mill.) Baumg., *Penicillaria italica* (L.) Oken, *Pennisetum germanicum* (Mill.) Baumg., *Pennisetum italicum* (L.) R.Br., *Pennisetum macrochaetum* J. Jacq., *Setaria asiatica* Rchb. pro syn., *Setaria californica* Kellogg, *Setaria compacta* Schur nom. nud., *Setaria erythrosperma* Hornem. ex Rchb. pro syn., *Setaria erythrosperma* (Vahl ex Hornem.) Spreng., *Setaria flavida* Hornem. ex Rchb. pro syn., *Setaria germanica* (Mill.) P. Beauv., *Setaria globularis* J. Presl, *Setaria italica* subsp. *colchica* Maisaya & Gorgidze, *Setaria italica* subsp. *germanica* K. Richt., *Setaria italica* subsp. *moharia* (Alef.) H. Scholz, *Setaria italica* subsp. *moharica* (Alef.) H. Scholz, *Setaria italica* subsp. *nigrofructa* F.T. Hubb., *Setaria italica* subsp. *rubrofructa* F.T. Hubb., *Setaria italica* subsp. *stramineofructa* F.T. Hubb., *Setaria italica* subvar. *densior* F.T. Hubb., *Setaria italica* subvar. *germanica* (Mill.) F.T. Hubb., *Setaria italica* var. *germanica* (Mill.) Schrad., *Setaria itieri* Delile, *Setaria italica* var. *moharia* (Alef.) A. Zimm., *Setaria japonica* Pynaert, *Setaria macrochaeta*

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(Jacq.) Schult., *Setaria maritima* (Lam.) Roem. & Schult., *Setaria melinis* Link ex Steud., *Setaria moharica* Menabde & Erizin, *Setaria multiseta* Dumort., *Setaria pachystachya* Borbás nom. illeg., *Setaria panis* Jess., *Setaria persica* Rchb. pro syn., *Setaria violacea* Hornem. ex Rchb. pro syn., *Setaria viridis* subsp. *italica* (L.) Briq., *Setariopsis italica* (L.) Samp.

Family

Poaceae

Common/English Names

Chinese Millet, Dwarf Setaria, Foxtail Bristle Grass, Foxtail Millet, German Millet, Hay Millet, Giant Setaria Hungarian Millet, Italian Millet, Japanese Millet, Liberty Millet, Red Rala.

Vernacular Names

Afrikaans: Boermanna, Giers;
Arabic: Durra, Dukhn;
Chinese: Bai Liang Mi, Huang Liang Mi, Liang, Qing Liang Mi, Xiao Mi;
Czech: Bér Italský;
Danish: Kolbehirse;
Dutch: Trosgierst, Vogelgierst,
Eastonian: Itaalia Kukeleib;
Finnish: Italianpantaheinä, Tähkähirssi;
French: Millet À Grappes, Millet d'Italie, Millet D'oiseau, Millet Des Oiseaux, Panic d'Italie, Petit Mil, Sétaire d'Italie;
Georgian: Gomi;
German: Italienische Borstenhirse, Kolbenhirse;
Hungarian: Ecsetpázsit Köles;
India: Kaon (Assamese), Kangu, Syama Dhan (Bengali), Karig, Ral Kang (Gujarati), Bertia, Chena, Kakni, Kakun, Kalakangni, Kamguni, Kang, Kanghuni, Kangni, Kangu, Kauni, Kirakang, Kirang, Koni (Hindi), Aarike, Bilikorla-Hollu, Kaango Akki, Kongu, Naoni, Navanaklu, Navane, Navani, Priyangi Thene, Raia, Vavani (Kannada), Shol (Kashimiri), Navana, Tauna, Tena, Tenayari, Tenna, Tina (Malayalam), Hoop (Manipuri), Bhadle, Chena, Kaang, Kamg, Kang, Kangni, Kangu, Raala, Raale, Rala, Rale (Marathi), Chinaka, Dhanyapriyangu, Kangaka, Kangu, Kanguh, Kanguka, Kanguni, Kangunika, Kanku, Pitatandula, Priyangu, Priyanguka, Shyamaka, Syamaka (Sanskrit), Alaitticam, Cai, Caivankam, Cakattiram, Celumaipiri, Ceyamakam, Cinattaniyam, Cittirattantulam, Elan, Enam, Irati, Kakkaram, Kanakavirutti, Kankur, Karcepam, Mancaltinai, Niriyam, Paintinai, Pantupocanam, Pontukatinai, Tenai, Tennai, Thinai, Tinai, Tirutti, Titti, Uttanam (Tamil), Kanguni, Kora, Koralu, Korra, Korralu, Nakka-Korra (Telugu);
Indonesia: Juwawut (Javanese), Jawawut (Sundanese);
Italian: Panico, Panico d'Italia, Panico Degli Uccelli;
Japanese: Awa, Awami, Hie;
Kenya: Mukobi (Embu), Mukobi (Kikuyu), Mukobi (Meru);
Khmer: Kuö Thpu;
Korean: Jo;
Laos: Khauz Fa:Ngz;
Malaysia: Rumput Ekor Kucing, Sekoi, Sekui;
Nepalese: Kaguno, Kagunu, Kaun, Kauni;
Norwegian: Stor Busthirse;
Philippines: Sammang (Bontok), Daua (Cebu Bisaya), Sabug (Igorot), Bikakau, Bukakau (Iloko), Rautnokara (Ivatan), Boroña (Pampangan), Daua (Panay Bisaya), Turai (Sulu), Daua (Tagalog);
Persian: Arzun, Gal;
Polish: Wonica Ber;
Portuguese: Milho Painço, Milho Painço De Itália;
Romanian: Vulpii Meiul;
Russian: Morap;
Slovaščina: Bar, Muhvič Laški;
Slovencina: Mohár Taliansky;
Sotho: Lebelebele;
Spanish: Mijo De Italia, Mijo Menor, Moha, Panizo;
Sri Lanka: Tanna-Hal, Ten-Nai;
Swahili: Kimanga;

Swedish: Kolvhirs;
Switzerland: Pabbio Coltivato (Italian), Fennich (German);
Thai: Fang Haang Maa (Southern), Khao Fang (Central);
Tibetan: Khre;
Turkish: Kunak;
Vietnamese: Kê.

Origin/Distribution

Foxtail millet is an ancient crop and was first domesticated in China. The earliest archeological relics of foxtail millet were found in northern China, in the Cishan and Peiligang in the Yellow River Valley, approximately 7,400 years before present (BP) and 7,935 years BP, respectively (Li and Wu 1996). It was also found in a succession of sites in the Yiluo valley of northern China indicating that foxtail millet was the dominant staple grain for four millennia (Lee et al. 2007). Archeological evidence of foxtail millet domestication in Europe and the Middle East were younger dating from around 4,000 years BP (Austin 2006).

Phylogenetic analyses using both chloroplast and nuclear genes reveal foxtail millet and green millet (*Setaria viridis*) to be close relatives (Giussani et al. 2001; Doust et al. 2007), and support the premise that foxtail millet is a domesticated derivative of green millet (Li et al. 1944; Wang et al. 1995; Le Thierry d'Ennequin et al. 2000). Today, foxtail millet is cultivated all over the world, in the Americas, Europe, Africa, Asia and Australia.

Agroecology

Setaria italica is principally a crop of subtropical and temperate regions, but is grown in the tropics at high altitudes of 2,000–3,300 m, between latitudes of 30°N and S. It frost intolerant. In China and India, foxtail millet is mainly grown in areas with an annual rainfall of 400–800 mm with a summer maximum. Foxtail millet is not particularly drought-resistant, but its short crop cycle and its early maturity makes it suitable for low-rainfall areas. It can be cultivated in semi-arid regions with rainfall <125 mm in the 3–4 months of growth. It is, however, susceptible to long periods of drought. Flowering is normally accelerated by short days, but day-neutral and long day cultivars also exist. Foxtail millet prefers fertile sandy loam to clayey loam soils with a pH of about 6.5, but can be grown successfully on a wide range of soils including poor or marginal soils. It abhors water-logged conditions.

Edible Plant Parts and Uses

Foxtail millet is used as staple food in south and east Asia, south-eastern Europe and north Africa. It is most important in China and India. The grain may be cooked in water or milk and eaten like rice, either as whole grain or broken grain. It can be ground into flour and made into cakes, porridges puddings and bread both unleavened and leavened when mixed with wheat flour. The flour can be made into noodles. In northern China, foxtail millet is usually mixed with pulses and cooked. In China, foxtail millet is used for the commercial manufacture of mini crisp chips, millet crisp rolls and flour for baby foods. In China, foxtail millet is also processed into vinegar and wine. In Russia and Myanmar it is used in the preparation of beer and alcohol. Sprouted seeds are eaten as a vegetable in China.

Foxtail millet is considered a nutritious food, more nutritious than rice and is often recommended for the elderly, pregnant women and for people suffering celiac disease with gluten intolerance. Foxtail millet, common millet, broadrood, grain and sweet sorghum together with pseudocereals like buckwheat, grain amaranth and quinoa were found by immunological test to have gliadin content below 10 mg/100 g and to be suitable for the diet in celiac disease (Petr et al. 2003). This was also confirmed by electrophoretic analysis PAGE analysis that showed these species to contain no or negligible level of α-gliadin.

Botany

An annul grass with robust, erect culms 60–150 cm high with glabrous nodes and internodes. Leaf sheaths glabrous or pubescent, ciliate and ligule small, 1–3 mm. Leaf lamina linear-lanceolate, to 45 cm long and 2 cm wide, usually glabrous, scabrous. Panicle 6–40×0.5–5 cm, dense, lobed, erect or pendent when mature, with densely pubescent rachis (Plates 1 and 2). Spikelets elliptic to ovate or subglobose, 2–3 mm with 2–3 bristles; 2 florets per spikelet, upper bisexual; lower glume 1/3–1/2 as long as spikelet; upper glume about as long as spikelet, 5–7(–9)-veined, obtuse; lower glume 1–3-nerved, 1/3–1/2 as long as spikelet; upper glume about as long as spikelet, 5–7(–9)-veined, obtuse; upper floret oblong or ovate-oblong, cartilaginous, deciduous at maturity, minutely papillose to nearly smooth and shiny. Fruit a caryopsis; grain of various colours; seeds enclosed in thin, papery hulls, largely removed by threshing, leaving free the small, convex oval or elliptical seed.

Plate 1 Harvested mature heads (panicles)

Plate 2 Close-up of harvested heads

Nutritive/Medicinal Properties

Nutrient composition of foxtail millet (*Setaria italic*a) whole grain was reported by Leung et al. (1972) as: energy 341 cal, moisture 11.3%, protein 9.5 g, fat 2.9 g, total carbohydrate 74.2 g, fibre 1.2 g, ash 1.6 g, Ca 33 mg, P 244 mg, Fe 5.5 mg, Na 7 mg, K 249 mg, thiamine 0.43 mg, riboflavin 0.12 mg and niacin 2.2 mg. *Setaria italica* grains were found to have 1.4 mg/L niacin, 11.97% moisture, 12.38% protein, and the following amino acids (g/16gN): arginine 2.31 g, cystine 1.36 g, histidine 1.22 g, isoleucine 6.06 g, leucine 10.50 g, lysine 0.73 g, methionine 2.42 g, phenylalanine 4.22 g, threonine 2.66 g, tryptophan 2.02 g, tyrosine 1.56 g and valine 4.47 g (Mangay et al. 1957). The amino acid composition of 13 samples of foxtail millet (*Setaria italica*) from six Chinese and one French varieties ranged from 1.82 to 3.65 g per 100 g of grain DM (Mossé et al. 1989). The levels of amino acids in grain dry matter increased linearly with N with correlation coefficients close to 1 for most of them. Amino acids in crude protein of grain (g/16gN) changed as quadratic functions of N, which decreased for glycine, cysteine, tysine, histidine and arginine, remained nearly constant for valine, threonine, tyrosine, methionine and aspartate plus asparagine, and increased for other amino acids. Foxtail millet appeared as the only cereal in which lysine was the only limiting essential amino acid. The composition of storage proteins accumulated in grains remained constant, with a prolamin to glutelin ratio close to three and independent of grain protein content.

The composition of foxtail millet grain per 100 g edible portion was also reported as: water 12 g, energy 1,470 kJ (351 kcal), protein 11.2 g, fat 4.0 g, carbohydrate 63.2 g, crude fibre 6.7 g, Ca 31 mg, Fe 2.8 mg, thiamin 0.6 mg, riboflavin 0.1 mg and niacin 3.2 mg (FAO 1995). The essential

amino-acid composition per 100 g grain was reported as: tryptophan 103 mg, lysine 233 mg, methionine 296 mg, phenylalanine 708 mg, threonine 328 mg, valine 728 mg, leucine 1,764 mg and isoleucine 803 mg (FAO 1970). Most foxtail cultivars are non-glutinous and are thus suitable for the diet of people with coeliac disease (Brink 2006). Foxtail millet bran contains about 9% oil and its starch granules are spherical, angular or polyhedral with a diameter of 6–17 μm.

The total protein of the 14 Italian millet varieties was fractionated into albumin-globulin, prolamin and glutelin fractions (Monteiro et al. 1982). The alcohol-soluble prolamin fraction constituted the major storage protein of the grain in the endosperm. There was a positive correlation between protein content and the prolamin levels of the seeds and the increase in protein content was largely due to an increase in the prolamin content. The limiting amino acids in the protein were lysine followed by tryptophan and the sulphur containing amino acids, methionine and cystine. The lysine content of the grain decreased with increase in protein content. The total protein had a rather high content of leucine. SDS-polyacrylamide gel electrophoresis of the protein fractions indicated similarities in the prolamin fraction and differences in the albumin-globulin and glutelin fractions of the different varieties. Ash and fibre content of Italian millet (*Setaria italica*) cultivars were comparable to that of other millets while protein and calcium levels were slightly higher (Monteiro et al. 1988; Gopal et al. 1988). The protein concentrates contained large amounts of non-essential amino acids. The amounts of essential amino acids in the concentrates were substantially higher than in whole-seed protein except for lysine and arginine. The overall composition of Italian millet was not very different from other millets. In-vitro protein digestibility (IVPD) studies showed that it was high with pepsin and papain but low with trypsin. Acid treatment of the flour increased IVPD with trypsin.

Sequential extraction of the defatted Italian millet flour resulted in three major protein fractions, namely, albumin-globulin (1.43%), setarin I (true prolamin) (6.60%), and setarin II (prolamin-like (2.24%)) (Naren and Virupaksha 1990). Further fractionation of setarin II yielded three protein preparations designated as γ-setarin (0.23%), β-setarin (0.09%) and α-setarin (0.14%). α- and β-Setarin constitute the major sulfur-rich proteins of the Italian millet prolamin fraction. They have rather similar amino acid profiles and molecular sizes. α-setarin had high amounts of the sulphur amino acids methionine and cysteine. Both α-setarin and β-setarin contained considerably higher amounts of the sulfur amino acids than setarin II; the levels of methionine in α-setarin and β-setarin were 7.3- and 6.5-fold higher, respectively. α-setarin had significantly lower amounts of glutamic acid, proline, and lysine and higher amounts of leucine and phenylalanine. Setarin II was distinct from both α-setarin and β-setarin in possessing negligible amounts of serine, tyrosine, andcysteine but had much higher levels of alanine, leucine, and glutamic acid.

The fatty acids (% total fatty acid mass) found in *Setaria italica* grains were: C5:0 (valeric acid) 37%, C16:0 (palmitic acid) 3.1%, C18:0 (stearic acid) 0.8%, C20:0 (arachidic acid) 0.5%, C18:1 (oleic acid) 9.9%, C18:2(linoleic acid) 42.5%; C18:3 (linolenic acid) 2.1%, C20:1(gadoleic acid) 0.5% and C22:1 (erucic acid) 0.3%. The grains contained 1% cholesterol and 99% phytosterols. The phytosterols found were ergostanol 0.164 mg/kg, γ-sitosterol 2.781 mg/kg, stigmasterol 0.398 mg/kg, cholest-5-en-3-ol,24-propylidene-,(3β)- 0.390 mg/kg, lanosterol 0.185 mg/kg, stigmasta-5,24(28)-dien-3-ol,(3β, 24 Z)- 0.200 mg/kg, 5-cholestene-3-ol, 24-methyl- 0.913 mg/kg, stigmastanol 1.006 mg/kg, stigmastan-3,5-diene 0.376 mg/kg, campesterol 0.867 mg/kg, stigmast-4-en-3-one 0.215 mg/kg and 9,19-cyclolanost-24-en-3-ol, acetate, (3β)- 0.229 mg/kg. The lipophylic fractions (mg/kg) found in *S. italica* grains were: pentanoic acid (valeric) 5.214 mg; pentadecanoic acid, methyl ether 0.112 mg; pentadecanoic acid, 14-methyl-, methyl ether 3.478 mg; hexadecanoic acid, methyl ether, (palmitic) 4.578 mg; hexadecanoic acid, ethyl ether, (palmitic) 0.089 mg; heptadecanoic acid, methyl ether, (margaric) 0.115 mg; 6-octadecenoic acid (Z), (petroselinic) 1.467 mg; 9,12-octadecadienoic (Z, Z), (linoleic) 2.610 mg;

octadecanoic acid, methyl ether, (stearic) 1.195 mg; 9-octadecynoic acid, methyl ether (E), (stearolic) 0.534 mg; 9,12-octadecadienoic acid, methyl ether (E, E) (linoleic) 2.623 mg; 9,12-octadecadienoic acid, methyl ether, (linoleic) 1.698 mg; 9,12,15-octadecatrienoic acid, methyl ether (Z, Z, Z), (linolenic) 0.781 mg; nonadecanoic acid, methyl ether 0.082 mg; . linoleic acid, ethyl ether 7.569 mg; eicosanoic acid, methyl ether, (arachidic) 0.402 mg; 11-eicosenoic acid, methyl ether, (gadoleic) 0.223 mg; heneicosanic acid methyl ether, 0.115 mg; docosanoic acid, methyl ether, (behenic) 0.465 mg; tricosanoic acid, methyl ether 0.233 mg; tetracosanoic acid, methyl ether, (lignoceric) 0.200 mg; hexacosanoic acid, methyl ether 0.223 mg and octacosanoic acid, methyl ether, (montanic) 0.242 mg.

Leaf Phytochemicals

Setaricin, a flavone glycoside was isolated from the methanol extract of *Setaria italica* leaves (Jain et al. 1989). The leaves of *Setaria italica* yielded six *O*-glycosylflavones and 10 C-glycosylflavones including the new compounds scoparin 2″-*O*-xyloside and scoparin 2″-*O*-glucoside, and six new acylated C-glycosylflavones, five of which were at partly elucidated: orientin 6″-*O*-(E)-ferulyl-2″-*O*-xyloside, orientin X″-*O*-(E)-ferulyl-2″-*O*-glucoside, vitexin X″-*O*-(E)-ferulyl-2″-*O*-xyloside, vitexin X″-*O*-(E)-ferulyl-2″-*O*-glucoside and vitexin X″-*O*-(E)-sinapyl-2″-*O*-xyloside (Gluchoff-Fiasson et al. 1989). A coumarin named setarin was isolated from *Setaria italica* leaves (Jain et al. 1991b). A new flavone glycoside identified as 8,3′-dimethoxy-5,4′-dihydroxyflavone 7-glucoside was isolated from *Setaria italica* leaves (Jain et al. 1991a).

Antioxidant Activity

Administration of ethanolic extract of *S. italica* to carrageen induced rheumatoid female rats significantly reduced the levels of cathepsin, uric acid, lactate dehydrogenase, alanine transaminase and aspartate transaminase which were elevated by injection of carrageenan to rats (Banu et al. 2010). The extract also increased the carrageenan-induced low levels of antioxidants superoxide dismutase, catalase and Vitamin C in serum, liver and kidney tissues. The study revealed that *S. italica* crude extract had effective control on scavenging free radicals and had potent antioxidant promoting ability due to the presence of its active flavonoids and alkaloids.

Antihyperglycemic and Hypolipidemic Activities

An amylase inhibitor from *Setaria italica* grains (Nagaraj and Pattabiraman 1985). When type 2 diabetic KK-Ay mice were fed a normal foxtail millet protein (FMP) diet or a high-fat-high-sucrose diet containing FMP for 3 weeks, in both experiments plasma concentrations of high-density lipoprotein cholesterol (HDL-cholesterol) and adiponectin increased markedly in comparison with a casein diet group, whereas concentrations of insulin decreased greatly and that of plasma glucose was comparable to that in the casein diet group (Choi et al. 2005). Based on the role of adiponectin, insulin, and HDL-cholesterol in diabetes, atherosclerosis, and obesity, they stated that FMP may improve insulin sensitivity and cholesterol metabolism through an increase in adiponectin concentration. Therefore, FMP would serve as another beneficial food component in obesity-related diseases such as type 2 diabetes and cardiovascular diseases. Similarly, Nishizawa et al. (2009) found that feeding of a high-fat diet containing Japanese millet protein concentrate (20% protein) to type 2 diabetic mice for 3 weeks significantly increased plasma levels of adiponectin and high-density lipoprotein cholesterol (HDL cholesterol) and decreased the levels of glucose and triglyceride as compared to control. The starch fraction of Japanese millet had no effect on glucose or adiponectin levels, but the prolamin fraction beneficially modulated plasma glucose and insulin concentrations as well as adiponectin and tumour necrosis factor-alpha gene expression.

Methanolic extract of *Setaria italica* exhibited strong in-vitro anti-lipase activity (above 80%) (Sharma et al. 2005). Park et al. (2011) showed that treatment of 3 T3-L1 adipocytes with *Sorghum bicolor*, *Setaria italica*, or *Panicum miliaceum* extract significantly inhibited adipocyte differentiation, triglyceride accumulation, and glycerol 3-phosphate dehydrogenase activity.

Aqueous extract of foxtail seeds (300 mg/kg body weight) produced a significant fall (70%) in blood glucose in diabetic rats after 6 h of administration of the extract (Sireesha et al. 2011). After 30 days of treatment with 300 mg of the extract there was a significant decrease in fasting blood glucose associated with a significant improvement in glycemic control as evidenced by lower levels of HbA1c in diabetic treated rats when compared to those in untreated diabetic rats. The aqueous extract also exhibited significant hypolipidemic effect which is evident from lower levels of triglycerides, total, LDL and VLDL cholesterol and increase in the levels of HDL cholesterol in diabetic treated rats compared to those in diabetic untreated rats (Sireesha et al. 2011). The antihyperglycemic and hypolipidemic activities of the aqueous extract were postulated to be due to the presence of alkaloids or glycosides as active principles.

A cross over randomized clinical study of 30 type 2 diabetic subjects showed consumption of low glycemic index (GI) foxtail millet (*Setaria italica*) biscuits (GI = 50.8) for 30 days caused a significant reduction in serum glucose (23%), serum cholesterol (6%), serum LDL (20%) and GHb (16.5%), and a slight decrease in serum triglycerides and VLDL (Thathola et al. 2011). Serum HDL increased significantly by 23%. Almost similar results were observed for foxtail millet burfi as for foxtail millet biscuits. All metabolic parameters except for HDL increased upon stopping the supplementation. The authors concluded that foxtail millet as a low GI food product led to modest improvement in long-term glycemic and lipidemic control in type 2 diabetics.

Trypsin Inhibitory Activity

A major trypsin inhibitor (FMTI-II) was isolated from seeds of foxtail millet (Tashiro et al. 1990). It consisted of 67 amino acid residues, including 10 half-cystine residues which are involved in 5 disulfide bridges in the molecule. Another subtilisin inhibitor, FMTI-III was also isolated from foxtail millet seeds (Tashiro et al. 1991a, b). The molecular weight and the amino acid composition together with the above nature were identical with those of another major trypsin inhibitor (FMTI-II). The protein contained 67 amino acid residues, the sequence of which was the same as that of FMTI-II except for the replacement of the C-terminal glutamine by glutamic acid. FMTI-III was shown to be specific and single-headed for trypsin.

Traditional Medicinal Uses

In China, foxtail millet grain is used as emollient and astringent in diarrhoeic and choleric affections. cholereic affections. In India, the seed are used as diuretic, for strengthening virility, for treatment of dyspepsia and indigestion, and for rheumatism.

Other Uses

Foxtail millet is cultivated in Europe, north and south America, north Africa, Australia and India mainly for hay, forage and silage, and also for birdseed. The straw is also used as fodder in China; and for thatching and bedding, e.g. in India. The bran serves as animal feed and can be used for oil extraction. Foxtail millet can be used as a quick-growing crop in contour strips in dense populations for erosion control.

An antifungal peptide with a molecular mass of 26.9 kDa was isolated from dry seeds of foxtail millet (*Setaria italica*) (Xu et al. 2011). The peptide inhibited mycelial growth in *Alternaria alternata* with an IC_{50} of 1.3 μmol/L, and it also exhibited antifungal activity against *Trichoderma viride*, *Botrytis cinerea* and *Fusarium oxysporum*.

Comments

Foxtail millet is the second most widely planted species of millet, and the most important in East Asia. China has the longest history of foxtail millet and cultivation is the leading producer of foxtail millet today.

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Sorghum bicolor

Scientific Name

***Sorghum bicolor* (L.) Moench.**

Synonyms

Agrostis nigricans (Ruiz & Pav.) Poir., *Andropogon besseri* Kunth, *Andropogon bicolor* (L.) Roxb., *Andropogon compactus* Brot., *Andropogon niger* (Ard.) Kunth, *Andropogon rubens* Kunth nom. nud., *Andropogon saccharatrus* Kunth, *Andropogon saccharatus* (L.) Roxb. nom. illeg., *Andropogon saccharatus* (Willd.) Roxb., *Andropogon sorghum* (L.) Brot., *Andropogon sorghum* f. *pallidus* Chiov., *Andropogon sorghum* subsp. *sativus* Hack., *Andropogon sorghum* subvar. *aethiops* (Körn.) Hack., *Andropogon sorghum* subvar. *badius* Hack., *Andropogon sorghum* subvar. *fragilis* Hack., *Andropogon sorghum* subvar. *japonicus* Hack., *Andropogon sorghum* subvar. *lividus* Hack., *Andropogon sorghum* subvar. *niger* (Ard.) Hack., *Andropogon sorghum* subvar. *rubens* Hack., *Andropogon sorghum* subvar. *splendidus* Hack., *Andropogon sorghum* var. *abyssinicum* Hack., *Andropogon sorghum* var. *aegyptiacus* Körn., *Andropogon sorghum* var. *aethiops* Körn., *Andropogon sorghum* var. *albofuscus* Körn., *Andropogon sorghum* var. *ankolib* Hack., *Andropogon sorghum* var. *arabicus* Körn., *Andropogon sorghum* var. *bicarinatus* Hack., *Andropogon sorghum* var. *bicolor* (L.) Körn., *Andropogon sorghum* var. *burmanicus* G.T. Benson & Subba Rao, *Andropogon sorghum* var. *cafer* (Ard.) Körn., *Andropogon sorghum* var. *campanus* Hack., *Andropogon sorghum* var. *caudatus* Hack., *Andropogon sorghum* var. *cernuus* (Ard.) Körn., *Andropogon sorghum* var. *corymbosus* Hack., *Andropogon sorghum* var. *dochna* (Forssk.) C. Chr., *Andropogon sorghum* var. *durra* (Forssk.) Hack., *Andropogon sorghum* var. *ehrenbergianus* Hack., *Andropogon sorghum* var. *elegans* Körn., *Andropogon sorghum* var. *eois* Burkart ex Benson & Subba Rao, *Andropogon sorghum* var. *fulvus* Hack., *Andropogon sorghum* var. *glaberrimus* Hack., *Andropogon sorghum* var. *globosus* Hack., *Andropogon sorghum* var. *hians* Hook.f., *Andropogon sorghum* var. *hirsutus* Busse & Pilg., *Andropogon sorghum* var. *hybridus* Hack., *Andropogon sorghum* var. *irungu* Burkill ex C. Benson & C.K. Subba Rao, *Andropogon sorghum* var. *javanicus* Hack., *Andropogon sorghum* var. *jucundus* Busse & Pilg., *Andropogon sorghum* var. *lasiorhachis* Hack., *Andropogon sorghum* var. *leiostachyus* Hack., *Andropogon sorghum* var. *leucospermus* Körn., *Andropogon sorghum* var. *melanospermus* Hack., *Andropogon sorghum* var. *miliiformis* Hack., *Andropogon sorghum* var. *neesii* Körn., *Andropogon sorghum* var. *nervosus* (Besser ex Schult.) Hack., *Andropogon sorghum* var. *nitidus* Chiov., *Andropogon sorghum* var. *obovatus* Hack., *Andropogon sorghum* var. *ovatoellipticus* Hack., *Andropogon sorghum* var. *ovulifer* Hack., *Andropogon sorghum* var. *pulcher* G.T. Benson & Subba Rao *Andropogon sorghum* var. *roxburghii* Hack., *Andropogon sorghum* var. *rubrocernuus*

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Körn., *Andropogon sorghum* var. *rufescens* Hack., *Andropogon sorghum* var. *rugulosus* Hack., *Andropogon sorghum* var. *saccharatus* (L.) Alef., *Andropogon sorghum* var. *schenkii* Körn., *Andropogon sorghum* var. *schimperi* Hack., *Andropogon sorghum* var. *subglabrescens* Hack., *Andropogon sorghum* var. *subglobosus* Hack., *Andropogon* sorghum var. *submuticus* Hack. nom. illeg., *Andropogon sorghum* var. *technicus* Körn., *Andropogon sorghum* var. *usorum* (Nees) Körn., *Andropogon sorghum* var. *vulgaris* (Pers.) Hack. nom. superfl., *Andropogon sorghum* var. *wightii* Hack., *Andropogon sorghum* var. *yemensis* Körn., *Andropogon subglabrescens* Steud., *Andropogon truchmenorum* Walp., *Andropogon usorum* Steud., *Andropogon vulgaris* (Pers.) Balansa nom. illeg., *Andropogon vulgaris* Raspail, *Holcus albus* Steud. nom. nud., *Holcus arduinii* J.F. Gmel., *Holcus bicolor* L., *Holcus cafer* Ard., *Holcus caffrorum* (Retz.) Thunb., *Holcus cernuus* Ard., *Holcus compactus* Lam., *Holcus dochna* Forssk., *Holcus dora* Mieg, *Holcus duna* J.F. Gmel. orth. var., *Holcus durra* Forssk., *Holcus ferrugineus* Schrad. ex Roem. & Schult. nom. nud.,*Holcus niger* Ard., *Holcus nigerrimus* Ard. orth. var., *Holcus nigricans* Steud. pro syn., *Holcus pyramidalis* Steud. pro syn., *Holcus rubens* Gaertn., *Holcus saccharatus* L nom. rej., *Holcus saccharatus* var. *technicus* (Körn.) Farw., *Holcus sorghum* L., *Holcus sorghum* var. *caffrorum* (Thunb.) L.H. Bailey, *Holcus sorghum* var. *durra* (Forssk.) L.H. Bailey, *Holcus sorghum* var. *saccharatus* (L.) L.H. Bailey, *Holcus sorghum* var. *technicus* (Körn.) L.H. Bailey, *Milium bicolor* (L.) Cav., *Milium compactum* (Lam.) Cav., *Milium maximum* Cav., *Milium nigricans* Ruiz & Pav., *Milium sorghum* (L.) Cav., *Milium sorgo* Garsault nom. nud., *Panicum caffrorum* Retz., *Panicum frumentaceum* Salisb. nom. superfl., *Panicum sacchariferum* Salisb. nom. superfl., *Rhaphis sorghum* (L.) Roberty, *Sorghum abyssinicum* (Hack.) Chiov. nom. illeg., *Sorghum album* Roem. & Schult. pro syn., *Sorghum ankolib* (Hack.) Stapf, *Sorghum anomalum* Desv., *Sorghum arduinii* (Gmel.) J. Jacq., *Sorghum basiplicatum* Chiov., *Sorghum basiplicatum* f. *eburneum* Chiov., *Sorghum basiplicatum* f. *jodolepis* Chiov., *Sorghum basiplicatum* f. *leucolepis* Chiov., *Sorghum basiplicatum* var. *atropaniculatum* Chiov., *Sorghum basiplicatum* var. *microcarpum* Chiov., *Sorghum basiplicatum* var. *pallescens* Chiov., *Sorghum basiplicatum* var. *paniculatellum* Chiov., *Sorghum basiplicatum* var. *pseudoanfetum* Chiov., *Sorghum basiplicatum* var. *rubellum* Chiov., *Sorghum basiplicatum* var. *rubrogeminum* Chiov., *Sorghum basiplicatum* var. *subflavescens* Chiov., *Sorghum basutorum* Snowden, *Sorghum bicolor* var. *cafer* (Körn.) Fosberg & Sachet, *Sorghum bicolor* var. *caffrorum* (Retz.) Mohlenbr., *Sorghum bicolor* var. *cernuum* (Ard.) Ghi'a, *Sorghum bicolor* var. *exaristatum* Doronina & Ivanjuk., *Sorghum bicolor* var. *miliiforme* (Hack.) Teplyak., *Sorghum bicolor* var. *obovatum* (Hack.) Fosberg & Sachet, *Sorghum bicolor* var. *rotundulum* (Snowden) Fosberg & Sachet, *Sorghum bicolor* var. *saccharatum* (L.) Mohlenbr., *Sorghum bicolor* var. *sikkimense* (Snowden) Teplyak., *Sorghum bicolor* var. *subglabrescens* (Steud.) Fosberg & Sachet, *Sorghum bicolor* var. *technicum* (Körn.) Stapf ex Holland, *Sorghum caffrorum* (Retz.) P. Beauv., *Sorghum caffrorum* var. *albofuscum* (Körn.) Snowden, *Sorghum caffrorum* var. *bicarinatum* (Hack.) Snowden, *Sorghum campanum* Ten. & Guss., *Sorghum caudatum* (Hack.) Stapf, *Sorghum caudatum* var. *angolense* (Rendle) Stapf, *Sorghum caudatum* var. *aristatum* Ivanjuk., *Sorghum caudatum* var. *coffeatum* Ivanjuk., *Sorghum caudatum* var. *dicarpum* Ivanjuk., *Sorghum caudatum* var. *purpureum* Ivanjuk., *Sorghum centroplicatum* Chiov., *Sorghum centroplicatum* var. *alborubr*um Chiov., *Sorghum centroplicatum* var. *dubium* Chiov., *Sorghum centroplicatum* var. *ellipsoideum* Chiov., *Sorghum centroplicatum* var. *erythromelas* Chiov., *Sorghum centroplicatum* var. *faregg* Chiov., *Sorghum centroplicatum* var. *globosum* Chiov., *Sorghum centroplicatum* var. *incertum* Chiov., *Sorghum centroplicatum* var. *pallidocernuum* Chiov., *Sorghum centroplicatum* var. *perlarium* Chiov., *Sorghum centroplicatum* var. *pseudoneesii* Chiov., *Sorghum centroplicatum* var. *sabderatense* Chiov., *Sorghum centroplicatum* var. *subcarneum* Chiov., *Sorghum centroplicatum* var. *tricolor* Chiov., *Sorghum cernuum* (Ard.)

Host, *Sorghum cernuum* var. *globosum* (Hack.) Snowden, *Sorghum cernuum* var. *truchmenorum* (Klokov) Snowden, *Sorghum cernuum* var. *yemense* (Körn.) Snowden, *Sorghum chinense* Jakusch. no Latin descr., *Sorghum commune* P. Beauv. nom. nud., *Sorghum compactum* Lag., *Sorghum conspicuum* Snowden, *Sorghum coriaceum* Snowden, *Sorghum dochna* (Forssk.) Snowden, *Sorghum dochna* var. *atrum* Snowden, *Sorghum dochna* var. *burmanicum* (Benson & Subba Rao) Snowden, *Sorghum dochna* var. *corymbosum* (Hack.) Snowden, *Sorghum dochna* var. *formosum* Snowden, *Sorghum dochna* var. *irungu* (Benson & Subba Rao) Snowden, *Sorghum dochna* var. *melliferum* Snowden, *Sorghum dochna* var. *obovatu*m (Hack.) Snowden, *Sorghum dochna* var. *pulchrum* (Burk. ex Benson & Subba Rao) Snowden, *Sorghum dochna* var. *technicum* (Körn.) Snowden, *Sorghum dochna* var. *wightii* (Hack.) Snowden, *Sorghum dora* (Mieg) Cuoco, *Sorghum dulcicaule* Snowden, *Sorghum dulcicaule* var. *griseolilacinum* Ivanjuk., *Sorghum durra* (Forssk.) Trab., *Sorghum durra* var. *elongatum* Snowden, *Sorghum durra* var. *eois* (Burk. ex Benson & Subba Rao) Snowden, *Sorghum durra* var. *fuscum* Snowden, *Sorghum elegans* (Körn.) Snowden, *Sorghum eplicatum* Chiov., *Sorghum eplicatum* f. *dichrolepis* Chiov., *Sorghum eplicatum* f. *geminatum* Chiov., *Sorghum eplicatum* f. *laxum* Chiov., *Sorghum eplicatum* var. *cereum* Chiov., *Sorghum eplicatum* var. *erythrocarpum* Chiov., *Sorghum eplicatum* var. *fiorii* Chiov., *Sorghum eplicatum* var. *hackelii* Chiov., *Sorghum eplicatum* var. *heterochromum* Chiov., *Sorghum eplicatum* var. *melanoleucum* Chiov., *Sorghum eplicatum* var. *virescens* Chiov., *Sorghum exsertum* Snowden, *Sorghum gambicum* Snowden, *Sorghum giganteum* Edgew., *Sorghum glycychylum* Pass., *Sorghum guineense* Stapf, Bull. *Sorghum halepense* var. *saccharatum* (L.) Goiran, *Sorghum japonicum* (Hack.) Roshev., *Sorghum margaritiferum* Stapf, *Sorghum medioplicatum* Chiov., *Sorghum melaleucum* Stapf, *Sorghum melanocarpum* Huber, *Sorghum mellitum* Snowden, *Sorghum membranaceum* Chiov., *Sorghum membranaceum* var. *baldratianum* Chiov., *Sorghum miliiforme* (Hack.) Snowden, *Sorghum miliiforme* var. *rotundulum* Snowden, *Sorghum miliiforme* var. *sikkimense* Snowden, *Sorghum nankinense* Huber, *Sorghum nervosum* Besser ex Schult. & Schult.f., *Sorghum nervosum* Chiov. orth. var., *Sorghum nigericum* P. Vig. no Latin descr., *Sorghum nigricans* (Ruiz & Pav.) Snowden, *Sorghum nigricans* var. *angolense* (Rendle) Snowden, *Sorghum nigrum* (Ard.) Roem. & Schult., *Sorghum notabile* Snowden, *Sorghum pallidum* Chiov. nom. illeg., *Sorghum papyrascens* Stapf, *Sorghum pyramidale* Roem. & Schult. pro syn., *Sorghum rigidum* Snowden, *Sorghum rollii* Chiov., *Sorghum roxburghii* Stapf, *Sorghum roxburghii* var. *farinosum* Snowden, *Sorghum roxburghii* var. *fulvum* (Hack.) Snowden, *Sorghum roxburghii* var. *hians* (Hook.f.) Stapf, *Sorghum roxburghii* var. *hirsutum* (Busse & Pilg.) Snowden, *Sorghum roxburghii* var. *jucundum* (Busse & Pilg.) Snowden, *Sorghum roxburghii* var. *mutabile* Snowden, *Sorghum roxburghii* var. *nanum* Snowden, *Sorghum roxburghii* var. *parvum* Snowden, *Sorghum rubens* Willd. pro syn., *Sorghum saccharatum* (L.) Moench, *Sorghum saccharatum* var. *atrum* (Snowden) Doronina & Ivanjuk., *Sorghum saccharatum* var. *bicolor* (L.) Kerguélen, *Sorghum saccharatum* var. *burmanicum* (Burk. ex Benson & Subba Rao) Doronina & Ivanjuk., *Sorghum saccharatum* var. *corymbosum* (Hack.) Doronina & Ivanjuk., *Sorghum saccharatum* var. *formosum* (Snowden) Doronina & Ivanjuk., *Sorghum saccharatum* var. *giganteum* Doronina & Ivanjuk., *Sorghum saccharatum* var. *irungu* (Burk. ex Benson & Subba Rao) Doronina & Ivanjuk., *Sorghum saccharatum* var. *melliferum* (Snowden) Doronina & Ivanjuk., *Sorghum saccharatum* var. *obovatum* (Hack.) Doronina & Ivanjuk., *Sorghum saccharatum* var. *papyraceum* Doronina & Ivanjuk., *Sorghum saccharatum* var. *pulchrum* (Burk. ex Benson & Subba Rao) Doronina & Ivanjuk.,*Sorghum saccharatum* var. *rubens* (Kunth) Nees, *Sorghum saccharatum* var. *technicum* (Körn.) Doronina & Ivanjuk., *Sorghum saccharatum* var. *vulgare* (Pers.) Kuntze, *Sorghum saccharatum* var. *wightii* (Hack.) Doronina & Ivanjuk., *Sorghum sativum* (Hack.) Trab., *Sorghum simulans* Snowden, *Sorghum sorghum* (L.) H. Karst. nom. inval.,

Sorghum splendidum (Hack.) Snowden, *Sorghum subglabrescens* (Steud.) Schweinf. & Asch., *Sorghum subglabrescens* var. *arabicum* (Körn.) Snowden, *Sorghum subglabrescens* var. *microcarpum* (Chiov.) Snowden, *Sorghum subglabrescens* var. *paniculatellum* (Chiov.) Snowden, *Sorghum subglabrescens* var. *rubrocernuum* (Körn.) Snowden, *Sorghum tataricum* Huber, *Sorghum technicum* (Körn.) Trab., *Sorghum truchmenorum* K. Koch, *Sorghum usorum* Nees, *Sorghum vulgare* Pers. nom. superfl., *Sorghum vulgare* var. *angolense* Rendle, *Sorghum vulgare* subsp. *bicolor* (L.) Maire & Weiller, *Sorghum vulgare* var. *bicolor* (L.) Pers., *Sorghum vulgare* var. *caffrorum* (Retz.) F.T. Hubb. & Rehder, *Sorghum vulgare* var. *cernuum* (Ard.) Fiori & Paoli, *Sorghum vulgare* var. *durra* (Forssk.) F.T. Hubb. & Rehder, *Sorghum vulgare* var. *nervosum* (Besser ex Schult.) Forbes & Hemsl., *Sorghum vulgare* var. *nigricans* (Ruiz & Pav.) Hill, *Sorghum vulgare* var. *roxburghii* (Hack.) Haines nom. superfl., *Sorghum vulgare* var. *saccharatum* (L.) Boerl., *Sorghum vulgare* var. *technicum* (Körn.) Ják.

Refer to notes under Comments.

Family

Poaceae

Common/English Names

African Millet, Beer Sorghum, Black Millet, Black Seeded Sorghum, Brown Durra, Brown-Seeded Sorghum, Broom Corn, Chicken Corn, Chinese Sugar Cane, Chinese Millet, Chinese Sorgum, Durra, Egyptian Corn, Feterita, Forage Sorghum, Gooseneck,Grain Sorghum, Guinea Corn, Guinea Wheat, Great Millet, Indian Grain Sorghum, Indian Millet, Italian Whisk, Jerusalem Corn, Kafir Corn, Kaffir-Corn, Milo, Kamerun Grass, Large-Seeded Sorghum, Maili, Negro Corn, Orange Sawgum, Orange Sorgum, Pampas Rice, Pearl Millet, Rhodesian Sudan Grass, Rice Corn, Rox Orange, Saccharine Sorghum, Shallu, Shattercane, Soft-Seeded Sorghum, Sordan, Sorghum, Sorghum Cane, Sorghum-Sudangrass, Sudanese Sorghum, Sugar Sorghum, Sweet Sorghum, Tennessee Rice, Turkish Millet, Venetian Whisk, Wacona Orange, West African Grain Sorgum, White Durra.

Vernacular Names

Arabic: Gafuli,Miknis;
Argentina: Sorgo, Sorgo Azucarero, Sorgo Granifero;
Brazil: Milho –De-Vassoura, Painco, Sorgo (Portuguese);
Burmese: Shallu;
Chinese: Duo Mai Gāoliáng, Gāoliáng, Gāoliáng G Mi, Li Yong Gāoliáng, Lu Shu, Lu Su, Lu Shu Tian Gāoliáng, Nan Fei Gāoliáng, Tian Gāoliáng, Shi Yong Gāoliáng, Shu Mi, Xi Fei Gāoliáng, Yin Gan Gāoliáng, Ying Gāoliáng Cao, Zhong Guo Gāoliáng;
Cook Islands: Tarapi (Maori);
Czech: Čirok Obecný;
Danish: Almindelig Durra, Ægte Durra, Durrah, Durra, Sukkerdurra, Sukkerhirse, Sukkersorghum;
Dutch: Dari, Durrha Kafferkoren, Suikersorgho, Suikergierst, Suiker-Sorghum;
Eastonian: Harilik Sorgo;
Ethiopia: Bachanta;
Finnish: Durra, Sokerihirssi;
French: Dari, Doura, Gros Mill, Gros Millet, Riz Égyptien, Sorgho, Sorgho À Balais, Sorgho Blanc, Sorgho Douro, Sorgho Feterita, Sorgho Du Soudan, Sorgho Durra, Sorgho Menu, Sorgho Penché;
German: Gewöhnliche Mohrenhirse, Grosse Hirse, Japanische Mohrenhirse, Kaffernhirse, Mohrenhirse, Nickende Mohrenhirse, Sorghum-Hirse, Sorghumhirse, Zucker-Mohrenhirse, Zuckerhirse, Zuckerrohr;
Huasa: Dawa;
Hungarian: Cirok;
India: Jowar (Bengali), Jowar, (Gujarati), Jowar, Chari (Hindu), Jola (Kannada), Jwari (Marathi), Janha (Oriya), Joar, Jawari (Sanskrit), Cholam, Karuncoolam (Tamil), Jannalu, Jonna (Telugu);
Indonesia: Cantel, Jagung Cantel;

Italian: Dura, Durra, Miglio, Saggina A Spazzola, Saggina Da Zucchero, Saggina Rossa, Sorgo Coltivo, Sorgo Saccarifero, Sorgo Zuccherino;
Japanese: Azuki Morokoshi, Beni Kooryan, Kouryan, Morokoshi, Morokoshi Kibi, Satou Morokoshi, Sorugami;
Kenya: Muvya (Kikamba);
Korean: Susu;
Laotian: Khauz Fangz;
Libya: Gafuli;
Malaysia: Jagung, Jagung Gerebang;
Mali: Kenike (Bamanankan);
Marshall Islands: Korn;
Nigeria: Igwu (Idoma);
Norwegian: Brundurra, Durra, Kaffer, Hvitdurra, Kjempehirse, Kvastdurra;
Philippines: Batad (Bikol), Batad (Bisaya), Bakau (Ibanag), Gau (Ifugao), Layagah (Sulu), Batad, Batag (Tagalog);
Portugal: Massambala, Milho Miúdo, Sorgo, Sorgo-Vassoura, Sorgo Para Vassouras;
Russian: Belaia Durra, Buroe Durra, Durra, Dzhugara, Džugara, Gaolian, Sakharnoe Sorgo, Sorgo Afrikanskoe, Sorgo Obyknovennoe, Sorgo Sakharnoe, Sorgo Tekhncheskoe, Sorgo Venichnoe;
Rwanda: Ishaka (Kinyarwanda);
Slovašcina: Krmni Sirek;
Slovencina: Cirok Dvojfarebný;
Spanish: Daza, Doura, Durra, Maiz Guineo, Maiz Milo, Mijo, Millo, Pasto Sudan, Popote, Sorgo, Sorgo Azucarado, Sorgo Común, Sorgo De Grano, Sorgo De Guinea, Sorgo Dulce, Sorgo Durra, Sorgo Forrajero, Sorgo Kaoliang, Sorgo Rojo, Sorgo Sacarífero, Zahina;
South Africa: Graansorghum (Afrikaans), Mabele (Ndedele), Mabele (Pedi), Mabele (Setswana); Mabele (Sotho), Amazimba (Xhosa), Amabele (Zulu);
Sudan: Dura;
Swahili: Mtama;
Swedish: Durra, Gaoliang, Jättehirs, Kvastdurra, Sockerdurra;
Thai: Kao Liang, Khao Fang, Khao Fang Hang Vhnag, Khao Fang Samut Khodom, Khao Khuang, Khao Pang Hang Vhang, Samut Kodom (Central Thailand);
Tongan: Kola;
Turkish: Misir Darisi, Dari, Zura;
Vietnamese: Cao Lương Đỏ, Cỏ Miến To, Miến To;
Yoruba: Baba, Oka Bab.

Origin/Distribution

Sorghum is an important tropical cereal being grown for food and fodder. It originated in northern Africa, probably in Ethiopia and is now cultivated widely in tropical and subtropical regions including other parts of Africa, India, Southeast Asia, China, Australia, South America, Mexico and the southern United States.

World's leading sorghum producing countries in terms of production quantity are:

USA 8,773,440 tonnes, India 6,980,000 tonnes, Mexico 6,940,230 tonnes, Nigeria 4,784,100 tonnes, Argentina 3,629,000 tonnes, Ethiopia 2,997,400 tonnes, Sudan 2,630,000 tonnes, Burkina Faso 1,990,230 tonnes, China 1,729,411 tonnes, Australia 1,598,000 tonnes, Brazil 1,505,340 tonnes, Niger 1, 304,830 tonnes, and Mali 1,256,810 tonnes (FAO 2012).

Agroecology

Sorghum is adapted to a wide range of ecological habitats. Primarily it is a plant of hot, dry regions, extremely drought tolerant but will still survive cool weather (12–15°C) , water-logged conditions (for short periods) and will grow in high rainfall areas. It thrives in areas with mean annual rainfall of 400–750 mm uniformly distributed during the growing season It is usually grown from sea-level to altitudes of 1,000 m and up to 2,300 m in the tropics from 40°N and S of the equator. Its optimum temperature range is 25–31°C; temperatures below 12–15°C have been reported to affect flowering by causing sterility, growth and yield. It is intolerant of frost. Sorghum thrives in full sun; it has a short–day requirement with a wide range of response to photoperiod. Weakly photoperiod-sensitive to photoperiod-insensitive sorghum cultivars have been developed.

Sorghum grows in a wide variety of soils with a pH range of 5.0–8.5. In the tropics, it is commonly grown on heavy vertisols but is equally adaptable to light sandy soils. It will grow on poor soils and saline soil as it more tolerant to salinity than maize. Best growth is produced on loams and sandy loams.

Edible Plant Parts and Uses

Sorghum is an important staple food in the semi-arid tropical regions of Africa and Asia. Whole grain sorghum is boiled like rice, roasted, or popped like maize. Grain sorghum after hulling, is usually ground or pounded into flour. Sorghum flour is used un-fermented or fermented to make thick or thin porridge, pancakes, bread, dumplings or couscous, opaque and cloudy beers and non-alcoholic fermented beverages. In many parts of Africa, various types of food are prepared from germinated and non-germinated grains. In Africa sorghum grain is germinated, dried and ground to form malt, which is used as a substratum for fermentation in local beer production. White grain sorghum is generally preferred for cooking while red and brown grain sorghums are normally used for beer making. In Sudan sorghum is usually consumed in the fermented form in such food as *injera*, a thick, unleavened bread made from fermented flour; *kisra*, a pancake or thin bread prepared from fermented sorghum; *nasha* or *medid*a, a thin gruel; *aceda*, a gruel made from fermented sorghum grains; *ugali*, a porridge, *hulu-mur* or *abreh*, a sorghum drink commonly consumed in the evening during breaking of fast during Ramadan and *marissa*, a sorghum beer (Eggum et al. 1983; Elkhalifa 2005; Mohammed et al. 2011b; Rahman and Osman 2011). In Burkin Faso, sorghum is used to make a thick porridge preparation "*tô*" and red sorghum cultivars used for local beer "*dolo*" (Dicko et al. 2002).

In many African countries, in eastern and southern Africa, Uganda, Nigeria malting sorghum for lager beer and stout brewing, and malt beverages have become important industries. In South Africa an instant breakfast cereal is made from sorghum that is similar in quality but much cheaper than wheat or maize products. The use of decorticated sorghum and pigeon pea flours in infants food, afford a product with high nutritional value and of better functional properties (Mohammed et al. 2011a). The dried product was found to provide adequate amounts of protein (15.15%) and energy values (414.25 kcal/100 g DM) capable to meet the international standards for infants' protein quality as recommended by the FAO/WHO/UN in 1985.

In India, sorghum flour is used to make *jowar rotti* or *jolada rotti* (an Indian bread). In Korea, sorghum is cooked with rice, or its flour is used to make cake that is called *susu bukkumi*. Sorghum was ground and the flour was the main alternative to wheat in north China for a long time. In China, sorghum is fermented and distilled to produce vinegar and a spirit, maotai, which is regarded as one of the country's most famous liquors.

The stems of sweet sorghum types are chewed like sugar cane and, mainly in the United States, a sweet syrup is pressed from them. Sorghum is one of a number of cereal grains used as wheat substitutes in gluten-free recipes and products. A dye can be extracted from the grain refuse (glumes and grain wall) of several red sorghum cultivars grown for food or for beer-making.

Botany

An erect, robust herbaceous annual, culm 3–4 m high with 1 or more tillers (Plate 1), glabrous or pubescent nodes and a fibrous root system. Leaf sheaths are glabrous, compressed and keeled with waxy bloom. Leaf blades are broadly linear (Plate 2) or linear-lanceolate, 40–70 × 3–8 cm, glabrous with prominent mid-rib, scabrous margins and ciliated, subrounded ligule. Panicles erect, dense or lax, 10–25 cm long, pyramidal or obovate in outline, central axis with primary branches ascending or spreading and secondary branches, sessile spikelets broadly obovate to subglobose, 4–6 mm long (Plates 2, 3, and 4). Mature glumes of sessiIe spikelets red, reddish brown, straw-coloured or yellowish,

Plate 1 Robust erect plant habit

Plate 2 Young lax terminal panicle and broadly linear leaves

sometimes flushed with dark red or reddish brown (Plate 4); lower glume leathery to papery, glabrous to pilose, upper lemma usually awned (Plate 5). Caryopsis large, rounded to slightly pointed, 4–8 mm across, variable colour yellow to orange or reddish depending on cultivar, often exposed between the gaping glumes

Plate 3 Maturing lax seed heads

Nutritive/Medicinal Properties

Nutrient composition of sorghum grains per 100 g edible portion was reported by USDA (2012) as follows: water 9.20 g, energy 339 kcal (1,418 kJ), protein 11.30 g, total lipid 3.30 g, ash 1.57 g, carbohydrate 74.63 g, total dietary fibre 6.3 g, Ca 28 mg, , Fe 4.40 mg, P 287 mg, K 350 mg, Na 6 mg, thiamin 0.237 mg, riboflavin 0.142 mg, niacin 2.927 mg, total saturated fatty acids 0.457 g, 12:0 (lauric acid) 0.007 g, 14:0 (myristic acid) 0.009 g, 16:0 (palmitic acid) 0.407 g, 18:0 (stearic acid) 0.035 g, total monounsaturated fatty acids 0.993 g, 16:1 undifferentiated (palmitoleic acid) 0.029 g, 18:1 undifferentiated (oleic acid) 0.964 g,

Plate 4 Sorghum with ripening dense seed heads ready for harvesting

Plate 5 Harvested sorghum

total polyunsaturated fatty acids 1.370 g, 18:2 undifferentiated (linoleic acid)1.305 g, 18:3 threonine 0.346 g,undifferentiated (linolenic acid) 0.065 g, tryptophan 0.124 g, isoleucine 0.433 g, leucine 1.491 g, lysine 0.229 g, methionine 0.169 g, cystine 0.127 g, phenylalanine 0.546 g, tyrosine 0.321 g, valine 0.561 g, arginine 0.355 g, histidine 0.246 g, alanine 1.033 g, aspartic acid 0.743 g, glutamic acid 2.439 g, glycine 0.346 g, proline 0.852 g and serine 0.462 g.

Sorghum kernels consisted of 68.7–70.6% starch, more than the B73 corn (67.4%) (Ai et al. 2011). Sorghum starches (6B73, 6C21, 6C69, 7R34, and X789) exhibited higher gelatinization temperatures (66.6–67.4°C), greater gelatinization enthalpy changes (13.0–14.0 J/g), and greater percentages of retrogradation (60.7–69.1%), but slower enzymatic hydrolysis rates (83.8–87.8% at 48 h) than the B73 corn starch (61.7°C, 10.1 J/g, 51.5%, and 88.5%, respectively). These differences could be attributable to sorghum amylopectins consisting of fewer short branch chains (Degree of Polymerization 6–12) (12.8–14.0%) than the corn amylopectin (15.0%). The sorghum starches displayed greater peak and breakdown viscosities but lower setback viscosities than the B73 corn starch, because of the lower amylose content of the sorghum starches. After 96 h of fermentation, most ground sorghums displayed lower ethanol yields (30.5–31.8%) than the ground B73 corn (31.8%). Heterowaxy sorghum starch had intermediate amylose content, pasting properties, and dynamic rheological properties (Sang et al. 2008). Cooked heterowaxy sorghum starch (10% solids) exhibited a viscoelastic-solid type of character, whereas cooked waxy sorghum starch behaved like a viscoelastic liquid. Amylopectin of normal sorghum starch had a slightly higher proportion of chains with degree of polymerization (DP) of 6–15 (45.5%) compared with amylopectin of heterowaxy starch (44.1%), which had a gelatinization peak temperature 2°C higher than normal sorghum starch. Heterowaxy sorghum starch contained significantly lower readily digestible starch (RDS) and higher resistant starch (RS) than waxy sorghum starch.

Kafirin, the alcohol soluble prolamin protein fraction in sorghum endosperm comprise about 50% of the grain storage protein (Paulis and Wall 1979). According to gel electrophoretic banding patterns and amino acid composition, there were no differences between the true kafirins and the cross-linked kafirin fractions (alcohol soluble reduced glutelin). Kafirins had been classified as α-, β-, and γ-kafirins according to differences in molecular weight, solubility, and structure (Shull et al. 1991). The kafirins were purified, amino acid composition was determined, and immunolocalization methods were used to determine the organization of the protein bodies and distribution of kafirins throughout the endosperm. All three groups of kafirins were low in lysine; β-Kafirins and γ-kafirins were relatively high in cysteine, and β-kafirins were relatively high in methionine (Shull et al. 1992). Protein bodies in the peripheral endosperm contain predominantly

α-kafirin with minor amounts of β- and γ-kafirin. Central endosperm protein bodies are also predominantly α-kafirin, but have a higher proportion of β-kafirin and γ-kafirin than the peripheral endosperm protein bodies.

El-Khalifa and El Tinay (1994) reported the percentage of the protein fractions albumin, globulin, prolamin, glutelin and insoluble fraction for the safra sorghum cultivar were 11.5, 8.2, 60.2, 10.2 and 10.1%, respectively, and for the sorghum cross 35:18 cultivar 10.0, 4.7, 67.9, 9.4 and 8.1%, respectively. The tannin contents of fractions for the safra cultivar were 0.228, 0.052, 0.028 and 0.304% for the first four soluble protein fractions, respectively, and for the cross 35:18 cultivar 0.376, 0.056, 0.136, 0.536%, respectively.

Grain sorghum and its proteins were deemed safe for celiac patients and individuals with varying levels of gluten intolerances (De Mesa-Stonestreet et al. 2010). However, the main sorghum proteins, kafirins, were found to be resistant to digestion. They were also difficult to extract and modify in an industrial-scale process and with food-compatible chemicals, thus limiting their use in foods. Extraction yields of 44.2, 24.2, and 56.8% kafirin proteins from sorghum distillers dried grains with solubles (DDGS) were achieved by using acetic acid, HCl-ethanol and NaOH-ethanol under reducing conditions, respectively (Wang et al. 2009). Acetic acid and NaOH-ethanol produced protein with higher purity than kafirins extracted with the HCl-ethanol protocol. The acetic acid extraction protocol produced protein with the highest purity, 98.9%. Fourier transform infrared spectroscopy (FTIR) showed alpha-helix dominated in all three samples, with only a small portion of beta-sheet present. Electrophoresis results showed alpha (1), alpha (2) band and beta kafirins were present in all three extracts. Extraction yields of 44.2, 24.2, and 56.8% kafirin proteins from sorghum distillers dried grains with solubles (DDGS) were achieved by using acetic acid, HCl-ethanol and NaOH-ethanol under reducing conditions, respectively (Wang et al. 2009). Acetic acid and NaOH-ethanol produced protein with higher purity than kafirins extracted with the HCl-ethanol protocol. The acetic acid extraction protocol produced protein with the highest purity, 98.9%. Fourier transform infrared spectroscopy (FTIR) showed alpha-helix dominated in all three samples, with only a small portion of beta-sheet present. Electrophoresis results showed alpha (1), alpha (2) band and beta kafirins were present in all three extracts.

Red sorghum spent grains (RSSG) and white sorghum spent grains (WSSG) by-product of beer production contained 23.4 and 19.3% crude protein (CP), 54 and 43% dietary fibre (NDF), 1.44 and 0.78% ash, 4.5 and 3.2% hexane extract and tannin content of 7.5 and 1.0 mg/g catechin equivalent respectively (Adewusi and Ilori 1994). Magnesium was the most abundant mineral in both RSSG and WSSG--185 and 140 mg/kg, respectively. Calcium, zinc, iron and copper were generally low. Both samples contained cadmium 1.12 (WSSG), 1.19 (RSSG) and lead at 1.38 mg/kg. Lysine was the limiting amino acid (chemical score 0.55) in both samples. Other essential amino acids were adequate or surplus. Stearic acid was the predominant fatty acid with varying levels of lauric, myristic, palmitic, and oleic acids in both samples. Feed intake and weight gain were highest in rats fed 26.3% WSSG (contributing 50% of the diet protein) but protein efficiency ratio (PER) and net protein retention (NPR) were highest in diets where spent grains contributed just 25% of the diet protein. True digestibility of diets decreased as dietary fibre content increased such that animals on diets containing 100% spent grain protein (above 20% NDF) lost weight.

Other Phytochemicals

The colour and the phenols of sorghum pericarp and testa were found to be controlled by the R, Y, B1, B2 and S genes (Hahn and Rooney 1986). Pericarp colour is determined by R-Y genes whether the pericarp is red (r-Y-), colourless or white (R-yy, rryy) or lemon –yellow (rrY-). Group II sorghums with a red pericarp (R-Y-B1-B2-ss) had higher levels of Folin-Ciocalteu-positive phenols or tannins than in group I sorghums (b1b2B1-, B1-b2b2), with a white pericarp (R-yy-B1-B2-ss). The pericarp and testa of group III sorghums

(B1-B2-S-) had similar levels of anthocyanidin pigments. Group III sorghums had higher levels of Folin-Ciocalteu phenols and tannins in the whole grain, pericarp, and testa fractions than group II sorghums. Sorghum containing condensed tannins possessed dominant genes B_1B_2 producing a thick, pigmented testa layer in the kernel upon maturation (Blakely et al. 1979; Earp and Rooney 1986). This layer varied in thickness, intensity and colour.

The anthocyanin pelargonidin and a flavanone eriodictyol were obtained from the acid hydrolysis of 3 anthocyanogen-type flavonoids -chromogens I, II, III in the seed coat of commercial sorghum (Yasumata et al. 1965). Apigeninidin, luteolinidin, 7-*O*-methtyl luteolinidin and its glycoside along with a polymeric pigment were identified in purple coloured glumes (Misra and Seshadri 1967). Two yellow pigments apigeninidin-5-glucoside and kaempferol-3-rutinoside-7-glucuronide, and an unidentified orange pigment having anthocyanin properties were isolated from three reddish-brown varieties of sorghum grains (Nip and Burns 1969). Two forms of apigeninidin and two forms of luteolinidin pigments were found in six white seeded sorghum varieties and hybrids (Nip and Burns 1971). An acylated cyanidin-3-glucoside, apigeninidin and luteolinidin and their 5-glucosides plus an unidentified acid-stable form were found in the first internodes, coleoptiles and roots of the Wheatland variety (1965). Red pericarp sorghums were reported to have flavan-4-ol compounds, such as luteoforol and apiforol (Awika and Rooney 2004), produced from flavanones (i.e., naringenin and eriodictyol) and may be precursors of anthocyanidins in sorghums. Wharton and Nicholson (2000) reported that sorghum synthesized a complex mixture of 3-deoxyanthocyanidin phytoalexins in response to inoculation with the non-pathogenic fungus *Bipolaris maydis*. The anthocyanin cyanidin 3-dimalonyl glucoside is also synthesized naturally in response to light. The following phytoalexins were detected from sorghum mesocotyls upon fungal inoculation: apigeninidin, apigeninidin 5-*O*-arabinoside, apigeninidin 7-methylether, luteolinidin, luteolinidin 5-methylether.

The chemical components of the sorghum grain cuticle were flavonoids, tannins and anthocyanidins (Kaluza et al. 1980). Average contents of free phenolic compounds (FPC) in sorghum were 0.5 (caryopses), 2.2 (glumes), 0.9 (stalks), and 6.2 mg/g (leaves) (Ring et al. 1988). Caryopses and glumes had higher FPC levels 15 days after anthesis (DAA). FPC contents in stalks did not change during maturity; young, lower leaves had higher FPC levels. Average concentrations of total phenolic acids (TPA) were 2.5 (caryopses), 10.6 (glumes), 4.8 (stalks), and 7.6 mg/g (leaves). Caryopses and stalks contained stable levels of TPA during maturation. Glumes contained maximum amounts of TPA at physiological maturity of caryopsis (27 DAA) while young, upper leaves contained more TPA. The most abundant phenolic acids, *p*-coumaric, salicyclic, and ferulic acids, were present at levels of 0.2–2.0 mg/g. Sorghum was found to be particularly rich in tannins and anthocyanidins; with apigeninidin as the main anthocyanidin (Sereme et al. 1993). Roots, stalks and grains of sorghum were found to be poor in phenolic compounds while sheaths and leaves were rich. In grains, anthocyanidins and tannins did not exceed 1.6% dry weight. In the sheaths, anthocyanidins and tannins reached 10.8 and 20.7% respectively 20 days after physiological maturation. An anthocyanidin identified as 7-*O*-methylapigeninidin was isolated from sorghum grains (Pale et al. 1997). This pigment was found in low concentration both in grains and in leaf sheaths. Sorghum brans were reported to have three to four fold higher anthocyanin contents than the whole grains (Awika et al. 2004); a rich source of anthocyanin (4.0–9.8 mg luteolinidin equivalents/g) compared to pigmented fruits and vegetables (0.2–10 mg/g), fresh weight basis. Luteolinidin and apigeninidin accounted for about 50% of the anthocyanins in the black sorghums. The 3-deoxyanthocyanins identified in red sorghum were apigenindin and luteolindin (Devi et al. 2011).

Red sorghum grains were found to contain 0.4–1 mg/kg amount of *trans*-piceid and up to 0.2 mg/kg *trans*-resveratrol (Bröhan et al. 2011). The white sorghum samples contained only traces of *trans*-piceid (up to 0.1 mg/kg), and no *trans*-resveratrol. Red sorghum could be the main source of *trans*-piceid in beer.

Sorghum varieties resistant to biotic and abiotic stresses were found to have on average higher contents of proanthocyanidins (PAs), 3-deoxyanthocyanidins (3-DAs), and flavan-4-ols than susceptible varieties (Dicko et al. 2005a). Results showed the content of 3-DAs to be a good marker for sorghum resistance to both biotic and abiotic stresses because it correlated with resistance to all stresses except for photoperiod sensitivity.

A study of 30 sorghum varieties used for food in Burkina Faso showed a relationship between tannin level and utilization of sorghum grain (Sereme et al. 1994). High tannin varieties (more than 0.2%) are generally used for local alcoholic beverages, while low tannin varieties (under 0.2%) are used for cooking and for non-fermented drinks. Most of the 50 Burkina Faso sorghum varieties (82%) had a tannin content less than 0.25% (w/w) and peroxidase specific activity was higher than the monophenolase and *O*-diphenolase specific activities of polyphenol oxidase (Dicko et al. 2002). There was a diversity of isoforms among varieties for peroxidase. Varieties good for a thick porridge preparation ("tô") had low phenolic compounds content and a medium peroxidase activity. From the red varieties, those used for local beer ("dolo") had a high content in phenolic compounds and polyphenol oxidase, and a low peroxidase activity. The variety considered good for couscous had a low peroxidase content.

The Sudanese cultivar showed significantly higher moisture, ash, protein, copper, calcium, iron, sodium and fat contents while the Indian cultivar was significantly higher in fibre, potassium and phosphorus and carbohydrate contents (Awadelkareem et al. 2009). Syringic, *p*-coummaric, ferulic acid were detected as free form of phenolic acids in the Indian cultivar while gallic, protocatechuic, gentisic, caffeic, *p*-coummaric, and ferulic acids were detected in free form in the Sudanese cultivar. Gallic, protocatechuic, gentisic, and *p*-coummaric were not detected in free form in the Indian cultivar while syringic acid was not detected in Sudanese cultivar in free form. The Indian cultivar contained high caffeic and ferulic acid in free form compared to the Sudanese cultivar. Syringic, caffeic, *p*-coummaric and ferulic acids were detected in bound form in the Indian cultivar while gallic, protocatechuic, caffeic, *p*-coummaric and ferulic acid were detected in bound form in the Sudanese cultivar. Gallic, protocatechuic and gentisic acids were not detected in free and bound form in the Indian cultivar while *p*-coummaric acid was only detected in bound form in the Indian cultivar. Syringic, caffeic, *p*-coummaric and ferulic acids content in bound form were high in the Indian cultivar than the Sudanese cultivar. Generally phenolic acids of the two cultivars existed mostly in bound form.

The chemical composition of sorghum was reported as approximately 75% starch, 12% protein, 3.6% oil, 2.7% fibre (cellulose and hemicellulose), 1.6% ash, and 0.2% wax (Hwang et al. 2002c). Bianchi and colleagues (Bianchi et al. 1979; Avato et al. 1990) reported that grain sorghum kernel wax contained 1.3% hydrocarbons, 4% wax esters, 34% fatty alcohols, 24% fatty acids, and 32% aldehydes, or 7% hydrocarbons, 13% wax esters, 32% fatty alcohols, 27% fatty acids, and 21% aldehydes. They found that aldehydes, alcohols, and acids in sorghum wax were mainly saturated C28 and C30 and the wax esters were mostly esters of C28 and C30 alcohols and acids. The hydrocarbon n-alkanes were mainly heptocosane (34%) and nonacosane (53.2%). Free acids of grain wax contained C28 (20.6%) and C30 (20.6%) chains and unsaturated scids (18:1 25, 18:2 20%) that were absent in epiculticular wax of the plant. Avato et al. (1990) also presented the following analysis of the composition of the wax esters: 1% C42, 2% C44, 3% C46, 1% C48, 1% C50, 1% C52, 4% C54, 1% C55, 19% C56, 1% C57, 37% C58, 1% C59, 25% C60, and 2% C62. The presence of hopanoids (fernenol, isoarborinol, sorghumol, trematol) in sorghum grain flour suggested that they could be significant chemotaxonomic markers for sorghum (Avato et al. 1990). Dotriacontanol was found to characterize the lipid content of sorghum grain flour. Hwang et al. (2002a, b) found that the major components of the wax-like material were long-chained aldehydes, alcohols, and acids. Grain sorghum wax was composed of 46.3% (w/w) fatty aldehydes, 7.5% fatty acids, 41.0% fatty

alcohols, 0.7% hydrocarbons, 1.4% wax esters and steryl esters, and 0.9% triacylglycerols. The major components of the long-chained lipids extracted from grain sorghum kernels comprised policosanols (37–44%), aldehydes (44–55%), and acids (4–5%) whilst long-chained lipids from sorghum dried distillers grains (DDG) contained 52% policosanols, 23% aldehydes, 6.4% acids and l7% wax esters/steryl esters (Hwang et al. 2004). Composition of policosanols in DDG matched the composition in grain sorghum kernels, but the content of policosanols in DDG was higher than in grain sorghum kernels. Policosonal composition ranges were 0–1% C22:0 (docosanol), 0–3%c C24:0 (tetracosanol). 6–8% C26:0 (hexacosanol), 1% C27:0. 43–47% C28:0 (octanosol). 1–2% C29:0 (nonacosanol) , 40–43% C30:0 (triacontanol) and 1–4% C32:0 (dotriacontanol). Thus sorghum can be a major source of policosanols, long-chained alcohols, that have beneficial physiological activities. Hwang et al. (2005) reported that yields of wax-like materials from unpolished and polished Korean grain sorghum were 223 and 36.6 mg/100 g dry kernels respectively. Unpolished and polished grain sorghum contained 4.8% and 2.6% w/w crude lipids respectively. Composition of wax-like materials in unpolished grain sorghum was aldehydes 56.8%, policosanols 33.4%, acids 4.3%, hydrocarbons 2.3%, traiglycerols 1.2% and wax esters and steryl esters were not detected. Composition of wax-like materials in polished grain sorghum was aldehydes 34%, policosanols 29.2%, acids 13.1%, hydrocarbons 4.4%, traiglycerols 5.3% and wax esters and steryl esters 13.3%. Total policosanol content in unpolished grain sorghum was 74.5 mg/100 g dry kernel, comprising l.l% (20:0) 6.2% (22:0) 1.3% (23:0) 3.4% (24:0) 9.2% (26:0) 1.0% (27:0) 45.5% (28:0) 2.1% (29:0) and 30.2% (30:0). Total policosanol content in polished grain sorghum was 9.8 mg/100 g dry kernel, comprising l.l% (20:0) 5.4% (22:0) 1.3% (23:0) 2.7% (24:0) 14.6% (26:0) 0.8% (27:0) 45.6% (28:0) 1.0% (29:0) and 27.3% (30:0).

Avato et al. (1984) found that the composition of wax from sorghum panicles was quite different from that of mature leaf blades and sheaths. Free fatty alcohols were the dominant class of wax from sorghum seedlings and C32 was the major homologue of alcohols and aldehydes. The major was components of the epicuticular waxes were free fatty acids. The typical chain lengths of aldehydes, free alcohols and free fatty acids were C28 and C30.

Sorghum procyanidins were composed mainly of high MW (molecular weight) DP (degree of polymerization > 10) polymers (Awika et al. 2003a). Processing of sorghum bran into cookies and bread significantly reduced the levels of procyanidins; this effect was more pronounced in the higher MW polymers. Cookies had a higher retention of procyanidins (42–84%) than bread (13–69%). Extrusion of sorghum grain resulted in an increase in the levels of procyanidin oligomers with DP ≤ 4 and decrease in polymers with DP ≥ 6, suggesting a possible breakdown of the high MW polymers to the lower MW constituents during extrusion.

Sorghum sourdoughs fermented with two binary strain combinations, *Lactobacillus plantarum* and *Lactobacillus casei or Lactobacillus fermentum* and *Lactobacillus reuteri*, were compared to chemically acidified controls (Svensson et al. 2010). Four glycerol esters were tentatively identified, caffeoylglycerol, dicaffeoylglycerol, coumaroyl-caffeoylglycerol, and coumaroyl-feruloylglycerol. Chemical acidification resulted in hydrolysis of phenolic acid esters and flavonoid glucosides. During lactic fermentation, phenolic acids, phenolic acid esters, and flavonoid glucosides were metabolized. Analysis of ferulic acid, caffeic acid, and naringenin-glucoside contents in single-strain cultures of lactobacilli demonstrated that glucosidase, phenolic acid reductase, and phenolic acid decarboxylase activities contributed to polyphenol metabolism. This study demonstrated that microbial fermentation of sorghum affected the content of polyphenols and could influence the nutritional value and antimicrobial activity of sorghum.

The following air-borne volatiles were detected emanating from 4 week old sorghum seedlings: toluene, hexanal, (Z)-3-hexen-1-ol, *m*-xylene, *o*-xylene, (Z)-3-hexen-1-ol acetate, nonanal and decanal (Lwande and Bentley 1987). Five major compounds were isolated from sorghum stem:

methyl ferulate, methyl *p*-hydroxycinnamate, *p*-hydroxybenzaldehyde, tricin and quercetin 3,4′-dimethyl ether (Kwon and Kim 2003).

The total anthocyanin content of the leaf sheaths of dye sorghum ranged from 13.7 to 35.5 mg of cyanidin 3-glucoside equivalent/g of dry matter (DM), with an average of 27.0 mg/g (Kayodé et al. 2011). The total anthocyanin content was 90 fold higher than levels usually reported in fruits and vegetables. Anthocyanin consisted essentially of apigeninidin and luteolinidin, two 3-deoxyanthocyanidins with many applications in food, beverage, and pharmaceutical industries. The apigeninidin content of the leaf sheaths was 30 times higher than that in cereal bran and varied from 14.7 to 45.8 mg/g, with a mean of 31.3 mg/g. The amount of luteolinidin ranged from 0.4 to 2.4 mg/g, with an average of 1.2 mg/g. The total phenolic content expressed as gallic acid equivalent averaged 95.5 mg/g. The free phenolic acids identified were benzoic acid, *p*-coumaric acid, and *o*-coumaric acid at levels of 801.4, 681.6, and 67.9 µg/g, respectively. The leaf sheaths of dye sorghum had an antioxidant capacity [3.8–5.6 mmol of Trolox equivalent (TE)/g of DM] much higher than that reported for cereal bran and fruits and vegetables.

Eight phenolic acids and three associated aldehydes were identified in a Sahelian sorghum (*Sorghum bicolor*) genotype (CE145–66), with *p*-hydroxybenzoic, *p*-coumaric, and ferulic acids the most abundant (Sène et al. 2001). Their totals reached 2.9–3.2 mg/g in 1996 and 2.6–2.8 µg/g in 1997 for the aerial part; and 3.3–3.6 mg/g in 1996 and 2.8–3.3 mg/g in 1997 for roots.

Sorgoleone, a major component of the hydrophobic root exudate of sorghum, had been extensively studied for its allelopathic activity (Dayan et al. 2010; Uddin et al. 2010). Sorgoleone was reported to interfere with several molecular target sites, including inhibition of photosynthesis in germinating seedlings. The root exudate also contained an equivalent amount of a lipid resorcinol analog as well as a number of minor sorgoleone congeners (Dayan et al. 2010). Synthesis of sorgoleone was reported to be constitutive and compartmentalized within root hairs, accumulating up to 20 mγ of exudate/mg root dry weight. Sorgoleone production was found to be high in young developing plants (Uddin et al. 2010). The maximum concentration (µg/mg root dry weight) was produced in 5-day-old seedlings; beyond this age, production declined. Among the innate immunity response elicitors, cellulose (an elicitor of plant origin) stimulated higher sorgoleone production than the others, and it produced 6.2 times more sorgoleone than the control. Combined treatment of sorghum seeds with half strength Hoagland solution and 5 mγ/mL of IBA auxin significantly increased both root growth and sorgoleone content in sorghum seedlings.

Sorghum is a rich source of various phytochemicals including tannins, phenolic acids, anthocyanins, phytosterols and policosanols (Awika and Rooney 2004). Scientific evidence suggests that sorghum consumption reduces the risk of certain types of cancer in animals, tannin-containing sorghum can help to reduce obesity and phytochemicals in sorghum also promote cardiovascular health in animals albeit clinical studies in human are still lacking. Some of the pharmacological properties of the sorghum plant are elaborated below.

Antioxidant Activity

The scavenging effects of all pigmented sorghum grain methanol extracts on the DPPH radical were greater than that of BHA and α-tocopherol and less than that of ascorbic acid (Mohamed et al. 2009). The relative abilities of sorghum grain extracts to scavenge the ABTS radical (ABTS•+) generated in the aqueous phase, were in the range of 32–74% compared to 82% for the trolox. Line LC-9 showed much higher ABTS radical scavenging activity (74%) than the other lines (32–63%). The reductive capabilities of grain extracts on ferric–ferricyanide complex, were extremely high (0.44–0.82 at 700 nm) compared to control (0.08 at 700 nm). Lines LC-9, LIND, L47, LC-13 and LDeib exhibited the highest antioxidant capacities and thus could be potential rich sources of natural antioxidants. The yield of methanolic extracts obtained from the

pigmented grains was in the range of 1.51–3.24%. The total polyphenols and caroteniods were in the range of 229–787 mg GAE/100 g and 8–21 mγ β-carotene/100 g, respectively. The total polyphenol contents were highly correlated with the DPPH ($R^2 = 0.915$), ABTS ($R^2 = 0.902$) and FRAP ($R^2 = 0.903$) values. The data indicated that polyphenols were the major contributors to antioxidant properties of sorghum grains. In another study, sorghums with a pigmented testa and spreader genes (B_1B_2S) had the highest levels of phenols and antioxidant activity (Dykes et al. 2005). Also, sorghums with purple/red plants (PQ) and thick pericarp (z) genes had increased levels of phenols and antioxidant activity. Sorghums with a black pericarp had higher levels of flavan-4-ols and anthocyanins than the other varieties and also had high antioxidant activity. The results suggested that genes for plant color, pericarp thickness, presence of a pigmented testa, and spreader genes increased phenols and antioxidant activity levels in sorghum.

Sorghum brans were found to have 3–4 times higher anthocyanin contents than the whole grains. Black sorghum grains and their brans had high antioxidant activity (52–400 μmol TE/g) compared to other cereals (<0.1–34 mg TE/g) and should be useful in food and other applications, because of itsa valuable source of anthocyanins with good antioxidant activity (Awika et al. 2005b). Black sorghum had the highest anthocyanin content (average = 10.1 mg/g in bran) whilst brown and red sorghum brans had anthocyanin contents of 2.8–4.3 mg/g (Awika et al. 2004). Only 3-deoxyanthocyanidins were detected in sorghum. The antioxidant properties of the 3-deoxyanthocyanidins were similar to those of the crude sorghum anthocyanins which were more stable than the pure 3-deoxyanthocyanidins. The high antioxidant capacity of black sorghum and their brans were correlated with their anthocyanin contents (Awika and Rooney 2004). Pigmented sorghum bran with high levels of unique 3-deoxyanthocyanidins, which were stable to change in pH may have good potential as natural food pigments. Awika et al. (2005a) found that the first two bran layers of decorticated sorghum had the highest levels of phenols and antioxidant activity (3–6 times as compared to whole grain). Brown (tannin-containing) and black sorghums had at least ten fold higher antioxidant activity than white sorghum or red wheat brans. Black sorghums had the highest 3-deoxyanthocyanin content (up to 19 mg/g bran). Dietary fibre in sorghum brans ranged between 36 and 45%, as compared to 48% for wheat bran. Specialty sorghum brans being rich in valuable dietary components may present promising opportunities for improving health attributes of food.

The screening of 50 sorghum varieties showed that, on average, germination did not affect the content in total phenolic compounds but decreased the content of proanthocyanidins, 3-deoxyanthocyanidins, and flavan-4-ols (Dicko et al. 2005b). Phenolic compounds and antioxidant activities were more positively correlated in ungerminated varieties than in germinated ones. Sorghum grains with pigmented testa layer, chestnut color glumes, and red plants had higher contents, larger diversity of phenolic compounds, and higher antioxidant activities than other sorghums. Some red sorghum varieties had higher antioxidant activities (30–80 μmol of Trolox equiv/g) than several sources of natural antioxidants from plant foods. Among varieties used for couscous and porridge preparation, the "dolo" (local beer) varieties had the highest average content and diversity in phenolic compounds as well as the highest antioxidant activities.

Specialty sorghums, their brans, and baked and extruded products exhibited antioxidant activity as evaluated by three methods: oxygen radical absorbance capacity (ORAC), 2,2′-azinobis (3-ethyl-benzothiazoline-6-sulfonic acid) (ABTS), and 2,2-diphenyl-1-picrylhydrazyl (DPPH) (Awika et al. 2003b). Both ABTS and DPPH correlated highly with ORAC ($R^2 = 0.99$ and 0.97, respectively). Phenol contents of the sorghums correlated highly with their antioxidant activity measured by the three methods ($R^2 > \text{or} = 0.96$).

The use of kafirin microparticles to encapsulate bioactive polyphenols, catechin and sorghum condensed tannins was found to have potential as an effective method of controlled release of

dietary antioxidants (Taylor et al. 2009). Stilbenoids, *trans*-piceid and *trans*-resveratrol present in lower amounts than procyanidins in sorghum did not contribute significantly to the high antioxidant activity of red sorghum (ORAC, 83–147 μmol TE/g; AAPH, 0.61–1.79 min/mg/kg) (Bröhan et al. 2011).

The ethyl acetate soluble fraction of sorghum stem exhibited potent free radical scavenging activity (Kwon and Kim 2003). Five major compounds were isolated and identified as methyl ferulate (1), methyl *p*-hydroxycinnamate (2), *p*-hydroxybenzaldehyde (3), tricin (4), and quercetin 3,4′-dimethyl ether (5). Of these compound 1 exhibited a strong, free radical scavenging activity on 1,1-diphenyl-2-picrylhydrazyl (DPPH) In rat liver microsomes induced by non-enzymatic method, all five compounds showed anti-lipid peroxidation activity (IC_{50} values of 0.5, 0.4, 0.3 and 0.3 μM, respectively).

Antiinflammatory Activity

A 1:200 dilution of a 10% (wt/vol) ethanol extract of black sorghum bran significantly inhibited the secretion of the pro-inflammatory cytokines interleukin-1beta and tumor necrosis factor-alpha (Burdette et al. 2010). Ethanolic extracts of both black and sumac varieties of sorghum bran significantly reduced edema in inflamed ears induced by TPA (12-*O*-tetradecanoylphorbol acetate). Black sorghum bran significantly diminished the increase in myeloperoxidase activity 24 h following the application of TPA. No anti-inflammatory activity was observed with white and Mycogen sorghum bran varieties or with oat, wheat, or rice brans in the mouse ear model. The antiinflammatory activity observed with these brans correlated with their phenolic content and antioxidant activity.

The ethanolic bran extracts (1:9 [wt/vol] of 50% ethanol) of six cultivated sorghum varieties extract inhibited hyaluronidase activity with this order of potency: Sumac > Shanqui Red > Black > Mycogen > Fontanelle > White sorghum (Bralley et al. 2008). Extracts of wheat and rice bran had weak inhibitory activities relative to the high phenolic sorghum brans. Hyaluronidase inhibition correlated positively with total phenolic content and ferric reducing antioxidant power values for each bran extract. Inhibition was not only attributable to condensed tannins (proanthocyanidins) because the Black sorghum cultivar lacks condensed tannins but has abundant anthocyanins and other polyphenols. Since hyaluronidase activity is important in chronic inflammatory conditions such as osteoarthritis and in skin aging, these sorghum varieties may have potential as nutraceutical and cosmeceutical ingredients.

Antidiabetic Activity

Abdelgadir et al. (2005) compared the effects on glycaemic and insulin responses of six traditional Sudanese carbohydrate-rich meals namely wheat gorasa (pancakes), sorghum kisra (flat bread) and sorghum acida (porridge), millet kisra and millet acida and maize acida in Type 2 diabetes subjects. A significant variation in AUC (area under the curve) for glucose and insulin responses were found between meals, the over all differences in incremental AUCs between the six meals were significant for both plasma glucose and insulin. The 2-h glucose values were 10.5 for sorghum flatbread, 9.5 for sorghum porridge, 10.3 for millet flatbread, 10.6 for millet porridge, 11.4 for maize porridge and 8.7 for the wheat pancakes. The comparison between the AUCs of the meals showed that millet acida (porridge) followed by wheat gorasa (pancakes) displayed significantly lower post-prandial glucose and insulin responses, whereas maize acida induced a higher post-prandial glucose and insulin response.

Sorghum brans with a high phenolic content and high antioxidant properties inhibited protein glycation, whereas sorghum brans low in these properties did not (Farrar et al. 2008). Although one high phenolic sorghum bran variety (sumac) inhibited protein glycation by approximately 60%, it produced only a 20% decrease in methylglyoxal mediated albumin glycation. The results suggested that certain varieties of sorghum bran may affect critical biological processes important

indiabetesandinsulinresistance.Proanthocyanidin-rich sumac sorghum bran extract inhibited α-amylase at a lower concentration (50%) inhibitory concentration (IC_{50} = 1.4 μg/mL) than did proanthocyanidin-free black sorghum bran extract (IC_{50} = 11.4 μg/mL) (Hargrove et al. 2011). Inhibition of α-amylase could reduce the glycemic effect of dietary starches.

Anticancer Activity

In-Vitro Studies

Wine phenolic fractions decreased melanogenic activity while sorghum tannins increased melanogenic activity (tyrosinase activity), although no increase was found in total melanin at the concentrations that least affected melanocyte viability (Gómez-Cordovés et al. 2001). Incubation of human melanoma cells with the wine fractions and sorghum tannins resulted in a decrease in colony formation, although the effect was not dose dependent in all cases. The results suggested that all of wine and sorghum phenolic fractions have potential as therapeutic agents in the treatments of human melanoma, although the mechanisms by which cellular toxicity was effected appeared to be different among the fractions.

Shih et al. (2007) demonstrated that the 3-deoxyanthocyanidins were more cytotoxic on human cancer cells than the 3-hydroxylated anthocyanidin analogues. At 200 μM concentration, luteolinidin reduced the viability of HL-60 and HepG2 cells by 90 and 50%, respectively. Sorghum is a major source of 3-deoxyanthocyanidins, which are present as seed pigments and as phytoalexins responding to pathogen attack. They demonstrated that inoculated sorghum seedlings could be utilized for convenient and large-scale production of 3-deoxyanthocyanidins. A quantity of almost 270 mγ/g (fresh weight) of luteolinidin was produced 72 h after fungal inoculation of 1-week-old seedlings. Crude black sorghum extract that contained high levels of methoxylated 3-deoxyanthoxyanins (3-DXA) was a strong inducer of NAD(P)H:quinone oxidoreductase (NQO) activity (3.0 times at 50 μg/mL), compared to red or white sorghum extracts with low or no methoxylated 3-DXA (1.6 times at 200 μg/mL) (Yang et al. 2009). All sorghum extracts exerted strong antiproliferative activity against HT-29 cells after 48 h of incubation (IC_{50} = 180–557 μg/mL). Among isolated fractions, nonmethoxylated 3-DXA were very effective against HT-29 cell growth (IC_{50} = 44–68 μM at 48 h), but were noninducers of NQO. In contrast, the methoxylated 3-DXA had both strong antiproliferative activity (IC_{50} < 1.5–53 μM) and NQO inducer activity (2–3.7 times). Dimethoxylated 3-DXA were more potent than monomethoxylated analogues. Methoxylation of 3-DXA was essential for NQO activity and also enhanced tumour cell growth inhibition. Anthocyanin from red sorghum bran showed high antioxidant activity and also showed moderate cytotoxic activity against HT 29 and HEP G2 cell lines (Devi et al. 2011). The authors postulated that the antioxidant and antiproliferative activity of the extract from red sorghum bran was due to apigenindin and luteolindin which were identified in red sorghum.

Kamath et al. (2007) demonstrated that chymotryptic hydrolysates of sorghum prolamin, α-kafirin, could serve as a good source of peptides with angiotensin I converting enzyme inhibitory activity. The IC_{50} values of these chymotryptic hydrolysate fractions ranged from 1.3 to 24.3 μg/mL. Two of the fractions were found to be competitively inhibiting the enzyme, while two other fractions were non-competitive inhibitors.

In-Vivo Animal Studies

Administration of a procyanidin-rich sorghum extract (150 mg/kg) to C57BL/6 J mice bearing Lewis lung cancer significantly reversed the d-galactose-induced oxidative stress by enhancing the activities of antioxidant enzymes (Wu et al. 2011). Further, the extract administration inhibited tumour growth and metastasis formation by suppressing vascular endothelial growth factor (VEGF) production. Sumac sorghum bran extract inhibited aromatase activity more strongly than black sorghum bran extract (IC_{50} = 12.1 μg/mL vs. 18.8 μg/mL, respectively) (Hargrove et al. 2011). Bovine serum albumin (BSA), which binds proanthocyanidins, reduced inhibition by sumac but not black sorghum bran extract.

Proanthocyanidins and simple flavonoids in Sephadex LH-20 fractions both inhibited aromatase with mixed kinetics and affected K(m) and V(max). Aromatase is a target for breast cancer therapy.

Antilipidemic Activity

Hwanggeumchal sorghum ethyl acetate extracts significantly reduced plasma total cholesterol and triglyceride levels significantly when given orally at a dose of 50 and 300 μg/kg/day to the high-fat diet-induced obese rats for 2 weeks (Chung et al. 2011b). The findings demonstrated the pharmacological potential of Hwanggeumchal Sorghum variety to prevent obesity.

Immunomodulatory Activity

Mixed linkage β-D-glucan were found in the subaleurone cells of sorghum grain (Ramesh and Tharanathan 2000). Alkali extracted β-D-glucan (fraction 2) of sorghum showed 30% activation of rat peritoneal macrophages (in-vitro) at 100μg/mL in 10 min. This activation was found mediated mainly through phospholipase A2 (PLA2) pathway. A phagocytic index k of 0.102 was observed in-vivo carbon clearance test in mice in the group treated with fraction 2.

Chal Sorghum variety ethyl acetate extract showed anticomplement activity with 50% inhibitory concentration (IC_{50}) value of 38.7 μg/mL (Chung et al. 2011a). Of three compounds; sorgoleone-362, sorgoleone-360 and sorgoleone-386 isolated from sorghum, sorgoleone-386 exhibited inhibitory activity in-vitro against complement system with 50% inhibitory concentration IC_{50} value of 148.3 μg/mL (Moon et al. 2012).

Anti tyrosinase Activity

Methanol extracts of sorghum distillery residue showed the highest radical-scavenging and tyrosinase-inhibiting activities (Wang et al. 2011).

Hemolytic Activity

A crude polysaccharide that hemolyzed human red blood cells of the ABO types was isolated from the condensed tannin fraction of *Sorghum bicolor* (Neucere et al. 1986). It contained primarily 2-hydroxybenzoic acid and glucose and had a molecular weight > 6,000. Limit hemolytic activity for each of four blood group cells corresponded to a range of 110–27 μg of carbohydrate per assay.

Antianaemic Activity

Oral administration of albino rats for 16 days with sorghum leaf sheath extract dose-dependently increased haemoglobin, red blood cell count, packed cell volume, and mean corpuscular haemoglobin levels. (Ogwumike 2002) However, mean corpuscular volume was decreased. The results of this study supported the traditional use of sorghum as a remedy for anaemia. Oral administration of aqueous extract of sorghum stem bark administration produced significant increase in haemoglobin, packed cell volume and red blood cells in iron sufficient and iron deficient weaning rats (Oladiji et al. 2007). There was also significant increase in the catalase activity of the rat liver and kidney without any significant change in the serum catalase activity. The results revealed that sorghum stem extract restored the anaemic condition in the iron deficient rats and supported its use in folklore medicine in the management of anaemia.

Neuroprotective Activity

Studies by Oboh et al. (2010) found no significant difference in average feed intake and weight gain of Wistar strain albino rats fed a basal diet and the sorghum red dye extract-supplemented diet. However, intraperitoneal administration of cyclophosphamide (75 mg/kg of body weight) 24 h prior to the termination of the experiment caused a significant increase in the brain malondialdehyde (MDA) content and serum activities of aspartate aminotransferase, alanine aminotransferase,

and alkaline phosphatase in those rats fed basal diet without the dye supplement, whereas there was a significant decrease in brain MDA content and serum enzyme activities in rats fed diet with the dye in a concentration-dependent fashion. The protective effect of the red dye against cyclophosphamide-induced oxidative stress could be attributed to the high phenolic content (56.2%) and antioxidant activities of the red dye as evaluated by 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging ability, reducing properties, and Fe(2+) chelating ability. The authors concluded that dietary inclusion of the red dye from sorghum stem could be harnessed in the management of neurodegenerative diseases associated with oxidative stress.

Antidiarrhoeal Activity

The aqueous methanolic extract of sorghum leaf base (100–400 mg/kg i.p) significantly and dose-dependently decreased the intestinal motility in mice, inhibited castor oil-induced diarrhoea in rats, and produced concentration dependent relaxation of rabbit jejunum with half maximal effective concentration (EC_{50}) of 0.21 mg/mL (Nwinyi and Kwanashie 2009a). The extract also produced both non-myogenic and slight relaxation effects on guinea pig ileum and a contraction on rat stomach fundus strips. Both aqueous and ethylacetate fractions also reduced intestinal motility. However, the ethyl acetate fraction caused greater reduction than the aqueous fraction. The oral LD_{50} value for the aqueous methanolic extract in both rats and mice was found to be ≥2,000 mg/kg while the intraperitoneal values were 1414.2 mg/kg in rats and 1341.6 mg/kg in mice. The intraperitoneal value for both aqueous and ethyl acetate fractions was ≥2,000 mg/kg in mice.

Sedative Effect

Wistar rats and Swiss albino mice treated with aqueous methanolic extract of sorghum leaf base exhibited: (i) a reduction in the exploratory behaviour as did diazepam (1 mg/kg i.p.); (ii) no change in apomorphine-induced stereotypic behaviour; (iii) prolonged pentobarbitone-induced sleep as did diazepam (1 mg/kg i.p.) and cimetidine (100 mg/kg p.o.) and exhibited no significant effect on rota-rod performance for motor coordination (Nwinyi and Kwanashie 2009b). The findings suggested that sorghum leaf base extracts contained sedative substances that acted via centrally-mediated actions rather than peripheral neuromuscular blockade and may also be microsomal enzyme inhibitor like cimetidine.

Antimicrobial Activity

The n-butanol purified saponin extract of sorghum inhibited the growth of *Staphylococcus aureus* in-vitro (Soetan and Oyekunie 2006). Kil et al. (2009) reported that sorghum extracts could be used as a source of antioxidant and antimicrobial ingredients in the food industry as its methanol extract exhibited inhibitrory activity against *Escherichia coli*, *Salmonella typhimurium*, *Klebsiella pneumonia*, *Bacillus subtilis* and *Candida albicans.* Methanol extracts of all the pigmented sorghum lines exhibited good antibacterial activity against *Escherichia coli* (14–30 mm) except the extract of line LKhs 8 (Mohamed et al. 2009). In contrast,none of the tested pigmented sorghum extracts inhibited the growth of *Bacillus subtilis*. Among the ten lines, the methanol extract of LIND had the highest level of antibacterial activity (32 mm) against *Pseudomonas aeruginosa. Salmonella typhimurium was* sensitive to methanolic extracts of lines LKhs 5, LKhs 10, LC-9, L47 and LDeib, but did not show any sensitivity to the other pigmented sorghum extracts.

Anthelminthic Activity

Studies showed that aqueous extract of sorghum plant possessed inhibitory effects in-vitro on the hatching and moulting of eggs of *Haemonchus contortus* (Iqbal et al. 2001).

Anti-Sickle Cell Disorder Activity

Niprisan (Nix-0699), which is a product of the extracts of four different plants, (*Piper guineensis* seeds, *Pterocapus osum* stem, *Eugenia caryophyllum* fruit, and *Sorghum bicolor* leaves) were shown to possess strong anti-sickling properties in-vitro (Iyamu et al. 2002). The concentration of Nix-0699 required to inhibit 50% of erythrocyte sickling was about 0.05 mg/mL. In a double-blind, placebo-controlled, randomised cross-over clinical trial with 82 patient with sickle cell disorder (SCD), Niprisan significantly reduced the frequency of SCD episodes associated with severe pains (Wambebe et al. 2001). The clinical and laboratory results of the phase IIB (pivot) clinical study suggested Niprisan to be a safe and efficacious phytomedicine for the management of patients with sickle cell disorder.

Bioavailability of Phenolic Compounds

Sorghum bran (containing 23.3 mg/g of procyanidins) dose dependently increased the urinary excretion of catechin (0–2.2 nmol/day) and 3′-*O*-methylcatechin (0–9.5 nmol/day) in female Sprague–Dawley rats (Gu et al. 2007). Their serum concentrations also increased with dose (range of 0–14 nM for 3′-*O*-methylcatechin). Among the 14 phenolic acids analyzed, 3,4-dihydroxybenzoic acid, 3-methoxy-4-hydroxybenzoic acid, and 4-hydroxyphenylacetic acid dominated in the serum (1.8–8 μmol/L). In the urine, 3-methoxy-4-hydroxyphenylacetic acid, 3-hydroxyphenylacetic acid, and 3-hydroxyphenylpropionic acid dominated and their excretion increased significantly with the level of sorghum bran in the diet. The summed phenolic acid excretion was 0.8 μmol/day in the control group and increased to 23 μmol/day for 40% sorghum bran group. The hippuric acid excretion ranged from 2.2 to 16.2 μmol/day and peaked in the 10% sorghum bran group. On the basis of chromic oxide, a non-absorbable marker, total procyanidins and polymers disappeared progressively, and significant degradation occurred in the cecum and colon. Catechins and procyanidins in sorghum were bioavailable; however, bacteria-derived phenolic acids were the predominant metabolites of procyanidins. Procyanidins were degraded in the gastrointestinal tract.

Toxicity Studies

Toxicity studies in rats showed that the methanolic sorghum leaf base extract widely used in ethnomedicine, was relatively safe (Nwinyi et al. 2009). No adverse clinical signs were observed. There was no significant change in the feed intake, body weight and relative organ weight except the significant reduction in weight of kidneys and increase in relative weight of the testes observed at doses of 200 and 400 mg/kg respectively. No gross or histopathological changes were seen in the kidneys, heart, spleen, lungs, liver and testes. No significant effect was observed in the haematological indices (packed cell volume, heamoglobin, total and differential white blood cells), hepatic function indices (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, direct bilirubin, total bilirubin, alkaline phosphatase, albumin, total protein) as well as renal function indices (urea and creatinine). Uric acid was however reduced significantly. Study of effect on serum lipid profile showed no significant effect on cholesterol but a significant reduction of triglyceride at 200 mg/kg p. o. dose.

Antinutrients – Effects and Removal

Sorghum contains antinutrients such as proteinase inhibitors, tannins, phytic acid and other compounds that can lower the nutritional values and digestibility of grain proteins. Tannins and phytic acid, compounds form complexes with proteins and minerals, respectively, decreasing sorghum's digestive value (Schons et al. 2011). However, not all sorghum contains tannin; 99% or more of the

sorghums in USA do not contain tannin (Rooney 2005). Tannins are present in sorghums with a pigmented testa layer controlled by B1-B2 genes. Sorghum genotypes without pigmented testa do not contain tannins. Further, tannins in sorghum are condensed tannins which are also present in grapes, blueberries, carobs, cranberries, dark chocolate, food now considered as health foods because of the antioxidant properties of the tannins (Rooney 2005). Studies by Elkin et al. (1996) suggested that condensed tannins we only partially responsible for variations in nutrient digestibilities of sorghum grain. Sorghums containing equivalent amounts of tannins exhibited different digestibilities suggesting that other components besides tannins we responsible for variations in the availability of nutrients in sorghum.

A nutritional limitation to sorghum use is the poor digestibility of its protein when wet cooked (Duodu et al. 2003). The authors categorised the factors affecting wet cooked sorghum protein digestibility into two main groups: exogenous factors (grain organisational structure, polyphenols, phytic acid, starch and non-starch polysaccharides) and endogenous factors (disulphide and non-disulphide crosslinking, kafirin hydrophobicity and changes in protein secondary structure). All these factors had been shown to influence sorghum protein digestibility and their interaction may be important depending on the nature or the state of the sorghum grain i.e. whether whole grain, endosperm, protein body preparation, high-tannin or condensed-tannin-free. The authors proposed that protein crosslinking may be the greatest factor influencing protein digestibility. This may be between γ- and β-kafirin proteins at the protein body periphery, which may impede digestion of the centrally located major storage protein, α-kafirin, or between γ- or β-kafirin and α-kafirin.

El-Khalifa and El Tinay (1994) reported that after 14 h fermentation, there was a decrease in the prolamin fraction, an increase in the glutelin and a slight increase in the albumin and globulin fractions for the safra sorghum (low tannin) cultivar. In the sorghum cross 35:18 (high tannin) cultivar, the prolamin content fluctuated during fermentation while the glutelin fraction increased towards the end of fermentation and the albumin fraction increased at the beginning of fermentation but decreased at the end. Most of the tannin was associated with the glutelin and albumin fractions. Fermentation decreased the tannin content for both cultivars, and the decrease of tannin reached 92% in the high-tannin variety. The tannin content of the protein fractions decreased during fermentation, especially in the albumin and glutelin fractions.

Trypsin inhibiting substances were detected in aqueous and acid extracts of sorghum grain powder (Filho 1974). The trypsin inhibitors had a broad distribution of molecular weight with the most significant peak of activity centered around 15,000 Da and in acidic conditions (pH 4) were stable to heat treatment of 100°C for 30 min Sorghum had been reported to contain the antinutrient cyanogenic glycoside, dhurrin (*p*-hydroxymandelonitrile-β-D-glucoside), abundant in seedlings but absent in mature plants and seeds (Akazawa et al. 1960). Sorghum contains phenolic compounds at all stages of growth, with higher levels in leaves and glumes compared to stalks and caryopses and these phenolic compounds had been reported to inhibit alpha- and glucoamylase activity (Waniska et al. 1988). Storage of sorghum resulted in increased levels of some phenolic acids. The phenolic compounds from sorghum appeared to be detoxified during anaerobic digestion.

On germination, both trypsin and chymotrypsin inhibitory activities were markedly reduced in sorghum seeds (Mulimani and Vadiraj 1991). A greater reduction in trypsin and chymotrypsin inhibitory activity was observed on soaking sorghum seeds in mixed salt solution than on soaking in distilled water (Mulimani and Vadiraj 1994). Of the processing treatments namely overnight soaking of sorghum in 2% NaHCO3, soaking in different alkalis, ammoniation and autoclaving, ammoniation was best for complete removal of tannins in sorghum (Mulimani and Supriya 1994). Soaking sorghum seeds in alkalis was also effective. Soaking the sorghum seeds for 18 h in mixed salt solution (containing 1.5% NaHCO3 + 0.5% Na2CO3 and 0.75% citric acid in w/v ratio) was also found to

be effective. Abrasive dehulling of sorghum grains to a yield between 75 and 80%, humidifying the grains with acetic acid (1% v/v) and storing them during 7 days at 20°C was found to be the most effective procedure for elimination of tannin (Agudelo et al. 1997) In this way tannin could be totally reduced and the in-vitro digestibility of protein e increased to 87.5%. Traditional khamir (bread) fermentation of 3 local sorghum varieties significantly improved the in-vitro digestibility of sorghum proteins by reducing trypsin inhibitory activity by 31–58% and phytic acid levels by 15–35% (Osman 2004). Idris Wisal et al. (2005) found that germination of sorghum for 24, 48 and 96 h or fermentation for up to 14 h followed by cooking decreased antinutrient (phytate and tannins) levels and enhanced availibilty of minerals. The reduction in phytate content was accompanied by an increase in HCl-extractable minerals of more than 100%.

Rahman and Osman (2011) reported that tannins, phytic acid and trypsin inhibitor activity levels varied significantly among the three Sudanese sorghum cultivars Fetarita, Safra and Ahmer. Tannin content of unfermented seeds was 0.32, 0.65 and 1.5 catechin equivalent for Fetarita, Safra and Ahmer, respectively. Safra showed the highest level of phytic acid among the three cultivars, while Fatarita showed the highest trypsin inhibitory activity level. After fermentation, tannin contents were significantly reduced by 56.3, 56.9 and 52.7% in Fetarita, Safra and Ahmer, respectively. Phytic acid contents of the three cultivars were markedly reduced by over 50%. The decrease in the trypsin inhibitory activity levels during fermentation was more obvious in Ahmer (87.4%) than in Safra (77.7%) and Fetarita (76.5%), suggesting that the enzyme inhibitors activity were not correlated with tannin contents.

Compared to the raw sorghum flour and fermented sorghum floor, injera (unleavened thick bread make from fermented flour) had low protein (11.55%), ash (1.57%) and fat (2.40%) contents but high in fibre content (Mohammed et al. 2011b). Injera was found to have significantly higher energy (389.08 Kcal/100 g) compared to raw and fermented sorghum flour. Injera contained lower levels of anti-nutritional factors (polyphenols, phytate and tannins) compared to raw and fermented sorghum. Also it was found to be rich in Ca (4.75 mg/100 g), Fe (3.95 mg/100 g), and Cu (0.7 mg/100 g) compared to that of raw and fermented flour. Moreover, both the extractable minerals and protein digestibility were high for injera due to low amount of anti-nutrients. Injera was found to contain an appreciable amount of amino acids except arginine and tyrosine. Fermentation makes the foods easier to digest and the nutrients easier to assimilate and also it retains enzymes, vitamins, and other nutrients that are usually destroyed by food processing. Fermentation is an oldest known form of food biotechnology, and is an important low-cost technique in the developing countries.

Studies in rats showed that enzymatic treatment (tannase and phytase) was effective in reducing tannins and promoting the increase of inorganic phosphorus (Schons et al. 2011). Enzymatically treated sorghum was better than raw sorghum in the apparent digestibility of phosphorus, in the level of glucose, cholesterol and triacylglycerol. Treatment of the sorghum also resulted in lower activity of the enzymes aspartate aminotransferase and alanine aminotransferase in rat serum. The enzymatic treatment of sorghum could improve the nutritional value of this cereal while also decreasing environmental pollution

Traditional Medicinal Uses

Sorghum has various applications in African traditional medicine. In Lagos state, Nigeria, sorghum leaf is used in local herbal medicine in an infusion with *Randia lucida* roots (sliced) and soaked in potash water is used as abortifacient; sorghum leaf, sliced root of *Baphia nitida* and wood pieces of *Pterocarpus osun* soaked in gin is taken as an abortifacient, and sorghum leaf in a mixture with *Xylopia aethiopica* fruit, *Aframomum melegueta* seeds in hot lemon juice is drank as a contraceptive (Balole 2009). In Lagos, Nigeria, sorghum is also used for anaemia, pain and inflammation. In South Western Nigeria, sorghum is employed for

headache, sickle-cell anaemia, leukemia, multiple myeloma, heart and blood-related problems. In India, it is used as an aphrodisiac. Decoction of sorghum grains is demulcent and diuretic; used for kidney and urinary tract complaints. The red pigment from sorghum is said to have antimicrobial and antifungal properties and is also used as a cure for anaemia in traditional medicine.

Other Uses

Globally sorghum is primarily cultivated for livestock feed and for alcohol (ethanol) production. Grain sorghum is used extensively for animal feeding in concentrate rations, with high-protein constituents. After the grain is harvested, the sorghum stover is cut and fed to cattle, sheep and goats, or may be grazed. Some farmers grind harvested stover and mix it with sorghum bran or salt to feed livestock. The whole plant is used for forage, hay or silage. Sorghum produced in Australia is used almost exclusively for feed, especially cattle, pigs and poultry. None is used for human consumption and a significant market exists in the pet food industry.

Sorghum grains and stalks are used for ethanol (biofuel) production. Sweet sorghum is best suited for ethanol production because of its higher content of reducing sugar content as compared to other plant sources. The cost of per liter ethanol production from sweet sorghum grain and juice has been reported to be lower than that from maize and sugarcane, respectively. Existing automobile engines can be operated with gasohol – petrol blended with ethanol usually 10% or upto 25% – withoutany need for engine modification as ethanol is a 'clean burning fuel' with high octane rating. Chohnan et al. (2011) demonstrated that fuel ethanol could be produced from sweet sorghum using repeated-batch fermentation. *Saccharomyces cerevisiae* cells could be recycled in 16 cycles of the fermentation process with good ethanol yields. Studies by Han et al. (2010) demonstrated that ethanol production from sweet sorghum stalks by advanced solid state fermentation (ASSF) technology was successful and economically competitive.

Sorghum plant residues are used extensively as material for roofing, wattle fencing, weaving mats and as fuel material. The stems can be used for the production of fibre board. Danish scientists have made good panelling using stem chips of sorghum. The recovered sorghum stalks are used to make a decorative millwork material marketed as Kirei board, a strong, lightweight, durable, environment free substitute for wood. Sorghum bagasse is a suitable source of paper pulp for the production of kraft paper, newsprint and fibre board. Sorghum panicles are used for making brushes, brooms and whisks. Sorghum is also used for the production of vegetable oil, waxes and dyes.

For dye production, non-edible sorghum cultivars are exclusively grown for the red dye present in the leaf sheaths and adjacent stem parts. In Africa, this dye is used particularly for goat-skin leather (e.g. in Nigeria), other leathers (e.g. in Morocco), for mats, textiles (*abata* and *ifala* fabrics in Nigeria), for dyeing strips of palm leaves and grasses used in basketry and weaving, ornamental calabashes, wool (e.g. in Sudan), as a body paint and to colour cheese and lickstones for cattle (e.g. in Benin). Sorghum is also used to provide the violet colours adorning the masks worn during certain dances by Yoruba communities in southern Benin and in south-western Nigeria. In China, sorghum culitvars with red panicles and leaf sheaths were also employed for dye production. In the nineteenth century red sorghums were exported to Europe where the dye extracted called 'carmin de sorgho' was used with wool or silk mordanted with tin or chrome, yielding a colourfast red-brown that was once known as '*rouge badois*'. Recently the use of sorghum dye in hair dying products has been patented.

Comments

The genus *Sorghum* was established in 1794 by Moench, who placed all the sorghums together under the name *Sorghum bicolor* (Clayton 1961). On the basis of the absence of genetic barriers among the *Sorghum* taxa, DeWet and Huckabay

(1967) combined the 52 species into a single species *S. bicolor*. Harlan and de Wet (1972), using inflorescence type as a grouping criterion, separted all the cultivated sorghum taxa of the world into 5 races and 15 intermediate races, under *S. bicolor* ssp. *bicolor*. Four of the five cultivated races are found in Ethiopia (Stemler et al. 1977).

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Triticum aestivum

Scientific Name

***Triticum aestivum* L.**

Synonyms

Frumentum triticum E.H.L.Krause, *Triticum album* Gaertn. ex Steud. pro syn., *Triticum aestivum* convar. *tetraristatum* Gandilyan, *Triticum aestivum* subsp. *hadropyrum* (Flaksb.) Tzvelev, *Triticum aestivum* subsp. *inflatum* (Kudr.) Tzvelev, *Triticum aestivum* subsp. *tibeticum* J.Z.Shao, *Triticum aestivum* subsp. *transcaucasicum* Dorof. & Laptev, *Triticum aestivum* subsp. *vavilovii* (Jakubz.) Sears, *Triticum aestivum* subsp. *vulgare* (Vill.) Thell., *Triticum aestivum* subsp. *yunnanense* King ex S.L.Chen, *Triticum aestivum* var. *albinflatocapitatum* Udachin, *Triticum aestivum* var. *australianum* Udachin & Schachm., *Triticum aestivum* var. *brezhnevii* Udachin & Shakhm., *Triticum aestivum* var. *dorofeevii* Udachin & Shakhm., *Triticum aestivum* var. *erythrospermum* (Körn.) Velican, *Triticum aestivum* var. *ferrugineum* (Alef) Velican, *Triticum aestivum* var. *hybernum* (L.) Fiori, *Triticum aestivum* var. *ischkaschimicum* Udachin & Shakhm., *Triticum aestivum* var. *japschorvi* Nigmat., *Triticum aestivum* var. *lutescens* (Alef.) Velican, *Triticum aestivum* var. *meridionale-inflatum* Nigmat., *Triticum aestivum* var. *milturum* Velican, *Triticum aestivum* var. *quasiheraticum* Nigmat., *Triticum aestivum* var. *quasimeridionale-inflatum* Nigmat., *Triticum aestivum* var. *ramifera* Koric, *Triticum aestivum* var. *ramosoalborubrum* Udachin & M.V.Novikova, *Triticum aestivum* var. *ramosomilturum* Udachin & M.V. Novikova, *Triticum aestivum* var. *ruchczianum* Nigmat., *Triticum aestivum* var. *subfalsegraecum* Udachin, *Triticum aestivum* var. *subfalseerythroleucon* Udachin, *Triticum aestivum* var. *subtadjicorum* Udachin & Shakhm., *Triticum aestivum* var. *uralicum* L.V.Semenova, *Triticum aestivum* var. *vavilovianum* Udachin & Shakhm. nom. illeg., *Triticum aestivum* var. *vavilovianum* Yakubts., *Triticum aestivum* var. *vigorovii* L.V.Semenova, *Triticum amylosum* Flaksb. nom. nud., *Triticum antiquorum* (Heer) Udachin, *Triticum antiquorum* var. *vavilovianum* Udachin, *Triticum aristatum* Haller f. ex Steud. pro syn., *Triticum arundinaceum* Schur nom. illeg., *Triticum asiaticum* Kudr., *Triticum bucharicum* Flaksb. nom. nud., *Triticum caeruleum* Ard. ex Bayle-Bar. nom. nud., *Triticum cereale* Bernh. nom. illeg., *Triticum cereale* Schrank pro syn., *Triticum clavatum* Seidl ex Opiz, *Triticum duriusculum* Flaksb. nom. nud., *Triticum erinaceum* Hornem., *Triticum hieminflatum* Flaksb. nom. nud., *Triticum horstianum* Clemente, *Triticum hybernum* L., *Triticum imberbe* Desv., *Triticum inflatum* Flaksb. nom. nud., *Triticum inflatum* Kudr., *Triticum koeleri* Clemente, *Triticum labile* Flaksb. nom. nud., *Triticum linnaeanum* Lag., *Triticum lutinflatum* Flaksb. nom. nud., *Triticum martius* Risso nom. nud., *Triticum pilosum* Hornem. nom. illeg., *Triticum poltawense* Flaksb. nom. nud., *Triticum pubescens* Hornem. nom.

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illeg., *Triticum pulverulentum* Hornem., *Triticum quadratum* Mill., *Triticum rossicum* Flaksb. nom. nud., *Triticum rufinflatum* Flaksb. nom. nud., *Triticum sativum* Lam., *Triticum sativum* subsp. *vulgare* (Vill.) Thell., *Triticum sativum* var. *aestivum* (L.) Alph.Wood, *Triticum sativum* var. *vulgare* (Vill.) Hack., *Triticum segetale* Salisb. nom. superfl., *Triticum sibiricum* Flaksb. nom. nud., *Triticum siliginum* Risso nom. nud., *Triticum spelta* subsp. *vavilovii* (Jakubz.) L.B.Cai, *Triticum sunpanii* Flaksb. nom. nud., *Triticum tustella* Risso nom. nud., *Triticum vavilovii* Jakubz., *Triticum vavilovii* var. *lorenze* Galst.-Avan., *Triticum vavilovii* var. *munuru* Gandilyan, *Triticum vavilovii* var. *mupuru* Gandilyan, *Triticum vavilovii* var. *ramocoeruleum* Galst.-Avan., *Triticum vavilovii* var. *ramomuticum* Galst.-Avan., *Triticum vavilovii* var. *sisianicum* Galst.-Avan., *Triticum vavilovii* var. *vavilovomil-turum* Udachin, *Triticum velutinum* Schübl., *Triticum vulgare* Vill., *Triticum vulgare* subsp. *hadropyrum* Flaksb., *Triticum vulgare* subsp. *irano-asiaticum* Flaksb., *Triticum vulgare* subvar. *inflatum* Flaksb. nom. nud., *Triticum vulgare* var. *aestivum* (L.) Spenn., *Triticum vulgare* var. *antiquorum* Heer, *Triticum vulgare* var. *caesium* Alef., *Triticum vulgare* var. *erythrospermum* Körn., *Triticum vulgare* var. *ferrugineum* Alef., *Triticum vulgare* var. *hybernum* (L.) Kunth, *Triticum vulgare* var. *lutescens* Alef.,

Family

Poaceae

Common/English Names

Bread Wheat, Common Wheat, Grass Wheat, Hard Wheat, Soft Wheat, Wheat, Wheat Bran, Wheat Germ, wheatgrass

Vernacular Names

Afrikaans: Koring;
Arabic: Hinta, Qamh;
Brazil: Trigo;
Chinese: Pu Tong Xiao Mai, Fu Xiao Mai, Xi Zang Xiao Mai, Xiao Mai, Yun Nan Xiao Mai;
Croatian: Pšenica;
Czech: Pšenice, Pšenice Naduřelà, Pšenice Setá;
Danish: Almindelig Hvede, Brød-Hvede, Hvede, Hvede-Slægten, Moderne Hvede, Slægten Hvede, Vinterhvede;
Dutch: Gewone Tarwe, Tarwe, Tarwesoort;
Eastonian: Harilik Nisu, Harutähkne Nisu;
Finnish: Leipävehnä, Vehnä;
French: Blé, Blé Ordinaire, Blé Tender, Froment;
German: Aat-Weize, Brotweizen, Gemeiner Weizen, Gewöhnlicher Weizen, Land-Weizen, Saat-Weizen, Weich-Weizen;
Georgian: Chorbali;
Greek: Malakós Sítos, Sitos Malakos;
Hebrew: Chita, Chita Raka, Hittah;
Hungarian: Búza, Kenyérbúza, Közönséges Búza, Őszi Búza, Termesztett Búza;
Icelandic: Hveiti;
India: Glun (Bengali), Gehun, Giun, Kanak (Hindu), Gahung (Marathi),Godhuma (Sanskrit), Godhuma (Tamil);
Indonesia: Gandum;
Italian: Frumento, Frumento Tenero, Grano Tenero;
Japanese: Komugi;
Kazjistan: Bidaj;
Korean: Mil;
Latvian: Kvieši
Lithuanian: Kviečiai
Malaysia: Gandum;
Nepali: Gahun;
Norwegian: Kveite;
Persian: Gandum;
Philippines: Trigo;
Polish: Pszenica, Pszenica Zwyczajna;
Portuguese: Trigo, Trigo Mole;
Romanian: Grâu;
Russian: Pšenica Chlebnaja, Pšenica Mjagkaja, Pšenica Mjagkaja Obyknovennaja;
Serbian: Pšenica;
Slovaščina: Pšenica Navadna;
Slovencina: Pšenica Letná;
Spanish: Trigo, Trigo Blando, Trigo Candeal, Trigo Chamorro, Trigo De Pan, Trigo Doméstico, Trigo Mole Trigo Pan;
Swahili: Ngano;

Swedish: Vanligt Vete, Vårvete, Vete;
Thai: Khao-Sa-Le, Sa-Le;
Turkish: Bughdaj, Yumuşak Buğday;
Vietnamese: Cây Lúa Mỳ;
Welsh: Gwenith.

Origin/Distribution

Wheat (*Triticu*m spp.) was reported to have originated from the Levant region of the Near East (Lev-Yadun et al. 2000). These earliest cultivated forms were diploid (genome AA) (einkorn) and tetraploid (genome AABB) (emmer) wheats and their phylogenetic relationships indicated that they originated from the south-eastern part of Turkey (Heun et al. 1997; Nesbitt 1998; Ozkan et al. 2002). Evidence from archeological excavations of early agricultural settlements nearby supports the conclusion that domestication of einkorn wheat began near the Karacadağ mountains (Heun et al. 1997). Wheat cultivation spread to the Near East by about 9,000 years ago when hexaploid bread wheat made its first appearance (Feldman 2001). Wheat is now widely cultivated in temperate areas world-wide.

Agroecology

Wheat is a temperate cereal species grown in areas between latitudes 30°N and 60°N and 27°S and 40°S (Briggle and Curtis 1987). The optimum temperature range for growth and development is 10–24°C, with a minima of 3–4°C and a maxima of 30–32°C. An average temperature of about 18°C is optimal for yield. Temperatures above 35°C halt photosynthesis and growth, and at 40°C the plant is killed by heat stress. It will grow in areas with 250–1,750 mm annual rainfall but most occur in areas receiving 375–875 mm annually (Briggle and Curtis 1987). It can be grown in the tropics at higher elevations (1,200–3,000 m) in the cooler months of the year. Most wheat cultivars are quantitative long-day plants although sensitivity to daylength differs among genotypes. Wheat flower earlier at long daylengths, but they do not require a particular daylength to induce flowering.

Wheat thrives best in well-aerated, well-drained, and deep soils with 0.5% or more organic matter from sea level up to 4,500 m elevation. Optimum soil pH ranges between 5.5 and 7.5. Wheat is intolerant of soil salinity.

Edible Plant Parts and Uses

Wheat grain is a staple food used primarily for the manufacture of wheat flour for bread and noodles. Wheat flour is used to make leavened or flat bread (baked, steamed or deep-fried), biscuits, cakes, cookies, muffins, rolls, doughnuts, pastries, crackers, biscuits, pretzels, noodles, pastas, couscous, gravy, boza (fermented beverage), farina, breakfast foods, baby foods and food thickeners.

Leavened (yeasted) breads, such as pan-type bread and hamburger and hot-dog buns are made from hard to medium-hard wheats as they yield strong flour doughs (Faridi and Faubion 1995). Those yielding medium-strong doughs are suitable for the production (generally semi-mechanized or manual) of French-type bread (yeast-fermented, hearth-baked breads, in general) and flat-type, such as Arab baladi bread, Indian chapati, Mexican flour tortilla, are made from medium-strong doughs (Qarooni 1996; Singh and Kulshrestha 1996). Soft wheats, which produce weak doughs, may be suitable for Asian steamed breads (Nagao 1995). Soft wheat is also more suitable for making cookies, cakes and pastries. Wheat flour is also used to make pastas and noodles. Soft wheat is also sutiable for the production of noodle flour and all-purpose flour (Nagao et al. 1977). There are two major types of wheat noodles: white salted noodles (WSN), made with wheat flour, salt and water, and yellow alkaline noodles (YAN), which in addition to the ingredients of WSN include alkali to develop their characteristic yellow colour (Huang 1996).

There are several types of wheat flours (Pena 2002): (a) all-purpose flour – made from finely ground endosperm of the wheat kernel separated from the bran and germ during milling, suitable for yeast breads, cakes, cookies, pastries and noodles;

(b) made from wheat kernel endosperm, mainly used by bakers for yeast bread; (c) self-raising flour with added salt and leavening; (d) whole wheat flour coarse textured flour made from entire wheat kernel (bran, germ and endosperm), suitable for baked products; (e) cake flour – milled from soft wheat, low in protein and gluten, suitable for cakes, cookies, crackers and pastries; (f) pastry flour – milled from soft, low gluten wheat; (g) gluten flour -for making gluten bread of high protein content; (h) semolina – coarsely ground endosperm of durum wheat, rich in protein used in high quality pasta products; (i) durum flour a by-product of semolina production, used to make commercial U.S. noodles and (j) farina – coarsely ground endosperm of hard wheat, high in dietary fibre, used for breakfast cereals and pastas.

Wheat flour is also used to produce vital wheat gluten or seitan (used as alternative to soy-based products) in vegetarian cooking and as a source of wheat proteins in meat substitutes. Wheat flour is also used as a brewing ingredient in certain alcoholic beverages (white beer). In Ethiopia, wheat grain is eaten as a snack and during social gatherings as '*nifro*' (boiled whole grain often mixed with pulses), '*kollo*' (roasted grain) and '*dabo-kollo*' (ground and seasoned dough, shaped and deep fried).Whole wheat grain can be milled to leave by-products such as bran and germ. Wheat bran is often use to enrich bread, muffins and breakfast cereals to enhance the intake of dietary fibre. Wheat germ sold as food supplement can be added to protein sakes, casseroles, muffins, pancakes, muffins, cookies, yogurt, smoothies and cookies. It is in vitamin E, folic acid, thiamine, essential minerals, notably phosphorus, zinc and magnesium, essential fatty acids and fatty alcohols and also dietary fibre.

Botany

An annual, tufted grass, upto 150 cm tall with 2–5 or more tillers. Stem (culm) terete, glabrous, hollow except at nodes. Leaves distichously alternate, simple and entire; leaf sheath rounded, auricled , wraps around stem; ligule ciliate and membranous (Plate 6). Lamina linear 10–60 cm long by 1–2 cm wide, parallel-veined, flat, glabrous or pubescent. Inflorescence (ear) a terminal, distichous spike 4–18 cm long, with sessile spikelets borne solitary on zigzag rachis (Plates 1 and 2). Spikelet 10–15 mm long, laterally compressed, 3–9-flowered, with bisexual florets, but 1–2 uppermost ones usually rudimentary, sometimes only 1 of the florets bisexual; floret enclosed by lemna and plaea and composed of carpel (ovary and stigma) and stamens; lemna keeled toward the apex, leathery, long-awned (Plates 3 and 4)or blunt (Plate 5); palea 2-keeled, pubscent or villous; stamens three with anther with four loculi enclosing pollen grains; ovary superior, topped by a small fleshy hairy appendage and with two plumose stigmas. Fruit an ellipsoid caryopsis (grain), at one side with a central groove, reddish brown to yellow or white.

Plate 1 Wheat with ripened ears

Plate 2 Wheat crop ready for harvest

Plate 3 Close-up of ripe ears in the field

Plate 4 Close-up ear showing florets with long-awned lemna

Plate 5 Wheat with developing ear with blunt lemna (A. Gardner)

Nutritive/Medicinal Properties

Nutritive values of soft white wheat (low gluten) per 100 g edible portion had been reported as: water 10.42 g, energy 340 kcal (1,423 kJ), protein 10.69 g, total lipid 1.99 g, ash 1.54 g, carbohydrate 75.36, dietary fibre 12.7 g, total sugars 0.41 g, Ca 34 mg, Fe 5.37 mg, Mg 90 mg, P 402 mg, K 435 mg, Na 2 mg, Zn 3.46 mg, Cu 0.426 mg, Mn 3.406 mg, thiamine 0.401 mg, riboflavin 0.107 mg, nicin 4.766 mg, pantothenic acid 0.859 mg, vitamin B-6 0.378 mg, total folate 41 μg, vitamin A 9 IU, vitamin E (α-tocopherol) 1.01 mg, luetin + zeaxanthin 220 μg, vitamin K (phylloquinone) 1.9 μg, total saturated fatty acids 0.368 g, 14:0 (myristic) 0.003 g, 16:0 (palmitic) 0.346 g, 18:0 (stearic) 0.018 g, total monounsaturated fatty acids (MUFA) 0.227 g, 16:1 undifferentiated (palmitoleic) 0.010 g, 18:1 undifferentiated (oleic) 0.217 g, total polyunsaturated fatty acids (PUFA) 0.837 g, 18:2 undifferentiated (linoleic) 0.800 g, and 18:3 undifferentiated (linolenic) 0.036 g (USDA 2012).

Nutritive values of hard white wheat (high gluten, 12–14%) per 100 g edible portion had been reported as: water 9.57 g, energy 342 kcal (1,431 kJ), protein 11.31 g, total lipid 1.71 g, ash 1.52 g, carbohydrate 75.90, dietary fibre 12.2 g, total sugars 0.41 g, Ca 32 mg, Fe 4.56 mg, Mg 93 mg, P 355 mg, K 432 mg, Na 2 mg, Zn 3.33 mg, Cu 0.363 mg, Mn 3.821 mg, thiamine 0.387 mg, riboflavin 0.108 mg, niacin 4.381 mg, pantothenic acid 0.954 mg, vitamin B-6 0.368 mg, total folate 38 μg, vitamin A 9 IU, vitamin E (α-tocopherol) 1.01 mg, lutein + zeaxanthin 220 μg, vitamin K (phylloquinone) 1.9 μg, total saturated fatty acids 0.277 g, 16:0 (palmitic) 0.261 g, 18:0 (stearic) 0.016 g, MUFA 0.203 g, 18:1 undifferentiated (oleic) 0.203 g, PUFA 0.750 g, 18:2 undifferentiated (linoleic) 0.715 g,

and 18:3 undifferentiated (linolenic) 0.035 g (USDA 2012).

Proximate nutrient values of whole-grain wheat flour per 100 g edible portion was reported as: water 10.74 g, energy 340 kcal (1,424 kJ), protein 13.21 g, total lipid 2.50 g, ash 1.58 g, carbohydrate 71.97, dietary fibre 10.7 g, total sugars 0.41 g, sucrose 0.36 g, fructose 0.05 g, starch 57.77 g, Ca 34 mg, Fe 3.60 mg, Mg 137 mg, P 357 mg, K 363 mg, Na 2 mg, Zn 2.60 mg, Cu 0.410 mg, Mn 4.067 mg, thiamine 0.502 mg, riboflavin 0.165 mg, niacin 4.957 mg, pantothenic acid 0.603 mg, vitamin B-6 0.407 mg, total folate 44 μg, total choline 31.2 mg, β-carotene 5 μg, vitamin A 9 IU, vitamin E (α-tocopherol) 0.71 mg, β-tocopherol 0.23 mg, g-tocopherol 1.91 mg, lutein + zeaxanthin 220 μg, vitamin K (phylloquinone) 1.9 μg, total saturated fatty acids 0.430 g, 16:0 (palmitic) 0.410 g, 18:0 (stearic) 0.020 g, MUFA 0.283 g, 18:1 undifferentiated (oleic) 0.273 g, 20:1 (gadoleic) 0.010 g, PUFA 1.167 g, 18:2 undifferentiated (linoleic) 1.093 g, and 18:3 undifferentiated (linolenic) 0.073 g tryptophan 0.174 g, threonine 0.367 g, isoleucine 0.443 g, leucine 0.898 g, lysine 0.359 g, methionine 0.228 g, cystine 0.275 g, phenylalanine 0.682 g, tyrosine 0.275 g, valine 0.564 g, arginine 0.648 g, histidine 0.357 g, alanine 0.489 g, aspartic acid 0.722 g, glutamic acid 4.328 g, glycine 0.569 g, proline 2.075 g, and serine 0.620 g (USDA 2012).

Wheat grains contain between 8 and 17% protein with gluten accounting about 78–85% of total wheat endosperm protein, comprising mainly of polymeric (multiple polypeptide chains linked by disulphide bonds) and monomeric (single chain polypeptides) proteins known as glutenins (high molecular weight glutenin and low molecular weight glutenin) and gliadins (γ-gliadin, ω-gliadin, α-gliadin, β-gliadin) (Pena 2002). Glutenins confer elasticity, while gliadins confer mainly viscous flow and extensibility to the gluten complex that is responsible for most of the viscoelastic properties of wheat flour doughs and is the main factor dictating the use of a wheat variety in bread and pasta making. Lipids, pentosans, soluble proteins and other minor grain constituents also play a role in determining wheat flour quality

Gluten proteins are the major storage protein fraction in the mature wheat grain, restricted to the starchy endosperm, which forms white flour on milling, and interact during grain development to form large polymers which form a continuous proteinaceous network when flour is mixed with water to give dough (Tosi et al. 2011). The high-molecular-weight subunits of glutenin (HMW-GS) and γ-gliadins are more abundant in the inner endosperm layers, while the with the low-molecular-weight subunits of glutenin (LMW-GS), ω- and α-gliadins are more abundant in the subaleurone. Seed storage proteins, prolamins found in wheat include the sulphur-rich prolamins α-gliadins, γ-gliadins, LMW (low molecular weight) glutenins, the S-poor w-gliadin and HMW glutenins (Shewry et al. 1995). Puroindoline-a (Pin-a), an indoline and β-purothionin (β-Pth), a thionines are basic amphiphilic and cysteine-rich proteins found in wheat (Clifton et al. 2011). Pin-a and β-Pth had been suggested to play a significant role in seed defence against microbial pathogens by binding to lipid monolayers composed of 1,2-dipalmitoyl-sn-glycero-3-phospho-(1′-rac-glycerol) (DPPG) in bacterial membranes.

Dehydrodiferulic acids (DFA) (8-5′- DFA, 8-8′-DFA, 5-5′-DFA, 8-*O*-4′-DFA) could be identified in both insoluble dietary fibre (IDF) and soluble dietary fibre (SDF) of wheat grains (Beunzel et al. 2001). Total dehydrodiferulic acid in IDF of wheats was quantified as 32,372 μg/g, in SDF 59 μg/g. In wheat, amounts of 8-5′-DFA reached up to 46.8% in IDF and 36.5% in SDF; 8-8′-DFA 16.5% in IDF and 39,8% in SDF; 5-5′-DFA 24.9% in IDF and 11.9% in SDF; 8-*O*-4′-DFA 20.6% in IDF and 11.8% in SDF; 4-*O*-5′ DFA 0.3% in IDF and not detected in SDF.

Mattila et al. (2005) reported that the total ferulic acid content of grains ranged from 458 (whole wheat) to 129 (oats and barley) μmol/100 g grain, the total *p*-coumaric acid content ranged from 24 (barley) to 9 (buckwheat) μmol/100 g grain, and the total *p*-hydroxybenzoic acid content ranged from 80 (buckwheat) to 4 (corn) μmol/100 g grain. The high total *p*-hydroxybenzoic acid content in buckwheat is most likely due to the contribution of the free fraction. Studies by

Adom et al. (2003) showed that total phenolic content (709.8–860.0 μmol of gallic acid equiv/100 g), total antioxidant activity (37.6–46.4 μmol of vitamin C/g), and total flavonoid content (105.8–141.8 μmol of catechin equiv/100 g) did not vary greatly among the 11 wheat lines. However, significant differences in total ferulic acid and carotenoid contents were observed among the varieties, with carotenoid content exhibiting the greatest range of values. Carotenoid content among the 11 wheat varieties exhibited 5-fold, 3-fold, and 12-fold differences in lutein, zeaxanthin, and β-cryptoxanthin, respectively. Total phenolic content of wheat bran/germ fractions (2,867–3,120 μmol of gallic acid equiv/100 g) was 15–18-fold higher than that of respective endosperm fractions (Adom et al. 2005). Ferulic acid content ranged from 1,005 to 1,130 μmol/100 g in bran/germ fractions and from 15 to 21 μmol/100 g in the endosperm fractions. The flavonoid content of the bran/germ fraction was 740–940 μmol of catechin equiv/100 g. On average, bran/germ fractions of wheat had 4-fold more lutein, 12-fold more zeaxanthin, and 2-fold more β-cryptoxanthin than the endosperm fractions.

Zhou et al. (2004b) found that ferulic acid (99–231 μg/g) was the predominant phenolic acid in all of the tested bran samples and accounted for about 46–67% of total phenolic acids on a weight basis. The concentrations for α-, δ-, and γ-tocopherols were 1.28–21.29, 0.23–7.0, and 0.92–6.90 μg/g, respectively. Lutein and cryptoxanthin were detected in all of the tested bran samples with levels of 0.50–1.80 and 0.18–0.64 μg/g, respectively. Zeaxanthin was detected in the six bran samples, and the greatest zeaxanthin concentration of 2.19 μg/g was observed in the Australian general purpose wheat bran. Beta-carotene was detected in four of the tested bran samples at a range of 0.09–0.40 μg/g. Zhou and Yu (2004) found that the extracting solvent significantly altered the antioxidant property estimations of wheat bran, and 50% acetone was recommended as the solvent for extracting phenolic antioxidants from wheat bran for analytical purpose. Moore et al. (2005) showed that all tested soft wheat grain samples contained alpha-tocopherol, with a range of 3.4–10.1 μg/g. Lutein was the primary carotenoid present in the grain samples at a level of 0.82–1.14 μg/g, along with significant amounts of zeaxanthin and β-carotene. Vanillic, syringic, *p*-coumaric, and ferulic acids were found in soluble free, soluble conjugated, and insoluble bound forms in the grain extracts, with ferulic acid as the predominant phenolic acid.

The following phenolic acids gallic, *p*-hydroxybenzoic, caffeic, syringic, *p*-coumaric, vanillic, gentisic, *o*-coumaric acid, and ferulic acids were detected in wheat bran of Chinese black-grained wheat (Li et al. 2005). Ferulic acid content was highest among the phenolic acids. Ferulic acid was identified as the major simple phenolic acid, with lesser amounts of *p*-hydroxybenzoic acid, caffeic acid, syringic acid and *p*-coumaric acid in dark blue grained wheat (*Triticum aestivum* cv. HedongWumai) (Hu et al. 2007). High variability was observed among 16 old and 6 modern Italian wheat varieties genotypes, both in the free and bound phenolic extracts (Dinelli et al. 2011). The total polyphenol content ranged from 885.5 to 1715.9 μmol GAE/100 g of grain and, on average, the bound fraction contributed for 72.0% to the total phenolic content. In flavonoid content, the free fraction ranged from 50.7 to 106.1 μmol CE/100 g of grain and the bound fraction from 78.3 to 148.9 μmol CE/100 g of grain. Thirty-four phenolic compounds (104 including isomer forms) belonging to the phenolic acid, flavonoid, coumarin, stilbene, proanthocyanidin and lignan chemical classes were detected. Six ancient wheat genotypes (Bianco Nostrale, Frassineto, Gentil Rosso, Gentil Rosso Mutico, Marzuolo d'Aqui, Verna) showed phenolic profiles with a number of total compounds and isomer forms much higher than that identified in the modern cultivars.

Total lignan content was 2.60 and 5.00 μg/g dry seed weight for modern and old Italian wheat cultivars, respectively (Dinelli et al. 2007). Secoisolariciresinol and pinoresinol were detected in all ten investigated soft wheat cultivars, whereas arctigenin, hinokinin, and syringaresinol were exclusively detected in old genotypes. Significant differences between modern and old

cultivars were also observed for the number of glycosidic forms. Spring wheat whole grain extract from various locations in Finland, was found to contain seven dietary lignans, i.e., 7-hydroxymatairesinol, secoisolariciresinol, matairesinol, lariciresinol, pinoresinol, medioresinol, and syringaresinol; total lignin content varied from 340 to 2,270 μg/100 g (Smeds et al. 2009). Lignan had proven health benefits.

Blue wheat was first investigated by the Crop Development Centre, Department of Plant Sciences, University of Saskatchewan in 1999 with the aim to develop highly pigmented wheat line as bioactive food ingredients and natural colorants (Abdel-Aal and Hucl 1999). The total anthocyanin content distribution in 160 blue wheat lines ranged from 35 to 507 μg/g with a mean of 183 μg/g. Total anthocyanins averaged 157 mg/kg in blue wheat whole meal and 104 mg/kg in purple wheat whole meal, whereas blue wheat bran contained 458 mg/kg as compared with 251 mg/kg in purple wheat bran. In a subsequent study, they found that the anthocyanin trait in blue wheat was relatively more stable to environmental changes in a 3 year study as compared to purple wheat grown under the same conditions (Abdel-Aal and Hucl 2003). Zeven (1991) reported that the purple pigments were mainly located in the pericarp outer layers, whereas the blue pigments were mainly found in the aleurone layer. The anthocyanina profile was different between the blue and purple wheat (Abdel-Aal and Hucl 1999, 2003). Delphinidin was found to be the primary aglycone or anthocyanindin in blue wheat and accounts for about 69% of the total anthocyanins followed by the aglycone cyanidin at 24% with smaller amounts of petunidin, malvidin, and peonidin (Abdel-Aal and Hucl 1999). Purple wheat cultivars Laval and Konini contained lower amounts of total anthocyanins, but they had a greater variety of anthocyanin compounds as compared to blue wheat, with cyanidin-3-glucoside being the only major anthocyanin. The blue aleurone spring wheat line "Purendo 38" and commercial cultivars of purple (Konini) and red (Katepwa) wheats had different and distinct anthocyanin profiles (Abdel-Aal and Hucl 2003). Four major anthocyanins were separated from blue wheat extracts as compared to five anthocyanins in purple wheat. Cyanidin 3-glucoside was the predominant anthocyanin in purple wheat, whereas it was the second major anthocyanin in blue wheat. Abdel-Aal et al. (2006) reported delphinidin-3-glucosdie as the most abundant anthocyanin in blue wheat. In a more recent study, four main anthocyanins, delphinidin-3-glucoside (45%), cyanidin-3-glucoside (28%), delphinidin-3-rutinoside (22%), and cyanidin-3-rutinoside (2%), were in the found in blue wheat cv. Purendo (Abdel-Aal et al. 2008). In addition to the main anthocyanins, blue wheat extracts contained low concentrations of petunidin-3-rutinoside, petunidin-3-glucoside, malvidin-3-rutinoside, and peonidin-3-rutinoside. Hu et al. (2007) found that a dark blue grained wheat cv. Hedong Wumai exhibited a different anthocyanin composition, with cyanidin-3-glucoside being the predominant pigment, together with cyanidin-3-galactoside, pelargornidin-3-glucoside, and peonidin-3-glucoside. All the data from the various studies suggested that the anthocyanin composition in wheat varied with genotype.

Seven hydroquinones substituted by β-1,6-linked oligosaccharides viz. 4-hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (1), 4-hydroxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (2), 4-hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside(3),4-hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (4), 4-hydroxy-3,5-dimethoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (5), 4-hydroxy-3,5-dimethoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (6), and 4-hydroxy-2-methoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (7), were isolated from wheat germ (Zhokhov et al. 2009). Compound 1 was the most abundant, approximately 2 mg isolated from each gram of wheat germ.

Several novel benzoxazinoid metabolites of the hydroxamic acids (2,4-dihydroxy-1,4-

benzoxazin-3-one, DIBOA; 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one, DIMBOA), lactams (2-hydroxy-1,4-benzoxazin-3-one, HBOA), and benzoxazolinones (1,3-benzoxazol-2-one, BOA) were identified, including double-hexose derivatives of DIBOA, DIMBOA, and HBOA in whole grain rye and wheat (Hanhineva et al. 2011).

Phytochemicals in Wheat Products

Wheatgrass is rich in chlorophyll, minerals like magnesium, selenium, zinc, chromium, antioxidants like β-carotene (pro-vitamin A), vitamin E, vitamin C, anti-anaemic factors like vitamin B12, iron, folic acid, pyridoxine and many other minerals, amino acids and enzymes, which have significant nutritious and medicinal value (Tirgar et al. 2011). Wheat grass is a rich source of phenolic and flavonoid content.

Wheat and rye breads generally contained low quantities of fructan (0.61–1.94 g/100 g), with rye bread being the richest source (1.94 g/100 g) (Whelan et al. 2011). Gluten-free bread also contained similar quantities of fructan (1.00 g/100 g) as other breads. There was wide variation in fructan content between individual brands of granary (0.76–1.09 g/100 g) and gluten-free breads (0.36–1.79 g/100 g). Although they contain only low quantities of fructan, the widespread consumption of bread may make a significant contribution to fructan intakes. Fructans are non-digestible carbohydrates with various nutritional properties including effects on microbial metabolism, mineral absorption and satiety.

The average total alkylresorcinol content in Swedish wheat was found to be 412 μg/g (ranging between 227 and 639 μg/g) (Chen et al. 2004). The alkylresorcinol content in cereal foods commonly consumed in Sweden varied widely, from non-detectable levels in white wheat flour and products not containing the outer parts of wheat and/or rye to >900 μg/g in some whole grain rye products. Alkylresorcinols appear to be good markers of whole grain wheat and rye in foods, and their analysis may be an objective way to identify foods rich in whole grain wheat and/or rye or brans thereof. Similarly alkylresorcinols with alkyl chains C17:0–C25:0 were found to be abundant in whole-grain wheat and rye (Linko-Parvinen et al. 2007). In a 1-week crossover design study of 15 volunteers, they demonstrated that alkylresorcinols in human plasma were mainly transported in lipoproteins. The plasma alkylresorcinol C17:0–C21:0 ratio reflected intake of whole-grain wheat and rye, and the plasma total alkylresorcinol concentration was found to be a useful biomarker of whole-grain cereal intake. The average alkylresorcinol content in selected Polish rye and wheat cereals was found to be about 1,100 and 800 mg/kg DM respectively (Kulawinek et al. 2008). The total alkylresorcinol content in tested cereal products available on the Polish market varied from very low levels in barley grain-based foods up to 3,000 mg/kg DM in wheat bran. Calculated ratios of C17:0–C21:0 homologues, a useful parameter used to distinguish between rye and wheat cereals and their derived products, was about 1.2–1.4 in rye products, about 0.2 in wheat products, and varied between 0.2 and 0.6 in cereal-derived products containing a mixture of whole rye and/or wheat.

Antioxidant Activity

Of the antioxidants in wheat, free and esterified phenolic acids appear to have the greatest potential to be beneficial to health (Baublis et al. 2000). Phenolic acids from whole wheat- and wheat bran-based ready-to-eat breakfast cereals possess potent antioxidant activity in-vitro at concentrations that would be obtained from a normal serving of whole wheat cereal. Further, acid conditions and enzymic hydrolysis increase the solubility and activity of wheat phenolics suggesting that the digestive process could be important in altering the antioxidant potential of wheat-based foods.

Wheat had second highest total phenolic content (7.99 μmol of gallic acid equiv/g of grain) after corn (15.55 μmol of gallic acid equiv/g of grain) and more than oats (6.53 μmol of gallic acid equiv/g of grain), and rice (5.56 μmol of gallic acid equiv/g of grain) (Adom and Liu

2002). The major portion of phenolics in grains existed in the bound form (85% in corn, 75% in oats and wheat, and 62% in rice), wheat had 13.43 μmol of gallic acid equiv/g of grain of bound phenolics and 1.9 μmol of gallic acid equiv/g of grain of free phenolics. Ferulic acid was the major phenolic compound in grains tested, with free, soluble-conjugated, and bound ferulic acids present in the ratio 0.1:1:100. Ferulic acid content of wheat grains (% contribution of fraction to the total μmol ferulic acid/100 g of grain) comprised total ferulic acid 333.44 μmol, free ferulic acid 0.57 μmol (0.2%), soluble ferulic acid conjugate 3.27 μmol (1%), and bound ferulic acid 329 μmol (98.8%). Wheat had a total flavonoid content of 1.29 μmol catechin equivalent per g of grain, made up of 1.15 μmol catechin equivalent per g of grain of bound flavonoids and 0.09 μmol catechin equivalent per g of grain of free flavonoids. Corn had the highest total antioxidant activity (181.42 μmol of vitamin C equiv/g of grain), followed by wheat (76.70 μmol of vitamin C equiv/g of grain), oats (74.67 μmol of vitamin C equiv/g of grain), and rice (55.77 μmol of vitamin C equiv/g of grain). Bound phytochemicals were the major contributors to the total antioxidant activity: 90% in wheat, 87% in corn, 71% in rice, and 58% in oats. Bound phytochemicals could survive stomach and intestinal digestion to reach the colon. This may partly explain the mechanism of grain consumption in the prevention of colon cancer, other digestive cancers, breast cancer, and prostate cancer, which is supported by epidemiological studies.

Wheat whole grain was found to have total phenolic content of 122 mg GAE/100 g grain and oxygen radical absorbance capacity (ORAC) of 2,730 μmol TE/100 g grain (Okarter 2012). Wheat contained 192 μmol/100 g grain of ferulic acid, and 12.1 μmol/100 g grain of *p*-coumaric acid and also caffeic acid in the insoluble bound fraction but contained no flavonoids (qurecetin, kaempferol, catechin, and rutin) in the insoluble-bound fraction of the grain. None of the phenolic compounds had any cellular antioxidant activity, most likely because these phenolic compounds did not have the structure necessary to impart cellular antioxidant activity. The data suggested that the potential health benefit of whole grain consumption in the lower gastrointestinal tract was independent of the cellular antioxidant activity of the phenolic compounds found in the insoluble-bound fraction of whole grains.

Soft wheat grain samples exhibited ED_{50} values against DPPH(*) of 23–27 mg of grain equiv/mL, ORAC of 32.9–48 μmol of Trolox equiv (TE)/g, and ABTS(*)(+) scavenging capacity of 14.3–17.6 μmol of TE/g (Moore et al. 2005). Significant radical scavenging and chelating capacities were detected in wheat bran extracts, along with significant levels of phenolic acids, tocopherols, and carotenoids (Zhou et al. 2005). Ferulic acid (130.60–146.38 μg/g) was the predominant phenolic acid in all of the tested bran samples and accounted for approximately 53–67% of total phenolic acids on a weight basis. Total tocopherol concentration ranged from 1.87 to 2.95 μmol/100 g of bran, whereas total carotenoid level was 0.20–0.33 μmol/100 g of bran. Hydrophilic antioxidant activity of wheat bran/germ samples (7.1–16.4 μmol of vitamin C equiv/g) was 13–27-fold higher than that of the respective endosperm samples (Adom et al. 2005). Similarly, lipophilic antioxidant activity was 28–89-fold higher in the bran/germ fractions (1,785–4,669 nmol of vitamin E equiv/g). Hydrophilic antioxidant activity contribution to the total antioxidant activity (hydrophilic + lipophilic) was >80%. In whole-wheat flour, the bran/germ fraction contributed 83% of the total phenolic content, 79% of the total flavonoid content, 51% of the total lutein, 78% of the total zeaxanthin, 42% of the total β cryptoxanthin, 85% of the total hydrophilic antioxidant activity, and 94% of the total lipophilic antioxidant activity.

Total phenolics of cultivars of five genotypes representing four commercial Canadian wheat classes with different intrinsic qualities were found to be concentrated in fractions from the first and second pearlings (>4,000 mg/kg) (Beta et al. 2005). Wheat fractions from the third and fourth pearlings still contained high phenolic content (>3,000 mg/kg). A similar trend was observed in antioxidant activity of the milled fractions with ≈4,000 mg/kg in bran and shorts,

≈3,000 mg/kg in bran flour, and <1,000 mg/kg in first middlings flour. Total phenolic content and antioxidant activity were highly correlated ($R^2 = 0.94$). There were no significant differences between red and white wheat samples. A strong influence of environment (growing location) was indicated.

Ferulic acid was the predominant phenolic acid in Swiss red wheat and accounted for approximately 57–77% of total phenolic acids on a weight basis (Zhou et al. 2004a). Ferulic acid concentration was well correlated with scavenging activities against radical cation and superoxide anion, total phenolic content, and other phenolic acid concentrations, suggesting the potential use of ferulic acid as a marker of wheat antioxidants. The oxygen radical absorbance capacity (ORAC) value of 50% acetone extracts was 3–20-fold greater than that of the ethanol extracts, indicating that 50% acetone may be a better solvent system for monitoring antioxidant properties of wheat. Among the blue wheat cv. Purendo milling products, the bran extract showed the highest capacity to scavenge DPPH free radicals, followed by whole grain and white flour (Abdel-Aal et al. 2008). They attributed this to a higher concentration of anthocyanins in the bran fraction as compared to whole grain and white flour. Blue wheat white flour exhibited a moderate scavenging capacity toward DPPH radicals despite its low content of anthocyanins indicating that other kernel constituents contributed to the total antioxidant activity in the white flour. Blue wheat anthocyanin powder and anthocyanin compounds, elicited exceptionally high scavenging capacities. Anthocyanin powder had a DPPH scavenging capacity 42-fold higher than blue wheat bran. Cyanidin-containing anthocyanins exhibited higher DPPH scavenging capacities as compared to delphinidin-based anthocyanins. Again, among the milling products, blue wheat bran showed the highest scavenging capacity followed by whole grain and white flour. Anthocyanin powder and anthocyanin compounds were exceptionally high in ABTS scavenging capacity as compared to the blue wheat milling products. Anthocyanin powder had an ABTS scavenging capacity 54-fold higher than blue wheat bran. In addition, there were significant differences between anthocyanin compounds in their ABTS scavenging capacity. Again, cyanidin-containing anthocyanins exhibited higher ABTS scavenging capacity as compared to delphinidin based anthocyanins. This trend was similar to that obtained with DPPH scavenging capacity. The sugar moiety was also found to influence ABTS scavenging capacity of anthocyanin compounds, with rutinose-containing anthocyanins showing higher scavenging capacity as compared to glucose-containing anthocyanins. Among blue wheat milling products, the bran fraction exhibited a greater inhibition capacity against oxidation of LDL cholesterol as compared to the whole grain and white flour. With a longer incubation time, differences in inhibition capacity between bran and whole grain were insignificant. Anthocyanin powder and anthocyanin compounds were appreciably high in their ability to inhibit copper-induced human LDL cholesterol oxidation as compared to the blue wheat milling products. For instance, anthocyanin powder exhibited inhibition capacity 25-fold higher than blue wheat bran and was comparable to that of the isolated anthocyanin compounds. Significant differences in antioxidant capacity were observed with anthocyanin powder and compounds exceeding that of butylated hydroxytoluene, indicating a potential for the development of blue wheat-based natural antioxidants and colorants. Hu et al. (2007) reported that 69% of the overall free radical scavenging capacity of dark blue grained wheat was attributed to the anthocyanin content, as compared to 19% for the extractable phenolic acids. Li et al. (2005) found that Chinese black-grained wheat had the strongest DPPH scavenging activity and the highest total phenolic content among the wheat samples prepared from four wheat genotypes (black, blue, purple, and white). The DPPH scavenging capacity of the bran extracts was about two fold higher than that of whole meal (grain) extracts. A positive correlation was found between DPPH radical scavenging activity and total phenolic content of bran ($R = 0.86$) and whole meal ($R = 0.96$). The presence of gallic, *p*-hydroxybenzoic, caffeic, syringic, *p*-coumaric, vanillic, gentisic, *o*-coumaric

acid, and ferulic acids were detected in wheat bran. Ferulic acid content was highest among the phenolic acids. They concluded that Chinese black-grained wheat may be considered as a potential source of natural antioxidants given its high free radical scavenging ability and phenolic content.

Among several potent antioxidants in blue wheat, anthocyanins (delphinidin-3-glucoside, delphinidin-3-rutinoside, cyanidin-3-glucoside, and cyanidin-3-rutinoside), tryptophan, and a novel phenolic trisaccharide (β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-(4-hydroxy-3-methoxyphenyl)-β-D-glucopyranoside) were the most active water-extractable constituents (Tyl and Bunzel 2012). However, anthocyanins were found to be major contributors to the overall blue wheat antioxidant activity only when the extraction steps were performed under acidic conditions. Alkylresorcinols were among the most active antioxidants extractable with 80% ethanol in the TEAC assay. Ferulic acid was found to be the major antioxidant in alkaline cell-wall hydrolysates.

Wheat germ protein hydrolysates prepared with alcalase, exhibited antioxidant activity close to that of α-tocopherol in a linoleic acid emulsion system (Zhu et al. 2006). The hydrolysate showed scavenging activity against free radicals such as DPPH, superoxide, and hydroxyl radicals. The radical-scavenging effect was in a dose-dependent manner, and the EC_{50} values for DPPH, superoxide, and hydroxyl radicals were found to be 1.30, 0.40 and 0.12 mg/m, respectively. Further, the hydrolysate also exhibited notable reducing power and strong chelating effect on Fe2+.

Li et al. (2007) found that DPPH* scavenging activity at 60 min was 50.6–59.9% for control and antho-beer (made from purple wheat grains) extracts, 15.0–54.1% for antho-bran extracts and hydrolysates. Total phenolic content ranged from 410 to 609 mg/L for control (from barley malt) and antho-beer original samples; from 84 to 95 mg/L for control and antho-beer extracts; and from 2,473 to 7,634 mg/kg for antho-bran extracts and hydrolysates. The corresponding ORAC values were 3,050–4,181 mg/L, 2,961–3,184 mg/L, and 74–213 g/kg, respectively. The major known phenolic acids comprised four types in control beer, five types in antho-beers, and seven types in antho-bran hydrolysates. Total anthocyanin content of antho-bran was up to 1,160 mg/kg. they found that brewing materials had an effect on the antioxidant, likely taste, and aroma properties of beers; and concluded that antho-grain may have potential as a novel brewing material.

Seven new compounds that demonstrated antioxidant properties, 4-hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside (1), 4-hydroxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside (2), 4-hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside (3), 4-hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside (4), 4-hydroxy-3,5-dimethoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside (5), 4-hydroxy-3,5-dimethoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside (6), and 4-hydroxy-2-methoxyphenyl β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (7), were isolated from wheat germ (Zhokhov et al. 2009). In antioxidant activity determined by the Trolox equivalent antioxidant capacity assay, compound 2 and 7 showed higher values than the other compounds. Compounds 1 and 3–6 reacted with the radical cation reagent within a few seconds, whereas 2 and 7 required several minutes for complete reaction. Compound 1 was shown to protect plasmid DNA from oxidative stress damage caused by hydrogen peroxide; this effect was concentration-dependent.

Ethanolic extract of freeze-dried wheatgrass gave the highest value of ferric-reducing antioxidant power assay (FRAP), while the α-tocopherol gave the lowest value (Das et al. 2012). In DPPH scavenging ability, freeze-dried wheatgrass samples again exhibited the highest activity compared to hot-air dried samples.

Wheatgrass samples had the highest amount of ascorbic acid and chlorophyll, but the lowest amount of total flavonoids and phenolics.

Antihyperlipidemic Activity

In a study of six normolipidemic males, adding fibres to the low-fibre test meal [2.8 g dietary fibre (TDF)] containing 70 g fat and 756 mg cholesterol induced no change in serum glucose or insulin responses (Cara et al. 1992). The serum triglyceride response was lower in the presence of oat bran, wheat fibre, or wheat germ and chylomicron triglycerides were reduced with wheat fibre. All fibre sources reduced chylomicron cholesterol. Cholesterolemia decreased postprandially for 6 h and was further lowered in the presence of oat bran. Serum apolipoprotein (apo) A-1 and apo B concentrations were not affected. Thus, dietary fibres from cereals may reduce postprandial lipemia in humans to a variable extent.

Studies showed that wheat grass supplementation with a high-fat diet in rabbits resulted in improved lipid levels (decreased total cholesterol and increased HDL-C) together with significantly reduced malondialdehyde (MDA) levels and increased GSH and vitamin C levels (Sethi et al. 2010). These results indicated the beneficial role of wheat grass in ameliorating hyperlipidemia and the associated oxidative stress. In another study, fresh wheat grass juice administration at 5 and 10 mL/kg resulted in dose dependent significant decline in total cholesterol (TC), triglycerides (TG), low density lipoprotein-cholesterol (LDL-C) and very low density lipoprotein-cholesterol (VLDL-C) levels in hypercholesterolemic rats (Kothari et al. 2011). Further, in comparison to atorvastatin, wheat grass juice administration at the dose of 10 mL/kg resulted in comparable decrease of TC, LDL-C, TG and VLDL-C levels. Fecal cholesterol excretion was significantly enhanced by wheatgrass juice administration. Phytochemical analysis revealed the presence of flavonoids, triterpenoids, anthraquinol, alkaloids, tannins, saponins and sterols in fresh wheat grass juice. The results suggested that fresh GJ could have potentially beneficial effect in atherosclerosis associated with hyperlipidemia. Similar results were observed in normal rats, fresh grass juice administration produced dose related significant reduction in total chloesterol, triglycerides, low density lipoprotein-cholesterol and very low density lipoprotein-cholesterol levels (Kothari et al. 2008). Juhel et al. (2011) found that 9% Nutriose6 (a new wheat starch-based low-digestible carbohydrate) significantly lowered plasma and LDL cholesterol by 14.5 and 23.8% in hamsters respectively as compared to a 0.25% cholesterol-enriched diet. Nutriose6 diets prevented hepatic cholesterol accumulation (−10 to −20%) and significantly decreased bile cholesterol (−47 to −68%) and phospholipids (−30 to −45%) concentrations. The 9% Nutriose6 diet significantly decreased the rate of dietary cholesterol absorption (−25%) and markedly stimulated faecal neutral sterol (+81%) and bile salts (+220%) excretion. No significant change in cholesterol 7-α-hydroxylase or LDL-receptor activities was observed whereas 3-hydroxy-3-methylglutaryl-coenzyme A reductase activity was reduced by 29%. The authors postulated that reduced cholesterol and bile salt absorptions and lowered cholesterol synthesis were likely mechanisms underlying the cholesterol lowering effect of Nutriose6.

In a randomized sequential crossover study of 15 healthy individuals (mean age 54.5, body mass index 27.4 kg/m^2) consumption of wholemeal wheat food for 3 weeks reduced significantly fasting plasma cholesterol as well as LDL cholesterol levels without major effects on glucose and insulin metabolism, antioxidant status and sub-clinical inflammation markers (Giacco et al. 2010).

Antidiabetic Activity

In-Vitro Studies

In-vitro studies suggested that wheat plant lectin (wheat germ agglutinin, WGA) at low concentrations increased the affinity of the insulin receptor and the insulin sensitivity of fat cells (Livingston and Purvis 1980). WGA (0.25–20 μg/mL) increased the binding of insulin by adipocytes, apparently by increasing the binding affinity of

the insulin receptor and this was accompanied by an increase in the sensitivity of the adipocytes to insulin stimulation of glucose transport. At higher concentrations, the lectin appeared to act at another site(s) to inhibit the activation of the transport system by insulin, vitamin K5, or H2O2, an effect that was reversed by the addition of ovomucoid. In-vitro studies by Lee et al. (2012) showed that wheat sprout polysaacharide extract had a stimulating effect on insulin secretion and production in pancreatic β-cells via K + channel closure and calcium influx. Their results suggested that wheat sprout polysaacharide extract may be useful as a candidate for the therapy of diabetes mellitus.

The acetic and lactic acid concentrations in wheat sourdough, bread chemical composition, total phenolics content and glycemic index (GI) in-vivo were found to vary significantly depending on the starter culture used (Novotni et al. 2011). The GI of control bread without sourdough (70) was significantly higher than that of bread containing sourdough prepared with *Saccharomyces cerevisiae* var. *chevalieri* starter (50), *Lactobacillus fermentum* starter (56) or *Lactobacillus fermentum* with phytase starter (56), but not from bread with *Lactobacillus plantarum* sourdough (60). The addition of 10% sourdough with a lower molar ratio of lactic to acetic acid (≤4) and higher total phenolics content was found preferable for producing bread with medium and low GI.

Animal Studies

Holm et al. (1989) investigated the effects of different thermal processes used to produce ready-to-eat cereals on the glycemic response to whole grain wheat in rats. Incompletely gelatinized steam flaked and dry autoclaved products were digested more slowly in vitro and elicited lower glucose responses in rats compared with completely gelatinized drum dried, extrusion cooked or boiled samples. The initial glycemic response in rats was closely related to the rate of starch hydrolysis in the pepsin/alpha-amylase assay. The peak glucose, insulin and C-peptide responses in humans after breakfast meals of porridge prepared from drum dried flour and from boiled flour were similar, whereas the rate of depression of the glucose curve was more rapid after consuming drum dried porridge. They concluded that the glycemic response to wheat products was affected by the processing conditions used. The more severe the processing conditions, the more rapid the digestion of starch.

The effect of exogenous opioid peptides, gluten exorphins A5 and B5, which were isolated from the enzymatic digest of wheat gluten, on the postprandial insulin level were examined in rats. The oral administration of wheat gluten opioid peptide exorphin A5 at a dose of 30 mg/kg weight potentiated the postprandial plasma insulin level in rat and the effect was reversed by naloxone (Fukudome et al. 1995). The administration of gluten exorphin B5 showed a similar effect at a higher dose (300 mg/kg w). Additionally, intravenous administration of gluten exorphin A5 at a dose of 30 mg/kg weight also stimulated the postprandial insulin release. The fact that orally and intravenously administered gluten exorphin A5 stimulated insulin release suggested that it modulated pancreatic endocrine function by the action after the absorption rather than within the gastrointestinal tract.

Clinical Studies

The results of a 6-week cross-over study of ten men and nine women aged 35–55 showed that the gastric inhibitory polypeptide response after a sucrose load (2 g/kg body weight) was significantly greater after the subjects consumed the sucrose rather than the wheat starch diet (Reiser et al. 1980). The gastric inhibitory polypeptide response was significantly greater after 6 weeks on diet than during pretest. The results suggested that the increases in insulin levels observed after sucrose feeding may be mediated by an effect on the enteric hormone gastric inhibitory polypeptide. Studies in ten healthy men showed that ingestion of partially hydrolysed wheat flour on 2 separate days induced greater lipid utilization, less hyperglycemia in the late postprandial period and less rapid and intense variations of blood glucose than ingestion of an equivalent amount of glucose (Pittet et al. 1981). In a 6-week randomized study of four young adult (18–26 years old), nonobese human subjects

(two men and two women) with insulin-dependent diabetes mellitus, a large reduction in triglycerides was noted with cellulose feeding but not with wheat bran (Harold et al. 1985). The mean daily insulin dose decreased in response to fibre addition (8 and 10% decrease for wheat bran and cellulose feeding, respectively). Mean biostator insulin requirements decreased 11% with wheat bran but not with cellulose. The wheat bran diet reduced peak blood glucose concentration and peak insulin infusion rate in comparison with baseline and cellulose diets. The data suggested that high levels of cellulose or wheat bran were of marginal benefit to insulin-dependent diabetic subjects.

Hagander et al. (1985) monitored the postprandial glucose and hormonal responses in nine non-insulin-dependent diabetics after four randomized breakfast meals containing mainly wheat products. The extruded whole-grain product gave significantly larger areas under the glucose and insulin curves than the corresponding baked bread, and resulted in higher C-peptide, gastric inhibitory polypeptide, and glucagon concentrations at certain time points. The mean incremental areas under the glucose curves were similar after white bread and the two extruded crispbread-like products. There were no significant differences between white and whole-grain wheat bread. The results indicated that baked whole-grain wheat bread was preferable to corresponding extruded products in non-insulin-dependent diabetes mellitus. In another study, unprocessed wheat bran significantly reduced the blood glucose and plasma immunoreactive insulin concentrations at 30 min of the tolerance test in ten obese children (Molnár et al. 1985). The results suggested that supplementation of obese children's diet with unprocessed bran was advantageous. In a study of seven processed wheat products (shortbread biscuits, custard, quick-cooking wheat, wholemeal bread, water biscuits, puffed wheat, and puffed crispbread), 50 g carbohydrate portions of the foods were fed to eight volunteers after an overnight fast (Ross et al. 1987). The calculated glycemic indices (GI) (mean) ranged from 43 for custard to 81 for puffed crispbread. Insulin responses paralleled the glycemic responses. The GI correlated positively with the percentage of starch digested in-vitro. The degree of starch gelatinization ranged from 0.4 to 60% and correlated positively with the percentage starch digested in-vitro. Differences in the glycemic and insulin responses to wheat products was elucidated in part by the extent of processing and the degree of gelatinization achieved.

In a self-controlled study using 11, non-obese patients with impaired glucose tolerance, the blood glucose levels were decreased as compared to the control values with simultaneous wheat bran intake (Rinfel et al. 1990). The glucagon response curve fell below that of the control. The serum gastrin levels did not show any change following either glucose or glucose plus wheat bran intake. They concluded that dietary fibres were able to decrease glucagon release, beside their direct inhibitory effect on the level of sugar absorption from gastrointestinal tract. Glucose and insulin responses to wheat bread products namely three white-wheat-bread (WWB) products varying in crust-crumb ratio and monoglyceride addition, three bread products with a high soluble fibre content (HSFB), and two coarse-wheat breads (CB) were evaluated in healthy subjects (Holm and Björck 1992). The metabolic responses to WWBs were in general higher than those to CB and HSFB products. The most prominent reduction in metabolic responses was noted with the CBs with intact kernels and the HSFBs with oat bran. The resistant starch content ranged from 0 to 1.7/100 g starch. HSFBs and the CB with intact kernels showed a higher satiety score than did the WWBs immediately after the test meal. Studies in nine healthy male volunteers aged 65–70 found no differences in the glycaemic and insulinaemic indices (IIs) between breakfast meals of rolled oat (muesli), rolled oat porridge and white bread (Granfeldt et al. 1995). In contrast, boiled intact oat and wheat kernels (kernel porridges) produced low glucose and insulin responses. No differences were obtained in GI values whether based on capillary or venous blood. The results suggested that neither incomplete gelatinization in rolled oats nor naturally occurring viscous dietary fibre in oats affect

postprandial glycaemia, whereas enclosure of intact kernels significantly blunt metabolic responses.

In a Latin square design study involving 12 physically active subjects (6 males and 6 females) resting carbohydrate oxidation rates and plasma insulin concentrations after oat ingestion were less than after wheat, and corn and wheat ingestion, respectively (Paul et al. 1996). During exercise, the change in plasma glucose from pre-exercise was greater after consuming wheat and corn compared with oat, and it was inversely related to pre-exercise plasma insulin concentration. Plasma free fatty acid concentrations were inversely related to plasma lactate concentrations. Free fatty acid concentrations and fat oxidation were greater in fasting trials than all others, but performance ride times did not differ among treatments. The results indicated that pre-exercise meal composition could influence glucose homeostasis during early exercise and plasma branched-chain amino acid concentrations over a substantial range of metabolic demands.

In a two 3-month phases of a randomized crossover study of 23 subjects with type 2 diabetes (16 men and 7 postmenopausal women), high-fibre cereal (wheat bran) breakfast foods did not improve conventional markers of glycemic control or risk factors for coronary heart disease (CHD)in type 2 diabetes over 3 months (Jenkins et al. 2002). Between the test and control treatments, no differences were seen in body weight, fasting blood glucose, HbA(1c), serum lipids, apolipoproteins, blood pressure, serum uric acid, clotting factors, homocysteine, C-reactive protein, magnesium, calcium, iron, or ferritin. They concluded that longer studies were required to demonstrate the benefits of cereal fibre.

In a study of 11 healthy young men, comparative insulinaemic, glycaemic responses to different breads: leavened Einkorn (*T. monococcum*) bread with added honey-salt, leavened Einkorn crushed whole grain bread and conventional leavened Einkorn bread and conventional modern leavened wheat (*T. aestivum*) bread were investigated (Bakhøj et al. 2003). Postprandial glucose-dependent insulinotrophic polypeptide response was significantly reduced by the Einkorn breads processed with honey-salt leavening and by using crushed whole grain bread compared to the yeast leavened bread made from modern wheat or from Einkorn. No significant differences were found in the responses of glucagon-like peptide 1, insulin or glucose.

In a crossover study of 4 healthy men ingested ingesting ^{13}C –enriched wholemeal wheat bread (WB) or glucose in water, starch in WB was found to be partly rapidly and partly slowly digestible (Priebe et al. 2008). The glucose influx rate after WB was comparable with that after glucose in the early postprandial phase (0–2 h) and higher in the late postprandial phase (2–4 h). Despite the same initial glucose influx rate the 0–2 h incremental area under the curve (IAUC) of insulin after WB was 41% lower than after glucose. Endogenous glucose production after WB was significantly more suppressed than after glucose. The results suggested that postprandial insulin response and endogenous glucose production after WB ingestion might not solely be determined by the digestive characteristics of starch; other components of WB appeared to affect glucose homeostasis. In subsequent cross-over study of 10 healthy male volunteers, they compared the rate of starch digestion of three different meals: pasta with normal wheat bran (PA) and bread with normal (CB) or purple wheat bran (PBB) (Eelderink et al. 2012). Plasma glucose concentrations (2-h incremental AUC) did not differ between the test meals. The rate of appearance of exogenous glucose was similar after consumption of CB and PBB, indicating that purple wheat bran in bread did not affect in-vivo starch digestibility. However, the 2-h incremental AUC in men who consumed PA was less than after they consumed CB despite the similar glucose response, suggesting that glycemic response did not always reflect the in-vivo starch digestibility. This could have implications for intervention studies in which the glycemic response is used to characterize test products. In a 6 month study of 30 diabetic subjects, supplementation of wheat bran was found to decrease serum fasting glucose, serum postprandial glucose and serum glycosylated haemoglobin levels compared to the control group without wheat bran supplementation (Haripriya and Premakumari 2010).

Anticancer Activity

Invitro Studies

In-vitro studies showed the aqueous and ethanol extract of wheat grass inhibited the growth of human chronic myeloid leukemia CML (K562) cell line in a time dependent manner (Aydos et al. 2011). The most apoptotic and antiproliferative effect was found with the aqueous extract at 48 h. Increases in antioxidant enzyme MDA level and CAT and SOD activities were observed. Commercial wheatgrass and fibre mixture elicited cytotoxic effect on human acute promyelocytic leukemia cells (HL60) (Alitheen et al. 2011). The IC_{50} of wheat grass-treated HL60 (17.5, 12.5, and 16 μg/mL for 24, 48 and 72 h, respectively) and fibres-treated HL60 (86.0, 35.0 and 52.5 μg/mL for 24, 48 and 72 h, respectively) showed that both extracts possessed optimum effect after 48 h of treatment. Wheat grass decreased the number of viable cells by 13.5, 47.1 and 64.9% after 24, 48 and 72 h exposure, respectively while the fibre mixture reduced the number of viable cells by 36.4, 57.1 and 89.0% after 24, 48 and 72 h exposure, respectively. Both extracts induced early apoptosis concurrently with the reduction of percentage of cell viability. Cell cycle analysis revealed that in HL60, the percentage of apoptosis increased with time (wheatgrass: 16.0, 45.3 and 39.6%; mixture of fibres: 14.6, 45.4 and 45.9%) after exposure for 24, 48 and 72 h, respectively at the concentration of 100 μg/mL and showed optimum effect at 48 h. The results suggested that these health products could be a potential alternative supplement for leukaemia patients. In a prospective matched control study of 60 patients with breast carcinoma, Bar-Sela et al. (2007) found that wheat grass juice intervention during three cycles of FAC (fluorouracil, doxorubicin (adriamycin), and cyclophosphamide) chemotherapy may reduce myelotoxicity, dose reductions, and need for GCSF (granulocyte colony-stimulating factors) support, without diminishing efficacy of chemotherapy.

In-vitro studies showed that fermented wheat aleurone and fermented wheat flour equally reduced cell growth of human HT29 colon adenocarcinoma cells ore effectively than the corresponding blank and the SCFA (short chain fatty acid) mixtures (Borowicki et al. 2010). After 48 h, fermented wheat aleurone significantly induced apoptosis and inhibited cell proliferation by arresting the cell cycle in the G0/G1 phase. The fermented wheat samples contained two- to threefold higher amounts of SCFA than the faeces control (blank), but had reduced levels of bile acids and increased concentrations of ammonia. They concluded that fermentation of wheat aleurone resulted in a reduced level of tumour-promoting deoxycholic acid (DCA), but higher levels of potentially chemopreventive SCFA and that fermented wheat aleurone was able to induce apoptosis and to block cell cycle – two essential markers of secondary chemoprevention.

Okarter (2011) found that the phenolic extracts from the insoluble-bound fraction of whole wheat but not the phenolic extracts from refined wheat inhibited the proliferation of human Caco-2 colon cancer cells, in-vitro. The total phenolic content of the insoluble-bound fraction of Barretta and Magnolia whole wheat was 97.5 and 95.8 mg gallic acid equivalents/100 g whole wheat, respectively. The total phenolic content of the insoluble-bound fraction of Barretta and Magnolia refined wheat was 13.8 and 12.8 mg gallic acid equivalents/100 g. Ferulic acid was the predominant phenolic acid found in both commercial blends of whole and refined wheat. *p*-Coumaric acid and caffeic acid were also detected in the insoluble-bound fraction of whole wheat.

Animal Studies

Studies in male F344 rats found that removal of phytic acid (WB-P) or lipids (WB-F) from wheat bran (WB) had no significant effect on colon tumuor incidence (% animals with tumours) or multiplicity (tumours/animal), whereas removal of both phytate and lipids from WB (WB-PF) significantly increased colon tumour multiplicity and volume (Reddy et al. 2000). They found that WB-PF fortified with excess bran oil or with bran oil plus phytate significantly inhibited colon tumour incidence, multiplicity, and volume; whereas supplementation of WB-PF with phytate alone had no significant effect on colon tumorigenesis in rats suggesting that lipid fraction of

WB possessed tumour-inhibitory properties. In addition, feeding WB-PF diet significantly increased iNOS, total COX and COX-2 enzyme activities, and iNOS protein expression in colon tumours as compared with wheat bran control diet. Feeding the WB-PF that was fortified with excess bran oil alone or with bran oil plus phytate significantly suppressed the activities of iNOS and COX-2 as well as the expression of iNOS and COX-2 in colon tumours compared with that in rats fed the WB diet or WB-PF diet. The study demonstrated time that the lipid fraction of wheat bran had strong colon tumour inhibitor properties.

Wheat samples with high ability to kill human colon cancer cell $CaCO_2$ cells in-vitro had high levels of orthophenolic acids and produced elevated blood caffeic acid levels when used in balanced diets of Min mice (Drankham et al. 2003). These factors correlated positively with their ability to prevent tumour formation in Min mice. When fibre content was equal in diets the content of orthophenolic acids in wheats predicted the antitumour activity in-vivo. Carter et al. (2006) reported that mice fed whole wheat diets for 10 weeks gained more weight than those fed wheat bran diets. Tumour multiplicity was reduced in the two groups fed wheat diets with the highest antioxidant potential. Tumour load was reduced in four of the wheat bran groups and in two of the whole wheat groups. Regression analysis revealed inverse relationships between dietary antioxidant potential and tumour multiplicity in whole wheat and wheat bran diet groups and tumour load in wheat bran diet groups.

Arya and Kumar (2011) reported that skin carcinogenesis tumour incidence, yield, and burden induced by 7, 12-dimethyl benz(a) anthracene (DMBA) and croton oil in all groups of mice treated with wheat grass extract i.e. pre-cancer initiation, peri-cancer initiation, post-cancer initiation and in combination (wheat grass extract given pre-, peri- and post-initiation) were significantly decreased as compared to control (alone with DMBA and croton oil). Additionally, the average latent period was significantly increased from 9.87 to 13.4 weeks in the combination group, together with significant elevation of reduced glutathione (GSH), superoxide dismutase (SOD) catalase (CAT) and reduction in lipid peroxidation (LPO) was observed as compared to the control group.

Clinical Studies

In a randomized, double-blind, placebo-controlled study over a 4-year period of 58 patients with familial adenomatous polyposis, analysis adjusted for patient compliance showed a strong benefit from the high-fibre wheat supplement during the middle 2 years of the trial (DeCosse et al. 1989). The results provided evidence for inhibition of benign large bowel neoplasia by wheat grain fibre supplements in excess of 11 g/day in the study population. They concluded that their findings were consistent with the hypothesis that dietary grain fibre and total dietary fat acted as competing variables in the genesis of large bowel neoplasia. Farkas (2005) reported that fermented wheat germ extract (code name: MSC, trade name: Avemar) exerted a growth inhibitory effect in HCR-25 human colon carcinoma xenograft, and had a synergistic effect with 5-FU in mouse C-38 colorectal carcinoma. On the basis of supportive therapy, he reported fermented wheat germ extract to be efficient in the treatment of colorectal cancer in humans. Thirty patients following radical operation were treated with standard postoperative therapy, 12 of them were given fermented wheat germ extract as additive treatment: following a 9 month long administration, no new distant metastases were detected, in contrast to 4 out of 18 treated with standard therapy alone. Out of 34 patients following radical surgery and treated with chemotherapy, 17 who were given fermented wheat germ extract, achieved an improved survival rate. In a controlled multicenter open label cohort study of 170 colorectal cancer patients, that received anticancer therapies (chemo/radiotherapy), 66 of them completed therapy with fermented wheat germ extract. The results obtained were: new recurrences: 3.0% vs. 17.3%; new metastases: 7.6% vs. 23.1%; deaths: 12.1% vs. 31.7%, progression-related events in total: 16.7% vs. 42.3%. Survival analysis showed significant improvements in the fermented wheat germ extract group, regarding progression-free and overall survival probabilities.

He recommended the supportive application of fermented wheat germ extract in colorectal cancer.

In an open-label, matched-pair (by diagnosis, stage of disease, age, and gender) pilot clinical trial of 22 patients, the continuous supplementation of anticancer therapies with the medical nutriment Avemar (fermented wheat germ extract) helped to reduce the incidence of treatment-related febrile neutropenia in children with solid cancers (Garami et al. 2004). During the treatment (follow-up) period, there was no progression of the malignant disease, whereas at end-point the number and frequency of febrile neutropenic events significantly differed between the two groups: 30 febrile neutropenic episodes (24.8%) in the avemar group versus 46 (43.4%) in the control group. In a randomized, pilot, phase II clinical trial, the efficacy of dacarbazine (DTIC)-based adjuvant chemotherapy on survival parameters of skin melanoma patients was compared to that of the same treatment supplemented with a 1-year long administration of fermented wheat germ extract (Avemar) (Demidov et al. 2008). At the end of an additional 7-year-long follow-up period, log-rank analyses (Kaplan-Meier estimates) showed significant differences in both progression-free and overall survival in favor of the fermented wheat germ extract. Avemar is a nontoxic wheat germ extract registered as a special nutriment for cancer patients in Hungary (Telekes et al. 2009). It had been reported to show potent anticancer activity on cell lines by interfering with glucose metabolism and affecting expressions of several kinases. In in-vivo experimental models, Avemar was also effective by enhancing the activity of the immune system such as stimulating NK cell activity (by reducing MHC I molecule expression), enhancing TNF secretion of the macrophages, increasing ICAM 1 molecule expression on the vascular endothelial cells and inducing apoptosis of tumour cells. "Avemar pulvis" is a powder consisting of an aqueous extract of fermented wheat germ, with the drying aids maltodextrin and silicon dioxide, standardized to contain approximately 200 μg/g of the natural constituent 2,6-dimethoxy-*p*-benzoquinone (Heimbach et al. 2007). Avemar pulvis has been used in Hungary since 1998 and is approved in that country, as well as in the Czech Republic, Bulgaria, and Romania, as a "medical nutriment for cancer patients." Acute and subacute toxicity studies using rodents orally administered Avemar pulvis showed that dose levels (2,000–3,000 mg/kg body weight [bw]/day) exceeding the normal recommended oral dosage (8.5 g/day or 121 mg/kg bw/day for a 70-kg individual) by up to approximately 25-fold caused no adverse effects (Heimbach et al. 2007). The test substance showed no evidence of mutagenicity or genotoxicity in-vitro or in-vivo. Clinical studies using Avemar pulvis as a supplement to drug therapy in cancer patients at doses of 8.5 g/day not only showed no evidence of toxicity, but also showed a reduction in the side effects of chemotherapy. Overall, it was concluded that Avemar pulvis would not be expected to cause adverse effects under the conditions of its intended use as an ingredient in dietary supplements

Antihypertensive Activity

Angiotensin I-converting enzyme (ACE) inhibitory peptide was isolated from wheat gliadin hydrolysate prepared with acid protease (Motoi and Kodama 2003). The ACE inhibitory activity (IC_{50} value) was 2.7 μM. In spontaneously hypertensive rats, the peptide inhibited the hypertensive activity of angiotensin I with intravenous injection, and decreased the blood pressure significantly with intraperitoneal administration. Five angiotensin I-converting enzyme (ACEI) inhibitory peptides were purified from wheat germ and identified as VEV, W, NPPSV, QV, and AMY (Yang et al. 2011). The IC_{50} values were 115.20, 94.87, 40.56, 26.82, and 5.86 μM, respectively.

Immunomodulatory Activity

In-vivo study in mice showed that cyclophosphamide significantly decreased serum hemolysin, phagocytic function of macrophages, liver superoxide dismutase, catalase activity and total

oxidation capacity and increased malondialdehyde (Dai et al. 2009). Wheat peptides restored serum hemolysin and spleen cell proliferation when orally administrated. In addition, they also enhance serum 2,2-diphenyl-1-picrylhydrazyl and *OH scavenging. The results suggested that wheat peptides could help body resist the stress related disorders in immune and antioxidant system.

Water extract of wheat grass was found to increase white blood cells, red blood cells and hemoglobin (Hb) concentration in both normal and myelosuppressed Swiss albino mice (Hemalatha et al. 2012). Further, there was significant increase in bone marrow cellularity and hemagglutinin (antibody to SRBC (sheep red blood cells)) titer in animals treated with wheatgrass compared to the control group. Wheatgrass water extract upregulated Th1 cytokines (TNF-α, IL-2 and IFN-γ) and Th2 cytokine (IL4) and suppressed interleukin IL-1β (a Th1 cytokine) and P65 subunit of NFκB transcription factor. In addition, the wheatgrass extract restored prednisolone suppressed TNF-α (tumour necrosis factor –alpha) and interleukin IL-2 cytokines. The results suggested wheat grass to have a significant role in immunity with a beneficial role in hemoglobin concentration and potential role in Th1 modulation. The authors suggested that the potential of wheatgrass as a candidate drug for inflammatory disorders including cancer management should be explored.

Antiurolithiasis Activity

Wheat bran extract was found to have marked inhibitory effect on calcium oxalate urolithiasis crystallization in-vitro (Sekkoum et al. 2011).

Neuroprotective Activity

In-vivo studies showed wheat to have neuroprotective effect in Sprague–Dawley rats (Jang et al. 2010). Wheat pretreatment suppressed beta-Amyloid (Abeta)-increased intracellular accumulation of reactive oxygen species (ROS) via up-regulation of glutathione, an essential endogenous antioxidant. In a water maze test, injection of Abeta or scopolamine of rats increased the time taken to find the platform during training trials, which was decreased by wheat pretreatment. one of the active components of wheat, total dietary fibre also effectively inhibited A beta-induced cytotoxicity and scopolamine-caused memory deficits. The results suggested that wheat may have preventive and/or therapeutic potential in the management of Alzheimer disease.

Anti thrombocytopenic Activity

Animal studies found that wheat grass had potential beneficial effect in thrombocytopenia and pancytopeniaand also possessed potent immunomodulatory effects Tirgar et al. (2011). Treatment with fresh wheat grass juice, methanol and acetone extracts showed significant increase in haemoglobin, RBC, total and differential WBC and platelet counts in pancytopenia Wistar rats as compared to disease control group. Disease control rats showed significant increase in bleeding and clotting time indicating hemophilia and thrombocytopenia. Treatment with fresh wheat grass juice, methanol and acetone extracts showed decrease in bleeding and clotting time period.

Antiulcerative Activity

In a randomized, double-blind, placebo-controlled study of 21 patients with ulcerative colitis who completed the study, treatment of wheat grass juice was associated with significant reductions in the overall disease activity index and in the severity of rectal bleeding (Ben-Arye et al. 2002). No serious side effects were found. Wheat grass juice appeared effective and safe as a single or adjuvant treatment of active distal ulcerative colitis.

Regina et al. (2006) employed RNA interference to down-regulate the two different isoforms of starch-branching enzyme (SBE) II (SBEIIa

and SBEIIb) in wheat endosperm to raise its amylose content. Suppression of SBEIIb expression alone had no effect on amylose content; however, suppression of both SBEIIa and SBEIIb expression resulted in starch containing >70% amylose. When the >70% amylose wheat grain was fed to rats in a diet as a wholemeal, several indices of large-bowel function, including short-chain fatty acids, were improved relative to standard wholemeal wheat. The results indicated high-amylose wheat to have a significant potential to improve human health through its resistant starch content.

Prebiotic Activity

In a double-blind, placebo-controlled, crossover study of 31 volunteers, ingestion of whole-grain wheat (WG) breakfast cereal elicited a significant increase of faecal bifidobacteria and lactobacilli compare with wheat bran (WB) (Costabile et al. 2008). Ingestion of both breakfast cereals resulted in a significant increase in ferulic acid concentrations in blood but no discernible difference in faeces or urine. No significant differences in faecal SCFA (short chain fatty acid), fasting blood glucose, insulin, total cholesterol (TC), TAG or HDL-cholesterol were observed upon ingestion of WG compared with WB. However, a significant reduction in TC was observed in volunteers in the top quartile of TC concentrations upon ingestion of either cereal. No adverse intestinal symptoms were reported and WB ingestion increased stool frequency. Daily consumption of WG wheat was found to exert a pronounced prebiotic effect on the human gut microbiota composition.

Anti-thalassemia Activity

In a pilot study of patients with thalassemia major, daily consumption of wheat grass juice, blood transfusion requirement of 8 (50%) patients fell by > 25% with a decrease of >40% documented in 3 of these (Marawaha et al. 2004). No adverse effects were observed. However, in a study of 53 patients of thalassemia major with a median age of 16 years wheat grass therapy for 1 year was found not effective in reducing the transfusion requirement in transfusion dependent thalassemia (Choudhary et al. 2009). In a recent study of 40 children with thalassemia major, wheat grass tablet (WGT) was found to have the potential to increase the haemoglobin levels, increase the interval between blood transfusions and decrease the amount of total blood transfused (Singh et al. 2010). The mean haemoglobin in the pre-WGT was 8.54 g% whereas in WGT period was 9.13 g%. The mean blood transfused as packed cells in pre-WGT period was 326.82 mL/kg/year whereas during WGT period it was 256.39 mL/kg/year. The percentage difference in the amount of packed cells transfused in pre-WGT and WGT period was 18.02. The decrease in the blood transfusion requirements was by 25% or more in 20 (60.6%) cases. The mean interval between the consecutive blood transfusions in pre-WGT period was 18.78 days whereas in WGT period was 24.16 days.

Water and methanol extracts of wheat grass were found to reduce markedly serum iron and ferritin levels in iron dextran induced iron overload animals similar to desferoxamine group, a standard iron chelator use in treatment of iron overload in thalassemia (Tirgar and Desai 2011). Reduction in serum iron and ferritin lever was due to an increase in the excretion of iron in urine and faeces, suggesting that wheat had iron chelating property.

Alpha-Amylase Inhibition Activity

The major wheat protein inhibitor of α-amylase was found to consist of a single polypeptide chain of 123 residues. Both serine and alanine were found in position 65, and further minor examples of micro-heterogeneity were observed in four other residues (Kashlan and Richardson 1981).

Opioid Activity

Peptides with opioid activity were found in pepsin hydrolysates of wheat gluten and α-casein

(Zioudrou et al. 1979). The opioid activity of these peptides was demonstrated by use of the following bioassays: (1) naloxone-reversible inhibition of adenylate cyclase in homogenates of neuroblastoma X-glioma hybrid cells; (2) naloxone-reversible inhibition of electrically stimulated contractions of the mouse vas deferens; (3) displacement of [3H]dihydromorphine and [3H-Tyr, dAla2]met-enkephalin amide from rat brain membranes. Substances which stimulated adenylate cyclase and increased the contractions of the mouse vas deferens but did not bind to opiate receptors were also isolated from wheat g luten hydrolysates. Four opioid peptides were isolated from the enzymatic digest of wheat gluten (Fukudome and Yoshikawa 1992). Their structures were Gly-Tyr-Tyr-Pro-Thr, Gly-Tyr-Tyr-Pro, Tyr-Gly-Gly-Trp-Leu and Tyr-Gly-Gly-Trp, and were designated gluten exorphins A5, A4, B5 and B4, respectively. The gluten exorphin A5 was highly specific for δ-receptors. Gluten exorphin B5, which corresponded to [Trp4,Leu5] enkephalin, showed the most potent activity among these peptides. Its IC_{50} values were 0.05 μM and 0.017 μM, respectively, on the guinea pig ileum (GPI) and mouse vas deferens (MVD) assays. A new opioid peptide, Tyr-Pro-Ile-Ser-Leu, was isolated from the pepsin-trypsin-chymotrypsin digest of wheat gluten (Fukudome and Yoshikawa 1993). Its IC_{50} values were 40 and 13.5 μM in the GPI and MVD assays, respectively. This peptide was named gluten exorphin C. Gluten exorphin C had a structure quite different from any of the endogenous and exogenous opioid peptides ever reported in that the N-terminal Tyr was the only aromatic amino acid. From the pepsin–pancreatic elastase digest of wheat gluten, opiod peptides gluten exorphin A5, B5 and B4 were isolated (Fukudome et al. 1997). The yield of gluten exorphin A5 in the pepsin–elastase digest was larger than that in the pepsin–thermolysin digest. The gluten exorphin A5 sequence is found 15 times in the primary structure of the high molecular weight glutenin. Intracerebroventricular administration of gluten exorphin B5 (GE-B5) 200 μg to rats strongly stimulated prolactin secretion, this effect strongly stimulated PRL secretion (Fanciulli et al. 2002). The results indicated that an opioid peptide derived from wheat gluten, GE-B5, had an effect on pituitary function when intracerebroventricular administered; its mechanism of action appeared to be mediated via classical opioid receptors.

Reproductive Enhancement Acitivity

The sprouted wheat contains great amounts of 6-methoxybenzoxazolinone (6-MBOA) a phenol compound that stimulates reproduction in certain small wild herbivorous mammals. Rodríguez-De Lara et al. (2007) found that the number of young born produced per doe rabbit during their study was significantly greater in does fed sprouted wheat (28.1 versus 23.6 control). Does fed sprouted wheat had 0.65 receptivity rate at artificial insemination over 28 per cent greater than does in the control treatment. Kindling rates for nulliparous, lactating and non-lactating does were 0.95, 0.63 and 0.78, respectively. Sexually receptive does had a greater kindling rate (0.95) than non-receptive females (0.63). Does fed sprouted wheat produced larger (litters than those in the control group: 7.7 and 6.8, respectively). Largest litters were born during autumn (7.9) than during summer (6.6). Feeding sprouted wheat as a source of biological 6-MBOA enhanced sexual receptivity and prolificacy in artificially inseminated doe rabbits bred in summer and autumn.

Study of short-term sprouted wheat (SW) dietary supplement on buck rabbit showed that the percentage of normal alive spermatozoa was 13.5% greater in SW-supplemented bucks than in the control and the percentage of abnormal alive spermatozoa was 44.1% greater in the control than in the SW-supplemented bucks (Fallas-López et al. 2011). The morphology of dead spermatozoa, integrity of acrosome, number of normal alive motile sperm and semen doses per ejaculate were not influenced by SW supplementation. The proportion of presence of gel and semen volume in the first ejaculate was greater than the second ejaculate. However, the semen quality in the latter was greater than the former in terms of an increase in motility. Reproductive

traits were more desirable (in winter than autumn). Dietary wilted SW as a source of biological 6-MBOA enhanced sperm characteristics in terms of a greater percentage of normal alive and lesser percentage of abnormal alive spermatozoa but did not affect the number of normal live sperm and suitable semen doses in rabbit bucks in autumn and winter.

Anti-endometrial Activity

Studies in 14 young women mean age 24 years with 2-week wheat sprout juice intervention suggested that the potential detoxification of wheat sprouts on bisphenol A induced toxicity could be mediated via antioxidative and interference of absorption, distribution, metabolism and excretion (ADME)-mediated mechanisms (Yi et al. 2011). Bisphenol A, an endocrine disrupting chemical had been suggested to induce reactive oxygen species (ROS) which play an important role in pathologies of female diseases such as endometriosis.

Wheat Protein Films and Tissue Engineering

The wheat protein (gluten, glutenin and gliadin) films were found to have good strength ranging from 8 to 30 MPa (Reddy et al. 2011). Gliadin films experienced about 50% weight loss whereas glutenin films had bout 90% weight loss after being in water (pH 7.2) for 15 days at 37°C. Gliadin was found to be cytotoxic and the presence of gliadin restricted osteoblast cell proliferation on wheat gluten films. However, gliadin-free glutenin films showed a higher rate of proliferation of osteoblast cells than the poly(lactic acid) films. The results suggested the potential of wheat gluten as a substrate for tissue engineering and other medical applications. Earlier, Hernández-Muñoz et al. (2003) reported that biodegradable protein films obtained from the wheat glutenin fraction presented higher tensile strength values and lower elongation at break and water vapor permeability values than gliadin films. Gliadin films disintegrated when immersed in water.

Antitrypanosomal Activity

Ethyl acetate extract of fermented wheat germ exhibited antitrypanosomal activity; it decreased proliferation of the parasite and extended survival extension *Trypanosoma brucei*- infected rats from 8 days of the control (infected-untreated) to 14 days (Yusuf and Ekanem 2010). The fermented wheat germ extract was found to contain a high amount of glycosides (19.513%), alkaloids (4.017%) and saponins (7.992%).

Antifungal Activity

Three histones H1, H2, H3, and H4 extracted from wheat were found to be active against non-germinated and germinating conidia of *Fusarium oxysporum*, *Fusarium verticillioides*, *Fusarium solani* and *Fusarium graminearum*, significantly reducing 99–100% viability at ≤10 μM or less for the histone mixture and pure H1 (De Lucca et al. 2011). The histones were inactive against all of the non-germinated conidia of *Penicillium digitatum* and *Penicillium italicum* but significantly reduced the viability of the germinating conidia of the *Penicillium* spp. with 95% loss at 2.5 μM. Non-germinated and germinating conidia viability of the *Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger* and *Greeneria uvicola* were unaffected when exposed to histones up to 10 μM. Results indicated that *Fusarium* spp. pathogenic to wheat were susceptible to wheat histones, indicating that these proteins may be a resistance mechanism in wheat against fungal infection.

Antinutrient Activity

The proteinase inhibitor WSCI, active in inhibiting bacterial subtilisin and a number of animal chymotrypsins, was purified from endosperm of hexaploid wheat (*Triticum aestivum*, c.v. San Pastore) (Poerio et al. 2003). The primary structure

of WSCI displayed high similarity with barley subtilisin-chymotrypsin isoinhibitors of the Cl-2 type and with maize subtilisinchymotrypsin inhibitor MPI. Significant degrees of similarity were also found between sequences of WSCI and of other members of the potato inhibitor I family of the serine proteinase inhibitors. A novel chymotrypsin inhibitor named WCI (wheat chymotrypsin inhibitor) was detected in the endosperm of *Triticum aestivum* (Di Maro et al. 2011). In-vitro, WCI inhibited strongly bovine pancreatic chymotrypsin as well as of chymotryptic-like activities isolated from the midgut of two phytophagous insects, *Helicoverpa armigera* (Hüb.) and *Tenebrio molitor* L., respectively. No inhibitory activities were detected against bacterial subtilisins, bovine pancreatic trypsin, porcine pancreatic elastase or human leukocyte elastase.

Wheat Allergy

IgE-mediated sensitization to wheat flour belongs to the most frequent causes of occupational asthma. Baker's asthma is a serious problem for a significant proportion of workers in bakeries, confectionaries, and the food industry caused mainly by inhalation of cereal flour such as wheat flour. Four allergens were identified in wheat flour by means of 2-dimensional immunoblotting; the IgE-binding proteins matched different isoforms of glycerinaldehyde-3-phosphate dehydrogenase from *Hordeum vulgare*, triosephosphate isomerase from *H. vulgare*, and serpin, a serine proteinase inhibitor from *Triticum aestivum* (Sander et al. 2001). The wheat thioredoxin-hB (Triticum aestivum allergen 25 [Tri a 25]) allergen exhibited distinct IgE cross-reactivity with its maize homologue thioredoxin-h1 (Zea mays allergen 25 [Zea m 25]) (Weichel et al. 2006). Two bakers also showed sensitization to human thioredoxin, which shares 29% identity with Tri a 25. A wheat serine proteinase inhibitor was identified as a new allergen in baker's asthma (Constantin et al. 2008). The recombinant allergen showed allergenic activity in basophil histamine release assays and reacted specifically with IgE from 3 of 22 baker's asthma patients, but not with IgE from grass pollen allergic patients or patients suffering from food allergy to wheat. The allergen is mainly expressed in mature wheat seeds localised in the starchy endosperm and the aleuron layer.

Wheat allergens include several salt-soluble proteins (albumins and globulins)–cereal alpha-amylase/trypsin inhibitors, peroxidase, thioredoxin, nonspecific lipid transfer protein, serine proteinase inhibitor, and thaumatin-like protein-as well as salt-insoluble storage proteins (prolamins, namely, gliadins and glutenins) as allergens associated with baker's asthma (Salcedo et al. 2011). Twenty-seven potential water/salt-soluble wheat allergens were identified; the following seven were new reports in food allergy: endogenous α-amylase/subtilisin inhibitor, trypsin/α-amylase inhibitor (AAI) CMX1/CMX3, thaumatin-like protein (TLP), xylanase inhibitor protein-1, β-glucosidase, class II chitinase and 26 kDa endochitinase (Sotkovský et al. 2011). TLP and wheatwin were shown to activate patients' basophils to a similar extent as two well-known allergens, lipid transfer protein (Tri a 14) and AAI 0.19 (Tri a 28.0101). Sander et al. (2011) reported that the highest allergen frequencies among German bakers were found for wheat α-amylase inhibitors (WTAI-CM1, WTAI-CM2, WTAI-CM3, WDAI-0.19 and WMAI-0.28), and CCDs (cross-reactive carbohydrate determinants). Most frequent was IgE to WDAI-0.19, HRP and MUXF (25% each), followed by WTAI-CM1 (20%), thiol reductase (16%), WTAI-CM3 (15%), WTAI-CM2 and thioredoxin (12.5%), WMAI-28, triosephosphate-isomerase, αβ-gliadin (10%), 1-cys-peroxiredoxin (7.5%), dehydrin, serpin, glyceraldehyde-3-phosphate-dehydrogenase (5%), ω-5-gliadin, nsLTP and profilin (2.5%). Fifteen bakers (38%) had IgE to any α-amylase inhibitor and 12 (30%) to at least one CCD. The controls reacted exclusively to CCDs (80%), profilin (60%), thioredoxin (30%), triosephosphate isomerase and nsLTP (10%).

The wheat protein fast ω-gliadin was the most potent allergen among wheat water/salt-insoluble proteins when evaluated by skin prick test and dot-blotting test in Japanese patients with

wheat-dependent exercise-induced anaphylaxis (Morita et al. 2003). Fast and slow ω-gliadin, and γ-gliadin caused dose-dependent inhibition of the serum IgE-binding to solid-phase gluten in the patients. The incubation with fast ω-gliadin of the patient's serum caused dose-dependent inhibition in the IgE-binding to γ-gliadin as well as slow ω-gliadin, indicating a cross-reactivity of these proteins in IgE-binding.

The S-poor prolamins of wheat such as ω-gliadin which lacked both cysteine and methionine residues, ω-secalin of rye and c hordein of barley have been implicated as major allergens in wheat-dependent exercise induced anaphylaxis (WDEIA) and wheat allergy and as immunodominant proteins in coeliac disease (Tatham and Shewry 2012).

Wheat and Coeliac Disease

Anand et al. (1978) found that beside wheat gluten, barley and rye were also involved in causing coeliac disease but not maize and rice. Coeliac disease or celiac spru or gluten-sensitive enteropathy is a digestive disorder of the small intestine caused by intolerance of genetically susceptible individuals to the ingestion of gluten from wheat, barley, and rye (Fraser and Ciclitira 2001; Fasano and Catassi 2001; Farrell and Kelly 2002; Kasarda 2004). Gluten is a complex storage protein found in endosperm kernels of the above cereals. The sensitivity response is triggered by the prolamin fraction of the storage proteins: in wheat gliadins and glutenins, in barley the hordeins and the secalins in rye (Shewry et al. 1995; OECD 2003) which causes villous atrophy, damage to the mucosal lining of the small intestine. In celiac sufferers, the consumption of gluten can result in diarrhoea, malabsorption, steatorrhoea, anaemia, fatigue, osteopenia, nutritional and vitamin deficiencies complications of pregnancy and associated autoimmune diseases, such as insulin dependent diabetes mellitus, hypothyroidism (Fraser and Ciclitira 2001; Fasano and Catassi 2001; Farrell and Kelly 2002). Some sufferers may have only minimal changes in the epithelium and exhibit a milder constellation of symptoms such as abdominal discomfort, bloating, indigestion, or non-gastrointestinal symptoms (or no obvious symptoms at all).

The fundamental method of therapy gluten-sensitive celiac disease is strict lifelong adherence to a gluten-free diet (GFD) that eliminates protein cereal – gluten contained in wheat, rye and barley (Fasano and Catassi 2001; Farrell and Kelly 2002; Krums et al. 2011). For diarrhea and malabsorption syndrome adsorbents, astringents, enzymes, intestinal antiseptic and probiotics are used. Intravenous electrolyte mixture containing potassium, calcium and magnesium are employed for correction of metabolic disorders. To eliminate protein deficiency, drugs used solid protein mixture of pure amino acids, gluten-free mixes for enteral feeding. A study showed that sweet baked goods made of fermented wheat flour with gluten completely degraded, was not toxic for patients with celiac disease (Di Cagno et al. 2010). In a subsequent study they found that a 60-day diet of baked goods made from hydrolyzed wheat flour, manufactured with sourdough lactobacilli and fungal proteases, was not toxic to patients with celiac disease (Greco et al. 2011). A combined analysis of serologic, morphometric, and immunohistochemical parameters was employed to assess this therapy for celiac disease.

Traditional Medicinal Uses

Triticum aestivum, wheatgrass has been traditionally used, to treat various diseases like cancers, diabetes, gastritis, ulcers, pancreas and liver problems, anaemia, skin problems and constipation (Tirgar et al. 2011).

Other Uses

Wheat is used in the production of wheat based cat and pet litter, wheat based raw materials for cosmetics, and to make wheat straw composites. Straw is fed to ruminants or used for bedding

material, thatching, wickerwork, newsprint, cardboard, packing material, fuel and as substrate for mushroom production. In many dry parts of the world it is chopped and mixed with clay to produce building material.

Wheat stubble is used as feed for sheep and fodder wheats are grown for hay and chaff production and for grazing live stock. Wheat middlings (leftover from flour milling) is used to a smaller and limited extent for the fish industry in USA. Sprouted wheat is suitable for animal feed and is used in the pig and poultry industries, beef feed lot and the dairy industry.

Industrial uses of wheat products revolves around the production of glues, alcohol, oil, biofuel and gluten. Wheat is used for biofuel production in Europe with France being the leading producer. By-products of flour milling, particularly the bran, are used almost entirely to feed livestock, poultry or prawns. Wheat germ (from wheat embryos) is sold as a human food supplement. Wheat protein can be used as an antiaging agent with vitamin C in cosmetic multiple emulsion formulation (Akhtar and Yazan 2008).

Comments

The leading wheat producing countries in terms of tonnes production in 2010 are: China 115,180,303 tonnes, India 80,710, 000 tonnes, USA 60,102,600 tonnes, Russian Federation 41,507,600 tonnes, France 38,207,000 tonnes, Germany 24, 106,700 tonnes, Pakistan 23,310,800 tonnes, Canada 23,166,800 tonnes, Australia 22,138,000 tonnes, Turkey 19,660,000 tonnes, Iran 15,028,800 tonnes, Argentina 14,914,500 tonnes and United Kingdom 14, 878, 000 tonnes (FAO 2012).

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Zea mays

Scientific Name

***Zea mays* L.**

Synonyms

Mays americana Baumg. nom. superfl., *Mays vulgaris* Ser., *Mays zea* Gaertn. nom. superfl., *Mayzea cerealis* Raf. nom. superfl., *Mayzea cerealis* var. *gigantea* Raf., *Mayzea vestita* Raf., *Thalysia mays* (L.) Kuntze nom. superfl., *Zea alba* Mill., *Zea altissima* J. F. Gmel. ex Steud. nom. nud., *Zea americana* Mill., *Zea amylacea* Sturtev., *Zea amyleosaccharata* Sturtev. ex L. H. Bailey, *Zea canina* S. Watson, *Zea cryptosperma* Bonaf. nom. superfl., *Zea curagua* Molina, *Zea erythrolepis* Bonaf., *Zea everta* Sturtev., *Zea gigantea* Voss pro syn., *Zea glumacea* Larrañaga, *Zea gracillima* Voss, *Zea hirta* Bonaf., *Zea indentata* Sturtev., *Zea indurata* Sturtev., *Zea japonica* Van Houtte, *Zea macrosperma* Klotzsch, *Zea mays* convar. *aorista* Greb., *Zea mays* f. *hanakibi* Makino, *Zea mays* f. *variegata* (G. Nicholson) Beetle, *Zea mays* subsp. *acuminata* Golosk., *Zea mays* subsp. *amylacea* (Sturtev.) Zhuk., *Zea mays* subsp. *amyleosaccharata* (Sturtev.) Zhuk., *Zea mays* subsp. *aorista* (Greb.) Golosk., *Zea mays* subsp. *ceratina* (Kuleshov) Zhuk., *Zea mays* subsp. *everta* (Sturtev.) Zhuk., *Zea mays* subsp. *huehuetenangensis* (Iltis & Doebley) Doebley, *Zea mays* subsp. *indentata* (Sturtev.) Zhuk., *Zea mays* subsp. *indurata* (Sturtev.) Zhuk., *Zea mays* subsp. *obtusa* Golosk., *Zea mays* subsp. *parviglumis* Iltis & Doebley, *Zea mays* subsp. *saccharata* (Sturtev.) Zhuk., *Zea mays* subsp. *tunicata* (A.St.Hil.) Zhuk., *Zea mays* var. *ceratina* Kuleshov, *Zea mays* var. *everta* (Sturtev.) L. H. Bailey, *Zea mays* var. *gracillima* Körn., *Zea mays* var. *hirta* (Bonaf.) Alef., *Zea mays* var. *huehuetenangensis* Iltis & Doebley, *Zea mays* var. *indentata* (Sturtev.) L. H. Bailey, *Zea mays* var. *japonica* (Van Houtte) Alph. Wood, *Zea mays* var. *multicoloramylacea* Yarchuk, *Zea mays* var. *pensylvanica* Bonaf., *Zea mays* var. *praecox* Torr., *Zea mays* var. *rugosa* Bonaf., *Zea mays* var. *saccharata* (Sturtev.) L. H. Bailey, *Zea mays*var. *striatiamylacea* Leizerson, *Zea mays* var. *subnigroviolacea* T. A. Yarchuk, *Zea mays* var. *tunicata* A. St. Hil., *Zea mays* var. *variegata* G. Nicholson, *Zea mays* var. *virginica* Bonaf., *Zea mexicana* subsp. *parviglumis* (Iltis & Doebley) Greb., *Zea minima* Voss pro syn., *Zea minor* J. F. Gmel. ex Steud. pro syn., *Zea mucronata* Poit. ex Vilm., *Zea odontosperma* Ten., *Zea oryzoides* Golosk., *Zea praecox* Steud. pro syn., *Zea rostrata* Bonaf., *Zea saccharata* Sturtev., *Zea segetalis* Salisb. nom. superfl., *Zea tunicata* (A. St. Hil.) Sturtev. ex L.H.Bailey, *Zea vaginata* Sturtev. nom. nud., *Zea vittata* Voss pro syn., *Zea vulgaris* Mill.

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Family

Poaceae

Common/English Names

Annual Teosinte, Blue Corn, Corn, Cultivated Maize, Field Corn, Grain Maize, Indian Corn, Maize, Mealie, Sweet Corn, Pop Corn, Turkish Corn, Turkish Wheat.

Vernacular Names

Albanian: Misër I Ëmbël;
Amharic: Bäqqollo, Bekolo, Boqqollo, Yäbahər Mašəlla;
Angola: Espiga De Milho, Milho (Portuguese), Pungu, Pungu-Osovo, Pumu (Umubundu);
Arabic: Dhurah, Durah-Kizan, Durah-Shami, Dhurah Shâmîyah, Durahkizan, Durahshami, Hintahe-Runu, Hintaherunu, Khalavan, Khandarus, Khandaruz, Surratul Makkah, Zora Sukaria, Zurratul-Makkah, Zurratulmakkah;
Armenian: Egipitacoren;
Aztec: Cintli;
Azerbiajani: Gargy Daly, QarğĐdalĐ;
Bangladesh: Bhootta (Bengali), Mokka (Tanchangya);
Belarusian: Cucuruz, Mais;
Benin: Bérétobourou, Gberebou (Bariba), Gbade, Gbadye (Fon), Gbade, Gbado, Gbli (Gbe-Fon), Ebli (Gen) Bayuri, Maana-Sore, Sege-Yore (Gurma), Ebli (Mina), Abirri, Birri, Ebli (Phera), Ámeláamelá (Tem-Dompago), Manzo (Yom), Agbado (Yoruba-Nago),Gbadé, Gbadésè (The Flower), (The Flower) (Fon), Gbadoda (Flower) (Goun), Tchara Igbado (The Flower) (Yoruba);
Bosnian: Kukuruz, Zrno (Pšenice), Žulj;
Brazil: Cabelo-De- Milho, Milho;
Breton: Ed-Turki, Ed-Indez;
Bulgaria: Carevica, Zacharna Carevica;
Burkina Faso: Magno, Kaba (Bambara), Kanian (Dagari), Maïs (French), Kamana (Gourounsi), Kamana (Mooré);
Burmese: Pyaung-Bu;
Burundi: Ikigori (Kirundi);
Catalan: De Blat De Moro;
Chechen: Hwaechk'a, H'äshk'a;
China: Sok Mai, Shu Mi, Su Mi (Cantonese), Pāo-Siôuc (Hakka), Bang Zi, Shu Mi, Yu Mi, Yu Shu-Shu, (Mandarin), Hoan-Béh (Min Nan), Yu Mi (Wu), Yu Gu Zi, Bao Gu (Xiang), Yu Mi, Shu Mi (Yue);
Comoros: Ndérou;
Cook Islands: Kōni, Kaoni;
Croatian: Kukuruz, Kukuruz Šecerac;
Czech: Kukurice Cukrová, Kukuřice Seta;
Danish: Majs, Sukkermays;
Democratic Republic Of Congo: Masasi (Kikongo), Nzefu Zi Masasi (Kitandu), Ilefo Kia Masisi (Kiyaka), Masangu (Kwilu), Poone (Sotho), Muhindi (Swahili);
Dutch: Korrelmaïs, Maïs, Suikermais, Turkse Koren, Turkse Tarwe;
Eastonian: Lõhenev Mais, Mais, Penikeel;
Espernato: Maizo;
Farsi: Awâri (Eastern), Balal, Javâri, Zorrat, Zurat (Western);
Fiji: Corn, Maize, Sila Ni Vavalagi (Fijian), Makai (Indian), Kono (Rotuman), Kon (Banaban/ Kiribati);
Finnish: Maissi, Sokerimaissi;
French: Blé D'egypte, Blé Des Indes, Blé De Turquie, Blé Turc, Maïs, Maïs Doux, Maïs Sucré;
French Haiti: Mayi (Creole);
Galician: Mainzo, Millo, Millo Grosso;
Gambia: Manyσ, Tubah-Nyσ (Manding-Mandinka);
Georgian: Simindi;
German: Echter Mais, Körnermais, Mais, Türkisches Korn, Tuerkisher Mais, Tuerkisher Weizen, Zuckermais;
Ghana: Kroju (Adangme-Krobo), Aburo, Awiaburo (Akan-Asante), Efíita (Akpafu), Aburo (Asante-Twi), Ò-Dóólí (Avatime), Kaloana, Kaluwana (Dagbani), Eburo (Fante), Abele, Able, Blafo (Ga), Akplẽ (Gbe-Vhe), Aburoo, Aburow (Twi), Kpledzi, Kple-Ti (Vhe);
Greek: Glyko Kalampoki, Kalamboki;
Guinea: Tubanyo (Badyara), Kènkáabe, K-Akabe, Kö-Bay, Ts-Akabe (Baga), I-Rundù (Basari), Gé-Maka (Bedik), Maka, Makaré (Fulu-Pulaar),

Sòâng (Kissi), Nyóde (Kono), Woloma Kpway (Kpelle), Kö-Babo (Landoma), Bura-Gué, Cissé-Nion, Diokoroni, Kaba, Mańo, Sagada (Mandingka-Manika), Kpèy (Mano), Kabè (Susu), Kémank (Temne);
Guinea-Bissau: Ntubanyo (Biafada), Midjo Bassil (Crioulo), Cába, Tubanhô (Fula-Pulaar), Bumaadsa, Bumbaawa (Pepel);
Hebrew: Tiras;
Huasa: Àgwààdóó;
Hungarian: Csemegekukorica, Kukorica, Tengeri;
Icelandic: Mais;
India: Gum Dhan, Gomdhan, Makoi (Assamese), Bhutta, Janar, Jonar (Bengali), Anaaj, Bara Jauvar, Barajuar, Bhutta, Jawdra, Junri, Kukri, Makaa,Makai, Makka, Makkah-Bhuttah, Makkah-Javar, Makkai, Makki, Makya, Mukka-Jauri, Mungri (Hindu), Bottah, Dodda Jola, Gocinajola, Goinjol, Govina Jola, Hallina Jola, Hidi Jola, Kundige Jola, Makkai-Jola, Makkejola, Mekke Jola, Mekkejola, Meksikan Jola, Musukina Jola, Musukojola, Musukujola (Kannada), Mako (Konkani), Cholam, Colam, Jagung, Makka Cholam, Makkaccolam (Malayalam), Chujak (Manipuri), Bhutta, Buti, Maka, Makaibonda, Makayi, Makka, Mako (Marathi), Vaimim (Mizoram), Kandaja, Mahakaya, Mahakayah, Makaya, Makayah, Samputantastha, Shikhalu, Yavanala, Yugandhara (Sanskrit), Macca Cholam, Makka Colam, Makka-Cholam, Makkac-Colam, Makkaccolam, Makkasholam, Mokkaiccoolam, Turka-Cholam (Tamil), Jonnapothu, Makka-Zonnalu, Makkazonnalu, Mokka, Mokka Javanalu, Mokka Jonna, Mokka-Jonna, Mokkajanna, Mokkajonna, Mokkajonnalu, Mosanam, Zonaloo (Telugu), Anaaj, Makai, Makka (Urdu);
Indonesia: Jajong, Jagung, Jagung Manis;
Hmong Daw: Pob Kws, Pob Kws Qab Zib;
Irish: Arbhar Indiach;
Isle On Man: Praase (Gaelic);
Italian: Formentone, Grano Di Turchia, Granoturco, Granoturco Da Zucchero, Granturco, Mais, Mais Dolce, Mais Zuccherino;
Ivory Coast: Kanian (Dagari), Kamana (Gourounsi);
Japanese: Fiirudo Koon, Tomorokoshi;
Kamba: Mbemba;
Kashmiri: Dŏda-Hĕdur; Maköyü;
Kazakh: Sacharnaja Kukuruza, Zhügeri;
Kenya: Mbembe (Kikuyu), Mûcakwe;
Khmer: Pôôt;
Kirghizstan: Jügörü, Kanttuu Žugeru;
Kiribati: Kaon;
Korean: Ok Soo Soo, Kangnaengi;
Kurdish: Gēnmēsāmi;
Laotian: Khauz Ph'ô:D, Khauz Sa:Li;
Latvian: Cucurkukurūza, Kukurūza;
Liberia: Gbu (Basa), Baai (De), Gbado, Gbai (Kpelle), Yibo, Yubwσ (Kru-Grebo), Gbáazi (Loma), Nyσ (Manding-Maninka), Kpai (Mano), Nyoru (Vai),' Gbuu, Pamu (Kru);
Lithuanian: Daržo Kukurūzai, Paprastasis Kukurūzas;
Luxembourg: Mais;
Macedonian: Slatka Pčenka;
Madagascar: Somo-Katsaka;
Malaysia: Jagung, Jagung Manis;
Mali: Kaba (Bambara), Mako (Khasonke), Manyò (Manding-Bambara);
Maltese: Qamh Ir-Rum;
Mauritius: Maïs;
Mongolian: Erdene Shish;
Morocco: Drâ, Drâ I-Hamra (Arabic), Âssengar, Tasengart: (Berber), Maïs (French), Mâser (Tecna), Mekkâ, I-Mekki (Moresque), Dra Squib (Tatouane Province), Tifsî Engafulî, Gafulî (Touareg);
Nepal: Makai;
Nicobar Islands : Peòk (Car);
Niger: Kòtòkòalí (Dendi), Makkari, Massaru (Fula-Fulfulde) Kólgótí, Kolkoti (Song-Hai);
Nigeria: Ansam (Agoi), Ejama, Esut (Agwagwune), Īkpāngkpà (Akpa), Ekpoi (Akpet-Ehom), ọka (Aoma), Dura Shami, Masar, Umm Abât, Umn Abat (Arabic-Shuwa), Kâ K'pa, Kúmkpà, Kũkpa (Ashuku), Anjam (Bakpinka), Sięk (Bandawa-Minda), Daené, Dawai, Mapinawo (Bata), Aku Kwan (Batu), Yara Kàpas (Birom), Ajo Kwana (Bitare), Nkurung (Bokyi), Damasar, Damasr (Bole), Pinau, Pino (Bura), Dir Kwozak (Chawai), Masiri (Chawai-Janji), Mìkĩ (Chomo), Ápónò (Dera), Ansam (Doko-Uyanga), Aagba, Aagwa, Agwawa (Ebira-Etuno), Ka, Oka (Edo), Ìbòkpòt, Ìbòkpòt Úmòn (Efik), Ekpai

(Ehom), Nchamm (Ejagham), Áka (Engenni), Àkân (Epie), Ókà (Eruwa), ọka (Esan), Nggulia (Fali), Butaali, Kaba (Fula-Fulfulde), Puno (Ga'anda), Pimisire, Pitigadin (Gbiri-Niragu), Som Kiva (Gengle),Okà (Ghotuo), Àmbàbât, Ngguleˌ (Gude), Gau Buza, Zakzak (Gudu), Dákú-Hye (Gwandara-Cancara), Agbado, Nyawi, Nyiawie (Gwari), Agwado, Dááwàr Másàr, Dawaa Baa Másàráá (Huasa), Hi Buku Hibéku (Huba), Panu (Hwana), Gupara (Hyam), Àkpà-Akpa, Akpakpa, Àkpàkpà (Ibibio), Amirkpa, Makpa, Mkpà (Icen), Ikpapka, Ọ̀gbàdụ, ọkà (Igbo), ịzọ́n Áká (Ijo-Izon), Ọ́kaa (Isoko), Àlàkpà (Ivbie), Ihwẹ (Janjo), Likam (Jara), Acim (Jiru), Azankpa, Kpankara, Za Kwa, Zaakim, Zakeim, Zakim, Zakpa, Zamkp (Jukun), Amaû (Jukun-Jibu), Nywat Épat, Yakpat (Kaje), Gọmbi (Kaka), Khàrẹ̀bì (Kambari-Auna), Limasára (Kamuku), Khauwa, Khavwa (Kamwe), Damasar, Damasr (Karekare), Àrgêm, Másàr, Masarmi (Kanuri), Dákúše (Karshi), Suwa Kpat, Okpat (Katab), Shwa Pa, Silok Akpat, Solak Akpat, Swá Pa (Katab-Kagoro), Nkwi (Korop), Aakalaaba (Kuda-Cham), Som Kiva (Kugama), Sopa (Kumba), Imasarim (Kurama), Khiya Masere, Masar (Kyibaku), Babir (Laamang), Akpe (Lenyima), Kwang Ufa (Libo), Esahma (Loke), Apenwa (Longuda), Nsam (Lubilo), Fuan (Magu), Idãnyagọ (Mala), Kọọm, Tap (Mambila), Apanau, Khiya Masere, Masar (Margi), Óghàk-Kpà (Mbembe), Fatuma (Mboi), Misakono (Mbula), Izitura (Mumbake), Za Ki, Zagin, Zakin (Mumuye), Mom Kwaẹ (Munga), Kâ-G'ba, Kumkpa (Nama), ẹ- Gú (Nde), Akwana (Ndoro), Haigim, Masar (Ngamo), Másármì (Ngizim), Dáza (Nimbia), Isangkpar (Ninzam), Nshamm (Nkukoli), Aakaaba, Káawa, Kàba (Nupe), Kwon Ga (Nyamnyam), Mapinawe, Mapinawin (Nzangi), Ọ̀bḭ̀àkà (Obulom), Kpákìrà (Ogoni-Gokana), Úbaakpâ (Okpamheri), ẹ̀-Gû, Ì-Gù (Olulumo), Diptura (Perema), Kóomò (Pero), Idal Tibok, Tibok: Hat (Piti), Kilbokta, Komberi Ma (Roba), Kkárábú (Salka), Ka Yiri, Kááda, Kai, Kaii (Samba-Daka), Idi-Manseri (Sanga), Tsaa Kpat (Sholio), Mu Buba (Somyewe), Béng Shwàa (Sura), Kofa (Teme), Likám (Tera), Jẹrldi, Pinodi (Tera-Pidlimdi), Gombie (Tikar-Nkom), Ikuleke, Ikuleko, Ikureke (Tiv), Dákúše (Toni), ọgbado (Uhami-Iyayu), Σσka (Ukue), Igbadoo (Ukue-Ehuen), Akpoi (Umon), ọka (Urhobo), Àgbàdo, Àgwàdo, Egbáado, Ìgbàdo, ọkà, Óoka, Yángán (Yoruba), Kụl Bọkta (Yungur);

Niuean: Ahi, Ahi Taina, Hana;

Norwegian: Mais, Sukkermais;

Persian: Bajri, Gandume-Makkah, Gaudume-Makkah, Gaudumemakkah, Hintahe-Rumi, Khoshahe-Makki, Khoshahemakki;

Philippines: Mais (Bisaya), Igi, Mais,Ngeya, Tibi, Tigi, Tongnga (Bontok), Mañgi (Ibanag), Gahilang (Igorot), Mais (Ilocano), Mait (Itogon), Mait (Itawit), Mais (Pampangan), Mais (Tagbanwa), Mais (Tagalog);

Polish: Kukurydza Cukrowa;

Portuguese: Milho, Milho Doce, Milho Forrageiro, Milho Grande; Milho Grosso; Milho-Maeês;

Romanian: Porumb, Porumb Zaharat;

Russian: Kukuruza, Sacharnaja Kukuruza;

Rwanda: Ibigori;

Samoan: Fiso, Sana;

Scottish: Cruithneachd (Gaelic);

Senegal: Ekôntibaba, Ékuntubaba, Sikutumbara, Husit, Sitikon (Diola), Kumorha (Diola-Flup), Maka, Makarbodiri, Makari, Mala (Fula-Pulaar), Mańo (Manding-Bambara), Mańo (Mandinka), Búmaagi (Mandyak), Mańo (Maninka), Bala, Maka, Makarbodiri (Peul), Mumbáawo, Púmaidsi, Pursin (Serer), Maka (Soninke-Sarakole), Bala, Gwari Makka, Makarbodiri, Makka, Mala, Sataba (Tukulor), Maka, Makandé, Mbogi, Mboha, Mboxa, Morha, Wende (Wolof), Mańo (Soce);

Serbian: Kukuruz, Kukuruza Obyknovennaia;

Seychelles: Maïs;

Shona: Bonore, Chibage, Chibahwe, Chibarwe, Chibere, Hupfu, Upfu;

Sierra Leone: Kã, Kã-Moɛ, Kaŋ-Dɛ, Khàŋ, Nkan, Nkang-Ntol, Nkison, Nkuskus (Bulom), Kaaba (Fula-Pulaar), Di, Diomɔkɔ, Kedĭ (Gola), Soã, Swahu (Kissi), Nyuɛ (Kono), Nyõ (Koranko), Kɔn (Krio), Kutanki, Taŋki, Teher-Baŋwuridi (Limba), Dahɔyɔ, Nyɔ (Loko) Kama (Manding-Mandinka), Nyɔ, Nyoo (Mende), Kaabɛ, Kabe (Susu), A-Mank (Temne), Nyóoroo, Nyɔrɔ, Nyuɛ, Tama-Nyɔ (Vai), Kabé-Na (Yalunka);

Slovaščina: Koruza, Koruza;

Slovencina: Kukurica Siata;
Sorbian: Kukurica, Majs (Lower), Kukurica, Kurjace Woko, Majs (Upper);
Sotho: Mahea, Poone;
South Africa: Mafela, Mavhele, Mielies, Suikermielie (Afrikaans), Mmidi, Mmopo, Umbila, Umbona;
Spanish: Cabellitos De Elote (Silk Of Immature Cob), Choclo, Elote (Immature Cob), Mazorca De Maíz, Maíz, Maíz Azucarado, Maíz Comun, Maíz Dulce, Maíz Tierno, Mijo Turquesco, Trigo De Indias;
Sudan: Manio (Bambara), (Malinke), Maka (Kasombe), Mako (Sominke);
Swahili: Mahindi, Mhindi, Punje, Mafaka, Ngano, Gunzi, Kigunzi;
Swedish: Majs, Sockermajs;
Tajikistan: Juvorimakka;
Tanzania: Dana, Mambatu'a, N/Ini (Sandawe);
Tongan: Koane;
Thai: Khaophot, Khaaophot On (Baby Corn);
Tibetan: Āshom;
Togo: Bli (Ewé), Ebli (Mina);
Tongan: Cingoma;
Turkish: Kokoroz, Mısır, Tatli Misir;
Turkmen: Mekgejöwen, Adaty Mekgejöwen;
Uganda: Duma;
Uyghur: Qonaq;
Uzbek: Makkajo'xori, Maccadjukhory;
Ukrainian: Cukrova Kukurudza;
Welsh: Corn Melys;
West Cameroons: Ngui (Bafok), Ánsáng (Bafut), Mbàsì (Duala), Ngun (Koosi), Mbasi, Mukala (Kpe), Ngui, Ngwi (Kundu), Ngui (Long), Begbabo (Lundu), Mgbi (Mbonge), Kwata, Ngesáng (Ngyemboon), Mbwe (Tanga), Gombie (Tikar-Nkom), Mbasi (Wovea);
Vietnamese: Ngô;
Yiddish: Kukuruzeh;
Zapotec: Lox Yela' (Silk Immature Cob);
Zulu: Mbila, Ummbila, Umumbu.

Origin/Distribution

Maize has its centre of origin in Mesoamerica, probably in the Mexican highlands from where it spread. Archaelogical data and phylogenetic analysis suggested that domestication of maize in Mexico began at least 6,000 years ago (Piperno and Flannery 2001). Maize was disseminated around the world after the European discovery of the Americas in the fifteenth century. It is now cultivated globally. Maize is only known in cultivation and its exact genealogy remains unclear.

Agroecology

Maize is cultivated from latitude 58°N in temperate Russia and Canada, throughout the subtropics and tropics, to latitude 42°S in South America and New Zealand, and in areas below sea level in the Caspian Plain up to a high altitude of 3,800 m in Peru and Bolivia. Maize is adapted to a wide range of agro-ecological environments but is essentially a crop of warm climate with the bulk of the crop being cultivated in tropical and subtropical regions. Maize requires an average daily temperature of at least 20°C for adequate growth and development, and warm daytime temperatures of 25–30°C and cool nights for optimum growth and development (Colless 1992). Temperatures above 35°C depress yields; temperatures below 8°C and above 40°C are extremely detrimental, causing cessation of growth. High temperature stress imposes adverse impact on kernel growth, kernel mass and endosperm zein protein accumulation (Jones et al. 1984, 1985; Monjardino et al. 2005, 2006). Maize is intolerant of frost. It cannot survive temperatures below 0°C for more than 6–8 h at the 5–7 leaf stage; damage from sub-zero temperatures, however, depends on the extent of temperatures below 0°C, length of freezing temperatures, soil condition, residue, wind movement, relative humidity, and stage of plant development (Hanway 1966). Light frosts in late spring in temperate areas can cause leaf scorching. Maize requires abundant sunlight for optimum yields and is deemed a quantitative short-day plant. The time of flowering is influenced by photoperiod and temperature.

Rainfall is a limiting factor to dry-land commercial maize production and irrigation is required in areas with dominant winter rainfall or

where amount of summer rain is highly variable (Birch et al. 2003). In the tropics, maize performs best in areas with 600–900 mm well-distributed rainfall during the growing season. Maize is less drought-tolerant than sorghum, pearl millet and finger millet. It is especially sensitive to water stress or drought and high temperatures around the time of flowering (Colless 1992; Birch et al. 2003). Significant yield losses can be caused by water-logging (Srinivasan et al. 2004).

Maize is adaptable to a wide range of soils (Norman et al. 1995), but thrives best on well-drained, well-aerated, deep soils containing adequate organic matter and well supplied with nutrients. It can be grown on soils with a pH of 5–8, but 5.5–7 is optimal. In the tropics oxisols, ultisols, alfisols and inceptisols are most suitable for maize production. Of particular concern is aluminium toxicity for maize on acid tropical soils; this however can be surmounted by liming. Maize is sensitive to soil salinity (Kaddah and Ghowali 1964).

Edible Plant Parts and Uses

Maize grain is the basic staple food for the population in many countries of Latin America and Africa and an important ingredient in the peoples 'diet'. Globally, just 21% of total maize production is consumed as food (OGTR 2008). Within the United States, the usage of maize for human consumption constitutes about 1/40th of the amount grown in the country.

Young, immature cobs of the sweet corn type are harvested 18–20 days after pollination and are used as vegetable (Plates 4 and 5). Very young female inflorescences ('baby cobs') are relished as a fancy vegetable in stir fries or salad in Western countries and in Asia. Sweet corn kernels are boiled or steamed and often used as a pizza topping, in salads or garnishes. Alternatively, the raw unripe kernels may also be shaved off the cobs and processed into a variety of cooked dishes, such as maize purée, tamales, *pamonhas* (Brazilan food, paste made from fresh corn and milk and boiled wrapped in corn husks), *curau* (Brazilian sweet custard-like dessert made from the expressed juice of unripe maize, cooked with milk and sugar), cakes, ice creams, etc. Corn on the cob is a sweet corn cob that has been boiled, steamed, or grilled whole; the kernels are then eaten directly off the cob or cut off. Corn on the cob is a common dish in the United States, Canada, United Kingdom, Cyprus, some parts of South America, and the Balkans. Creamed corn is sweet corn kernels served in a milk or cream sauce or in soups. In Mexico, immature corn smut galls are relished as an edible delicacy known as *cuitlacoch*e, and sweet corn smut galls have become a high value crop for some growers in the northeastern United States who sell them to Mexican restaurants. Corn smut is an extremely common disease of sweet, pop, and dent corn throughout the world. Roasted dried maize cobs with intact semi-hardened kernels, coated with a seasoning mixture of fried chopped spring onions with salt added to the oil, is a popular snack food in Vietnam. Another very popular type of corn is popcorn which explodes when heated into puffed, fluffy corn which is a popular snack food eaten all over the world. *Cancha* a homemade Andean snack consists of toasted corn kernels which pop without puffing and is made from a special large-grained corn called maize chulpe. *Cancha* is a popular snack in Peru and Ecuador. *Cancha* also appears in Peruvian *ceviche* (latinoamerican seafood dish). Dried maize kernels are also processed into *hominy* or *nixtamal* or by soaking and cooking in an alkali solution usually lime and hulled. *Hominy* or *nixtamal* are commonly consumed in southeastern United States. The Brazilian dessert *canjica* is made by boiling maize kernels in sweetened milk. Tepache, maize beer also know as chichi, a light refreshing beer, is also made from maize kernels and is consumed throughout Mexico, but nowadays various fruits such as pineapple, apple and orange are used. *Chicha* a fermented and alcoholic drink and *chicha morada* (purple chicha) a soft drink, are made from special types of maize and consumed in Peru. Bourbon whisky is made from mash that contains more than 51% of corn. Corn flakes made from milled corn, is widely consumed as a crispy breakfast cereal, popular in North America and the United Kingdom, and in many other countries all over the world.

Maize meal (ground dried maize) is made into various types of porridge or cooked corn meals in various cultures such as *polenta* in Italy, *angu* in Brazil, *mămăligă* (porridge of yellow corn) of Romania, *meali pap* in south Africa, *sadza*, *nshim*a and *ugali* in other parts of Africa, *hominy* in south-eastern USA or *cornmeal mush* in other parts of USA. Maize dough or corn flour is also used as a replacement for wheat flour, to make cornbread and other baked products. An unleavened corn bread called *makki di roti* is a popular bread eaten in the Punjab region of India and Pakistan. *Masa* or corn dough is made from freshly prepared *hom-in*y, and is used for making corn *tortillas* (flat, cornbread), *tamales* (steamed or boiled *masa* wrapped in leaf wrapper), *tostadas* (bowl-shaped tortilla toasted or deep fried), *pupusas* (a traditional Salvadoran dish made of thick, hand-made corn *tortilla*), *arepas* (corn cakes made from precooked corn flour, salt and water), *pozole* (soup or stew), *pinole* (corn drink made from coarse corn flour from toasted kernels mixed with other seeds and herbs), *atole* (masa based hot drink) and many other Latin American dishes.

Corn starch is a well-known product in its own right and is also used in the manufacture of raw material for extractive industries and on a number of industrial traits such as: high fructose corn syrup, fuel alcohol, starch, glucose, and dextrose (Tsaftaris 1995) and is a major ingredient in home cooking. The starch is widely used for a number of purposes in cooking, as in the making of deserts and the thickening of gravy, soups, etc. Corn starch has the advantage of being almost tasteless. The glucose (corn syrup) is not as sweet as that of case sugar. It is much used in combination with cane sugar and maple syrup, and also in the manufacture of jams, jellies, and other sweets. Maize starch can be hydrolyzed and enzymatically treated to produce syrups, particularly high fructose corn syrup, a sweetener; and also fermented and distilled to produce grain alcohol. Grain alcohol from maize is traditionally the source of Bourbon whiskey. Maize is also a major source of cooking oil (corn oil) and of maize gluten. Corn oil is oil extracted from the germ of maize. Its main use is in baking and cooking, where its high smoke point makes refined corn oil a valuable frying oil. Corn oil is also a key ingredient in some margarine.

Botany

Zea mays is a tall, monoecious annual grass, 1.1.2 m high with a single erect stem made up of nodes and internodes. Leaves broadly linear 50–10 cm long by 3–7 cm wide arranged distichously, with leaf sheath surrounding the stem (Plates 1 and 2). Male flowers in terminal open, branched panicle, (tassel) (Plate 3) spikelets 9–14 mm, lower glume lanceolate, pubescent, keeled, long-ciliate, 9–11-nerved, as long as the spikelet; upper glume oblong-lanceolate, 7- nerved, nearly as long as the lower; lower lemma minutely hairy on the back and margins, 3-nerved; palea as long as the lemma; upper lemma smaller than the lower palea; anthers 3 orange, about 6 mm long. Female inflorescence consist of sessile spikelets densely arranged in many vertical rows on a fleshy cylindrical axis (cob), glumes equal, veinless, margins ciliate; florets hyaline, from each floret style begins to elongate towards the tip of the cob, forming long threads or silks. The silks have short hairs, trichomes, which form an angle to the stylar canals and help to capture pollen grains. Receptive silks are moist and sticky. Pistillate inflorescence is enclosed by numerous foliaceous bracts and matures into ear or cob (Plates 1, 3, 6, and 7). The fruit of maize is a caryopsis, a dry indehiscent single seeded fruit. The pericarp (ovary wall) and testa (seed coat) are fused to form the fruit wall. Fruit also called kernel or grain and seed. Kernel composed of three main parts – the embryo, endosperm and fruit wall. Each ear contains 200–400 kernels which can be variously coloured blackish, bluish-gray, purple, green, red, white and yellow (Plate 7).

Nutritive/Medicinal Properties

Nutrients in Corn Kernels

Proximate nutrient composition of raw, yellow sweet corn per 100 g edible portion was reported

Plate 1 (**a**, **b**) Corn leaves and young cobs with apical buanch of silks

Plate 2 Male inflorescence

Plate 3 Mature corn cobs

Plate 4 Young immature cobs harvested for baby corn

Plate 5 Close-up of baby corn cob used as vegetables

Plate 6 Harvested corn cobs for sale in local market

Plate 7 Mature con cobs with ripe yellow kernels

as: water 76.05 g, energy 86 kcal (360 kJ), protein 3.27 g, total lipid 1.35 g, ash 0.62 g, carbohydrate 18.70 g, total dietary fibre 2.0 g, total sugars 6.26 g, sucrose 0.89 g, glucose 3.43 g, fructose 1.94 g, starch 5.70 g, Ca 2 mg Fe 0.52 mg, Mg 37 mg, P 89 mg, K 270 mg, Na 15 mg, Zn 0.46 mg, Cu 0.054 mg, Mn 0.163 mg, Se 0.6 µg, vitamin C 6.8 mg, thiamine 0.155 mg, riboflavin 0.055 mg, niacin 1.770 mg, pantothenic acid 0.717 mg, vitamin B-6 0.093 mg, total folate 42 µg, total choline 23 mg, vitamin A 9 µg RAE, β-carotene 47 µg, α-carotene 16 µg, β-cryptoxanthin 115 µg, vitamin A 187 IU, lutein + zeaxanthin 644 µg, vitamin E (α-tocopherol) 0.07 mg, γ-tocopherol 0.15 mg, vitamin K (phylloquinone) 0.3 µg, total saturated fatty acids 0.325 g, 10:0 (capric) 0.003 g, 12:0 (lauric) 0.001 g, 14:0 (myristic) 0.001 g, 15:0 (pentadecanoic) 0.001 g, 16:0 (palmitic) 0.262 g, 17:0 (margaric) 0.001 g, 18:0 (stearic) 0.045 g, 20:0 (arachidic) 0.007 g, 24:0 (lignoceric) 0.003 g, total monounsaturated fatty acids 0.432 g, 14:1 (myristoleic) 0.002 g, 16:1 undifferentiated (palmitoleic) 0.004 g, 16:1 *cis* 0.004 g, 18:1 undifferentiated (oleic) 0.419 g, 18:1 *cis* 0.416 g, 18:1 *trans* 0.003 g, 20:1 (gadoleic) 0.006 g, total polyunsaturated fatty acids 0.487 g, 18:2 undifferentiated (linoleic) 0.472 g, 18:2 n-6 *cis*,*cis* 0.468 g, 18:2 *trans* 0.004 g, 18:3 n-3 *cis*,*cis*,*cis* (ALA) 0.014 g, 20:4 undifferentiated (arachidonic) 0.001 g, total *trans* fatty acids 0.007 g, fatty acids, total *trans*-monoenoic 0.003 g, tryptophan 0.023 g, threonine 0.129 g, isoleucine 0.129 g, leucine 0.348 g, lysine 0.137 g, methionine 0.067 g, cystine 0.026 g, phenylalanine 0.150 g, tyrosine 0.123 g, valine 0.185 g, arginine 0.131 g, histidine 0.089 g, alanine 0.295 g, aspartic acid 0.244 g, glutamic acid 0.636 g, glycine 0.127 g, proline 0.292 g and serine 0.153 g (USDA 2012).

Proximate nutrient composition of raw, white sweet corn per 100 g edible portion was reported as: water 75.96 g, energy 86 kcal(358 kJ), protein 3.22 g, total lipid 1.18 g, ash 0.62 g, carbohydrate 19.02 g, total dietary fibre 2.7 g, total sugars 3.22 g, Ca 2 mg Fe 0.52 mg, Mg 37 mg, P 89 mg, K 270 mg, Na 15 mg, Zn 0.45 mg, Cu 0.054 mg, Mn 0.161 mg, Se 0.6 µg, vitamin C 6.8 mg, thiamine 0.200 mg, riboflavin 0.060 mg, niacin

1.700 mg, pantothenic acid 0.760 mg, vitamin B-6 0.055 µg, total folate 46 µg, total choline 23 mg, β-carotene 1 µg, vitamin A 1 IU, lutein + zeaxanthin 34 µg, vitamin E (α-tocopherol) 0.07 mg, γ-tocopherol 0.15 mg, vitamin K (phylloquinone) 0.3 µg, total saturated fatty acids 0.182 g, 16:0 (palmitic) 0.171 g, 18:0 (stearic) 0.011 g, total monounsaturated fatty acids 0.347 g, 18:1 undifferentiated (oleic) 0.347 g, total polyunsaturated fatty acids 0.559 g, 18:2 undifferentiated (linoleic) 0.542 g, 18:3 undifferentiated (linolenic) 0.016 g, tryptophan 0.023 g, threonine 0.129 g, isoleucine 0.129 g, leucine 0.348 g, lysine 0.137 g, methionine 0.067 g, cystine 0.026 g, phenylalanine 0.150 g, tyrosine 0.123 g, valine 0.185 g, arginine 0.131 g, histidine 0.089 g, alanine 0.295 g, aspartic acid 0.244 g, glutamic acid 0.636 g, glycine 0.127 g, proline 0.292 g and serine 0.153 g (USDA 2012).

The primary carotenoids in fresh market sweet corn were found to be lutein and zeaxanthin, with γ-tocopherol predominating among the tocopherols (Kurilich and Juvik 1999). Mean values among the sweet and dent corn genotypes were observed to range from 0 to 20.0 and 2.4 to 63.3 µg/g dry weight for lutein and γ-tocopherol.

Typical mature kernel comprises 70–75% starch, 8–10% protein and 4–5% oil (Boyer and Hannah 1964). The two major structures of the kernel are the endosperm and embryo (germ), making up 80 and 10% of the kernel dry weight respectively. Maize endosperm is largely starch (about 90%) and the germ contains high levels of fats (about 433%) and protein about 18%. Starch contains two types of glucose homopolymers, amylase and amylopectin. In amylase, the glucose residues are mainly linked via α-1, 4 linkages which results in a linear chain. In amylopectin, the majority of the linkages are α-1, 4 linkages with α-1, 6 linkages providing the branching.

Storage protein (a 7S globulin) was found in the embryo and endosperm. The relative content of protein was found highest in the embryo but because the endosperm comprised a greater part of the kernel, it contributed greater amount of protein. The endosperm protein was reported to be divided into prolamins, collectively referred to as zeins, comprising about 52% of kernel nitrogen, glutelin (ca 25% of kernel nitrogen), albumins (ca 70%) and globulins (ca 5%) (OGTR 2008). Normal and Opaque corn cultivars showed different contents of corn proteins (Ortiz de Bertorelli and Guerra 1983). The latter showed a low level of zein and a high content of alcohol-insoluble reduced glutelins (AIG), albumins and globulins in relation to the normal kernel. The relative increase of these protein fractions, rich in lysine and tryptophan, resulted in a higher concentration of these amino acids in the opaque kernel. Ortíz de Bertorelli (1993) found that zeins accounted for 36.57% of the total protein present in normal corn grain and 9.38% in Opaque-2 corn. Prolamines presented a soluble fraction in 95% ethanol (α zeins) which represented 33, 12% of zeins and another insoluble (β zeins) the 66.88%.

Lipids (oil) are found mainly in the embryo more specifically the scutellum (OGTR 2008). The embryo contains about 33% oil, while a typical kernel contains about 4% oil. Fatty acids in corn oil always occur esterified to the hydroxyl groups of glycerol forming triacylglycerides which contain a mixture of saturated and unsaturated fatty acids. Maize contains low levels of anti-nutrient such as phytate which chelate metal ions including iron and making them inaccessible to humans and other animals. Another anti-nutrient in maize is raffinose which is indigestible and is responsible for gas production and resulting in flatulence. It can be removed from food and feed by soaking, cooking and irradiation or by enzyme or solvent treatment (OECD 2002). Both trypsin and chymotrypsin inhibitors are present in low levels in maize (OECD 2002). They are not considered important for human or animal nutrition.

Zeins were isolated from corn ethanol coproduct distiller's dried grains (DDG) and fractionated into α- and β γ-rich fractions (Paraman and Lamsal 2011). Around 29–34% of the total zein was recovered from DDG, whereas 83% of total zein was recovered from corn gluten meal (CGM). Compared to the α-zein of CGM, the α-zein of DDG showed lower recovery and purity but retained its solubility, structure, and film forming characteristics, indicating the potential of producing functional zein from a low-value co-product for uses as industrial bio-based product.

Other Phytochemicals in Corn Kernels

Dehydrodiferulic acids (DFA) (8-5′- DFA, 8-8′-DFA, 5-5′-DFA, 8-*O*-4′-DFA, 4-O-5′ DFA) could be identified in both insoluble dietary fibre (IDF) and soluble dietary fibre (SDF) of corn grains (Beunzel et al. 2001). Total dehydrodiferulic acid in IDF of corn was quantified as 12,596 μg/g, in SDF 58 μg/g. In corn, amount of 8-5′-DFA reached up to 37.7% in IDF and 36.5% in SDF; 8-8′-DFA 16.5% in IDF and 39.8% in SDF; 5-5′-DFA 24.9% in IDF and 11.9% in SDF; 8-*O*-4′-DFA 20.6% in IDF and 11.8% in SDF; 4-*O*-5′ DFA 0.3% in IDF and not detected in SDF.

Similar anthocyanin composition (cyanidin 3-monoglycosides) and concentration (314 mg/kg) was observed for both blue corn genotypes as was their non-anthocyanin polyphenolic composition ((+)-catechin, free and esterified ferulic acid, and *p*-coumaric acid derivatives) (Pozo-Insfran et al. 2006). Six derivatives of ferulic acid (88.8–816 mg/kg) along with the free form (2,480 mg/kg), *p*-coumaric acid (6.6 mg/kg), two protocatechuic acid derivatives (4.2 and 14.2 mg/kg), and gallic acid (3.9 mg/kg) were identified in the white corn genotype. In nine Bolivian purple corn (four red and five blue) varieties, ferulic acid values ranged from 132.9 to 298.4 mg/100 g, and *p*-coumaric acid contents varied between 251.8 and 607.5 mg/100 g dry weight (DW), and were identified as the main nonanthocyanin phenolics (Cuevas Montilla et al. 2011). The total content of phenolic compounds ranged from 311.0 to 817.6 mg gallic acid equivalents (GAE)/100 g DW, and the percentage contribution of bound to total phenolics varied from 62.1 to 86.6%. The total monomeric anthocyanin content ranged from 1.9 to 71.7 mg cyanidin-3-glucoside equivalents/100 g DW. Cyanidin-3-glucoside and its malonated derivative were detected as major anthocyanins. Several dimalonylated monoglucosides of cyanidin, peonidin, and pelargonidin were present as minor constituents. Cell wall-bound ferulic acid dehydrodimers and dehydrotrimers namely the 5-5/8-O-4-, 8-O-4/8-O-4-, and 8-8(aryltetralin)/8-*O*-4-dehydrotrimers were found in minor levels in cereals including corn (Dobberstein and Bunzel 2010). Of 26 Brazilian maize landraces, the Roxo 41 purple-coloured landrace showed the highest concentration of pigments, e.g. 11.72 10^{-3} g/kg of total carotenoids and 2.16 g/kg of total anthocyanins (Kuhnen et al. 2011). Similarly, the yellow-coloured MPA 1 and the purple-coloured Roxo 29 landraces showed prominent amounts of carotenoids (10.86 10^{-3} g/kg) and anthocyanins (2.60 g/kg), respectively. The major carotenoids detected in the whole grain flour were zeaxanthin and lutein.

Three major sterols found in developing maize kernels were sitosterol, campesterol and stigmaterol (Davis and Poneleit 1974). Sterol levels in three inbred lines ranged from 173 to 235 μγ per kernel. Sitosterol accounted for 75–85% of the sterols. Cholesterol was found at level of <1% of the dry weight. Free sterols and steryl esters were the major sterol fractions and steryl glycosides and acylated steryl glycosides were only minor components during kernel development. Unrefined corn oils had ester levels from 0.18 to 8.6 mg/g for oil from hexane-extracted bran and the predominant esters from corn were sitostanyl and campestanyl ferulate, and sitostanyl and campestanyl *p*-coumarate (Norton 1995).

Nutrients and Phytochemicals in Corn Silk

Corn silk is an excellent source of many bioactive compounds such as volatiles, phenols, flavonoids, saponins, alkaloids, tannins, chlorogenic acid, phytosterols, allantoin, vitamin E and K. β-sitosterol was found to be one of the major phytoconstituents in cornsilk (Sarfare et al. 2010). They found that β-sitosterol was absorbed when administered in rabbits in the form of slurry of powdered cornsilk confirming significant bioavailability β-sitosterol from cornsilk and the potential use of cornsilk as a natural source of β-sitosterol. Corn silk and kernel were found to contain epicatechin, rutin, ascorbic acid, kaempferol, chlorogenic acid and quercetin (Lin et al. 2007). The leaf contained epicatechin and rutin, vitamin C, kaempferol and quercetin. Corn silk was found to contain very high chlorogenic acid level, about 200 times that in the kernel. Corn silk

was found to be rich in allantoin with a concentration range between 215 and 289 mg per 100 g of dry plant material (Maksimović et al. 2004). Allantoin was also detected in seed and corn silk and the amount of allantoin in samples found was between 14 and 271 mg/100 g of dry plant material (Haghi et al. 2008).

Proximate nutrient value of corn silk was reported by Wan Rosli et al. (2008) as follows: fresh corn silk 83.91% water content, 1.28% crude lipid, 0.18% nitrogenous compound, 7.60 %ash, 0.00% soluble dietary fibre, 0.00% insoluble dietary fibre, 0.0% total dietary fibre; aqueous extract of corn silk : 1.40% crude lipid, 01.40% nitrogenous compound, 21.55%ash, 0.05% soluble dietary fibre, 0.00% insoluble dietary fibre, 0.05% total dietary fibre, and ethanol extract of corn silk: 28.63% crude lipid, 0.41% nitrogenous compound, 6.11 %ash, 0.00% soluble dietary fibre, 0.08% insoluble dietary fibre, 0.08% total dietary fibre. Crude lipids content of ethanolic corn silk extract recorded the highest value (28.0%) compared to fresh (1.30%) and water extracts (0.20%).Water extract sample recorded the highest amount of ash (21.55%) compared to the fresh corn silk and ethanolic extract which recorded lower percentage of ash (7.60 and 6.11%), respectively. Further analysis of macro and micro-minerals of the ash revealed that Ca, Mg, Fe, Na, K, Cu, Zn and Mn were present at the highest concentration in water extract corn silk as compared to other samples (Wan Rosli et al. 2008).

Sixty-three volatile compounds were identified in corn silk with alcohols predominating 2-heptanol as the major constituent (Flath et al. 1978). A highly odorous compound, geosmin, was found among the volatiles. Volatile compounds emitted by corn silk were found to be 1-butanol, 1-pentanol, 1-hexanol, (E)-4-hexen-1-ol, 3-methyl-1-butanol, acetaldehyde, 2-furancarboxaldehyde (furfural) and phenylacetaldehyde (Cantelo and Jacobson 1979). A total of 44 compounds were identified in Korean corn silk including 9 alcohols, 7 aldehydes and ketones, 14 terpenes and terpene alcohols, 3 pyrazines, 5 hydrocarbons and 6 miscellaneous compounds (Kwag et al. 1999). The major components were 2-propanol (8.08%), nonal (7.93%), heptanal (7.40%), hexanal (3.68%), hexanol (2.86%), decanal (2.04%), α-copaene (2.20%), pentanol (1.82%), limonene (1.68%), β-caryophyllene (1.43%), α-selinene (1.03%), and β-selinene (1.03%). A total of 36 compounds, which comprised 99.4% of the extract, were identified in the volatile dichloromethane extract obtained from Egyptian corn silk (El-Ghorab et al. 2007). The main constituents of the volatile extract were *cis*-α-terpineol (24.22%), 6,11-oxidoacor-4-ene (18.06%), citronellol (16.18%), *trans*-pinocamphone (5.86%), eugenol (4.37%), neo-iso-3-thujanol (2.59%), and *cis*-sabinene hydrate (2.28%).

Five flavonoid monomers were isolated from corn silk (Ren et al. 2009). Two were novel flavones glycosides identified as 2″-*O*-α-L-rhamnosyl-6-C-3″-deoxyglucosyl-3′-methoxyluteolin and 6,4′-dihydroxy- 3′-methoxyflavone-7-*O*-glucoside. Three identified as ax-5″-methane-3′-methoxymaysin, ax-4″-OH-3′-methoxymaysin and 7,4′-dihydroxy-3′-methoxyflavone-2″-*O*-a-L-rhamnosyl-6-C-fucoside had been previously isolated and identified (Ren and Ding 2004, 2007). The three major C-glycosyl flavones isolated from maize (*Zea mays*) silk tissue, maysin [2″-*O*-α-L-rhamnosyl-6-C-(6-deoxy-xylo-hexos-4-ulosyl) luteolin], apimysin [2″-*O*-α-L-rhamnosyl-6-C-(6-deoxy-xylo-hexos-4-ulosyl) apigenin] and 3′-methoxymaysin [2″-*O*-α-L-rhamnosyl-6-C (6-deoxy-xylo-hexos-4-ulosyl)-3′-methoxyluteolin] in high concentration conferred natural resistance to corn ear worm, *Heliotis zea* (Waiss et al. 1979; Elliger et al. 1980; Snook et al. 1993, 1994, 1995). Maysin levels ranged from 0 to 0.9% fresh weight with approximately 19% of both the inbreds and populations containing maysin levels above 0.2%, a level considered to be necessary for resistance (Snook et al. 1993). Ellinger et al. (1980) also found the 6-C-glycosylated analog of chrysoeriol besides maysin and apimaysin. Snook et al. (1995) isolated and identified from several corn inbreds, reduced derivatives of maysin and 3′-methoxymaysin. These included 2″-*O*-α-L-rhamnosyl-6-C quinovosylluteolin (equatorial 4″-OH-maysin, eq-4″-OH-maysin), 2″-*O*-α-L-rhamnosyl-6-C-fucosylluteolin (axial 4″-OH-maysin, ax-4″-OH-maysin), and 2″-*O*-α-L-rhamnosyl-6-C-fucosyl-3′ methoxyluteolin (ax-4″-OH-3′ methoxymaysin).

An antifungal aldehyde, furfural (2-furancarboxaldehyde), was one of the volatiles generated from corn silk (Zeringue 2000). Bioassay-guided fractionation of petroleum ether and ethyl acetate extracts of corn silk afforded the isolation of stigmast-7-en-3-ol, β-sitosterol, stigmasterol and ergosterol from the petroleum ether extract, while apigenin, luteolin, chlorogenic acid, 8-C-glucopyranosyl apigenin [vitexin] and 8-C-glucopyranosyl luteolin [orientin] were isolated from the ethyl acetate extract (Abdel-Wahab et al. 2002). Four major unbranched alkanes (C25, C27, C29, and C31) and three isoalkanes (C27i, C29i, and C31i) were identified (Miller et al. 2003). Total alkane contents were highest in the exposed silk followed by the silk channel silk, with the lowest in the youngest silk closest to the kernels.

The cyclic hydroxamic acid, DIMBOA (2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one) was found to be the most abundant derivative in *Zea mays* and was strongly dependent on cultivar and environmental growth conditions (Nie et al. 2004). Hydroxamic acids were not found in seeds. After germination, the level of DIMBOA increased, reaching a maximum level in young seedlings a few days after germination. DIMBOA existed in all parts of the maize plant, and its concentration was generally higher in shoots than in roots. In all stages, the young leaves of *Zea mays* had relatively high content of DIMBOA. Because of their phytotoxic properties, cyclic hydroxamic acids showed a great variety of biological activities. They could be the defensive agents against plant diseases, pests, nematodes and other plants. DIMBOA prevalent in large amounts in young maize shoots was converted enzymatically to its aglycone upon tissue damage (Larsen and Christensen 2000). The aglycone DIMBOA possessed strong biologically activity toward various organisms whereas the glucoside was almost biologically inactive. DIMBOA, the major active component in those corn seedling extracts was found to be inhibitory to soft rot bacteria, *Erwinia* species (Corcuera et al. 1978). Cambier et al. (2000) found that the concentration of hydroxamic acids, 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one glucoside (DIMBOA-Glc) and its 8-methoxylated analogue (DIM2BOA-Glc) was high after seed germination and then decreased with plant age. Variation in concentration of N-*O*-methylated DIMBOA-Glc (HDMBOA-Glc) was similar to the one of hydroxamic acids in aerial parts. However in the roots HDMBOA-Glc became the main compound. This compound was also present in higher level than hydroxamic acids in the oldest leaf of 20-day-old maize. Four different fractions of phenolic compounds were extracted from *Fusarium graminearum* inoculated and non-inoculated (control) corn pith tissues: insoluble cell-wall-bound, free, soluble ester-bound, and soluble glycoside-bound phenolics (Santiago et al. 2007). *p*-coumaric acid and ferulic acid were the most abundant compounds in the soluble and cell-wall-bound fractions. The quantity of free, glycoside-bound, and ester-bound phenolics in the pith was lower than the level required for the inhibition of *Fusarium* growth or mycotoxins production; however, significant negative correlations between diferulic acid contents in the cell walls and disease severity ratings 4 days after inoculation were found. Diferulates may play a role in genotypic resistance of maize to *Gibberella* stalk rot as preformed barriers to infection. Two major simple phenolic acids [*p*-coumaric and *trans*-ferulic acids] were identified in free and cell-wall fractions of maize stalk, whereas four isomers of diferulic acid (DFA) (8-5′l, 5-5′, 8-*o*-4′, and 8-5′ benzofuran form) were present in the cell-wall bound fraction (Santiago et al. 2008). Results showed that the cell-wall bound phenolics could have a determinative role in the resistance of corn to the Mediterranean corn borer.

Flavonoids from corn silk had been investigated and confirmed to possess various pharmacological activities such as antihypertensive, anti-infectious, anti oxidative and anti diabetic (Li and Yu 2010; Liu et al. 2011). In recent years, corn silk flavonoids had been reported to be scavenger of hydroxyl and peroxyl radicals (Ren et al. 2005; Ebrahimzadeh et al. 2008; Hu et al. 2010). Also, it was reported that corn silk flavonoids had anti-fatigue activity (Hu et al. 2010; Hu and Deng 2011).

Antioxidant Activity

Total phytochemicals (free + bound) of corn had highest antioxidant activity of 181.68 μmol vitamin C equivalent/g of grain compared to wheat, rice, and oats (Adom and Liu 2002). Antioxidant activity of free phytochemicals was 24 μmol and bound phytochemicals 157.68 μmol. Ferulic acid content of corn grains (% contribution of fraction to the total μmol ferulic acid/100 g of grain) comprised total ferulic acid 906.13 μmol, free ferulic acid 0.92 μmol (0.1%), soluble ferulic acid conjugate 8.95 μmol (0.2%), and bound ferulic acid 896.27 μmol (98.9%). Corn had the highest total phenol content of all grains tested, determined as 15.55 μmol gallic acid equivalent/ g of grain comprising bound phenols 13.43 μmol and free phenols 2.12 μmol. Total flavonoid content in corn grains was 1.68 μmol catechin equivalent per g of grain, free flavonoids 0.16 μmol, bound flavonoids 1.52 μmol. Bound phytochemicals were the major contributors to the total antioxidant activity: 90% in wheat, 87% in corn, 71% in rice, and 58% in oats. Bound phytochemicals could survive stomach and intestinal digestion to reach the colon. This may partly explain the mechanism of grain consumption in the prevention of colon cancer, other digestive cancers, breast cancer, and prostate cancer, which is supported by epidemiological studies (Adom and Liu 2002).

Corn whole grain was found to have total phenolic content of 255 mg GAE/100 g grain and oxygen radical absorbance capacity (ORAC) of 10089 μmol TE/100 g grain (Okarter 2012). Corn contained 558 μmol/100 g grain of ferulic acid, and 70.2 μmol/100 g grain of *p*-coumaric acid and also caffeic acid in the insoluble bound fraction but contained no flavonoids (quercetin, kaempferol, catechin, and rutin) in the insoluble-bound fraction of the grain. None of the phenolic compounds had any cellular antioxidant activity, most likely because these phenolic compounds did not have the structure necessary to impart cellular antioxidant activity. The data suggested that the potential health benefit of whole grain consumption in the lower gastrointestinal tract was independent of the cellular antioxidant activity of the phenolic compounds found in the insoluble-bound fraction of whole grains.

The highest total content of polyphenols, anthocyanins, flavonoids, flavonols, and flavanols of purple corn extract was obtained with the 80:20 methanol:water extract, acidified with 1% HCl (1 N) (Ramos-Escudero et al. 2012). The 50% inhibitory concentration values obtained by the DPPH and ABTS assays with this extract were 66.3 and 250 μg/mL, respectively. The antioxidant activity by the FRAP assay was 26.1 μM Trolox equivalent/g, whereas the deoxyribose assay presented 93.6% inhibition. Eight phenolic compounds were identified: chlorogenic acid, caffeic acid, rutin, ferulic acid, morin, quercetin, naringenin, and kaempferol. Furthermore, it was observed that the purple corn extract was capable of significantly reducing lipid peroxidation (lower malondialdehyde [MDA] concentrations by the TBARS assay) and at the same time increasing endogenous antioxidant enzyme (CAT, TPX, and SOD) activities in isolated mouse kidney, liver, and brain. Thus, it was concluded that the purple corn extract contained various bioactive phenolic compounds that exhibited considerable in-vitro antioxidant activity, which correlated well with the decreased MDA formation and increase in activity of endogenous antioxidant enzymes observed in the isolated mouse organs. The DPPH* scavenging activity at 60 min was 34.39–44.51% in methanol extracts and 60.41–67.26% in HCl/methanol (1/99, v/v) extracts of typical and mutant corn genotypes (typical-1, waxy, typical-2, and high-amylose (Li et al. 2007)). The DPPH* scavenging activity of alkaline hydrolysates of corn ranged from 48.63 to 64.85%. The total phenolic content ranged from 0.67 to 1.02 g and from 0.91 to 2.15 g of ferulic acid equiv/kg of corn in methanol and HCl/methanol extracts, respectively. The total phenolic content of alkaline hydrolysates ranged from 2.74 to 6.27 g of ferulic acid equiv/kg of corn. The antioxidant capacity of lipid-soluble substances (ACL) values were 0.41–0.80 and 0.84–1.59 g of Trolox equiv/kg of corn in methanol and HCl/methanol extracts, respectively. The oxygen radical absorbance capacity (ORAC), values were 10.57–12.47 and 18.76–24.92 g of Trolox equiv/kg of corn in

methanol and HCl/methanol extracts, respectively. ORAC values of alkaline hydrolysates ranged from 42.85 to 68.31 g of Trolox equiv/kg of corn. The composition of phenolic acids in alkaline hydrolysates of corn was *p*-hydroxybenzoic acid (5.08–10.6 mg/kg), vanillic acid (3.25–14.71 mg/kg), caffeic acid (2.32–25.73 mg/kg), syringic acid (12.37–24.48 mg/kg), *p*-coumaric acid (97.87–211.03 mg/kg), ferulic acid (1552.48–2969.10 mg/kg), and *o*-coumaric acid (126.53–575.87 mg/kg). Levels of DPPH* scavenging activity, TPC, ACL, and ORAC in HCl/methanol extracts were much higher than those present in methanol extracts. There was no significant loss of antioxidant capacity when corn was dried at relatively high temperatures (65 and 93°C) postharvest as compared to drying at ambient temperatures (27°C). Alkaline hydrolysates showed very high TPC, ACL, and ORAC values when compared to methanol and HCl/methanol extracts. High-amylose corn had a better antioxidant capacity than did typical (non-mutant) corn genotypes. Lee et al. (2010) reported that all ethanolic extracts of 18 maize varieties tested inhibited yeast (*Saccharomyces cerevisiae*) α-glucosidase with the highest potency (49–54%) found for 2 purple and a yellow varieties. Maize extracts were capable of scavenging NO• at the level of 0.25 mg/mL with efficacies ranging from 24 to 50% and 26 to 57%, respectively, for aqueous and ethanolic extracts. All tested aqueous extracts were also capable of scavenging •O(2)(-), with efficacies ranging from 8 to 38%, at the level of 1.5 mg/mL, whereas almost none of the ethanolic extracts scavenged •O(2)(-), except for one purple strain (approximately 10% effective). The results suggested that certain maize varieties tended to exert higher biological activities and may have potential to be used in dietary regimes that are designed to promote human health.

Results of studies of yellow maize plant at stages M1 (74 DAS (days after seeding)), M2 (86 DAS), M3 (98 DAS), and maturity stage (116 DAS), revealed that during maturation of corn grains, the content of reducing sugar and crude protein decreased while starch and total lipids increased (Xu et al. 2010). Total carotenoids first decreased, then increased, and then decreased to minimum at maturity stage. Analysis of the main carotenoid compounds showed that lutein first increased and then decreased, whereas the reverse was found for β-cryptoxanthin. The change in zeaxanthin was consistent with total carotenoids. Total phenolic content decreased; nevertheless, different phenolic fractions varied with various maturation stages. The antioxidant activity determined by DPPH and FRAP assay in total phenolic extracts of yellow corn grains decreased during maturation, which may explain that antioxidant activity can be attributed to soluble phenolic and total phenolic content. Hu and Xu (2011) found that black waxy corn had the highest quantity of anthocyanins, phenolics and the best antioxidant activity, yellow corn contained a relatively large amount of carotenoids, while white corn had the lowest amounts of carotenoids, anthocyanins, phenolics, and antioxidant capacity. For each type of waxy corn, the higher carotenoids were found at the M2 stage (no major difference between the M1 and M2 stages for yellow corn). The levels of anthocyanin and phenolics decreased for white and yellow corns, contrary to those for black corn during maturation. The antioxidant activity determined by scavenging 2,2-diphenyl-1-picrylhydrazyl (DPPH), the ferric reducing antioxidant power (FRAP), and the Trolox equivalent antioxidant capacity (TEAC) assays increased with ripening, but no difference was found between the M2 and maturity stages for yellow and black corns. For white corn, the DPPH radical scavenging activity first increased and then decreased, while the antioxidant activity determined by TEAC and FRAP assay decreased during maturation. Differences in these parameters indicate that types and harvesting time have significant influences on functional properties of waxy corns.

Methanolic extracts of fully developed, mature corn silk exerted significant inhibition of lipid peroxidation in liposomes induced by Fe(2+)/ascorbate system (Maksimovic and Kovacevic 2003) The same test, performed after fractionation of the most active extract, showed that most of the activity was concentrated in fractions with moderate lipophilicity, containing phenolic acids, flavonoid aglyca and resembling monosides.

Ren et al. (2005) reported that the corn silk flavonoid, ax-5″-methane-3′-methoxymaysin exerted stronger antioxidant activity than the ax-4″-OH-3′-methoxymaysin with IC_{50} values of 0.5 and 4.9 µg/mL respectively. The petroleum ether, ethanol, and water and the volatile dichloromethane extract exhibited clear antioxidant activities at levels of 50–400 µg/mL in the 2,2-diphenyl-1-picrylhydrazyl (DPPH)/linoleic acid assay (El-Ghorab et al. 2007). The ethanol extract inhibited DPPH activity by 84% at a level of 400 µg/mL. All samples tested via the β-carotene bleaching assay also exhibited satisfactory antioxidant activity with clear dose responses. The result indicated that corn silk could be used to produce novel natural antioxidants as well as a flavoring agent in various food products. The ethanol-water extract of corn silk was found to have antioxidant activity (Ebrahimzadeh et al. 2008). The percentage of DPPH radical scavenged by corn silkextract was 92.6 at a concentration of 1.6 mg/mL. IC_{50} of the extract and the standard compounds butylated hydroxytoluene (BHA) and quercetin was 0.59, 0.053, and 0.025 mg/mL, respectively. Iron chelating activity of the extract was less than the standard compounds. The extract also exhibited nitric oxide-scavenging effect but the effect was less than the reference agent (quercetin). Corn silk extract displayed a high reducing ability. According to ferric thiocyanate (FTC) method, the extract showed more than 88% inhibition of linoleic acid peroxidation. The extract was found to have a significant amount of phenol and flavonoids.

N-butanol fraction (BF) of corn silk demonstrated the highest total phenolic content (164.1 µg GAE/g DCS) and total flavonoids content (69.4 µg RE/g DCS), and also the highest antioxidant activity compared to other fractions through all antioxidant assays (Liu et al. 2011). Two flavone glycosides showing potent antioxidant activity were isolated from the butanol fraction and identified to be isoorientin-2″-*O*-α-L-rhamnoside and 3′-methoxymaysin. The two isolated flavone glycosides, particularly isoorientin-2″-*O*-α-L-rhamnoside, demonstrated significant total antioxidant activity, DPPH radical scavenging activity, reducing power and iron chealting capacity with EC_{50} values of 14.24, 22.69, 6.58 and 30.25 µg /mL respectively Results indicated that corn silk can be used potentially as a read and accessible and valuable bioactive source of natural antioxidants. Administration of corn silk ethanol extract to γ-irradiated mice, dose-dependently and significantly abolished elevation of malondialdehyde levels in liver, normalised the decreased hepatic GSH/GSSG ratio and ameliorated hematological abnormalities induced by γ-radiation (Bai et al. 2010). Further the extract upregulated the hepatic protein expression of Nrf2. The findings suggested corn silk ethanol extract had a protective role against oxidative stress.

The 80% ethanol extract of supersweet corn powder (SSCP) was found to have 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging activity and 7-(*O*-β-Glucosyloxy)oxindole-3-acetic acid (GOA) was found to be the component most strongly contributing to the antioxidative activity (Midoh et al. 2010). The presence of its aglycone, 7-hydroxy-oxindole-3-acetic acid (HOA) was confirmed. GOA and HOA respectively contributed 35.1 and 10.5% to the DPPH radical-scavenging activity of the SSCP ethanol extract. Mice orally administered with HOA at doses of both 500 and 1,500 mg/kg showed a significantly lower level of thiobarbituric acid reactive substances (TBARS) in the plasma than the vehicle-treated control. The results suggested that GOA and HOA were at least partly involved in the antioxidative activity of SSCP in-vitro and that HOA might have possessed antioxidative activity in-vivo. Supersweet corn powder is commonly used in corn soup and snacks in Japan.

Both Mexican blue, and American blue corn genotypes contained higher antioxidant capacity (>8.3 µmol Trolox equivalents/g) yet lower polyphenolic levels (3.6–4.4 g/kg) than the white corn genotype (Pozo-Insfran et al. 2006). Comparable anthocyanin losses were observed when the blue genotypes were processed into nixtamals (cooked kernels), (37%), tortillas (54%), and chips (78%) that correlated to polyphenolic ($R^2=0.91$) and antioxidant capacity ($R^2=0.94$) losses. Acidification was mainly effective in reducing anthocyanin (9–17%), polyphenolic (10%), and antioxidant

capacity (6–14%) losses for the blue genotypes. The nixtamalization process (lime-cooking of coran grains to obtain masa) reduced total phenolics, anthocyanins and antioxidant activities and the ability for quinone reductase induction when was compared to raw corn grains (Lopez-Martinez et al. 2011). Processing masa into tortillas also negatively affected total phenolics, anthocyanin concentration, antioxidant activities, and quinone reductase induction in the colored corn varieties. The blue variety and its corresponding masa and tortillas did not induce quinone reductase. Veracruz 42 genotype and their products (masa and tortilla) showed the greatest antioxidant activity and capacity to induce quinone reductase and had the highest concentration of total phenolics, anthocyanins and antioxidant index.

Antiinflammatory Activity

A crude ethanolic extract of corn silk exhibited significant tumour necrosis factor-α (TNF) activity (Habtemariam 1998). The extract at concentrations of 9–250 μg/mL effectively inhibited the TNF- and *E. coli* lipopolysaccharide (LPS) -induced adhesiveness of EAhy 926 endothelial cells to monocytic U937 cells. Similar concentration ranges of corn silk extract also obstructed the TNF and LPS but not the phorbol 12-myristate 13-acetate-induced ICAM-1 expression on EAhy 926 endothelial cell surface. The extract did not alter the production of TNF by LPS-activated macrophages and failed to inhibit the cytotoxic activity of TNF. It was concluded that corn silk possessed important therapeutic potential for TNF- and LPS-mediated leukocyte adhesion and trafficking. Both petroleum ether and ethyl acetate extracts of corn silk exerted significant and dose-dependent analgesic and anti inflammatory activities (Abdel-Wahab et al. 2002). At the dose of 500 mg/kg, both extracts exerted analgesic activity with 80% protection in *p*-benzoquinone-induced writhings. They markedly inhibited formalin-induced oedema at the same dose with percentage reduction 57 and 52% respectively. No effect was observed for antipyretic activity. Treatment of Sprague-Dawley rats with induced colitis with enzymatic hydrolysate of corn gluten significantly decreased the severity of injury and reduced myeloperoxidase activity and histamine levels in the distal colon mucosa (Mochizuki et al. 2010). The results suggested that the enzymatic hydrolysate of corn gluten may have therapeutic benefit as a supplement in enteral nutrition for patients with inflammatory bowel diseases.

Owoyele et al. (2010) demonstrated that corn husk extract at 25, 50, 100, and 200 mg/kg body weight significantly reduced pain stimuli and inflammatory activity when compared with the control group. The reductions in paw licking time and granuloma weight in the formalin and cotton pellet models were both dose dependent. The authors suggested that the analgesic and anti-inflammatory effects of corn husk may be attributable to its tannins and polyphenolic constituents.

Antifatigue Activity

Studies reported that corn silk flavonoids had anti fatigue activity (Hu et al. 2010; Hu and Deng 2011). Results from exhaustive swimming exercise indicated that corn silk flavonoids had anti-fatigue activity on mice by inhibiting oxidative stress caused by the production of blood lactic acid, retarding the formation of blood urea nitrogen and increasing hepatic glycogen concentration (Hu et al. 2010). Flavonoids with content of 63.15% was obtained with a flavonoid recovery of 94.27% in the purification process. Hu and Deng (2011) found that corn silk flavonoids could elevate the exercise tolerance of mice, and provide protection against oxidative stress induced by exhaustive exercise in mice, by inhibiting lipid per oxidation and increasing anti oxidant enzymes levels.

Antidiabetic Activity

A 4-week study in rats by Zhou and Kaplan (1997) found that soluble amylose cornstarch in

the form of modified amylomaize-7 starch was more digestible than soluble amylopectin potato starch and may be useful in the development of food products for liquid nutritional supplements because of the high digestibility and the low resultant insulin levels. Commercial cornstarch, dextrose, modified potato starch and modified amylomaize-7 starch were 100, 100, 69.0 and 91.5% digestible, respectively. The insulin to glucagon ratios were significantly lower in the modified potato starch-fed and amylomaize-7 starch-fed groups than in the dextrose-fed control group.

Administration of *Zea mays* saponin to streptozocin induced diabetic rats was found to decrease blood glucose and prevented kidney and pancreas injury induced by streptozocin (Miao et al. 2008). Li and Yu (2009) demonstrated that flavonoids in corn silk could dose-dependently and markedly decreased serum glucose in alloxan-induced diabetic mice. Corn silk flavonoids improved activity of serum superoxide dismutase and decreased malondialdehyde activity in alloxan-induced diabetic mice suggesting the involvement of antioxidative mechanism. It was also postulated that Corn silk flavonoids triggered β-cell damage repair system, and enhanced the secretion of insulin function to lower the high blood sugar. Findings of studies by Suzuki et al. (2005) indicated that the water extract of corn silk (style) suppressed the progression of diabetic glomerular sclerosis in streptozotocin-induced diabetic rat. Corn silk extract was found to prevent glomerular hyperfiltration. Guo et al. (2009) reported corn silk extract to markedly reduce hyperglycemia in alloxan-induced diabetic mice. The action of corn silk extract on glycaemic metabolism was not via increasing glycogen and inhibiting gluconeogenesis but through increasing insulin level as well as repairing the injured pancreating β-cells. The results suggested that corn silk extract may be used as a hypoglycemic food or medicine for hyperglycemic people.

In a study of six healthy volunteers, consumption of a breakfast composed of a complex carbohydrate in the form of "arepa" prepared with precooked corn flour showed that the corn bread arepa to have high a glycemic index 71.5% and was increased not significantly with the addition of protein and fat (Semprún-Fereira et al. 1994). Total glucose as well as insulin obtained for corn bread and for corn bread plus protein and fat were similar to the oral glucose tolerance test (OGTT). In contrast in another study of healthy subjects in Sweden, arepa meals containing high amylose (70% amylose) corn flour produced lower areas under the glucose and insulin response curves (57 and 42% lower, respectively) than did the meals containing ordinary cornmeal (25% amylose) (Granfeldt et al. 1995). The rate of starch hydrolysis measured in-vitro was slower in the high amylose corn products than in the ordinary corn product. Resistant starch in the ordinary product was 3/100 g dry matter, vs. approximately 20/100 g dry matter in the high amylose products. They concluded that high amylose corn products have a potential to promote favorably low metabolic responses and high resistant starch contents. Rats fed maize bread presented higher body weight gain and cholesterol level, lower fecal pH, and postprandial blood glucose response than the group fed wheat bread, a poor source of dietary fibre, typically containing less than 2%. (Brites et al. 2011). The resistant starch-wheat bread rats showed significant reductions in feed intake, fecal pH, postprandial blood glucose response, and total cholesterol. The resistant starch-maize group displayed significant reductions of body weight gain, fecal pH, and total cholesterol levels; however, for the glycemic response, only a reduction in fasting level was observed. The results suggested that maize bread had a lower glycemic index than wheat bread, and the magnitude of the effect of resistant starch on glycemic response depends of type of bread.

Studies showed that consumption of waxy maize starch (WM), a slow-digestible starch, provided sustained glucose availability in young, insulin-sensitive adults (Sands et al. 2009). Compared to white bread control, the 4-h glucose response was not different for a maltodextrin-sucrose mixture (MS) and WM, and the 4-h insulin response was higher for MS and lower for (WM). Compared to MS, WM led to lower 4-h glucose and insulin responses. These differences

were driven by blunted glucose and insulin responses during the first hour for WM. Postprandial energy expenditure and appetite were not different among treatments. In a randomised, cross-over, intervention study of 10 healthy men, dietary supplementation with hydroxypropyl-distarch phosphate (HDP) from waxy maize starch lowered postprandial glucose-dependent insulinotropic polypeptide (GIP) (Shimotoyodome et al. 2011). The HDP meal led to significantly lower postprandial glucose, insulin and GIP responses than the waxy maize starch meal. Further, HDP increased postprandial resting energy expenditure and fat utilisation in healthy humans indicating an of hydroxypropyl-distarch phosphate -rich diet may therefore have beneficial implications in weight management.

In a study of six patients with non-insulin-dependent diabetes mellitus (NIDDM) consumption of fructose meal was superior to a high-fructose corn syrup (HFCS) as a sweetening agent as it caused less increment in plasma glucose (Akgün and Ertel 1981). In another study of 16 NIDDM patients, the authors (Akgün and Ertel 1985) found that sucrose and HFCS caused greater increments of plasma glucose than fructose in patients with NIDDM, but did not differ from each other. Thus, regardless that HFCS was less expensive than fructose, its effect on plasma glucose and insulin was not different from that of sucrose, and the useful function for HFCS in diets for persons with diabetes could not be validated on scientific basis. Also, they found that diabetic patients with higher basal plasma glucose (i.e., >140 mg/daily) showed similar increase in plasma glucose whether they were given sucrose, HFCS, or fructose meals suggesting fructose has potential value only in patients with mild diabetes mellitus. The study of Hung (1989) in 8 normal and 21 non-insulin dependent diabetes mellitus (NIDDM) subjects, also did not support the use of HFCS as a substitute for fructose for diabetic management because of the high glycemic index of HFCS. His results showed that the glycemic effect of HFCS was 73% of glucose. The AUC (area under the curve) of immunoreactive insulin after HFCS was 56% of that of glucose. The AUC of immunoreactive C-peptide after HFCS was 57% of that of glucose. In a more recent study of 30 lean women, Melanson et al. (2007) compared the effects of HFCS and sucrose based on the premise that fructose had been implicated in obesity, partly due to lack of insulin-mediated leptin stimulation and ghrelin suppression. They found no significant differences between the two sweeteners were seen in fasting plasma glucose, insulin, leptin, and ghrelin. There were no differences in energy or macronutrient intake on day 2. Their short-term results suggested that, when fructose was consumed in the form of HFCS, the measured metabolic responses did not differ from sucrose in lean women.

Hypolipidemic/Antihyperlipidemic Activity

The marked body weight loss in Sprague-Dawley streptozotocin-induced diabetic rats was not recovered by feeding resistant starch from corn or rice, even though there were no differences in food intake compared to the non-diabetic control rats (Kim et al. 2003). No significant effect of resistant starch feeding on blood glucose and insulin was found. Nonetheless, both resistant starch from corn and rice significantly lowered plasma total lipid and cholesterol concentrations compared to the diabetic control. Neither immunoglobulin G nor C(3) were influenced by resistant starch.

Results of a 3-year study of 40 patients with exudative retinopathy, suggested that a diet containing appreciable quantities (60 g) of unsaturated fatty acid (corn oil) and reduced (20 g) animal fat, could achieve significant reduction in the amount of retinal exudates in diabetic retinopathy (King et al. 1963). However, there was no improvement in visual acuity and it appeared that exudates was the end result of neuronal degeneration which impaired vision. Total blood serum lipid and cholesterol levels were also lowered. Cataract formation in streptozotocin-induced diabetes in rats was reduced by approximately 85% when a diet rich in corn oil (300 g/kg diet) (corn oil diet) was administered (Hutton et al. 1976). However, the concentration of sorbitol in the lens

of diabetic animals remained high, the values for diabetic rats given the standard diet and the fat diet being 65 and 40 μmol/g protein respectively. With the standard diet, the fatty acid profile of the triglycerides of the epididymal fat pads was characterized by a greater relative proportion of saturated fatty acids for the diabetic animals compared to that for the normal animals while the corn oil diet moderated the tendency towards saturation in the diabetic animals. The corn oil diet had other effects on the diabetic animals that included a reduced mortality rate, increased body-weight, a decrease in the daily water intake, and in the daily urinary excretion of glucose and urea. In diabetic animals the corn oil diet had no effect on the specific activities of hexokinase, glucokinase, phosphofructokinase and pyruvate kinase in the liver. However, the specific activity of glucose-6-phosphatase was reduced, while that of malate dehydrogenase (decarboxylating) (NADP) was increased. The NAD+: NADH ratio, as calculated from liver pyruvate and lactate concentrations, tended to increase. The results suggested that the corn oil diet moderated the long-term metabolic effects of diabetes.

The results of the first 10 years of a prospective study of the effect of corn-oil and standard diets given to diabetic children since diagnosis suggested that the corn-oil diets available in Britain then were not acceptable to most diabetic children and adolescents in the management of hyperlipidaemia in juvenile diabetes (Chance et al. 1969). Attempts to administer such diets may result in hyperpre-β-lipoproteinaemia. In most diabetic children normal serum lipid levels can be maintained with adequate diabetic control and a standard diabetic diet.

Cardioprotective Activity

Studies showed that chronic dietary intake of maize rich in flavonoids (anthocyanins) could protect the rat heart against ischemia-reperfusion injury (Toufektsian et al. 2008). After 8 weeks feeding anthocyanins were significantly absorbed and detected in the blood and urine of only rats fed the anthocyanin -rich diet.

The hearts of rats fed the anthocyanin-rich diet were more resistant to regional ischemia and reperfusion challenge. Further, on an in-vivo model of coronary occlusion and reperfusion, infarct size was reduced in rats that ate the anthocyanirich diet than in those that consumed the anthocyani-free diet. Cardioprotection was associated with increased myocardial glutathione levels, suggesting that dietary anthocyanins might modulate cardiac antioxidant defences.

Antilithiasic Activity

Maize herb infusion was found to have antilithiasic in Wistar rats (Grases et al. 1993) and was attributed to some diuretic activity. Impact on important urinary risk factors such as citraturia, calciuria or urinary pH values were not detected.

Diuretic and Kaliuretic Activity

Studies by Velazquez et al. (2005) found that in water-loaded conscious rats (2.5 mL/100 body wt.), corn silk aqueous extract was diuretic at a dose of 500 mg/kg body wt. and kaliuretic at doses of 350 and 500 mg/kg body wt. In water-loaded conscious rats (5.0 mL/100 g body wt.), corn silk aqueous extract was kaliuretic at a dose of 500 mg/kg body wt., but glomerular filtration and filtered load decreased without affecting proximal tubular function, Na+, or uric acid excretion.

Immunological Enhancing Activity

The bio active substances with immunological enhancing function was isolated and purified from corn silk and found to be a non-starch polysaccharide (Tang et al. 1995).

Vasodilatory Activity

The hydroalcoholic extract of *Zea mays* (Andean purple corn) at doses of 0.1, 0.5 and 1.0 mg/mL

produced nitric oxide dependent vasodilation in the rat aortic rings (Moreno-Loaiza and Paz-Aliaga 2010).

Inhibition of IgE Antibodies Activity

Glycoproteins extracted from a hot water extract of corn silk was found to inhibit formation of IgE antibodies after primarily and secondarily challenged responses with dinitrophenyl (DNP)-ovalbumin (OVA) antigen in mice using the passive cutaneous anaphylaxis (PCA) test (Namba et al. 1993). The glycoproteins may be clinically applicable to type I allergic diseases.

Drug Potentiating Activity

Studies showed that polyamine oxidase from maize conditionally expressed in the nucleus of MCF-7 human breast cancer cells conferred sensitivity to etoposide a DNA topoisomerase II inhibitor widely used as antineoplastic drug (Marcocci et al. 2008). The data suggested polyamine oxidases as a potential tool to improve the efficiency of antiproliferative agents despite the difficulty to interfere with cellular homeostasis of spermine and spermidine.

Antimicrobial Activity

Several small, acid-soluble, basic peptides with anti-microbial properties were isolated from maize kernels (Duvick et al. 1992). One of these peptides (MBP-1) inhibited in-vitro spore germination or hyphal elongation of several plant pathogenic fungi, including two seed pathogens of maize (*Fusarium moniliforme*) and *Fusarium graminearum* (*Gibberella zea*e), and several bacteria, including a bacterial pathogen of maize (*Clavibacter michiganense* ssp. *nebraskense*). Both petroleum ether and ethyl acetate extracts of corn silk showed a potent antibacterial activity against certain Gram +ve and Gram –ve bacteria (Abdel-Wahab et al. 2002).

Prebiotic Activity

In a double-blind, placebo-controlled human feeding study of 32 healthy men and women, after 21 days consumption of whole grain maize enriched breakfast mean group levels of faecal bifidobacteria increased significantly compared with the non-whole grain control cereal (Carvalho-Wells et al. 2010). After a 3-week wash-out period, bifidobacterial levels returned to pre-intervention levels. No statistically significant changes were observed in serum lipids, glucose or measures of faecal output. The authors concluded that whole grain maize enriched breakfast cereal mediated a bifidogenic modulation of the gut microbiota, indicating a possible prebiotic mode of action.

Alleviating Vitamin A Deficiency

The conversion factor of yellow maize β-carotene to retinol by weight was 3.2–1. In a random study of six healthy women, the consumption of β-carotene biofortified maize porridge showed β-carotene in biofortifed maize to have good bioavailability as a plant source of vitamin A (Li et al. 2010). The major carotenoid was all *trans* β-carotene followed by 9-*cis* β-carotene, which reflects the high 9-*cis* β-carotene content present in the raw β-carotene–biofortified maize. The provitamin A carotenoid content in the β-carotene fortified porridge were (in μg/240 g serving): α-carotene 40 μg, β-cryptoxanthin 96 μg, 9-*cis* β-carotene 101 μg, 13-*cis* β-carotene 98 μg, *trans* β-carotene 328 μg, total β-carotene 527 μg, total *trans* β-carotene equivalents 495 μg. Mean areas under the curve for retinyl palmitate in the triacylglycerol-rich lipoprotein fractions (nmol/hour) were 24.0, 89.7, and 80.1 after ingestion of the β-carotene-biofortified maize porridge, the white maize porridge with the β-carotene reference dose, and the white maize porridge with the vitamin A reference dose, respectively. On average, 6.48 μg (mean) of the β-carotene in β-carotene-biofortified maize porridge and 2.34 μg of the β-carotene in the reference dose were each equivalent to 1 μg retinol. In a study of 8 healthy

Zimbabwean men, 300 g cooked yellow maize containing 1.2 mg β-carotene that was consumed with 20.5 g fat showed the same vitamin A activity as 0.38 mg retinol and provided 40–50% of the adult vitamin A Recommended Dietary Allowance (Muzhingi et al. 2011).

Adverse Effects

Mycotoxin Contamination

Fumonisins are mycotoxins produced by various species of *Fusarium* (*F. verticillioides* and *F. proliferatum*) and occur naturally in contaminated maize and maize-based foods (Gong et al. 2009; Feng et al. 2011; Ndube et al. 2011). Fumonisins mycotoxins that contaminate maize, disrupt the folate and sphingolipid metabolism, are associated with neural tube defects, and are considered by the International Agency for Research on Cancer (IARC) as possible human carcinogens (Torres-Sánchez and López-Carrillo 2010). Gong et al. (2009) found from an analysis of a total of 282 corn samples harvested in 2005 from six provinces, the main corn-producing areas of China, the distribution pattern for fumosin B1 to be 43.6% of tested samples had fumosin B1 concentrations below 1,000 ng/g, while 25.2% contained in excess of 5,000 ng/g. The average exposure to fumosin B1 (1.1 μg/kg body weight/day) was within the provisional maximum tolerable daily intake of 2 μg/kg body weight/day set by the Joint FAO/WHO Expert Committee on Food Additives. Feng et al. (2011) found in a total of 255 corn samples collected in 2010 from three main corn production provinces of China (Liaoning, Shandong, and Henan) approximately 80.0% of the samples from Liaoning were contaminated with fumonisins FB1 and FB2, with a mean total fumonisin concentration of 3,990 ng/g. In contrast, the mean total fumonisin concentrations were 845 and 665 ng/g in samples from Shandong and Henan, respectively. The probable daily intake of fumonisins (0.3 μg/kg of body weight) was within the provisional maximum tolerable daily intake of 2.0 μg/kg of body weight set by the Joint Food and Agriculture Organization and World Health Organization Expert Committee on Food Additives Ndube et al. (2011) found naphthalene-2,3-dicarboxaldehyde (NDA) to be an effective derivatization reagent of fumonisin in naturally contaminated maize samples following immunoaffinity column (IAC) clean-up in the detection of the mycotoxin.

Mutagenic/Aneugenic Activity

From the sprouts of Gramineae such as wheat, maize and rye, two most abundant benzoxazinoids, namely 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one (DIMBOA) and 2,4-dihydroxy-1,4-benzoxazin-3-one (DIBOA) exhibited mutagenic activities in the *Salmonella*/microsome assay and additionally, in micronucleus assay and single cell gel electrophoresis (SCGE) assay in a human-derived liver cell line (HepG2) (Buchmann et al. 2007). DIBOA caused significant induction of his(+) revertants in all three strains in the range between 0.02 and 0.50 mg/plate; the highest activity was observed in TA100. In general, DIMBOA was less active than DIBOA. Addition of rat liver homogenate (S9-mix) led to a significant (twofold) increase of the mutagenic activities of both benzoxazinoids. In micronucleus assay, DIMBOA caused significant effects already at concentrations > or =1 μM; at the highest dose (20 μM) the micronucleus frequency was sevenfold higher than the background level. DIBOA caused weaker effects and was positive at doses > or =2.5 μM, the maximal induction (twofold over background) was observed with 20 μM. Overall, DIMBOA was about 30-fold more active as DIBOA. Subsequent experiments with pancentromeric probes showed that >80% of the micronucleus induced at the highest doses gave a centromere positive signal indicating both benzoxazinoids to be aneugenic. Aneuploidy has been reported to be a key event in cancer induction.

Tolerogenic/Immunogenic Response

In a study of 661 Mexican patients, 56 (8.5%) manifested allergic symptoms attributable to maize, which correlated with a positive cutaneous response to its antigens (Valencia Zavala et al. 2006). Fifty (88%) of them worked with

maize and had a significant relative risk value. The remaining six patients did not work with maize, four of them were included in the group who had a positive response for both allergens, and two in that one with positive response for only one of these allergens. The low frequency (8.5%) to which the allergic disease was attributed to maize, and the strong association (88%) with workers of maize suggest the development of either tolerogenic or immunogenic response to an antigen.

Maize Allergy

Pastorello et al. (2000) identified a 9-kDa lipid-transfer protein (LTP) as the major allergen of raw maize in a population of 22 anaphylactic patients. The allergic reaction can cause skin rash, swelling or itching of mucous membranes, diarrhea, vomiting, asthma and, in severe cases, anaphylaxis. They demonstrated that the LTP cross-reacted completely with rice and peach LTPs but not with wheat or barley LTPs. N-terminal sequence of the 16-kDa allergen (recognized by 36% of patients) showed it to be the maize inhibitor of trypsin. This protein cross-reacted completely with grass, wheat, barley, and rice trypsin inhibitors. In further studies (Pastorello et al. 2003), they found that maize LTP maintained its IgE-binding capacity after heat treatment, thus being the most eligible candidate for a causative role in severe anaphylactic reactions to both raw and cooked maize. In a more recent double-blind placebo-controlled study of maize-challenge-positive patients Pastorello et al. (2009) found besides LTP other maize allergens namely 14-kDa α-amylase inhibitor, 30-kDa endochitinase A and endochitinase-B, 19 kDa zein-β precursor, and 26 kDa zein-α precursor; a newly described allergen, the globulin-2 precursor.

Anticoagulant/Coagulopathy Activity

An anticoagulant purified from corn silk, with a molecular mass of 135 kDa was found to compose of neutrosugar and aminosugar (Choi and Choi 2004). Galactose, glucose, mannose, fucose, glucosamine, and galactosamine were detected. It was not sensitive to heat and protease treatment. However, periodate oxidation of the anticoagulant resulted in loss of activity significantly, implying that a carbohydrate was responsible for the anticoagulant activity. Godier et al. (2010) found maize- and potato-derived hydroxyethyl starches to have similar effects on coagulation. Both the starch preparations tested led to more severe haemostatic defects than crystalloid solutions, and impairment of fibrin polymerization appeared to be a leading determinant of this coagulopathy.

Oesophagus Cancer

Endemic cancer of the oesophagus in Africa was found to be associated with the consumption of maize as the staple (Sammon 1999: Sammon and Iputo 2006; Pink et al. 2011). High levels of non-esterified fatty acids (11–42% of contained fatty acids) were found both in maize meal and in foods prepared from it (Sammons 1999). In food prepared from maize meal, 49–363 mg non-esterified linoleic acid per 100-g sample was found. High levels of non-esterified linoleic acid in the diet, causing raised intragastric production of prostaglandin E2 (PGE2) and profoundly affecting the normal pH and fluid content of the esophagus, may create a predisposition to esophageal carcinogenesis. The molecular mechanisms by which a high-maize diet could lead to increased incidence of squamous cancer of the esophagus was elucidated by Pink et al. (2011). They confirmed that levels of PGE(2) were high (606.8 pg/mL) in the gastric fluid of individuals from Transkei, South Africa. They also demonstrated that treatment of oesophageal cells with linoleic acid, found at high levels in maize and a precursor to PGE(2), led to increased cell proliferation. Similarly, treatment of cells with PGE(2) or with gastric fluid from Transkeians also led to increased proliferation. Their data suggested that the high levels of PGE(2) associated with a maize-rich diet stimulated cell division and induced the enzyme COX 2, resulting in a positive feedback mechanism that predisposed the oesophagus to carcinoma.

Traditional Medicinal Uses

Traditionally, in many parts of the world, corn silk has been used as diuretic, antilithiasic, uricosuric, and antiseptic. It is used for the treatment of edema as well as for cystitis, gout, diabetes mellitus, kidney stones, nephritis, and prostatitis (Grases et al. 1993; Velazquez et al. 2005; Ebrahimzadeh et al. 2008). Corn kernel is considered to be diuretic and a mild stimulant (Grieve 1971). Corn is a good emollient poultice and is used for ulcers, wounds sore, swelling and rheumatic pains. An infusion of parched corn is taken for nausea and vomiting in many diseases. Stuart (2010) reported the following traditional folkloric uses In the Philippines, a decoction of fresh or dried stalk, cob as well as corn silk is used as a diuretic (Stuart 2010). Decoction of roots, leaves, and corn silk is used for dysuria, bladder complaints, and bedwetting. In China corn silk has been used for fluid retention and jaundice A decoction of pith of cob as tea is used for stomach complaints (Burkill 1966). In Europe corn silk is used for has been used for treating urinary and venereal diseases and in cardiac and renal dropsy. Young cob is known to be diuretic owing to its potassium content and In Indonesia, the cob is used for kidney stones (Burkill 1966). Maize has been widely used in traditional African medicine (Burkill 1994). Urinogenital problems are treated with prescriptions based on the whole or parts of the maize plant, especially a decoction of the cornsilk, which is also used to treat jaundice. A maize leaf maceration is drunk to treat fever. Charcoal made from maize stalks is included in medicines to treat gonorrhoea; an infusion from the burnt cob is used to wash wounds. Maize spike heated with powdered leaves of *Glossonema boveanum* used to treat intestinal schistosomiasis in Mali (Bah et al. 2006). In Burundi, corn silk decoction is used as a diuretic and depurative, and macerated maize leaves used to treat fever (Baerts and Lehmann (1989). In Ghana, powdered corn and leaves used as poultice for boils and carbuncles (Agyare et al. 2009). In southwestern Nigeria, a decoction of the kernel and silk is used for management of diabetes mellitus (Abo et al. 2008). In Togo, carbonised and powdered corn silk is used for oedma and rash, and a decoction of the corn silk is used for hypertension (Adjanohoun et al. 1986). In Benin, corn silk used to treat convulsion, hepatic disorders, jaundice, and kernels also used for diarrhoea, dysentery and liver disorders (Adjanohoun et al. 1989). In Morocco, corn silk decoction is used as a diuretic and for kidney ailments (Bellakhdar 1997). In the Errachidia province of Morocco, dried, roasted kernels used to treat hypertension Tahraoui et al. 2007) and the stalk for renal diseases in Fez-Boulemane, Morocco (Jouad et al. 2001). In Uganda, maize stalk ashes are applied to the gums to treat tooth caries (Tabuti et al. 2003). In Burkina-Faso, decotion of corn flowers and slat is used as a mouth wash for tooth-ache (Tapsoba and Deschamps 2006). In Kenya, the sap from boiled kernels is applied externally for skin diseases (Njoroge and Bussmann 2007). In Nigeria, corn silk is used for treating measles (Kayode et al. 2008) and a towel dip in a decoction of corn cob is applied to bleeding nose (Ogie-Odia and Oluowo 2009).

Other Uses

Corn By-Products

Corn oil beside being edible is also used in the manufacture of soaps and paints. Starch from maize can also be made into plastics, fabrics, adhesives, and many other chemical products. Corn starch is also used extensively for laundry purposes. A sticky gum containing dextrin is used for sealing envelops, and on gummed labels.

Corn is used for making alcohol. The cobs may be used to supply potash, and by distillation they can be made to produce acetic acid and acetone. Materials for the manufacture of nitrocellulose lacquers may also be obtained from them by controlled fermentation. The corn steep liquor, a plentiful watery byproduct of maize wet milling process, is widely used in the biochemical industry and research as a culture medium to grow many kinds of microorganisms. Maize meal is also a significant ingredient of some commercial animal food products, such as dog food.

Animal Feed

In industrialised countries corn is used for animal feed, directly in the form of grain and forage, fodder, silage (fermentation of chopped green cornstalks) or sold to the feed industry; and maize breeders in North America and Europe focus on agronomic traits for its use in the animal feed industry. Corn provides a greater quantity of epigeous mass than other cereal plants, so can be used for fodder. Digestibility and palatability are higher when ensiled and fermented, rather than dried. Feed corn is sometimes used by hunters to bait animals such as deer or wild hogs.

Ethanol Fuel Production

Various aerial parts of the corn plant can be used for ethanol biofuel production. The value of corn as a feedstock for ethanol production is due to the large amount of carbohydrates, specifically starch, present in corn (Mosier and Illeleji 2006). Starch can be rather easily processed to break it down into simple sugars which can then be fed to yeast (*Saccharomyces cerevisiae*) to produce ethanol by fermentation. For each pound of simple sugars, yeast can produce approximately 0.5 lb (0.15 gal) of ethanol and an equivalent amount of carbon dioxide. Modern ethanol production can produce approximately 2.7 gal of fuel ethanol per bushel of corn. Cellusosic feedstocks such as corn stover which consists of the leaves, stalks, husk and cob of corn plants left in a field after harvest can be converted into ethanol (Mosier 2006) through a biological process using enzymatic hydrolysis followed by fermentation.

Insecticidal, Insect Attractants and Antifungal Compounds

Corn silk contains compound with insecticidal and antifungal compounds which can thwart attacks from insect pests and plant pathogens. Maysin (rhamnosyl-6-C-(4-ketofucosyl)-5,7,3′,4′ tetrahydroxyflavone), isolated from corn silks of the exotic cultivar ‘Zapalote Chico’ had been shown to severely retard the growth of *Heliothis zea* (Boddie) when incorporated into the insect’s diet (Waiss et al. 1979). Flavone contents in corn silks of three maize lines exhibited different resistance to larvae of fall amyworm (FAW), *Spodoptera frugiperda* Smith, and Southwestern corn borer (SWCB), *Diatraea grandiosella* Dyar. The main compound in the resistant (CML 67) and in the intermediate (CML 135) lines was apimaysin (Guevara et al. 2000).

Volatiles generated from corn silks of individual genotypes of maize were found to exhibit differences in biological activities when the volatiles were exposed to 5-day solid cultures of *Aspergillus flavus* (Zeringue 2000). Aflatoxin field-resistant maize genotypes exhibited a larger relative concentration of the antifungal aldehyde, furfural (2-furancarboxaldehyde), when compared to the relative concentrations of the field-susceptible varieties tested. The presence of furfural appeared to contribute to a defense mechanism for protecting the developing maize kernel from fungal attack. Corn silk also contain compound which can be used as insect attractants. Phenylacetaldehyde, a volatile component of corn silk was found to attract the corn earworm, European corn borer, soybean looper, tarnished plant bug, *Cisseps fulvicollis*, and forage looper. Combining phenylacetaldehyde with other components viz. butanol or acetaldehyde increased attractiveness to some species; other combinations reduced attractiveness.

Miscellaneous Uses

An unusual use for maize plants is to create a “corn maze” (or “maize maze”) as a tourist attraction. Maize kernels can be used in place of sand in a sandboxlike enclosure for children’s play. Corncobs can be hollowed out and treated to make inexpensive smoking pipes. A brown dye can be obtained from the cob. The sheaths of the cob have been used for matting and paper making and as wrappers for cigarettes in parts of America and ceroots in Myanmar. Dry corn stalks can be used to build fences. Maize kernels and cobs are also used as a biomass fuel source and is

relatively cheap and home-heating furnaces have been developed which use maize kernels as a fuel. Maize is also used as a fish bait, called "dough balls".

Comments

Maize can be categorized into different types based on endosperm and kernel characteristics and composition (Purseglove 1972; Paliwal 2000; Darrah et al. 2003):

Flint maize – kernels with a hard outer core surrounding a small soft centre. This type is cultivated predominantly in Latin America and Europe for food.

Dent maize – takes its name from the dent that develop at the top of the kernel at maturity. It is characterized by hard endosperm on the sides and base of kernel and remainder filled with soft starch. It is grown mainly for grain and silage for animal feed and is the predominant type in USA. Dent corn requires special processing for human consumption.

Floury maize – the endosperm is composed of soft starch, making it easy to grind and process into food. It is cultivated predominantly in the Andean region.

Waxy maize – kernels contain entirely of amylopectin and no amylose starch compared to the normal 70% amylopection and 30% amylose composition. Waxy maize is the preferred for food in parts of East Asia and for some industrial uses; it produces a starch similar to tapioca.

Pop maize – better known as popcorn or popping corn, has kernels characterized by high a hard moisture sealed hull and a dense starchy core. amount of hard endopserm, much higher than any other maize kernel. The kernel expand and puffed up when heated. Pop corn is a popular snack food consumed all over the world.

Sweet maize – or sweet corn is grown for its immature green ears (sweet corn) and is often prepared and eaten as a vegetable. Ears are harvested 18–20 days post pollination when the kernel moisture is around 70%. Developing grain of sweet corn is higher in sugar and lower in starch due to one or more recessive mutations in the genes blocking conversion of sugar to starch inside the endosperm.

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Zizania palustris

Scientific Name

***Zizania palustris* L.**

Synonyms

Melinum palustre (L.) Link, *Zizania aquatica* subsp. *angustifolia* (Hitchc.) Tzvelev, *Zizania aquatica* var. *angustifolia* Hitchc., *Zizania palustris* fo. *purpurea* Dore.

Family

Poaceae

Common/English Names

Canada Rice, Indian Rice, Interior Wild Rice, Interior Zizania, Manomin, Northern Wild Rice, Northern Zizania, Water Oats, Wild Rice.

Vernacular Names

French: Folle Avoine, Zizanie Des Marais;
German: Wilder Reis;
Japanese: Jizania Barusutorisu
Russian: Dikii Ris;
Spanish: Arroz Silvestre;
Swedish: Indianris.

Origin/Distribution

Zizania palustris is a native to the Great Lakes region of North America, it is predominantly found in the aquatic areas of the Boreal Forest regions of Alberta, Saskatchewan and Manitoba in Canada, and Minnesota, Wisconsin and Michigan in the USA. In the US the main producers are California and Minnesota. In Canada the largest producer is the province of Saskatchewan. Wild rice is also produced in Hungary and Australia. In Australia, production is located at Deniliquin in Southern New South Wales.

Agroecology

In its native range, Northern Wild Rice grows as an annual, emergent, aquatic grass in shallow lakes and slow-moving rivers in the boreal forest. It thrives luxuriantly in the northern temperate latitudes of North America but is not productive in the southern United States. However, it performs well in the warmer temperate climate of northern California, Idaho and Oregon where cultivars have been developed for that environ and where humidly is very low with little consequential leaf diseases. It grows on organic soils (shallow peats) and inorganic soils (clays or sandy loams) in flat areas that are flooded for most of the growing season, similarly to rice (*Oryza sativa*). The majority of wild rice fields have been developed on shallow peats. It thrives

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well in cooler and deeper water than rice thus requiring fewer weed control chemicals compared to rice.

Edible Plant Parts and Uses

American Indians (Chippewa, Sioux) popped wild rice, like popcorn, and occasionally served it with maple sugar as a special treat. Popped wild rice is also eaten by men in hunting and fishing trips. Traditionally, wild rice is used by cooks as a side dish or a stuffing for roasted game-birds, pheasant and turkeys. Nowadays, it is considered a gourmet food, eaten on its own, or mixed with regular rice (*Oryza sativa*) or as a substitute for potatoes, plain rice and pasta. Wild rice is also used in dressings, casseroles, soups, salads (e.g. wild rice, asparagus, snow-pea salad; wild rice chicken salad, wild rice prawn salad), mixed in vegetable chowder, deserts (e.g. wildrice nutty desert, wild rice berry dessert) and wild rice stuffings with almonds, mushroom. In recent years, wild rice has been used in breakfast cereals, and mixes for pancakes, muffins, and cookies. Wild rice is increasing in popularity among health enthusiasts.

Botany

Annual, monoecious, aquatic grass 60–70(150) cm tall with shallow root system with a spread of 2,030 cm with spongy, straight roots with sparse root hairs. Stem is strongly tillering with up to 50 tillers per plant. Stems are hollow except at nodes where leaves, tillers, roots, and flowers appear. Leaf blades are linear (ribbon-like), 6–32 mm wide; mature plants with five or six leaves per stem or tiller above the water. Inflorescence a slender, much- branched panicle with female (pistillate) florets at the top and pendulous male (staminate) florets on the lower portion. Female florets have a long awn. branching Cross pollination is common since female flowers emerge first and become receptive and are pollinated before male flowers shed pollen on the same panicle. The caryopsis has an impermeable pericarp, large endosperm, and small embryo and is tightly enclosed by the palea and lemna. The seed (grains) with the palea and lemma (hulls) removed, are narrowly cylindrical 8–16 mm long by 1.5–4.5 mm across. Immature seeds are green, but turn a purple-black colour as they reach maturity (Plate 1).

Plate 1 Mature northern wild rice grains

Nutritive/Medicinal Properties

Proximate nutrient composition of raw wild rice per 100 g edible portion was reported as: water 7.76 g, energy 357 kcal (1,494 kJ), protein 14.73 g, total lipid 1.08 g, ash 1.53 g, carbohydrate 74.90 g, total dietary fibre 6.2 g, total sugars 2.50 g, sucrose 0.67 g, Ca 21 mg, Fe 1.96 mg, Mg 177 mg, P 433 mg, K 427 mg, Na 7 mg, Zn 5.96 mg, Cu 0.524 mg, Mn 1.329 mg, Se 2.8 µg, thiamin 0.115 mg, riboflavin 0.262 mg, niacin 6.733 mg, pantothenic acid 1.074 mg, vitamin B-6 0.391 mg, total folate 95 µg, total choline 35.0 mg, β-carotene 11 µg, vitamin A 19 IU, lutein + zeaxanthin 220 µg, vitamin E (alpha-tocopherol) 0.82 mg, vitamin K (phylloquinone) 1.9 µg, total saturated fatty acids 0.156 g, 16:0 (palmitic) 0.145 g, 18:0 (stearic) 0.011 g, total monounsaturated fatty acids 0.159 g, 18:1 undifferentiated (oleic) 0.159 g, total polyunsaturated fatty acids0.676 g, 18:2 undifferentiated (linoleic) 0.377 g, 18:3 undifferentiated (linolenic) 0.300 g, tryptophan 0.179 g, threonine 0.469 g, isoleucine 0.618 g, leucine 1.018 g, lysine

0.629 g, methionine 0.438 g, cystine 0.174 g, phenylalanine 0.721 g, tyrosine 0.622 g, valine 0.858 g, arginine 1.136 g, histidine 0.384 g, alanine 0.825 g, aspartic acid 1.419 g, glutamic acid 2.565 g, glycine 0.672 g, proline 0.519 g and serine 0.778 g (USDA 2012).

The lipid content of wild rice (*Zizania palustris*) ranging from 0.7 to 1.1% , were lower than in regular brown rice, 2.7% (Przybylski et al. 2009). Wild rice lipids comprised mainly linoleic (35–37%) and linolenic (20–31%) acids and other fatty acids palmitic (14.1–18.4%), stearic (1.1–1.3%), and oleic (12.8–16.2%). Wild rice lipids contained very large amounts of sterols, ranging from 70 g/kg for a Saskatchewan sample to 145 g/kg for Minnesota Naturally Grown Lake and River Rice. The main sterols found in an unsaponified fraction were: campesterol (14–52%), β-sitosterol (19–33%), δ-5-avenasterol (5–12%), and cycloartenol (5–12%). Other sterols, γ-oryzanols, were present as the phenolic acid esters; the content t ranged from 459 to 730 mg/kg in wild rice lipids. The highest levels of tocopherols and tocotrienols, 3,682 and 9,378 mg/kg, were observed in North Western Ontario wild rice samples, whereas the lowest were 251 mg/kg in an Athabasca Alberta sample and 224 mg/kg in regular long-grain brown rice. The α isomer was the most abundant among tocopherols and tocotrienols. The results of this study showed that wild rice lipids contain large amounts of nutraceuticals with proven positive health effects.

This grain has a high protein and carbohydrate content, and is very low in fat (USDA 2012; Anderson 1976). The nutritional quality of wild rice appears to equal or surpass that of other cereals and lysine and methionine constitute a higher concentration of the amino acids in the protein than in most other cereals. The SLTM value (sum of lysine, threonine, and methionine contents) often serve as a measure of the nutritional quality of cereals, is a little higher for wild rice than for oat groats, which is one of the better cereals for humans (Oelke et al. 1997). Processed and unprocessed wild rice have similar amino acid composition indicating little loss in nutritional quality during processing. Wild rice contains less than 1%fat, of which linolenic and linoleic acids together comprise a larger proportion of the fatty acids (68%) than in wheat, rice, or oats (Oelke et al. 1997). Although both fatty acids are easily oxidized and develop rancid odours in wild rice, the high levels of linolenic acid make the lipid in wild rice highly nutritious. Also, the high potassium and phosphorus mineral content, compares favourably with wheat, oats, and corn. Processed wild rice contains no vitamin A, but serves as an excellent source of the B vitamins: thiamine, riboflavin, and niacin.

The cell wall of wild rice grain when fractionated afforded pectin (7%), hemicellulose (71%), and cellulose (22%) (Motoko and Akira 2001). The hemicellulose content was significantly higher than that of cultivated rice, while the pectin content was lower. Soluble hemicelluloses when further fractionated afforded three components: H1, H2, and H3. H1 was a neutral arabinoxylan, with a lower degree of branching than that in rice, H2 was a glucuronoarabinoxylan, and H3 was a pectic polysaccharide containing a galacturonan backbone.

Wild rice (*Zizania palustris*) has been reported to be diuretic and refrigerant, and is used in folkloric remedy for burns, heart ailments, hepatoses, nephrosis, pulmonosis, and stomach ailments.

Other Uses

Wild rice is also a staple food for wild waterfowl, ducks, mallards, woodducks.

Wild rice is grown as an ornamental plant in garden ponds. Several Native American Indian cultures, such as the Ojibwa, reverently regard wild rice (known as manoomin to the Objiwa) as a sacred component in their culture.

Comments

Based on electrophoretic evidence, annual members of the genus *Zizania* were classified into two species: *Z. aquatica* with three varieties (vars. *aquatica*, *subbrevis*, and *brevis*) and *Z. palustris* with two varieties (vars. *palustris* and *interior*)

(Warwick and Aiken 1986). *Z. aquatica* is a non-cultivated wild rice and its smaller seeds are not commonly used for food (Oelke 1993).

Wild rice seed needs to be stored for 90 days in cold (3°C) water before dormancy is surmounted.

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Xanthophyllum amoenum

Scientific Name

***Xanthophyllum amoenum* Chodat.**

Synonyms

Xanthophyllum stipitatum var. *nitidum* Chodat, *Xanthophyllum stipitatum* var. *pachyphyllum* Chodat.

Family

Polygalaceae

Common/English Name

Langgir, Nyalin

Vernacular Names

Borneo: Langgir, Nyalin (Sarawak), Minyak Berok, Pokok Minyak Berok (Sabah), Keranji, Lahal, Langir, Menyerin, Nyalin Paya, Sianglam, Tampasak;
Indonesia: Gading, Gading Batu, Lilin, Medang Tanduk, Mendjalin, Minat Angkat;
Malaysia (Peninsular): Kapas, Minyak Berok, Pokok Minyak Berok;
Philippines: Mararing (Palawan).

Origin/Distribution

The species is indigenous to Peninsular Malaysia, Sumatra, Borneo (throughout the island) and the Philippines.

Agroecology

In nature it occurs wild in undisturbed mixed dipterocarp forest, coastal (mangrove), keranga, (peat)-swamp and sub-montane forests from near sea level up to 1,500 m altitude. In secondary forests it is usually present as a pre-disturbance remnant or planted. It is common on alluvial, swampy localities as well as on hillsides and ridges. It is also found on sandy to clayey soils.

Edible Plant Parts and Uses

The fruit is edible and the cream-like fibrous aril is sweet.

Botany

A mid-canopy, evergreen, branched, perennial tree up to 30 m tall with 66 cm bole diameter. Leaves are alternate, exstipulate with short petiole 0.5–1 cm. Lamina is simple, oblong elliptic with tapering apex, 6–12 cm long by 3–6 cm wide, shiny, glabrous with entire margin and

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Plate 1 Globose, greenish-yellow Langgir fruit

Plate 2 Globose fruit halved to show the creamy-white flesh

inconspicuous venation. Flowers are reddish-white in unbranched racemose, axillary and terminal inflorescences. Flowers are 18 mm across with five ovate sepals, five free petals with one hooded keel enclosing the eight free stamens, style, and one-loculed ovary with four or more ovules. Fruit is globose, fleshy berry, 4.5–5.0 cm diameter, glabrous, green turning to yellow or orangey-yellow when ripe, with several brown, ovoid seeds embedded in the white mucilaginous, sweetish pulp (Plates 1 and 2).

Nutritive/Medicinal Properties

The food nutrient composition of the fruit of *Xanthophyllum amonum* per 100 g edible portion based on analyses made in Sarawak (Voon and Kueh 1999) is: water 71.0%, energy 124 kcal, protein 2.3%, fat 2.9%, carbohydrates 22.1%, crude fibre 1.6%, ash 0.2%, P 29 mg, K 139 mg, Ca 20 mg, Mg 9 mg, Fe 0.6 mg, Mn 11 ppm, Cu 8.4 ppm, Zn 33.1 ppm and vitamin C 1.2 mg.

Fruit has been used medicinally in local folkloric medicine against pain (paste of fruit on painful spot) and the fruit skin is used as hair shampoo. It is held by the locals in Sarawak that prolonged use of the shampoo will result in glossy black hair.

Other Uses

X. amoenum is a major species that provides nyalin timber classified as medium hardwood timber in Malaysia. The ASEAN name for the timber is Lilin. The timber is suitable for medium and heavy construction, which is temporary or protected from attacks by drywood termites as it is susceptible to drywood termites. It is also suitable for panelling, mouldings, flooring (heavy traffic), joists, staircase (angle block, rough bracket, newel, riser, tread, bullnose, round end and winder), planking, plywood, tool handles (impact) and pallets (permanent and heavy duty). When treated, it is suitable for telegraphic and power transmission posts and cross arms. The timber has also been successfully used for the manufacture of blockboards.

Comments

The species is not a threatened species in its native range.

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Coccoloba uvifera

Scientific Name

***Coccoloba uvifera* (L.) L.**

Synonyms

Coccoloba uvifera (L.) Jacq., *Coccolobis uvifera* (L.) Crantz, *Coccolobis uvifera* (L.) Jacq., *Polygonum uvifera* L.

Family

Polygonaceae

Common/English Names

Bay Grape, Bow Pigeon, Caracas Kino, Coccoloba Kino, Columbian Kino, Hopwood, Horsewood, Jamaican Kino, Mangrove Grape, Platterleaf, Pigeon Wood, Sea Grape, Seaside Grape, Seaside Plum, Shore Sea-Grape, Shore Grape, South American Kino, West Indian Kino, Wild Grape, Wild Mangrove Grape, Wild Seaside Grape.

Vernacular Names

Brazil: Cocoloba, Uva-Do-Mar (Portuguese);
British West Indies: Bow Pigeon, Hopwood, Horsewood, Mangrove Grape, Pigeonwood, Seaside Grape, Seaside Plum, Wild Grape, Wild Mangrove Grape, Wild Seaside Grape;
Central America : Uva, Uva Caleta, Uva De La Mar, Uva De Playa, Uverillo, Uvero (Spanish);
Finnish: Norsunkorva;
French: Raisin Marine, Raisinier, Raisinier Bord De Mer, Raisinier Des Bords De Mer, Raison De Mer;
French West Indies: Bois Baguette, Bois Rouge Montagne, Raisinier À Grappes;
German: Meertraube, Seetraube, Gemeine Seestraube, Meertraubenbaum, Strandtraube;
Portuguese: Cipo Branco De Pernambuco, Uva-Da-Praia;
Puerto Rico: Cucubano, Gateado, Uva-Del Mar, Uvero, Uvillo;
Spanish: Arahueque, Cumare Blanco, Manzano, Micongo, Nula, Palo Mulato, Papatón, Uva Caleta, Uva De La Playa, Uva De La Costa, Uva De Mar, Uverna, Papaturro; Uvero, Uvero De Playa, Uvero Macho, Zapatero;
Surinam: Dreifi, Droifi (Creole), Zeedruif, Zee-Druif (Dutch), Matora (Arawak);
Trinidad: Cuchape, Uvero Del Monte.
Venezuela: Uvero De Playa.

Origin/Distribution

The species is indigenous to Mexico, northern South America, the Caribbean and southern Florida. It is now found pantropically and has been introduced to Taiwan, Australia and the Philippines.

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Agroecology

In its native tropical range from Argentina north throughout the West Indies and in Florida, it occurs on sandy coasts, coastal hammocks, coastal scrub, coastal grasslands and beach strands. It thrives in full sun to partial shade. It is drought tolerant and highly tolerant of salt spray and salty soils as well as strong sun and wind. It is often planted as a windbreak near beaches and as a hedge. It is sensitive to frost.

Edible Plant Parts and Uses

The fruit is edible, the pulp can be eaten fresh or made into jams, jellies or fermented to make wine.

Botany

A tall shrub to a small tree 2–15 m high with a bole of 30–60 cm with spreading or sprawling branches and a sparse crown. Stem with grey brown bark that peels off in flakes, with reddish sap, twigs green and puberulent when young, grey at maturity, glabrous or pubescent. Leaves of normal shoots with stout petioles, 7–10 mm long, alternate, puberulent to pilose, lamina pale green below, green to bluish green above, round to transversely elliptic, (6–)10–20(–27)×6–20(–27) cm, coriaceous, base cordate, margins sometimes revolute, apex rounded to blunt or emarginate, abaxial surface dull, adaxial surface shiny or dull, minutely punctate, glabrous (Plates 2 and 3). Inflorescences 10–30 cm, puberulent or glabrous, pistillate pendent in fruit; peduncle 1–5 cm, glabrous. Pedicels 1–4 mm, glabrous. Flowers are fragrant with round to broadly elliptic, white tepals margins entire, apex obtuse. Staminate flowers 1–7 per fascicle, stamens to 4 mm long. Pistillate flowers 1–5 per fascicle, flower inconspicuous with obpyriform tube, 12–20×8–12 mm, becoming fleshy. Fruit included within the succulent perianth, obpyriform, 12–20 mm by 8–10 mm across, narrowed at the base, rounded truncate at the apex, the perianth green turning shiny rose-purple when mature and formed in pendant bunches (Plates 1, 2, and 3).

Plate 1 Immature seagrape fruits

Plate 2 Pendant bunch of fruits

Plate 3 Ripening fruits and leaves

Nutritive/Medicinal Properties

The leaves, bark and roots were traditionally used by the Native Americans to make medicinal teas. Both the juice and decoctions of wood, bark, and roots of the sea grape are astringent and were used to treat diarrhea, dysentery, hemorrhages, and venereal diseases, and applied externally for rashes and other skin afflictions. A tea made from the leaves was used to treat hoarseness and asthma, and to bathe wounds. The resinous gum of the bark was also used against throat ailments, while the root decoction was used against dysentery.

There was an application to the United States Patent Office, for United States Patent 6103242 for "Method of controlling blood sugar levels using *Coccoloba uvifera*" (Buckley 2000). This patent application included a method of treating diabetes in a patient comprising the steps of administering a quantity of an ingestible medium of *Coccoloba uvifera* leaf extract to the patient, monitoring the patient's change in serum glucose level, and modifying the dose and frequency of intake as required. The application also listed the following phytochemicals found in *C. uvifera* and associated bioactivities: α-amyrin (antitumour, cytotoxic), chrysophanol (antiseptic, bactericial, cathartic, hemostat, purgative), emodin (anti-aggregant, antiinflammatory, antitumour, antiulcer, immunosuppressive, viricide), physcion (antiseptic, cathartic, purgative), rhein, anticarcinomic, antitumour, fungicide), royleanone, β-sitosterol (hypoglycemic, hypolipidemic, hypocholesterolemic, hepatoprotective).

The methanol seed extract of *C. uvifera* was active against *Salmonella typhimurium* and *Staphylococcus aureus* (Morales et al. 2008). The ethyl acetate fraction inhibited the growth of *Escherichia coli* and *Pseudomonas aeruginosa*, and showed antifungal activity against *Candida albicans*, *Fusarium oxysporum* and *Fusarium decencellulare*. A tannic compound, an organic acid and a benzopyran was obtained from the bioactive fraction and identified as gallic acid, hexenedioic acid and 1,3,4,6,7,8–hexahydro-4,6,6,8,8,8-hexamethylcyclopenta-2-benzopyran respectively.

Recent studies showed *Coccoloba uvifera* extract to have photoprotective potential (Silveira et al. 2008). Exposure to ultraviolet (UV) radiation induced generation of reactive oxygen species, production of proinflammatory cytokines and melanocyte-stimulating hormone (MSH) as well as increase in tyrosinase activity. The extract exhibited antioxidant and antityrosinase activities and also inhibited the production of interleukin-1alpha (IL-1alpha), tumour necrosis factor alpha (TNF-alpha) and alpha-MSH in melanocytes subjected to UV radiation. Additionally, the extract inhibited the activity of tyrosine kinase in cell culture under basal and UV radiation conditions, corroborating the findings of the mushroom tyrosinase assay.

Other Uses

Sea-grape is used as hedges and as an ornamental street tree in coastal cities throughout the tropics. It is also used as windbreak and is planted along the sea-shore to stabilise the sandy soils. The wood is used for furniture, carvings and for fuel. The resin of the bark is used in tanning and yields a red dye. The plant is also valued for honey production.

Comments

Sea-grape is readily propagated from seeds and stem cuttings.

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Fagopyrum esculentum

Scientific Name

***Fagopyrum esculentum* Moench.**

Synonyms

Fagopyrum cereale (Salisb.) Raf., *Fagopyrum emarginatum* (Roth) Meisn., *Fagopyrum emarginatum* var. *kunawarense* Meisn., *Fagopyrum fagopyrum* Karst., *Fagopyrum sagittatum* Gilib. Nom. inval., *Fagopyrum sarracenicum* Dumort., *Fagopyrum vulgare* Hill nom. illeg., *Fagopyrum vulgare* T. Nees, *Fagopyrum zuogongense* Q.F. Chen, *Helxine fagopyrum* Kuntze, *Kunokale carneum* Raf., *Phegopyrum esculentum* (Moench) Peterm., *Polygonum cereale* Salisb., *Polygonum emarginatum* Roth, *Polygonum fagopyrum* L., *Polygonum tataricum* Lour. non L.

Family

Polygonaceae

Common/English Names

Buckwheat, Common Buckwheat, Japanese Buckwheat, Silverhull Buckwheat, Sweet Buckwheat.

Vernacular Names

Bhutan: Jare;
China: ER, Er Chi, Qiao Mai, Tian Qiao Mai;
Czech: Pohanka Obecná;
Danish: Almindelig Boghvede, Boghvede;
Dutch: Boekweit, Gewone Boekweit;
Eastonian: Harilik Tatar, Tatar;
Esperanto: Fagopiro, Fagopiro Ordinara;
Finnish: Tattari, Viljatatar;
French: Blé Noir, Bouquette, Renouée, Sarrasin, Sarrasin Commun;
Gaelic: Lus Na Gcearc;
German: Blenden, Bokert, Brein, Buchweizen, Echte Buchweizen, Gricken, Heidekorn, Heiden, Heidenkorn, Heidensterz, Sarazenenkorn, Schwarz-Plent, Schwarzes Welschkorn, Schwarzpolenta, Tater, Türkischer Weizen;
Hungarian: Hajdina, Közönséges Pohánka, Pohánka;
Icelandic: Bókhveiti;
India: Kaspat, Kuttu, Phaphra (Hindu), Rajgira (Maharashtra), Ogal;
Italian: Faggina, Fagopiro, Grano Saraceno, Grano Saraceno Commune, Sarasin;
Japanese: Soba;
Korean: Memil;
Nepal: Mite Phapar, Pharphar;
Norwegian: Bokhvete, Bokkveite;
Poland: Gryka Zwyczajna, Poganka, Tatarka Gryka;

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Portguese: Trigo Sarraceno;
Russian: Grecicha Kul'furnaja, Grečicha Posevnaja;
Slovaščina: Ajda Navadna, Navadna Ajda;
Slovencina: Pohánka Jedlá, Pohánka Streliciová;
Spanish: Alforfón, Grano Sarraceno, Grano Turco, Trigo Sarraceno;
Swedish: Bovete;
Thai: Khao Sam Liam;
Turkish: Karabuğday;
Vietnamese: Kiều Mạch;
Welsh: Gwenith Yr Hydd.

Origin/Distribution

The discovery of the wild ancestor of common buckwheat, *Fagopyrum esculentum* subsp. *ancestralis* in Yongsheng-xiang in Yunna province in China combined with the observation of the richest distribution of wild species in southern China clearly indicated that the birth place of cultivated common buckwheat is southern China, probably Yunnan province (Ohnishi 1996, 1998a, b). This discovery dismissed De' Candolle'e theory of 1883 that buckwheat originated in the area of Amur River, Siberia or the northern part of China. *Fagopyrum esculentum* ssp. *ancestralis* Ohnishi and four species, *F. homotropicum* Ohnishi, *F. pleioramosum* Ohnishi, *F. capillatum* Ohnishi, and *F. callianthum* Ohnishi in the genus *Fagopyrum* were found in southern China, either in Yunnan or Sichuan province (Ohnishi 1998a). Three species *F. cymosum* (4x form), *F. gracilipes* and *F. tataricum* ssp. *potanini* are widely distributed from central China to western India, northern China to Bhutan, and central China to northern Pakistan, respectively. All other species have relatively narrow endemic distribution either in northwestern Yunnan province or in the upper Min river valley of Sichuan province. The location where Ohnishi discovered the wild ancestor of common buckwheat (*F. esculentum* ssp. *ancestralis*) is just in the center of species diversity of *Fagopyrum. F. tataricum* ssp. *potanini* Batalin was found to be the wild ancestor of tatary buckwheat and its original birthplace was found to be the northwest part of Sichuan based on allozyme variability in wild tatary buckwheat (Ohnishi 1998b). *F. cymosum* was found not to be the ancestor of cultivated buckwheat, it is only distanly related in morphology, isozymes and cpDNA. Li and Yang's (1992) study of the origin of buckwheat supports Ohnishi's hypothesis that the province of Anion is the area in which common buckwheat originated. Buckwheat is known to have been cultivated in China as early as the second-first centuries BC (Li and Yang 1992).

Buckwheat is grown throughout a large area of Asia as a crop that fits the farming system on marginal and fairly unproductive land as found in China, Tibet, Bhutan, Korea, Japan, Mongolia, Myanmar, Nepal, Russia, and Sikkim. It is also cultivated in Australia, Europe, and North America. Common buckwheat is by far the most important *Fagopyrum s*pecies, economically, accounting for over 90% of the world's buckwheat production. The main producers are China, Russian Federation, Ukraine and Kazakhstan.

Agroecology

Buckwheat is a cool climate crop and grows well in temperate and subtropical areas; it can be successfully grown in the highlands in the tropics. It is a short- season crop of 3–4 months and is killed by freezing temperatures in both spring and autumn. It has been reported to grow optimally within the temperature range of 18–25°C; it tolerates night temperatures of 5–10°C and day temperatures of 18–30°C. Temperatures above 30°C have been reported to be detrimental causing fruit desiccation and reducing yield. Buckwheat is susceptible to strong winds that cause lodging during crop growth and shattering during seed maturity. The plant is intolerant of drought because of tis shallow and poorly developed root system. Drought coupled with high temperatures will cause poor fruit setting and rains during flowering will hamper pollination and fruit set though it will stimulate vegetative growth. Buckwheat cultivars are usually day-neutral or exhibit short day photoperiodism.

Buckwheat grows on a wide range of soil types and fertility levels. It produces a better crop

than other grains on infertile, poorly drained soils if the climate is moist and cool. Buckwheat has higher tolerance to soil acidity than any other grain crop. It is best suited to light to medium textured, well-drained soils such as sandy loams, loams and silt loams with pH levels of 4.5–7. It performs poorly in heavy, wet soils or in soils that contain high levels of limestone. On soils high in nitrogen, lodging may occur and cause yield reduction. Buckwheat is suitable for freshly cleared infertile, well-drained marshland, rough land or acid soils with a high amount of decomposing organic matter.

Edible Plant Parts and Uses

The buckwheat grain, leaves and germinated sprouts are edible raw or cooked. Buckwheat grain is a pseudo cereal and not classified as a true cereals but share similar usage. Unlike common cereals, the protein of buckwheat is of excellent quality and is high in the essential amino acid lysine, buckwheat is also rich in vitamins (especially vitamin B6), minerals, dietary fibre and antioxidant phenolic compounds. Buckwheat is gluten free and thus is suitable for people with gluten allergies or suffering from coeliac disease. (see below). However, buckwheat ca be a potent allergen in sensitive people and provoke Ig E-mediated anaphylaxis.

Most of the buckwheat grain utilized as food for human consumption is marketed in the form of flour. The flour is generally dark coloured due to presence of hull fragments not removed during the milling process. Buckwheat flour is used primarily for making buckwheat griddle cakes, and is more commonly marketed in the form of pancake mixes than as pure buckwheat flour. These prepared mixes may contain buckwheat mixed with wheat, corn, rice, or oat flours and a leavening agent. Buckwheat flour is also used for making noodles, bread, biscuits, cereals, thickening agents, and used as a meat extender. Buckwheat flour is never produced from tartary buckwheat because of a bitter taste that makes it undesirable as human food.

Some buckwheat grains are utilized in the form of groats (that part of the grain that is left after the hulls are removed from the kernels). The product may be marketed as whole groats, cracked groats, or as a coarse granular product. These products are used for breakfast food, porridge, and thickening materials for soups, gravies, and dressings.

Buckwheat grain is also used to brew an excellent beer, alcoholic beverage and vinegar. It can be used as a substitute for other gains in a gluten free beer. It can be utilised similarly like barley to produce a malt to form a the basis of a mash free of gluten (gliadin or hordein) and therefore can be suitable for coeliacs or others sensitive to certain glycoproteins. In Danzig, cordial water is made from the spirit dsitilled from buckwheat.

Buckwheat is of ten grown as a leafy vegetable crop in the Indian subcontinent, The small leaves and tender young leafy shoots are harvested and consumed in various dishes. The leaves are rich in rutin and present a very healthy addition to the diet. Green flour, obtained by milling of the dried common buckwheat plants, is used as a natural food colorant (Kalinova et al. 2006). Dried buckwheat leaves for tea were manufactured in Europe under the brand name “Fagorutin”. Buckwheat sprouts are used in salads and as vegetables.

Buckwheat plant provides an excellent nectar source for honey production. Relatively pure buckwheat honey is monofloral, dark-coloured and has a strong flavour and can fetch a premium price.

Buckwheat Edible Uses Around the World

Common buckwheat is consumed in many diverse cuisines around the world. Since ancient time buckwheat noodles have been eaten by people from Tibet and northern China where wheat cannot be grown in the mountainous areas. Buckwheat noodles commands a major role in the cuisines of Japan (*soba*), (*makguksu, memil guksu* and *naengmyeon*,) and the Valtellina region of Northern Italy (*pizzoccheri*). In Korea, *guksu*

(noodles) were widely made from buckwheat before it was replaced by wheat. Buckwheat strach is used to nake a jelly called *memilmu*k in Korea. *Soba* noodles are the subject of deep cultural importance in Japan. In Japan, prior to the sixteenth century, the common way of eating buckwheat flour was to add water to the flour and beat into a firm, steamy, gelatin-like substance and make into small dumplings called *soba-gaki* (Shiratori and Nagata 1986). From the sixteenth century onwards, buckwheat flour was processed into noodles called *soba-kiri*. Although *soba-kiri* was appreciated for its delicious taste, it required much time and effort to make. In mountain and rural areas, the making of noodles was reserved for special occasions such as weddings and funerals etc., as well as being served as a dish for visitors. A good example is the old custom of eating buckwheat noodles on New Years' Eve (called *Toshi-koshi Soba*). This is done to symbolize their wish for a life of longevity. In China, buckwheat grains are used for the production of vinegar.

In south Asia, buckwheat forms the staple food for people in the mountainous areas. Here, buckwheat flour is used to prepare unleavened bread, *chapattis* or mixed with some water and fried to make a crisp *pakora*. Buckwheat flour is also mixed with mashed potatoes to make *parathas*. It is also used for fasts and for religious celebrations by the Hindus in the Himalayas.

In North America and Europe buckwheat flour is normally mixed with wheat flour to make prepare pancakes, biscuits, noodles, cereals, and is used as a meat extender. In North America, buckwheat flour is baked into cakes and eaten with maple syrup as breakfast cakes. In Russia and Poland the groats and flour are used to make porridge and soup. In Sweden it is used to stuff fish. Buckwheat pancakes made from buckwheat raised with yeast is commonly etean in many countries. In Russia, they are called buckwheat *blinis*; *ploys* in Acadia; *boûketes* in the Wallonia of Belgium and in France, *galettes* (savoury *crêpes* made with buckwheat flour with or without eggs). In Ukraine, yeast rolls called *hrechanyky* are made from buckwheat flour. Bukwheat flour is also made into crumpets which are popular among Dutch children.

Buckwheat groats were the most widely used form of buckwheat worldwide during the twentieth century, eaten primarily in western Asia and eastern Europe especially in Russia, Ukraine and Poland. In the Russian army, buckwheat groats are served as part of a soldier's ration and cooked with butter, tallow or hemp seed oil. Buckwheat groats are used to make farina breakfast food, porridge and thickening agents in soups, gravies and dressings. Porridge made from groats are cooked with broth to a texture similar to rice or *bulgur*. Russians and Polish called it *kasha* and mixed it with pasta or used it as a filling for *knishes* and *blintzes*. Buckwheat also used with wheat, maize (*polenta taragna* in Northern Italy) or rice in bread and pasta products. In Germany, the groats are used as an ingredient in pottage, puddings and other food.

Studies on Buckwheat Food Products

Studies showed that *erişte*, Turkish noodles containing buckwheat up to a 25% level were appreciated by the panelists, especially in terms of overall acceptability (Bilgiçli 2009). Bread prepared with buckwheat flour had improved quality: an increased specific volume, a sof ter texture, color characteristics, and gas-cell size distribution similar to French bread (Mezaize et al. 2009). Bread with 1.9% guar gum (w/w, total flour basis) and 5% buckwheat flour (of all flours and substitutes) mimicked French bread quality attributes. Recent studies showed that gluten-free cake could be produced with satisfactory results by the addition of debittered lupin flour and whole buckwheat flour up to 30 and 10%, respectively (Levent and Bilgicli 2011). Lupin flour increased the protein, calcium, iron, manganese, phosphorus and zinc contents of the cakes, while buckwheat flour caused a significant increase especially in potassium and magnesium contents of the gluten-free cakes.

Botany

An erect, annual, branched herb, 30–120 cm high with short tap roots and fine lateral roots. Stems green or red when mature, angular and hollow. Leaves alternate, upper leaves subsessile, lower ones on 1.5–5 cm long petioles; petiole surrounded by short, tubular, membranous, caducous ocrea (sheath); lamina hastate-triangular, sagittate-triangular, 2.5–7 × 2–5 cm, or base cordate or nearly truncate, apex acute to acuminate, 7–9 primary basal veins, both surfaces papillate along veins. Inflorescence axillary or terminal, racemose or corymbose; peduncles 2–4 cm; bracts green, ovate, margin membranous, each 3- or 5-flowered. Perianth pink or white, tepals 5 elliptic, 3–4 mm long persistent; stamens 8 alternating at he base with 8 honey glands, anthers pinkish; ovary 1-celled, trigonous, style tripartite with purplish, capitate stigmas. Flowers exhibit heterostyly, some with eight long styles and three short styles, other flowers have eight short stamens and three long styles. Fruit a trigonous achene, 5mm × 6 mm, grey brown to dark brown to black, surfaces smooth, angles prominent containing a single seed, light green turning reddish-brown, slightly smaller than fruit (Plate 1).

Plate 1 Common buckwheat grains

Nutritive/Medicinal Properties

Proximate nutrient composition of buckwheat (*Fagopyrum esculentum*) had been reported as: water 9.75 g, energy 343 kcal (1435 kJ), protein 13.25 g, total lipid 3.40 g, ash 2.10 g, carbohydrate 71.50 g, total dietary fibre 10.0 g, Ca 18 mg, Fe 2.20 mg, Mg 231 mg, P 347 mg, K 460 mg, Na 1 mg, Zn 2.40 mg, Cu 1.1 mg, Mn 1.3 mg, Se 8.3 µg, thiamin 0.101 mg, riboflavin 0.425 mg, niacin 7.020 mg, pantothenic acid 1.233 mg, vitamin B-6 0.210 mg, total folate 30 µg, total saturated fatty acids 0.741 g, 8:0 (caprylic) 0.035 g, 10:0 (capric) 0.018 g, 12:0 (lauric) 0.010 g, 14:0 (myristic) 0.025 g, 16:0 (palmitic) 0.450 g, 18:0 (stearic) 0.047 g, total monounsaturated fatty acids 1.040 g, 16:1 undifferentiated (palmitoleic) 0.023 g, 18:1 undifferentiated (oleic) 0.988 g, 22:1 undifferentiated (erucic) 0.012 g, total polyunsaturated fatty acids 1.039 g, 18:2 undifferentiated (linoleic) 0.961 g, 18:3 undifferentiated (linolenic) 0.078 g, tryptophan 0.192 g, threonine 0.506 g, isoleucine 0.498 g, leucine 0.832 g, lysine 0.672 g, methionine 0.172 g, cystine 0.229 g, phenylalanine 0.520 g, tyrosine 0.241 g, valine 0.678 g, arginine 0.982 g, histidine 0.309 g, alanine 0.748 g, aspartic acid 1.133 g, glutamic acid 2.046 g, glycine 1.031 g, proline 0.507 g and serine 0.685 g (USDA 2012).

Proximate nutrient composition of roasted, dry buckwheat groats (kasha) had been reported as: water 8.41 g, energy 346 kcal (1448 kJ), protein 11.73 g, total lipid 2.71 g, ash 2.20 g, carbohydrate 74.95 g, total dietary fibre 10.3 g, Ca 17 mg, Fe 2.47 mg, Mg 221 mg, P 319 mg, K 320 mg, Na 11 mg, Zn 2.42 mg, Cu 0.624 mg, Mn 1.618 mg, Se 8.4 µg, thiamin 0.224 mg, riboflavin 0.271 mg, niacin 5.135 mg, pantothenic acid 1.233 mg, vitamin B-6 0.353 mg, total folate 42 mγ, total choline 54.2 mg, betaine 2.6 mg, total saturated fatty acids 0.591 g, 8:0 (caprylic) 0.028 g, 10:0 (capric) 0.014 g, 12:0 (lauric) 0.008 g, 14:0 (myristic) 0.020 g, 16:0 (palmitic) 0.359 g, 18:0 (stearic) 0.038 g, total monounsaturated fatty acids 0.828 g, 16:1 undifferentiated (palmitoleic)

0.018 g, 18:1 undifferentiated (oleic) 0.788 g, 22:1 undifferentiated (erucic) 0.009 g, total polyunsaturated fatty acids 0.828 g, 18:2 undifferentiated (linoleic) 0.766 g, 18:3 undifferentiated (linolenic) 0.062 g, tryptophan 0.170 g, threonine 0.448 g, isoleucine 0.441 g, leucine 0.736 g, lysine 0.595 g, methionine 0.153 g, cystine 0.202 g, phenylalanine 0.461 g, tyrosine 0.213 g, valine 0.600 g, arginine 0.869 g, histidine 0.273 g, alanine 0.662 g, aspartic acid 1.003 g, glutamic acid 1.811 g, glycine 0.912 g, proline 0.449 g and serine 0.606 g (USDA 2012).

Mineral components (mg/100 g) in buckwheat and its products were reported as follows:- grain: K 244.1, Mg, 168.6, Mn 5.44, Fe 4.82, Zn 3.40, Cu 0.59, ; flour: K 299.4, Mg 160.8, Mn 2.22, Fe 5.26, Zn 3.72, Cu 0.53; testa K 248.0, Mg 120.6, Mn 13.09, Fe 5.61, Zn 2.49, Cu 0.49; groat K 301.5, Mg 172.9, Mn 1.53, Fe 3.69, Zn 2.96, Cu 0.79 (Amarowicz and Fornal 1987). Dietary fibre contents and its components in buckwheat grains and its products (% DM) were reported as follows: grain dietary fibre 24.75, acid detergent fibre 20.39, hemi-celluloses 4.36, celluloses 9.81, lignins 10.58; flour dietary fibre 3.94, acid detergent fibre 3.98, hemi-celluloses 0.00, celluloses 2.34, lignins 1.64; testa: dietary fibre 80.31, acid detergent fibre 61.98, hemi-celluloses 18.33, celluloses 29.93, lignins 32.05; groat dietary fibre 4.51, acid detergent fibre 2.29, hemi-celluloses 2.22, celluloses 1.81, lignins 0.48. Compared to cereal grain buckwheat seed coat was found to be rich only in iron and manganese, while compared to whole buckwheat grain it contained less zinc, copper and potassium, and less manganese. Thus removal of seed coat would not affect qualitative-quantitative composition of flours mineral salts. Compared to buckwheat flour buckwheat groats were found to contain less zinc, manganese and iron, and more potassium and magnesium. Dietary fibre content in groats and flour was much lower than in buckwheat grain while seed coat was found to contain 3 times more fibre than the grain. In fractional composition of dietary fibre in the examined material there is a noticeably higher amount of lignins and celluloses in comparison to hemicelluloses. The seed coat fibre contained the greatest amount of celluloses and lignins. An interesting finding was the presence of hemicelluloses in buckwheat groats.

Buckwheat contained 12% protein (similar to wheat), 3% fat and high crude fibre (12.7 and 18.7% for two varieties) and low soluble carbohydrate level of 48.7% (Eggum et al. 1980). Both buckwheat varieties had a high tannin content of 1.76 and 1.54%, respectively. Unlike other cereals, the protein quality was very high, with biological values above 90% attributable to a high concentration of most essential amino acids especially lysine, threonine, tryptophan, and the sulphur-containing amino acids. However, due to the high contents of crude fibre and tannin, the true protein digestibility was slightly below 80%.

In general roasted buck wheat groat had lower nutrient values than raw buckwheat grain. Roasting significantly decreased the total protein content of buckwheat groats, whereas this parameter was not affected by the thermal treatment of whole buckwheat seeds (Zielinski et al. 2009). The formation of Maillard Reaction Products (MRPs) was induced by the thermal treatment of both whole seeds and groats, thus suggesting deterioration of protein quality due to this chemical event. A significant degradation in natural antioxidants due to thermal processing was observed.

Proximate nutrient composition of whole-groat buckwheat flour had been reported as: water 11.15 g, energy 335 kcal (1402 kJ), protein 12.62 g, total lipid 3.10 g, ash 2.54 g, carbohydrate 70.59 g, total dietary fibre 10.0 g, total sugars 2.60 g, sucrose 1.70 g, Ca 41 mg, Fe 4.06 mg, Mg 251 mg, P 337 mg, K 577 mg, Na 11 mg, Zn 3.12 mg, Cu 0.515 mg, Mn 2.030 mg, Se 5.7 μg, thiamin 0.417 mg, riboflavin 0.190 mg, niacin 6.150 mg, pantothenic acid 0.440 mg, vitamin B-6 0.582 mg, total folate 54 μg, total choline 54.2 mg, luetin + zeaxanthine 220 μg, vitamin E (α-tocopherol) 0.32 mg, γ-tocopherol 7.14 mg, δ-tocophero l0.45 mg, vitamin K (phylloquinone) 7.0 μg, total saturated fatty acids 0.677 g, 8:0 (caprylic) 0.032 g, 10:0 (capric) 0.016 g, 12:0 (lauric) 0.009 g, 14:0 (myristic) 0.023 g, 16:0 (palmitic) 0.411 g, 18:0 (stearic) 0.043 g, total monounsaturated fatty acids 0.949 g, 16:1 undifferentiated (palmitoleic) 0.021 g, 18:1 undifferentiated (oleic)

0.902 g, 22:1 undifferentiated (erucic) 0.011 g, total polyunsaturated fatty acids 0.949 g, 18:2 undifferentiated (linoleic) 0.877 g, 18:3 undifferentiated (linolenic) 0.071 g, tryptophan 0.183 g, threonine 0.482 g, isoleucine 0.474 g, leucine 0.792 g, lysine 0.640 g, methionine 0.164 g, cystine 0.218 g, phenylalanine 0.495 g, tyrosine 0.230 g, valine 0.646 g, arginine 0.935 g, histidine 0.294 g, alanine 0.712 g, aspartic acid 1.078 g, glutamic acid 1.948 g, glycine 0.981 g, proline 0.482 g and serine 0.652 g (USDA 2012). Seeds of common buckwheat contained 1.5–3.7% total lipids (Campbell 1997). The highest concentration was in the embryo at 7–14% and the lowest in the hull at 0.4–0.9%. Groats or dehulledseeds of Mancan, Tokyo and Manor buckwheat contained 2.1–2.6% total lipids, of which 81–85% were neutral lipids, 8–11% are phospholipids and 3–55% are glycolipids. The major fatty acids of common buckwheat were palmitic, oleic, linoleic, stearic, linolenic, arachide, behenic and lignoceric. Of these, the 16 and 18-carbon acids were commonly found in all cereals. The long-chain acids – arachidic, behenic and lignoceric – which represented approximately 8% of the total acids in buckwheat, were only minor components or were not present in cereals.

Amino acid composition (% amino acid/total amino acid) of buckwheat sample was reported as lysine 6.66%, histidine 1.89%, arginine 8.46%, aspartic acid 10.60%, threonine 4.03%, serine 4.68%, glutamic acid 18.90%, proline 4.52%, glycine 5.74%, alanine 5.095, cystine 1.15%, valine 5.92%, methionine 2.38%, isoleucine 3.70%, leucine 7.31%, tyrosine 2.96% and phenylalanine 4.85%(Javornik and Kreft 1984). Amino acid composition (% amino acid/total amino acid) of buckwheat albumin was reported as lysine 7.86%, histidine 2.07%, arginine 8.68%, aspartic acid 10.49%, threonine 4.40%, serine 5.20%, glutamic acid 18.38%, proline 3.66%, glycine 5.21%, alanine 4.76, cystine 2.50%, valine 4.93%, methionine 2.69%, isoleucine 3.46%, leucine 6.67%, tyrosine 3.76% and phenylalanine 4.28%. Amino acid composition (% amino acid/total amino acid) of buckwheat globulin was reported as lysine 5.04%, histidine 2.27%, arginine 12.17%, aspartic acid 11.04%, threonine 3.30%, serine 5.64%, glutamic acid 20.91%, proline 3.79%, glycine 5.42%, alanine 3.64, cystine 0.91%, valine 4.81%, methionine 1.77%, isoleucine 3.63%, leucine 6.82%, tyrosine 2.52% and phenylalanine 6.38%. Amino acid composition (% amino acid/total amino acid) of buckwheat glutelin was reported as lysine 6.40%, histidine 2.56%, arginine 9.98%, aspartic acid 9.89%, threonine 4.82%, serine 5.76%, glutamic acid 17.45%, proline 4.52%, glycine 6.66%, alanine 5.59, cystine 0.00%, valine 5.12%, methionine 2.56%, isoleucine 4.10%, leucine 8.19%, tyrosine 3.41% and phenylalanine 2.99%.

The range of starch content in buckwheat groats was reported as 37–70%(db), depending on the species (Javornik 1986). Buckwheat starch granule size ranged from 1.0–11.4 μm, were polygonal and slightly larger than rice with a 25% amylose content by iodine colorimetry; a gelatinization temperature of 61–65°C; and high cool paste viscosity in a Brabender Visco-Amylograph (Kim et al. 1977). Qian et al. (1998) found that buckwheat starch granules (2.9–9.3 μm) were round and polygonal with some holes and pits on the surface (Qian et al. 1998). Buckwheat starch had higher amylose content, waterbinding capacity, and peak viscosity, and it had lower intrinsic viscosity whencompared with corn and wheat starches. Buckwheat starch also showed restricted swelling power at 85–95°C and lower solubility in water at 55–95°C and was more susceptible to acid and enzymatic attack. Gelatinization temperatures, determined by differential scanning calorimetry, were 61.1–80.1°C for buckwheat starch compared to 64.7–79.2°C and 57.1–73.5°C for corn and wheat starches, respectively. Li et al. (1997) found common buckwheat starch to have a swelling volume in water of 27.4–28.0 mL and peak gelatinization temperature in water of 66.3–68.8°C. A comparison of pasting characteristics of common and tartary buckwheat starches to wheat starch indicated similar peak viscosity, higher hot paste viscosity, higher cool paste viscosity, smaller effect of NaCl on peak viscosity, and higher resistance to shear thinning. Texture profile analysis of starch gels showed significantly greater hardness for all buckwheat samples when compared to wheat

starch. Buckwheat starch granules were polygonal in shape and had a smaller diameter than the wheat starch granule (Acquistucci and Fornal 1997). Buckwheat starch possessed a higher swelling power than the wheat one, probably as a consequence of the weaker but more extensive bonding forces in the granule. During cooling, buckwheat starch showed good paste stability. Yoshimoto et al. (2004) found that the actual amylase content of buckwheat starches was 16–18%, which was lower than the apparent amylose content (26–27%), due to the high iodine affinity (IA) of amylopectin (2.21–2.48 g/100 g). Amylopectins resembled each other in average chain-length (23–24) and chain-length distributions. The long-chains fraction (LC) was abundant (12–13% by weight) in all the amylopectins, which was consistent with high IA values. A comparison of molecular structures of buckwheat starches to cereal starches indicated buckwheat amylopectins had a larger amount of long-chain fractions, and their distributions of amylose and short chains of amylopectin on molar basis were similar to those of wheat and barley starches.

The highest concentration of resistant starch was found in boiled buckwheat groats (6% total starch basis) (Skrabanja et al. 2001). The resistant starch level in bread products based on different proportions of buckwheat flour or buckwheat groats (30–70%) varied from 0.9 to 4.4%. The rate of in-vitro amylolysis was significantly lower in all buckwheat products in comparison with the reference, white wheat bread. The calculated hydrolysis indices (HI) were lowest in boiled buckwheat groats (HI = 50) and in bread with 70% buckwheat groats (HI = 54). Buckwheat groats prepared by using the traditional procedure of cooking before dehusking followed by warm-air drying, were found to have less than 48% of rapidly available starch, in comparison to white wheat bread, where the corresponding value was almost 59%(Skrabanja et al. 1998). In untreated groats and in groats dry-heated to 110°C there was significantly less rapidly digested starch than in hydrothermally treated samples. Buckwheat groat starch with a reduced rate of digestion could be a possible complement to or a substitute for common carbohydrate sources. Steam jet-cooking caused structural breakdown and starch gelatinization of buckwheat flour, thus increasing its water hydration properties (Min et al. 2010). When shortening in cakes was replaced with steam jet-cooked buckwheat gels, the specific gravity of cake batters significantly increased, consequently affecting cake volume after baking. However, shortening replacement with steam jet-cooked buckwheat up to 20% by weight appeared to be effective in producing low fat cakes with comparable volume and textural properties to the control.

Ikeda et al. (2000) reported the following mineral and protein composition per 100 g flour of 22 buckwheat flour fractions: Zn 217–1940 mg, Cu 159–580 mg, Mn 97–456 mg, Ca 2.08–9.44 mg, Mg 15–150 mg, K 60–597 mg, P 35–178 mg, protein 0.23–4.70 mg. Water-soluble essentia l minerals and watersoluble protein were found at relatively high levels in buckwheat semolina flour fractions, BS and SS flour fractions, especially the SS8 flour fraction, except for water-soluble calcium. On the other hand, water-soluble essential minerals and water-soluble protein were found at relatively low levels for some buckwheat flour fractions, CF and FF flour fractions, especially the FFI, FF2, FF3 and FF5 flour fractions. A considerable variation in gross chemical composition was found among the 23 milling fractions of buckwheat seeds namely seven fine flours, three coarse flours, four small semolina, two big semolina, six bran, and one husk fraction (Skrabanja et al. 2004). The protein content varied from 4.4 to 11.9%(db) in flours and from 19.2 to 31.3% in bran fractions; starch varied from 91.7 to 70.4% in flours and from 42.6 to 20.3 in bran. The percentage of soluble dietary fibre contained in total dietary fibre was higher in flours than in semolina and bran fractions. Ash, Fe, P, tannin, phytate content, and colour were also investigated. A unique distribution of phytate was found in starch. Correlation was significantly positive in husk, bran, and semolina fractions, while correlation was significantly negative in flour fractions.

Of four buckwheat species viz. *Fagopyrum esculentum* Moench, *F. sagittatum* Gilib.,

F. kashmirianum Munshi and *F. tataricum* Gaertn, grains of *F. esculentum* had the lowest content of phenolics, relatively low fat, free sugar and protein content but a higher starch content compared to the other three cultivars (Tahir and Farooq 1985). Further, *F. esculentum* had lower albumin-globulin and glutelin contents but a higher content of residual insoluble proteins. The content of prolamins was generally low in all the four species. Low content of phenolics in the groat fraction of *F. esculentum* accounted for its better palatability compared to other three species which possessed astringent taste. There was a prevalence of unsaturated fatty acids – C18:1, C18:2, C18:3 and C20:1 in common and tartary buckwheat (Bonafaccia et al. 2003b). In both species most lipid substances were concentrated in the bran. In common buckwheat bran, protein content was 21.6%, and in tartary buckwheat, 25.3%. There were relatively small differences in the contents of vitamins B1 and B2 between the two main utilisable milling fractions, but more substantial differences in the contents of vitamins B6 (up to 0.61 mg/100 g in the tartary buckwheat bran fraction). Total B vitamin content was higher in tartary buckwheat than in common buckwheat.

Bonafaccia et al. (2003a) analysed the contents of Se, Cr, Rb, Zn, Fe, Co, Sb, Ba, Ni, Ag, Hg and Sn in the flour and bran of common and tartary buckwheat, and found that in both species most trace elements were concentrated mainly in the bran. However, there were relatively small differences in the contents of iron, antimony, and chromium between flour (extraction rate 55%) and bran fractions. The potential use of buckwheat bran as a dietary source of Zn, and Se, was indicated.

Buckwheat (*Fagopyrum esculentum*) proteins are nutritionally important because of their high and balanced content of essential amino acids making their biological value much higher than that of cereal proteins (Licen and Kreft 2005). Buckwheat endosperm and embryo proteins were found in the range of molecular weights (M.W.s) from 50 to 60 kDa. Protein of 57 kDa has been shown not to cross-react against antibodies raised against proteins of M.W. ranging between 23 and 25 kDa. Thus far there were no reports about the allergenicity of other endosperm proteins. Watanabe et al. (1998) found that a thiamin-binding protein from buckwheat seeds was different from those from rice seeds and sesame seeds as to subunit structure or immunological properties, but resembled them in the mechanism of binding thiamine. Bharali S, Chrungoo A vicilin-like 8S storage globulin was identified from buckwheat seed (Milisavljević et al. 2004). A partial cDNA was also isolated, showing high homology with cDNAs coding for vicilin-like storage proteins from various plant species. A methionine-rich legumin-like protein was isolated and characterised from buckwheat seed (Samardži et al. 2004). Based on amino acid sequence this specific buckwheat storage polypeptide should be classified in the methionine-rich legumin subfamily present in the lower angiosperm clades, a representative of which was first characterized in *Magnolia salicifolia*. The salt-soluble globulin extracted from common buckwheat (*Fagopyrum esculentum*) seeds comprised acidic and basic polypeptides linked by disulfide bonds (Choi and Ma 2006). The basic polypeptide has an estimated molecular weight of 23–25 kDa, an isoelectric point in slightly alkaline region (pH 8–9), and showed a high degree of homology with other legumin-like proteins. The protein content of buckwheat globulin (BWG) was over 90%. BWG exhibited beneficial functional properties such as high solubility, emulsifying activity and emulsion stability, while the foaming properties were relatively poor. BWG had lower water holding capacity and comparable fat binding capacity when compared to a commercial soy protein product. Tang and Wang (2010) characterised globulin and albumin fraction from common buckwheat and compare with those of buckwheat protein isolates (BPI). The polyphenol content in albumin was much higher than that in globulin, and most of the polyphenols in the albumin was in the free form, whilst that in the globulin and BPI was mainly in the protein-bound form. Albumin higher content of uncharged polar amino acids, but lower acidic amino acids than globulin. The protein solubility-pH profile of globulin and albumin were very different, especially at pH 4.0–6.0. The properties of globulin and albumin varied considerably, and

were largely dependent upon their polyphenol levels and the interactions of the polyphenols and the proteins.

Fagopyritols are galactosyl cyclitols in buckwheat (*Fagopyrum esculentum*) seeds with structural similarities to a putative insulin mediator deficient in non-insulin dependent diabetes mellitus and polycystic ovary syndrome (Ueda et al. 2005). Fagopyritols, mono-, di-, and trigalactosyl derivatives of D-chiro-inositol, found in common buckwheat seeds and other soluble carbohydrates were assayed in mature groats and 11 milling fractions of common buckwheat seeds (Steadman et al. 2000). Bran milling fractions contained 6.4 g of total soluble carbohydrates per 100 g of dry weight, 55% of which was sucrose and 40% fagopyritols. Flour milling fractions had reduced fagopyritol concentration [0.7 g/100 g of dry weight total fagopyritols in the dark (Supreme) flour and 0.3 g/100 g in the light (Fancy) flours]. Fagopyritol B1 amounted to 70% of total fagopyritols in all milling fractions. Fagopyritols were 40% of total soluble carbohydrates in groats of two cultivars of common buckwheat but 21% in groats of tartary buckwheat. Fagopyritols may be important for seed maturation and as a dietary supplement. Two digalactosyl D-chiro-inositols and two trigalactosyl D-chiro-inositols, members of the fagopyritol A series and fagopyritol B series, were isolated from buckwheat (*Fagopyrum esculentum*) seeds (Steadman et al. 2001). Structures of fagopyritol B2 was elucidated as α-D-galactopyranosyl-(1 → 6)-α-D-galactopyranosyl-(1 → 2) -1D-chiro-inositol, and fagopyritol A2 as α-D-galactopyranosyl-(1 → 6)-α-D-galactopyranosyl-(1 → 3)- 1D-chiro-inositol. Fagopyritol A3, a trigalactosyl D-chiro-inositol, as α-D-galactopyranosyl-(1 → 6)-α-D-galactopyranosyl-(1 → 6)-α-D-galactopyranosyl-(1 → 3)- 1 D-chiro-inositol. From analysis of hydrolysis products, the second trigalactosyl D-chiro-inositol, fagopyritol B3, was determined as α-D-galactopyranosyl-(1 → 6)-α-D-galactopyranosyl-(1 → 6)-α-D-galactopyranosyl-(1 → 2)-1D-chiro-inositol. The molecular structure of fagopyritol A1, a novel galactopyranosyl cyclitol from buckwheat seeds, was determined to be *O*-α-D-galactopyranosyl-(1 → 3)-D-chiro-inositol (Obendorf et al. 2000).

Studies revealed that buckwheat sprouts not only have the soft and slightly crispy texture, and attractive fragrance, but also have abundant nutrients. (Kim et al. 2004) Linoleic acid (C18:2) was found to be the major fatty acid of buckwheat sprouts and increased up to 52.1% at 7 days after seeding (DAS), and total unsaturated fatty acid composition was greater than 83%. As seeding days progressed, monosaccharides in buckwheat sprouts were rapidly increased, while di-, tri-, and tetrasaccharides were gradually decreased. Free amino acid contents in buckwheat sprouts were almost four-times higher than those of buckwheat seeds. Based on these results, it was concluded that the abundance of lysine, γ-amino-n-butyric acid (GABA) and sulfur containing amino acids in buckwheat sprouts provides a high nutritional value as a new vegetable. Rutin (quercetin-3-*O*-rutinoside), quericitrin (quercetin-3-*O*-rhamnoside), chlorogenic acid, and two unknown compounds were presented in both buckwheat seeds and sprouts. As seeding days progressed, rutin, quercitrin, and unknown compound B (431 m/z) were notably increased, while chlorogenic acid and unknown compound A (451 m/z) were moderately increased. Vitamin C contents of buckwheat sprouts were increased and its maximum content (171.5 mg/100 g) was observed at 7 DAS while vitamin B1 + B6 contents were moderately increased.

The content of alcohol soluble solids (2.73% FW), alcohol insoluble solids (10.91% FW) and total solids (13.65% FW) was lower in the leaves of *F. esculentum* than in the other three species (Farooq and Tahir 1989). Total sugar levels in the leaves of *F. esculentum* (1.0% FW) and *F. sagittatum* (1.05% FW) were higher concentration than *F. kashmirianum* (0.87% FW) and *F. tataricum* (0.77% FW). Leaf starch content of *F.esculentum* (0.60% FW) were higher than the other three species. Leaf phenolic content of *F. esculentum* (0.58% FW) and *F. tataricum* (0.47% FW) were lower than in *F. sagittatum* (0.96% FW) and *F. kashmirianum* (0.82% FW). The concentration of alcohol soluble nitrogen (0.039% FW) and total free amino nitrogen (0.024% FW)

was lower in *F. esculentum* than in the other three species. The concentration of alcohol insoluble nitrogen was higher in the leaves of *F. kashmirianum* (0.54% FW) and *F. tataricum* (0.054% FW) than in *F. esculentum* (0.039% FW) and *F. sagittatum* (0.045% FW). *F. esculentum* possessed thicker and more succulent leaves with a higher content of total sugars and starch, besides a relatively lower phenolic content. The findings suggested *F. esculentum* was more suited as a green vegetable compared to the other three species.

Other Phytochemicals

Polyphenolic compounds in buckwheat differed considerably from the composition of polyphenols in other kinds of cereals. Cereals contain mainly ferulic and other hydrocinnamic acids but they usually do not contain tannins or in trace amounts in barley and millet. Gorinstein et al. (2007) reported that the total phenolic content of buckwheat was 91 GAE/100 g of grain. Zadernowski et al. (1992) found total phenolics in commercial buckwheat groats produced by steam treatment before dehulling to be 1.33% and 1.87% in the hulls. The proportion of tannins in the total amount of phenolic compounds was 0.24% in buckwheat groats and 1.04% in buckwheat hull and the share of phenolic acids in the total polyphenols of buckwheat groats was 1.07% and in buckwheat hull 0.5%. Among aromatic acids in buckwheat groats, mainly *p*-coumaric, caffeic and sinapic acids were identified. Most acids (54.2%) occurred in a free form, while about 28% were bound to esters and glycosides. Buckwheat hull was found to contain 16 identified aromatic acids, but only *p*-coumaric acid exceeded 1 mg per 100 g of sample. Sinapic and gentisic acids also occurred at levels of about 1 mg/100 g of sample. Buckwheat groats contained 1.33% total polyphenols, 14.25 mg/100 g derivatives of phenolic acids and 3.23 mg/100 g tannins. Buckwheat hull contained hull 1.87% total polyphenols, 8.72 mg/100 g derivatives of phenolic acids, 19.64 mg/100 g. Six flavonoids namely rutin, orientin, vitexin, quercetin, isovitexin, and isoorientin were isolated and identified in buckwheat grain (Dietrych-Szostak and Oleszek 1999). Rutin and isovitexin were the only flavonoid components of buckwheat seeds while hulls contained all six flavonoids. The total flavonoid concentration in the seeds was 18.8 mg and in the hulls 74 mg/100 g of dry matter. Dehulling the grain by using different temperature regimes resulted in drastic reductions of the total flavonoid concentration in the grain (by 75% of the control) and smaller but significant (15–20%) reduction in the hulls.

Phenolic acids (mg/100 g) in free form identified from buckwheat groats were : benzoic 0.350 mg, mandelic traces, salicylic 0.115 mg, cinnamic 0.050 mg, pyrogallic 0.065 mg, *m*-OH-benzoic 0.225 mg, piperonylic 0.034 mg, *p*-OH-benzoic 0.659 mg, *p*-OH-phenyloacetic 0.207 mg, veratic 0.200 mg, homovanilic and vanillic 1.035 mg, protocatechuic traces, homogenistic 0.223 mg, syringic 0.078 mg, *p*-coumaric 1.989 mg, gallic 0.789 mg, iso-ferulic 0.200 mg, ferulic traces, cafeic 1.333 mg and sinapic 0.770 mg (Zadernowski et al. 1992). Phenolic acids (mg/100 g) in free form identified from buckwheat hull were : benzoic traces, salicylic 0.200 mg, piperonylic 0.098 mg, *p*-OH-benzoic 0.364 mg, *p*-OH-phenyloacetic 0.098 mg, veratic 0.213 mg, homovanilic and vanillic 0.645 mg, gentisic 0.083 mg, protocatechuic 0.110 mg, *p*-coumaric 1.619 mg, gallic 0.075 mg, ferulic traces, caffeic 0.150 mg and sinapic 0.275 mg. Watanabe et al. (1997) isolated and identified antioxidant fractions from buckwheat hull containing proanthocyanidins (condensed tannins) and five antioxidant compounds: quercetin, hyperin, rutin, protocatechuic acid, and 3,4-dihydroxybenzaldehyde. Also two non-antioxidant compounds vitexin and isovitexin were also identified. Four catechins (−)-epicatechin, (+)-catechin 7-*O*-β-d-glucopyranoside, (−)-epicatechin 3-*O*-*p*-hydroxybenzoate, and (−)-epicatechin 3-*O*-(3,4-di-O-methyl)gallate and rutin were isolated from ethanol extracts of buckwheat groats (Watanabe 1998). Canadian buckwheat were found to contain 12-16 g/kg total phenolics, about 3 g/kg of esterifed phenolic acids and 8-13 g/kg etherified phenolic acids (Oomah et al.

1996). The latter represented 70–79% of the total phenolics. Variation in phenolics was attributable mainly to cultivar, seasonal effects and their interactions and not locality. Similarly, Ohsawa and Tsutsumi (1995) reported intervarietal and seasonal variation in rutin content of Japanese buckwheat cultivars. Four flavonol glycosides: rutin, quercetin, kaempferol-3-rutinoside and a trace quantity of a flavonol triglycoside were found in the methanol extract of buckwheat (Tian et al. 2002). The main phenolic compounds found in buckwheat hulls and flour were identified as: (2)-epicatechin, rutin, hyperoside, and quercetin (Peng et al. 2004).

The flavonoid rich grain of buckwheat (*Fagopyrum esculentum*) is of high nutritional value (Ölschläger et al. 2008). Seven flavonoid compounds were purified from methanol extracts of buckwheat (*Fagopyrum esculentum*) grains. Beside the procyanidin epicatechin-[4–8]-epicatechin-3-*O*-(3,4)-dimethylgallate, the following propelargonidins were identified: epiafzelechin-[4–6]-epicatechin, epiafzelechin-[4–8]-epiafzelechin-[4–8]-epicatechin, epiafzelechin-[4–8]-epicatechin-3-*O*-(3,4-dimethyl)-gallate, epiafzelechin-[4–8]-epiafzelechin-[4–8]-epicatechin-3-*O*-(3,4-dimethyl)-gallate, epiafzelechin-[4–8]-epicatechin-3-*O*-4-methyl-gallate and epiafzelechin-[4–8]-epicatechin-*p*-OH-benzoate.

The phenolic compounds in buckwheat grain existed primarily in free form, whereas the flavonoids rutin and quercetin existed in insoluble bound forms, bound to cell wall materials (Hung and Morita 2008). The amounts of ferulic acid and rutin increased from 2.5 and 2.5 μg/g flour of the phenolics less rich fraction to 609.5 and 389.9 μg/g flour of the phenolics rich fraction of grain, respectively. The higher phenolic contents in the phenolics rich fractions exhibited the stronger antioxidant capacity than the phenolics less rich fractions.

In buckwheat (*Fagopyrum esculentum*) bran fractions the concentration of rutin determined was 131 – 476 ppm, and in flour fractions 19 – 168 ppm (Kreft et al. 1999). On average, about 300, 1000, and 46000 ppm of rutin were found in leaves, stems, and flowers, respectively. The results indicated that buckwheat could be an important nutritional source of flavonoids, especially in countries with a low mean daily flavonoid intake. Japanese buckwheat flour was found to contain rutin (12.7 mg/100 g), catechin (3.30 mg/100 g), epicatechin (20.5 mg/100 g), and epicatechin gallate (1.27 mg/100 g) (Danila et al. 2007). The embryo proper and cotyledons of a mature buckwheat seed were found to contain highest concentration of rutin compared to other parts. Inglett et al. (2011) evaluated commercial buckwheat flours for their antioxidant activities, free, and bound phenolic compositions. The found farinetta flour contained the highest free and bound phenolic contents, followed by Supreme, whole buckwheat, and Fancy flour, respectively. Studies on whole buckwheat flour showed that *p*-coumaric and gallic acids were found in the bound phenolics along with isoquercitrin but were not present in the free phenolic compounds. The free flavonol-glycosides were found in whole buckwheat flour but not in any other buckwheat flours. Thirty-two free and 24 bound phenolic compounds in buckwheat flour and spaghetti were characterized and quantified including protochatechuic-4-*O*-glucoside acid and procyanidin A detected in buckwheat for the first time (Verardo et al. 2011). The results demonstrated a decrease of total free phenolic compounds from farm to fork (from flour to cooked spaghetti) of about 74.5%, with a range between 55.3 and 100%, for individual compounds. The decrease in bound phenols was 80.9%, with a range between 46.2 and 100%. The spaghetti-making process and the cooking caused losses of 46.1 and 49.4% of total phenolic compounds, respectively. Of the total phenolic compounds present in dried spaghetti, 11.6% were dissolved in water after cooking.

Twenty-one tartary and 18 common buckwheat cultivars exhibited high variations in colour properties, nutritional composition and flavonoid content (Qin et al. 2010). The flour of common buckwheat showed a higher whiteness index than that of tartary buckwheat and contained very low levels of flavonoids. On average, the tartary buckwheat flour contained a higher level of ash (2.38%) and lower levels of total starch (70.22%),

amylose (22.32%), resistant starch (17.66%) than the common buckwheat flour (2.17%, 73.69%, 23.01%, 18.69% respectively) whereas the contents of proteins, fats and crude fibre of the tartary buckwheat flour were similar to those of common buckwheat flour. The Mei-Hua-Shan tartary buckwheat flour contained the highest level of total flavonoids and quercetin (22.74 mg/g and 2.38 mg/g, respectively).

Kalinová et al. (2004) found the following phenolic compound in buckwheat herb extract: quercetin, rutin, catechin, epicatehin, benzoic and cinnamic acids and 2,4,5-trimethylphenol, 3,4,5-trimethoxyphenol, 2-methoxy-6-(2-propenyl) fenol (*o*-allylguajakol) and 4-(3-hydroxy-1-propenyl)-2-methoxyfenol. α-tocopherol was found as the main component of vitamin E in all parts of the buckwheat plant; epicatechin and squalene were also detected (Kalinova et al. 2006). For the use of buckwheat as an antioxidant source in the human diet, the most suitable part of the plants appeared to be the leaves and the flowers at the stage of full flowering due to the considerable amounts of rutin and epicatechin. α-tocopherol content correlated positively with temperature, drought, and duration of solar radiation. Some differences appeared among varieties of buckwheat, especially in their squalene and rutin contents. Four anthocyanins, cyanidin 3-*O*-glucoside, cyanidin 3-*O*-rutinoside, cyanidin 3-*O*-galactoside, and cyanidin 3-*O*-galactopyranosyl-rhamnoside, were isolated from the sprouts of common buckwheat (Kim et al. 2007). The following phenolic compounds: isoorientin, orientin, rutin, and vitexin were found as the main phytochemicals of buckwheat sprouts cultivated under dark conditions (Kim et al. 2011). The accumulation of these metabolites caused the phenolic compound content and antioxidant activity of the sprouts to increase. GABA (γ-aminobutyric acid) and rutin concentrations of common and tartary buckwheat peaked at 42 DAS (days after sowing), whereas anthocyanin, 2″-hydroxynicotianamine (2HN), and minor flavonoid concentrations declined with the age of the plants (Suzuki et al. 2009). However, at 42 DAS, anthocyanin concentrations in the leaves of tartary buckwheat Hokkai T10 leaves were at least tenfold greater than in the other buckwheats tested. The results indicated that, in terms of GABA, rutin, and anthocyanin concentrations, leaf powder from 42 day old Hokkai T10 had the potential to be a useful food ingredient, such as Ao-jiru juice.

Buckwheat flavour volatiles: hexanal, tentative butanal, tentative 3-methylbutanal and tentative 2-methylbutanal showed significant positive correlation with lipase and/or peroxidase activity, indicating that enzymatic reactions were important in flavor generation in boiled buckwheat noodles (Suzuki et al. 2010). In contrast, pentanal, which showed no significant correlation with any enzyme activity, showed a significant positive correlation to the levels of C18:2 and C18:3 FFAs suggesting the existence of a 'non-enzymatic' and/or 'uncertain enzymatic pathway' for flavour generation in boiled buckwheat noodles. Salicylaldehyde (2-hydroxybenzaldehyde) was identified as a characteristic component of buckwheat groats aroma (Janeš and Kreft 2008). Traditionally dehulled buckwheat grain, which had the strongest odour, contained the highest concentration (1.6 ppm) of salicylaldehyde with an odour activity value (OAV) of 216. Direct extraction of volatiles from buckwheat flour with methanol and distillation proved to be very efficient (Janeš et al. 2009). In these extracts 25 and 35 compounds were identified, respectively. The first extract contained more hydrophilic compounds and the latter more volatile compounds. Only two compounds (salicylaldehyde and phenylacetaldehyde) were found in both extracts. The compounds with the highest contribution to the buckwheat aroma were: 2,5-dimethyl-4-hydroxy-3(2 H)-furanone, (E,E)-2,4-decadienal, phenylacetaldehyde, 2-methoxy-4-vinylphenol, (E)-2-nonenal, decanal, hexanal and salicylaldehyde (2-hydroxybenzaldehyde). Apart from the aroma molecules present in all fractions of the buckwheat kernel (flour, bran, and husk), compounds that were present only in flour or bran, but not in groats, were also found (Janeš et al. 2010). Furthermore, some aroma compounds identified only in buckwheat groats but not in buckwheat flour or bran were octanal, (*E,E*)-2,4-heptadienal, (*E*)-2-decenal, and (*E,E*)-2,

4-decadienal, others were identified only in husks (*E*)-2-hexenal, heptanal, (*E,E*)-2,4-hexadienal, phenylacetaldehyde, and α-bisabolol.

Gorinstein et al. (2007) reported that the total phenolic content of quinoa was 912 mγ GAE/g of grain dw, 111.3 mg/100 g cyanidin-3-glucoside dw, and 146 mg/100 g (+) catechin dw. Thirty phenolic compounds were found in buck wheat flour and 2-hydroxy-3-*O*-β-d-glucopyranosil-benzoic acid, 1-*O*-caffeoyl-6-*O*-α-rhamnopyranosyl-β-glycopyranoside and epicatechin-3-(3″-*O*-methyl) gallate were tentatively identified in buckwheat for the first time (Verardo et al. 2010).

In common buckwheat plants obtained from seeds soaked in water, regardless of UV-B radiation levels, the highest concentration of selenium was found in leaves, with values between 45 and 66 ng Se/g (Ožbolt et al. 2008). In buckwheat leaves 44.5–63.6 mg/100 g d.m. of fagopyrin was found, and in stems 14.3–26.4 mg/100 g d.m. The content of total flavonoids in leaves was 7.8–15.9% and in stems 1.4–4.1%. Tartary and common buckwheat, fagopyrin occurred mainly in the leaves and flowers and slightly in the stems, hulls, and groats (Eguchi et al. 2009). The fagopyrin contents of the leaves and flowers of tartary buckwheat 'Rotundatum' were approximately 2.6 and 2.8 times higher than those in common buckwheat 'Miyazakiootsubu', respectively. Tartary buckwheat grains were found to contain three-times more resveratrol than common buckwheat grains but common buckwheat leaves contained ten times more resveratrol than tartary buckwheat leaves (Němcová et al. 2011). The lowest level of *trans*-resveratrol was in hulls of common buckwheat.

Four anthocyanins, cyanidin 3-*O*-glucoside, cyanidin 3-*O*-rutinoside, cyanidin 3-*O*-rhamnoside, and cyanidin 3-*O*-galactosyl-rhamnoside were isolated from the flower petals of common buckwheat, *Fagopyrum esculentum* (Suzuki et al. 2007). In every variety/breeding line tested, cyanidin 3-*O*-rutinoside was detected as the major anthocyanin followed by cyanidin 3-*O*-glucoside whereas cyanidin 3-*O*-rhamnoside and cyanidin 3-*O*-galactosyl-rhamnoside occurred in traces or were not detectable in white and pink flowered buckwheat. Of all the varieties/breeding lines tested, Gan-Chao, a Chinese variety, contained the highest amount of anthocyanins. The largest part of cyanidin moiety comprised a proanthocyanidin form (PAs-Cy). Anthocyanins and PAs-Cy in petals were increased along with increase of flower development stages. Therefore, fully developed petals of red flowered buckwheat, especially Gan-Chao, could be promising as a new anthocyanin-rich material for food processing. The highest content of rutin was found in flowers of both kinds of buckwheat (99,400 mg/kg in *F. esculentum*, 108,000 mg/kg in *F. tataricum*) (Dadáková and Kalinová 2010). Free quercetin was found in flowers and achenes of *F. esculentum*, whereas flowers and achenes of *F. tataricum* contained quercitrin.

Buckwheat noodles were found to contain much less rutin, 78 mg/kg, dwb (dry weight basis) than the dark buckwheat flour (218 mg/kg, dwb) from which they are produced (Kreft et al. 2006). In raw (uncooked) groats there was 230 mg/kg (dwb) of rutin and in precooked groats, 88 mg/kg (dwb) Buckwheat leaf flour contained about 2700 mg/kg (dwb) rutin, and thus could be a suitable material for enriching functional foods, endowing the potential for preventive nutrition.

Common buckwheat (*Fagopyrium esculentum*) was used to substitute 15% of wheat flour to make husked and unhusked buckwheat breads that contained more sugars and had higher sugar contents than white bread (Lin et al. 2009). Both buckwheat breads contained more total free amino acids (86.36–87.73 mg/g) than white bread (73.90 mg/g). Contents of flavor 5′-nucleotides were higher in both buckwheat breads. Both buckwheat breads had higher umami intensities than white bread. All 3 breads had different profiles of volatile compounds, and total volatile contents in buckwheat breads (3564.36–4951.39 μg/g) were two to three folds higher than that in white bread (1,706.46 μg/g). Additionally, buckwheat breads possessed a more characteristic aroma than white bread. The results suggested that buckwheat could be incorporated into bread and provide buckwheat bread with more sugars, a stronger umami taste and a more characteristic aroma.

Buckwheat was found to be a rich source of starch and contains many valuable nutraceutical compounds, such as proteins, antioxidative substances, trace elements and dietary fibre (Krkošková and Mrázová 2005). Besides high-quality proteins, buckwheat seed contained several components with healing benefits: flavonoids and flavones, phytosterols, fagopyrins and thiamin-binding proteins. It has strong potential for development of new functional foods, and health benefit products. There is an increasing trend in research on pseudocereals amaranth, quinoa and buckwheat; focusing on their use in the formulation of high nutritional quality, healthy gluten-free products such as bread and pasta (Alvarez-Jubete et al. 2010). The availability of palatable pseudocereal-containing gluten-free products would represent a significant advance towards ensuring an adequate intake of nutrients in subjects with celiac disease.

Antioxidant Activity

Buckwheat contained an average of 387 and 1314 mg/100 g of flavonoid and 47 and 77 mg/100 g of rutin in the seed and hull, respectively (Oomah and Mazza 1996). The flavonoid and rutin contents of the seed varied with location, while growing season had significant influence on the flavonoid content of the hulls. Variation in antioxidative activities was mainly due to a cultivar × environment effect. Antioxidative activities expressed as AOX (Δ log A470/min), AA (% inhibition relative to control), and ORR (oxidation rate ratio) ranged from 0.42, 114, and 0.16 to 1.63, 48, and 0.59, respectively. Flavonoid content in buckwheat was strongly correlated with rutin content and weakly associated with antioxidative activities, while rutin content was not related to antioxidative activities.

Five of the fractions of the ethanolic extract of buckwheat hull exhibited peroxyl radical-scavenging activity by inhibiting the oxidation of methyl linoleate in solution (Watanabe et al. 1997). Two of the antioxidant fractions contained proanthocyanidins (condensed tannins) and five antioxidant compounds were isolated and identified as quercetin, hyperin, rutin, protocatechuic acid, and 3,4-dihydroxybenzaldehyde. The contents of these active compounds in the buckwheat hulls were as follows: protocatechuic acid (13.4 mg/100 g of dried hulls), hyperin (5.0 mg/100 g), 3,4-dihydroxybenzaldehyde (6.1 mg/100 g), rutin (4.3 mg/100 g), and quercetin (2.5 mg/100 g). Additionally, two major compounds that showed no peroxyl radical-scavenging activity in the extract were isolated and identified as vitexin and isovitexin. Four catechins (−)-epicatechin, (+)-catechin 7-*O*-β-d-glucopyranoside, (−)-epicatechin 3-*O*-p-hydroxybenzoate, and (−)-epicatechin 3-*O*-(3,4-di-*O*-methyl)gallate isolated from ethanol extracts of buckwheat groats exhibited higher antioxidant activity than rutin (Watanabe 1998). The yields of these antioxidant compounds suggested that they were as abundant as rutin in buckwheat groats.

In in-vitro studies, buckwheat hull extract scavenged super oxide anion produced in the xanthine/xanthine oxidase system ($IC_{50} = 11.4$ μg phenolic compound/mL), and strongly inhibited autoxidation of linoleic acid ($IC_{50} = 6.2$ μg phenolic compound/mL) (Mukoda et al. 2001). Low-density lipoprotein (LDL) oxidation induced by Cu^{2+} ion was also protected by the extract. In in-vivo studies, ddY mice fed a standard diet supplemented with 0.75% buckwheat extract for 14 days had significantly lower concentration of TBARS and fluorescent substance in blood, liver and brain compared with those of non-treated mice. SOD like activity in serum was significantly elevated by the extract. The results suggested that buckwheat hull extract was effective in protecting biological systems against various oxidative stresses in-vitro and in-vivo.

Holasova et al. (2002) evaluated the antioxidant activities of buckwheat seeds, dehulled seeds, hulls, straws and leaves and compared them with those of oats and barley. They reported protection factor to range from 1.3 to 8 in the order: buckwheat straws < buckwheat hulls = oats < barley < buckwheat seeds < buckwheat dehulled seeds < buckwheat leaves. Methanol extract of buckwheat seeds showed higher antioxidant activity in comparison with

petrol-ether extract, protection factors amounted to 2.9 and 1.9, respectively. Statistically significant relationship between total phenolics content as well as rutin content and antioxidant activity of buckwheat material was observed. The ethanol extracts of common buckwheat and tartary buckwheat seeds both displayed DPPH free radical-scavenging effect, and the main anti-oxidative constituents of buckwheat seed extract identified were mainly rutin and quercetin, and the anti-oxidative activity of quercetin was higher than that of rutin (Yao et al. 2008). Initial pepsin digestion of buckwheat protein (BWP) decreased its antioxidant activity; however, subsequent pancreatin digestion fully recovered the reducing power and increased the ability to chelate Fe(2+) (45%), scavenge ABTS(+•) (87%), and curtail lipid peroxidation (45%) when compared with intact BWP (Ma and Xiong 2009). The final BWP digest exhibited a 67% increase in cholic acid binding capability over that of the non-digested BWP control but was comparable to the control in binding chenodeoxycholic and deoxycholic acids. Digestion-resistant peptides were largely responsible for bile acid elimination. Mattila et al. (2005) reported that the total ferulic acid content of grains ranged from 458 (whole wheat) to 129 (oats and barley) μmol/100 g grain, the total *p*-coumaric acid content ranged from 24 (barley) to 9 (buckwheat) μmol/100 g grain, and the total *p*-hydroxybenzoic acid content ranged from 80 (buckwheat) to 4 (corn) μmol/100 g grain. The high total *p*-hydroxybenzoic acid content in buckwheat is most likely due to the contribution of the free fraction.

Gorinstein et al. (2007) reported the antioxidant activity of polyphenol dry matter methanol extract of buckwheat in the DPPH assay to be 80%, in the β-carotene linoleate model system to be 75.6% and 2.601 μM TE/g TEAC (trolox equivalent coefficient).

Buckwheat whole grain was found to have total phenolic content of 23.5 mg GAE/100 g grain and oxygen radical absorbance capacity (ORAC) of 921 μmol TE/100 g grain (Okarter 2012). Buckwheat contained 5.3 μmol/100 g grain of ferulic acid, and 6.3 μmol/100 g grain of *p*-coumaric acid in the insoluble bound fraction but contained no flavonoids (qurecetin, kaempferol, catechin, and rutin) in the insoluble-bound fraction of the grain. None of the phenolic compounds had any cellular antioxidant activity, most likely because these phenolic compounds did not have the structure necessary to impart cellular antioxidant activity. The data suggested that the potential health benefit of whole grain consumption in the lower gastrointestinal tract was independent of the cellular antioxidant activity of the phenolic compounds found in the insoluble-bound fraction of whole grains.

Studies by Hur et al. (2011) confirmed that the main phenolics of buckwheat extract were rutin, quercitrin, and quercetin. The rutin content increased with digestion of the buckwheat (from 48.82 to 96.34 μg/g) and rutin standard samples (from 92.76 to 556.56 μg/g) in an in-vitro human digestion model. Antioxidant activity was more strongly influenced by in vitro human digestion of both buckwheat and rutin standard. After digestion by the small intestine, the antioxidant activity values were dramatically increased (from 5.06 to 87.82%), whereas the antioxidant activity was not influenced by digestion in the stomach for both buckwheat extract and rutin standard. Inhibition of lipid oxidation of buckwheat in mouse brain lipids increased after digestion in the stomach for both buckwheat extract and the rutin standard. The major finding of this study was that in- vitro human digestion may be an important modulator of the antioxidant capacity of buckwheat.

The major anthocyanin compound in buckwheat sprouts was determined to be cyanidin 3-*O*-rutinoside (C3R) (Watanabe 2007). Investigation of the content of phenolic compounds in commercial buckwheat sprouts indicated that hypocotyls had abundant C3R and rutin, whereas all of the detected flavonoids were abundant in cotyledons. The superoxide anion radical-scavenging activities SOD (superoxide dismustase-like activities) of phenolic compounds in buckwheat sprouts and their contents indicated that rutin, isoorientin, and orientin contributed mainly to the SOD-like activity of the extract from buckwheat sprouts. In contrast, the contribution of C3R was substantially lower than

that of flavonoids. Buckwheat sprouts produced in dark or light, contained a high level of isoorientin, orientin, vitexin, rutin, and isovitexin whereas ungerminated buckwheat grain contained only rutin (Zielinska et al. 2007). The flavonoid content in sprouts produced under light was almost 2 times higher than those of sprouts produced in the dark. The antioxidant capacity of light-grown sprouts was higher than that of dark-grown ones. The results from voltammetric experiments obtained for buckwheat seeds and 6 and 8 DAS (days after seeding) sprouts harvested under dark or light conditions highly correlated with those obtained by photochemiluminescence antioxidant capacity of water-soluble substances ($R^2=0.99$), photochemiluminescence antioxidant capacity of lipid-soluble substances ($R^2=0.99$), TEAC ($R^2=0.99$), and Folin-Ciocalteu reducing capacity ($R^2=0.99$). Buckwheat sprouts grown in trace element water (TEW) (3000 ppm) increased the Cu, Zn, Mn, and Fe contents in buckwheat sprout but not the Se content (Liu et al. 2007). However, the levels of rutin, isoorientin, vitexin, and isovitexin did not differ between buckwheat sprouts grown in TEW and deionized water (DIW). The ethanolic extract from buckwheat sprout grown in 300 ppm of TEW showed higher ferrous ion chelating activity and inhibitory activity toward lipid peroxidation than that grown in DIW. The extract in the TEW group also enhanced intracellular superoxide dismutase activity and lowered reactive oxygen species and superoxide anion in the human Hep G2 cell. The results suggested that TEW could increase the antioxidant activities of buckwheat sprouts. The ethanol extracts of tartary buckwheat sprouts (TBS) exhibited higher reducing power, free radical scavenging activity, and superoxide anion scavenging activity than those of common buckwheat sprouts (CBS) (Liu et al. 2008). As for chelating effects on ferrous ions, CBS had higher values than TBS. Rutin was the major flavonoid found in both types of buckwheat sprouts, and TBS had5 fold higher rutin than CBS. The antioxidant effects of buckwheat sprouts on human hepatoma HepG2 cells revealed that both of TBS and CBS could decrease the production of intracellular peroxide and remove the intracellular superoxide anions in HepG2 cells, but TBS reduced the cellular oxidative stress more effectively than CBS, possibly because of its higher rutin (and quercetin) content. Nutrient levels in buckwheats that peaked in day 8 sprouts (D8SP) included total phenolics, quercetin, and l-ascorbic acid, whereas those of oxalic, malic, tartaric, and citric acids, rutin, and γ-aminobutyric acid (GABA) were found to reach maximum levels on day 10 (Lin et al. 2008). Ethanolic extract of D8SP (2.5 mg/mL) revealed potent free-radical scavenging and antioxidative capabilities but moderate Fe2+-chelating capability.

Jiang et al. (2007) found the contents of both rutin and total flavonoids were significantly different depending on species, 0.02 and 0.04% in *F. esculentum*, 0.10 and 0.35% in *F. homotropicum*, and 1.67 and 2.04% in *F. tataricum*, respectively. All three buckwheat species exhibited a dose–response effect in inhibiting low-density lipoprotein (LDL) peroxidation. The antioxidant activity decreased in the order: *F. tataricum* > *F. homotropicum* > *F. esculentum*. Linear regression analysis revealed a correlation between antioxidant activity and rutin content ($R^2=0.98$) or total flavonoids content ($R^2=0.77$) in all buckwheat cultivars/accessions. In another study, phenolic compounds, including chlorogenic acid, four C-glycosylflavones (orientin, isoorientin vitexin, isovitexin), rutin and quercetin, were determined in the seed sprouts of common (*Fagopyrum esculentum*) and tartary (*Fagopyrum tataricum*) buckwheats (Kim et al. 2008). In the edible parts of common buckwheat sprouts, individual phenolics significantly increased during sprout growth from 6 to 10 days after sowing (DAS), whereas in tartary buckwheat sprouts they did not. While the sum contents of phenolic compounds in the edible part (mean 24.4 mg/g DW at 6–10 DAS) of tartary buckwheat sprouts were similar to those of common buckwheat sprouts, rutin contents in the non-germinated/germinated seeds (mean 14.7 mg/g DW) and edible parts (mean 21.8 mg/g DW) of tartary buckwheat were 49- and 5-fold, respectively, higher than those of common buckwheat. Extracts of the edible parts of both species showed very similar free radical-scavenging activities (mean 1.7 μmol trolox eq/g DW),

suggesting that the overall antioxidative activity might be affected by the combination of identified phenolics and unidentified (minor) components. They recommended buckwheat seed sprouts for their high antioxidative activity, as well as being an excellent dietary source of phenolic compounds, particularly tartary buckwheat sprouts, being rich in rutin.

Buckwheat flour exhibited higher antioxidative efficiency than the hull though both contained total phenols, flavonoids, total flavanols, oligomeric proanthocyanidins (Quettier-Deleu et al. 2000). The higher efficiency of the flour extract could be related to its higher flavanolic content rather than to flavonoids which were predominant in the hull extract. Buckwheat flour, which is used for various dishes in the world, is a good source of proanthocyanidins. Proanthocyanidins in the buckwheat flour reduced nitrous acid producing nitric oxide (NO) when the flour was suspended in acidified saliva or in acidic buffer solution in the presence of nitrite (Takahama et al. 2010). The intake of dough prepared from buckwheat flour enhanced the concentration of NO in the air expelled from the stomach, suggesting that the proanthocyanidins also reduced nitrite to NO in the stomach. The increase in the concentration of NO could improve the activity of stomach facilitating the digestion of ingested foods and the nitration and nitrosation of the proanthocyanidins could contribute to the scavenging of reactive nitrogen oxide species generated from NO and nitrous acid. In-vitro studies by Awatsuhara et al. (2010) demonstrated that rutin , the highly antioxidative ingredient of buckwheat flour, displayed antioxidative activity against hydroxyl radicals in a DNA protection assay. When combined with ovalbumin, it formed a rutin-ovalbumin complex that markedly enhanced the peroxyl, but not the hydroxyl, radical scavenging activity of rutin and markedly improved DNA protection from apurinic/apyrimidinic site formation caused by hydroxyl radicals. Polyphenolics content in buckwheat flour was four times higher than in wheat flour and ranged between 476.3 and 618.9 mg GAE/g extract (Sedej et al. 2010). Ethanolic extracts of buckwheat flours exhibited higher antioxidant activities in all antioxidative Assays (DPPH, reducing power), except for chelating activity.

Extrusion cooking of buckwheat caused a significant decrease in all the compounds tested, except for phenolic acids (Zieliński et al. 2006). The content of inositol phosphates decreased by 13%, that of reduced glutathione by 42%, and that of tocopherols and tocotrienols by 62%. A three-fold lower level of melatonin and total polyphenols was observed whereas the superoxide dismutase-like activity disappeared when compared to the nonextruded material. A two-fold higher content of phenolic acids (free and released from ester bonds) was observed. In spite of the clear decrease in the investigated antioxidants, the extruded dehulled buckwheat seeds contained still significant content of bioactive compounds, which resulted in as little as an average 10% decrease of the antioxidant capacity.

Roasting of buckwheat caused a decrease in ABTS*+radical cation (TEAC) and 2,2-diphenyl-1-picrylhydrazyl radical (DPPH RSA) free radical scavenging and Folin-Ciocalteu reagent reducing capabilities by 70% (Zielinska et al. 2007b). The lowest TEAC, DPPH RSA, and FCR reducing capacities were noted for roasted groats. Both DPPH RSA and TEAC methods were highly positively correlated with the FCR reducing capacity assay ($r=0.98$ and $r=0.99$). The enzymatic hydrolysis of buckwheat protein isolate resulted in remarkable decrease in the globulins or protein aggregates and concomitant increase in peptide fragments (Tang et al. 2009). The hydrolysates exhibited excellent antioxidant activities, including DPPH radical scavenging ability, reducing power and ability to inhibit linoleic acid peroxidation. The antioxidant activities of these hydrolysates were closely related to their polyphenol contents. The results indicated polyphenol-rich buckwheat proteins to be unique protein materials for the production of the hydrolysates with good nutritional and antioxidant properties. Phenolic contents in microwave irradiated buckwheat extracts were higher than those heated with a water bath (Inglett et al. 2010). The highest phenolic content, 18.5 mg/g buckwheat, was observed in the extract that was microwave irradiated in 50% aqueous ethanol at

150°C. The highest antioxidant activities, 5.61–5.73 μmol Trolox equivalent/g buckwheat, were found in the 100% ethanol extracts obtained at 100 and 150°C, independent of heat source. The results indicated that microwave irradiation could be used to obtain buckwheat extracts with higher phenolic content and similar antioxidant activity as extracts heated in a water bath.

Sun and Ho (2005) found that the properties of the extracting solvents significantly affected the yield, total phenolics and antioxidant activity of buckwheat extract. The methanol buckwheat extract showed the highest antioxidant activity coefficient (AAC) of 627 at 200 mg/L by the β-carotene bleaching method and longest induction time of 7.0 h by the Rancimat method. The acetone extract showed the highest total phenolics of 3.4 g catechin equivalents/100 g and the highest scavenging activity of 78.6% at 0.1 mg/mL by the DPPH method.

Photoprotective Activity

Buckwheat extract displayed antioxidant and photoprotective activities (Hinneburg et al. 2006). In the 1,1-diphenyl-2-picryl-hydrazyl radical (DPPH) assay the extract had significantly better antioxidant activity than pure rutin, the major constituent of the extract. The extract prevented more effectively the UV-induced peroxidation of linolic acid than rutin itself or the commercial UV absorber. The use of the extract from buckwheat herb appeared to be more beneficial than the use of pure rutin.

Hypotensive Activity

An inhibitor of angiotensin-I converting enzyme (ACE) activity was isolated from buckwheat powder (Aoyagi 2006). Its chemical structure was determined to be 2″-hydroxynicotianamine, hydroxy derivative of nicotianamine. The compound showed a very high inhibitory activity toward ACE, and the IC_{50} was 0.08 μM. Only this hydroxy analog was found in buckwheat powder, at about 30 mg/100 g, and no nicotianamine was detected. However, nicotianamine was detected in the buckwheat plant body. Spontaneously hypertensive rats treated with germinated buckwheat extract (GBE) had lower systolic blood pressure than that in the 600 mg/kg in raw buckwheat extract(RBE) -treated group (Kim et al. 2009). The treatment with both buckwheat extracts significantly reduced oxidative damage in aortic endothelial cells by lowering nitrotyrosine immunoreactivity RBE and GBE contained a mean content of rutin of 1.52 and 2.92 mg/g, respectively. The results suggested that germinated buckwheat extract had an antihypertensive effect and may protect arterial endothelial cells from oxidative stress.

Fermented buckwheat sprouts, produced by fermentation with lactic acid bacteria such as *Lactobacillus plantarum, Lactobacillus brevis, Lactobacillus pentosus, Lactococcus lactis subsp. lactis,* and *Pediococcus pentosaceus*, are used as multifunctional foods (Maejima et al. 2011). Two functional components, nicotianamine (NA) and 2″-hydroxynicotianamine (HNA) were identified as angiotensin I-converting enzyme (ACE) inhibitors. NA and HNA increased during fermentation. Indole-3-ethanol was identified as an antioxidant (a SOD active substance), and may have been generated from tryptophan during fermentation because it was not contained in green buckwheat juice. A safety test demonstrated that fermented buckwheat sprouts contained safe functional food components, showing negative results in buckwheat allergy tests.

Anticancer Activity

The buckwheat protease inhibitor designated BWI-1, a member of the potato inhibitor I family, inhibited trypsin, chymotrypsin, and subtilisin, whereas the buckwheat protease inhibitor designated BWI-2a, a novel protease inhibitor homologous to the vicilin family, inhibited only trypsin (Park and Ohba 2004). Both inhibitors significantly suppressed the growth of T-acute lymphoblastic leukemia (T-ALL) cells such as Jurkat and CCRF-CEM. Jurkat cells showed slightly higher susceptibility to buckwheat inhibitors

than CCRF-CEM. Modification of Arg residue(s) in inhibitors by 1,2-cyclohexandione inactivated their trypsin inhibitory activity, considerably abolishing their suppressive activity. This suggested trypsin inhibitory activity to be involved in the suppression of growth of human T-ALL cell lines. It was further found that both inhibitors triggered programmed cell death (apoptosis) of these cell strains with DNA fragmentation.

Of the various fraction of a 70% ethanol extract of buckwheat hull , the hexane and ethyl acetate fractions at 1 mg/mL concentration exerted higher inhibition effects 89 and 93.2%, respectively against MCF-7 cells (Kim et al. 2007a). They also exhibited high inhibition rates at 1 mg/mL against Hep3B cells of 83.6 and 75.3%, respectively. All the fractions (including chlorof orm, butanol and water) displayed higher inhibition effects against AGS human gastric carcinoma than any other cancer cells. The inhibition rates against HeLa cells were 81.2 and 82.0% for the chlorof orm and butanol fraction with 0.5 mg/mL, respectively. All the fractions at doses of 25 and 50 mg/kg showed decreases of more than 20 and 42%, respectively, in tumour formation in sarcoma-180 implanted mice except for the aqueous fraction. The results suggested buckwheat to possess anticancer properties against a variety of different cancer cell lines. An antifungal peptide, isolated from buckwheat seeds, inhibited proliferation of Hep G2 (hepatoma) cells, L1210 (leukemia) cells, breast cancer (MCF-7) cells, and liver embryonic WRL 68 cells with an IC_{50} of 33, 4, 25, and 37 μM, respectively (Leung and Ng 2007).

MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assays showed that the recombinant buckwheat trypsin inhibitor (rBTI) could specifically inhibit the growth of human chronic myeloid leukemia K562 cells in a dose-dependent manner, and there were minimal effects on normal human peripheral blood mononuclear cells (PBMCs) (Wang et al. 2007). Flow cytometric analysis indicated that the apoptosis of K562 cells were 31.0, 32.8, 35.3 and 52.1% after treated by rBTI in range of 12.5–100 mγ/mL, respectively. The results suggested that rBTI could be a potential protein drug of the trypsin inhibitor family. Studies showed that the growth of HL-60 cells was inhibited evidently after treatment with recombinant common buckwheat trypsin inhibitor (rBTI) in a dose-dependent manner, and there were minimal effects on normal human peripheral blood mononuclear cells (PBMNCs) (Gao et al. 2007). The nuclei of HL-60 cells showed the characteristics of apoptosis and flow cytometry analysis indicated that the apoptosis rate of HL-60 cells was 52% after treatment with rBTI (100 mγ/mL), It was concluded that rBTI could inhibit growth of HL-60 and induced its apoptosis providing a foundation for use of recombinant common buckwheat trypsin inhibitor to cure the acute myeloid leukemia.

Buckwheat polysaccharides (BWPSs) were found to exert antiproliferative effects in THP-1 human leukemia cells by inducing differentiation (Wu and Lee 2011). In the indirect treatment, BWPS significantly stimulated cytokine secretion (differentiation inducer) in mononuclear cells (MNCs) from peripheral blood mononuclear cells in MNC-conditioned medium (BWPS-MNC-CM) following a 24-h treatment, and THP-1 cell differentiation and maturity were significantly increased after 5 days of treatment with the BWPS-MNC-CM. Conversely, BWPS directly induced THP-1 cell differentiation and maturity following 3-day and 5-day treatments in a dose-dependent manner and exerted phagocytic activity and superoxide anion production in these mature cells. The findings indicated that BWPS had potential for differentiation therapy in leukemia. BWI-1 (buckwheat trypsin inhibitor), a member of the potato inhibitor I family, was found to suppress the growth of T-acute lymphoblastic leukemia cells and induced apoptosis in human solid tumour cell lines (Wang et al. 2011). A recombinant protein of BWI-1 was found to undergo conformational change at the P(8)′ position upon binding to trypsin.

Hypocholesterolemic Activity

In a study of 850 Yi people, an ethnic minority in southwest China, multiple regression analysis showed that buckwheat intake (100 g/day) was associated with lower serum total cholesterol

(−0.07 mmol/L) and low-density-lipoprotein cholesterol (−0.06 mmol/L,) and a higher ratio of HDL to total cholesterol (0.01) (He et al. 1995). These findings suggested a role for buckwheat consumption in the prevention and treatment of hypercholesterolemia. Bijlani et al. (1985) demonstrated that supplementing the daily diet of human volunteers for 4 weeks with 100 g whole buckwheat flour raised the high density lipoprotein cholesterol (HDL-C)/cholesterol ratio and improved glucose tolerance. The other changes in lipid profile were not significant. Animal Studies showed that rabbits fed a high fat diet and buckwheat had significantly lower concentration of malondialdehyde and the number of ascorbate free radicals, examined in vitro, in the liver was markedly elevated (Wojcicki et al. 1995). The level of testosterone in rabbit blood serum was increased, but the insulin concentration was significantly diminished in comparison with rabbits fed a high fat diet containing cholesterol and coconut oil. The content of total cholesterol and triglyceride in the liver of animals maintained on buckwheat extract was decreased.

Buckwheat protein product (BWP) was found to have a strong hypocholesterolemic activity in rats fed a cholesterol-enriched diet (Kayashita et al. 1997). The results suggested that the cholesterol-lowering effect of BWP was mediated by higher faecal excretion of neutral sterols and that lower digestibility of BWP was at least partially responsible for the effect. The consumption of buckwheat protein product suppressed plasma cholesterol by enhancing the fecal excretion of both neutral and acidic steroids excretion in rats fed on a cholesterol-free diet (Tomotake et al. 2001). The effects of buckwheat protein product were stronger than those of soy protein isolate.

Oral administration of germinated buckwheat along with a high-fat diet caused significant reductions in triglyceride and total cholesterol levels in the liver C57BL/6 mice after 8 weeks (Choi et al. 2007). Oral administration of germinated buckwheat also down-regulated mRNA expressions of PPARgamma and C/EBPalpha in hepatocytes, in a dose-dependent manner. These results suggested germinated buckwheat to have potent anti-fatty liver activities caused partially by suppressing the gene expression of certain adipogenic transcription factors like PPARgamma and C/EBPalpha a in hepatocytes.

Findings of a random cross-sectional study of 3542 Mongolians in two adjacent counties of Inner Mongolia, China, reported that the consumption of buckwheat seed may be a preventative factor for hypertension, dyslipidaemia and hyperglycaemia in the pastureland Mongolian population (Zhang et al. 2007). The age-adjusted prevalence rate of hypertension in Kulun participants who consumed buckwheat seed as a staple food was 18.22% whereas that in Kezhuohou participants, who consumed corn as a staple food, was 23.31%. Age-adjusted prevalence rates in Kulun participants compared with Kezhuohou participants for hypercholesterolaemia, hypertriglyceridaemia and abnormalities in low-density lipoprotein-cholesterol were 4.02% versus 7.76%, 26.58% versus 31.04% and 4.66% versus 8.81%, respectively. The age-adjusted prevalence rate of hyperglycaemia in Kulun participants was 1.56% versus 7.70% in Kezhuohou participants.

Buckwheat (*Fagopyrum esculentum*) protein (BWP) had been shown to exhibit hypocholesterolemic activity in several animal models by increasing fecal excretion of neutral and acidic sterols (Metzger et al. 2007). Further studies showed that the insoluble fraction of buckwheat protein possessed cholesterol-binding properties that reduced micelle cholesterol solubility and uptake by Caco-2 cells. Cholesterol uptake in Caco-2 cells from micelles made in the presence of BWP (0.2%) was reduced by 47, 36, 35, and 33% when compared with buckwheat flour, bovine serum albumin, casein, and gelatin, respectively. Reduction in cholesterol uptake in Caco-2 cells was dose-dependent, with maximum reductions at 0.1–0.4% BWP. In cholesterol-binding experiments, 83% of the cholesterol was associated with an insoluble BWP fraction, indicating strong cholesterol-binding capacity that disrupted solubility and uptake by Caco-2 cells.

Animal studies showed day 8 buckwheat sprouts (D8SP) to contain high polyphenolic and moderate quercetin contents and to exert hypocholesterolemic, hypotriglyceridemic, and antioxidative activities (Lin et al. 2008). Groups of Syrian hamsters were fed (i) control meal, (ii)

high fat plus high cholesterol meal, (iii) high fat plus high cholesterol plus 2.5% of buckwheat seeds, (iv) high fat plus high cholesterol plus 25% of buckwheat seeds, (v) high fat plus high cholesterol plus 2.5% of D8SP, and (vi) high fat plus high cholesterol plus 25% of D8SP. High seed meal prominently enhanced body weight gain, whereas high sprout meal exhibited the highest feed efficiency. Ratios of liver/body weight (L/B) were significantly lowered by all buckwheat meals. Although low seed meal reduced serum total cholesterol (TC) levels, its effect was still inferior to the high seed and sprout meals. In contrast, serum triglyceride (TG) levels were lowered only by the high seed and sprout meals. Levels of serum low-density lipoprotein cholesterol (LDL-C) were significantly suppressed by all buckwheat meals; however, serum high-density lipoprotein cholesterol (HDL-C) levels were increased insignificantly. Both LDL-C/HDL-C and TC/HDL-C ratios were significantly lowered. Hepatic TC levels were significantly reduced, whereas hepatic TG levels were totally unaffected. The results of studies by Watanabe and Ayugase (2010) suggested that buckwheat sprouts had various in-vivo activities in relation to antidiabetic effects in type 2 diabetic mice, especially for improvement in lipid metabolism. Concentrations of hepatic parameters, such as lipids, total cholesterol, triglyceride, and thiobarbituric acid reactive substances (TBARS) levels in buckwheat sprout-fed groups, were lower than those in the diabetic control group. It was deduced that excretion of bile acids in feces by feeding the in buckwheat sprout diet would contribute to the suppression of the cholesterol concentration in the plasma and liver tissues of mice.

In a double blind crossover study of female day-care centre staff, intake of tartary buckwheat cookies was found to reduce the serum level of myeloperoxidase (MPO) by a factor 0.84 (Wieslander et al. 2011). When grouping tartary and common buckwheat cookies together, there was a reduction of total serum cholesterol and HDL-cholesterol during the study period, with improved lung vital capacity. The degree of reduction in total and HDL cholesterol levels was similar in individuals with low and high body mass index. It was concluded that intake of tartary buckwheat cookies with high level of the antioxidant rutin may reduce levels of MPO, an indicator of inflammation and intake of both types of buckwheat cookies may lower cholesterol levels.

Anticholethiasis and Activity

Animal studies showed that after 2 weeks, plasma and liver concentrations of cholesterol in the hamsters fed buckwheat protein product (BWP) were significantly lower than those in the hamsters fed casein and soy protein isolate (SPI) (Tomotake et al. 2000). The molar proportion of cholesterol in gallbladder bile was significantly lower in the BWP group than in the other groups, whereas that of bile acids was slightly higher in the BWP group resulting in the lowest lithogenic index in the BWP animals. None of the hamsters fed BWP had gallstones, whereas they were present in some of the hamsters fed other proteins. Compared with casein ingestion, BWP ingestion resulted in significantly higher ratios of cholic acid to chenodeoxycholic acid and of cholic acid to lithocholic acid in the gallbladder bile. The excretions of faecal neutral and acidic steroids were distinctly higher in the BWP group compared with the other groups. SPI intake also significantly lowered cholesterol level in gallbladder bile and caused higher faecal bile acids compared with casein intake, but the effects were significantly less than those of BWP. The results suggested that buckwheat protein product suppressed gallstone formation and cholesterol level more strongly than soy protein isolate by enhancing bile acid synthesis and faecal excretion of both neutral and acidic steroids.

Antiinflammatory Activity

An extract of buckwheat sprouts exerted antiinflammatory activity in lipopolysaccharide-activated human colon cancer cells and was confirmed by oral administration of lipopolysaccharide (LPS) to mice (Ishii et al. 2008).

Inflammatory cytokines (interleukin 6 and tumour necrosis factor α) were markedly up-regulated in the spleen and liver from LPS-administrated mice, and combinatory treatment with LPS and the extract decreased up-regulation of them in both cytokines. Oral administration of the extract also showed protective activity as to hepatic injury induced by galactosamine/LPS treatment. The results suggested that buckwheat sprouts contained anti inflammatory compounds.

Antidiabetic Activity

Buckwheat was found to contain relatively high levels of D-chiro-inositol, component of an insulin mediator with antihyperglycemic properties (Kawa et al. 1996). In streptozotocin rats , administration of buckwheat concentrate containing 10 and 20 mg of D-chiro-inositol/kg of body weight were effective in lowering serum glucose concentrations by 12–19% at 90 and 120 min after administration. The findings demonstrated that a buckwheat concentrate wais an effective source of D-chiro-inositol for lowering serum glucose concentrations in rats and therefore may be useful in the treatment of diabetes. Nestler et al. (1999) showed that D-chiro-inositol increased the action of insulin in obese women patients with the polycystic ovary syndrome, thereby improving ovulatory function and decreasing serum androgen concentrations, blood pressure, and plasma triglyceride concentrations. Women with the polycystic ovary syndrome have insulin resistance and hyperinsulinemia, possibly because of a deficiency of a D-chiro-inositol-containing phosphoglycan that mediates the action of insulin. Iuorno et al. (2002) also demonstrated that in lean women with the polycystic ovary syndrome, D-chiro-inositol reduced circulating insulin, decreased serum androgens, and ameliorated some of the metabolic abnormalities (increased blood pressure and hypertriglyceridemia) of syndrome X.

Consumption of boiled buckwheat groats or bread based on wheat flour and 50% buckwheat groat induced significantly lower postprandial blood glucose and insulin responses compared with the white wheat bread (Skrabanja et al. 2001). The calculated glycemic and insulinemic indices (GI and II) for boiled buckwheat groats were 61 and 53 and for the buckwheat bread, 66 and 74, respectively. The highest satiety score was found with boiled buckwheat groats. It was concluded that buckwheat had potential use in the design of foods with lower GI properties. Kreft and Skrabanja (2002) evaluated in-vitro the rate of starch hydrolysis and the resistant starch formation in boiled buckwheat noodles, boiled wheat noodles, boiled buckwheat groats, and white wheat bread. The highest content of resistant starch (total starch basis) was found in boiled buckwheat groats (6%), compared with the boiled buckwheat noodles (3.4%), boiled wheat noodles (2.1%), and white wheat bread (0.8%). The rate of in-vitro amylolysis was significantly reduced in both studied buckwheat products in comparison to the reference white wheat bread. The calculated hydrolysis index (HI) was lower in boiled buckwheat noodles (61) in comparison to boiled wheat noodles (71), but higher in comparison to boiled buckwheat groats (50). They confirmed that boiled buckwheat noodles had some potential in diets designed in accordance with the dietary recommendations for diabetic patients and for healthy subjects. Similar results were reported by Skrabanja et al. (2001). The rate of in-vitro amylolysis was significantly lower in all buckwheat products in comparison with the reference white wheat bread. The calculated hydrolysis indices (HI) were lowest in boiled buckwheat groats (HI = 50) and in bread with 70% buckwheat groats (HI = 54). Consumption of boiled buckwheat groats or bread based on wheat flour and 50% buckwheat groats induced significantly lower postprandial blood glucose and insulin responses compared with the white wheat bread. The calculated glycemic and insulinemic indices (GI and II) for boiled buckwheat groats were 61 and 53 and for the buckwheat bread, 66 and 74, respectively. The highest satiety score was found with boiled buckwheat groats. They concluded that buckwheat had potential use in the design of foods with lower GI properties.

Amézqueta et al. (2012) separated the iminosugar, D: -fagomine in buckwheat seed from its diastereomers 3-epi-fagomine and 3, 4-di-epi-fagomine using a single run by cation

exchange high-performance liquid chromatography (HPLC) with detection and quantification by mass spectrometry using electrospray ionisation and a simple quadrupole analyser (ESI-Q-MS). The content of d-fagomine in buckwheat groats (6.7–44 mg/kg), leaves, bran and flour and 3,4-di-epi-fagomine (1.0–43 mg/kg) were determined. D-fagomine if used as a dietary supplement or functional food component may reduce the risks of developing insulin resistance, becoming overweight and suffering from an excess of potentially pathogenic bacteria. When ingested together with sucrose or starch, D-fagomine iminosugar originally isolated from buckwheat seeds, lowered blood glucose in a dose-dependent manner without stimulating insulin secretion (Gomez et al. 2012). D-fagomine reduced the area under the curve (0–120 min) by 20% and shifted the time to maximum blood glucose concentration (Tmax) by 15 min at doses of 1–2 mg/kg body weight when administered together with 1 g sucrose/kg body weight. Further, D-fagomine agglutinated 60% of Enterobacteriaceae (*Escherichia coli, Salmonella enterica* serovar *typhimurium)* populations (Gomez et al. 2012), while it did not agglutinate *Bifidobacterium* spp. or *Lactobacillus* spp. At the same concentration, D-fagomine significantly inhibited the adhesion of Enterobacteriaceae (95–99% cells in the supernatant) and promoted the adhesion of *Lactobacillus acidophilus* (56% cells in the supernatant) to pig intestinal mucosa. D-fagomine did not show any effect on bacterial cell viability. Based on all this evidence, the scientists suggested that D-fagomine may be used as a dietary ingredient or functional food component to reduce the health risks associated with an excessive intake of fast-digestible carbohydrates, or an excess of potentially pathogenic bacteria.

Coeliac Disease Management

Gluten-free breads made from pseudocereals namely amaranth, quinoa and buckwheat showed significantly higher levels of protein, fat, dietary fibre and minerals than the control bread (Alvarez-Jubete et al. 2009). The attributes of these breads conformed to the expert's nutritional recommendations for the gluten-free diet and gluten-free foods and could represent a healthy alternative to frequently used ingredients in gluten-free products for patients with coeliac disease.

Leg Oedema Protective Activity

In a single-centre, randomised, double-blind, placebo-controlled clinical trial of patients (22–74 years) with chronic venous insufficiency (CVI), treatment with buckwheat herbal tea did not change the mean partial leg volume which was increased in the placebo group by 110 mL (Ihme et al. 1996). The difference between the groups was significant. The subjective clinical symptoms were significantly reduced in both groups. The mean diameters of the femoral veins were reduced and capillary permeability was improved, but neither change was statistically significant. The treatment with buckwheat herb tea was safe and could have a favourable influence on patients with CVI such that further oedema development is prevented.

Antimicrobial Activity

An antifungal peptide with a molecular mass of approximately 4 kDa was isolated from buckwheat seeds (Leung and Ng 2007). It inhibited mycelial growth in *Fusarium oxysporum* and *Mycosphaerella arachidicola* with an IC_{50} of 35 and 40 μM, respectively. It inhibited HIV-1 reverse transcriptase with an IC_{50} of 5.5 μM. Tannins fractionated from acetone extract of *Phaseolus vulgaris, Fagoypyrum esculentum, Corylus avellana* and *Juglans nigra* showed antibacterial activity, especially against *Listeria monocytogenes* with MIC of 62.5–125 mγ/mL (Amarowicz et al. 2008). Methanol extract of buckwheat showed inhibitory action against *Enterobacter aerogenes* and *Pseudomonas fluorescens* (Zadernowski et al. 1992). Two antimicrobial peptides (AMP), designated Fa-AMP1 and Fa-AMP2, were purified from the seeds of buckwheat (Fujimura et al. 2003). Half of all

amino acid residues of Fa-AMP1 and Fa-AMP2 were cysteine and glycine, and they had continuous sequences of cysteine and glycine. The concentrations of peptides required for 50% inhibition (IC_{50}) of the growth of plant pathogenic fungi, and Gram-positive and -negative bacteria were 11–36 mγ/mL. The structural and antimicrobial characteristics of Fa-AMPs indicated that they were a novel type of antimicrobial peptides belonging to a plant defensin family.

Nephroprotective Activity

Studies showed that buckwheat extract ameliorated the renal injury induced by ischemia-reperfusion (Yokozawa et al. 2001). In ischemic-reperfused control rats, the activities of antioxidative enzymes in renal tissue and blood and renal parameters deviated from the normal range, indicating dysfunction of the kidneys. In contrast, when buckwheat extract was administered orally for 20 consecutive days before ischemia and reperfusion, the activities of the antioxidation enzymes superoxide dismutase, catalase, and glutathione peroxidase were higher, while thiobarbituric acid-reactive substance levels in serum and renal tissue were lower in the treated rats than in the controls. Decreased levels of urea nitrogen and creatinine in serum demonstrated a protective effect against the renal dysfunction caused by ischemia and recirculation. Further, it was demonstrated that buckwheat extract had a protective effect on cultured proximal tubule cells subjected to hypoxia-reoxygenation, probably by preventing oxygen free radicals from attacking the cell membranes. The renal protective activity of buckwheat was also demonstrated in another study (Yokozawa et al. 2002). Rats subjected to partial resection of the parenchyma showed reduced radical-scavenging activity in the remaining kidney and increased severity of renal tissue lesions. However, in similarly nephrectomized rats given buckwheat extract, the state of oxidative stress was ameliorated by the restoration of the decreased activities of reactive oxygen species-scavenging enzymes such as superoxide dismutase and catalase. The degree of mesangial proliferation, severity of extratubular lesions such as crescents and adhesions, glomerulosclerosis index, and severity of tubular interstitial lesions also improved. Additionally, nephrectomized rats administered buckwheat extract showed improvement in renal function, as indicated by decreased serum level of creatinine, with a significant decrease in the level of methylguanidine, a uremic toxin produced from creatinine in the presence of hydroxyl radical.

Neuroprotective Activity

Buckwheat polyphenol (600 mg/kg, continuous 21-day p.o.) significantly ameliorated not only the impairment of spatial memory in the 8-arm radial maze, but also necrosis and TUNEL-positive cells in the hippocampal CA1 area subjected to repeated cerebral ischemia in rats (Pu et al. 2004). A 14-day buckwheat polyphenol treatment of rats significantly inhibited the excess release of glutamate after the second occlusion. Additionally, the extract markedly suppressed a delayed increase in and NO^{x-} ($NO^{2-} + NO^{3-}$) production induced by repeated cerebral ischemia in the dorsal hippocampus. The results suggested that buckwheat polyphenol might ameliorate spatial memory impairment by inhibiting glutamate release and the delayed generation of NO^{x} in rats subjected to repeated cerebral ischemia.

Antiallergic Activity

Oral, intraperitoneal and intradermal administration of buckwheat grain extract significantly inhibited the compound 48/80-induced vascular permeability (Kim et al. 2003). The extract displayed potent inhibitory effect on passive cutaneous anaphylaxis activated by anti-dinitrophenyl (DNP) IgE when orally administered. In an in-vitro study, the extract exhibited inhibitory potential on the compound 48/80-induced histamine release from rat peritoneal mast cells. Additionally, the extract inhibited the IL-4 and TNF-α mRNA induction by PMA and A23187 in human leukemia mast cells, HMC-1. The results suggested

that anti-allergic action of buckwheat grain extract may be due to the inhibition of histamine release and cytokine gene expression in the mast cells.

Enzyme Activity

A metalloproteinase (MW 34,000) isolated from buckwheat seed exhibited limited proteolysis of the following seed storage proteins: 13 S globulin from buckwheat seeds and 11 S globulin from soybean (*Glycine max*) seeds (Belozersky et al. 1990). In its main properties the enzyme was similar to metalloproteinases of animal and bacterial origin. A triacylglycerol lipase (LIP) of two isozymes, LIP I and LIP II consisting were purified from buckwheat seed (Suzuki et al. 2004). Molecular weights were found to be 150 (LIP I) and 28.4 kDa (LIP I) by gel filtration and 171 (LIP I) and 26.5 kDa (LIP II) by SDS-PAGE. LIP I and II ecerted higher activity against triolein than monoolein or tri/monopalmitin. Most of the LIP activity was distributed in the embryo. A flavonol-3-*O*-β-heterodisaccharide glycosidase (FHG I) with molecular mass 74.5 kDa was isolated from dried aerial tissues of *Fagopyrum esculentum* (Baumgertel et al. 2003). FHG I exhibited high substrate specificity, preferring flavonol 3-*O*-glycosides comprising the disaccharide rutinose. Another flavonol 3-*O*-β-heterodisaccharide glycosidase (FHG II) with a molecular mass of 85.3 kDa could also be detected in buckwheat herb.

Adverse Effects: Protease Inhibition Activity

A trypsin inhibitor was isolated from buckwheat seeds (Ikeda and Kusano 1978). Subsequently, trypsin inhibitors I, II III were isolated from buckwheat seeds (Ikeda and Kusano 1983). They were found to be homogenous proteins with similar amino acid composition and molecular weight of about 8000. Trypsin inhibitory activity was more pronounced than chymotrypsin activity. In a study on the potency of antinutrients on the in-vitro digestibility of buckwheat seed protein, globulin, showed that protein protease inhibitor exhibited the highest inhibitory capacity amongst the substance (fibre sources, tannins, phytates, etc.) and phytate the lowest (Ikeda et al. 1986). Ikeda et al. (1994) also found buckwheat seed to contain an α-amylase inhibitor. The buckwheat inhibitor exhibited inhibitory activity against α-amylase from human saliva and α-amylase from porcine pancrease, but less or virtually no inhibitory activity against α-amylase from *Bacillus subtilis* and β-amylase from sweet potato.

Two major trypsin isoinhibitors BTI-1 and BTI-2, were purified from buckwheat seeds (Pandya et al. 1996). The buckwheat trypsin isoinhibitors exhibited distinct sequence similarities with the potato chymotrypsin inhibitor I family of serine proteinase inhibitors. Studies indicated that both trypsin inhibitors BWI-2b and BWI-1 from buckwheat seeds possessed IgE binding activity, albeit to a low extent, suggesting that they might be minor allergenic proteins in buckwheat seeds (Park et al. 1997). Sequence comparison of BWI-2b showed BWI-2b to be significantly homologous to the N-terminal region of storage proteins classified in the vicilin family. BWI-2b showed no relationship to the other buckwheat trypsin inhibitor (molecular mass 7743 Da) reported by Belozersky et al. (1995) which had an active site containing Arg45-Asp46 bond. Three protease trypsin inhibitors (BWI-1, BWI-2 and BWI-4) from buckwheat seeds with molecular masses of 7.7–9.2 kDa were found to contain a high content of glutamic acid and valine and a low content of isoleucine, aromatic and sulfur-containing amino acids (Dunaevsky et al. 1996). Each of the inhibitors contained an Arg residue at the reactive site. In addition to trypsin, BWI-1 and BWI-2 inhibited chymotrypsin, however, less effectively. None of the isolated inhibitors suppressed activity of papain, leukocyte elastase, pepsin and subtilisin. Proteinase inhibitors in buckwheat seeds (*Fagopyrum esculentum*) were purified, characterised and separated into 2 main groups – anionic (BWI-1a, BWI-2a and BWI-4a) and cationic inhibitors (BWI-2c and BWI-4c),

according to their behaviour on ion-exchange chromatography (Dunaevsky et al. 1998). Molecular masses of anionic inhibitors were in the range 7.7–9.2 kDa and of cationic 6.0 kDa. Both anionic and cationic inhibitors were highly pH- and thermostable. All anionic and cationic inhibitors inhibited trypsin. In addition to trypsin, BWI-1a and BWI-2a inhibited chymotrypsin, however, less effectively. Besides trypsin and chymotrypsin, cationic inhibitor BWI-4c also inhibited bacterial subtilisin. Inhibitors BWI-1a, BWI-2a, BWI-4a and BWI-2c contain an Arg residue at the reactive site whereas BWI-4c contains a Lys residue. According to determined amino acid sequences anionic inhibitors BWI-1a, BWI-2a and BWI-4a belong to the potato proteinase inhibitor I family.

Buckwheat seeds were found to contain anionic protease inhibitors (Belozersky et al. 1996). Analysis of amino acid sequences of IT1, IT2 and IT4 protease inhibitors suggested that the proteins were members of the potato proteinase inhibitor 1 family and include Arg-Asp residues in their active site.

The protease inhibitor BWI-4a of buckwheat seeds occurred in two isof orms differing by a single amino acid substitution of Gly40 for Ala40 (Belozersky et al. 2000). The reactive site of the inhibitor contained an Arg43-Asp44 bond. Analysis of the amino acid sequence of the BWI-4a inhibitor indicated the inhibitor to be a member of the potato proteinase inhibitor I family. Buckwheat seeds were found to contain cationic trypsin inhibitors BWI-1c (molecular mass 5203 Da), BWI-2c (5347 Da), BWI-3c (7760 Da) and BWI-4c (6031 Da) (Tsybina et al. 2001). In addition to trypsin, BWI-3c and BWI-4c inhibited chymotrypsin and subtilisin-like bacterial proteases. BWI-3c and BWI-4c appeared to belong to the potato proteinase inhibitor I family. All four cationic inhibitors demonstrated high efficiency in binding bovine trypsin and chymotrypsin as well as their broad antiprotease effect, including inhibition of proteinases secreted by fungi and bacteria suggesting their role in the defense of plants against fungal and bacterial infection (Tsybina et al. 2004).

Hyposensitization Activity

A haptenic substance, BWD II 22-3, isolated from the dialysate of the aqueous extract of buckwheat was composed of Asp(1), Thr(1), Ser(1), Gly(1), Gly(4), Ala(1), Val(1), Leu(1), Orn(2), Lys(1), Arg(1), Cys(1) and glucose (Vagi et al. 1982) It was demonstrated to be homogenous with an estimated molecular weight of 1600. The haptenic substance apparently had -SH group determinant and caused about 50% inhibition at a concentration of 100 mγ/disc in the radioallergosorbent test (RAST) procedure using human serum sensitive to buckwheat. An active component, BWD II 22-3, might prove effective in the hyposensitization therapy of buckwheat-sensitive patients. Earlier studies by the researchers (Yanagihara and Koda) demonstrated that the haptenic substance was capable of neutralizing specific IgE antibodies on mast cells and may be useful as an hyposensitization agent in buckwheat hypersentivity.

Buckwheat Allergy

Inhalation of buckwheat flour and ingestion of buckwheat foods had been reported to induce bronchial asthma (Hong et al. 1987). Buckwheat flour adhering to husks used as bed pillows can provoke bronchial asthma in patients sensitized to buckwheat. There was good correlation of skin test results between house dust mites, *Dermatophagoides farinae*, an important allergenic substance and buckwheat pillow extract. The authors reported 10 of 40 cases who tested positive to the skin test of buckwheat husk-pillow manifested weakly positive to buckwheat radioallergosorbent test. Buckwheat can be a potent allergen when ingested or inhaled (Stember 2006). A case was reported of a 36-year-old man who experienced nausea, vomiting, urticaria, a sensation of throat closing, inability to speak, dyspnea, and dizziness shortly after ingesting a large portion of buckwheat that required emergency room treatment. In the previous 2 years he had experienced asthma, contact urticaria, allergic conjunctivitis, and allergic rhinitis from sleeping

with a buckwheat pillow. Six months after the first ingestion reaction, the patient again experienced anaphylaxis requiring emergency treatment when he accidentally ate crackers with a small amount of buckwheat. Skin-prick testing showed a strong positive response to buckwheat, and a radioallergosorbent assay test was highly positive to buckwheat. Heffler et al. (2007) reported a case of anaphylaxis in a 20 year old woman after ingestion of buckwheat fl our as the hidden allergen in pizza dough on 4 different occasions. A prick-to-prick test with buckwheat fl our was positive. Double-blind, placebo controlled food challenges with buckwheat flour were positive after the administration of a cumulative dose of 2.3 g of the culprit flour. A study from 2006 to 2008 in Italy, of 72 patients with suspected buckwheat allergy, 30 (41.7%) were sensitized to buckwheat and 24 had a positive double-blind placebo-controlled food challenge. Several IgE-binding proteins were identified and grouped into three patterns: a 16-kDa band in patients with predominantly gastrointestinal symptoms with grass and wheat flour co-sensitization, a 25-kDa band in patients with predominantly cutaneous symptoms and a low frequency of co-sensitization, and a 40-kDa band in patients with anaphylaxis and a low frequency of co-sensitization.

Studies in Korea found buckwheat pillows, commonly used in Korea, to be a source of very high endotoxin levels that may be of relevance to asthma severity of atopic asthmatics (Nam et al. 2004). After 3 months, endotoxin were significantly higher on new buckwheat pillows compared to synthetic pillows. No *Der f* 1(house dust mite allergen) was detected on the new pillows. After three months *Der f* 1 levels were similar on buckwheat and synthetic pillows.

Traditional Medicinal Uses

Buckwheat is a bitter but pleasant tasting herb that is frequently used medicinally. The leaves and leafy shoots are rich sources of rutin which is useful in the treatment of a wide range of circulatory problems, it dilates the blood vessels, reduces capillary permeability and lowers blood pressure and used internally in the treatment of high blood pressure, gout, varicose veins, chilblains, radiation damage etc. Often combined with lime flowers (*Tilia* species), it is a specific treatment for haemorrhage into the retina. A homeopathic remedy has been made from the leaves; it is employed in the treatment of eczema and liver disorders. An infusion of the herb has been used in the treatment of erysipelas (an acute infectious skin disease). However, some caution should be exercised in the use of this herb because it has been known to cause photo-sensitive dermatitis. A poultice made from the flour and buttermilk has been used for restoring the flow of milk in lactating mothers.

Other Uses

Common buckwheat is a useful and good green manure crop as it grows rapidly and produces a green manure crop in a short time, it is used to reclaim low-productivity and badly degraded soils. Buckwheat is used a smother crop for the control of weeds like leafy spurge, knapweed, Canadian thistle, sow thistle and quakegrass. It germinates readily and grows rapidly and has also been reported to exude allelopathic substance that inhibits the growth of other plant species. Kalinova et al. (2007) reported the following allelopathic root exudates of common buckwheat that were exuded into agar medium: palmitic acid, squalene, epicatechin, vitexin, a gallic acid derivative, and a quercetin derivative whereas in the soils the root exudates detected were palmitic acid methyl ester, vanillic acid, rutin, a gallic acid derivative, and a 4-hydroxyacetophenone derivative. Plant growth inhibition effects were observed with 4-hydroxyacetophenone and vanillic and gallic acids suggesting that these compounds could have important function in the allelopathic root response of buckwheat. Buckwheat is well-known as a crop rich in flavonoids such as rutin, isoquercitrin, quercetin, catechin, and myricetin, however, most attention had been focussed on the main flavonoid, rutin as an important natural antioxidant or as a

possible allelopathic compound (Kalinova and Vrchotova 2009). In buckwheat, isoquercitrin represented the largest component of the selected compounds. The strongest inhibitory allelopathic effects on the growth of those selected plants were produced by catechin. Quercetin and isoquercitrin had weak inhibitive effects. Myricetin did not show any influence on plant growth. The results showed that myricetin, isoquercetin and quercetin did not have important function in allelopathy of buckwheat.

Buckwheat can be used as satisfactory partial substitute for other grains in feeding livestock. The grain is usually ground and mixed with at least two parts of corn, oats, or barley to one part buckwheat. Buckwheat middlings are rich in protein, fat, and minerals, and are considered a good feed for cattle when fed in moderate amounts and not as the only concentrate. Buckwheat middlings have been reported to have no harmful effect on dairy cows or dairy products.

Sportsmen have long known that buckwheat is useful as a food and cover crop for wildlife and as a honey plant in North America. The grain is sought after by deer, wild turkeys, pheasant, grouse, waterfowl and other birds. Buckwheat seed is an ingredient in commercial bird feed mixes. Buckwheat is currently being assessed, and actively used, as a pollen and nectar source to increase natural enemy numbers (hyperparasites, parasitoids) to control crop pests in New Zealand (Berndt et al. 2002) and USA (Lee and Heimpel. 2005). Storage pests *Tribolium confusum* and *T. destructor* were found to be most sensitive to the presence of buckwheat hull (Zadernowski et al. 1992). Buckwheat hull contained six times as much tannin as dehulled seeds, thus it was assumed that tannins may be a factor inhibiting the reproductive abilities of these two species.

Buckwheat hulls are used for pillow filling, which manufacturers claim has health benefits over traditional foam, polyester, or down fillings. In Korea, buckwheat hulls are commonly used as filling for a variety of upholstered goods, including pillows and *zafu*. However cases of bronchial asthma have been reported on buckwheat pillows made with poorly processed and uncleaned hulls that harbour high levels of a potential allergen that may trigger onset of asthma in susceptible individual. A blue dye can be obtained from buckwheat stems and a red dye from the flowers.

Comments

Four newly discovered and seven previously known *Fagopyrum* species were classified based on their morphology, isozyme variability, and RFLP of chloroplast DNA (cpDNA)(Ohnishi and Matsuoka 1996) The new classification differed from Steward (1930)'s classification in the position of *Fagopyrum tataricum* and *F. gracilipes*; *F. tataricum* was found to be closer to *F. cymosum*. Three new species, *F. pleioramosum*, *F. callianthum* and *F. capillatum* were found to be closely related to *F. gracilipes*. The new species *F. homotropicum* was very close to *F. esculentum* in morphology as well as in isozyme variability.

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Macadamia integrifolia

Scientific Name

***Macadamia integrifolia* Maiden & Betche.**

Synonyms

Macadamia ternifolia auct. non F. Muell., *Macadamia ternifolia* F. Muehl. var. *integrifolia* (Maiden & Betche) Maiden & Betche.

Family

Proteaceae

Common/English Names

Australian Bush Nut, Bauple Nut, Bopple Nut, Bush Nut, Macadamia Nut, Nut Oak, Queensland Nut; Smooth Macadamia, Smooth-Shelled Macadamia, Smooth-Shelled Queensland-Nut.

Vernacular Names

Chinese: Ao Zhou Jian Guo;
Czech: Makadámie Celolistá;
Eastonian: Tervelehine Makadaamia;
French: Macadamia À Coque Lisse, Macadamier, Noisetier D'australie, Noix De Macadamia, Noix De Queensland, Noix Du Queensland, Noyer Du Queensland;
German: Australische Haselnuß, Glattschalige Macadamia, Macadamianuss, Macadamia Nuß;
Hungarian: Makadámdió;
Japanese: Kuinsurandonatto Nattsu;
Portuguese: Macadâmia, Nogueira-Do-Havaí, Nogueira-Macadâmia, Noz De Macadamia;
Russian: Avstralijskij Orech, Makadamia Trojčatolistnaja;
Slovaščina: Makadamija, Makadamski Oreh;
Spanish: Macadamia, Nuez De Macadamia;
Swedish: Macadamia;
Taiwan: Ao Zhou Hu Tao.

Origin/Distribution

Macadamia integrifolia is native to coastal rainforests of central eastern Australia. The species occurs naturally in remnant forests from Mt Bauple, north of Gympie to Currumbin Valley in the Gold Coast hinterland in Queensland. While specimens have been collected from the North Coast of NSW, this species is not known to occur naturally in NSW. Along with the Rough-shelled Bush Nut, this species forms the basis of the commercial macadamia nut industry in Australia and Hawaii, usually as a hybrid selection. Australia and Hawaii are the world's leading producers followed by Costa Rica, but macadamias are now grown in other countries including

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Kenya, South Africa, Malawi, Tanzania, Brazil, Sri Lanka, New Zealand, Thailand and in Central America.

Agroecology

The eastern slopes of the Great Dividing Range in southern Queensland and northern NSW in Australia ranging from 25° to 31° south are the native habitat of the macadamias, *M. integrifolia* and *M. tetraphylla*. Roughly from Bundaberg to Coffs Harbour and at elevations near sea level up to 600 m. This area provides the best conditions for macadamias to flourish – deep, well drained, moist soil rich in organic matter, high humidity, high rainfall, a warm climate with minimal summer and winter temperature variation and frost free. Optimum temperature range for macadamias is between 20° and 25°C. Ground temperatures less than −1°C can severely affect young trees and frosts of −6°C will kill young trees and damage flowers and foliage of older trees. Prolonged exposure to over 35°C will also cause stress. Average annual precipitation should be at least 1,200 mm, otherwise irrigation is needed. Rainfall between 1,500 and 2,500 mm is ideal for most soils. Prolonged wet periods can cause trunk canker and blossom blight.

Macadamias perform well in deep, well drained loams and sandy loams. Well-drained topsoil about 1 m deep to a minimum 0.5 m is ideal for macadamias. Macadamias will thrive in a wide variety of soils from pH 4.5 to 8.0 but abhors heavy clay soil and gravelly ridges. Macadamias develop a deep tap root and relatively few lateral roots and as such they need protection of windbreaks in exposed areas.

Edible Plant Parts and Uses

Macadamia nuts are eaten raw or after cooking in oil are roasted and salted. The nuts have an excellent flavour, containing up to 76% colorless oil, suitable for human food and has no starch. Macadamia is available in variety of styles to suit different applications in snacks, confectionery, catering, baking and home use. In addition, macadamia nuts are sold by the primary processor as raw, roasted, salted or flavoured. Macadamias are eaten as snack or used in food dishes, desserts and confectionery. Fancy pastries, candies and ice cream, have been made from it. It has the advantage of retaining texture and flavour without becoming stale when used this way. It goes well with poultry, pork, beef lamb or seafood dishes. It is commonly use in salads, soups, noodle, fritters, spaghetti and couscous dishes. Confectionary uses include muffins, cakes, cookies such as Macadamia and fruit Florentines, biscuits, tartlets, brownies, chocolates, chocolate Macadamia biscotti, chocolate wedges. It is also relish in desserts like ice cream, mousse, meringue, marzipan, macadamia baklava, parfait, macadamia and mixed berry mille. In recent years many new and exciting products have been developed. Cold-pressed macadamia oil is not only revered as a salad and cooking oil, other applications have found a growing market in therapeutic oils and cosmetics as it is one of the known 'vanishing oils' which penetrate the skin. Years ago a coffee-like beverage known as "almond coffee" was marketed from the seeds.

Botany

An evergreen tree with a spread of 13 m, rough trunk with a diameter of 30 cm and reaching heights of 12–20 m and a roundish crown. Leaves usually in whorls of 3, pale green or bronze when young becoming dark green; petiole 4–18 mm. Lamina is simple, narrow-elliptical to oblanceolate, 10–30 cm long, leathery, base attenuate, margin irregularly spiny toothed when young becoming smooth, entire, apex acute to obtuse and sometimes retuse (Plates 1, 2, and 3). Flowers are creamy white (Plates 1 and 2), zygomorphic, bisexual, apetalous, scented, borne in groups of 3 or 4 along a long axis in pendant axillary racemes. Tepals 4, strap-like, dilated distally, coherent to free, cream-coloured. Filaments 4, with 4 anthers, connective slightly exceeding anthers. Ovary glabrous to sericeous, sessile to shortly stipitate; ovules 2, orthotropous; style terete to slightly

Plate 1 Dense foliage and white-flowered inflorescences

Plate 2 Foliage and fruits

quadrate; stigma ovoid, clavate. Fruit a globular follicle, with an apical horn, 25 mm diameter, consisting of a fleshy green pericarp 3 mm thick, enclosing a globular to broadly ovoid smooth-testa seed (nut) (Plate 4). Seed is 20–30 mm across, hard, brown, smooth or nearly so, shell (testa) and an inner, edible cream-coloured kernel (Plate 5).

Plate 3 Leaves and fruits

Plate 4 Harvested macadamia nuts

Plate 5 Macadamia nut kernels

Nutritive/Medicinal Properties

Food value of raw, unroasted macadamia nut (refuse 69%shells) per 100 g edible portion was reported as follows (USDA 2012): water 1.36 g, energy 718 kcal (3,004 kJ), protein 7.91 g, total lipid (fat) 75.77 g, ash 1.14 g, carbohydrate 13.82 g; fibre (total dietary) 8.6 g, total sugars 4.57 g, sucrose 4.43 g, glucose 0.07 g, fructose 0.07 g, starch 1.05 g, minerals – calcium 85 mg, iron 3.69 mg, magnesium 130 mg, phosphorus 188 mg, potassium 368 mg, sodium 5 mg, zinc 1.30 mg, copper 0.756 mg, manganese 4.131 mg, Se 3.6 μg; vitamins – vitamin C (total ascorbic acid) 1.2 mg, thiamin 1.195 mg, riboflavin 0.162 mg, niacin 2.473 mg, pantothenic acid 0.758 mg, vitamin B-6 0.275 mg, folate (total) 11 μg, vitamin E (α tocopherol) 0.54 mg, lipids – fatty acids (total saturated) 12.061 g, 12:0 (lauric acid) 0.076 g, 14:0 (myristic acid) 0.659 g,16:0 (palmitic acid) 6.036 g, 17:0 (margaric acid) 0.124 g,18:0 (stearic acid) 2.329 g, 20:0 (arachidic acid) 1.940 g, 22:0 (behenic acid) 0.616 g, 24:0 (lignoceric acid) 0.281 g; fatty acids (total monounsaturated) 58.877 g, 16:1 undifferentiated (palmitoleic acid) 12.981 g, 18:1 undifferentiated (oleic acid) 43.755 g, 20:1 (gadoleic acid) 1.890 g, 22:1 undifferentiated (erucic acid) 0.233 g, 24:1c (nervonic acid) 0.018 g; fatty acids (total polyunsaturated) 1.502 g, 18:2 undifferentiated (linoleic acid) 1.296 g, 18:3 undifferentiated (linolenic acid) 0.206 g; phytosterols 116 mg, campesterol 8 mg, β-sitosterol 108 mg; amino acids – tryptophan 0.067 g, threonine 0.370 g, isoleucine 0.314 g, leucine 0.602 g, lysine 0.018 g, methionine 0.023 g, cystine 0.006 g, phenylalanine 0.665 g, tyrosine 0.511 g, valine 0.363 g, arginine 1.402 g, histidine 0.195 g, alanine 0.388 g, aspartic acid 1.099 g, glutamic acid 2.267 g, glycine 0.454 g, proline 0.468 g, serine 0.419 g. Studies in China reported macadamia nut lipid profile to be predominated by a high triacylglycerol content of 98.4%, made up of 14.7% SFA, low PUFA (18:2n-6 (linoleic acid) and 18:3n-3 (linolenic acid) (<4%)) but high MUFA (monounsaturated fatty acids) of 82.6% (Li et al. 2006). No C20 fatty acids were detected. This was also reported in another study where macadamia nut oil was found to have the highest level (79%) of MUFA (Ako et al. 1995) and was low (4%) in the omega-6 fatty acid 18:2n-6 and saturated fatty acids. Curb et al. (2000) also reported macadamia nut to be a rich source of MUFA 58.877 g/100 g comprising 12.981 g/100 g of 16:1 undifferentiated (palmitoleic acid) and 43.755 g/100 g 18:1 undifferentiated (oleic acid). Macadamia nuts had 75% fat by weight, 80% of which was monounsaturated. The main PUFA present were linoleic acid (C18:2) and linolenic acid (C18:3).

Nuts including macadamia nuts are an excellent source of vitamin E and magnesium. Individuals consuming nuts also have higher intakes of folate, β-carotene, vitamin K, lutein + zeaxanthin, phosphorus, copper, selenium, potassium, and zinc per 1,000 kcal (King et al. 2008). Regular nut consumption increases total energy intake by 250 kcal/day (1.05 MJ/day), but the body weight of nut consumers is not greater than that of nonconsumers. Nuts are an excellent source of phytochemicals (phyotsterols, phenolic acids, flavonoids, stilbenes, and carotenoids). The total phenolic constituents probably contribute to the total antioxidant capacity of nuts, which is comparable to broccoli and tomatoes. Macadamia nuts were also reported to contain catechol, pyrogallol, and 3,4,5-trihydroxy phenolic compounds (Quinn and Tang 1996). Four phenolic compounds were identified 2,6-dihydroxybenzoic acid, 2′-hydroxy-4′-methoxyacetophenone, 3′,5′-dimethoxy-4′-hydroxyacetophenone, and 3,5-dimethoxy-4-hydroxycinnamic acid.

In one study, the levels of the elements in Macadamia nuts from different sampling sites in the south east coast region of South Africa were found to be in the decreasing order of Mg > Ca > Fe > Zn > Cu > Cr > As (Moodley et al. 2007a). The exception was Mn, which exhibited large variability with concentrations in nuts ranging from 10.21 to 216.4 μg/g. The scientists also compared the total elemental concentrations and proximate chemical composition of five different tree nuts, almond (*Prunus dulcis*), Brazilnut (*Bertholletia excelsa*), pecan (*Carya pecan*), macadamia (*Macadamia integrifolia*) and walnut

(*Juglans nigra*) that are consumed in South African households (Moodley et al. 2007b). With maximum and minimum limits being set by the almond and pecan nut samples, Cr ranging from 0.94 to 2.02 μg/g was detected in the nut samples. Generally, the order of the concentrations of the elements in the nut samples was found to be Mg > Ca > Fe > Cu > Cr > As > Se. The concentrations of Mn and Zn showed greater variation amongst the different types of nuts. The extracted oils showed low acid values and high saponification values with the macadamia nut sample having the highest oil content (76.0 g per 100 g of sample), the lowest acid value (0.42 mg KOH per g of oil) and highest saponification value (193.7 mg KOH per g of oil). The findings would be useful in calculating the Dietary Reference Intakes of these nutrients.

In another study of oil extracted from freshly ground nuts namely walnuts, almonds, peanuts, hazelnuts and the macadamia nut, α-tocopherol was the most prevalent tocopherol except in walnuts (Maguire et al. 2004). The levels of squalene detected ranged from 9.4 to 186.4 μg/g. β-sitosterol was the most abundant sterol, ranging in concentration from 991.2 to 2071.7 μg/g oil. Campesterol and stigmasterol were also present in significant concentrations. The data indicated that all five nuts are a good source of monounsaturated fatty acid, tocopherols, squalene and phytosterols.

Other Phytochemicals

Crain and Tang (1975) isolated pyrazines, furanones and carbonyl compounds (typical aromatic Maillard reaction products) from roasted macadamia nuts. They found that methyl sulphide, methylpropanal, 2-methylbutanal, 3-methylbutanal were present in high levels in roasted macadamia nuts. The main volatile compounds identified in raw/wet, raw/dry and roasted macadamia kernels were dihydro-2-methyl-3 (2 H)-furanone-, furfural phenol, benzeneacetaldehyde, 5-methyl-2- furancarboxaldehyde, benzyl methyl ketone, nonanal, and enzenepropanal (Netiwaranon et al. 2000). However, in raw/dry and roasted macadamia kernels, other volatiles were identified including sulphur compounds and pyrazines, which may also contribute to the characteristic macadamia flavour. One hundred and eleven volatile compounds were identified in macadamia nut (Pino et al. 2009). The composition of the nuts was characterized by many terpene compounds, particularly limonene (55.5% of the total composition), and the presence of esters and lactones. The concentration of volatile compounds found in stored unroasted macadamia nuts were not significantly different with regards to storage temperature (Srichamnong et al. 2010). Volatile compounds detected in unroasted macadamia nut-in-shell nuts stored for 2 months were hexanal, octanal, butenal, ester indole, nonyl aldehyde, heptanal, butanone, propenal and octyldodecan-1-ol. After roasting at 125°C oven, the compounds detected were pyridinamine, pentanamine, pyrazine, thiazole, oxazine, hexanol, cyclobutane, pyrrolidine, porpenal, butanone, pyran, furan, pyranose, pyrrolepyran, aziridine and amine. These compounds contribute to the overall flavour of roasted macadamia nuts.

Macadamia and Cardiovascular Diseases

Concentrations of releasable cyanide were measured in tissues of mature nuts and seedlings of *Macadamia integrifolia* Maiden & Betche, *M. tetraphylla* L.A.S. Johnson and *M. ternifolia* F. Muell (Dahler et al. 1995). Root, cotyledon and leaf samples were assayed at several developmental stages from germination to maturation of the first leaves. All samples contained detectable levels of cyanide. Concentrations were low (0.15 μmol/g fresh weight) in cotyledons of mature *M. integrifolia* and *M. tetraphylla* seeds, corresponding to the edibility of the seeds of these commercial species, and much higher (9.6 μmol/g) in the inedible *M. ternifolia* seeds. Root cyanide concentrations of 6–23 μmol/g were measured. The immature first leaf of the commercial species contained the highest concentrations (38–77 μmol.g). Levels decreased with leaf maturity, correlating with toughening of the leaf and possibly a consequent diminished requirement for cyanide as a herbivory deterrent.

Epidemiologic studies and clinical trials have demonstrated that the unique fatty acid profile of tree nuts beneficially affects serum lipids/lipoproteins, reducing cardiovascular disease (CVD) risk (Griel and Kris-Etherton 2006; Griel et al. 2008). Nuts have been reported to be low in saturated fatty acids (SFA) and high in polyunsaturated fatty acids (PUFA) and monounsaturated fatty acids (MUFA) and to be rich sources of other nutrients. Macadamia nuts have been reported to be a rich source of MUFA. Extensive evidence consistently showed total and LDL cholesterol-lowering effects of diets low in saturated fat and cholesterol and high in unsaturated fat provided by a variety of tree nuts. Studies had shown that tree nuts reduced LDL cholesterol by 3–19% compared with Western and lower-fat diets (Griel and Kris-Etherton 2006). Nuts also contain many nutrients and bioactive compounds that appear to contribute to the favourable effects on lipids and lipoproteins – these include plant sterols, dietary fibre and antioxidants. Because of their unique nutrient profile, nuts can be part of a diet that features multiple heart-healthy foods resulting in a cholesterol lowering response that surpasses that of cholesterol-lowering diets typically used to reduce CVD risk.

Frequent nut consumption was found to be associated with a reduced risk of both fatal coronary heart disease and non-fatal myocardial infarction in women (Hu et al 1998). After adjusting for age, smoking, and other known risk factors for coronary heart disease, women who ate more than five units of nuts (one unit equivalent to 1 oz of nuts) a week (frequent consumption) had a significantly lower risk of total coronary heart disease than women who never ate nuts or who ate less than one unit a month (rare consumption). The magnitude of risk reduction was similar for both fatal coronary heart disease (0.61, 0.35 to 1.05, P for trend = 0.007) and non-fatal myocardial infarction (0.68, 0.47 to 1.00, P for trend = 0.04). Frequent nut consumption may offer postmenopausal women modest protection against the risk of death from all causes and coronary heart disease (CHD) (Ellsworth et al 2001). Epidemiological studies found there was an inverse but not statistically significant association between frequent nut consumption (two or more 28.5 g servings per week compared with less than one serving per month) and death from CHD. There was also a weak inverse association between frequent nut intake and all-cause mortality.

Palmitoleic acid is a minor monounsaturated fatty acid in the human diet and in blood plasma. Macadamia oil being a potentially rich source of palmitoleic acid, was tested against two other dietary fatty acids, oleic acid and palmitic acid for its effect on plasma lipid levels (Nestel et al. 1994). Thirty-four hypercholesterolemic men ate the three test diets in random order in 3-week periods. Plasma total cholesterol and low density lipoprotein (LDL) cholesterol concentrations were similar with palmitic and palmitoleic acids and significantly higher than with oleic acid. High density lipoprotein (HDL) cholesterol was significantly lower with palmitoleic than with palmitic acid. The study confirmed that, at least in hypercholesterolemic men, a modest increase in palmitic acid (+4% en) raised LDL cholesterol relative to oleic acid (+3% en), even when dietary cholesterol was low (< 165 mg/day). Palmitoleic acid (+4% en) behaved like a saturated and not a monounsaturated fatty acid in its effect on LDL cholesterol.

In one notable study, a diet rich in macadamia nut (MAC) was compared with an average American diet (AAD) (Griel et al. 2008). Serum concentrations of total cholesterol (TC) and LDL cholesterol (LDL-C) following the MAC diet (4.94 mmol/L, 3.14 mmol/L) were lower than the AAD diet (5.45 mmol/L, 3.44 mmol/L). The serum non-HDL cholesterol (HDL-C) concentration and the ratios of TC:HDL-C and LDL-C:HDL-C were reduced following consumption of the MAC diet compared with the AAD. There was no change in serum triglyceride concentration. The findings strongly suggested that macadamia nuts could be included in a heart-healthy dietary pattern to reduce lipid/lipoprotein CVD risk factors. Nuts as an isocaloric substitute for high SFA foods increase the proportion of unsaturated fatty acids and decrease SFA, thereby lowering CVD risk. This was also confirmed in another study where a “typical American” diet high in saturated fat (37% energy from fat); an

American Heart Association Step 1 diet (30% energy from fat); and a macadamia nut–based monounsaturated fat diet (37% energy from fat) were assessed (Curb et al. 2000). Mean total cholesterol level after the typical American diet was 5.20 mmol/L (201 mg/dL). After the Step 1 diet and the macadamia nut diet, total cholesterol level was 4.99 mmol/L (193 mg/dL) and 4.95 mmol/L (191 mg/dL), respectively. Low-density lipoprotein cholesterol level was 3.37 mmol/L (130 mg/dL) (typical diet), 3.21 mmol/L (124 mg/dL) (Step 1 diet), and 3.22 mmol/L (125 mg/dL) (macadamia nut diet). High-density lipoprotein cholesterol level was 1.43 mmol/L (55 mg/dL) (typical), 1.34 mmol/L (52 mg/dL) (Step 1), and 1.37 mmol/L (53 mg/dL) (macadamia nut). Lipid values after the Step 1 and macadamia nut diets were significantly different from those after the typical diet.

In another study conducted in Japan in young, healthy Japanese female students; 3 week interventions of diet high in MUFA based on macadamia nuts, coconuts and butter were compared (Hiraoka-Yamamoto et al. 2004). After 3 weeks intervention, serum concentrations of total cholesterol and low-density lipoprotein-cholesterol were significantly decreased in the macadamia nut and coconut diets; and bodyweight and body mass index were decreased in the group fed macadamia nuts, although there were no statistically significant changes in the group fed butter.

One study demonstrated that macadamia nut consumption as part of a healthy diet favourably modified the plasma lipid profile in 17 hypercholesterolemic men despite their diet being high in fat (Garg et al. 2003). Plasma total cholesterol and LDL cholesterol concentrations decreased by 3.0 and 5.3%, respectively, and HDL cholesterol levels increased by 7.9% in hypercholesterolemic men after macadamia nut consumption. Plasma triglyceride and homocysteine concentrations were not affected by treatment. Macadamia nut consumption was associated with a significant increase in the relative intake of MUFA and a reduced relative intake of saturated fatty acids and PUFA. Research also showed that frequent nut consumption may offer postmenopausal women modest protection against the risk of death from all causes and coronary heart disease. Frequent nut consumption was associated with a reduced risk of both fatal coronary heart disease and non-fatal myocardial infarction. These data, and those from other epidemiological and clinical studies, support a role for nuts in reducing the risk of coronary heart disease.

Other Uses

Macadamia is also planted as an ornamental or shade tree in home gardens. In Kenya, it has been inter-cropped with coffee and food crops without affecting the yield of these crops. The tree provides timber but is not generally exploited. The wood is reddish, hard and tough, attractively marked, used in small turnery jobs. Macadamia shell may be used as fuel, generating sufficient energy to dry wet, in shell nuts. The decomposed husk is used in potting soils and the ground shell supplied to the plastic industry.

Comments

Macadamia integrifolia is favoured over *Macadamia tetraphylla* in the commercial cultivation of macadamia nuts for the following reasons: the higher sugar content of *M. tetraphylla*, leads to browning of the kernels when roasted; *M. integrifolia* is more resistant to water stress; research, selection work and breeding programs have mainly focused on *M. integrifolia*.

Cases of dogs developing toxicoses after consuming macadamia were reported in USA (Hansen 2002). Clinical signs commonly reported from most to least frequent were weakness, depression, vomiting, ataxia, tremors, and hyperthermia.

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Macadamia tetraphylla

Scientific Name

***Macadamia tetraphylla* L.A.S. Johnson.**

Synonyms

None recorded

Family

Proteaceae

Common/English Names

Macadamia Nut, Queensland-Nut, Rough-Leaved Queensland Nut, Rough-Shelled Bush Nut, Rough-Shelled Macadamia, Rough-Shelled Queensland-Nut.

Vernacular Names

Chinese: Si Ye Ao Zhou Jian Gu;
Czech: Makadámie Čtyřlistá;
Eastonian: Neljalehine Makadaamia;
French: Macadamia À Coque Ridée, Macadamier, Noisetier D'australie, Noix De Macadamia, Noix Du Queensland, Noyer Du Queensland;
German: Macadamia Nuß, Rauhschalige Macadamia;
Japanese: Hawai Makadamia Nattsu;
Portuguese: Macadâmia, Nogueira-Macadâmia, Noz De Macadamia;
Russian: Avstralijskij Orech, Makadamia Cetverolistnaja;
Spanish: Nogal De Australia, Nuez Australiana, Nuez De Macadamia.

Origin/Distribution

Macadamia tetraphylla is native to Australia. This species occurs naturally in subtropical rainforest in the coastal areas from northern NSW (mainly the Richmond and Tweed River valleys) to south-east Queensland (from the Gold Coast hinterland north to Mt Wongawallan). *M. integrifolia* and *M. tetraphylla* (and their cultivars and hybrids), are grown in a number of countries including the United States (Hawaii, California), southern Africa, Thailand and central America.

Agroecology

In its native range, Rough-shelled Bush Nut generally occurs in subtropical rainforest and complex notophyll vine-forest, at the margins of these forests and in mixed sclerophyll forest. It occurs in restricted habitat, growing on moderate to steep hillslopes on alluvial soils at well-drained sites, growing at altitudes from 10 to 460 m above sea level. It does best in areas with 1,250 mm of rainfall

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equally distributed throughout the year and a mild frost-free climate. Growth is optimal between temperatures of 20–25°C, ceasing when they fall below 10°C or rise above 30°C. *M. tetraphylla* appears to be slightly more cold-tolerant than *M. integrifolia*. It thrives in full sun in a sheltered position as the trees are easily damaged by strong winds Globally, both species will perform on a wide range of soil types from open sands and lava rock soils to heavy clay soils, as long as the soil is well drained. They do best, however, in deep, rich soils with a pH of 5.5–6.5. Macadamias will not tolerate soil or water with high salt concentrations. Both species, however, grow well in the coastal areas of California, although varieties often respond differently to a given location. Mature macadamia trees are fairly frost hardy, tolerating temperatures as low as −4.4°C, but the flower clusters are usually killed at −2.2°F. Young trees can be killed by light frosts.

Edible Plant Parts and Uses

The edible uses of rough-shelled bush nuts are similar to that described for the smooth-shelled bushnut, *M. integrifolia*.

Botany

Rough-shelled bush nut is a small to medium sized, much-branched tree, often branching near the base, densely bushy and growing to 20 m tall. The trunk is cylindrical, with a diameter of 45 cm (dbh). The outer bark greyish-brown, smooth or finely wrinkled, with numerous cream horizontal lenticels. Branchlets brown to greyish-brown (Plates 4 and 5), young shoots hairy. New foliage is pinkish-red (Plate 2). Leaves are in whorls of 4 usually, petioles are 2–4 mm long, lamina is narrowly oblong-obovate, 6–20 cm long and 2–4 cm wide, glabrous, leathery, green, apex usually acute or acuminate, margin regularly spiny serrate, with 13–20 pairs of main lateral veins (Plates 1, 4, and 5). Inflorescences are axillary, simple, 5.5–38 cm long and pendent, densely brownish yellow tomentose; bracts of flower pairs subulate to linear, 0.2–1.4 mm. Pedicel 2–3 mm. Perianth yellowish or pink to

Plate 1 Whorls of juvenile and mature leaves

Plate 2 Inflorescences with pinkish flowers and young leaves

Plate 3 Closer view of pinkish flowers

Plate 4 Mature leaves and fruits

Plate 5 Pendant cluster of fruits

lilac, 5.5–15 mm, tomentose (Plates 2 and 3). Ovary and base of style brownish yellow pubescent. Fruit globose, green turning (Plates 3 and 4) woody brown, 2.5–5 cm in diam., apex apiculate. Seed usually 1, testa bony, brown, wrinkled or tuberculate.

Nutritive/Medicinal Properties

Analysis conducted among four cultivars of macadamia nut (*M. tetraphylla*) in New Zealand reported that the major fatty acids were oleic acid, palmitoleic acid and palmitic acid; oleic acid accounted for 40.6–59% of the total fatty acids (Kaijser et al. 2000). The polyunsaturated fatty acid (18:2 + 18:3) content was low, ranging from 3.0 to 4.7%. α-Tocopherol (0.8–1.1 μg/g lipids) and δ-tocopherol (3.5–4.8 μg/g lipids) were the only two tocopherols identified in the

extracted oil. The major sterols identified were sitosterol (901–1,354 μg/g lipids), Δ5-avenasterol (82–207 μg/g lipids), campesterol (61–112 μg/g lipids) and stigmasterol (8–19 μg/g lipids).

The nutritive and medicinal attributes are as described for *M. integrifolia*.

Other Uses

As described for *M. integrifolia.*

Comments

Macadamia nuts are readily propagated by using fresh seeds. Cuttings are also successful but vegetative propagation is usually carried out by grafting or budding of selected varieties onto seedlings.

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Nigella sativa

Scientific Name

***Nigella sativa* L.**

Synonyms

Nigella cretica Mill.

Family

Ranunculaceae

Common/English Names

Black Caraway, Black Cumin, Blackseed, Black Seedflower, Edible Love-In-A-Mist, Fennel-Flower Nigella, Fitches, Nutmeg Flower, Onion Seed, Roman Coriander.

Vernacular Names

Albanian: Fara E Zezë;
Amharic: Tik'ur Azmud;
Arabic: Habah Al-Brekah, Habbah Al-Baraka, Habbah Sauda, Habbeh As-Sudah, Habbeh Al-Suda, Habbet Al-Suda, Habbet As-Suda, Kamun Aswad, Sanouz, Shunez, Shuniz, Sinouj;
Azeri: Çörək Out;
Brazil: Nigela;
Bulgarian: Chelebitka Posevna, Cheren Kimion;
Catalan: Sanuj, Barba D'ermità;
Chinese: Hak Jung Chou, Hei Xian Hao, Hei Zhong Cao;
Coptic: Shouniz, Stikeme;
Croatian: Crni Kumin;
Czech: Černucha Seta, Černý Kmín;
Ethiopia: Abasuda, Orsudu, T'ikur Azmud;
Danish: Nigella, Sort Kommen;
Dutch: Tamme Nigelle, Zwarte Komijn;
Eastonian: Aed-Mustköömen, Mustköömen;
Farsi: Siah Daneh;
Finnish: Mustakumina, Mustasiemen, Rohtoneidonkukka, Sipulinsiemen, Ryytineito;
French: Cheveux De Vénus, Cumin Noir, Nigelle, Nigelle Cultivée, Nigelle De Crète, Poivrette, Toute Épice;
Gaelic: Lus An Fhograidh;
German: Echter Schwarzkümmel, Nigella, Römischer Kümmel, Schwarzer Coriander, Schwarzkümmel, Zwiebelsame;
Hebrew: Ketzah, Kezah;
Hungarian: Borzaskata Mag, Fekete Kömény, Kerti Katicavirág, Parasztbors, Szőrös Kandilla;
India: Kaljeera, Kaljira, Kalzira, Kolajeera, Kolazira (Assamese), Kalo Jira (Bengali), Kala-Jira, Kala-Zira, Kalajira, Kalomji, Kalonji, Kulangji, Mangrail, Maṃgarail, Mugrela (Hindu), Kare-Jirage, Karejeerage, Karejirage, Karijeerige, Karijirigae, Karijirigay, Karijirigi, Karimsiragam, Krishnajeerige, Neeruli Beeja (Kannada), Mangrela (Maithili), Karim Jeerakam,

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Karinchirakam, Karincirakam, Karinjirakam, Karinjeeragam, Karun-Chirakam, Karunchirakam, Karunshiragam, Karuta jirakam (Malayalam), Kalongji, Kalonjee Jeere, Krishnajira (Marathi),Kalajira (Oriya), Kalonji (Punjabi), Ajaji, Aranyajeeraka, Asitajirakah, Bashpika, Jiraka, Kala-Ajaji, Kalajaji, Kalika, Kalvanjika, Karava, Karave, Karavi, Krishna Jiraka, Krishna-Jiraka, Krsnajiraka, Kunchi, Kunchika, Kuncika, Kunjika, Musavi, Prathvika, Prithu, Prithuka, Prithvi, Prthu, Prthvika, Susavi, Sushave, Sushavi, Upakunchika, Upakunchiraka, Upakunci, Upakuncika (Sanskrit), Acaci, Aciyacirakam, Aciyam, Aniyam, Aranam, Arattuvakki, Attakam, Attimai, Attimaiccirakam, Attulaccirakam, Attulakiyam, Attulakki, Attulakkinam, Attulakkiyam, Attuvakkayam, Attuvakkiyam, Attuvarkkayam, Cailaciritam, Caitini, Cannikanayan, Canninayakam, Canninayan, Carin Siragum, Cariyaccirakam, Copakunci, Culakkini, Irucitari, Irulakam, Iruli, Iruliccirakam, Kaketali, Kakoniyacirakam, Kakoniyam, Kalcirakam, Kamanam, Kanakacciram, Kanakaciram, Kanakam, Kapitaciram, Kapitam, Karaciram, Karavi Kariya Cirakam, Kariyacirakam, Kariyaciram, Kariyamani, Kariyamaniccirakam, Karkanacirakam, Karkanam, Karkkoli, Karkol, Karkolam, Karkoli, Karum Cheerakam, Karum Ciragam, Karun-Shiragam, Karuncetakam, Karuncheerakam, Karuncirakam, Karunciri, Karunjchirakam, Karunjeeragam, Karunjiragam, Karunshirogam, Karutakacirakam, Kattukkarucirakam, Kattukkaruncirakam, Kattumaiccirakam, Kiruttinacirakam, Kiruttinaciram, Kiruttinamuli, Kittinacaci, Kommatticcirakam, Kotticciram, Kutakam, Kutamanakam, Kutamanam, Kutampan, Kuttanam, Kuttinam, Maciyam, Maiccirakam, Malattakkutampu, Miti, Narcirakam, Pakutam, Palampacakam, Palampacam, Palappacam, Pankumam, Pankutam, Pilacam, Pilaccam, Pilecam, Pilicam, Puppacam, Purruccirakam, Putpaciram, Putparacan, Tecalati, Tecalaticceti, Terikkam, Umataviyam, Upakancikam, Upakuncam, Upakuncikai, Upakuncikai, Uppukkuncam, Vanticotani, Vengaya Vidhai. Viluttam (Tamil), Nalla Jeelakarra, Nalla-Jilakara, Nallailakarra, Nallajilakara, Nellajeelakaira, Nullajilakara, Ullithnam (Telugu), kalajirege (Tulu), Kalonji, Kalauṃjī, Kaloṃjīkulajan, Tukhm Gandana (Urdu);

Indonesia: Jintan Hitam;

Italian: Cuminella, Cumino Romano, Erba Spezie, Gittaione, Grano Nero, Melanzio Domestico;

Japanese: Kuro Tanetsou, Nigera, Nijera;

Kazakh: Sodana;

Korean: Nigella, Pullaek-Kumin, Tae-Hoehyang;

Kurdish: Siawasa;

Latvian: Melnsēklīte;

Libya: Kaműn Aswad, Kemun;

Lithuanian: Juodgrūdė;

Malaysia: Jintan Hitam;

Nepali: Mugrelo, Mungrelo;

Newari: Mugrela, Haji;

Norwegian: Svartfrø, Svartkarve;

Pakistan: Kalonji;

Persian: Siyah-Biranj, Siyah-Danah, Siyahbirinj, Siyahdana, Shoneez, Shuneez, Shuniz;

Polish: Czarnuszka Siewna;

Portuguese: Cominho-Negro;

Russian: Černuška Posevnaja, Chernushka;

Serbian: Crno Seme;

Slovaščina: Navadna Črnik, Vzhodna Črnika A;

Slovencina: Černuška, Černuška Siata;

Spanish: Agenuz, Ajenuz, Ajenuz Comun, Arañuel, Neguilla, Pasionara, Toda Especia;

Sri Lanka: Kaladuru, Kalu Duru (Sinhalese);

Swedish: Svartkummin;

Thai: Thian-Dam;

Turkish: Çörek, Çörek Out, Türk Çörekotu, Çörekotu Tohumu, Ekilen, Garacocco, Hakiki Çöreotu, Karamuk, Kara Çörek Otu, Sehniz, Siyah Kimyon, Siyah Susam;

Ukrainian: Chornushka;

USA: Charnushka;

Vietnamese: Thì Là Đen;

Yiddish: Nigele, Tshernitshke.

Origin/Distribution

Its origin is unknown, most probably in south-eastern Europe or southwestern Asia. Its seeds were found in the tomb of the pharaoh

Tutankhamun in Egypt. During antiquity, Nigella was already cultivated by the Jews, Arabs and Indians. Subsequently, it was introduced into several countries of Europe, Asia, and Africa. The species, formerly cultivated in Central Europe too, has lost somewhat of its economic importance.

Agroecology

N. sativa is a hardy cool season crop, with an optimum temperature of 15°C and a range of 5–25°C. It grows in full-sun on a wide range of well-drained soils from pH 6–7, but prefers sandy loam soils. It is quite drought tolerant and can survive in dry soils but requires regular watering during prolonged dry periods.

Edible Plant Parts and Uses

Nigella sativa seeds are used as a spice to flavor buns, breads and pastries, sauces as well as beverages, It is employed primarily in candies, curries and liquors. In the Middle East, Nigella is used in Armenian string cheese called Majdouleh or Majdouli. Egyptians spread the seeds on bread or put them on cakes like comfits. In Bosnia, nigella is commonly used to flavour pastries. Peshawari naan bread is topped with nigella seeds. Kalonji is one the five ingredients in the spice blend called *panch phoron*, popularly used in eastern India and Bangladesh particularly in Mithilia, Bengali, Assamese and Oriya cuisine.

Botany

An annual stout, erect, flowering herb growing to 30–50 cm tall with well-developed tap root and branched, subterete, weakly ribbed, pubescent, dark green stem. Leaves 7–5 cm, bipinnately, tripinnately to multipinnately divided into thin sublinear, pilose lobes. Flowers are terminal and solitary, actinomorphic, hermaphrodite, pentamerous, hypogynous on 4–11 mm minutely hairy and ribbed pedicels. Floral parts on a pale yellow fleshy, depressed conical receptacle. Calyx with 5 imbricate, greenish-white, ovate sepals; petals 5–10, pale bluish-white or white, and with short, thick, subulate-capitate appendix; stamens indefinite, polyandrous, spirally arranged with long filaments and yellow anthers; gynoecium 5–12 carpellary, syncarpous, ovary superior, with many ovules in each locule; stigmas free and as many as carpels. Fruit an inflated, ribbed, oblongoid, tuberculate capsule (Plate 1), 6–16 mm × 5–12 mm, greyish-green to brown at maturity and with long persistent stigma and containing numerous seeds. Seeds triquetrous to obpyramidal, rugose, white turning black (Plate 2) when exposed to the air, containing a small embryo embedded in copious fatty endosperm.

Nutritive/Medicinal Properties

Babayan et al. (1978) reported the following proximate nutrient composition for *Nigella sativa* seeds: 21% protein, 35.5% fat, 5.5% moisture, 3.7% ash and the rest being total carbohydrate. Fatty acid analysis of the extracted oil showed 56% linoleic acid, 24.6% oleic acid, 12% palmitic acid, 3% stearic acid, 2.5% eicosadienoic acid, 0.7% linolenic acid and 0.16% myristic

Plate 1 Inflated fruit capsule with persistent stigma remnants

Plate 2 *Nigella sativa* seeds

acid. Traces of few unidentified fatty acids were also found. Amino acid analysis of the seed protein hydrolysate of the n-propyl, N-acetyl derivatives showed the presence of 15 amino acids including 9 essential amino acids. Proximate analysis of black cumin seeds showed a composition of 20.85% protein, 38.20% fat, 4.64% moisture, 4.37% ash, 7.94% crude fibre and 31.94% total carbohydrates (Al-Jassir 1992). Potassium, phosphorus, sodium and iron were the predominant elements present. Zinc, calcium, magnesium, manganese and copper were found at lower levels. Linoleic and oleic acids were the major unsaturated fatty acids while palmitic acid was the main saturated acid. Glutamic acid, arginine and aspartic acid were the main amino acids present while cystine and methionine were the minor amino acids. Tee et al. (1997) reported the following proximate nutrient composition of *Nigella sativa* seeds per 100 g edible portion was reported as: water 13 g, energy 349 kcal, protein 12.7 g, fat 14.8 g, carbohydrate 41.3 g, fibre 12.5 g, ash 5.7 g, Ca 664 mg, P 704 mg, Fe 29.9 mg, Na 21 mg, K 929 mg vitamin B1 0.63 mg, vitamin B2 0.20 mg and niacin 5.9 mg. Takruri and Dameh (1998) reported the following average values of the proximate analysis on dry matter basis (g/kg) of black cumin seeds 216 g crude protein, 406 g fat, 45 g ash, 84 g crude fibre and 249 g nitrogen-free extract, whereas moisture content 38 g. The mineral and vitamin analyses showed that black cumin seeds contained iron, (105 mg/kg) copper (18 mg), zinc (60 mg) phosphorus (527 mg), calcium (1,860 mg), thiamin (15.4 mg), niacin (57 mg), pyridoxine (5.0 mg) and folic acid (160 μg). The protein quality of black cumin seeds was evaluated using net protein utilisation (NPU), protein efficiency ratio (PER) and net dietary protein energy percent (NDPE%) for two samples imported from Syria and Turkey, while PER was determined for the Syrian sample only. They found that the net protein utilisation (NPU) of Turkish black cumin seeds (63.1) was significantly higher than that of Syrian type (54.6). The net dietary protein energy percent (NDPE%) results were 5.3 and 5.6 for the Syrian and the Turkish samples, respectively. The protein efficiency ratio (PER) adjusted value for the Syrian samples was 1.9. The results of protein quality evaluation and those of the nutrient composition suggested black cumin to be of relatively good nutritional value.

Nigella sativa seeds from three different regions, Marib, Sadah and Taiz in Yemen were found to have a moisture content of was 6.83, 4.6 and 7.2%, total dietary fibre of 36.88, 26.50, 30.40%, insoluble dietary fibre 27.10, 20.56, 22.40% and soluble dietary fibre 8.90, 6.50, 8.13% respectively (Al-Naqeep et al. 2009b). *N. sativ*a seeds were also found to be a rich source of calcium, magnesium, potassium, phosphorus and iron.

Nigella sativa seeds were reported to contain fixed and volatile oils (Nickavar et al. 2003). Fatty acid composition of the fixed oil of *Nigella sativa* comprised eight fatty acids*:* linoleic acid 55.6%, oleic acid 23.4%, palmitic acid 12.5%, stearic acid 3.4%, eicosadienoic acid 3.1%, lauric acid 0.6%, myristic acid 0.5% and linolenic acid 0.4%. Thirty-two fatty acids (99.9%) were identified in the fixed oil of black cumin seeds (Amin et al. 2010). The dominant fatty acids were linoleic acid (50.2%), oleic acid (19.9%), margaric acid (10.3%), *cis*-11,14-eicosadienoic acid (7.7%) and stearic acid (2.5%). Hassanein et al. (2011) reported that *Nigella sativa*, lupin and artichoke seed oils to be rich in oleic and linoleic acids The triacylglycerols of the three oils showed some similarity with sunflower oil. *N. sativa* seed oil was found to have the highest

content of free sterols and acylated sterols, and had a high content of isofucosterol. *Nigella sativa* and lupin oils contained over 90% γ-tocopherol while artichoke oil comprised about 100% α-tocopherol.

Al-Naqeep et al. (2009b) found *Nigella sativa* seeds to contain high amount of oil (30–48%) and the major unsaturated fatty acids were linoleic acid (57.96, 58.04 and 57.04%) followed by oleic acid (21.49, 20.87 and 20.60%), while the main saturated fatty acids were palmitic (11.56, 11.23 and 11.22%), followed by stearic and myristic acids in cv. Marib, Taiz and Sadah samples respectively. The oil extracts were found to be rich in α-tocopherol content 290, 170 and 120 mg/100 g, in cv. Marib, Sadah and Taiz samples, respectively. The main fatty acids of the fixed oil of black cumin seeds were linoleic acid, oleic acid and palmitic acid (Tulukcu 2011). The lowest linoleic acid content (54.32%) was found in Kutahya Tavsanli. Additionally, the highest linoleic acid content (70.81%) is found to be in Iran. Palmitic acid is mostly found in samples obtained from Konya Karakaya and Konya Seydisehir and the palmitic acid, contributing approximately 8.23–13.34% to the total palmitic acid content. In general, black cumin contained about 24.6% oleic acid (C18:1), 56% linoleic acid (C18:2), 12% palmitic acid (C16:0), 0.7% linolenic acid (C18:3) and 6.7% other fatty acid. The total oil content of the *Nigella sativa* seeds ranged from 30.4 to 36.4%. Linoleic acid was found to be to be the highest (56.9–58.9%) (Matthaus and Ozcan 2011). The fatty acid profile was found to be: 14:0 (myristic) 0–0.6%, 16:0 (palmitic) 11.5–12.3%, 18:0 (stearic) 2.6–3.2%, 16:1 (palmitoleic) 0–0.3%, 18:1 Δ9 (oleic) 18.7–21.9%, 18:1Δ11 1.0–1.2%, 18:2 (linoleic) 56.9–58.9%, 18:3 (linolenic) 0.3–0.4%, 20:0 (arachidic) 0.0.2%, 20:1 (gadoleic) 0.4%, 20:2 (eicosadienoic) 3.2–3.8%, 22:1 (erucic) 0–0.01% and 24:0 (lignoceric) 0–0.4%. The total tocopherol content of *N. sativa* seeds ranged from 9.15–27.92 mg/100 g. The tocopherol profile was shown to be: α-tocopherol 0.63–4.80 mg/100 g, α-tocotrienol 0.035 mg, β-tocopherol 0–6.96 mg, γ-tocopherol 0.97–5.53 mg, β-tocotrienol 8.21–17.91 mg, γ-tocotrienol 0–1.00 mg, δ-tocopherol 0–0.48 mg and δ-tocotrienol 0–0.4%. The total sterol content of the seeds ranged from 1993.07–2887.28 mg/kg. The profile of sterol in the seeds comprised: cholesterol 0.7–1.25 mg, 24-methylen-cholesterol 1.21–2.36 mg, campesterol 9.88–14.06 mg, campestanol 0.54–0.94 mg, stigmasterol 9.95–18.38 mg, 7-camersterol 0.35–0.72 mg, 5,23-stigmastadienol 0.18–0.21 mg, clerosterol 0.18–0.21 mg, β-sitosterol 46.68–51.92 mg, sitostanol 2.29–2.78 mg, 5-avenasterol 7.35–16.60 mg, 5,24-stigmastadienol 1.05–1.29 mg, δ 7-avenastenol 1.11–2.38 mg and 7-avenastenol 1.82–2.99 mg. *N. sativa* seed oil was found to contain cholesterol, campesterol, stigmasterol, β-sitosterol and α-spinasterol (Salama 1973). The total unsaponifiable matter found in *N. sativa* seed oil was 15.58 oil and 14.82 g/kg oil in the Tunisian and Iranian seed oils, respectively (Cheikhrouhou et al. 2008). The total sterol content was 17.41 and 42.66% of the unsaponifiable matter, respectively. Beta-sitosterol was the major sterol in all oils with 44 and 54% in Tunisian and Iranian Nigella seed oils, respectively. The next major sterol was stigmasterol (16.57–20.92% of total sterols). TMS (trimethylsilyl sterol) 484, Delta 7-stigmasterol, Delta 7-avenasterol and cholesterol were detected at lower levels. *Nigella sativa* seed oil was found to contain free sterols, steryl esters, steryl glucosides and acylated steryl glucosides (Menounos et al. 1986). Steryl glucosides were the major sterol form. Steryl esters appeared relatively richer in 4-methylsterols and triterpene alcohols than free sterols. Delta 7 sterols were found only in the steryl ester fraction which was also richer in obfusifoliol (Δ8-4a-methysterol). The total fatty acids of the seed oil appeared richer in unsaturated acids than those of the steryl esters and acylated steryl glucosides.

Amount of total lipid extracted from black cumin seeds was higher in the chloroform/methanol mixture (39.2% of seed fresh weight) than in the hexane extract (37.9%) (Ramadan and Morsel 2002). The major fatty acid was linoleic acid C18:2n-6 (about 57% of total fatty acid methyl esters (FAME)) followed by oleic acid C18:1n-9.

Palmitic acid C16:0 was the major saturated fatty acid and detected in appreciable level. Chromatography on a silica column with solvent of increasing polarity yielded 96.1–97.2% neutral lipids and about 3% of polar lipids. The major fatty acids present in all lipid classes was C18:2n-6 followed by C18:1n-9 and C16:0 acids. The major individual phospholipid classes were found to be phosphatidylcholine (46–48% of total phospholipid) followed by phosphatidylethanolamine, phosphatidylserine and phosphatidylinositol. Phosphatidylglycerol, lysophosphatidylcholine and lysophosphatidylethanolamine were isolated in smaller quantities. The level of saturated fatty acids, namely palmitic C16:0 and stearic C18:0 acids, was considerably higher in phospholipid classes than in the corresponding triacylglycerols. Six glycolipids subclasses were detected in black cumin seed oil, with diglucosyldiacylglycerol predominating, followed by glucocerebroside (Ramadan and Morsel 2003). The fatty acid profiles of glycolipid fraction was dominated by linoleic acid C18:2n-6 was the dominating fatty acid, followed by oleic acid C18: ln-9. Four sugar and sterol moieties were identified and glucose was the only component sugar detected. A lipid-transporting protein (Ns-LTP1) with a molecular mass of 9,602 Da and containing eight cysteine residues forming four disulfide bridges was isolated from *N. sativa* seeds (Oshchepkova et al. 2009). Two defensins designated as Ns-D1 and Ns-D2, were isolated from *Nigella sativa* seeds (Rogozhin et al. 2011). The peptides differed by a single amino acid residue and showed high sequence similarity to *Raphanus sativus* defensins Rs-AFP1 and Rs-AFP2.

Other Phytochemicals

Nigella sativa seed had been reported to contain 1.3% volatile oil and 35% fixed oil and an amorphous, glucoside melanthin, which is decomposed by diluted hydrochloric acid into melanthigenin and sugar (Grieve 1971). Takruri and Dameh (1998) reported that the seeds contained 30.0%–38.0% (by weight) of total oil which is composed of approximately 97.5–99.9% fixed oil and about 2.5–0.1% volatile.

The following pharmacologically active constituents were isolated from the volatile *N. sativa* seed oil: thymoquinone, dithymoquinone, thymohydroquinone, and thymol (Ghosheh et al. 1999). A new compound 2-(2-methoxypropyl)-5-methyl-1,4-benzenediol (1) and two known compounds, thymol (2), carvacrol (3), from the methanol portion of *N. sativa* seed oil (Enomoto et al. 2001).

Thirty-two constituents were isolated from *N. sativa* seed volatile oil comprising phenyl propanoid compounds 46.1%, monoterpenoid hydrocarbons 26.9%, monoterpenoid ketones 6.0%, nonterpenoid hydrocarbons 4.0%, monoterpenoid alcohols 2.7% and sesquiterpenoid hydrocarbons 1.0% (Nickavar et al. 2003). The major components were *trans*-anethole (38.3%), *p*-cymene (14.8%), limonene (4.3%), carvone (4.0%) and α-thujene 2.4%. Other minor constituents included estragole 1.9%, dill apiole 1.8%, anisaldehyde 1.7%, *n*-nonane 1.7%, carvacrol 1.6%, sabinene 1.4%, myristicin 1.4%,β-pinene 1.3%, α-pinene 1.2%, fenchone 1.1%, apiole 1.0%, longifolene 0.7%, terpinen-4-ol 0.7%, α-phellandrene 0.6%, thymoquinone 0.6%, γ-terpinene 0.5%, 1,3,5-trimethyl benzene 0.5%,1-methyl-3-propyl benzene 0.5%, *p*-cymene-8-ol 0.4%, *n*-decane 0.4%, myrcene 0.4%, α-longipinene 0.3%, 3-methyl nonane 0.3%, dihydrocarvone 0.3%, 1-ethyl-2,3-dimethyl benzene 0.2%, *n*-tetradecane 0.2% and *n*-hexadecane 0.2%. Nine components were identified from the volatile oil of *N. sativa* seeds (Adamu et al. 2010). The major component was 2-methyl-5(1-methyl ethyl)-bicyclo[3.1.0]hex-2-ene (62.28%) followed by 1-methyl-2-(1-methyl ethyl)benzene (45.7%), 2-methyl-5-(1-methyl ethyl)-2,5- cyclohexadiene-1,4-dione (30.8%), 4-methyl −1-(1-methyl ethyl)-3- cyclohexen-1-ol (4.8%), 2-methyl-5-(1-methyl ethyl)phenol (4.45%), decahydro-4,8,8-trimethyl-9-methylene-1,4-methanoazulene (4.2%), β-pinene (2.49%), 2,6,6,9-tetramethyl tricyclo[5.4.0.0(2,8)]undec-9-ene (2.49%), and α-pinene (2.28%). The main constituents of *N. sativa* seed essential oil were

found to be *p*-cymene, thymoquinone, α-thujene, 4-terpineol and carvacrol (Benkaci-Ali et al. 2006). Forty-eight compounds were identified in the essential oil from *Nigella sativa* seeds and two monoterpenoids: *cis*-4-methoxythujane and *trans*-4-methoxythujane were isolated for the first time from plants (Wajs et al. 2008).

A total of 47 different compounds comprising quinines, monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons, oxygenated sesquiterpenes, diterpenes, alkane, alkenes, fatty acids and fatty acid esters were identified in *N. sativa* seed oils extracted by supercritical CO2 (SFE 1 and SFE 2) and hydrodistillation of SFE 1 (HD SFE) (Venkatachallam et al. 2010). About 31 compounds were identified in SFE 1 oil, 22 compounds in SFE 2 oil and 23 compounds in HD SFE oil. The major phenolic compounds isolated were thymoquinone (35.05% for SFE1, 33.12% for SFE2, 38.41% for HDSFE), thymohydroquinone (1.17% for SFE1, 1.12% for SFE2, 2.31% for HDSFE) and thymol (7.43% for SFE1, 5.30% for SFE2, 16.95% for HDSFE) (Venkatachallam et al. 2010). Dithymoquinone could not be detected. Sixteen volatile compounds were reported for the first time namely n-nonane (0.12% for SFE1), allo-ocimenol (0.11 for SFE2), terpinen-1-ol (0.11 for HDSFE), 1,5,8-ρ-menthatriene (0.43% for SFE1, 0.38 for SFE2), dihydrocarvone (0.37% for SFE1, 2.06 for SFE2), ocimenone (E) (0.54% for SFE1, 1.50 for SFE2), n-octyl isobutyrate (0.12% for HDSFE), citronellyl acetate (0.50% for HDSFE), thymohydroquinone methyl ether (trace for HDSFE), (Z)-caryophyllene (0.23% for SFE1), thymohydroquinone dimethyl ether (0.12% for SFE1), aromadendrene (1.05% for HDSFE), davanone (0.31% for SFE1), 8-heptadecene (1.23% for SFE1, 1.13% for SFE2, 0.86% for HDSFE), dihydro farnesyl acetate (2.28% for SFE1, 4.68% for SFE2) and pimaradiene (1.23% for SFE1, 2.25% for SFE2). The other known compounds isolated included: tricyclene (trace for SFE1), camphene (1.64% HDSFE), β-pinene (0.4% for HDSFE), 2,4,(10)-thujadiene (4.74% for SFE1, 0.19% for SFE2), sabinene (1.05% for SFE1), β-myrcene (0.31% for SFE1), 1,8cineole (0.98% HDSFE), α-terpinene (2.34% for SFE1), limonene (0.18% for SFE1, 0.38% for SFE2, 1.03% for HDSFE), γ-terpinene (27.46% for SFE1, 13.20% for SFE2, 12.87% for HDSFE), *cis*-sabinene hydrate (0.38% for SFE2, trace for HDSFE), linalool (0.25% for SFE1, 0.19% for SFE2), terpinolene (trace for HDSFE), *trans*-sabinene hydrate (0.37% for SFE1), borneol (1.02% for HDSFE), pinocarvone (2.96% for SFE1, 3.00% for SFE2), *trans*-dihydrocarvone (0.19% for SFE2), carvacrol (1.98% for SFE1, 1.73% for SFE2, 0.81% for HDSFE), 2-undecanone (13.72% for HDSFE), α-longipene (0.26% for SFE1), cyclosativene (1.43% HDSFE), α-longicyclene (0.43% for SFE1, 5.25% for SFE2), α-copaene (1.54% for SFE1, 2.00% for SFE2, 0.41% for HDSFE), α-longifolene (0.51% for HDSFE), β-caryophyllene (2.89% for SFE1, 5.07% for SFE2, 4.80% for HDSFE), palmitic acid (0.18% for SFE1), pimara-8(14),15-diene (0.92% for SFE1), and octadecanoic acid (0.26% for SFE1, 12.31% for SFE2). Fractionation of the essential oil from *N. sativa* seeds afforded four terpenoids: *trans*- sabinene hydrate methyl ether (1), *cis*-sabinene hydrate methyl ether (2), 1,2-epoxy-menth-4-ene (3) and 1,2-epoxy-menth-4(8)-ene (4) (Bourgou et al. 2012).

Alkaloids isolated from *N. sativa* seeds included: nigellicine (pyridazinoindazolium alkaloid) (Atta-ur-Rahman et al. 1985b), nigellimine (isoquinoline alkaloid) (Atta-Ur-Rahman et al. 1992), nigellimine-N-oxide (Atta-ur-Rahman et al. 1985a), nigellidine (idazole alkaloid) (Atta-Ur-Rahman et al. 1995), nigellidine-4-*O*-sulfite (Ali et al. 2008), dolabellane-type alkaloids nigellamines A(1), A(2), B(1) and B(2) (Morikawa et al. 2004b); A(3), A(4), A(5), and C, (Morikawa et al. 2004a). Three new flavonoid glycosides quercetin and kaempferol 3-glucosyl (1→2) galactosyl (1→2) glucoside and quercetin 3-(6-feruloylglucosyl)(1→2) galactosyl (1→2) glucoside were isolated from seeds of *Nigella sativa* seeds (Merfort et al. 1997). Saponins isolated from *N. sativa* seeds included: 3-*O*-[β-D-xylopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-l-arabinopyranosyl]-28-*O*-[α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl]-

hederagenin (Ansari et al. 1988); 3 hederagenin type saponins triterpene 3-*O*-[β-D-xylopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl]-28-*O*-[α-L-rhamnopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl]-hederagenin (1), 3-*O*-[α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl]-28-*O*-[α-L-rhamnopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl]-hederagenin (2), and 3-*O*-[β-D-xylopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl] -hederagenin (3) (Taksin et al. 2005). Two monodesmosidic triterpene saponins α-hederin and kalopanaxsaponin I were found in *N. sativa* leaves (Scholz et al. 2009). The two saponins accounted for approximately 10% of the dry plant matter, of which 93% was kalopanaxsaponin I and 7% α-hederin. An isobenzofuranone derivative, 5-hydroxy-2,2-dimethyl-2,8-dihydro-6*H*-furo[3,4-*g*]chromen-6-one was isolated from *N. sativa* seeds (Joshi et al. 2001). A triterpene saponin and known steroidal glucoside were isolated from the alcohol extract, and a new cycloartenol from n-hexane extract of seeds of *Nigella sativa* and were identified as 3-*O*-[β-D-xylopyranosyl-(1 → 2)-α-L-rhamnopyranosyl-(1 → 2)-β-D-glucopyranosyl]-11-methoxy-16,23-dihydroxy-28-methylolean-12-enoate (1), stigma-5,22-dien-3-β-D-glucopyranoside (2) and cycloart-23-methyl-7,20, 22-triene-3β,25-diol (3), respectively (Mehta et al. 2009b). A glycosylated pentahydroxy pentacyclic triterpene saponin identified as 3-*O*-[β-D-xylopyranosyl-(1 → 3)-α-l-rhamnopyranosyl-(1 → 4)-β-D-glucopyranosyl]-11-methoxy-16-hydroxy-17-acetoxy hederagenin from an ethanolic extract of *Nigella sativa* seeds (Mehta et al. 2009a). An antitumour principle saponin, α-hederin, a triterpene was isolated from *Nigella sativa* seeds (Kumara and Huat 2001).

Besides proteins, carbohydrates, crude fibre, fats, vitamins, minerals, *N. sativa* seeds also contain phytosterols, flavonoid glycosides, and bioactive alkaloids (nigellicines, nigellimine-N-oxide, and nigelledine) and bioactive saponins (alpha-hederin) in substantial amounts. Its fixed oil fixed oil (lipid fraction), is rich in unsaturated fatty acids, fatty acid esters and phytosterols while its essential oil contains quinines, monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons, oxygenated sesquiterpenes, diterpenes, alkane, alkenes among which are many bioactive compounds such as thymoquinone, thymohydroquinone, dithymoquinone, thymol, *p*-cymene and carvacrol. *N. sativa* seed, its oil and bioactive components especially thymoquinone have been reported to possess a diverse range of pharmacological properties (Ali and Blunden 2003; Saleem 2005; Yi et al. 2008; Butt and Sultan 2010; Randhawa and Alghamdi 2011; Woo et al. 2012) that include antioxidant, antiinflammatory, analgesic, antipyretic, antimicrobial, antineoplastic, immunomodulatory, immunotherapeutic, hypoglycemic, antihypertensive, antiasthmatic, antiparasitic, antidyslipidemic antiepileptic, antihypercholesterolemic, antiarthritic, spasmolytic, antiallergic, antiepileptic properties; and a host of other pharmacological activities that include cardioprotective, gastroprotective, hepatoprotective, neuroprotective, nephroprotective and other activities elaborated below.

Antioxidant Activity

Nigella sativa essential oil and four of its components, thymoquinone, carvacrol, t-anethole and 4-terpineol demonstrated respectable radical scavenging property (Burits and Bucar 2000). These four constituents and the essential oil possessed variable antioxidant activity when tested in the DPPH assay for non-specific hydrogen atom or electron donating activity. They were also effective OH radical scavenging agents in the assay for non-enzymatic lipid peroxidation in liposomes and the deoxyribose degradation assay.

Thymoquinone, a main constituent of *N. sativa* seed volatile oil, and a synthetic structurally-related tert-butylhydroquinone (TBHQ) exhibited strong in-vitro antioxidant potentials through scavenging ability of different free radicals (Badary et al. 2003). Both TQ and TBHQ efficiently inhibited iron-dependent microsomal lipid peroxidation in a concentration-dependent manner with median inhibitory concentration

(IC_{50}) values of 16.8 and 14.9 μM, respectively. TBHQ was stronger than thymoquinone as a scavenger of 2,2′-diphenyl-*p*-picrylhydrazyl radical (DPPH) (IC_{50} = 5 μM, 200-fold more active than thymoquinone) and as a scavenger of hydroxyl radical (OH*) with an IC_{50} of 4.6 μM (approximately 10 times more active than thymoquinone). Thymoquinone was more active than TBHQ as a superoxide anion scavenger with IC_{50} of 3.35 μM compared to 18.1 μM for TBHQ. Only TBHQ significantly promoted DNA damage in the bleomycin-Fe(III) system.

Nigella sativa seed oil extracts exhibited strong antioxidant properties when compared to α-tocopherol with 78–82% inhibition in the ferric thiocyanate method and 70–80% in the thiobarbituric acid assays (Al-Naqeep et al. 2009a). The oil extracts were found to be rich in α-tocopherol content 290, 170 and 120 mg/100 g, in cv. Marib, Sadah and Taiz samples, respectively. Among the main quinone constituents of *Nigella sativa* seeds, namely dithymoquinone, thymohydroquinone and thymoquinone, the best scavenging activity was produced by thymohydroquinone, which showed notable activity of 2.60 Trolox equivalents (TE) in a concentration range between 1.6 and 6.4 μg/mL and IC_{50} value of 2.4 μg/mL in ORAC and DPPH assays, respectively (Tesarova et al. 2011). In contrast, thymoquinone possessed only weak DPPH scavenging efficacy (IC_{50} = 170 μg/mL) but significant antioxidative action of 1.91 TE in the ORAC assay. No effect was observed for dithymoquinone.

Fractionation of the essential oil from *N. sativa* seeds afforded four terpenoids: *trans*- sabinene hydrate methyl ether (1), *cis*-sabinene hydrate methyl ether (2), 1,2-epoxy-menth-4-ene (3) and 1,2-epoxy-menth-4(8)-ene (4) (Bourgou et al. 2012). All four compounds exhibited oxygen radical absorbance capacity (ORAC) antioxidant activity in-vitro. Compounds 1, 2 and 4 strongly inhibited oxidative stress in human skin WS-1 fibroblasts cells, with IC_{50} values of 0.32, 0.005 and 0.43 μm, respectively. Moreover, all four compounds significantly inhibited nitric oxide release by lipopolysaccharide-activated RAW 264.7 macrophages. The results revealed that the most effective compound was *cis*-sabinene hydrate methyl ether (2).

Treatment of mice with the different doses of thymoquinone (25, 50 and 100 mg/kg/day orally) for 5 successive days, produced significant reductions in hepatic superoxide dismutase (SOD), catalase and glutathione peroxidase activities (Mansour et al. 2002). Cardiac SOD activity was also markedly inhibited with the higher doses of thymoquinone. Additionally thymoquinone (100 mg/kg/day), significantly reduced hepatic and cardiac lipid peroxidation as compared with the respective control group but enhanced cardiac and renal DT-diaphorase activity. DT-diaphorase reduced thymoquinone to dihydrothymoquinone (DHTQ). Both thymoquinone and its metabolite dihydrothymoquinone acted not only as superoxide anion scavengers but also as general free radical scavengers which contributed to the beneficial protective effect of thymoquinone. The IC_{50} for thymoquinone and DHTQ in biochemical and photochemical assays were in the nanomolar and micromolar range respectively.

In-vivo studies showed that *N. sativa* exerted a protective effect against cadmium-induced oxidative stress in the blood of rats (Kanter et al. 2005b). Cd + *N. sativa* treatment decreased significantly the elevated malondialdehyde and enhanced oxidative levels in the plasma and erythrocyte, and also decreased the activity of iron levels in the plasma compared to the Cd-treated group. There were less membrane destruction and hemolytic changes in erythrocytes in the Cd + NS-treated group compared to the Cd-treated group.

Nigella sativa extract and oil elicited significant protection against CCl(4)-induced changes in biochemical parameters (increased plasma protein oxidation, nitric oxide, TNF-alpha and decreased total antioxidant power and total thiol molecules) in rats indicating the potential of *N. sativa* in preventing CCL(4)-induced toxic nitrosative stress (Soleimani et al. 2008). The authors concluded that *N. sativa* had marked antioxidant potentials that may be beneficial in alleviating complications of many illnesses related to oxidative/nitrosative stress in humans.

Thymoquinone-rich fraction (TQRF) extracted from *Nigella sativa* and its bioactive compound, thymoquinone (TQ), effectively improved the plasma and liver antioxidant capacity and enhanced the expression of liver antioxidant genes of hypercholesterolemic rats (Ismail et al. 2010). Treatment with TQRF and TQ caused the up-regulation of the superoxide dismutase 1 (SOD1), catalase, and glutathione peroxidase 2 (GPX) genes compared to untreated rats. Further, liver antioxidant enzyme levels, including SOD1 and GPX, were also apparently increased in the TQRF- and TQ-treated rats compared to untreated rats. *N. sativa* extracts were found to prevent protein carbonyl formation as well as depletion of intracellular glutathione (GSH) in fibroblasts exposed to toluene (Ashraf et al. 2011). Although fractions rich in thymoquinone were found to be most potent in terms of antioxidant capacity against petrochemical-induced oxidative stress, the data indicated that the protective effects of *N. sativa* may not only be due to thymoquinone, but perhaps other antioxidants.

In the methanolic extract of *N. sativa* shoots and roots, vanillic acid was the major phenolic compound with a mean concentration of 143.21 and 89.94 mg per 100 g dry weight of shoots and roots, respectively (Bourgou et al. 2008). Shoots and roots showed comparable and potent superoxide scavenger activity; however, shoots exhibited higher DPPH radical scavenging, reducing and chelating activities than roots. Shoots and roots demonstrated important antimutagenic effects. Roots exhibited stronger activity than shoots with an inhibition percentage of 71.32%.

Haemeostasis Activity

After 12 weeks of *N. sativa* seed oil treatment, serum cholesterol, triglycerides and glucose levels and the count of leukocytes and platelets decreased significantly by 15.5, 22, 16.5, 35 and 32% in rats compared to control values, respectively while haematocrit and haemoglobin levels increased significantly by 6.4 and 17.4%, respectively (Zaoui et al. 2002b). In parallel, significant slowdown of the body weight development was observed in *N. sativa* treated animals comparatively to the animal control group. The results supported the traditional use of *N. sativa* seeds as a treatment of dyslipidemia, hyperglycaemia and related abnormalities.

Partial replacement of soybean meal in control diet of New Zealand white rabbit by *Nigella sativa* and/or *Thymus vulgaris* showed that the percentages of hemoglobin, hematocrate, the mean corpuscular hemoglobin and white blood cells (WBCs) count were significantly increased with the presence of black cumin seeds in the diets while WBCs count and the mean corpuscular volume in rabbit blood tended to decrease in *Thymus vulgaris* diets (Tousson et al. 2011). Feeding diet supplemented with *N. sativa* increased the plasma total proteins, albumin, globulin, serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) and decreased total lipids, cholesterol and triglycerides. The use of *N. sativa* alone or either mixture with *Thymus vulgaris* were good supplements for growing rabbits without any adverse effect on histological structure of liver, kidney and testis in rabbits.

Homeopathic Activity

Hansen et al. (2003) demonstrated that exposure of Hep-2 cells to lipopolysaccharide resulted in an alteration in the metabolic function (increase in malonaldehyde level), decrease in cell proliferation and this phenomenon was further escalated under stressful conditions (increased cortisol exposure); however treatment with *N. sativa* reversed the traumatic condition. The results supported the ancient traditional use of *N. sativa* in the Middle east and southeast Asia for its homeopathic effects.

Antidyslipidemic/ Antihypercholesterolemic Activity

Dolabellane-type diterpene alkaloids, nigellamines in particular nigellamine A(5), A(1) (1),

B(1) (3), and B(2) isolated from *N. sativa seeds* were found to lower triglyceride levels in primary cultured mouse hepatocytes (Morikawa et al. 2004a, b). Their activities were equivalent to that of the hypolipidemic PPAR-α agonist, clofibrate. Treatment of HepG2cells with thymoquinone-rich fraction (TQRF) from *Nigella* seeds and thymoquinone (TQ) resulted in a seven and twofold upregulation of low-density lipoprotein receptor (LDLR) mRNA level and suppression of 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) mRNA, compared with untreated cells (Al-Naqeep et al. 2009c). The study showed that TQRF and TQ regulated genes involved in cholesterol metabolism by two mechanisms, the uptake of low-density lipoprotein cholesterol via the upregulation of the LDLR gene and inhibition of cholesterol synthesis via the suppression of the HMGCR gene.

N. sativa (30 mg/kg body weight) administration to albino rats for 20 week induced significant decrease in serum low density lipoprotein cholesterol level, and increase in serum high density lipoprotein cholesterol levels (Dahri et al. 2005). Dietary supplementation of rats with *Nigella sativa* seeds at a dose of 400 mg for 1 week's duration produced a significant increase in high-density lipoprotein-cholesterol levels (Kocyigit et al. 2009). There was a significant decrease in very low-density lipoprotein-cholesterol levels after one week for 200, 400, and 600 mg doses, and all doses for 2 and 4 weeks. A 400 mg dose for 2 weeks, and all doses for 4 weeks caused a significant decrease in triglyceride levels. There was a significant decrease of total cholesterol levels in all doses after 4 weeks of supplementation. The results indicated that *N. sativa* may ameliorate the alteration in the lipid levels caused by diseases or toxic agents.

Administration of propolis or thymoquinone with cholesterol-enriched diet to rabbits significantly reduced TC, LDL-C, triglycerides and thiobarbituric acid-reactive substances concentrations, while increased high density lipoprotein-cholesterol concentration, as well as glutathione content compared to high cholesterol (HC) control group (Nader et al. 2010). Kidney function parameters were significantly affected by cholesterol diet and both propolis and thymoquinone counterregulated the cholesterol-induced changes. Histopathologically, early atherosclerotic changes were observed in high cholesterol control group represented by endothelial damage and thickened foam cells while propolis or thymoquinone provided protection against such high cholesterol-induced damage.

Feeding hypercholesterolemic rabbits with *N. sativa* either in powder or oil forms was shown to significantly reduce total cholesterol and low-density lipoprotein cholesterol levels and enhance high-density lipoprotein cholesterol levels after treatment for 2, 4, 6 and 8 weeks compared to the positive control group (Al-Naqeep et al. 2011). Plaque formation was significantly inhibited while the intima: media ratio was significantly reduced in the nigella powder and oil supplemented groups compared to the positive control group. The authors concluded that treatment of hypercholesterolemic rabbits with *N. sativa* seed powder or oil showed hypocholesterolemic and antiatherogenic cardioprotective properties.

Cardioprotective Activity

Studies by Hosseinzadeh et al. (2006) suggested that *N. sativa* seed extracts could have a therapeutic effect against cerebral ischemia. In ischemic rats, the aqueous (1 g/kg) and ethanolic (1.6 g/kg) extracts significantly reduced neural cell injuries in the CA1 and CA3 regions of rat hippocampus. The LD_{50} values (i.p.) of the aqueous and ethanolic extracts were 1.69 g/kg and 2.25 g/kg, respectively. *Nigella sativa* oil treatment of rats caused an increase in the activities of superoxide dismutase, catalase and glutathione peroxidase compared to the control group (Ebru et al. 2008). Malondialdehyde (MDA), nitric oxide and protein carbonyl levels were increased in the cyclosporine A-treated group in comparison with the control and *N. sativa* groups. Co-administration of *N. sativa* oil and cyclosporine A annulled the cyclosporine A-induced MDA, *N. sativa* oil and protein carbonyl increase compared to the cyclosporine A group. The results of their study showed that pre-treatment with *N. sativa*

oil reduced the subsequent cyclosporine A injury in rat heart, evidenced by normalized cardiac histopathology, decrease in lipid peroxidation, improvement in antioxidant enzyme status and cellular protein oxidation. *N. sativa* oral supplementation to normal adult rats had a favourable effect on the intrinsic cardiac contractile properties without evidence of an increased cardiac work load or energy consumption in-vivo (Al-Hariri et al. 2009). The isolated hearts *of Nigella*-treated rats maintained their normal cardiac adrenergic responsiveness, with a selective enhancement of both the tension-rate product and the inotropic reserve. The findings suggested *N. sativa* to be an attractive inotropic agent with an economic haemodynamic profile.

Administration of thymoquinone prior to doxorubicin ameliorated the doxorubicin-induced cardiotoxicity in rats (Nagi and Mansour 2000). Thymoquinone significantly decreased the elevated levels of lactate dehydrogenase and creatine phosphokinase induced by doxorubicin. In addition to its potent superoxide radical scavenging effect, thymoquinone also inhibited lipid peroxidation induced by Fe(3+)/ascorbate. Oral pretreatment of rats with thymoquinone for a week completely protected against methionine-induced hyperhomocysteinemia (El-Saleh et al. 2004). Similar results were obtained with *N. sativa* oil pre-treatment. Both pretreatments increased the antioxidant status and decreased the elevated plasma levels of triglycerides, lipid peroxidation, cholesterol and in the activities of glutathione peroxidase and superoxide dismutase associated with hyperhomocysteinemia.

Data from animal study suggested that thymoquinone supplementation attenuated cyclophosphamide -induced cardiotoxicity by a mechanism related, at least in part, to its ability to decrease oxidative and nitrosative stress and to preserve the activity of antioxidant enzymes as well as its ability to improve the mitochondrial function and energy production (Nagi et al. 2011). Recent studies by Sultan et al. (2012) found that supplementation of Sprague Dawley rats with *N. sativa* fixed and essential oil was effective in reducing the extent of potassium bromate induced oxidative stress and multiple organ toxicity. Abnormal elevated levels of cardiac enzymes such as lactate dehydrogenase (LDH), creatine phosphokinases CPK and CPK-MB and liver enzymes were reduced. The study showed that *N. sativa* essential oil to be helpful in reducing the extent of myocardial and liver necrosis.

Antidiabetic Activity

In-Vitro Studies

El-Mahmoudy et al. (2005) showed that thymoquinone treatment normalised the decreased inflammatory mediators (interleukin IL-1β and TNF-alpha) of peritoneal macrophages from Otsuka Long-Evans Tokushima Fatty rats (Type II diabetes mellitus) and the elevated inflammatory mediators (nitrite, IL-1Beta and TNF-alpha) of macrophages from streptozotocin-injected Long-Evans Tokushima Otsuka rats (Type I diabetes mellitus).

Thymoquinone was found to significantly reduce advanced glycation end products-induced redox-sensitive transcription factor nuclear factor kappa B (NF-kappaB) and interleukin-6 expression in human proximal tubular epithelial cells (Sayed and Morcos 2007). This indicated the potential antioxidative qualities of thymoquinone.

Results from western immunoblot assays indicated that in C2C12 skeletal muscle cells as well as in H4IIE hepatocytes, but not in 3 T3-L1 cells, *N. sativa* ethanol seed extract augmented activity of Akt, a key mediator of the effects of insulin, and activity of AMP-activated protein kinase (AMPK), a master metabolic regulating enzyme (Benhaddou-Andaloussi et al. 2010). *N. sativa* extract was found to exhibit potent uncoupling activity in isolated liver mitochondria. Also *N. sativa* extract behaved as an agonist of PPARgamma, stimulating PPARgamma activity in adipocytes. The data supported the ethnobotanical use of *N. sativa s*eed oil as a treatment for diabetes, and suggested potential uses of this product, or compounds derived thereof, against obesity and the metabolic syndrome.

Animal Studies

Intraperitoneal administration of the volatile oil of *N. sativa* seeds (50 mg/kg) to fasting normal and alloxan-diabetic rabbits produced significant hypoglycemic effects (Al-Hader et al. 1993). These effects were consistent and time-dependent. In normal animals, 15 and 23% decreases in fasting plasma glucose levels were detected 4 and 6 h, respectively, after treatment. The same treatment produced 12 and 21% decreases in the fasting glucose levels in diabetic rabbits at the 46 h time intervals, respectively. The administration of the volatile oil was not found to alter basal insulin levels in all animal groups, which might suggest a non-insulin-mediated mechanism of action for the demonstrated hypoglycemic activity.

Treatment with *N. sativa* seed extract for 2 months decreased the elevated glucose and malondialdehyde concentrations, increased the lowered glutathione and ceruloplasmin concentrations, and prevented lipid-peroxidation-induced liver damage in alloxan-diabetic rabbits (Meral et al. 2001). The authors concluded that *N. sativa* might be used in diabetic patients to prevent lipid peroxidation, increase anti-oxidant defence system activity and also prevent liver damage. Fararh et al. (2002) demonstrated that *N. sativa* oil elicited a hypoglycemic effect in streptozotocin plus nicotinamide-induced diabetic hamsters. The effect resulted, at least partly, from a stimulatory effect on β-cell function with consequent increase in serum insulin level. The results indicated that *N. sativa* oil had insulinotropic properties in type 2-diabetes model. They also found that *N. sativa* oil reduced blood glucose from 391 mg/dl before treatment to 325, 246, 208 and 1,791 mg/dl after the first, second, third and fourth weeks of treatment, respectively (Fararh et al. 2004). Hepatic glucose production from gluconeogenic precursors (alanine, glycerol and lactate) was significantly lower in *N. sativa* treated diabetic hamsters. Treatment with *N. sativa* oil significantly increased the phagocytic activity and phagocytic index of peritoneal macrophages and lymphocyte count in peripheral blood compared with untreated diabetic hamsters. Their data indicated that the hypoglycaemic effect of *N. sativa* oil was due to, at least in part, a decrease in hepatic gluconeogenesis, and that the immunopotentiating effect of *N. sativa* oil was mediated through stimulation of macrophage phagocytic activity either directly or via activation of lymphocytes.

Nigella sativa oil significantly lowered blood glucose concentrations in streptozocin-diabetic rats after 2, 4 and 6 weeks (El-Dakhakhny et al. 2002b). The blood lowering effect of *N. sativa* oil was, however, not paralleled by a stimulation of insulin release in the presence of *N. sativa*, nigellone or thymoquinone. Their data indicated that the hypoglycemic effect of *N. sativa* may be mediated by extrapancreatic actions rather than by stimulated insulin release. Studies by Kanter et al. (2004) suggested that *N. sativa* treatment exerted a therapeutic protective effect in diabetes by decreasing oxidative stress namely decreasing lipid peroxidation and serum NO, increasing antioxidant enzyme activity and preserving pancreatic β-cell integrity in streptozotocin-induced diabetic rats. Studies showed that *N. sativa* treatment of cadmium-treated mice may decrease the Cd-treated disturbances on heart rate, some hematological values, and preserve pancreatic β-cell (Demir et al. 2006). *N. sativa* treatment increased the lowered insulin levels, red blood cell and white blood cell counts, packet cell volume and neutrophil percentage in Cd-treated rats. Nigella treatment also decreased the elevated heart rate and glucose concentration of Cd-treated rats and reduce degeneration, necrosis, and weak degranulation in the β-cells of the pancreatic islets caused by cadmium.

Oral administration of ethanol seed extract of *N. sativa* s (300 mg/kg body weight/day) to streptozotocin induced diabetic rats for 30 days significantly lowered the elevated levels of blood glucose, lipids, plasma insulin and improved altered levels of lipid peroxidation products (TBARS and hydroperoxides) and antioxidant enzymes such as catalase, superoxide dismutase, reduced glutathione and glutathione peroxidase in liver and kidney (Kaleem et al. 2006). Treatment with *Nigella sativa* seed extract alone or in combination with human parathyroid hormone significantly increased the area of

insulin immunoreactive β-cells in diabetic rats; however, human parathyroid hormone treatment alone only led to a slightly increase in the insulin-immunoreactivity (Altan et al. 2007). The results suggested that *N. sativa* might be used in a similar manner to insulin as a safe and effective therapy for diabetes and might be useful in the treatment of diabetic osteopenia. Altan (2007) also reported that combined treatment of *N. sativa* and human parathyroid hormone was more effective on bone histomorphometry and mechanical strength than treatment with either of them alone for streptozotocin-induced diabetic osteopenia, which notably decreased bone volume. Chandra et al. (2009b) reported that concomitant *N. sativa* oil treatment reduced hyperinsulinemia in Sprague–Dawley rats treated with a daily HAART (highly active antiretroviral therapy) regimen for 7 months. The antiretroviral drugs used for HIV-1 therapy, consisted of nelfinavir (200 mg/kg), zidovudine (50 mg/kg), and efavirenz (20 mg/kg). Significant increases in insulin and C-peptide levels were observed in HAART-treated groups. The study showed that chronic HAART may increase serum insulin levels by dysregulating both insulin production by β-cells and insulin action at the periphery and that these deleterious effects may be prevented by dietary supplementation with *N. sativa* oil. They also demonstrated that exposure to several different HIV-1 protease inhibitors, nelfinavir (5–10 μM), saquinavir (5–10 μM) and atazanavir (8–20 μM), decreased glucose stimulated insulin secretion from rat pancreatic β-cells (INS-1) (Chandra et al. 2009a). Nelfinavir significantly increased reactive oxygen species (ROS) generation and suppressed cytosolic, but not mitochondrial superoxide dismutase (SOD) levels. Nelfinvair also decreased both glutathione and ATP and increased UCP2 levels in these cells. Simultaneous treatment with thymoquinone (TQ) (2.5 μM), an active ingredient of black seed oil, significantly inhibited the effect of nelfinavir on augmented ROS production and suppressed SOD levels. Both TQ and black seed oil exposure increased glucose stimulated insulin secretion and ameliorated the suppressive effect of nelfinavir. The findings implied a direct role of ROS in protease inhibitor induced deleterious effects on pancreatic β-cells.

N. sativa oil treatment caused a decrease in the elevated serum glucose, an increase in the lowered serum insulin concentrations and partial regeneration/proliferation of pancreatic β-cells in streptozotocin-induced diabetic rats (Kanter et al. 2003b). The authors concluded that the hypoglycaemic action of *N. sativa* could be partly due to amelioration in the β-cells of pancreatic islets causing an increase in insulin secretion. In another study, treatment of streptozotocin-induced diabetic rats with both *N sativa* and thymoquinone caused a sharp decrease in the elevated serum, and an increase in the lowered serum insulin concentrations in rats with diabetic neuropathy (Kanter 2008a). Streptozotocin induced a significant decrease in the area of insulin immunoreactive β-cells which was reversed by *N. sativa* and thymoquinone treatment. Myelin breakdown in sciatic nerves decreased significantly after treatment with nigella and thymoquinone. *N. sativa* seed volatile oil exhibited a therapeutic protective effect on streptozotocin-induced diabetic rats evidenced by decreasing morphological changes and preservation of β-cell integrity (Kanter et al. 2009). The results suggested that nigella may be clinically useful for protecting β-cells against oxidative stress. Meddah et al. (2009) demonstrated that *Nigella sativa* aqueous directly inhibited the electrogenic intestinal absorption of glucose in-vitro. Nigella extract exerted dose-dependent inhibition of sodium-dependent glucose transport across isolated rat jejunum. Maximal inhibition exceeded 80% and IC_{50} was close to 10 μg/mL. Together with the observed improvement of glucose tolerance and body weight in rats after chronic oral administration in-vivo, these effects further validated the traditional use of *Nigella sativa* seeds against diabetes. In another study, oral administration of thymoquinone (80 mg/kg b.w.) for 45 days, dose dependently improved the glycemic status in streptozotocin- nicotinamide induced diabetic rats (Pari and Sankaranarayanan 2009). The levels of insulin, Hb increased with significant decrease in glucose and HbA(1C) levels. The altered activities of carbohydrate metabolic

enzymes were restored to near normal. No significant changes were noticed in normal rats treated with thymoquinone.

Studies demonstrated that treatment of thymoquinone during pregnancy of streptozotocin-diabetic mice inhibited the rate of embryo malformations by reducing the free radicals, in addition to increasing the size and maturation of embryos (Al-Enazi 2007). Thymoquinone significantly reduced MDA and increased GSH in diabetic mice. The results suggested that the use of thymoquinone may be useful in pregnancy of diabetic females. Administration of *N. sativa* oil and its constituent, thymoquinone, attenuated the effects of oxidative stress and neuropathy in streptozotocin-induced diabetic rats (Hamdy and Taha 2009). The elevated heart and brain nitric oxide and malondialdehyde levels and increased norepinephrine and dopamine concentrations caused by streptozotocin were all lowered. The decreased activities of glutathione and antioxidant enzyme activities, i.e. glutathione-S-transferase and catalase, serum CK-MB (creatine kinase- muscle-brain) and serotonin concentration in streptozotocin-induced diabetic rats were restored or reversed by oral administration of either *N. sativa* oil or thymoquinone. The authors concluded that *N. sativa* oil or thymoquinone could rectify streptozotocin-induced diabetic alterations in CK-MB and brain monoamines due to their antioxidant properties.

Treatment of rats with *N. sativa* extract and oil, as well as thymoquinone, significantly decreased the diabetes-induced increases in tissue MDA and serum glucose and significantly increased serum insulin and tissue superoxide dismutase thus preserving pancreatic β-cell integrity (Abdelmeguid et al. 2010). Ultrastructurally, thymoquinone ameliorated most of the toxic effects of streptozotocin, including segregated nucleoli, heterochromatin aggregates (indicating DNA damage), and mitochondrial vacuolization and fragmentation. The aqueous extract of *N. sativa* also reversed these effects of streptozotocin, but to a lesser extent. The *N. sativa* oil restored normal insulin levels, but failed to decrease serum glucose concentrations to normal. The results suggest that *N. sativa* and thymoquinone may prove clinically useful in the treatment of diabetics and in the protection of β-cells against oxidative stress.

Benhaddou-Andaloussi et al. (2011) reported that diabetic rodents, *Meriones shawi*, treated with *N. sativa* seed ethanol extract showed a progressive normalization of glycaemia, albeit slower than that of metformin controls. Further, nigella extract increased insulinemia and HDL-cholesterol, compared to diabetic controls while leptin and adiponectin were unchanged. Nigella treatment decreased oral glucose tolerance test (OGTT) and tended to decrease liver and muscle triglyceride content. The results showed in-vivo treatment with nigella extract exerted an insulin-sensitizing action by enhancing acetyl-CoA carboxylase (ACC) phosphorylation, a major component of the insulin-independent AMPK signaling pathway, and by enhancing muscle Glut4 expression.

Clinical Studies

In a prospective study involving 60 patients, *N. sativa* oil was found to be effective as an add-on therapy in patients of insulin resistance syndrome (Najmi et al. 2008). Nigella treated patients showed significant improvement with reference to total cholesterol, low density lipoprotein cholesterol (LDL-C), and fasting blood glucose. The results indicated *N. sativa oil* to have a significant activity in diabetic and dyslipidemic patients. Results of a randomised study indicated a dose of 2 gm/day of *Nigella sativa* might be a beneficial adjuvant to oral hypoglycemic agents in type 2 diabetic patients (Bamosa et al. 2010). *Nigella sativa* caused significant reductions in fasting blood glucose, blood glucose level 2 h postprandially (2 hPG), and glycosylated hemoglobin (HbAlC) without significant change in body weight. Fasting blood glucose was reduced by an average of 45, 62 and 56 mg/dl at 4, 8 and 12 weeks respectively. HbAlC was reduced by 1.52% at the end of the 12 weeks of treatment. Insulin resistance calculated by the homeostatic model assessment (HOMA2) was reduced significantly, while β-cell function was increased at 12 weeks of treatment

Hypotensive/Antihypertensive Activity

An oral dose of *Nigella sativa* extract significantly increased diuresis and urinary excretion of Cl–, Na+, K+ and urea in spontaneously hypertensive rats after 15 days of treatment (Zaoui et al. 2000). Simultaneously, the mean arterial pressure was also decreased. In a randomized, double-blind, placebo-controlled study of patient with mild hypertension, oral supplementation of *N. sativa* seed extract for 2 months significantly reduced systolic blood pressure (SBP) compared to baseline values and placebo group (Dehkordi and Kamkhah 2008). Nigella extract administration reduced both SBP and DBP in a dose-dependent manner. Also Nigella extract caused a significant decline in the level of total and low-density-lipoprotein (LDL)-cholesterol relative to baseline data. No complications caused by the extract were observed. The results suggested that the daily use of nigella seed extract for 2 months may have a blood pressure-lowering effect in patients with mild hypertension.

Treatment of hypertensive L-NAME (NG-nitro-L-arginine methyl esters)-induced rats with thymoquinone decreased the elevated creatinine and systolic blood pressure, and increased glutathione to normal levels (Khattab and Nagi 2007). Thymoquinone inhibited the in-vitro production of superoxide radical in enzymatic and non-enzymatic systems. The results suggested thymoquinone to be effective in protecting rats against l-NAME-induced hypertension and renal damage possibly via antioxidant activity.

Thymoquinone, the main constituent of the volatile oil of black seed, elicited a concentration-dependent decrease in the tension of the isolated rat pulmonary arterial rings precontracted by phenylephrine (Suddek 2010). The effect was found to be mediated partly by activation of ATP-sensitive potassium channels and possibly by non-competitive blocking of serotonin, alpha1 and endothelin receptors. In-vitro studies showed that oleic and linoleic acids, two active principles in *Nigella sativa* seed oil, stabilized an E(2)P conformation of the Na, K-ATPase (Mahmmoud and Christensen 2011). Oleic and linoleic acids were found to increase the number of static sodium pump units and enhance ouabain interaction with Na, K-ATPase. The fatty acids differentially modulated cardiac glycoside interaction with the pump. On the basis of the possible involvement of the cardiac glycoside binding site on Na, K-ATPase in the regulation of hypertension, the authors suggested oleic acid to be a specific chaperon that modulated interaction of cardiac glycosides with the sodium pump.

Drug Potentiating Activity

Black cumin oil (5% v/v) exhibited the highest enhancement in in-vitro percutaneous permeation of the of the model lipophilic drug carvedilol (Amin et al. 2010). The increase in the permeability of the drug was due to increased drug diffusivity through the stratum corneum under the influence of black cumin oil. A higher content of linoleic acid (and other unsaturated fatty acids) in the oil was postulated to be responsible for the enhancement of in vitro percutaneous absorption of the drug.

Studies showed thymoquinon, from black cumin seeds and cisplatin to be an active therapeutic combination in lung cancer (Jafri et al. 2010). Thymoquinone inhibited cell proliferation, reduced cell viability and induced apoptosis. Thymoquinone at 100 μM and CDDP at 5 muM inhibited cell proliferation by nearly 90% and the combination showed synergism. Thymoquinone was able to induced apoptosis in both human lung cancer NCI-H460 and human small lung cancer NCI-H146 cell lines. Thymoquinone also appeared to affect the extracellular environment inhibiting invasion and reducing the production of two cytokines ENA-78 and Gro-alpha which were involved in neo-angiogenesis. The combination of thymoquinone and cisplatin was well tolerated and significantly reduced tumour volume and tumour weight without additional toxicity to the mice. In the combination arms (Thymoquinone 5 mg/kg/Cisplatin 2.5 mg/kg) tumour volume was reduced by 59% and (Thymoquinone 20 mg/kg/Cisplatin 2.5 mg/kg) by 79% as compared to control. Thymoquinone down regulated NF-kappaB

expression which may explain its various cellular activities and this activity may prove useful in overcoming cisplatin resistance from over expression of NF-kappaB.

Thymoquinone improved the anti-cancer properties of doxorubicin in a cell line-specific manner (Effenberger-Neidnicht and Schobert 2011). A significant rise of the growth inhibition by doxorubicin in human leukaemia HL-60 and multi-drug-resistant MCF-7/TOPO breast carcinomas cells was found when thymoquinone was added. The impact of the drug mixture on the mitochondria of HL-60 cells was also greater than those of the individual quinones alone. In addition, the drug mixture led to a higher concentration of reactive oxygen species in HL-60 cells.

Cytochrome Metabolic Activity

N. sativa seed significantly inhibited CYP2D6 and CYP3A4 mediated metabolism of dextromethorphan in human liver microsomes and healthy human volunteers indicating that it had the potential to interact with CYP2D6 and CYP3A4 substrates (Al-Jenoobi et al. 2010).

Analgesic/Antinociceptive Activities

Oral administration of *N. sativa oil* (50–400 mg/kg) to mice dose-dependently suppressed the nociceptive response in the hot-plate test, tail-pinch test, acetic acid-induced writhing test and in the early phase of the formalin test (Abdel-Fattah et al. 2000). The systemic administration (2.5–10 mg/kg, p.o. and 1–6 mg/kg, i.p.) and the i.c.v. injection (1–4 μg/mouse) of thymoquinone attenuated the nociceptive response in not only the early phase but also the late phase of the formalin test. The antinociceptive effect of *N. sativa* oil were blocked by naxolone and that of thymoquinone by the mu(1)-opioid receptor antagonist, naloxonazine, or the kappa-opioid receptor antagonist, nor-binaltorphimine. The results suggested that *N. sativa* oil and thymoquinone elicited antinociceptive effects through indirect activation of the supraspinal mu(1)- and kappa-opioid receptor subtypes.

The aqueous extract of *Nigella sativa* extract was found to have an antiinflammatory effect demonstrated by its inhibitory effects on Carrageenan induced paw edema (Al-Ghamdi 2001). It also produced significant increase in the hot plate reaction time in mice indicating analgesic effect. The results confirmed its use in folk medicine both as analgesic and anti-inflammatory agent. The aqueous and methanol extracts of defatted *Nigella sativa* seeds were found to have a potent central nervous system (CNS) and analgesic activity (depressant action especially in the case of the methanolic extract) (Al-Naggar et al. 2003). Black cumin seed essential oil was found to produce a significant analgesic effect in acetic acid-induced writhing, formalin and light tail flick tests (Hajhashemi et al. 2004). Oral administration of the essential oil at doses of 100, 200 and 400 μl/kg did not exert a significant antiinflammatory effect in the carrageenan test but intra peritoneal injection of the same doses significantly inhibited carrageenan-induced paw oedema. The oil at doses of 10 and 20 μl/ear could also reduce croton oil-induced oedema. Both systemic and local administration of the oil showed antiinflammatory activity. Thymoquinone (13.7%), as one of the major components was postulated to have an important role in both pharmacological effects, the other major component was *p*-cymene (37.3%). Studies by Ghannadi et al. (2005) showed that *N. sativa* seed polyphenols (NSP) possessed analgesic and anti-inflammatory activities. In the acetic acid-induced writhing test, oral administration of NSP decreased the number of abdominal constrictions. Both oral and intraperitoneal administration of NSP significantly suppressed in a dose-dependent manner the nociceptive response in the early and late phases of the formalin test, and the effect on the late phase was more pronounced. Oral administration of NSP did not produce a significant reduction in carrageenan-induced paw edema but, when injected intraperitoneally, NSP inhibited paw edema in a dose-dependent manner. NSP did

not produce a significant analgesia in the light tail flick test in mice. The lack of analgesic effect of NSP in the light tail flick test and also the failure of naloxone to reverse the analgesia in the formalin test revealed that mechanisms other than stimulation of opioid receptors were involved.

The p.o. administration of *N. sativa* oil (50–400 mg/kg) in mice dose-dependently suppressed the nociceptive response in the hot-plate test, tail-pinch test, acetic acid-induced writhing test and in the early phase of the formalin test (Fatah et al. 2000). The systemic administration (2.5–10 mg/kg, p.o. and 1–6 mg/kg, i.p.) and the i.c.v. (intracerebroventricular) injection (1–4 μg/mouse) of thymoquinone attenuated the nociceptive response in not only the early phase but also the late phase of the formalin test. Naloxone injected s.c. (1 mg/kg) significantly blocked *N. sativa* oil-induced and thymoquinone-induced antinociception in the early phase of the formalin test. Moreover, the i.c.v. injection of naloxone (10 μg /mouse), the mu(1)-opioid receptor antagonist, naloxonazine (1–5 μg/mouse), or the kappa-opioid receptor antagonist, norbinaltorphimine (1–5 μg/mouse), significantly reversed thymoquinone-induced antinociception in the early phase but not the late phase of the formalin test. The antinociceptive effect of morphine was significantly reduced in thymoquinone- and *N. sativa* oil-tolerant mice, but not vice versa. These results suggested that *N. sativa* oil and thymoquinone produced antinociceptive effects through indirect activation of the supraspinal mu(1)- and kappa-opioid receptor subtypes. The ethanolic extract of *Nigella sativa* seeds administered intraperitoneally to mice caused significant analgesic effect on nociceptive response initiated by 0.6% acetic acid; although this analgesic effect was less than that produced by diclofenac sodium (Bashir and Qureshi 2010).

Antiinflammatory Activity

The crude fixed *N. sativa* seed oil and pure thymoquinone both inhibited the cyclooxygenase and 5-lipoxygenase pathways of arachidonate metabolism in rat peritoneal leukocytes stimulated with calcium ionophore A23187 (Houghton et al. 1995). Thymoquinone was highly potent, with IC_{50} values of < 1 μg/mL and 3.5 μg/mL, against 5-lipoxygenase and cyclo-oxygenase respectively. Both substances also inhibited non-enzymatic peroxidation in ox brain phospholipid liposomes, but thymoquinone was about ten times more potent. However, the inhibition of eicosanoid generation and lipid peroxidation by the fixed oil was greater than thymoquinone, indicating that other components such as the unusual C20:2 unsaturated fatty acids may contribute also to its anti-eicosanoid and antioxidant activity. These pharmacological properties of the oil supported the traditional use of *N. sativa* and its derived products as a treatment for rheumatism and related inflammatory diseases. Oberg et al. (2009) showed that herbal melanin from *N. sativa* could modulate the inflammatory response by inducing interleukin IL-8 and IL-6 production via TLR4-dependent activation of the NF-kappaB signaling pathway in TLR4-transfected HEK293 cells and THP-1 cells.

Nigella sativa oil produced a concentration dependent inhibition of 5-lipoxygenase and 5-hydroxy-eicosa-tetra-enoic acid (5-HETE) production in the rat polymorphonuclear leukocytes with half maximal effects (IC_{50}) at 25 μg/mL, respectively 24 μg/mL (El-Dakhakhny et al. 2002a). Nigellone (polythymoquinone) caused a concentration-related inhibition of 5-HETE production (IC_{50}: 11.9 μg/mL). Similarly, thymoquinone, the active principle of the oil inhibited the production of 5-lipoxygenase products (IC_{50}: 0.26 μg/mL) and 5-HETE production (IC_{50}: 0.36 μg/mL). The data may partly elucidate the effect of the oil, its derived thymoquinone and nigellone in ameliorating inflammatory diseases. The aqueous extract of *N. sativa* seeds exhibited an inhibitory effect on nitric oxide production by murine macrophages activated with *Escherichia coli* lipopolysaccharide (Mahmood et al. 2003). The authors concluded that in view of the fact that nitric oxide is a pro-inflammatory mediator, the results validated the traditional use of the *Nigella sativa* seeds for the treatment of rheumatism.

Kanter (2009) showed that *N. sativa* treatment inhibited the inflammatory pulmonary responses, (reducing significantly) peribronchial inflammatory cell infiltration, alveolar septal infiltration, alveolar edema, alveolar exudate, alveolar macrophages, interstitial fibrosis, granuloma and necrosis formation in different pulmonary aspiration models in male Wistar rats. The data indicated a significant reduction in the activity of inducible nitric oxide synthase (iNOS) and a rise in surfactant protein D in lung tissue of different pulmonary aspiration models after Nigella therapy suggesting that Nigella treatment might be beneficial in lung injury and may have potential clinical use.

Antiinflammatory screening revealed that *N. sativa, N. orientalis, N. hispanica, N. arvensis* n-hexane, and *N. hispanica* chloroform extracts had strong inhibitory activity (more than 80%) on COX-1 and *N. orientalis, N. arvensis*, and *N. hispanica* n-hexane extracts were most effective against COX-2 (Landa et al. 2009). *Nigella sativa* was reported to have antiinflammatory effect. Majdalawieh et al. (2010) found that the secretion of IL-6, TNFalpha, and NO, key pro-inflammatory mediators, by primary macrophages was significantly suppressed by the aqueous extract of *N. sativa*.

Dithymoquinone, thymohydroquinone, thymol and thymoquinone, compounds derived from *N. sativa seeds*, were found to possess significant inhibitory activity against at least one cyclooxygenase form at concentrations comparable to the active one of indomethacin (Marsik et al. 2005). Thymol was the most active against COX-1 with an IC_{50} value of 0.2 μM while thymohydroquinone and thymoquinone exhibited the strongest inhibitory effect on COX-2 with IC_{50}values of 0.1 and 0.3 μM, respectively. The authors concluded that dithymoquinone, thymohydroquinone, thymol and thymoquinone could participate in the general antiinflammatory activity of *N. sativa* and may have potential use as non-steroidal antiinflammatory drugs. Thymoquinone induced a significant concentration-dependent inhibition of both leukotrienes LTC4 and LTB4 formation from endogenous substrate in human granulocyte suspensions with IC_{50} values of 1.8 and 2.3 μM, respectively, at 15 min (Mansour and Tornhamre 2004). Major inhibitory effect was on the 5-lipoxygenase activity (IC_{50} 3 μM). Further, thymoquinone induced a significant inhibition of LTC4 synthase activity, with an IC_{50} of 10 μM. The findings demonstrate that thymoquinone potently inhibited the formation of leukotrienes in human blood cells in a dose- and time-dependent and its inhibitory effect was exerted on both 5-lipoxygenase and LTC4 synthase activity.

N. sativa seed oil and it constituent, *p*-cymene completely suppressed lipopolysaccharide (LPS) induced sialidase activity in live BMC-2 macrophage cells, but its main constituent, thymoquinone, exhibited no inhibitory effect (Finlay et al. 2010). Contrariwise, thymoquinone induced a vigorous Neu4 sialidase activity in live BMC-2 macrophage cells in a dose dependent manner as well in live DC-2.4 dendritic cells, HEK-TLR4/MD2, HEK293, SP1 mammary adenocarcinoma cells, human WT and 1,140 F01 and WG0544 type I sialidosis fibroblast cells. This stimulatory effect on Neu4 sialidase activity was mediated via potentiation of G-protein coupled receptor (GPCR)-signaling by thymoquinone via membrane targeting of Galphai subunit proteins and matrix metalloproteinase-9 activation.

Antiasthmatic Activity

N. sativa treatment of mice sensitized and challenged with conalbumin significantly reduced peripheral blood eosinophil count, IgG1 and IgG2a levels, cytokine profiles and inflammatory cells in lung tissue (Abbas et al. 2005). These effects were equivalent to the effects of Dexamethasone except for unchanged interferon IFN-y level. The anti-airway inflammation and immunoregulatory effect exhibited by *N. sativa* may be useful for treatment of allergic asthma. Another study demonstrated that thymoquinone exerted antiinflammatory effect in a mouse model of allergic asthma (El Gazzar et al. 2006). Mice sensitized and challenged with ovalbumin (OVA) antigen had an increased amounts of leukotriene B4 and C4, Th2 cytokines, and

eosinophils in bronchoalveolar lavage (BAL) fluid and a marked increase in lung tissue eosinophilia and goblet cell numbers. Administration of thymoquionone before OVA challenge inhibited 5-lipoxygenase, the main enzyme in leukotriene biosynthesis, expression by lung cells and significantly reduced the levels of LTB4 and LTC4. This was accompanied by a notable decrease in Th2 cytokines and BAL fluid and lung tissue eosinophilia, all of which are characteristics of airway inflammation.

In a randomised placebo-controlled study involving 29 asthmatic patients, boiled aqueous extract of nigella seed significantly improved respiratory symptoms, chest wheezing, and pulmonary function test values (Boskabady et al. 2007). The usage of inhaler and oral beta-agonists, oral corticosteroid, oral theophylline and even inhaler corticosteroid in the nigella treated group decreased at the end of the study while there were no obvious changes in usage of the drugs in control subjects. The results suggested a prophylactic effect of *N. sativa* on asthma disease. Similar results were reported in a 2-month randomized, double-blind, placebo-controlled trial involving 40 chemical war victims, boiled aqueous extract of nigella seed significantly improved respiratory symptoms, chest wheezing, and pulmonary function test values (Boskabady and Farhadi 2008). Boiled extract of *Nigella sativa*, 50 and 100 mg/kg, caused significant increases in all measured pulmonary function tests in asthmatic patients (Boskabady et al. 2010). However, forced expiratory volume in one second, maximal mid expiratory flow and maximal expiratory flow at 50% due to both doses of boiled extract and increase in MEF(75) and MEF(25) due to its lower doses were significantly lower than those of theophylline. The results showed that *Nigella sativa* had a relatively potent antiasthmatic effect on asthmatic airways but its effect was less than those of theophylline. Treatment of the ovalbumin-sensitized guinea pigs with thymoquinone, a constituent of *N. sativa*, significantly improved their pathological changes to the lung and decreased their interleukin IL-4 levels but increased their interferon IFN-γ levels (Keyhanmanesh et al. 2010b). The results showed a preventive effect of thymoquinone on lung inflammation in sensitized guinea pigs. They also reported improvement in tracheal responsiveness, total WBC, eosinophils and lymphocytes changes in the sensitized guinea pigs treated with thymoquinone were significantly greater those of than those of fluticasone propionate (Keyhanmanesh et al. 2010a). The results showed thymoquinone had a preventive effect on tracheal responsiveness and inflammatory cells of lung lavage of sensitized guinea pigs which was comparable or even greater than that of the inhaled steroid, fluticasone propionate. Shafei et al. (2005) reported the potent inhibitory effect of aqueous extract from *N. sativa* on calcium channel of guinea pig heart was found comparable and even greater than that of diltazem. The results may also indicate an opening effect for Nigella on potassium channel of isolated heart. *N. sativa* seed essential oil dose-dependently inhibited human neutrophil elastase (HNE) activity (Kacem and Meraihi 2006). One of its constituent, carvacrol (5-isopropyl-2-methylphenol) also exhibited marked HNE inhibitory activity with a very low IC_{50} value (12 μM). The antielastase property of carvacrol suggested it to have potential as a phytotherapeutic candidate in the treatment of injuries that appear in some pathologic cases such as chronic obstructive pulmonary disease and emphysema.

Boskabady et al. (2011a) demonstrated the preventive effect of a hydro-ethanolic extract of *Nigella sativa* against methacholine and ovalbumin on the tracheal responsiveness and lung inflammation in sensitized guinea pigs. The white blood cell counts in both high and low concentration *N. sativa* treated groups showed significant improvements. They also demonstrated that *N. sativa* oil alone and in combination with dexamethasone, decreased tracheal muscle responsiveness and lung inflammation in sulfur mustard exposed guinea pigs (Boskabady et al. 2011c). Treatment of ovalbumin sensitized guinea pigs with *N. sativa* extract led to a significant decrease in pathological changes of the lung, except for the oedema in the sensitized group treated with low concentration of the extract, but an increased interferon-γ (Boskabady

et al. 2011b). The results confirmed the preventive effect of *N. sativa* extract on lung inflammation of sensitized guinea pigs.

Anti - encephalomyelitis Activity

Studies showed that administration (injection) of thymoquinone, active constituent of *N. sativa* seed, to female Lewis rats induced with experimental allergic encephalomyelitis (EAE), inhibited oxidative stress and led to improvement in EAE (Mahmood et al. 2003). Thymoquinone injection at days 1–5 resulted in 75% EAE animals with no symptoms, no perivascular inflammation and high spinal cord glutathione (GSH) level and 25% exhibited mild tail and hind limb weakness. Thymoquinone injection at days 12–17 resulted in 63% EAE animals showing improved symptoms, no perivascular inflammation and higher GSH level while 37% of animals showed no symptoms prior and post thymoquinone injections. In contrast, in thymoquinone-untreated EAE animals, 63% developed hind limb weakness and/or paralysis while 37% developed mild tail weakness, perivascular inflammation and low spinal cord GSH level. The results indicated that thymoquinone may have a role in the treatment of human multiple sclerosis as EAE, an autoimmune demyelinating disease of the central nervous system, is widely accepted as an animal model for human multiple sclerosis.

Studies showed that *N. sativa* protected brain and medulla spinalis tissues against oxidative stress induced by experimental autoimmune encephalomyelitis (EAE) in rats (Ozugurlu et al. 2005). *N. sativa* inhibited ROS production and regulated NO levels to some extent. *N. sativa* displayed its antioxidant and regulatory effects via inflammatory cells rather than the host tissue (brain and medulla spinalis) for EAE in rats.

Mohamed et al. (2005a) also showed that in EAE rats thymoquinone was able to counter perivascular cuffing and infiltration of mononuclear cells in the brain and spinal cord, increase the red blood cell glutathione, and inhibit the activation of NF-kappaB in the brain and spinal cord. The results were consistent with the clinical signs and suggested a beneficial effect of thymoquinone against experimental autoimmune encephalomyelitis in the rat model of multiple sclerosis. They also compared phase II enzymes inducers, namely the butylhydroxyanisole (BHA) and thymoquinone (glutathione inducer) (El-Gouhary et al. 2005). They found that EAE animals with BHA in their diets had higher red cell GSH indicating induction of phase II enzymes and asserted that BHA may also have ability to ameliorate multiple sclerosis. In subsequent study, Mohammad et al. (2009) found thymoquinone due to its potent antioxidant effect, was almost 90% preventive and 50% curative in chronic relapsing EAE. They advocated that the possibility of thymoquinone to treat human chronic relapsing multiple sclerosis phase should be investigated.

Antiarthritic Activity

Thymoquinone was reported to suppress Freund's incomplete adjuvant-induced arthritis in rats (Tekeoglu et al. 2007). This was confirmed by reduced inflammation on the claw, reduced levels of TNF-alpha and IL-1beta and radiologically. Thymoquinone inhibited matrix metalloproteinase MMP-1, MMP-3 and MMP-13 expression in rabbit chondrocytes and cartilage in animal osteoarthritis induced by anterior cruciate ligament transaction (Chen et al. 2010). In addition, nuclear factor NF-κB p65 protein level as well as its translocation induced by interleukin-1β were inhibited by thymoquinone. The results suggest the potential of thymoquinone in the treatment of osteoarthritis.

In isolated human rheumatoid arthritis fibroblast-like synoviocytes (FLS), thymoquinone was not cytotoxic and inhibited slightly lipopolysaccharide (LPS)-induced FLS proliferation and strongly H_2O_2-induced 4-hydroxynonenal (HNE) generation (Vaillancourt et al. 2011). Thymoquinone significantly abrogated LPS-induced interleukin-1beta (IL-1β), tumour necrosis factor-alpha (TNFα), metalloproteinase-13, cyclooxygenase-2, and prostaglandin E(2). Thymoquinone also suppressed LPS-induced the phosphorylation of p38

mitogen-activated protein kinase, extracellular-regulated kinases ½, and nuclear factor-kappaB-p65. In the experimental models of rheumatoid arthritis, oral administration of thymoquinone 5 mg/kg/day significantly reduced the serum levels of HNE, IL-1β and TNFα as well as bone turnover markers, such as alkaline phosphatase and tartrate-resistant acid phosphatase. The protective effects of thymoquinone against rheumatoid arthritis were also evident from the decrease in arthritis scoring and bone resorption.

In a placebo controlled study involving 40 female rheumatoid arthritis, the disease activity score (DAS-28) significantly decreased after receiving the *N. sativa* capsules (4.55) compared with before and after placebo (4.98 and 4.99, respectively) (Gheita and Kenawy 2012). Similarly, the number of swollen joints and the duration of morning stiffness improved. A marked improvement in the disease activity was shown by both the American College of Rheumatology 20% (ACR20) and European League Against Rheumatism (EULAR) response criteria in 42.5 and 30% of the patients, respectively, after intake of Nigella.

Anti allergic Activity

Nigellone, the carbonyl polymer of thymoquinone, isolated from *N. sativa* seeds, in relatively low concentrations was very effective in inhibiting histamine release induced by the secretagogues: antigen in sensitized cells, compound 48/80, and the calcium ionophore A23187 in rat peritoneal mast cells (Chakravarty 1993). The mechanism of action appeared to be through decreasing intracellular calcium by inhibiting its uptake and stimulating the efflux, and by an inhibition on protein kinase C. There was also indication for a mild inhibition of oxidative energy metabolism contributing to some inhibition of the release.

In a mouse model of allergic airway inflammation, intraperitoneal injection of thymoquinone for 5 days before ovalbumin challenge attenuated airway inflammation as indicated by the significant decrease in Th2 cytokines, lung eosinophilia, and goblet cell hyperplasia (El Mezayen et al. 2006). This attenuation of airway inflammation was concomitant to the inhibition of COX-2 protein expression and pProstaglandinPGD2 production. The findings suggested thymoquinone exerted an anti inflammatory effect during the allergic response in the lung through the inhibition of PGD2 synthesis and Th2-driven immune response.

Administration of thymoquinone significantly suppressed the ocular symptoms in allergic conjunctive, inflammatory cell infiltration in conjunctiva, blood and ophthalmic lavage fluid (OLF), increased level of serum IgE and ovalabuminum (OVA)-specific IgE, and OLF histamine level in OVA-exposed mice (Hayat et al. 2011). In addition, thymoquinone abrogated the mRNA expression and serum level of interleukin including 1L-4, IL-5, IL-13 and transforming growth factor beta (TGF-β) in mice immunized and exposed to OVA.

In a study of 152 patients with allergic diseases (allergic rhinitis, bronchial asthma, atopic eczema), administration of *Nigella sativa* oil, given in capsules at a dose of 40–80 mg/kg/day decreased the score of subjective feeling (Kalus et al. 2003). A slight decrease in plasma triglycerides and a discrete increase in HDL cholesterol occurred while the lymphocyte subpopulations, endogenous cortisol levels and ACTH release remained unchanged. The study suggested *N. sativa* oil to be an effective adjuvant for the treatment of allergic diseases. In another study of patients (mean age 34 years) sensitive to house dust mites with allergic rhinitis, there was a statistically significant increase in the phagocytic and intracellular killing activities of polymorphonuclear leukocyte of patients receiving specific immunotherapy, especially after the supplementation of *N. sativa* seed (Işik et al. 2010). The CD8 counts of patients receiving specific immunotherapy plus *N. sativa* seed supplementation significantly increased compared to patients receiving only specific immunotherapy. Polymorphonuclear leukocyte functions of healthy volunteers significantly increased after *N. sativa* seed supplementation compared to baseline. The results showed that *N. sativa* seed supplementation during specific immunotherapy of allergic rhinitis may be considered a potential adjuvant therapy.

In a clinical trial conducted as prospective and double blind with descriptive analytic involving 66 patients (case and placebo) with allergic rhinitis, exposure to *N. sativa* oil reduced the presence of the nasal mucosal congestion, nasal itching, runny nose, sneezing attacks, turbinate hypertrophy, and mucosal pallor during the first 2 weeks (day 15) (Nikakhlagh et al. 2011). The findings were consistent with evidence that the antiallergic effects of *N. sativa* components could be attributed to allergic rhinitis. Moreover, the authors advocated that *N. sativa* should be considered for treating allergic rhinitis when the effects of other antiallergic drugs need to be avoided.

Respiratory Stimulant Activity

Intravenous administration of *N. sativa* volatile oil in the dose range (4–32 μl/kg) induced dose-dependent increases in the respiratory rate and the intratracheal pressure in guinea pigs (El Tahir et al. 1993). The effects of the oil were significantly antagonized by treatment of the animals with mepyramine, atropine and reserpine but not with indomethacin, diethyl carbamazine or hydrocortisone. Intravenous administration of its constituent thymoquinone in the dose range (1.6–6.4 mg/kg) induced significant increases in the intratracheal pressure without any effect in the respiratory rate. The results suggested that *N. sativa* oil-induced respiratory effects were mediated via release of histamine with direct involvement of histaminergic mechanisms and indirect activation of muscarinic cholinergic mechanisms.

Relaxant/Spasmolytic Activity

The ethanol extract and volatile oil of *N. sativa* seeds inhibited spontaneous movements of the rabbit jejunum (Aqel 1993). Further, the volatile oil inhibited contractions of the rabbit jejunum which were induced by high potassium (K^+) solution or acetylcholine. This inhibition was dose-dependent, reversible and not affected by the addition of calcium to the organ bath. The data suggested that *N. sativa* seed had an antispasmodic effect, possibly due to a calcium antagonistic activity. Aqel (1995) also reported that *N. sativa* volatile seed oil inhibited contractions of rabbit aortic rings induced by norepinephrine stimulation in Ca^{2+}-containing solution. This inhibition was dose- dependent and reversible. The data suggested that the volatile oil of *N. sativa* seeds possessed a direct vascular smooth muscle relaxant effect, possibly by interfering with the influx of extra cellular Ca^{2+}. The crude extract of *Nigella sativa* seeds exhibited spasmolytic and bronchodilator activities in isolated rabbit jejunum and guinea-pig tracheal preparations mediated possibly through calcium channel blockade (Gilani et al. 2001). This activity was concentrated in the organic petroleum ether fraction, which was found to be approximately 10 times more potent than the crude extract.

Thymoquinone, the main constituent of the *N. sativa* volatile oil caused a concentration-dependent decrease in the tension of guinea-pig isolated tracheal smooth muscle precontracted by carbachol (Al-Majed et al. 2001). The effects of thymoquinone were significantly potentiated by pretreatment of the tracheal preparations with quinacrine, a phospholipase A2 inhibitor, nordihydroguaiaretic acid, a lipoxygenase inhibitor and by pretreatment with methylene blue, an inhibitor of soluble guanylyl cyclase. Thymoquinone totally abolished the pressor effects of histamine and serotonin on the guinea-pig isolated tracheal and ileum smooth muscles. The results suggested that thymoquinone induced relaxation of precontracted tracheal preparation was probably mediated, at least in part, by inhibition of lipoxygenase products of arachidonic acid metabolism and possibly by non-selective blocking of the histamine and serotonin receptors. This relaxant effect of thymoquinone, further supported the traditional use of black seeds either alone or in combination with honey to treat bronchial asthma. Two active constituents of *N. sativa*, nigellone and thymoquinone, were found to inhibit Ba^{2+}-induced and leukotriene-induced trachea contractions (Wienkötter et al. 2008). The cholinergic system (stimulation by carbachol) was hardly involved. The rate of ciliary clearance (mucociliary transport) was slightly modified by a high thymoquinone

concentration but was highly increased by nigellone. The study provided evidence for an antispasmodic effect and an increase in mucociliary clearance for nigellone but not for thymoquinone and that the former may be useful in treatment of different respiratory diseases.

Boskabady et al. (2005) showed that aqueous and macerated extracts from *N. sativa* potently reduced heart rate and inhibited contractility of isolated guinea pig heart that was comparable and even higher than that of diltazem. The inhibitory effect was suggested to be due to calcium channel inhibitory or an opening effect for Nigella on potassium channels of the isolated heart. The aqueous and macerated extracts from *Nigella sativa* showed inhibitory effects on pre-contracted tracheal chains in the presence of both ordinary and calcium free Krebs solution, the absence of inhibitory effects of the extracts on KCl induced contraction of tracheal chains suggested that the calcium channel blocking effect of this plant did not contribute to the relaxant effect of nigella on the tracheal chains of guinea pigs (Boskabady et al. 2004). The n-hexane, dichloromethane, methanol and aqueous fractions of *N. sativa* was found to have relaxant effects on guinea pig tracheal chains, with greater effect being elicited by the for methanol and dichloromethane fractions (Boskabady et al. 2008). Theophylline also showed significant relaxant effects.

Antineoplastic/Anticancer Activity

The anti-carcinogenic activities of *N. sativa* seed essential oil and purified components have been documented in innumerable in-vitro and in-vivo studies.

In-Vitro Studies

The ethyl acetate fraction of *Nigella sativa* ethanolic seed extract elicited cytotoxicity against different classes of cancer cell lines, P388, Molt4, Wehi 164, LL/2, Hep G2, SW620 and J82, as measured by 3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay (Swamy and Tan 2000). The ethyl-acetate column chromatographic fraction (CC-5) showed selectivity against Hep G2, Molt4, and LL/2. CC-5 was relatively non-toxic against human umbilical cord endothelial cells at 50 μg/mL. CC-5 had no stimulatory effect on mouse splenocytes as such. CC-5 and water fraction, however, enhanced the proliferative response in the presence of ConA (3 μg/mL). The data indicated that CC-5 possessed a potent cytotoxic effect as well as a potentiating effect on the cellular immune response. *N. sativa* seed extracts and pure thymoquinone showed markedly reduced levels of MDA in A549 (adenocarcinomic human alveolar basal epithelial) cells for the duration (72 h) of the study (Farah et al. 2005). Cell number was decreased after 24 h in thymoquinone treated cells, and remained reduced for the duration of the study. The aqueous seed fraction showed a similar trend to thymoquinone, where as the ethanol seed fraction showed a negative shift in cell number at 48 h when compared with the control. The aqueous fraction showed greater effect on cell viability and cellular metabolism than the ethanol fraction.

Methanolic, n-hexane and chloroform extracts of *Nigella sativa* seeds effectively extirpated HeLa cancer cells (Shafi et al. 2009) The IC_{50} values of methanolic, n-hexane, and chloroform extracts were 2.28 μg/mL, 2.20 μg/mL and 0.41 ng/mL, respectively. All three extracts induced apoptosis in HeLa cells. Apoptosis was confirmed by DNA fragmentation, western blot and terminal transferase-mediated dUTP-digoxigenin-end labeling (TUNEL) assay. The aqueous extract of *Nigella sativa* was found to significantly enhance NK (natural killer) cytotoxic activity against YAC-1 (T cell lymphoma) tumour cells, suggesting that the documented anti-tumour effects of *Nigella sativa* may be, at least in part, attributed to its ability to serve as a stimulant of NK antitumour activity (Majdalawieh et al. 2010). Salem et al. (2011) reported that addition of low concentrations of thymoquinone during antigen-specific CD85+ T-cell activation resulted in enhanced survival of the activated T cells and sustained expression of CD62L (Salem et al. 2011). These effects coincided with enhancement in the capability of CD8+ T cells to produce the effector cytokine interferon-gamma (IFNgamma). The results

suggest thymoquinone to have a beneficial effect in conditioning T cells in-vitro for adoptive T-cell therapy against cancer and infectious disease.

N. sativa ethanol extract alone or in combination with oxidative stress (hydrogen peroxide) were found to be effective in-vitro in inactivating MCF-7 breast cancer cells (Farah and begum 2003). In-vitro studies showed direct administration of epigallocatechin gallate (EGCG), alone or in combination with thymoquinone could limit PANC-1 (human pancreas carcinoma) cell line proliferation (Tan et al. 2006). Woo et al. (2011) showed that thymoquinone increased PPAR-γ activity and down-regulate the expression of the genes for Bcl-2, Bcl-xL and survivin in breast cancer cells. In addition, thymoquinone activated caspases 8, 9 and 7 in a dose-dependent manner. The results showed that thymoquinone may have potential implication in breast cancer prevention and treatment, and that the anti-tumour effect of thymoquinone may also be mediated through modulation of the PPAR-γ activation pathway.

Ait Mbarek et al. (2007) found the essential oil (IC_{50} = 0.6%, v/v) and ethyl acetate (IC_{50} = 0.75%) extracts of *N. sativa* seeds were more cytotoxic against the P815 (murine mastocytoma) cell line than the butanol extract (IC_{50} = 2%) Similar results were obtained with the Vero (monkey kidney carcinoma) cell line. Although all extracts had a comparable cytotoxic effect against the ICO1 (sheep heart carcinoma) cell line, with IC_{50} values ranging from 0.2 to 0.26% (v/v), tests on the BSR (hamster kidney carcinoma) cell line revealed a high cytotoxic effect of the ethyl acetate extract (IC_{50} = 0.2%) compared to the essential oil (IC_{50} = 1.2%). These data showed that the cytotoxicity of each extract depended on the tumour cell type. In-vivo, using the DBA2/P815 (H2d) mouse model, the results clearly showed that the injection of the essential oil into the tumour site significantly inhibited solid tumour development, the incidence of liver metastasis development and improved mouse survival. The essential oil contained the following major components (62.17% TQ, 16.84% carvacrol, 8.29% 2-methyl-5-prop-2-enyldihydroquinone, 6.99% dihydrothymoquinone, 2.07% terpini-4-en-1-ol, 3.11% monoterpenes). *Nigella sativa* oil produced a concentration-dependent inhibition of tissue-type plasminogen activator (t-PA), urokinase-type plasminogen activator (u-PA) and plasminogen activator inhibitor type 1 (PAI-1) in fibrosarcoma cell line (HT1080) (Awad 2005). When subconfluent HT1080 cells were conditioned with the oil, a concentration-dependent decrease in t-PA, u-PA and PAI-1 antigen was observed the results showed that black cumin oil decreased the fibrinolytic potential of the human fibrosarcoma cell line (HT1080) in-vitro, implying that inhibition of local tumour invasion and metastasis may be one such mechanism.

In a comparative study of chemotherapeutic agents, treatment with green tea rich in epigallocatechin-3-gallate (EGCG), and thymoquinone, bioactive ingredient from black cumin seeds, caused a significant decrease in SW-626 colon cancer cell numbers compared to 5-fluorouracil (Norwood et al. 2006). A sustained drug delivery of EGCG and thymoquinone demonstrated significant cellular destruction and interference of cellular metabolic functions of SW-626 human colon cancer cells, which was comparable to SW-626 cells exposed to sustained drug delivery of 5-FU. Reduced cell numbers in the treated groups suggested the possibility that epigallocatechin-3-gallate and thymoquinone may have similar chemotherapeutic effects on cancer cells as 5-fluorouracil, the chemotherapeutic drug. Recent studies showed that pretreatment with thymoquinone (TQ) significantly increased the apoptotic effects induced by 5-fluorouracil (5-FU) in gastric cancer cell lines in-vitro (Lei et al. 2012). TQ enhanced the 5-FU-induced killing of gastric cancer cells by mediating the downregulation of the anti-apoptotic protein bcl-2, the upregulation of the pro-apoptotic protein bax, and the activation of both caspase-3 and caspase-9. Moreover, the combined treatment of TQ with 5-FU provided a significantly more effective anti-tumour agent than either agent alone in a xenograft tumour mouse model. The data suggested that TQ inhibited growth and augmented 5-FU induced apoptosis by enhancing the activation of both caspase-3 and caspase-9 in gastric cancer cells.

N. sativa supplementation inhibited colon carcinogenesis induced by azoxymethane(AOM) in rats (Al-Johar et al. 2008). *N. sativa* exhibited inhibitory effects only on DNA damage (day 34) in the AOM-treated rat group. Its antioxidant constituents selenium, thymoquinone and vitamins decreased MDA (malondialedhye) content in the liver while its vitamin were effective in reducing colonic aberrant crypt foci.

The crude gum or oil of *N. sativa* was devoid of cytotoxicity, but both purified components of *N. sativa* seeds, thymoquinone (TQ) and dithymoquinone (DIM) were cytotoxic for all of the tested parental and multi-drug resistant (MDR) human tumour cell lines (IC_{50}′s 78 to 393 μM) (Worthen et al. 1998). Both the parental cell lines and their corresponding MDR variants, over ten fold more resistant to the standard antineoplastic agents doxorubicin (DOX) and etoposide (ETP), as compared to their respective parental controls, were equally sensitive to TQ and DIM. Further studies confirmed that TQ and DIM, which were cytotoxic for several types of human tumour cells, may not be MDR substrates, and that radical generation may not be critical to their cytotoxic activity. Shoieb et al. (2003) reported that thymoquinone demonstrated selective cytotoxicity *in vitro* for human and canine tumour cells tested (canine osteosarcoma (COS31), its cisplatin-resistant variant (COS31/rCDDP), human breast adenocarcinoma (MCF7), human ovarian adenocarcinoma (BG-1) and Madin-Darby canine (MDCK) cancer cell lines) when compared to normal kidney cells. They found that COS31/rCDDP (cisplatin-resistant variant of Cos 31) resistant cells were the most sensitive cell line to thymoquinone and Madin-Darby canine (MDCK) cells were the least sensitive. Thymoquinone (25 μM) induced apoptosis of canine osteosarcoma (COS31) cells 6 h after treatment and decreased the number of COS31 cells in S-phase and increased cells in G1-phase, indicating cell cycle arrest at G1. These results suggested that thymoquinone killed cancer cells by a process that involved apoptosis and cell cycle arrest. Non-cancerous cells were relatively resistant to thymoquinone. Thymoquinone treatment of mouse keratinocytes, papilloma cells reduced the proliferation of neoplastic keratinocytes by 50% by induction of G0/G1 cell-cycle arrest, concomitant with sharp increases in the expression of the cyclin-dependent kinase inhibitor p16 and a decrease in cyclin D1 protein expression (Gali-Muhtasib et al. 2004a). Thymoquinone also caused growth inhibition in spindle (I7) carcinoma cells by inducing G2/M cell-cycle arrest, which was associated with an increase in the expression of the tumour suppressor protein p53 and a decrease in cyclin B1 protein. The results supported a potential role for thymoquinone as a chemopreventive agent, particularly at the early stages of skin tumorigenesis. Nigella seed volatile oil exhibited cytoxicity against a panel of five human cancer cell lines and a fibroblast line with LC_{50} values of 155.02, 185.77, 120.40, 384.53 and 286.83 μg/mL respectively against the small cell lung SCL, SCL-6, SCL-37′6, NUGC-4 (gastric cancer) cancer lines and murine 3 T6 fibroblast line (Islam et al. 2004). T

Roepke et al. (2007) found that thymoquinone decreased cell survival dose-dependently and, more significantly, in p53-null MG63 (human osteosarcoma cells) (IC_{50} = 17 muM) than in p53-mutant MNNG/HOS cells (IC_{50} = 38 muM). Cell viability was reduced more selectively in MG63 tumour cells than in normal human osteoblasts. The findings showed that thymoquinone induced p53-independent apoptosis in human osteosarcoma cells and augmented capase activation in human osteosarcoma cells. As the loss of p53 function is frequently observed in osteosarcoma patients, their findings suggested the potential clinical usefulness of thymoquinone for the treatment of these malignancies. The combined dose of thymoquinone and selenium produced decreased osteoblasts cell (MG 63) counts, increased cellular damage, decreased alkaline phosphatase levels, and decreased glutathione levels as compared to control (Barron et al. 2008). The results suggest that the combined use of thymoquinone and selenium may be an effective treatment option against human osteosarcoma cells.

Sethi et al. (2008) found that thymoquinone suppressed tumour necrosis factor–induced NF-κB activation in a dose- and time-dependent

manner and inhibited nuclear factor (NF-κB) activation induced by various carcinogens and inflammatory stimuli. The suppression of NF-κB activation correlated with sequential inhibition of the activation of IκBα kinase, IκBα phosphorylation, IκBα degradation, p65 phosphorylation, p65 nuclear translocation, and the NF-κB–dependent reporter gene expression. thymoquinone specifically suppressed the direct binding of nuclear p65 and recombinant p65 to the DNA. Thymoquinone also down-regulated the expression of NF-κB–regulated antiapoptotic (IAP1, IAP2, XIAP Bcl-2, Bcl-xL, and survivin), proliferative (cyclin D1, cyclooxygenase-2, and c-Myc), and angiogenic (matrix metalloproteinase-9 and vascular endothelial growth factor) gene products. Overall, their results indicated that the anticancer and antiinflammatory activities previously assigned to thymoquinone may be mediated in part through the suppression of the NF-κB activation pathway, and thus may have potential in treatment of myeloid leukemia and other cancers

Results of in-vitro studies by El-Mahdy et al. (2005) indicated that thymoquinone-induced apoptosis in myeloblastic leukemia HL-60 cells was associated with the activation of caspases 8, 9 and 3, with caspase-8 acting as an upstream activator. Activated caspase-8 initiated the release of cytochrome c during thymoquinone -induced apoptosis. The results offered a potential mechanism for thymoquinone -induced apoptosis in p53-null HL-60 cancer cells. Studies by Abusnina et al.(2011) showed that thymoquinone repressed cyclic nucleotide phosphodiesterase PDE1A in lymphoblastic leukemia Jurkat cell line by sequential deregulation of the expression of the tumour suppressor protein p73 and the epigenetic integrator UHRF1 (Ubiquitin-like, PHD Ring Finger 1). The data suggested that a forced inhibition of PDE1A expression might be a new therapeutic strategy for the management of acute lymphoblastic leukemia.

Chehl et al. (2009) found that thymoquinone dose- and time-dependently significantly reduced pancreatic ductal adenocarcinoma cell synthesis of monocyte chemoattractant protein-1(MCP-1), tumour necrosis factor (TNF)-alpha, interleukin (IL)-1beta and Cox-2. Thymoquinone significantly and dose-dependently reduced the intrinsic activity of the MCP-1 promoter; inhibited the constitutive and TNF-alpha-mediated activation of NF-kappaB in pancreatic ductal adenocarcinoma cells and reduced the transport of NF-kappaB from the cytosol to the nucleus. The data demonstrated thymoquinone to be a novel inhibitor of proinflammatory pathways providing a promising strategy that combined antiinflammatory and proapoptotic modes of action. Recent studies demonstrated that thymoquinone exerted anti-metastatic activity on pancreatic cancer both in-vitro and in-vivo (Wu et al. 2011). Thymoquinone suppressed the migration and invasion of Panc-1 cells in a does-dependent manner. The antimetastatic activity may be related to down-regulation of NF-kappaB and its regulated molecules such as MMP-9 protein. The high molecular weight glycoprotein mucin 4 (MUC4) is aberrantly expressed in pancreatic cancer and contributes to the regulation of differentiation, proliferation, metastasis, and the chemoresistance of pancreatic cancer cells (Torres et al. 2011). They found that treatment of MUC4-expressing pancreatic cancer cells FG/COLO357 and CD18/HPAF with thymoquinone suppressed MUC4 expression through the proteasomal pathway and induced apoptosis in pancreatic cancer cells by the activation of c-Jun NH(2)-terminal kinase and p38 mitogen-activated protein kinase pathways. Their findings suggested thymoquinone to have potential for the development of novel therapies against pancreatic cancer. Among the synthesized analogs of thymoquinone, TQ-2 G, TQ-4A1 and TQ-5A1 (patent pending) were found to be more potent than thymoquinone in terms of inhibition of pancreatic cancer cell growth, induction of apoptosis and modulation of transcription factor-NF-kappaB (Banerjee et al. 2010). They found that their novel analogs were able to sensitize gemcitabine and oxaliplatin-induced apoptosis in MiaPaCa-2 (gemcitabine resistant) pancreatic cancer cells, which was associated with down-regulation of Bcl-2, Bcl-xL, survivin, XIAP, COX-2 and the associated prostaglandin E2.

Gali-Muhtasib et al. (2004b) reported that thymoquinone inhibited the growth of HCT-116 human colon cancer cells which was correlated with G1 phase arrest of the cell cycle. Thymoquinone triggered apoptosis in a dose- and time-dependent manner. The apoptotic effects of thymoquinone were found to be modulated by Bcl-2 protein and were linked to and dependent on p53. Thymoquinone was cytotoxic towards human cervical squamous carcinoma cells (SiHa) cells with IC_{50} values of 10.67 and 9.33 μg/mL (Ng et al. 2011). Thymoquinone was more cytotoxic than cisplatin but was less toxic towards the normal cells (3 T3-L1 and Vero). Thymoquinone was more potent than cisplatin in elimination of SiHa cells via apoptosis with down-regulation of Bcl-2 protein.

Thymoquinone inhibited proliferation, induced apoptosis and chemosensitized human multiple myeloma cells through suppression of both constitutive and IL-6-inducible STAT3 phosphorylation which correlated with the inhibition of c-Src and JAK2 activation (Li et al. 2010). Thymoquinone was found to have anti-myeloma activity (Badr et al. 2011a). It inhibited chemokine receptor CXCL12-induced chemotaxis of multiple myeloma cells and increased their susceptibility to Fas/CD95-mediated apoptosis. Additionally, it significantly down-regulated CXCR4 expression and CXCL12-mediated CXCR4/CD45 association in multiple myeloma cells. Thymoquinone also significantly potentiated the apoptotic effects of thalidomide and bortezomib in multiple myeloma cells. In another study, thymoquinone decreased F-actin polymerization and the proliferation of human multiple myeloma cells by suppressing STAT3 phosphorylation and Bcl2/Bcl-XL expression (Badr et al. 2011b). Thymoquinone induced growth arrest of MDN and XG2 multiple myeloma cells in a dose- and time-dependent manner and also inhibited CXC ligand-12 (CXCL-12)-mediated actin polymerization and cellular proliferation. The results suggest that thymoquinone would potentially be applied toward the treatment of multiple myeloma and other malignancies.

Gurung et al. (2010) demonstrated that thymoquinone induced DNA damage, cell cycle arrest and apoptosis in the human glioblastoma cells. Thymoquinone facilitated telomere attrition by inhibiting the activity of telomerase which was dependent on the status of DNA-PKcs. The data suggested that thymoquinone could be useful as a potential chemotherapeutic agent in the management for brain tumours. Kolli-Bouhafs et al. (2012) found that thymoquinone reduced migration and invasion of human glioblastoma cells (U-87 and CCF-STTG1) accompanied by a drastic down-regulation of FAK (focal adhesion kinase) protein and matrix metalloproteinases, MMP-2 and MMP-9.

Thymoquinone in combination with single dose of ionizing radiation (2.5 Gy) was found to exert supra-additive cytotoxic effects on both human breast carcinoma cells (MCF7 and T47D) as measured by cell proliferation and colony-formation assays (Velho-Pereira et al. 2011). Annexin V binding and Fluorescence activated cell scanning (FACS) revealed the role of enhanced apoptosis and cell cycle modulation in the mechanism of thymoquinone-mediated radiosensitization, thus supporting thymoquinone as an adjuvant for preclinical testing in cancer chemo-radiotherapy. Thymoquinone potently inhibited doxorubicin-resistant human breast cancer MCF-7/DOX cell proliferation by up-regulating expression of the key upstream signalling factor, PTEN (Arafa et al. 2011). Breyer et al. (2009) reported that the 6-hencosahexaenyl conjugate 3 e of thymoquinone to be most active in all resistant tumour cells, with IC_{50} (72 h) values as low as 30 nM in MCF-7/Topo breast carcinoma cells. The conjugates appeared likely to operate by mechanisms different from that of thymoquinone. For instance, 3 e induced distinct caspase-independent apoptosis in human HL-60 leukemia and 518A2 melanoma cells concomitant with a loss of mitochondrial membrane potential and a subsequent rise in the levels of reactive oxygen species. Thymoquinone was found to induce growth inhibition and apoptosis in several primary effusion lymphoma (PEL) cell lines (Hussain et al. 2011). Thymoquinone treatment resulted in down-regulation of constitutive activation of AKT via generation of reactive oxygen species (ROS) and it caused conformational changes in Bax protein, leading to

loss of mitochondrial membrane potential and release of cytochrome c to the cytosol. This also led to activation of caspase-9, caspase-3, and poly-adenosine 5′-diphosphate ribose polymerase cleavage, leading to caspase-dependent apoptosis.

Terpene conjugates of thymoquinone, constituent of *N. sativa* seed oil, were found to be more efficacious in treating cancer cells (Effenberger et al. 2010) Derivatives with a short four-atom spacer between quinone and cyclic monoterpene moieties were more antiproliferative than analogues with longer spacers. 6-(menthoxybutyryl) thymoquinone (3a) exhibited single-digit μmolar IC_{50} (72 h) values in all four cell lines. It was seven times more active than thymoquinone in 518A2 melanoma cells and four times in multi-drug-resistant KB-V1/Vbl cervix carcinoma cells, while only half as toxic in the non-malignant human foreskin fibroblasts. Compound 3a was also not a substrate for the P-gp and BCRP drug transporters of the resistant cancer cells. The caryophyllyl and germacryl conjugates 3e and 3f specifically inhibited the growth of the resistant MCF-7 breast carcinoma cells. Conjugation of thymoquinone with the triterpene betulinic acid via the OH group as in 3 g led to a loss in activity, while conjugation via the carboxylic acid afforded compound 4 with nanomolar IC_{50} (72 h) activity against human HL-60 leukemia cells. All anti-cancer-active derivatives of thymoquinone induced apoptosis associated with DNA laddering, a decrease in mitochondrial membrane potential and a slight increase in reactive oxygen species.

Ravindran et al. (2010) demonstrated that encapsulation of thymoquinone into nanoparticles enhanced its antiproliferative, antiinflammatory, and chemosensitizing effects. Thymoquinone nanoparticles were more active than thymoquinone in inhibiting NF-kappaB activation and in suppressing the expression of cyclin D1, matrix metalloproteinase (MMP)-9, vascular endothelial growth factor (VEGF), markers of cell proliferation, metastasis and angiogenesis, respectively. Thymoquinone nanoparticles were also more potent than thymoquinone in suppressing proliferation of colon cancer, breast cancer, prostate cancer, and multiple myeloma cells. Esterase staining for plasma membrane integrity revealed that thymoquinone nanoparticles were more potent than thymoquinone in sensitizing leukemic cells to TNF- and paclitaxel-induced apoptosis. Using in-vivo zebrafish angiogenesis model, thymoquinone was found to have anti-angiogenic activity (Paramasivam et al. 2012). Thymoquinone inhibited the growth of intersegmental vessel (ISV) of zebrafish embryos in a dose-dependent manner down-regulate the expression of VEGF-A mRNA. The study confirm its anti-angiogenic potential and revealed its role as a therapeutic agent against diseases like cancer.

In-vitro cytotoxic studies of *Nigella sativa* seeds containing antitumour principles showed 50% cytotoxicity to Ehrlich ascites carcinoma, Dalton's lymphoma ascites and Sarcoma-180 cells at a concentration of 1.5, 3 and 1.5 μg respectively with little activity against lymphocytes (Salomi et al. 1992). The cell growth of KB (human nasopharynx carcinoma) cells in culture was inhibited by the active principle while K-562 (erythroleukemia) cells resumed near control values on day 2 and day 3. Tritiated thymidine incorporation studies indicated the possible action of an active principle at DNA level. In-vivo Ehrlich ascites carcinoma tumour development was completely inhibited by the active principles at the dose of 2 mg/mouse per day for 10 days.

Alpha-hederin and thymoquinone, the two principal bioactive constituents of *Nigella sativa* separately induced a dose- and time-dependent effect on four human cancer cell lines [A549 (lung carcinoma), HEp-2 (larynx epidermoid carcinoma), HT-29 (colon adenocarcinoma) and MIA PaCa-2 (pancreas carcinoma)] (Rooney and Ryan 2005a). HEp-2 cells were the most sensitive, exhibiting apoptosis with a higher incidence following thymoquinone treatment. Pre-treatment of cells with α-hederin, followed by thymoquinone or cisplatin, did not enhance the cytotoxicity or apoptosis induced by either drug. Further studies on Hep-2 human laryngeal carcinoma cells showed that buthionine sulfoximine (BSO), a selective inhibitor of glutathione (GSH) significantly enhanced α-hederin- and cisplatin-mediated toxicity, without changes in apoptosis or necrosis levels (Rooney and Ryan 2005b).

Thymoquinone and cisplatin significantly decreased GSH levels in a dose-dependent manner, with BSO pre-treatment synergistically depleting GSH levels in only thymoquinone-treated cells. As the caspase 3 inhibitor, Z-DEVD-fmk significantly decreased thymoquinone- and cisplatin-induced apoptosis indicating that GSH depletion and caspase 3-activation mediated thymoquinone-induced apoptosis, in this cell line.

Thymoquinone inhibited DNA synthesis, proliferation, and viability of cancerous (LNCaP, C4-B, DU145, and PC-3) but not noncancerous (BPH-1) prostate epithelial cells by suppressing androgen receptor and E2F-1 (Kaseb et al. 2007). Thymoquinone blunted progression of synchronized LNCaP cells from G1 to S phase. In a xenograft prostate tumour model, thymoquinone inhibited growth of C4-2B-derived tumours in nude mice. This in vivo suppression of tumour growth, as with C4-2B cell growth in culture, was associated with a dramatic decrease in AR, E2F-1, and cyclin A. The findings showed that thymoquinone suppressed the expression of androgen receptor and E2F-1 necessary for proliferation and viability of androgen-sensitive as well as androgen-independent prostate cancer cells both in-vitro and in-vivo and, moreover, produced no noticeable side effects in mice. The authors concluded that thymoquinone, a naturally occurring herbal product, may prove to be effective in treating hormone-sensitive as well as hormone-refractory prostate cancer and because of its selective effect on cancer cells, thymoquinone could also be used safely to help prevent the development of prostate cancer. Koka et al. (2010) showed that 24–48 h exposure to thymoquinone inhibited the growth of both androgen receptor (AR)-independent (C4-2B) and AR naïve (PC-3) prostate cancer cells with IC_{50} values of approximately 50 and 80 μmol/L, respectively. Within 1 h, TQ increased reactive oxygen species (ROS) levels (3-fold) and decreased glutathione (GSH) levels (60%) in both cell types. Pretreatment with N-acetylcysteine (NAC) inhibited both thymoquinone-induced ROS generation and growth inhibition. Thymoquinone significantly promoted the expressions of growth arrest and DNA damage inducible gene (GADD45alpha) and apoptosis-inducing factor-1 and suppressed the expressions of several Bc12-related proteins. Thymoquinone dose dependently inhibited both total and nuclear AR levels (4–5 fold) and AR-directed transcriptional activity (10–12-fold). This suppressive effect on AR was not prevented by NAC, which clearly suggested that thymoquinone -induced cytotoxicity was not due to changes in AR regulation. These data suggested thymoquinone-induced cell death to be primarily due to increased ROS generation and decreased GSH levels, and was independent of AR activity.

Treatment of HepG2 cells with bee honey and *N. sativa* alcohol extract elicited a significant decrease in both the number of viable HepG2 cells by apoptosis and the levels of nitric oxide and improved total antioxidant status and caspase-3 activity (Hassan et al. 2010).

In-Vivo Studies

Topical application of *Nigella sativa* extract inhibited two-stage initiation/promotion [dimethylbenz[a]anthracene (DMBA)/croton oil] skin carcinogenesis in mice (Salomi et al. 1991). A dose of 100 mg/kg body wt of the extract delayed the onset of papilloma formation and reduced the mean number of papillomas per mouse. Intraperitoneal administration of *Nigella sativa* (100 mg/kg body wt) 30 days after subcutaneous administration of 20-methylcholanthrene (MCA)-(745 nmol×2 days) restricted tumour incidence to 33.3% compared with 100% in MCA-treated controls. Administration of 0.01% of thymoquinone in benzo(a)pyrene -treated tumour-bearing mice inhibited both benzo(a) pyrene-induced forestomach tumour incidence and multiplicity by 70 and 67%, respectively (Badary et al. 1999). thymoquinone alone showed a significant induction in the enzyme activities of hepatic glutathione-S-transferase and DT diaphorase. Mice treated with thymoquinone along with benzo(a)pyrene showed almost normal hepatic lipid peroxides and glutathione levels, and normal enzyme activities compared to the control group. The data suggest the potential of thymoquinone, the main constituent of the volatile oil of *Nigella sativa* seed, as a powerful chemopreventive agent against benzo(a)pyrene -induced

forestomach tumours in mice. In another study, administration of thymoquinone, (0.01% in drinking water), 1 week before and after 20-methylcholanthrene (MC) treatment significantly inhibited fibrosarcoma incidence and tumour burden by 43 and 34%, respectively, compared with the results in the mice receiving MC alone (Badary and Gamal El-Din 2001). Further, thymoquinone delayed the onset of MC-induced fibrosarcoma tumours that appeared at 12 weeks and produced less MC-induced mortality. Thymoquinone alone showed a significant induction in the enzyme activities of hepatic glutathione S-transferase and quinone reductase. Mice treated with thymoquinone along with MC showed reduction in hepatic lipid peroxides and increased glutathione content and increased enzyme activities of glutathione S-transferase and quinone reductase as compared to results of the control group. The in-vitro studies showed that thymoquinone inhibited the survival of fibrosarcoma cells with IC_{50} of 15 μM. The data indicate the potential of thymoquinone as a powerful chemopreventive agent against MC-induced fibrosarcoma tumours. Studies showed that daily intake of thymoquinone, the main constituent of the volatile *N. sativa* seed oil, by mice after and before or during exposure to benzo(a)pyrene [B(a)P] significantly reduced the frequencies of chromosomal aberrations and damaged cells compared to the highly clastogenic activity of B(a)P alone (Badary et al. 2007). The results suggest the chemopreventive activity of thymoquinone against B(a)P-induced forestomach carcinogenesis.

Yi et al. (2008) showed that thymoquinone suppressed angiogenesis in-vitro and in-vivo, prevented tumour angiogenesis in a xenograft human prostate cancer (PC3) model in mouse, and inhibited human prostate tumour growth at low dosage with almost no chemotoxic side effects. They found that endothelial cells were more sensitive to thymoquinone-induced cell apoptosis, cell proliferation, and migration inhibition compared with PC3 cancer cells. Thymoquinone inhibited vascular endothelial growth factor-induced extracellular signal-regulated kinase activation but showed no inhibitory effects on vascular endothelial growth factor receptor 2 activation. Their results indicated that thymoquinone inhibited tumour angiogenesis and tumour growth and could be used as a potential drug candidate for cancer therapy. Administration of thymoquinone, active ingredient from *N. sativa* seed, produced significant increase in the activities of quinone reductase and glutathione transferase in mice liver suggesting thymoquinone to be a promising prophylactic agent against chemical carcinogenesis and toxicity (Nagi and Almakki 2009).

A cytotoxic fraction of an ethanolic extract of *Nigella sativa* seeds exerted significant tumour inhibition rate against intraperitoneally implanted murine P388 leukemia and (subcutaneously implanted LL/2 (Lewis lung carcinoma) cells in BDF1 mice (Kumara and Huat 2001). alpha-hederin isolated from the cytotoxic fraction also produced significant dose-dependent tumour inhibition rate. Studies by Khan et al. (2003b) suggested *Nigella sativa* to be a potent chemopreventive agent and may suppress potassium bromate -mediated renal oxidative stress, toxicity and tumour promotion response in rats. Prophylaxis of rats orally with *Nigella sativa* extract resulted in a significant decrease in renal microsomal lipid peroxidation, gamma-glutamyl transpeptidase, H2O2 and xanthine oxidase. There was significant recovery of renal glutathione content and antioxidant enzymes. There was also reversal in the enhancement of blood urea nitrogen, serum creatinine, renal ODC activity and DNA synthesis). In another study, Khan and Sultana (2004) found *Nigella sativa* to be a potent chemopreventive agent in suppressing ferric nitrilotriacetate-induced oxidative stress, hyperproliferative response and renal carcinogenesis in Wistar rats. Treatment of rats orally with *Nigella sativa* (50 and 100 mg/kg body weight) resulted in significant decrease in γ-glutamyl transpeptidase, lipid peroxidation, xanthine oxidase, H2O2 generation, blood urea nitrogen, serum creatinine, renal ODC activity, DNA synthesis and incidence of tumours. Renal glutathione content, glutathione-metabolizing enzymes and antioxidant enzymes were also recovered to significant levels.

Salim and Fukushima (2003) demonstrated that the volatile oil of *N. sativa* seeds had the ability to inhibit colon carcinogenesis of rats in the postinitiation stage, with no evident adverse side effects, and that the inhibition may be associated, in part, with suppression of cell proliferation in the colonic mucosa. Studies showed that supplementation of diet with honey and *Nigella sativa* had a protective effect against methylnitrosourea -induced oxidative stress, inflammatory response and carcinogenesis in Sprague Dawely rats (Mabrouk et al. 2002). *Nigella sativa* seeds administered orally protected against methylnitrosourea-induced oxidative stress and carcinogenesis by 80% and combated this effect by lowering malondialdehyde and nitric oxide. Whereas honey and *Nigella sativa* together protected 100% against methylnitrosourea-induced oxidative stress, carcinogenesis and abolished the nitric oxide and malondialdehyde elevations shown in sera of untreated animals. Alenzi et al. (2010) found that administration of *N. sativa* oil or its active ingredient, thymoquinone to albino rats could lower cyclophosphamide -induced toxicity characterised by a decrease in haemoglobin concentration and increases in blood sugar levels, activities of liver enzymes, bilirubin, urea, creatinine, lipids (triglyceride, cholesterol and low-density lipoprotein (LDL)-cholesterol) and lipid peroxidation in the liver. The antitoxic effects of *N. sativa* oil and thymoquinone were associated with induction of antioxidant mechanisms, indicating a potential clinical application for these agents to minimise the toxic effects of treatment with anticancer drugs. Results of studies by el-Aziz et al. (2005) showed that the administration of melatonin, retinoic acid and *Nigella sativa* reduced the carcinogenic effects of methylbenz(a) anthracene mammary carcinoma in rats, suggesting a protective role.

A decoction of *Nigella sativa* seeds, *Hemidesmus indicus* root and *Smilax glabra* rhizome, commonly used by traditional medical practitioners in Sri Lanka to treat cancer was shown to prevent chemically induced carcinogenesis in rats (Thabrew et al. 2005). The decoction exerted a strong dose-dependent cytotoxic activity in human hepatoma HepG2 cell line. The greatest inhibitory effects were observed on DNA synthesis with both the decoction (91% inhibition) and *N. sativa* plant extract (88%) even at low concentrations (5 mg/mL). The three individual plant extracts were cytotoxic in the order of potency *N. sativa* > *H. indicus* > *S. glabra*. Flow cytometric analysis using Annexin V and propidium iodide staining showed that after 24 h exposure to the decoction, cells were in the late stage of apoptosis and/or necrosis. Studies demonstrated that protection against diethylnitrosamine-mediated carcinogenic changes in rat liver can be achieved by long term treatment (16 months) with a decoction comprising *N. sativa* seeds, *Smilax glabra* rhizome and *Hemidesmus indicus* root bark (Iddamaldeniya et al. 2006). No overt tumours or histopathological changes leading to tumour development and GST-P (glutathione S-transferase placental) positive foci were detected in any of the decoction treated groups.

Radioprotective Activity

Studies by Cemek et al. (2006) showed that *Nigella sativa* (NS) and reduced glutathione (GSH) treatment significantly antagonize the effects of radiation may have beneficial radioprotective effect against ionizing radiation-related tissue injury. The blood oxidative stress marker levels in irradiated rats that were pretreated with NS and GSH were significantly decreased. Also NS and GSH administration prior to irradiation prevent the number of α-naphthyl acetate esterase peripheral blood T lymphocytes from declining. Ethanolic extract of *Nigella sativa* displayed significant free radical scavenging and protection against DNA damage in cell free systems (Rastogi et al. 2010). Pre-treatment of mouse splenic lymphocytes with the extract prior irradiation showed significant prevention of the formation of lipid-peroxides and intracellular reactive oxygen species (ROS), associated with radiation-induced apoptosis and prevented radiation-induced DNA damage. Oral feeding of extract to Swiss albinmo mice prior to whole body irradiation significantly

protected against oxidative injury to spleen and liver as measured by lipid peroxidation and the activity of antioxidant enzymes and increased survival in mice exposed to irradiation. Oral administration of *Nigella sativa* oil to rats before irradiation considerably normalized all the adverse effect of irradiation and produced significant regeneration in spleen and thymus lymphoid follicles (Assayed 2010). Irradiation adverse effects in rats included a significant reduction in hemolysin antibodies titers and delayed type hypersensitivity reaction, significant decrease in plasma total protein and globulin concentrations and depletion of lymphoid follicles of spleen and thymus gland, significant leukopenia and a significant increase in malondialdehyde concentration with a significant decrease in plasma glutathione peroxidase, catalase and erythrocyte superoxide dismutase activities. The results strongly suggested *Nigella sativa* oil to be a promising natural radioprotective agent against immunosuppressive and oxidative effects of ionizing radiation.

Gastroprotective Activity

Pretreatment of rats with *N. sativa* oil before ethanol-induction of ulcers, produced a significant increase in glutathione level, mucin content and free acidity and a significant decrease in gastric mucosal histamine content with a protection ratio of 53.56% as compared to the ethanol group (El-Dakhakhny et al. 2000a). Ethanol administration produced a 100% ulcer induction and caused a significant reduction in free acidity and glutathione level while it produced a significant increase in mucosal histamine content. *Nigella sativa* oil and its main component, thymoquinone, were found to have gastroprotective effect against ischaemia/reperfusion (I/R) induced gastric lesion in mice which may be related to the conservation of the gastric mucosal redox state (El-Abhar et al. 2003). Both treatments normalised the elevated the levels of lipid peroxide and lactate dehydrogenase and the decreased reduced glutathione (GSH) and superoxide dismutase levels caused by ichaemia/reperfusion. Both treatments also reduced gastric lesions formation. Another animal study showed that aqueous suspension of black cumin seed had gastroprotective effect against necrotizing agents-induced gastric injury (Al Mofleh et al. 2008). The suspension significantly prevented gastric ulcer formation induced by necrotizing agents and significantly ameliorated the ulcer severity and basal gastric acid secretion in pylorus-ligated Shay rats. Further, the suspension significantly replenished the ethanol-induced depleted gastric wall mucus content levels and gastric mucosal non-protein sulfhydryl concentration.

Separate studies in surgically thyroidectomised rats showed that low thyroid hormone level increased stress gastritis as indicated by the increase in number of gastric ulcer and malonaldehyde; this effect was decreased by treatment with *N. sativa* oil (Abdel-Sater 2009). *N. sativa* seeds and natural honey were found to be equally effective in healing of gastric ulcers induced by acetylsalicylic acid in rats, similar to cimetidine (Bukhari et al. 2011). Oral administration of *N. sativa* oil was found to have protective effect against trinitrobenzene sulfonic acid (TNBS) experimental ulcerative colitis in rats (Isik et al. 2011). Nigella oil decreased proinflammatory cytokines (tumour necrosis factor-alpha (TNF-α), interleukin (IL)-1β, and IL-6), lactate dehydrogenase activity, and triglyceride and cholesterol levels which were increased in colitis. Mahgoub (2003) reported that pretreatment of rats for 3 days with thymoquinone (10 mg/kg) was able to give complete protection against acetic acid-induced colitis an effect significantly higher than sulfasalazine (500 mg/kg) control group.

Both *N. sativa* oil and thymoquinone, protected the rat gastric mucosa from acute alcohol-induced mucosal injury and promoted ulcer healing as evidenced from the ulcer index (UI) values (Kanter et al. 2005a). The oil prevented alcohol-induced increase in thiobarbituric acid-reactive substances (TBARS), an index of lipid peroxidation and also augmented gastric glutathione content (GSH), enzymatic activities of gastric superoxide dismutase (SOD) and glutathione-S-transferase (GST). Likewise, thymoquinone protected against the ulcerating effect

of alcohol and mitigated most of the biochemical adverse effects induced by alcohol in gastric mucosa, but to a lesser extent than the oil. They also found that Nigella oil significantly decreased the number of mast cells and reduced the area of gastric erosions induced by ethanol in rats (Kanter et al. 2005c). Likewise, thymoquinone treatment was also able to reduce the number of mast cells and the gravity of gastric mucosal lesions, but to lesser extent compared to the oil Both treatments reversed the elevated gastric tissue histamine levels and myeloperoxidase activities induced by ethanol. They concluded that the gastroprotective effect of both treatments, in particular *N. sativa oil* could be attributed to their antiperoxidative, antioxidant and antihistaminic effects.

Studies showed that *N. sativa* treatment protected the rat's intestinal tissue against intestinal ischemia-reperfusion injury (Terzi et al. 2010). Pretreatment of rats with *N. sativa* before ischemia and before reperfusion had significantly lower levels of liver enzymes, total oxidative status, oxidative stress index and myeloperoxidase in their ileum tissues compared to ischemia-reperfusion rats infused with saline solution. Total antioxidant capacity and catalase activity levels were also significantly higher in *N. sativa* treated group. And histological tissue damage was milder in the *N. sativa* treated group than in the control group.

N. sativa (NS) seed was found to possess clinically useful anti-*Helicobacter pylori* activity, comparable to triple therapy (TT, clarithromycin, amoxicillin, omeprazole) in a study of 88 adult patients with dyspeptic symptoms and found positive for *H. pylori* infection (Salem et al. 2010). *H. pylori* eradication was 82.6, 47.6, 66.7 and 47.8% with TT, 1 g NS + 40 mg omeprazole, 2 g NS + 40 mg omeprazole and 3 g NS + 40 mg omeprazole, respectively. Eradication rates with 2 g NS and TT were statistically not different from each other, whereas *H. pylori* eradication with other doses was significantly less than that with TT. Negative *H. pylori* stool antigen test 4 weeks after end of treatment was considered as eradication. Dyspepsia symptoms improved in all groups to a similar extent.

Nephroprotective Activity

Cisplatin [*cis*-dichlorodiammineplatinum (II)] is a widely used chemotherapeutic drug that is toxic to the kidney (el Daly 1998). Concurrent administration of cysteine together with vitamin E, *Crocus sativus* and *Nigella sativa* reduced the toxicity of cisplatin in rats. The combination mixture significantly reduced blood urea nitrogen (BUN) and serum creatinine levels as well as cisplatin-induced serum total lipids increases. Administration of the combined mixture together with cisplatin partially reversed many of the kidney enzymes changes induced by cisplatin. The combined mixture tended to protect from cisplatin-induced declines in leucocyte counts, haemoglobin levels and mean osmotic fragility of erythrocytes and also prevented the increase in haematocrit. The authors concluded that cysteine and vitamin E, *Crocus sativus* and *Nigella Sativa* may be a promising compound for reducing cisplatin-toxic side effects including nephrotoxicity. In an earlier study, an extract of *Nigella sativa* seed was found to protect from cisplatin-induced falls in hemoglobin levels and leucocyte counts in mice (Nair et al. 1991). *Nigella sativa* oil protected rat kidney tissue against oxygen free radicals and prevented renal dysfunction and morphological abnormalities associated with chronic cyclosporine – induced nephrotoxicity (Uz et al. 2008). They also found that *N. sativa* oil with its potent free radical scavenger and antioxidant properties, protected against ischaemia/reperfusion (I/R) injury in rat kidneys (Bayrak et al. 2008). Pre- and post-treatment with Nigella oil reduced serum levels of blood urea nitrogen and creatinine caused by I/R and significantly improved serum enzymatic activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) and also tissue enzymatic activities of catalase (CAT), SOD and GSH-Px. Nigella oil treatment resulted in lower total oxidant status and higher total antioxidant capacity levels and also significant reduction in serum and tissue malondialdehyde , nitric oxide (NO) and protein carbonyl content that were increased by renal I/R injury. The kidneys of untreated ischaemic rats

had a higher histopathological score, while treatment with *N. sativa* oil nearly preserved the normal morphology of the kidney.

Oral administration of rats with *N. sativa* oil protected rats against gentamicin nephrotoxicity (Ali 2004). Treatment with *N. sativa* oil produced a dose-dependent amelioration of the biochemical and histological indices of gentamicin nephrotoxicity that was statistically significant at the two higher doses used. Compared to controls, treatments of rats with *N. sativa* did not cause any overt toxicity, and it increased reduced glutathione (GSH) and total antioxidant status concentrations in renal cortex and enhanced growth. *N. sativa* was found to have protective effect against gentamicin-induced nephrotoxicity in rats (Yaman and Balikci 2010). Nigella administration with gentamicin injection resulted in significantly decreased malondialdehyde and NO generation and increased superoxide dismutase and glutathione peroxidase activities when compared with gentamicin group. Proximal tubular necrosis, vacuolation, desquamation and degeneration in epithelial cells of the proximal tubules, hyaline casts in tubular lumen, mononuclear cell infiltration, glomerular and basement membrane alterations histopathologically detected in the kidneys of the gentamicin group were considerably decreased by co-treatments with *N. sativa* (low and high dose).

Oral administration of thymoquinone to rats before or after cisplatin induction ameliorated cisplatin nephrotoxicity as evidenced by significant reductions in serum urea and creatinine and significant improvement in polyuria, kidney weight, and creatinine clearance (Badary et al. 1997). The protective effects of thymoquinone against cisplatin-induced nephrotoxicity in the rat were further confirmed by histopathological examination. Administration of thymoquinone (TQ) with the drinking water of rats before and during ifosfamide (IFO) treatment, significantly improved IFO-induced Fanconi syndrome characterised by phosphaturia, glucosuria, elevated serum creatinine and urea, and significantly normalized creatinine clearance rate (Badary 1997). TQ also significantly prevented IFO-induced renal glutathione (GSH) depletion and lipid peroxide accumulation. In mice bearing Ehrlich ascites carcinoma (EAC) xenograft, TQ significantly enhanced the antitumour effect of IFO. The findings suggested that TQ may improve the therapeutic efficacy of IFO by decreasing IFO-induced nephrotoxicity and improving its antitumour activity. In another study, treatment of rats with thymoquinone (10 mg/kg per day) supplemented with the drinking water for 5 days before doxorubicin (DOX), and daily thereafter, significantly lowered serum urea, total triglycerides and total cholesterol and lipid peroxides in the kidneys compared with DOX alone (Badary et al. 2000). Moreover, non-protein sulfhydryl content and catalase activity in the kidneys of thymoquinone -treated DOX group were significantly elevated compared with DOX alone. Treatment with thymoquinone significantly suppressed DOX-induced proteinuria, albuminuria, and urinary excretion of N-acetyl-β-D-glucosaminidase. The results confirmed the involvement of free radicals in the pathogenesis of nephropathy induced by DOX. The study also revealed the high antioxidant potential of thymoquinone and suggest that it might be applicable as a protective agent for proteinuria and hyperlipidemia associated with nephrotic syndrome.

Studies showed that thymoquinone supplementation prevented the development of gentamicin-induced acute renal toxicity in rats (Sayed-Ahmed and Nagi 2007). Thymoquinone supplementation resulted in a complete reversal of the gentamicin-induced increase in blood urea nitrogen, creatinine, thiobarbituric acid-reactive substances and total nitrate/nitrite and decrease in GSH (reduced glutathione), glutathione peroxidase, catalase and ATP to control values. Thymoquinone supplementation prevented gentamicin-induced degenerative changes in kidney tissues. *N. sativa* was found to exhibit protective effects against ischemia-reperfusion injury of rat kidneys (Yildiz et al. 2010). It was effective in reducing serum urea and creatinine levels as well as decreasing the tubular necrosis score. It also significantly reduced oxidative stress index and total oxidant status levels and increased total antioxidant capacity levels in both kidney tissue and blood. Results of animal studies suggested that thymoquinone protected against

renal ischaemia-reperfusion -induced damage through an antioxidant mechanism as well as the decrease of CYP3A1 mRNA expression and spermidine/spermine N-1-acetyl-transferase (SSAT) mRNA expression in rat's liver and kidney (Awad et al. 2011).

Anti-nephrolithiasis Activity

Treatment of rats with ethanolic extract of *N sativa* seeds reduced the number of calcium oxalate deposits in a group of rats with ethylene glycol-induced kidney calculi (Hadjzadeh et al. 2007). The extract also lowered the urine concentration of calcium oxalate. In another study they reported that after 28 days, urine oxalate concentration significantly decreased and calcium oxlate deposits were smaller in the thymoquinone-treated rat groups compared to the ethylene glycol group (Hadjzadeh et al. 2008). Also, serum calcium levels were significantly higher in the thymoquinone group. The results showed thymoquinone significantly decreased the number and size of calcium oxalate deposits in the renal tubules. The dose and duration of treatment, however, did not have a linear relation with the outcomes. Treatment of rats with N-butanol fraction and N-butanol phase remnant of *N. sativa* significantly reduced the number and size of kidney calcium oxalate deposits compared with ethylene glycol group (Hadjzadeh et al. 2011). Urinary concentration of oxalate in all experimental groups increased compared with control group on days 14 and 28, whereas the urine citrate concentration was lower in all experimental groups compared with control group on days 14 and 28. The authors suggested the use of butanolic fraction of *N. sativa* for the prevention of calcium oxalate calculi in humans.

Hepatoprotective activity

Administration of *N. sativa* oil to male albino rats for 4 weeks prior to induction of hepatotoxicity by D-galactosamine or carbon tetrachloride, it was able to give complete protection against d-galactosamine and partial protection against carbon tetrachloride hepatotoxicity (el-Dakhakhny et al. 2000b). *N. sativa* oil showed a favourable effect on the serum lipid pattern where the administration of the oil (800 mg/kg orally for 4 weeks) caused a significant decrease in serum total cholesterol, low density lipoprotein, triglycerides and a significant elevation of serum high density lipoprotein level in male spontaneously hypertensive rats of stroke prone strain and Wistar Kyoto rats.

N. sativa seeds appeared to be safe and protective against CCL4-induced hepatotoxicity in animals (Al-Ghamdi 2003). Animals pretreated with *N. sativa* had significantly reduced centrilobular fatty changes and inflammatory infiltrate in the form of neutrophil and mononuclear cells. Elevated lactate dehydrogenase was restored to normal and decreased L-alanine aminotransferase and aspartic transaminase levels were increased in animals pretreated with *N. sativa. Nigella sativa* or *Urtica dioica* treatments (alone or combination) for 45 days starting day 46 decreased the elevated lipid peroxidation and liver enzyme levels and also increased the reduced antioxidant enzyme levels in CCl4-treated rat and also increased live weights of rats (Kanter et al. 2003b; Kanter et al. 2005a). They concluded that *Nigella sativa* and *Urtica dioica* decrease the lipid peroxidation and liver enzymes, and increase the antioxidant defence system activity in the CCl4-treated rats. They also found from animal studies that *N. sativa* and/or *U. dioica* treatments may ameliorate CCl4-induced disturbances of anemia, some minerals and body defense mechanism (Meral and Kanter 2003). Similarly, Türkdoğan et al. (2003) found *U. dioica* and *N. sativa* to be effective in the prevention of carbon tetrachloride-induced liver fibrosis and cirrhosis in rats.

Preincubation of rat hepatocytes with 1 mM of either thymoquinone or silybin, (a known hepatoprotective agent), resulted in the protection of isolated hepatocytes against tert-butyl hydroperoxide (TBHP) induced toxicity evidenced by decreased leakage of alanine transaminase (ALT) and aspartic transaminase (AST) (Daba and Abdel-Rahman 1998). Both thymoquinone

and silybin prevented TBHP induced depletion of glutathione to the same extent. Oral administration of thymoquinone (TQ) in a single dose (100 mg/Kg) resulted in significant protection against the hepatotoxic effects of CCl4 in mice (Nagi et al. 1999). TQ appears to undergo reduction to dihydrothymoquinone (DHTQ). TQ and DHTQ inhibited the in- vitro non-enzymatic lipid peroxidation in liver homogenate (induced by Fe(3+)-ascorbate) in a dose dependent manner. In this in-vitro model DHTQ was more potent in comparison with TQ and butylated hydroxytoluene (BHT). The data suggested that the in-vivo protective action of TQ against CCl4-induced hepatotoxicity may be mediated through the combined antioxidant properties of TQ and its metabolite DHTQ. Mansour et al. (2001) reported that thymoquinone (12.5 mg/Kg, i.p.) may play an important role as antioxidant and may efficiently act as a protective agent against chemically-induced hepatic damage; however, higher doses were found to induce oxidative stress leading to hepatic injury. Pretreatment of mice with different doses of thyoquinone 1 h before CCl_4 injection showed that the only dose of TQ that ameliorated hepatotoxicity of CCl_4 was 12.5 mg/Kg i.p. as evidenced by the significant reduction of the elevated levels of serum enzymes as well as hepatic malondialdehyde content and significant increase of the hepatic nonprotein sulfhydryl (−SH) concentration. Treatment of mice with the other volatile oil constituents, *p*-cymene or α-pinene did not induce any changes in the serum ALT measured. In addition, i.p. administration of these compounds 1 h before CCl_4 injection, did not protect mice against CCl_4-induced hepatotoxicity.

Farrag et al. (2007) reported that lead acetate caused significant elevations in AST, urea, creatinine, total cholesterol and triglycerides in serum in rats, significantly decreased serum total protein and albumin and damaged the liver and kidneys. Combined treatment of lead-exposed animals with *N. sativa* showed marked improvement in both biochemical and histopathological findings as well as reduction in the damaged areas. The results strongly indicated the protective effect of *N. sativa* seeds against toxic effect of lead on liver and kidney tissues. Studies suggested that *N. sativa* treatment protected rat liver against hepatic ischemia-reperfusion injury (Yildiz et al. 2008). The levels of serum aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase levels, and total oxidative status, oxidative stress index and myeloperoxidase in *N. sativa* treated rats were significantly lower than those in the control group while total antioxidant capacity were significantly higher. Al-Ghasham et al. (2008) showed that both treatment with *N. sativa* and date reduce the toxic effects of aflatoxin-B(1) (AFB(1)) in the liver and kidney of rats. But date treatment was more cytoprotective for liver than NS treatment against aflatoxicosis in rats. Treatment with AFB(1) induced histopathological changes in the tissues of the rat's liver and kidney and significantly augmented plasma levels of alanine transaminase (ALT), aspartate transaminase (AST), creatinine and urea.

Oral administration of 1 mL/kg *N. sativa* oil to rats every day for 1 week prior to CCl4 injection alleviated CCl4-induced suppression of cytochrome CYP2B, CYP3A2, CYP2C11, and CYP1A2 (Ibrahim et al. 2008). Moreover, CCl4 increased iNOS and TNFalpha mRNA, while *N. sativa* oil administration prior to CCl4 injection suppressed the CCl4-induced iNOS mRNA and up-regulated interleukin IL-10 mRNA. The results indicated that *N. sativa* oil administration had a protective effect against the CCl4-mediated suppression of hepatic CYPs and that this protective effect was attributed partly to the downregulation of NO production and up-regulation of the antiinflammatory IL-10.

Sayed-Ahmed et al. (2010) showed that thymoquinone supplementation prevented the development of diethylnitrosamine NA-induced initiation of liver cancer in rats by decreasing oxidative stress and preserving both the activity and mRNA expression of antioxidant enzymes such as glutathione peroxidase (GSHPx), glutathione-s-transferase (GST) and catalase (CAT). Studies by Coban et al. (2010) showed that nigella exerted a therapeutic effect on cholestatic liver injury in bile duct ligated (BDL) rats possibly through attenuation of

enhanced neutrophil infiltration and oxidative stress in the liver tissue. A decrease in γ-glutamyl transferase, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase activities were observed in nigella treated rats when compared with BDL group. Nigella treated rats' tissue levels of total oxidant status, oxidative stress index, and myeloperoxidase were significantly lower than that of the BDL group. Increases in total antioxidant capacity and catalase levels were statistically significant in the nigella treated rats compared to BDL group. Administration of nigella in the rats with biliary obstruction resulted in inhibition of necro-inflammation.

Oral intake of NSE (*N. sativa* extract), GSE (grape seeds), CUR (curcumin) or SYL (silymarin) to tamoxifen -intoxicated rats, attenuated histopathological changes and elevated decreased liver antioxidant enzymes levels (glutathione peroxidase, glutathione reductase, superoxide dismutase and catalase), reduced glutathione (GSH) and GSH/GSSG ratio and lowered elevated lipid peroxides, oxidized glutathione (GSSG), tumour necrosis factor-alpha (TNF-alpha) and serum liver enzymes; alanine transaminase, aspartate transaminase, alkaline phosphatase, lactate dehydrogenase and gamma glutamyl transferase levels (El-Beshbishy et al. 2010). Improvements were prominent in case of NSE (similarly SYL)>CUR>GSE. The results indicated that NSE, GSE or CUR acted as free radicals scavengers and protected tamoxifen -induced liver injury in rats.

Pretreatment with omega3 and *N. sativa* seed oil prior γ-hexachlorocyclohexane, (γ-HCH) administration restored the altered biochemical features and alleviated the hazardous effects induced by γ-HCH on the liver and kidney and also protected acetylcholinesterase from the inhibitory action of γ-HCH as well as suppressed the lipid peroxidation in rats (Attia et al. 2011).

In recent animal studies, the aqueous *N. sativa* seed waste extract was found to attenuate CCl_4 -induced liver damage likely due to the decrease of proinflammatory cytokines and T-cell proliferation (Michel et al. 2011). This was accompanied by a significant decrease in both serum and tissue cytokines; tumour necrosis factor-alpha (TNF-α), interferon-gamma (INF-γ) and interleukin-beta (IL-1β), in the markers of liver functions; bilirubin and glutamic pyruvic transaminase (GPT) and in the oxidative stress markers; malondialdehyde (MDA) and glutathione content (GSH). Fractionation of the aqueous extract yielded protein, saponin, and polyphenol fractions. The protein fraction not the saponin and polyphenol fractions exhibited a promising hepatoprotective effect in the management of different liver disorders. The protein fraction improved hepatic biochemical changes manifested by a significant reduction in both serum and tissue cytokines in the liver markers and in the oxidative stress markers. The protein fraction reduced the incidence of liver lesions including hepatic cells cloudy swelling, lymphocytes infiltration, hepatic necrosis and fibrous connective tissue proliferation induced by CCl_4 in mice. Aqueous *N. sativa* seed extract (50 mg/kg) and thymoquinone (5 mg/kg in corn oil) countered the elevations in serum alanine aminotransferase activity, oxidized glutathione level, and stress ratio caused by CCl(4) in rats (El-Sayed 2011). Both treatments ameliorated the reductions in the activities and messenger RNA (mRNA) levels of glutathione S-transferase, NAD(P)H-quinone oxidoreductase, and microsomal epoxide hydrolase, as well as the reductions in reduced glutathione and cysteine levels produced by CCl(4).

Thymoquinone supplementation to lipopolysaccharide (LPS)-treated rats resulted in normalization of liver GSH and decreases in the levels of malondialdehyde (MDA) and caspase-3 activity in the liver with reduction of serum TNF-alpha, serum total bilirubin and the activities of ALP and gamma-glutamyl transferase (gamma-GT) enzymes (Helal 2010). Histopathological examination revealed that rhymoquinone administration improved LPS-induced pathological abnormalities in liver tissues. The author concluded that thymoquinone reduced acute endoxemia-induced liver dysfunction at least in part by its anti inflammatory, antiapoptotic and antioxidant activities.

Neuroprotective Activity

Animal studies showed *N. sativa* had neuroprotective effect against experimental spinal cord injury in rats. Methylprednisolone and *N. sativa* treatment decreased tissue malondialdehyde (MDA) and PC levels and prevented inhibition of superoxide dismutase, glutathione peroxidase, and catalase enzymes in the rat's spinal cord tissues (Kanter et al. 2006a). The most significant results were obtained when *N. sativa* was given. The morphology of neurons in methylprednisolone and *N. sativa*-treated groups were well protected against degeneration. Radad et al. (2009) demonstrated in primary dopaminergic neurons from mouse mesencephala, the potential of thymoquinone to exert neuroprotective effect in-vitro against MPP(+) and rotenone toxicities relevant to Parkinson's disease. Pretreament with *N. sativa* and its active component thymoquinone, reduced serum/glucose deprivation-induced cytotoxicity in PC12 cells after 6 and 18 h (Mousavi et al. 2010). Pretreament also reversed the elevated reactive oxygen species (ROS) production following ischemic insult. The results suggested the potenial therapeutic application of *N. sativa* extract and thymoquinone for managing cerebral ischemic and neurodegenerative disorders.

Studies by Hosseinzadeh et al. (2007) showed that pre-treatment of rats with *N. seed* oil and thymoquinone protected against cerebral ischemia-reperfusion injury (IRI) in rat hippocampus. Pretreatments resulted in a significant decrease in malondialdehyde level as compared with ischemic group and may have protective effects on lipid peroxidation process during IRI in rat hippocampus. *Nigella sativa* and derived thymoquinone caused morphologic improvement on neurodegeneration in hippocampus after chronic toluene exposure in rats (Kanter 2008b). Chronic toluene exposure caused severe degenerative changes, shrunken cytoplasma, slightly dilated cisternae of endoplasmic reticulum, markedly swollen mitochondria with degenerated cristae and nuclear membrane breakdown with chromatin disorganization in neurons of the hippocampus. The distorted nerve cells were mainly absent in the thymoquinone and Nigella-treated rats. Intraperitoneal administration of *N. sativa* protected rats against induced subarachnoid hemorrhage (Erşahin et al. 2011). *N. sativa* treatment markedly improved the neurological scores while all oxidant responses were prevented, implicating that *N. sativa* treatment may be of therapeutic use in preventing oxidative stress due to subarachnoid hemorrhage.

N. sativa exhibited protective effect against neuronal injury in the frontal cortex and brain stem after chronic toluene exposure in rats (Kanter 2008c). Chronic toluene exposure caused severe degenerative changes, shrunken cytoplasma, severely dilated cisternae of endoplasmic reticulum, markedly swollen mitochondria with degenerated cristae and nuclear membrane breakdown with chromatin disorganization in neurons of the frontal cortex and brain stem. *N. sativa* therapy for 12 weeks caused morphologic improvement on neurodegeneration in frontal cortex and brain stem after chronic toluene exposure in rats.

Repeated administration of *N. sativa* oil (4 mL/kg, p.o.) along with tramadol (50 mg/kg, s.c.) inhibited the development of tramadol tolerance in mice (Abdel-Zaher et al. 2011). Concomitantly, nitric oxide overproduction and increase in brain malondialdehyde level induced by repeated administration of tramadol to mice or by administration of naloxone to tramadol-dependent mice were inhibited by co-administration of the oil. Also, the decrease in brain intracellular reduced glutathione level and glutathione peroxidase activity induced by both treatments was inhibited by co-administration of the oil. The data showed that *N. sativa* oil appeared to have a therapeutic potential in tramadol tolerance and dependence through blockade of NO overproduction and oxidative stress induced by the drug.

Skin-Darkening Activity

Significant skin darkening activity of *N. sativa* seed extract and its active compound thymoquinone was observed on the isolated melanophores of the wall lizard (Ali and Meitei 2011). It appeared that

the extract and thymoquinone mimicked the action of acetylcholine in melanin dispersion leading to skin darkening via stimulation of cholinergic receptors of muscarinic nature within the melanophores of wall lizard. The results suggested a potential for thymoquinone, as a novel melanogen for its clinical application in skin disorders such as hypopigmentation or vitiligo.

Skeletal Muscle Protective Activity

Hosseinzade et al. (2012) reported that thymoquinone exhibited some protective effects against the muscle tissue injury caused by lower limb ischemia-reperfusion. The average peak-to-peak amplitude during ischemic reperfusion was significantly increased in thymoquinone groups in comparison with the control group. Following thymoquinone intraperitoneal administration, the total sulfhydryl contents and antioxidant capacity were elevated in muscle flap. The malondialdehyde (MDA) level was lowered significantly in test groups.

Sedative Activity

Methanolic extract of *N. sativa* seeds was found to modulate amino acid release in cultured cortical neurons (El-Naggar et al. 2010). Gamma-aminobutyric acid (inhibitory amino acid) was increased while secretion of glutamate, aspartate (both excitatory amino acids), and glycine (inhibitory) were decreased. The in-vitro findings supported the hypothesis that the sedative and depressive effects of *N sativa* observed in-vivo could be based on changes of inhibitory/excitatory amino acids levels.

Anxiolytic Activity

After 4 weeks of daily administration of *N. sativa* oil, the rats exhibited an increase in open field activity (Perveen et al. 2009). *N. sativa* also produced anti-anxiety effect in rats when tested in elevated plus maze. Result shows that oral administration of *N. sativa* oil increased brain levels of 5-hydroxytryptamine (5-HT) but the levels of brain 5-hydroxyindoleacetic acid (5-HIAA) decreased significantly. Brain and plasma levels of tryptophan also increased significantly following oral repeated administration of *N. sativa* oil. Based on this, they suggested that *N. sativa* oil may be a useful choice for the treatment of anxiety. Gilhotra and Dhingra (2011) reported that thymoquinone (10 and 20 mg/kg) produced significant antianxiety effects in unstressed mice without altering nitrite levels, but only the higher dose (20 mg/kg) of thymoquinone increased the GABA content in unstressed mice. In stressed mice, thymoquinone (20 mg/kg) showed anxiolytic effects, with a significant decrease in plasma nitrite and reversal of the decreased brain GABA content. Pre-treatment with methylene blue enhanced the antianxiety effect of thymoquinone in both unstressed and stressed mice. The results suggest an involvement of NO-cGMP and GABAergic pathways in the anxiolytic-like activity of thymoquinone.

Antioxytocic Activity

Nigella sativa seed volatile oil dose-dependently inhibited the spontaneous movements of rat and guinea pig uterine smooth muscle in-vitro and also the contractions induced by oxytocin stimulation (Aqel and Shaheen 1996). The data suggested that the volatile oil may have some anti oxytocic potential.

Anti-sepsis Activity

Studies showed that treatment of *Nigella sativa* oil in sepsis adult Wistar albino rats lowered endothelin-1 level and malondialdehyde but enhanced superoxide dismutase levels (Alici et al. 2011). The results suggested that *N. sativa* oil may have a positive impact on endothelin-1 levels and oxidative stress induced by sepsis in experimental rat models. Thymoquinine was

found to have a protective effect from sepsis-related morbidity, mortality and associated organ dysfunction in mice induced separately by endotoxin Gram-negative bacteria and live *Escherichia coli* (Alkharfy et al. 2011). Thymoquinone reduced mortality by 80–90% and improved both renal and hepatic biomarker profiles. Mice treated with thymoquinone had reduced levels of interleukins IL-1α, IL-10, IL-2 and TNF-α.

Immunomodulatory Activity

Nigella sativa was reported to have immunomodulatory effect. Majdalawieh et al. (2010) demonstrated in-vitro that the aqueous extract of *N. sativa* significantly enhances splenocyte proliferation in a dose-dependent manner. Further, the aqueous extract promoted the secretion of Th2, versus Th1, cytokines by splenocytes. The in-vitro effects of *N. sativa* on lymphocyte response to different mitogens and on polymorphonuclear leukocyte phagocytic activity were reported by Haq et al. (1995). No stimulatory effect of *N. sativa* was detected on lymphocyte response to phytohemagglutinin, concanavalin-A or pokeweed mitogen. A stimulatory effect of *N. sativa* was observed on the lymphocyte response to pooled allogeneic cells; the effect was pronounced when low locular weight soluble fractions were used. *N. sativa* enhanced the production of interleukin-3 by human lymphocytes when cultured with pooled allogeneic cells or without any added stimulator, but did not enhance or suppress interleukin-2 secretion by mitogen activated peripheral blood mononuclear cells. *N. sativa* increased interleukin-1 beta, suggesting therefore, that it has an effect on macrophages. In mixed lymphocyte cultures (MLC), whole *N. sativa* and its purified proteins were found stimulatory as well as suppressive and this effect varied from one donor to another (Haq et al. 1999). In MLC, maximum stimulation was observed with fractionated *N. sativa* proteins (P1) (10 μg/mL) while *N. sativa* were stimulatory at all concentrations (10 μg/mL, 1 μg/mL or 0.1 μg/mL) used. In contrast, a uniformly suppressive effect of *N. sativa* and its all four peaks at a concentration of 10 μg/mL was noticed when lymphocytes were activated with pokeweed mitogen. Large quantities of IL-1 beta were secreted by whole *N. sativa* in culture medium with non-activated peripheral blood mononuclear cells (PBMC) (450 μg/mL) and with allogeneic cells (410 μg/mL). Fractionated *N. sativa* was less effective when compared with whole *N. sativa* proteins. Stimulatory effect of whole *N. sativa* and fractionated proteins was also noticed on the production of TNF-alpha either using non-activated or mitogen activated cells.

Administration of volatile nigella seed oil to Long-Evans rats challenged with a specific antigen (typhoid TH) elicited a significant decrease in splenocytes and neutrophils counts, but a rise in peripheral lymphocytes and monocytes, indicating it to have potential immunosuppressive effect (Islam et al. 2004). The cytokine production of splenic mononuclear cells of ovalbumin-sensitised BALB/c mice that were given *Nigella sativa* for 30 days was not significantly different than those who took saline solution instead (Büyüköztürk et al. 2005). The findings suggested that *N. sativa* oil appeared not to have an immunomodulatory effect on Th1 and Th2 cell responsiveness to allergen stimulation. *N. sativa* essential oil significantly inhibited isolated human neutrophil chemotaxis from 0.05 to 0.5 mg/mL (Kacem and Meraihi 2009). The inhibitory concentrations IC_{50} value for induced neutrophil chemotaxis, and control movement were 0.08 and 0.07 mg/mL, respectively. The human neutrophil elastase secretion was inhibited by essential oil at a concentration dependent manner from 0.5 to 2.5 mg/mL. The results suggested that *N. sativa* essential oil to be potent inhibitor of polymorphonuclear leukocyte functions.

Macrophages showed reduced growth in comparison to monocytes 24 h after treatment with *Nigella sativa* oil (Mat et al. 2011). The mean cell diameter was significantly different between untreated and treated condition in monocytes and macrophages. In addition, intracellular lipid accumulation was hindered in combined treatment with *Nigella sativa* oil. More cells differentiated into macrophage-like cells when monocytes were supplemented with oxidized LDL alone.

The results showed that *N. sativa* modulated cell growth and differentiation in monocyte and monocyte-derived macrophages. No effect of *N. sativa* or its fractions were noticed on bacterial phagocytosis.

Thymoquinone (IC_{50} 1.4–2.76 μM) dose- and time-dependently reduced nitrite production in lipopolysaccharide (LPS)-stimulated rat peritoneal macrophages without affecting the cell viability and inhibited the increase in iNOS mRNA expression induced by LPS (El-Mahmoudy et al. 2002). The inhibitory effect of thymoquinone may be useful in ameliorating the inflammatory and autoimmune conditions. Thymoquinone was found to compromise the maturation, cytokine release and survival of dendritic cells derived from the mouse bone marrow (Xuan et al. 2010). Lipopolysaccharide (LPS) increased the percentage of CD11c(+) CD86(+), CD11c(+)MHCII(+), CD11c(+)CD40(+) and CD11c(+)CD54(+) cells and stimulated the release of IL-10, IL-12p70 and TNF-alpha in dendritic cells. These effects were blunted by thymoquinone in a concentration dependent manner (1–20 μM). LPS-induced phosphorylation of prosurvival kinases Akt and ERK1/2 was anulled by thymoquinone. Further LPS decreased and thymoquinone increased caspase 3 and caspase 8 activation and annexin V binding.

In a 4-week study of 30 male volunteers (age 24 years), daily intake of 39 mg/kg black cumin seeds was found to increase total leukocytes and CD3+ cells significantly (Kaya et al. 2003). The results suggested black cumin seed intake may increase activity of human immune system.

Antiplatelet Activity

The methanol soluble portion of black cumin oil showed inhibitory effects on arachidonic acid (AA)-induced platelet aggregation and blood coagulation (Enomoto et al. 2001). A new compound 2-(2-methoxypropyl)-5-methyl-1,4-benzenediol (1) and two known compounds, thymol (2), carvacrol (3), having very strong inhibitory activity were isolated from the methanol portion. The isolated compounds (1–3) and eight related compounds showed arachidonic acid induced platelet aggregation. Compounds possessing aromatic hydroxyl and acetoxyl group had more potent activity than aspirin, well known as a remedy for thrombosis.

N. sativa oil at 50 μg oil/mL in conditioned medium elicited maximum increase in tissue-type plasminogen activator (t-PA) in human umbilical vein (HUV) and human uterine arterial (HUA) endothelial cells (Awad and Binder 2005). At 100 μg/mL, there was a significant change in the amount of t-PA antigen produced by either HUVEC or HUA-EC. Plasminogen activator inhibitor-type 1 increased the conditioned medium significantly and concentration-dependently in both cells. The results suggested a role for *N. sativa* oil in modulating the balance of fibrinolysis/thrombus formation by modulating the fibrinolytic potential of endothelial cells.

Haemostatic Activity

Feeding studies in adult male albino rats showed that as compared to the control (plain flour dough), the equivalent dose of *N. sativa* powdered seeds (180 mg NS/kg rat/day) induced significant hyperfibrinogenemia (14%) after 4 weeks while the double dose induced significant transient prothrombin time prolongation (7.8%) and thrombin time reduction (13%) after 2 weeks and the triple dose induced significant transient activated partial thromboplastin time reduction (16%), and thrombin time reduction (13%) after 1 week (Al-Jishi and Abuo Hozaifa 2003). There was an increase in the albumin level and alanine aminotransferase activity paralleling that of fibrinogen. No changes were noticed in platelet count, antithrombin III level, and aspartate aminotransferase activity. The authors concluded *that N. sativa* within the doses employed appeared to induce transient changes in the coagulation activity of rats.

Antiepileptic Activity

Nigella sativa oil was found to be the most effective in preventing pentylenetetrazol -induced seizures

in mice relative to valproate, a major antiepileptic drug (Ilhan et al. 2005). *N. sativa* oil showed antiepileptogenic properties as it reduced the sensitivity of kindled mice to the convulsive and lethal effects of pentylenetetrazol; valproate was ineffective in preventing development of any of these effects.

In pentylenetetrazole-induced seizure, the intraperitoneally injection of thymoquinone at doses of 40 and 80 mg/kg in mice, prolonged the onset of seizures and reduced the duration of myoclonic seizures (Hosseinzadeh and Parvardeh 2004). The protective effect of thymoquinone against mortality was 71.4 and 100% respectively. In the maximal electroshock (MES)-induced seizure model, thymoquinone failed to reduce the duration of seizure, butexhibited a complete protection against mortality. Thymoquinone (40 and 80 mg/kg) did not have any hypnosis effect in the pentobarbital-induced hypnosis, but impaired the motor coordination and reduced the locomotor activity. Their results indicated that thymoquinone may have anticonvulsant activity in the *petit mal* epilepsy probably through an opioid receptor-mediated increase in GABAergic tone. They also showed in another study, that intracerebroventricular (i.c.v.) injection of thymoquinone suppressed epileptic seizures in rats (Hosseinzadeh et al. 2005). Flumazenil reversed the anticonvulsant activity of thymoquinone. Also, pretreatment with naloxone antagonized the prolongation of tonic-clonic seizure latency as well as the reduction in seizure duration induced by thymoquinone The results again indicated that thymoquinone may have anticonvulsant activity, probably through an opioid receptor-mediated increase in GABAergic tone.

All of *N. sativa* seed constituents except for fixed oil protected mice effectively against pentylenetetrazole Z-induced convulsions (Raza et al. 2008). Its volatile oil and its component *p*-cymene suppressed convulsions induced by maximal electroshock. All of the Nigella seed constituents induced varying degrees of minimal neurological deficit in the chimney test. Exploration on the role of receptors suggested that picrotoxin and bicuculline-sensitive GABA receptors, most probably GABAA receptors, mediated an increase in GABAergic response. Also thymoquinone increased the potency of valproate in both pentylenetetrazole and maximal electroshock models. In another study, treatment with curcumin, *Nigella sativa* oil or valproate ameliorated most of the changes induced by pilocarpine and restored Na^+, K^+-ATPase activity in the hippocampus to control levels in rats (Ezz et al. 2011). The study indicated the promising anticonvulsant and potent antioxidant effects of curcumin and Nigella oil in reducing oxidative stress, excitability and the induction of seizures in epileptic animals and improving some of the adverse effects of antiepileptic drugs.

In a double-blinded crossover clinical trial conducted on children with refractory epilepsy, the frequency of intractable pediatric seizures was significantly decreased during a month – long treatment with aqueous *N. sativa* seed extract (Akhondian et al. 2007). In a pilot, double-blinded crossover clinical trial study on children with refractory epilepsy, thymoquinone at a dose of 1 mg/kg administered as an adjunctive therapy significantly reduced the frequency of intractable pediatric seizures (Akhondian et al. 2011).

Antifertility and Fertility Activity

Hexane extract of the seeds of *Nigella sativa* prevented pregnancy in Sprague–Dawley rats treated orally at 2 g/kg daily dose on days 1–10 postcoitum (Keshri et al. 1995). At contraceptive dose, the active hexane extract exhibited only mild uterotrophic activity and but was devoid of any estrogenicity in the immature rat bioassay.

Adult male albino rats treated with *Nigella sativa* 300 mg/kg body weight for 60 days recorded a significant increase in the weight of reproductive organs as compared to control animals (Mohammad et al. 2009). The sperm motility and count in cauda epidydimides and testicular ducts were significantly increased. Spermatogenesis was increased at primary and secondary spermatocyte stages. Epididymides showed elevated number of spermatozoa and lumen of vas deferentia were full of sperms. The secretary activities of seminal vesicle and ventricular prostate were also increased. A significant

increase in spermatogenesis activity was observed in seminiferous tubule. Treated rats testicular cell population showed a increase in number of spermatocytes and spermatids when compared to control animals. Increased in number female rats impregnated by males receiving treatment was also observed.

Antimicrobial Activity

The diethyl ether extract of *Nigella sativa* seeds (25–400 μg extract/disc) caused concentration-dependent inhibition of Gram-positive *Staphylococcus aureus* and Gram-negative bacteria, *Pseudomonas aeruginosa* and *Escherichia coli* and a pathogenic yeast *Candida albicans* (Hanafy and Hatem 1991). The extract showed antibacterial synergism with streptomycin and gentamicin and showed additive antibacterial action with spectinomycin, erythromycin, tobramycin, doxycycline, chloramphenicol, nalidixic acid, ampicillin, lincomycin and sulphamethoxyzole-trimethoprim combination. The extract successfully eradicated a non-fatal subcutaneous staphylococcal infection in mice when injected at the site of infection. The volatile oil of *Nigella sativa* seeds exhibited antibacterial activity against 37 isolates of *Shigella dysenteriae, Shigella flexneri, Shigella sonnei* and *Shigella boydii* and 10 strains of *Vibrio cholerae* and *Escherichia coli* (Ferdous et al. 1992). The minimum inhibitory concentration (MIC) of the volatile oil for *Shigella*, *Vibrio* and *Escherichia* strains tested was between 50 and 400 μg/mL. Most of the strains were clinically resistant to ampicillin, co-trimoxazole and tetracycline. Crude alkaloid and water extracts of *N. sativa* were found to be more effective against Gram negative bacterial isolates including multiple antibiotics-resistant bacteria than the Gram positive isolates (Morsi 2000).

All Turkish black cumin oils showed antibacterial activity in-vitro against all the bacteria tested namely pathogenic and spoilage bacteria*: Aeromonas hydrophila, Bacillus cereus, Bacillus subtilis, Corynebacterium xerosis, Enterobacter aerogenes, Enterococcus faecalis*, *Escherichia coli*, *Escherichia coli* O157:H7, *Klebsiella pneumoniae, Listeria monocytogenes, Mycobacterium smegmatis, Proteus vulgaris, Pseudomonas aeruginosa, Pseudomonas fluorescens, Salmonella typhimurium, Staphylococcus aureus, Yersinia enterocolitica* and the following lactic acid bacteria: *Streptococcus salivarius* ssp. *thermophilus, Lactobacillus delbrueckii* ssp. *bulgaricus, Lactobacillus casei* ssp. *casei, Lactobacillus paracasei* ssp. *paracasei, Leuconostoc pseudomesenteroides, Leuconostoc gelidum* and *Weissella paramesenteroides* (Arici et al. 2005). The oils at 2.0% concentration were more effective than at other concentrations. The most sensitive bacterium against all of the oil concentrations was *Aeromonas hydrophila*, while the most resistant was *Yersinia enterocolitica*. Generally, lactic acid bacteria had more resistance than pathogenic and spoilage bacteria. They thus concluded that black cumin oil may be used as an antimicrobial agent in food products to prevent spoilage.

Ether extract of *N. sativa* seed and its active principle, thymoquinone, were found to have antifungal activity against 8 isolates of dermatophytes: four isolates of *Trichophyton rubrum* and one each of *Trichophyton interdigitale, Trichophyton mentagrophytes, Epidermophyton floccosum* and *Microsporum canis* (Aljabre et al. 2005; Randhawa 2008). The MICs of the *N. sativa* ether extract and thymoquinone were between 10 and 40 and 0.125 and 0.25 mg/mL, respectively. Similarly, thymoquinone was shown to inhibit three opportunistic fungi: *Aspergillus, Fusarium* and *Scopulariopsis* species, with an MIC of 0.1–1.0 mg/mL (Randhawa 2008). *N. sativa* seed essential oils obtained by hydrodistillation and dry steam distillation were dominated by *p*-cymene, whereas the major constituent identified in both volatile fractions obtained by dry steam distillation of extracted oils was thymoquinone (ranging between 0.36 and 0.38 g/mL, while in oils obtained by hydrodistillation and dry steam distillation, it constituted only 0.03 and 0.05 g/mL, respectively) (Kokoska et al. 2008). Both oils distilled directly from seeds showed lower antimicrobial activity (MICs > or = 256 and 32 μg/mL for hydrodistillation and dry steam distillation, respectively) than those obtained by steam distillation plus solvent extraction and

supercritical fluid extraction (MICs>or=4 μg/mL). All oil samples were significantly more active against Gram-positive than against Gram-negative bacteria. Thymoquinone exhibited potent growth-inhibiting activity against gram-positive bacteria, with MICs ranging from 8 to 64 μg/mL.

Nigella sativa seed oil and methanolic extract exhibited marked dose dependant antibacterial activity against *Staphylococcus epidermidis* and other coagulase-negative Staphylococci resistant to clinically used antibiotics up to a dilution of 1:50 as evident from the zones of inhibition (Salman et al. 2008a). No cross resistance was observed with any of the tested antibiotics, amikacin, tetracycline, cotrimoxazole, ciprofloxacin, ampicillin, ceftriaxone, tobramycin, gentamicin and erythromycin. In another study, they reported that *Nigella sativa* essential oil exhibited pronounced antibacterial activity against multidrug resistant clinical strains of *Pseudomonas aeruginosa* (Salman et al. 2009). Resistance was highest for ampicillin, gentamicin, ciprofloxacin, amikacin, ceftazidime, cefotaxime, ofloxacin and ceftriaxone. It was active up to 1:50 dilution against 1 strain resistant to 6 antibiotics, up to 1:10 dilution against 5 strains resistant to 2–11 antibiotics and in undiluted state against 6 strains resistant to 6–11 antibiotics. Salman et al. (2008b) also reported that *N.* oil showed pronounced dose dependent antibacterial activity which was more against Gram positive than Gram negative bacteria. Among Gram positive bacteria tested, *Staphylococcus aureus, S. epidermidis*, other coagulase −ve Staphylococci and *Streptococcus pyogenes* were sensitive to the oil while *Enterococcus faecalis, Streptococcus agalactiae* were resistant. Among Gram −ve bacteria tested, only *Pseudomonas aeruginosa* was sensitive to oil and the rest (*Acinetobacter baumannii, Citrobacter freundii, Klebsiella pneumoniae, Proteus mirabilis, P. vulgaris* and *Vibrio cholerae*) were insensitive. Out of 144 strains tested, most of which were resistant to a number of antibiotics, 97 were inhibited by the oil.

Ethanolic extract of *N. sativa* seed exerted inhibitory effect on methicillin resistant *Staphylococcus aureus* with an MIC range of 0.2–0.5 mg/mL (Hannan et al. 2008). Water extract of ground *N. sativa* seeds (300 mg/mL) was found to inhibit growth of *Staphylococcus aureus* and the authors (Bakathir and Abbas 2011) attributed the activity to the two important active ingredients of *N. sativa*, thymoquinone and melanin. Saponin compounds isolated from *N. sativa* seeds were found to have inhibitory effect on the in-vitro growth of *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Klebsiella pneumoniae, Proteus vulgaris* and *Salmonella typhi* (Mohammed et al. 2009)

Thymohydroquinone, isolated from *N. sativa* volatile seed oil, exhibited high antimicrobial effect against Gram positive microorganisms (El-Fatatry 1975). Thymoquinone, an active principle of *Nigella sativa* seed, exhibited a significant bactericidal activity against the majority of the tested bacteria (MICs values ranged from 8 to 32 μg/mL) especially Gram positive *Staphylococcus aureus* and *Staphylococcus epidermidis* (Chaieb et al. 2011). Crystal violet assay demonstrated that the minimum biofilm inhibition concentration (BIC_{50}) was attained with 22 and 60 μg/mL for *Staphylococcus aureus* and *Staphylococcus epidermidis* respectively. Thymoquinone prevented cell adhesion to glass slides surface.

N. sativa seed oils exhibited antifungal activity against pathogenic and industrial fungi: *Aspergillus flavus, Aspergillus niger, Candida crusii, Cryptococcos neaformans, Pichia membranaefaciens, Humicola* sp., *Rhizopus arrhizus, Rhizopus oligosporous, Rhizopus. oryzae, Saccharomyces cerevisiae, Saccharomyces cerevisiae* var. *ellepsoideus, Saccharomyces occidentalis, Trichoderma* spp, *Trichophyton mentagrophytes*, and wine yeast (Islam et al. 1989). The lowest MIC value was found against *Aspergillus fumigatus*. The seed oils were found to contain traces of nigellimin, nigellimin-N-oxide, nigellidin and nigellicin, and four dolabellane-type diterpene alkaloids (nigellamines).

An intravenous inoculation of mice with *Candida albicans* produced colonies of the organism in the liver, spleen and kidneys (Khan et al. 2003a). Treatment of candidasis mice with

Nigella sativa seed extract 24 h after the inoculation caused a considerable inhibitory effect on the growth of *Candida albicans* in all organs studied. A 5-fold decrease in *Candid*a in kidneys, 8-fold in liver and 11-fold in spleen was observed in the groups of animals post-treated with *N. sativa* seed extract which was confirmed by istopathological examination of the respective organs. The results indicated that the aqueous extract of *Nigella sativa* seeds exhibited inhibitory effect against candidiasis and validated the traditional use of the plant in fungal infections. The hexane and alcohol extract of *N. sativa* seeds showed antimicrobial activity (Mehta et al. 2009a). Thymohydroquinone and thymoquinone from black cumin seeds possessed significant antiyeast activity and affected the growth of all dairy spoilage yeast strains tested with MICs ranging from 8 to 128 μg/mL (Halamova et al. 2010). The findings suggested thymohydroquinone and thymoquinone to be effective antiyeast agents that could be used in the dairy industry as chemical preservatives of natural origin. *N. sativa* essential oil could be used as natural inhibitors in foods at low concentrations to protect from fungal and toxin contaminations by *Aspergillus parasiticus* (Khosravi et al. 2011). It exhibited a MIC 90 (minimum inhibitory concentration 90) value of 2.75 mg/mL and MFC (minimum fungicidal concentration) of 6.25 mg/mL.

The lipid-transporting protein (Ns-LTP1) protein from *N. sativa* seeds was found to inhibit the development of some phytopathogenic fungi and oomycetes (Oshchepkova et al. 2009). Two defensins Ns-D1 and Ns-D2 isolated from *Nigella sativa* seeds exhibited strong although varied antifungal activity towards a number of phytopathogenic fungi (Rogozhin et al. 2011). High antifungal activity of *N. sativa* defensins make them promising candidates for engineering pathogen-resistant plants.

Studies in BALB/c mice showed that intraperitoneal administration of *N. sativa* seed oil exhibited antiviral effect against murine cytomegalovirus infection (Salem and Hossain 2000). On day 10 of infection, the virus titer was undetectable in spleen and liver of Nigella-treated mice, while it was detectable in control mice. In addition, *N. sativa* oil upregulated suppressor function of Mφ CD4(+) T cells and IFN-gamma. The results suggested the antiviral effect may be mediated by increasing of Mφ number and function, and IFN-gamma production.

Testicular Protective Activity

Thymoquinone was found to have protective effect against methotrexate-induced testicular injury in mice (Gökçe et al. 2011). Thymoquinone treatment decreased total antioxidant capacity and prevented the increase in the myeloperoxidase activity in testes of methotrexate-treated mice. Light microscopy showed in mice that receiving methotrexate resulted in interstitial space dilatation, edema, severe disruption of the seminiferous epithelium and reduced diameter of the seminiferous tubules. Administration of thymoquinone reversed histological changes of methotrexate significantly.

Antisickling Activity

The fixed oil extracted from *N. sativa* seeds was found to have in-vitro antisickling activity (Ibraheem et al. 2010). The 0.1% concentration resulted in an approximately 80% reduction in the formation of sickle cells and a considerable reduction in the formation of irreversibly sickled cells of blood taken from patients with sickle cell disease.

Bone Healing Activity

Male rats with femoral defect were surgically implanted with, TCPL (tri-calcium phosphate lysine) capsule loaded with 0.02 g thymoquinone and 200 mg vancomycin and after 30 days all animals were sacrificed and vital as well as reproductive organs were collected and analyzed histopathologically (Kirui et al. 2004). The results showed that sustained levels of thymoquinone could enhance bone healing with little or no side effects on major vital and reproductive

organs. There were no significant differences in cholesterol, proteins, malondialdehyde, alkaline phosphatise levels, wet weights of vital as well as reproductive organs in all groups.

Antiparasitic Activity

Kalonji was reported to possess significant efficacy against fascioliasis in buffalos (Kailani et al. 1995). Single oral treatment with 25 mg/kg of kalonji exerted highly significant antifasciolic efficacy on day 15 after treatment, decreasing EPG (eggs per gram faeces) by 88.2%. *N. sativa* oil was found to reduce the number of *Schistosoma mansoni* worms in the liver and decreased the total number of ova deposited in both the liver and the intestine of infected mice (Mahmoud et al. 2002). Further, it increased the number of dead ova in the intestinal wall and reduced the granuloma diameters markedly. When *N. sativa* oil was administered in combination with praziquantel, the most prominent effect was a further lowering in the dead ova number over that produced by praziquantel alone. Administration of *Nigella sativa* oil succeeded partially to correct the previous changes in L-alanine aminotransferase, gamma-glutamyl transferase, alkaline phosphatase, activity, as well as the albumin content in serum. However, it failed to restore either liver lipid peroxide and reduced glutathione (GSH) content or lactate dehydrogenase and superoxide dismutase activities to normal level in the liver. In another study, *Nigella sativa* seeds exerted strong biocidal effects against miracidia, cercariae, and adult worm stages of against *Schistosoma mansoni* and also showed an inhibitory effect on egg-laying of adult female worms (Mohamed et al. 2005b). *N. sativa* crushed seeds induced an oxidative stress against adult worms which was indicated by a decrease in the activities of both antioxidant enzymes, superoxide dismutase, glutathione peroxidase, and glutathione reductase and enzymes of glucose metabolism, hexokinase and glucose-6-phosphate dehydrogenase. Disruption of such enzyme activities in adult worms could render the parasite vulnerable to damage by the host and may play a role in the antischistosomal potency of *N. sativa*. Both *N. sativa* extract and thymoquinone were found to act as protective agents against the chromosomal aberrations induced in mouse cells as a result of schistosomiasis (Aboul-Ela 2002). Karyotyping of the mice cells illustrated that the main abnormalities were gaps, fragments and deletions especially in chromosomes 2, 6 and some in chromosomes 13 and 14. Another study showed garlic extract (AGE) and *Nigella sativa* oil separately prevented most of the hematological and biochemical changes caused by schistomiasis and markedly improved the antioxidant capacity of *Schistosoma mansoni*-infected mice compared to the infected-untreated ones (El Shenawy et al. 2008). Moreover, marked reduction in worms, tissue eggs and alteration in oogram pattern were recorded in all the treated groups.

Nigella sativa oil reduced both infection of *Aspiculuris tetraptera* and its eggs (Ayaz et al. 2007) in mice. Its antiparasitic effect was related to its stimulating immune system. Studies proved that *N. sativa* aqueous extract could be useful in the treatment of intestinal protozoan parasite *Blastocystis hominis* (El Wakil 2007). *N. sativa* aqueous extract at concentrations of 100 and 500 μg/mL showed a potent lethal effect on both *B. homninis* isolates. There was no significant difference between the inhibitory effect of *N. sativa* and metronidazole on the living cell count on the 6th day. On assessment of living cell rate which calculate percentage rate of living cell, *N. sativa* at 500 μg/mL concentration exhibited a significant inhibitory effect on both isolates.

Studies found *t*hat *N. sativa* and *Allium-cepa* oils had anthelmintic effect in the rats infected with *Trichinella spiralis* infection and increased the production of antibodies generated during life cycle of the parasite (Abu El Ezz 2005). *N. sativa* oil as prophylactic treatment prior to *T. spiralis* infection was more effective than *A. cepa* oil on both adult worms and muscle larval count

Treatment with methanolic extract of *Nigella sativa* seeds significantly attenuated the serum and hepatic malondialdehyde levels in *Plasmodium yoelli nigeriensis* -infected mice (Okeola et al. 2011). Additionally, nigella extract restored the activities of red cell antioxidant enzymes in

the infected mice to near normal. Further, nigella extract was found to be more effective than chloroquinone in parasite clearance and, in the restoration of altered biochemical indices by *P. yoelli* infection. The results suggested that *N. sativa* seeds had strong antioxidant property and, may be a good phytotherapeutic agent against *Plasmodium* infection in malaria.

Therapeutic Activity in Opioid Tolerance and Dependence

In a study of 35 known addicts of opiates, non opioid drug *N. sativa* was found to be effective in long-term treatment of opioid dependence; it significantly decreased withdrawal effects (Sangi et al. 2008). It not merely cured opioid dependence but also cured the infections and weakness from which majority of addicts suffered. In another study in mice, repeated administration of *Nigella sativa* oil (4 mL/kg, p.o.) along with morphine (5 mg/kg, s.c.) attenuated the development of tolerance, as measured by the hot plate test, and dependence, as assessed by naloxone (5 mg/kg, i.p.)-precipitated withdrawal manifestations (Abdel-Zaher et al. 2010). Concomitantly, nitric oxide overproduction and increase in brain malondialdehyde level induced by repeated administration of morphine to mice or by administration of naloxone to morphine-dependent mice were inhibited by co-administration of Nigella oil. Also, the decrease in brain intracellular reduced glutathione level and glutathione peroxidase activity induced by both treatments were inhibited by co-administration of the oil. The inhibitory effect of the oil was enhanced by concurrent i.p. administration of the NMDA receptor antagonist, dizocilpine; and concurrent i.p. administration of the NO synthase inhibitors; L-N (G)-nitroarginine methyl ester, aminoguanidine and 7-nitroindazole or the antioxidant, N-acetylcysteine. The results provided evidence that *N. sativa* oil, through inhibition of morphine-induced NO overproduction and oxidative stress, appeared to have a therapeutic potential in opioid tolerance and dependence.

Toxicity/Safety Studies

The total aerobic bacterial count was 7×10^7 cfu/g and the yeast and mould counts were 4×10^2 cfu/g in black cumin seeds. The low numbers observed for *Staphylococcus aureus* and *Bacillus cereus* made black cumin seeds acceptable, without any associated health hazard (Al-Jassir 1992). *N. sativa* seeds were characterized by a very low degree of toxicity (Ali and Blunden 2003). The low toxicity of *Nigella sativa* fixed oil administered orally and intraperitoneally in mice, evidenced by high LD_{50} values, key hepatic enzyme stability and organ integrity, suggesting a wide margin of safety for therapeutic doses of *Nigella sativa* fixed oil, but the changes in hemoglobin metabolism and the fall in leukocyte and platelet count must be taken into consideration (Zaoui et al. 2002a).

The aqueous, methanol and chloroform extracts of *N. sativa* seeds in four different doses, 6, 9, 14 and 21 g/kg caused no mortality of mice (Vahdati-Mashhadian et al. 2005). Methanol extracts at all doses and chloroform extract at the concentration of 21 g/kg significantly decreased animals weight. Degenerative changes in hepatic cells were observed only with aqueous extract of the seeds.

Safety assessment studies using Sprague dawley rats as test animals showed that 4% black cumin fixed oil (BCFO) and 0.30% black cumin essential oil (BCEO) were safe as serological indices like liver and kidney functioning tests, serum protein profile, level of cardiac enzymes, electrolytes balance were remained in the normal ranges even after 56 days of study (Tauseef Sultan et al. 2009). Rats fed on BCFO gained less weight as compared to control indicating slight anorexic effect of BCFO which could be useful in obesity related disorders.

Cardiac Hypertrophic Activity

The hearts of *N. sativa*-treated rats (treated for 1 month) developed a moderate but significant hypertrophy that was evident by an increase in

the heart weight to body weight ratio (Yar et al. 2008). The observed Nigella-induced cardiac hypertrophy was associated with an increase in the baseline cardiac inotropic properties as well as the maximal peak tension generation upon progressive cardiac stress by isoproterenol infusion. The demonstrated selective enhancement of the inotropic reserve favoured the physiological nature of Nigella-induced cardiac hypertrophy, similar to that provoked by exercise training. They also reported that long term (2 months) oral supplementation of *N. sativa* to rats induced moderate global (homogenous) cardiac hypertrophy, evident by significant increases in left ventricular and whole heart weights as well as the relative heart weight/body weight ratio (El-Bahai et al. 2009). The isolated perfused hearts of Nigella-treated rats showed enhanced levels of baseline peak tension, maximum rate of tension development, heart rate and myocardial flow rate. There was also a significant increase in the tension developed per gram left ventricular weight.

Allergy Problems

One case of contact dermatitis on the skin was reported after topical use of *N. sativa* oil (Steinmann et al. 1997). Another recent case of contact dermatitis due to *N. sativa* oil developed symptoms of generalized erythema mutliforme (Nosbaum et al. 2011).

Traditional Medicinal Uses

Black cumin, is used in herbal folk medicine all over the world especially in the Middle East, Europe and Asia since antiquity for the treatment and prevention of a number of diseases and disorders that include asthma, bronchitis, diarrhoea, dyslipidaemia, diabetes, hyperglycaemia, and related abnormalities headache, dysentery, infections, obesity, back pain, hypertension, gastrointestinal problems, eczema, boils, rheumatism, cancer, fungal infections, diabetes, hypertension, cardiac diseases, hemorrhoids, sexual diseases and as an abortifacient (Zaoui et al. 2002b; Al-Majed et al. 2001; Ali and Blunden 2003; Mahmood et al. 2003; Khan et al. 2003a; Salem 2005; Taskin et al. 2005; Thabrew et al. 2005; Meddah et al. 2009). For centuries, people in the Middle East and Southeast Asia have used *N. sativa* seeds for its homeopathic effects (Hansen et al. 2003). The seeds are considered as stimulant, diaphoretic, emmenagogue, and used by nursing mothers to increase milk secretion and as anthlemintic, analgesic and antiinflammatory agent (Grieve 1971; Al-Ghamdi 2001; Duke et al. 2002). Black cumin is also used as a corrigent or adjuvant of purgative and tonic medicines; and as a carminative in indigestion and bowel complaints. *N. sativa* oil has also been used to treat skin conditions such as eczema, abscesses, and boils and to treat cold symptoms and to fight parasitic infections.

The medicinal uses of *N. sativa* can also be found in oldest religious and medical texts. For example it is referred to as 'Melanthion' by Hippocrates and Dioscorides whereas in Islamic culture the seeds are the common drug used in Tibbe-Nabvi (Prophet's Medicine) through out the world (Mohammad Ismail 2009). Since prophet Muhammad mentioned its therapeutic efficacy and potential of cure, *N. sativa* is stated in books of Seerat that Prophet Muhammad himself used to take these seeds with the syrup of honey for therapeutic purposes.

Other Uses

Kalonji seeds are also used in India for putting among linen to keep away insects and also served as insecticides.

Comments

Nigella Sativa currently has five FDA separate patents in the U.S. and one in the UK for the treatment of: diabetes, inhibition of cancer growth, improvement of immune system, viral infections, psoriasis and asthma.

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Hovenia dulcis

Scientific Name

***Hovenia dulcis* Thunberg.**

Synonyms

Hovenia dulcis var. *glabra* Makino, *Hovenia dulcis* var. *latifolia* Nakai ex Y. Kimura, *Hovenia dulcis* var. *tometnella* Makino, *Hovenia pubescens* Sweet.

Family

Rhamnaceae

Common/English Names

Chinese Raisin Tree, Coral Tree, Japanese Raisin Tree, Korean Raisin Tree, Oriental Raisin Tree

Vernacular Names

Brazil: Cajú-Japonês, Chico-Magro, Uva-Do-Japão;
Chinese: Bei Zhi Ju, Chi-Chu, Ji Zhao Zi, Wan Zi Guo;
Czech: Dužistopka Sladká;
Dutch: Japanse Rozijnboom;
Eastonian: Magus Kompvekipuu;
French: Hovenia À Fruits Doux;
German: Japanischer Rosinenbaum, Japanisches Mahagoni, Quaffbirne;
Italian: Ovenia Dolce;
Japanese: Kemponashi;
Korean: Heotgeanamu, Hutgenamu;
Polish: Szypulatka Słodka;
Russian: Konfetnoe Derevo;
Spanish: Pasa Japonesa, Sarmiento Japonés;
Vietnamese: Chi Cu, Ké Trao, Khting Khéng, Van Tho.

Origin/Distribution

Hovenia dulcis is native to Japan, China, North and South Korea, It also occurs in montane forests of northern Thailand (Kopachon et al. 1996) and North Vietnam (Nguyen and Doan 1989) up to altitudes of 2,000 m. the tree is widely cultivated in China, Japan, Korea, India, North Africa, Southern Europe, Brazil, Cuba, USA mostly as a fruit tree and has been introduced as an ornamental tree to several countries and naturalized in some countries.

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Agroecology

In its native range, *H. dulcis* occurs in shady glens in humid situations where it forms extensive thickets, in secondary forests and also in stream-irrigated valleys in lower montane evergreen forests, 1,075 m to 1,250 above sea level as in Northern Vietnam and northern Thailand. It tolerates a wide pH range and soil types from acidic sandy, loamy to alkaline soils but does best in well-drained, moist sandy or loamy soils. It abhors waterlogged soils. It thrives in full sun but will tolerate partial shade. It is moderately drought tolerant.

Edible Plant Parts and Uses

The ripe fruit and fleshy, swollen contorted fruit peduncle and inflorescence rachis are sweet and edible raw or cooked. Dried the ripe fruits resemble raisins. These edible parts can be used as a substitute for honey and are used in making candy and wine.

Botany

A large canopy, deciduous tree reaching 20–30 m and a dbh (diameter at breast height) of 22–55 cm. Leaves, arranged spirally, ovate to oblong, 11–13 cm long by 5–9 cm wide, papery, apex acuminate, base rounded, truncate or cuneate with irregularly and shallowly serrated margins, glabrous above, veins prominent below with three primary nerves covered with fine brown hairs, petiole pilose, 12–14 mm long (Plates 1, 2, and 3). Flowers produced in terminal or axillary asymmetrical cymes, hermaphrodite, greenish–yellow, 6–8 mm across, pedicel and rachis glabrous, sepals ovate-deltoid and glabrous, petals obovate-spatulate, clawed, disk sparsely pilose, ovary globose, style shortly 3-fid and glabrous. Fruit stalks contorted above each fruit becoming swollen irregularly, fleshy and juicy, 3–7 mm diameter, green turning to reddish–brown or black as the fruit matures and edible (Plates 1, 2, and 3). Fruit globose, dehiscent capsule, 6.9–8.5 mm long by 6–7.5 mm wide, three-lobed, lime green becoming brown or black when ripe and edible. Each lobe with1 seed. Capsule sits on a small calyx cup with a stylar scar at the top of the fruit. Seed deep brown to purple black, 5–6 mm long, 4.8–6.0 mm wide, thin endosperm surrounding the embryo.

Plate 1 Oriental raisin tree fruits and leaves

Plate 2 Raisin tree leaves

Plate 3 Close-up of fruit with swollen, contorted fruit stalks.

Nutritive/Medicinal Properties

The major minerals found in the leaf and fruit stalk were K, Ca, Mg, Na Mn and the vitamin C content in the leaf was 4.8 mg/dL and in the fruit stalk 3.8 mg/dL (Jeong and Shim 1999). The leaf contained 7.30% crude protein, 1.37% fructose, 1,715.21 mg/dL malic acid, 497.99 mg/dL glutamic acid, 43.54 mg/dL linolenic acid and 1214.36 ppm of volatile compound *trans*-geraniol. The fruit stalk was found to be rich in total sugars (51.64%) with 8.83% sucrose, 439,18 mg/dL malic acid, 751.78 mg/dL proline, 23.15 mg/dL palmitic acid and 292.67 ppm of volatile compound isobutyric acid. The total sugar content was the highest in the fruits stalk than in the leaf and stem (Park and Kim 2005). Glucose was the highest followed by sucrose and fructose in the fruits stalk. Fructose was also high in the leaf and stem. Among free amino acids, aspartic acid, glutamic acid and alanine in descending order were dominant. Among organic acids, malic acid was the abundant in the fruits stalk, leaf and stem. Potassium contents were the highest among minerals from the fruits stalk, leaf and stem followed by calcium and magnesium. Nineteen organic acid compounds were identified in the fruit peduncle of *H. dulcis* (Jia et al. 2005). Nine compounds of them belong to polyhydric acids and 10 were fatty acids. Malic acid predominated accounting for about 2.88%, total unsaturated fatty acids accounted for 9.71% with linolenic acid and linoleic acid accounting for 5.06% and 3.35% respectively.

The combined yields of sugars and polyols in *trans Hovenia dulcis* (peduncles) was 18.4 (Hussain et al. 1990). This yield was much higher than the total saccharide and polyol content (2.4% w/w) of the sweet dried fruits of *Thladiantha grosvenorii* (Cucurbitaceae), a species that contained more than 1% w/w of the intensely sweet triterpene, mogroside V.

Hovenia species namely *Hovenia dulcis, H. acerba* and *H. trichocarpa* were found to contain triterpenoids, saponins, flavonoids and alkaloids (Xu et al. 2003b)

Three new dihydrofravonols named hovenitins I, II, and III were isolated from the soluble methanol fraction of the fruit and seeds together with four known flavonoids, (+)-ampelopsin, laricetrin, myricetin, and (+)-gallocatechin (Yoshikawa et al. 1997).

Hovenia dulcis seed contained about 8.0% oil, which was predominated by unsaturated fatty acids (over 87.46%) and linolenic acid was about 45.56%.The physicochemical properties of the oil were as follows: refraction index (n20) 1.478 9, relative density 0.918 7, iodine value 170.7 g I/100 g, saponification value 178.9 mg KOH/g. Four flavanoids were isolated from *Hovenia dulcis* seed and identified as dihydrokaempferol (I), quercetin (II), (+)-3,3′,5′,5,7-pen tahydroflavanone (III) and (+)-dihydromyricetin (IV) (Ding et al. 1997).

Three new saponin, saponin C_2(1a), D (2a), and G (3a), were isolated from *Hovenia dulcis* leaves and their structures were identified as 3-*O*-(2-*O*-α-L-rhamnopyranosyl-3-*O*-β-D-glucopyranosyl-α-L-arabinopyranosyl)jujubogenin, 3-*O*-(2-*O*-α-L-rhamnopyranosyl-β-D-glucopyranosyl)-20-*O*-α-L-rhamnopyranosyljujubogenin, and 3-*O*-β-D-glucopyranosyl-20-*O*-α-L-rhamnopyranosyljujubogenin, respectively (Kimura et al. 1981). Saponin E, isolated from the leaves of *Hovenia dulcis*, afforded a new dammarane triterpene aglycone, hovenolactone (H), on treatment with naringinase (Kobayashi et al. 1982). The molecular structure of saponins E and H were determined to be 3-*O*-(2-*O*-α-L-rhamnopyranosyl-β-D-glucopyranosyl)hovenolactone and 3-*O*-β-D-glucopyranosylhovenolactone, respectively. Treatment of saponin D from *H. dulcis* leaves with sodium metal in ethanol afforded the aglycone jujubogenin, saponin G and a new compound whose structure was characterized as 20-*O*-α-L-rhamnopyranosyljujubogenin (Ogihara et al. 1987). From the fresh leaves of *Hovenia dulcis* var. *tomentella,* two new aroma glycosides named kenposide A and B were isolated together with the known glycoside, icariside C1 (Yoshikawa et al. 1993a).

Three peptide alkaloids, frangulanine, hovenin-A and hovenin -B were isolated from the root bark of *Hovenia dulcis* and *H. tommentella* (Takai et al. 1973). Hovenin-A was shown to be des-N-methylfrangulanine. Hovenoside G of

Hovenia dulcis (root bark) which produced ebelin lactone on acid hydrolysis was found to yield jujubogenin on Smith-de Mayo degradation (Kawai et al. 1974). Two major saponins, hovenosides D (1) and G (2) and a minor saponin, hovenoside I (3), were isolated from the root barks of *Hovenia dulcis* (Inoue et al. 1978). The full molecular structures of these saponins were elucidated as 3-*O*-[(2-*O*-β-D-xylopyranosyl)-3-*O*-(2-*O*-β-D-xylopyranosyl-6-*O*-β-D-glucopyranosyl-β-D-glucopyranosyl)-α-L-arabinopyranosyl]- jujubogenin, 3-*O*-[(2-*O*-β-D-xylopyranosyl)-3-*O*-(2-*O*-β-D-xylopyranosyl-β-D-glucopyranosyl)-α-L-arabinopyranosyl] jujubogenin, and 3-*O*-[(2-*O*-β-D-xylopyranosyl)-3-*O*-β-D-glucopyranosyl-α-L-arabinopyranosyl] jujubogenin respectively.

Extracts from *H. dulcis* had been reported to accelerate detoxification of ethanol, and to possess hepatoprotective, antioxidative, antimicrobial, antidiabetic properties (Hyun et al. 2010). Also *H. dulcis* had been reported to have antisweet, antigiardia, anticancer, nootropic, adaptogenic, trypanocidal, antiobesity and neuroprotective activities as presented below.

Antioxidant Activity

Vanillic acid (3-methoxy-4-hydroxybenzoic acid) and ferulic acid (3-methoxy- 4-hydroxycinnamic acid) isolated from hot aqueous extract of *H. dulcis* exhibited antioxidative activity (Cho et al. 2000). The DPPH-radical scavenging activity of ferulic acid appeared more active than that of vanillic acid. DPPH-radical scavenging concentration of ferulic acid and vanillic acid were 14 μg/mL and 100 μg/mL respectively. Ethanol extracts of *H. dulcis* leaf and fruit stalk and its ethyl acetate fraction showed the highest antioxidant and nitrite scavenging activity (Jeong and Shim 2000).

Oral administration of a homogenated extract of *H. dulcis* for 14 days accelerated free radical scavenging by increasing superoxide dismutase activity in the brain and kidney of mice and significantly decreasing malondialdehyde level in the blood serum and tissues of the brain and liver (Wang et al. 1994). Among the eight phenolic compounds isolated from a methanolic extract of *Hovenia dulcis*, (−)-catechin had a DPPH free radical scavenging effect with an IC_{50} value of 57.7 μM, and a superoxide anion radical scavenging effect with an IC_{50} value of 8.0 μM (Li et al. 2005). Both (−)-catechin and (+)-afzelechin had ABTS cation radical scavenging effects with IC_{50} values of 7.8 μM and 23.7 μM, respectively.

Antisweet Activity

An aqueous extract of *Hovenia dulcis* leaves was found to selectively reduced sweetness perception in humans (Saul et al. 1985; Kennedy et al. 1988). The taste-active sweetness inhibitor was found to be triterpene saponin glycoside, 'hodulcin'. It was suggested that some saponins having jujubogenin as their genin, by analogy with the anti-sweet jujubogenin saponin from *Ziziphus jujuba*, the saponin from *H. dulcis* might have similar sweet-taste-suppressing qualities. From the fresh leaves of *H. dulcis*, five new dammarane glycosides named hodulosides I–V (1–5) were isolated besides the known saponins hovenoside I (6), saponins C_2,(7), E (8) and H (9) and jujuboside B (10); all showed antisweet activity (Yoshikawa et al., 1991). Five new dammarane glycosides named hodulosides VI–X (1–5) were isolated from the leaves; hodulosides VII–X showed antisweet activities (Yoshikawa et al. 1993b).

Suttisri et al. (1995) reviewed the phytochemistry and biological activity of more than 40 triterpenoid sweetness inhibitors based on the oleanane and dammarane skeletons. These saponins were isolated from the leaves of three medicinal plants, namely, *Gymnema sylvestre, Ziziphus jujuba* and *Hovenia dulcis.*

Alcohol Detoxification Activity

Administration of *H. dulcis* extract to rats prior to alcohol ingestion decreased blood alcohol and

acetaldehyde levels by 40% and 37% respectively (Okuma et al. 1995). When the ethanol extract was administered to men prior to alcohol intake, decreases in alcohol and acetaldehyde concentrations in saliva were observed, and the expiratory alcohol concentration at 1 h after drinking beer was significantly decreased in five men out of eight. Level of alcohol in mouse and human sera were significantly reduced by 42% by oral administration of a mixture of *Hovenia dulcis* and *Alnus japonica* (An et al. 1999). A single treatment of *H. dulcis* reduced serum alcohol concentration to 32% compared to 13% with *A. japonica*. Both extract enhanced the activity of alcohol dehydrogenase and glutation-S-transferase in the live. The mixture of both extracts also significantly reduced cathepsin activity but *A. japonica* extract alone had no effect. The mixture of both extracts had synergistic effect in reducing serum alcohol concentration and improving the detoxification process in the liver.

H. dulcis fruit was found to significantly reduce sleeping time and reduce alcohol concentration in the blood of mice with acute alcohol toxicity (Ji et al. 2001)

The aqueous extract of *H. dulcis* was found to increase the activity of alcohol dehydrogenase and to reduce the alcohol concentration in blood of male Kuming mice after given alcohol (Chen et al. 2006). The results suggested that extract could relive alcohol toxicity and prevent drunkenness by restraining the absorption of alcohol in the gastrointestinal tract and promoting the metabolism of alcohol in the liver. Results of studies suggested that n-butanol extract of fruits and ethyl acetate extract of stem of *H. dulcis* were found to have relatively higher alcohol dehydrogenase activity; also, the n-butanol extract, hot water extract of fruits, and water extract of stem had relatively higher aldehyde dehydrogenase activity (Xu et al. 2003a). Studies found the microplate reader screening to be a quick, accurate, and effective method to assay both enzymes in-vitro. The hot, aqueous fruit extract of *Hovenia dulcis* compared to the stem and leaf extracts gave the highest activity for decreasing alcohol concentration which was 138% of control (Kim et al. 2006).

Hepatoprotective Activity

The methanol extract of *Hovenia dulcis* fruits exhibited significant hepatoprotective activity against carbon tetrachloride induced toxicity in rats and D-galactosamine /lipopolysaccharide induced injury in mice (Hase et al. 1997b). Hase et al (1997a) also found that the aqueous seed extract of *H. dulcis* markedly inhibited the increase of ALT, AST, MDA, TG (triglyceride) and TC (total cholesterol) induced by alcohol plus lipopolysaccharide in rats. The methanol-soluble fraction from the seed and fruit of *Hovenia dulcis* was found to show an inhibitory effect on the alcohol-induced muscular relaxation and a protective activity on the D-galactosamine /lipopolysaccharide or carbon tetrachloride-induced liver injury (Yoshikawa et al. 1997). Three new dihydrofravonols named hovenitins I, II, and III were isolated from the fraction together with four known flavonoids, (+)-ampelopsin, laricetrin, myricetin, and (+)-gallocatechin (Yoshikawa et al. 1997). Hovenitin I and (+)-ampelopsin, exhibited an inhibitory activity on the ethanol-induced muscle relaxation in rats. In addition, hovenitin I showed a protective activity on the liver injury induced by D-galactosamine/lipopolysaccharide or carbon tetrachloride in mice.

Administration of *H. dulcis* extract to male Sprague-Dawley rats attenuated hepatic fibrosis induced by carbon tetrachloride and was attributable to inhibition of TIMP-1 mRNA expression in hepatic tissues by the extract (Liu et al. 2006). The methanol extract also significantly protected against cultured primary rats hepatocytes. The active ingredient in the methanol extract was found to be (+)-ampelopsin. Studies showed that plasma activities of GPT and GOT, and hepatic levels of malondialdehyde were significantly lowered in mice treated with *Hovenia dulcis* fruit ethanol extract as compared to mice treated with carbon tetrachloride only (Fang et al. 2007). Histological observations showed that the extract could attenuate the liver fibrosis and necrosis caused by carbon tetrachloride. Treatment with the extract decreased hepatic collagen (alpha1)(I) and collagen (alpha1)(III) mRNA expression and significantly reduced the elevate changes in

methionine adenosyltransferase (MAT) 2A gene expression caused by carbon tetrachloride.

Pretreatment of mice with *H. dulcis* leaf methanol extract lowered the elevated activities of serum aminotransferase and hepatic cytochrome P450 induced by benzo(α)pyrene (B(α)P) (Park et al. 2009). The extract also significantly prevented the elevation of hepatic malondialdehyde content and depletion of glutathione content induced by B(α)P. In addition, the increased activities of superoxide dismutase, catalase and glutathione peroxidase after B(α)P-treatment were decreased and glutathione S-transferase activity was increased. The results suggest that *Hovenia dulcis* leaf extract had a protective effect on liver damage by B(α)P through the mechanisms of decreasing lipid peroxide and activities of free radical generating enzymes.

Results of in-vivo studies in mice demonstrated that *Hovenia dulcis* seed extract could protect against acute alcohol-induced liver injury without any toxic side effects (Du et al. 2010). Administration of the extract significantly decreased the activities of serum alanine aminotransferase (ALT) and aspartate transaminase (AST) and protected against alcohol-induced alcohol dehydrogenase (ADH) elevation in mice. Acute toxicity tests showed that a single dose of oral *Hovenia dulcis* seed extract up to 22 g/kg did not result in any death or toxic side effects in mice during 14 days' observation.

Antidiabetic Activity

Treatment of alloxan diabetic mice with *H. dulcis* extract significantly reduced blood sugar and increase hepatic glycogen (Ji et al. 2002). Blood glucose level in hyperglycemic mice induced by streptozotocin was significantly reduced after administration of *Hovenia dulcis* extract compared to the control mice (Kim et al. 2005).

Antimicrobial Activity

Vanillic acid and ferulic acid isolated from hot aqueous extract of *H. dulcis* exhibited antimicrobial activity against Gram-positive bacteria, Gram-negative bacteria and yeast (Cho et al. 2000). Vanillic acid (500 μg/disc) showed stronger activity than that of ferulic acid at the same concentration against Gram-positive bacteria, such as *Staphylococcus aureus*, *Staphylococcus epidermidis, Bacillus subtilis, Micrococcus luteus, Pediococcus damnosus* and Gram-negative bacteria namely *Escherichia coli, Pseudomonas aeruginosa* and *Salmonella typhi*. Methanol-soluble fraction of hot-water extracts from *Hovenia dulcis* leaves showed antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli* (Cho et al. 2004). The antimicrobial-active compound, was isolated elucidated as a 3(Z)-dodecenedioic acid; the compound inhibited growths of *S. aureus* and *E. coli* at 500 μg.

Anticancer Activity

Ethanol extract of *H. dulcis* exhibited more potent growth inhibitory activity of Hep3B and MCF-7 cell lines than the aqueous extract (Lee et al. 1999). The ethanol bark extract of bark (0.5 mg/mL) inhibited the growth of MCF-7 by 90%. The extract at the tested concentration did not show considerable cytotoxicity on HEL299 cell line. Methanol extract of young leaves of *H. dulcis* exhibited inhibitory activity against tumour cells lines tested while the ethanol extracts of pseudofruit showed high degree of selectivity against to SP2/0 mouse myeloma and BW lymphoma cells in-vitro (Castro et al. 2002).

Adaptogenic Activity

Oral administration of a homogenated extract of *H. dulcis* for 14 days increased tolerance towards cold and heat and prolonged swimming time of mice (Wang et al. 1994).

Neuroprotective Activity

The ethylacetate-soluble fraction from a methanolic extract of *Hovenia dulcis* exhibited neuroprotective activity against glutamate-induced

neurotoxicity in mouse hippocampal HT22 cells (Li et al. 2005). The neuroprotective activity-guided isolation resulted in 8 phenolic compounds (1–8), such as vanillic acid (1), ferulic acid (2), 3,5-dihydroxystilbene (3), (+)-aromadendrin (4), methyl vanillate (5), (−)-catechin (6), 2,3,4-trihydrobenzoic acid (7), and (+)-afzelechin (8). Among these, compounds 6 and 8 had a neuroprotective effect on the glutamate-induced neurotoxicity in HT22 cells.

Antigiardia Activity

The dichloromethane fraction of *H. dulcis* leaf methanol extract was found to inhibit growth of *Giardia lamblia* the causative agent of giardiasis, a common parasitic infection of the human and animal digestive tract (Gadelha et al. 2005). The fraction caused degenerations in the surface, modifications in the cell shape and alterations in the localization of nuclei and adhesion of G lamblia. The fraction did not elicit cytotoxic effects in mammalian cells.

Antiallergic Activity

Two bioactive novel triterpene glycosides with a migrated 16,17-seco-dammarane skeleton named hovenidulciosides A1 and A2 were isolated from the seeds and fruit of *Hovenia dulcis* (Yoshikawa et al. 1995). Hovenidulciosides A1 and A2 exhibited inhibitory activity on the histamine release from rat mast cells induced by compound 48/80 or calcium ionophore A-23187. Four bioactive methyl-migrated 16,17-seco-dammarane type triterpene glycosides designated hovenidulciosides A1, A2, B1, and B2 were isolated from the seeds and fruit of *Hovenia dulcis* together with hoduloside III and (+)-gallocatechin (Yoshikawa et al. 1996). All were found to inhibit the histamine release from rat peritoneal exudate cells induced by compound 48/80 and calcium ionophore A-23187.

Cardiovascular Activity

Methanol and water extract of *H. dulcis* cortex inhibited angiotensin converting enzyme (ACE) activity by 81 and 76%, respectively, at the concentration of 4,000 μg/mL which were similar to level obtained with (85%) of commercial peptide-type ACE inhibitor. Superoxide radical scavenging activity of two extracts (99.5%–99.9%) were stronger than that (69%) of ascorbic acid at the final concentration of 200 μg/mL.

Nootropic Activity

Six saponins were isolated from *H. dulcis* and elucidated as 3-*O*-stigmasterol-(6-*O*-palmitoyl)-β-D-glucopyranoside (1), β-daucosterin (2), hovenidulcioside A1 (3), hoduloside I (4), hoduloside IV (5), and saponins C2 (6) (Yi and Fu 2009). Among them, compounds 5 and 6 had an enhancing effect on the learning and memory ability of natural senile mice, and they could improve the impairment of memory acquirement, consolidation and recurrence in mice induced by scopolamine, sodium nitrite and 40% ethanol, respectively. The results suggested that the aglycone of jujubogenin might be the main saponins contributing to the nootropic effect of total saponins from *Hovenia dulcis.*

Mitochondrial Swelling Activity

Frangulanine a cyclopeptide alkaloid isolated from *Hovenia dulcis* induced mitochondrial swelling in 0.15 M KCl solution at the concentration of 6.5 μM (Kawai et al. 1977).

Antiobesity Activity

Recent studies in mice showed that *H. dulcis* fruit vinegar had weight reducing function by inhibiting body weight increase and fat content (Du et al. 2012). The fruit vinegar also markedly reduced the denaturation of mouse blood lipid, and attenuated

hepatomegaly caused by chronic alcoholism. It also decreased MDA (malondialdehyde) content in the liver, increased GSH (glutathione) content and improved ADH (alcohol dehydrogenase) activity. Further the fruit vinegar could also prevent arteriosclerosis through reducing blood lipid.

Neuroleptic Activity

Hovenosides, saponin fraction from H. dulcis, was found to have neuroleptic activity at a low dose of of 30 mg/kg i.p. without undesirable effects such as motor incoordination, muscle relaxation, hypothermia and antidiuresis (Saito et al. 1979). Hovenosides also enhance intestinal motility.

Trypanocidal Activity

Aqueous extract of pseudofruit and methanolic extracts of young leaves of *H. dulcis* exhibited trypanocidal activity against *Trypanosoma cruzi* with mortality rates of 95 and 100% respectively (Castro et al. 2002).

Traditional Medicinal Uses

According to traditional Chinese medicine, *H. dulcis* is neutral in nature, sweet and sour in flavour, attributive channel to spleen and lung, possesses the effect of clearing away heat, promoting diuresis and detoxifying alcoholic intoxication (Xu et al. 2004). *H. dulcis* has been used to treat alcohol abuse safely and effectively in China for more than a millennium. It is traditionally known as having the effect of alleviating lingering intoxication, treating thirsty, emesis, urinal disorder and constipation. Both the fruits and the fleshy peduncles are deemed to be antifebrile, laxative, diuretic and to have antivinous properties (Stuart 1979). The bark of the tree is used in rectal diseases. In Vietnam, ripe fruit and peduncles used for the treatment of alcoholic intoxication, dysuria, general ability and dry throat (Nguyen and Doan 1989).

Other Uses

The tree provides fine and hard timber that is used for building construction and fine furniture. In Thailand, it is one of 30 potential species identified as a substitute for *Eucalyptus* spp., commonly planted for reforestation. It is also planted as an ornamental tree.

Comments

Seeds are spread mainly by birds, but also by many other animals.

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Ziziphus jujuba

Scientific Name

***Ziziphus jujuba* Miller**.

Synonyms

Rhamnus lucidus Salisb., *Rhamnus soporifer* Lour., *Rhamnus ziziphus* L., *Ziziphus jujuba* var. *spinosa* (Bunge) Hu ex H. F. Chow, *Ziziphus nitida* Roxb., *Ziziphus sativa* Gaertn., *Ziziphus sinensis* Lam., *Ziziphus spinosa* (Bunge) Hu ex F. H. Chen, *Ziziphus soporifer* (Lour.) Schult., *Ziziphus vulgaris* Lam., *Ziziphus vulgaris* var. *spinosa* Bunge, *Ziziphus zizyphus* (L.) Meikle, *Zizyphus jujuba* Mill.

Family

Rhamnaceae

Common/English Names

Chinese Date, Chinese-Date, Chinese Jujube, Chinese Plum, Chinese Red Date, Common Jujube, Jujube, Jujube Tree.

Vernacular Names

Afghanistan: Berra (Pashto);
Arabic: Annab, Aunnabe-Hindi, Aunnabehindi, Ennab, Unnab, Unab, Nabec, Nabig, Nabiq, Sidr, Zenzeli;
Bangladesh: Bozoi, Kool, Kul;
Brazil: Jujuba;
Burmese: Hsi:, Zee-Pen, Zi, Ziben, Zizidaw;
Chinese: Da Zao, Beijing Mi Zao, Hei Zao, Hei Tsao, Hong Zao, Hung Tzao, Peiching Mi Tzao, Suan Zao Ren, Tzao, Wu He Hong Zao, Wu Ho Hung Tzao, Zao, Zao Shu;
Czech: Cicimek Datlový, Čínská Datle, Jujuba;
Danish: Almindelig Jujube, Brystbærtræ;
Dutch: Jujubeboom;
Eastonian: Harilik Kreektürn;
Fiji: Ber;
Finnish: Kiinanjujuba:
French: Circoulier, Dattier De Chine, Guindanlier, Jujube De Chine, Jujubier, Jujubier Commun, Jujubier De Chin;
German: Brustbeerbaum, Brustbeere, Chinesische Dattel, Chinesische Jujube, Domjujube, Jujube, Judendom, Rote Dattel;
Greek: Tzintzola;
Hungarian: Jujuba (Fa), Kínai Datolya, Zsidótövis;
India: Boguri (Assamese), Boroi (Bengali), Badara, Badari, Ber, Beri, Baer, Bor, Kath Ber (Hindu), Badari, Bare, Bari, Barihannu, Ber, Bogare, Bogari, Bogori, Bogri, Bore, Egaci, Egasi, Elaci, Elachi, Elasi, Ilanji, Ilantai, Ilici, Ilisi, Jati, Jelachi, , Karkandhu, Karkhandhyalachi, Yalachi-Hannuyagachi, Yalachi, Yelachi, Yelanji, Yelchi, Yellachi (Kannada), Badaram, Badari,

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Elanta,Elantap-Pazham, Elantha, Elenda, Elentha, Ilanta, Ilantha, Kolam, Lantaparintoddali, Parintudai, Perimtoddali, Perintoddah, Perintutali, Yelanda (Malayalam), Boroi (Manipuri), Bori, Bor, Baher, Ber, Bera, Bhor, Bora (Marathi), Borai, Kawl-Sun-Hlu (Mizoram), Ubhayakantaka (Oriya), Ajapriya, Badara, Badari, Balashta, Dridhabija, Dviparni, Ghonta, Grddhanakha, Gudaphala, Kantaki, Karkarmadhu, Kola, Koli, Kuvali, Madhuraphala, Mahadebara, Nakhi, Nripabadari, Nripeshta, Phalashayshira, Prithukoli, Rajabadari, Rajakoli, Rajavallabha, Sauvira, Srigalakoli, Sukrapriya, Sukshmapatrika, Sukshmaphala, Suphala, Svachha, Tanubija, Ubhayakantaka, Vadari, Vatadalla (Sanskrit), Adidaram, Atitaram, Attiram, Elandai, Elandei Vayr, Elandap-Pazham, Ilandai, Ilantai, Ilantai Ilai, Ilantai Ppalam, Ilandai Maram, Iradi, Iratti, Koli, Kondai, Korkoti, Kulari, Kullari, Kulavali, Kulvali Kol, Padari, Sivagam, Vadari, Vatari (Tamil), Badaramu, Badari, Badarika, Ganga-Regu-Pandu, Gangaregu, Gangarenu, Karkandhuvu, Karkhanduvu, Ragu, Regi, Regu, Regu-Pandu, Renga, Rengha, Reni, Renu, Reyghoo, Reygoo (Telugu), Baer, Ber ,Annab, Unab, Unnab (Urdu), Barholi, Bodokoli, Bodori, Koli (Uriya);
Indonesia: Bidara, Dara, Widara;
Iran: Kanar, Kunar, Nabik;
Iraq: Aunnaberhindi, Nabig, Sidr;
Italian: Giuggiole, Giuggiolo;
Japanese: Sanebuto Natsume;
Kampuchea: Putrea;
Korean: Dae-Choo, Moet-Dae-Choo, Moettaec-hunamu;
Laos: Than;
Malaysia: Bedara, Bedara Cina, Bidara, Epal Siam, Jujub, Langkeng;
Nepal: Baer;
Pakistan: Baryan, Singli, Unnab;
Persian: Annab, Kanar, Kunar, Nabik, Sinpo-I-Jilani;
Philippines: Manzanas, Mansanitas (Spanish), Mansanitas (Tagalog);
Polish: Chiński Daktyl, Jujuba, Jujuba Pospolita;
Portuguese: Açofeifeira;
Russian: Kitajskij Finik, Unabi;
Slovaščina: Čičimak Navadni;
Spanish: Azufaifo, Azufaifo Chino, Jinjolero;
Thai: Bhud-Saar, Phutsaa Cheen;
Tibetan: Gya-Sug, Ko La, Rgya Sug;
Turkish: Hünnap;
Vietnamese: Táo, Táo Tàu.

Origin/Distribution

Chinese jujube originated in China where they have been cultivated for more than 4,000 years. It was distributed beyond China centuries ago and today it is cultivated to some extent in Russia, northern Africa, southern Europe, the Middle East, Caribbean and the southwestern United States. It is widely cultivated and naturalized in Eurasia.

Agroecology

Chinese jujube although a mild temperate species can withstand extremely hot, dry temperatures, as well as cold temperatures down to −22°C. Winter dormancy allows it to withstand temperatures to subzero temperatures, yet it requires only a small amount of winter chill in order for it to set fruit. In its native range it is found in mountains, hills, sunny dry slopes, plains and is also widely cultivated below 1,700 m. Chinese jujube is fairly adaptable, but should be grown in full sun as they are shade intolerant. It is rather drought tolerant once established, but regular watering is important to ensure optimum productivity. It is adaptable on a wide diversity of soils including saline and alkaline soils but prefers a sandy-loamy, well-drained soil. It does not perform well in heavy, poorly drained soils.

Edible Plant Parts and Uses

Mature near ripe and ripe fruits are eaten fresh, dried, preserved, boiled or pickled. Ripe fresh fruits as well as the dried candied fruit are eaten

as snack or in herbal teas. Chinese dates are available in dried, unsmoked red form called *hóng zǎo* or in blacked smoked form called *hēi zǎo*. Smoking enhanced its flavour. In Asian groceries store in America, Europe and Australia, four types of preserved Chinese jujube are available: two shrivelled with intact skin, the dull maroon *hóng zǎo* (red jujube) (Plate 9) and the black *hēi zǎo* (black jujube) and two scored skin sugar preserves the *mi-zǎo* (honey jujube) and the seedless *wu-he-zǎo* (pitted jujube). Jujube powder and jujube oil are also processed from the fruit. Poached jujubes can be added to fruit compotes. A candy called "jujube", which is made from jujube paste, is available in the United States. In China, Korea, and Taiwan, a sweetened or honey tea syrup containing jujube pulps is available in glass jars (Plate 10), and canned jujube tea or dried, pulverized jujube pulp in the form of teabags is also available. The honey or sweetened syrup when diluted with cold water makes a refreshing and nutritious drink. Jujube juice made from preseed jujubes and jujube vinegar from fermented fruits are also available. In China, a wine made from fermented jujubes called *hong zao jiu* . The ripe fruits are sometimes preserved by storing in a jar filled with Chinese liquor which allows them to store longer over the winter, such jujubes are called *jiu zao* (spirited jujubes). In West Bengal and Bangladesh, the fruits are pickled. In Vietnam and Taiwan, fully mature near ripe fruits are harvested and sold in the local markets and also exported to other southeast Asian countries (Plates 5, 6, 7, and 8). They are crispy, sweet and delicious.

Jujubes fresh or the dried are relished in an array of Asian culinary cuisines – food dishes and desserts. Dried, candied jujubes can added to cakes and other desserts, soups, stews, or stuffings; or substituted in recipes that call for raisins or dates In Vietnam, the dried fruits are used in desserts such as *sâm bổ lượng,* a cold beverage that comprised the dried jujube, longan, fresh seaweed, barley, and lotus seeds. In Korea, jujubes are featured in the popular ginseng chicken dish called *samgyetang*. To prepare the dish, whole young chicken is stuffed with glutinous rice and boiled in a broth of Korean ginseng, dried seeded jujube fruits, garlic, and ginger. A popular Chinese dish is chicken stewed with Goji berries, red dates and shitake mushroom. Other common, but noteworthy recipes include, braised chicken red dates with bacon, pork, scallop and red dates soup, tomato and red date porridge and Chinese jujube and cheddar strudel. Chinese jujube butter can be made by cooking the ripe fruits with water, sugar and seasonings such as cinnamon, clove, nutmeg, lemon and vinegar. In Tamil Nadu, India, the dried fruits minus the seed are pounded with tamarind, red chillies, salt, and jaggery to make a dough and dried again. This is used to make delicious cakes such as *ilanthai vadai* or *regi vadiyalu* and in various dishes.

A jujube honey is produced in the Atlas Mountains of Morocco.

Botany

A small, deciduous, erect tree, 5–10 m high, spinose or unarmed with brown to gray-brown bark (Plate 1) and spreading often drooping branches. Suckers frequently arise from the roots near the trunk. Young branchlets gray brown or green, flexuose, zig-zag with or without 2 stipular spines (Plate 2). Stipular spines slender, caducous long spines erect, to 3 cm, stout; short spines recurved. Petioles 1–6 mm, glabrous. Leaves alternate, dark green above, pale green below, ovate, ovate-elliptic, or elliptic-oblong, 3–7 × 1.5–4 cm, papery, 3- veined from base, base slightly asymmetric, obtuse, margin crenate-serrate, apex obtuse or rounded, rarely acute (Plates 2, 3, and 4). Flowers yellow-green, fragrant, bisexual, pentamerous, glabrous, solitary or 2–8 clustered in axillary cymes, shortly pedunculate (Plates 2, 3, and 4). Pedicel 2–3 mm; sepals ovate triangular distinctly keeled below; petals obovate, clawed at base, disk orbicular, flesh and 5-lobed; ovary basally slightly immersed in disk; style 2 connate halfway. Drupe green in colour, but as it ripens it goes through a yellow-green stage becoming red or red-purple at maturity, subglobose, oblong, ellipsoid, or narrowly ovoid,

Plate 1 Old jujube tree with gray-brown bark and drooping branches

Plate 2 Flowering, drooping branches

Plate 3 Close-up of leaves and greenish-yellowish flowers

2.5–5 cm by 2–3.5(–4.5) cm in diameter (Plates 5, 6, 7, and 8); mesocarp fleshy, thick, sweet to acid-sweet; stone acute or obtuse at both ends, 2-loculed, 1- or 2-seeded (Plate 8); fruiting pedicel 2–5 mm or longer. Seeds compressed-orbicular, 10×8 mm.

Plate 4 Fertilised flowers with very young fruits

Plate 5 Harvested mature, unripe fruits

Plate 6 Close-up of mature fruit

Nutritive/Medicinal Properties

Food value of raw, Chinese jujube fruit per 100 g edible portion was reported as follows (USDA

Plate 7 Crispy white flesh and one seeded

Plate 8 Ripe jujbe fruits

Plate 9 Dried, red ripe jujubes, *hóng z o*

Plate 10 Bottle of honey jujube tea concentrate

2012): water 77.86 g, energy 79 kcal (331 kJ), protein 1.20 g, total lipid (fat) 0.20 g, ash 0.51 g, carbohydrate 20.23 g; minerals – calcium 21 mg, iron 0.48 mg, magnesium 10 mg, phosphorus 23 mg, potassium 250 mg, sodium 3 mg, zinc 0.05 mg, copper 0.073 mg, manganese 0.084 mg; vitamins – vitamin C (total ascorbic acid) 69 mg, thiamin 0.020 mg, riboflavin 0.040 mg, niacin 0.900 mg, vitamin B-6 0.081 mg, and vitamin A 40 IU (2μg RAE). Ripe *Ziziphus jujuba* fruit contained 42.25% water and 44.0% soluble solids (Vidrih et al. 2008). Mesocarp contained on dry matter basis 1.1% proteins, 0.73% total phenols and 1.7% of ash, 12.4% of insoluble and 6.7% of soluble fibres, 36.5.0% glucose, 33.4% fructose and 0.22% sucrose, 83.8 mg/100 g ascorbic acid and 39.4 mg/100 g dehydro ascorbic acid. Jujube seeds contained 2.5% total fat.

Triglycerides having medium-chain fatty acids were most abundant in the Spanish varieties studied (Guil-Guerrero et al. 2004). The main fatty acids were 12:0 (18.3%), 10:0 (12.5%), 18:2n6 (9.27%), 16:1n7 (8.50%), 16:0 (7.25%), and 18:1n9 (5.34%) on total saponifiable oil. The fruits yielded 1.33/100 g saponifiable oil on a dry weight basis. Fatty acid profiles of fruits were found to be influenced by their developmental stage. Carotenes were found to be in good agreement with other fruits, varying from 4.12 to 5.98 mg/100 g on a dry weight basis. The

contribution to vitamin value reach a medium of 38 μg RE/100 g on a fresh weight basis.

Food value of dried, Chinese jujube fruit per 100 g edible portion was reported as follows (USDA 2012): water 19.70 g, energy 287 kcal (1,202 kJ), protein 3.70 g, total lipid (fat) 1.10 g, ash 1.90 g, carbohydrate 73.60 g; minerals – calcium 79 mg, iron 1.80 mg, magnesium 37 mg, phosphorus 100 mg, potassium 531 mg, sodium 9 mg, zinc 0.19 mg, copper 0.265 mg, manganese 0.305 mg; vitamins – vitamin C (total ascorbic acid) 13 mg, thiamin 0.210 mg, riboflavin 0.360 mg, and niacin 0.500 mg.

Other Fruit Phytochemicals

Guanosine 3′: 5′-monophosphate was identified in *Z. jujube* fruit and its content increased 90-fold during fruit ripening (Cyong and Takahashi 1982). Zizyphus-pectin A from *Ziziphus jujuba* fruits contained *O*-acetyl groups located at positions 2,3,6 of the 2,3,6 tri-O acetylated D-galactopyranosyl residues in galactan side chains (Tomoda et al. 1985). Daechualkaloid-A a new pyrrolidine alkaloid was found in the fruit of *Z. jujube* (Han et al. 1987). Seventy eight volatile compounds were identified in the fruit of *Z. jujuba* var. *inermis* among which aliphatic acids and carbonyl compounds accounted for 62.97 and 29.56% of total volatiles respectively (Wong et al. 1996). The major constituents were decanoic acid (19.98%) and dodecanoic acid (15.64%).

Eleven triterpenoids, namely colubrinic acid (0.74%), alphitolic acid (0.09%), 3-*O*-*cis*-*p*-coumaroyl alphitolic acid (0.19%), 3-*O*-*trans*-*p*-coumaroyl alphitolic acid (0.19%), 3-*O*-*cis*-*p*-coumaroyl maslinic acid (0.08%), 3-*O*-*trans*-*p*-coumaroyl maslinic acid (0.08%), betulinic acid (0.41%), oleanolic acid (0.05%), betulonic acid (0.50%), oleanonic acid (0.59%) and zizyberenalic acid (0.19%) were isolated quantitatively from *Ziziphus jujube* (Lee et al. 2003). Eleven triterpenoides were isolated from the fruits of *the Zizyphus jujuba*: ceanothane-type triterpenes: colubrinic acid (1), zizyberenalic acid (11); lupane-type triterpenes: alphitolic acid (2), 3-*O*-*cis*-*p*-coumaroyl alphitolic acid (3), 3-*O*-*trans*-*p*-coumaroyl alphitolic acid (4), betulinic acid (7), betulonic acid (9); and oleanane-type triterpenes: 3-*O*-*cis*-*p*-coumaroyl maslinic acid (5), 3-*O*-*trans*-*p*-coumaroyl maslinic acid (6), oleanolic acid (8), oleanonic acid (10) (Lee et al. 2004a, b).

Jujube fruit were a good source of phenolics (especially flavonoids), comparable to prunes, and therefore should be recommended by nutritionists to be part of our diet (Hudina et al. 2008). Two phenolic acids from the hydroxycinnamate sub-class (chlorogenic acid and caffeic acid) and three flavonoids (catechin, epicatechin and rutin) were found in the fruit of seven Chinese jujube cultivars. Acid jujube fruit had the highest content of hydroxycinnamic acids, as well rutin and epicatechin, while 'Zizao' had the highest catechin content. One new ceanothane-type triterpene and one new sesquiterpene, together with two known triterpenes, zizyberanalic acid and ursolic acid were isolated from the fruits of *Ziziphus jujuba* (Guo et al. 2009b). The structures of two new compounds were elucidated as 2α-aldehydo-A(1)-norlup-20(29)-en-27,28-dioic acid (zizyberanal acid), and zizyberanone. Ten triterpenoid acids (ceanothic acid, alphitolic acid, zizyberanal acid, zizyberanalic acid, epiceanothic acid, ceanothenic acid, betulinic acid, oleanolic acid, ursonic acid and zizyberenalic acid) were identified in the dried fruit of *Ziziphus jujuba* which has been widely used as one of the traditional Chinese medicines (TCMs) (Guo et al. 2009a). Guo et al. (2010a) found that the contents of triterpenic acids in the fruits of *Ziziphus jujuba* var. *spinosa* were higher than those in the fruits of *Z. jujuba*, especially for the compound pomonic acid.

The fruit of *Ziziphus jujube* contains zizybeoside II, the content ranged from 0.013 to 0.041% (Niu et al. 2008). Five compounds were isolated from *Ziziphus jujuba* var. *spinosa* and their structures were established as jujuboside D, jujuboside A, 5,7,4′-trihydroxyflavonol-3-*O*-β-*D*-rhamnopyranosy l-(1→6)-β-*D*-glucopyranoside, 6′″-coumaroylspinosin and phenylalanine (Liu et al. 2004). *Ziziphus jujuba* alcoholic fruit extract was found to contain 0.013 mg myricetin/mL extract, 0.057 mg kaempferol/mL extract and

0.030 mg rutin/mL extract (Cacig et al. 2006). Twelve flavonoid compounds from methanol fruit extracts of *Zizyphus jujuba* and *Zizyphus spina-christi* were identified as quercetin, kaempferol, and phloretin derivatives (Pawlowska et al. 2009). *Zizyphus jujuba* showed a content of flavonoids than *Z. spina-christi.* Nine nucleosides and nucleobases in 49 jujube samples from 43 cultivars from 26 cultivation regions were characterised and quantified (Guo et al. 2010b). In g/100 g dry weight, total free amino acid content ranged from 5.2 to 9.8 g, total phenolic content measured by Folin–Ciocalteu ranged from 1.1 to 2.4 g and flavonoids ranged from 0.7 to 1.8 g in the fruit pulp of Korean *Z. jujuba* cultivars (Choi et al. 2011). Jujube fruits contained the following flavonoids: procyanidin B2, epicatechin, quercetin-3-*O*-rutinoside (Q-3-R), quercetin-3-O-galactoside (Q-3-G), kaempferol-glucosyl-rhamnoside (K-G-R), and two unidentified compounds.

A novel water-soluble polysaccharide (ZSP3c) was isolated from *Zizyphus jujuba* cv. Jinsixiaozao (Li et al. 2011b). ZSP3c was composed of L-rhamnose, D-arabinose and D-galactose in a molar ratio of 1:2:8. The main backbone chain of ZSP3c comprised (1 → 4)-D-galacturonopyranosyl residues interspersed with (1 → 2)-L-rhamno pyranosyl residues and (1 → 2,4)-L-rhamnopyranosyl residues.

Guo et al (2011a) found ultra-high-performance liquid chromatography (UHPLC)-TOFMS coupled with multivariate statistical analysis method to be a powerful technique for rapid study of differentiating components between two *Ziziphus* species, (*Z. jujuba* and *Z. jujuba* var. *spinosa*). By comparing the mass/UV spectra and retention times with those of reference compounds, these components were finally characterized as zizyberenalic acid, palmitoleic acid, oleic acid, pomonic acid and rutin, and these compounds would be the potential chemical markers for discrimination of these jujube products.

Seed Phytochemicals

Ebelin lactone was obtained on hydrolysis of the saponin fraction of the seeds of *Zizyphus jujuba* var. *spinosus* (Shibata et al. 1970). Acid hydrolysis of the saponin of the seeds of *Zizyphus jujuba* afforded ebelin lactone, which yielded the sapogenin, jujubogenin, on Smith-de Mayo degradation (Kawai et al. 1974). Enzymatic hydrolyses of jujubosides A and B, the saponins of the seeds of *Zizyphus jujuba*, afforded prosapogenins I, II and III (Otsuka et al. 1978). Sanjoinine-A (frangufoline), nuciferine and their congeners were found in the seeds of *Zizyphus vulgaris* var.*spinosus* (Han and Park (1987a). A C-glycosyl flavane named spinosin (2″-*O*-β-glucosylswertisin) and its acylated derivatives and swertisin isolated from the seeds (Woo et al. 1979). Three acylated flavone-C-glycosides, namely 6‴-sinapoylspinosin, 6‴-feruloylspinosin and 6‴-*p*-coumaroylspinosin) were identified from *Z. jujuba* seeds (Woo et al. 1980). From the methanol fraction of jujub*e* seeds (Suan Zao Ren), triterpenoid saponins, jujuboside B and jujuboside A, phenolic acid, ferulic acid and a flavonoid compound, spinosin were isolated (Zeng et al. 1987). A new flavonoid compound named zivulgarin, 4″-β-D-glucopyranosyl swertisin, was also found.

From seeds of *Zizyphus vulgaris* var.*spinosus* a cyclic peptide, sanjoinenine, four new peptide alkaloids (sanjoinine-B, -D, -F and -G2), together with the known cyclic peptide alkaloids, frangufoline and amphibine-D were isolated (Han et al. 1990). From the seeds of *Zizyphus vulgaris* var. *spinonus*, aporphine alkaloids: nuciferine, N-methylasimilobine, nornuciferine, norisocorydine, caaverine and tetrahydrobenzylisoquinoline alkaloid: (+)-coclaurine were isolated and identified. Zyzyphusine, a new quaternary aporphinium alkaloid from butanol soluble fraction was isolated and characterized.

New dammarane-type triterpene oligoglycosides, jujubosides A1 and C and acetyljujuboside B1 were isolated from *Zizyphus jujuba* var. *spinosa* seeds, together-with three known saponins (Yoshikawa et al. 1997). Following the elucidation of jujubosides A1 and C and acetyljujuboside B1, novel protojujubogenin type triterpene bisdesmosides, protojujubosides A, B, and B1, were isolated from *Zizyphus jujuba* var. *spinosa* seeds (Matsuda et al. 1999).

Eight flavonoid compounds were isolated from the seeds of *Ziziphus jujuba* var. *spin osa* and elucidated as swertish (1), puerarin (2), 6‴-feruloylspinosin (3), apigenin-6-C-β-D-glucopyranoside (4), spinosin (5), 6‴-feruloylisospinosin (6), isospinosin (7), and isovitexin-2 -*O*-β-D-glucopyranoside (8) (Cheng et al. 2000). Jujuphenoside and jujuphenoside were isolated from the seeds of *Ziziphus jujuba* var. *spinosa* together with 22 known compounds (Li et al. 2005b). A furanoflavonol rhamnoside named spinorhamnoside was isolated from the of *Ziziphus jujuba* var. *spinosa* seeds (Wang et al. 2005). the triglyceride, 1,3-di-*O*-[9(Z)-octadecenoyl]-2-*O*-[9(Z),12(Z)-octadecadienoyl]glycerol (3), and a fatty acid mixture of linoleic, oleic and stearic acids, were found to be the major active components in *Z. jujuba* seeds (Su et al. 2002). A new pentacyclic lupane-type triterpene derivative, 3-*O*-[9(Z)-octadecenoyl]betulinic acid and betulinic acid were also isolated. Eleven major components of 2 saponins and 9 fatty acids, namely jujuboside A, jujuboside B, lauric acid, myristic acid, palmitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid, arachidic acid and docosanoic acid were identified in the seeds of *Ziziphus jujuba* (Suanzaoren) (Zhao et al. 2006). Saponins and fatty oil contains several fatty acids in Suanzaoren were responsible for its therapeutic activities. Other alkaloids, terpenoids and saponins were also found. A new keto-dammarane type of saponin jujuboside G(1), along with three known triterpene saponins,jujuboside A(2), jujuboside B(3) and jujuboside A_1 (4), were isolated from the seeds of *Zizyphus jujuba* var. *spinos*a (Wang and Yang 2008). Zhang et al. (2008) developed a reverse phase high performance liquid chromatography-evaporative light scattering detection for the simultaneous determination of jujuboside A, B and betulinic acid in jujube seeds. Seven compounds were isolated from the seeds of *Ziziphus jujuba* var. *spinosa* (Bai et al. 2003). Their structures were established as jujuboside E (1), jujuboside B (2), jujuboside A (3), betulic acid (4), stearic acid (5), sucrose (6) and inosine (7). A new cyclopeptide alkaloid, jubanine-E, was isolated from *Zizyphus jujube* (Pandey et al. 2008a). In g/100 g dry weight, total free amino acid content ranged from 4.0 to 5.3 g, total phenolic content measured by Folin–Ciocalteu ranged from 3.6 to 4.6 g and flavonoids ranged from 3.2 to 4.0 g in the seed of Korean *Z. jujube* cultivars (Choi et al. 2011). Seeds contained the following flavonoids: saponarin, spinosin, vitexin, swertish, 6‴-hydroxybenzoylspinosin (6‴-HBS), 6‴-feruloylspinosin (6‴-FS), and one unidentified substance.

Leaf Phytochemicals

Terephthalic acid and its methyl esters were found in the leaves and stems of *Zizyphus sativa* (Thakur et al. 1975). The alkaloids coclaurine, isoboldine, norisoboldine, asimilobine, iusiphine iusirine and juziphine and juzirine juziphine and juzirine were isolated from *Z. jujuba* leaves by (Ziyaev et al. 1977). Juziphine had the structure of 8-hydroxy-1R-(4′-hydroxybenzyl)-7-methoxytetrahydroisoquinoline, and juzirine that of 7-hydroxy-1-(4′-hydroxybenzyl)-6-methoxyisoquinoline. A damarane-type saponin was isolated from the leaf and stem *of Z. vulgaris* and assigned as 3-*O*-[(2-*o*-a-1)-fucopyranosyl-3-O-b-1(-glucopyranosyl)-a-L-arabinosyl] jajubogenin (Ikram et al. 1981). Ziziphin an antisweet compound was found in the leaves (Kennedy and Halpern 1980) and elucidated as 3-0-(4-0-α-L-rhamnopyranosyl-α-L-arabinopyranosyl)-20-0-(2,3- di-0-acetyl)-α-L-rhamnopyranosyljujubogenin (Kurihara et al. 1988). Three new jujubogenin glycosides, jujubasaponins I–III were isolated from the fresh leaves of *Zizyphus jujuba*, (Yoshikawa et al. 1991).

Sixteen compounds were isolated from the leaves of *Ziziphus jujuba*: 8 monomeric catechins -(−)-epiafzelechin, (−)-epicatechin, (−)-epigallocatechin, (−)-epicatechin gallate, (−)-epigal-locatechin gallate, (+)-catechin, (+)-catechin gallate, and (+)-gallocatechin; 4 dimeric proanthocyanidins – (−)-epiafzelechin-(4β-8)-(−)-epicatechin, proanthocyanidin B-2, (−)-epicatechin-(4β-8)-(−)-epigallocatechin, and (−)-epiafzelechin-(4β-8)-(−)-epigallocatechin; and 4 oligomeric proanthocyanidins consisting of epiafzelechin, epigallocatechin, catechin, and epicatechin with

different degrees of polymerization (Malik et al. 1997).

Fourteen constituents including three flavonoids, two saponins and nine triterpenic acids were identified from *Ziziphus jujuba* and *Z. jujuba* var. *spinosa* leaves and characterized (Guo et al. 2011b). This included: quercetin-3-O-rutinoside, zizyphus saponins I and II, ceanothic acid, alphitolic acid, maslinic acid, 2α-hydroxyursolic acid, zizyberanalic acid, epiceanothic acid, ceanothenic acid, betulinic acid, and oleanolic acid.

Stem Bark Phytochemicals

From the stem bark of *Z. jujuba*, cyclopeptide alkaloids: mauritine-A, mucronine-D, amphibine-H, nummularine-A, nummularine-B and jubanine-A and -B were isolated (Tschesche et al. 1976). From the bark of *Zizyphus sativa*, 14-membered ring cyclopeptide alkaloids: sativanine-A (1) and sativanine-B (2), were isolated; compound 1 belonged to the integerrine type, while 2 was similar to nummularine-G with an additional ring in the side chain (Tschesche et al. 1979). From the bark of *Zizyphus sativa* a 13 membered cyclopeptide alkaloid, sativanine-C was isolated (Shah et al. 1984a). A damarane-type saponin was isolated from the stem *of Z. vulgaris* and assigned as 3-*O*-[(2-*o*-a-1)-fucopyranosyl-3-*O*-b-1(-glucopyranosyl)-a-L-arabinosyl] jajubogenin (Ikram et al. 1981). From the bark of *Zizyphus sativa* two 13 membered cyclopeptide alkaloids were isolated, sativanine-C (Shah et al. 1984a) and sativanine-G (Shah et al. 1984b). From the bark of *Zizyphus sativa*, a 13-membered cyclopeptide alkaloids were isolated sativanine-D (1) (Shah et al. 1985a), sativanine-F (Shah et al. 1985b), Sativanine-E (Shah et al. 1985c), sativanine-H (Shah et al. 1986), and sativanine-K, a 13-membered *N*-formyl cyclopeptide alkaloid containing a short side chain (Shah et al. 1987). The 14-membered cyclopeptide alkaloid mauritine-C and the 13-membered cyclopeptide alkaloid sativanine-C were isolated from *Zizyphus sativa* (Shah et al. 1989b). Two cyclopeptide alkaloids, sativanine-N and sativanine-O were isolated from the stem bark of *Zizyphus sativa* (Singh et al. 2006). A cyclopeptide alkaloid, sativanine-M (1), together with known alkaloid nummularine-P were isolated from *Zizyphus sativa* stem bark (Pandey et al. 2008b).

Sixteen compounds were isolated from the bark of *Ziziphus jujuba*: 8 monomeric catechins -(−)-epiafzelechin, (−)-epicatechin, (−)-epigallocatechin, (−)-epicatechin gallate, (−)-epigal-locatechin gallate, (+)-catechin, (+)-catechin gallate, and (+)-gallocatechin; 4 dimeric proanthocyanidins – (−)-epiafzelechin-(4β-8)-(−)-epicatechin, proanthocyanidin B-2, (−)-epicatechin-(4β-8)-(−)-epigallocatechin, and (−)-epiafzelechin-(4β-8)-(−)-epigallocatechin; and 4 oligomeric proanthocyanidins consisting of epiafzelechin, epigallocatechin, catechin, and epicatechin with different degrees of polymerization (Malik et al. 1997). The pentameric proanthocynidine called proanthocyanide PZ-5 was isolated from the bark and its structure elucidated as (−)-epiafzelechin-(4β-8)-(−)epigallocatechin-(4β-8)-(+)-catechin-(4α-8)-(−)-epigallocatechin-(4β-8)-(+)-catechin (Malik et al. 2002). A new cyclopeptide alkaloid, jubanine-C (1), together with known alkaloids scutianine-C (4) and zizyphine-A (5), were isolated from the stem bark of *Zizyphus jujuba* (Tripathi et al. 2001).

Root Phytochemicals

A lanostane-type triterpene, zizyphulanostane-21-oic acid, and a terpenic δ-lactone, zizyphulanostan-18-oic acid, were isolated from the roots of Zizyphus *vulgaris* and characterized as lanosta-25 (26)-en-9α-ol-21-oic acid and lanosta-25 (26)-en-22β-ol-18-oic acid 3(19)-olide, respectively (Mukhtar et al. 2004). A novel pentacyclic triterpenoid, zizyberanalic acid, was isolated from both bark and roots of *Zizyphus jujuba* and elucidated as 3α-hydroxy-2β-aldehydo-A(1)-norlup-20(29)-en-28-oic acid (Kundu et al. 1989).

Three triterpene esters: 2-*O*-protocatechuoylaliphitolic acid, 2α-hydroxypyracrenic acid and 3-*O*-protocatechuoylceanothic acid were isolated from the water-insoluble fraction of the

ethanol extract of *Zizyphus jujuba* var. *spinosa* root (Lee et al. 1996).

Pectic polysaccharides were found to be the major components in all water-soluble polysaccharides (WSPs) in Chinese jujube leaves, fruits and flowers (Zhao et al. 2008).

Antioxidant Activity

Studies showed that extracts of six kinds of common food including *Ziziphus jujuba*, could scavenge (O_2) free radical, inhibit lipid peroxidation of mice liver homogenate (in vivo and in vitro), decrease hyaluronic acid depolymerization induced by (O_2), and inhibit the adenosine deaminase activity of mice liver homogenate (in vivo) (Wang and Chen 1991). These actions were very similar to the actions of those traditional Chinese tonic prescriptions and their individual herbal drugs studied earlier.

Results of studies indicated that the antioxidant capacity differed in the five Chinese jujube cultivars (Li et al. 2005a). The antioxidant activities, scavenging effect on the 2,2-diphenyl-1-pycril-hydrazyl (DPPH) radical and reducing power of extracts decreased in the order of *Z. jujuba* cv. jinsixiaozao, *Z. jujuba* cv. yazao, *Z. jujuba* cv. jianzao, *Z. jujuba* cv. junzao, *Z. jujuba* cv. sanbianhong. The antioxidant activities of extracts from cv. jinsixiaozao, cv. yazao and cv. jianzao were stronger than a-tocopherol. Significant differences were found between α-tocopherol and both *Z. jujuba* cv. jinsixiaozao and *Z. jujuba* cv. yazao, while no significant differences were found between α-tocopherol and *Z. jujuba* cv. jianzao. Additionally, no correlation was found between total phenolic contents and antioxidant capacities of extracts from five cultivars. Contrariwise, high correlation was found between phenolic content and antioxidant capacity in another study. The total phenolic content in peel was five to six times higher than that in the pulp of all the three Chinese jujube cultivars *(Z. jujuba* cv. mayazao, *Z. jujuba* cv. dongzao and *Z. jujuba* cv. yuanzao) (Xue et al. 2009). The phenolics contents in the jujube were different among cultivars. The EC_{50} (concentration of lyophilized samples needed to decrease the initial DPPH radical concentration by 50%), FRAP and TEAC values of the peel and pulp were remarkably correlated to their total phenolic contents ($R^2 = -0.922$, $R^2 = 0.985$ and $R^2 = 0.997$, respectively). The results indicated that the high capacity of antioxidant of Chinese jujube fruit could be attributed to the high phenolic contents in the fruit.

Studies showed that jujube peel of all cultivars had the highest antioxidant capacities, reflecting the highest content of total phenolics, flavonoids, and anthocyanins found in this part (Zhang et al. 2010). Further, the predominant phenolic acid in jujube was found to be protocatechuic acid, followed by gallic acid, chlorogenic acid and caffeic acid. The results clearly indicated Chinese jujube to have significant potential to use as a natural antioxidant agent.

One neutral polysaccharide fraction (ZJPN) and three acidic polysaccharide fractions (ZJPa1, ZJPa2 and ZJPa3) with the average MW ranging from 40,566 to 129,518 Da were isolated from jujube fruit (Chang et al. 2010). Six monosaccharides, namely, rhamnose, arabinose, xylose, mannose, glucose and galactose were present in polysaccharide fractions. The galacturonic acid content in polysaccharide fractions followed the order: ZJPa3 > ZJPa2 > ZJPa1 > ZJPN. All the four polysaccharide fractions were found to be more effective in scavenging superoxide anions than hydroxyl radicals, while acidic polysaccharides showed a more pronounced effect in chelating ferrous ion.

Geographical condition was found to impact on the antioxidant levels in *Ziziphus jujuba* var. *spinosa* (Sun et al. 2011). Jujube fruits exhibited significant DNA damage protection activity and in-vitro antiradical potentials. Correlation analyses indicated that both altitude and annual precipitation exerted profound effects on natural antioxidant levels. Jujube fruits in arid harsh and high-altitude areas were found to accumulate higher levels of natural antioxidants and to display stronger antioxidant activities.

Antisweet Activity

An aqueous ethanol extract of *Ziziphus jujuba* leaves was fractionated into two components – ZjE-A, which had surface active properties, and

ZjE-B, which did not. Bioassay by psychophysical tests on humans revealed sweetness-modifying activity in ZjE-A, but not in ZjE-B. ZjE-A the potent, purified component, was found to consist of 60–80% ziziphins, triterpene saponin glycosides (Kennedy and Halpern 1980). One of the fractions obtained from the extract of *Zizyphus jujuba* leaves suppressed the response of the chorda tympani to sucrose, both in the rat and hamster (Yamada and Imoto 1987). In the rat and man, the inhibitory effect was found to be significant in responses to various sugars and artificial sweeteners but not in some sweet amino acids. The sweetness inhibiting substance (ziziphin) contained in *Z. jujuba* leaves was elucidated as 3-0-(4-0-α-L-rhamnopyranosyl-α-L-arabinopyranosyl)-20-0-(2,3- di-0-acetyl)-α-L-rhamnopyranosyljujubogenin (Kurihara et al. 1988). Ziziphin suppressed the sweetness induced by D-glucose, D-frutose, stevioside, glycine, sodium saccharin, aspartame and naringin dihydrochalcone. Ziziphin however showed no suppressive effect on the sour taste of hydrochloric acid and the bitter taste of quinine indicating it to be highly specific to sweet taste (Kurihara 1992). Ziziphin was found to inhibit the sweet taste receptors in humans (Smith and Halpern 1983). Sweetness was reduced after either a 10 s or a 90 s whole mouth treatment with ziziphins, but not after quinine sulfate or apple juice control treatment. The reduction in sweetness was weak with 10 s 3.5% W/V ziziphin treatment, but strong after 90 s 0.88% W/V ziziphin treatment; duration of suppression was about. 70 s. On comparison with known gymnemic acids, effects suggested that net dissociation of ziziphins from taste receptor membranes and/or inactivation in the membrane may be much faster than with gymnemic acids. Three new jujubogenin glycosides, jujubasaponins I–III were isolated from the fresh leaves of *Zizyphus jujuba*, compound 2 and 3 exhibited antisweet activity (Yoshikawa et al. 1991).

Anticancer Activity

Jujube seed oil at 0.35 or 1.40 mL/kg could prolong life-span over 50% and inhibit increase of body weight of Ehrlich Ascites Cancer mice (Wang et al. 1995). The seed oil also displayed antineoplastic effects on Ehrlich Ascites cancer mice. Among 11 triterpenoic acids isolated from the fruits of *Zizyphus jujuba*, the lupane-type triterpenes, such as compounds 3-*O*-*cis*-*p*-coumaroylalphitolic acid (3), 3-*O*-*trans*-*p*-coumaroylalphitolic acid (4), 3-*O*-*cis*-*p*-coumaroylmaslinic acid, 3-*O*-*trans*-*p*-coumaroylmaslinic acid, betulinic acid (7), oleanolic acid, betulonic acid (9), showed high in-vitro cytotoxic activities against K562 (human erythromyeloblastoid leukemia), B16(F-10) (murine melanoma), SK-MEL-2 (human skin melanoma), PC-3 (human prostate cancer), LOX-IMVI (human melanoma), and A549 (human lung adenocarcinoma) tumour cell lines (Lee et al. 2003). In particular, the cytotoxic activities of 3-*O*-*p*-coumaroylalphitolic acids (compounds 3 and 4) were better than those of non-coumaroic triterpenenoids (compounds 7 and 9). These results suggested that the coumaroyl moiety at the C-3 position of the lupane-type triterpene may play an important role in enhancing cytotoxic activity.

Studies showed that the chloroform fraction of *Z. jujuba* fruit extract CHCl(3)-F induced a concentration dependent effect on apoptosis and a differential cell cycle arrest in human hepatoma HepG2 cells (Huang et al. 2007). Apoptosis, an increase in intracellular ROS (reactive oxygen species) level, a decline of mitochondrial membrane potential at low *Z. jujuba* concentrations, and a ROS-independent mitochondrial dysfunction pathway at high concentrations were all observed. CHCl(3)-F-induced G1 arrest in HepG2 cells was associated with an increase in hypohosphorylation of Rb and p27(Kip1), and a decrease of phosphorylated Rb. Subsequent studies showed that that combination of the chloroform fraction of *Z. jujuba* fruit extract and green tea extract produced an enhanced cell growth inhibition effect, and that the resultant G1 arrest was caused via a different mechanism as that of CHCl(3)-F treatment alone (Huang et al. 2008a). Further studies showed that the CHCl(3)-F and green tea extract enhanced anticancer activity by reducing the expression of APRIL (a proliferation-inducing ligand), which was expressed in HepG2 cells (Huang et al. 2009). The scientists speculated

that the CHCl(3)-F and green tea extract mixture might provide a lead to a new drug design to treat hepatocellular carcinoma in the future. *Z. jujuba* aqueous extract showed inhibitory effects against human tumour cell lines, HEp-2, HeLa and Jurkat leukemic cell lines (Vahedi et al. 2008). Jurkat leukemic line was the most sensitive cells with IC_{50} of 0.1 μg/mL. This cell line also displayed a typical DNA laddering. The crude methanolic extract of *Zizyphus jujuba* was highly cytotoxic (73.33%) at the concentration of 1,000 (μg/mL) while the rest of the test fractions were low in toxicity at the same concentration (Ahmad et al. 2011).

Deproteinized polysaccharide isolated from *Z. jujuba* was found to compose of two fractions with average molecular weights of 143,108 and 67,633 Da (Hung et al. 2012). The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide test showed that the antiproliferation effect of the deproteinized polysaccharide on melanoma cells followed a dose- and time-dependent course with IC_{50} values of 3.99 mg/mL after 24-h treatment but decreased significantly to 3.36 mg/mL after 48 h. The cell cycle assay revealed melanoma cells to be arrested in G2/M phase. Moreover, with the deproteinized polysaccharide treatment, the apoptotic bodies were generated, accompanied by an increase in caspase-3 and caspase-9 activity. The results suggested that the deproteinized polysaccharide may be used as a potential anti-skin cancer agent.

Antiangiogenic Activity

The medicinal herb of *Aspergillus usamii* var. *shirousamii*-transformed *Angelicae gigantis* Radix and *Zizyphus jujuba* (tAgR and tZj) was found to have antiangiogenic activity (Kang et al. 2009). The medicinal herb significantly suppressed phorbol 12-myristate 13-acetate (PMA)-induced matrix metalloproteinases MMP-2 production and prevented vascular endothelial growth factor-stimulated endothelial cell transmigration and tube formation. Invasive cancer cells had been reported to utilize MMP to degrade the extracellular matrix and vascular basement membrane during metastasis, where MMP-2 had been implicated in the development and dissemination of malignancies. The medicinal herb-mediated inhibition of endothelial MMP may boost a therapeutic efficacy during vascular angiogenesis.

Antiinflammatory Activity

Ethanolic jujube fruit extract significantly inhibited carrageenan-induced paw oedema and cotton pellet-induced granuloma pouch (Shah et al. 1989a). Pharmacological studies demonstrated that the compound prescription Huangqin Tang and its component drugs: roots of *Paeonia lactiflora, Scutellaria baicalensis* and *Glycyrrhiza uralensis*, and the fruit of *Ziziphus jujuba* showed marked anti inflammatory effect (Huang et al. 1990). The compound prescription and its component drugs, except the peony root, also possessed significant antispastic effect. Studies showed that the % inhibition of paw oedema at 3 h after carrageenan administration produced by *Z. jujuba* leaf extracts at 200, 400 and 600 mg/kg was 44.5, 62.2 and 81.8%, respectively, compared to the control (Kumar et al. 2004). The paw oedema attenuating effect of *Z. jujuba* leaf extracts at the dose of 600 mg/kg was comparable with that produced by diclofenac sodium (88.6%). The results showed that *Ziziphus jujuba* leaf extracts possessed significant antiinflammatory activity against carrageenan-induced rat paw oedema. *Z. jujuba* leaf extract was found to possess significant antiinflammatory activity against carrageenan-induced rat paw edema in rats (Shiv et al. 2004).

Bioactivity-guided fractionation of petroleum ether- and EtOAc-soluble extracts of the seeds of *Ziziphus jujuba* using a cyclooxygenase-2 assay as a monitor indicated that the triglyceride, 1,3-di-*O*-[9(Z)-octadecenoyl]-2-*O*-[9(Z),12(Z)-octadecadienoyl]glycerol (3), and a fatty acid mixture of linoleic, oleic and stearic acids, were the major active components (Su et al. 2002). A new pentacyclic lupane-type triterpene derivative, 3-*O*-[9(Z)-octadecenoyl] betulinic acid (1), and betulinic acid (2) were

also isolated and identified. All isolates as well as pure linoleic, oleic and stearic acids were evaluated for their inhibitory effects against both cyclooxygenases-1 (COX-1) and -2 (COX-2). Cox inhibitors have antiinflammatory properties. This study was undertaken to evaluate the effect of essential oil from seeds of *Zizyphus jujuba* on TPA(12-*O*-tetradecanoylphorbol-13-acetate)-induced skin inflammation model in mice, treatment with 1 and 10% of essential oil of *Z. jujuba* seeds caused significant decrease in ear thicknesses and reduced respectively. Further, histological analysis clearly confirmed that *Z. jujuba* essential oil inhibited the inflammatory responses of skin inflammation in mice.

Pretreament of Wistar albino rats with *Ziziphus jujuba* fruit hydroalcoholic extract elicited marked dose-dependent attenuation in paw edema compared to control (Goyal et al. 2011). The extract significantly decreased granuloma tissue formation caused by interscapular implantation of sterile cotton pellets compared to control. The extract also decreased the elevated serum nitrite/nitrate level caused by chronic inflammation. The extract was found to contain jujubosides, flavonoids and terpenes, which may produce the marked anti-inflammatory effect of jujube fruit in acute and chronic inflammation, possibly by inhibiting nitric oxide expression. The results suggested the potential for the therapeutic use of *Z. jujuba* fruit as an anti-inflammatory agent. Among six fractions extracted from *Z. jujube*, fraction F (triterpene acids fraction) was demonstrated to be the most active part in inhibitory effects the inflammatory cells activated by *Euphorbia kansui* and prostratin, a phorbol ester isolated from *Euphorbia fischeriana* (Yu et al. 2012). Of 21 compounds isolated from *Z. jujube,* 7 compounds were found to have pronounced inhibitory action on the activated inflammatory cells. The scientist asserted that these compounds may be helpful in attenuating the irritant action of Euphorbiaceae plants and protect the gastrointestinal tissue from potent inflammatory injury, and would be beneficial to some diseases, like inflammatory bowel disease.

Antiulcerogenic Activity

In the pylorus ligation-induced ulcer model, *Ziziphus jujuba* leaf extract pretreatment in rats caused significant reduction in gastric volume, free acidity, total acidity and ulcer index compared to the control group (Ganachari and Kumar 2004a). In ethanol-induced ulcers, the extract was effective in reducing lesion index and increasing the gastric mucus content. It was also effective in decreasing ulcer index in aspirin-induced ulcers. All the results obtained with the extract were dose dependent. All the results suggested that *Ziziphus jujuba* leaf extract possessed significant and dose-dependent antiulcer activity. The antiulcer activity of the extract could be attributed to its cytoprotective and antisecretory action.

Antiobesity and Antihypercholesterolemic Activities

Studies found that *Z. jujuba* seeds at 64 mg/kg/day administered intra-peritoneally for 20 days could reduce the levels of total cholesterol and LDL-cholesterol, increase HDL-cholesterol and HDL 2 -cholesterol of rats fed on normal diet (Yuan and Li 1990). The extract at the same dosage could reduce triglycerides, and increase HDL2-cholesterol of rats fed on rich-fat diet.

The hydroalcoholic extract of *Ziziphus jujuba* leaves at the doses of 200, 400 and 600 mg/kg, p.o. given daily to sucrose induced- obese rats for 125 days caused reduction in body weight, daily food intake and serum total cholesterol, LDL-cholesterol, VLDL-cholesterol and triglycerides along with an increase in HDL-cholesterol levels (Ganachari and Kumar 2004b). The results obtained with 400 and 600 mg/kg dose of *Ziziphus jujuba* extract were significant when compared to sucrose control group. These results suggested that *Ziziphus jujuba* leaf extract possessed significant weight reducing, hypophagic and hypolipidemic properties in sucrose-induced obese rats. In a recent study, treatment with an extract of *Z. jujuba* suppressed lipid accumulation

and glycerol-3-phosphate dehydrogenase (GPDH) activity without affecting cell viability (Kubota et al. 2009). Further fractionation of the initial *Z. jujuba* extract with organic solvent revealed that the chloroform fraction (CHCl(3)-F) elicited the most inhibitory effect, which involved significant attenuation of the expression of key adipogenic transcription factors, including peroxisome proliferator-activated receptor (PPAR)γ and CCAAT enhancer binding proteins (C/EBPs) at the protein level. The results suggested that the chloroform fraction may block adipogenesis, at least in part, by decreasing the expression of PPARgamma, C/EBPα and β.

Effect on Chronic Constipation

Z. jujuba extract was found to be an effective and safe treatment for chronic constipation (Naftali et al. 2008). Clinical studies showed that patients with a prolonged transit time (TT), taking the extract had their TT decreased from 12.2 particles to 3 particles at week 11. Symptom severity ratings decreased from 6 and 6.2 to 2 and 5, and the quality of life score improved from 1.9 and 2.3 to 1.3 and 1.4 in the extract and control groups, respectively.

A water-soluble carbohydrate concentrate (WSCC) prepared from Chinese jujube contained carbohydrates (771 g/kg of WSCC) including glucose, fructose, pectin polysaccharide, and hemicelluloses (Huang et al. 2008b). The administration of WSCC (5.0 and 15 g/ kg of diet) effectively shortened gastrointestinal transit time, reduced caecal ammonia, elevated total short-chain fatty acid concentrations in caecum (3-4-fold), increased faecal moisture, reduced daily faecal ammonia output and decreased the activities of β-D-glucuronidase (by 73.0–73.8%), β-D-glucosidase (by 58.2–85.7%), mucinase (by 46.2–72.6%), and urease (by 31.9–48.7%) in faeces. This study suggested that adequate consumption of jujube WSCC (at least 5.0 g/kg of diet or 40 mg/day) might exert favourable effects on improving the gastrointestinal milieu and reduce the exposure of intestinal mucosa to toxic ammonia and other detrimental compounds.

Antiamnesic Activity

Among 50 Korean traditional plants tested, the methanolic extracts from *Zizyphus jujuba* showed the highest activation effect (34.1%) on choline acetyltransferase in vitro (Heo et al. 2003). By sequential fractionation of *Zizyphus jujuba*, the active component was finally identified as *cis*-9-octadecenoamide (oleamide). After isolation, oleamide showed a 65% activation effect. Administration of oleamide (0.32%) to mice significantly reversed the scopolamine-induced memory and/or cognitive impairment in the passive avoidance test and Y-maze test. Injection of scopolamine to mice impaired performance on the passive avoidance test (31% decrease in step-through latency), and on the Y-maze test (16% decrease in alternation behavior). In contrast, mice treated with oleamide before scopolamine injection were protected from these changes (12–25% decrease in step-through latency; 1–10% decrease in alternation behavior). These results suggested that oleamide should be a useful chemo-preventive agent against Alzheimer's disease.

Anticonvulsant Activity

The hydroalcoholic extract of *Zizyphus jujuba* (HEZJ) fruit (1,000 mg/kg) exhibited maximum protection (100%) against generalized tonic-clonic seizures in the pentylenetetrazole (PTZ) seizure model and 66.7% protection against tonic hindlimb extension in the maximal electroshock (MES) seizure model (Pahuja et al. 2011). Significant impairment in cognitive functions was observed in both PTZ- and MES-challenged rats. Pretreatment with the extract resulted in significant improvement in learning and memory. The extract also reversed the oxidative stress induced by both PTZ and MES. The significant decrease in cholinesterase activity observed in the PTZ and MES models was significantly reversed by pretreatment with the extract. The results demonstrated the anticonvulsant effect of jujube fruit extract as well as amelioration of cognitive impairment induced by seizures in rats.

Anxiolytic/Sedative Activity

A C-glycosyl flavane named spinosin (2"-*O*-β-glucosylswertisin) and its acylated derivatives isolated from the seeds were found to possess mild sedative activity (Woo et al. 1979). Swertisin was also found in small quantity. Three acylated flavone-C-glycosides, (namely 6‴-sinapoylspinosin, 6‴-feruloylspinosin and 6‴-*p*-coumaroylspinosin) were identified from *Z. jujuba* seeds (Woo et al. 1980). All showed mild sedative activity in pharmacological tests. The seeds and leaves of jujube exerted a similar inhibiting effect on central nervous system function, while the fruits was synergistic with pentobarbitol sodium and thiopental sodium on prolongation of sleep and sedation, and also decreased coordinated action (Wu et al. 1993). Jujuboside A exerted no inhibiting effect, but was synergistic with phenylalanine on central nervous system function. Jujuboside A, an effective component of sanzaoren (*Z. jujuba* seed), a Chinese herbal medicine, was found to be a non-competitive inhibitor of calmodulin (Zhou et al. 1994). Calmodulin is a primary Ca2+-binding protein found in all eukaryotic cells (Zhang and Yuan 1998). It couples the intracellular Ca2+ signal to many essential cellular events by binding and regulating the activities of more than 40 different proteins and enzymes in a Ca2+-dependent manner. Jujuboside inhibition of calmodulin was thought to be linked to its sedative properties (Zhou et al. 1994). In another study, a high dose of Jujuboside A inhibited the hyperactivity of rat hippocampal CA1 neurons induced by penicillin sodium (Shou et al. 2001). Further research showed that penicillin increased the hippocampal glutamate concentration and a high dose of Jujuboside A (0.1 g/L) significantly blocked penicillin-induced glutamate release (Zhang et al. 2003). It was found that glutamate (0.5 mM) induced an intracellular [Ca^{2+}] increase and Jujuboside A significantly inhibited the glutamate-induced Ca^{2+} increase. The calmodulin (CaM) antagonist trifluoperazine (TFP) showed a similar inhibitory effect as Jujuboside A. These observations suggested that JuA had inhibitory effects on glutamate-mediated excitatory signal pathway in hippocampus and probably acted through its anti-calmodulin action.

The ethanolic extract of *Ziziphus jujuba* seed (SZJE) orally administered to male ICR mice at the dosage 0.5–2.0 g/kg increased the first time entry, total changes and times spent in the white chamber of the black and white test (BWT) (Peng et al. 2000). The SZJE at the dosage 0.5–1.0 g/kg increased the percentage of time-spent and the percentage of arm entries in the open arms of the elevated plus maze (EPM) and decreased the percentage of time-spent and the percentage of arm entries in the closed arms of the EPM. Furthermore, the SZJE at the dosage of 1. 0 g/kg prolonged the hexobarbital-induced sleeping time in mice and decreased the locomotor activity in rats. These results suggested that SZJE possessed anxiolytic effect at lower dose and sedative effect at higher dose. The flavonoid isolated from *Z. jujuba* seeds, spinosin and swertish were found to possess significant sedative activity (Cheng et al. 2000). Studies showed that Jujuboside A administered intracerebroventricular in urethane-anaesthetized rats significantly decreased the slopes of excitatory postsynaptic potential (EPSP) and the amplitudes of population spike (PS) in the first responses of granule cells and significantly decreased EPSP and PS in the responses of CA1 pyramidal cells (Shou et al. 2002). There was good correlation between *in-vivo* and *in-vitro* results. Jujuboside A is a main component of jujubogenin extracted from the seed of *Ziziphus jujuba* var spinosa which is widely used in Chinese traditional medicine for the treatment of insomnia and anxiety, a Chinese herbal medicine, has long been known as a sedative-hypnotic drug.

Saponins from *Ziziphus jujuba* seeds exhibited sedative and hypnotic effect (Jiang et al. 2007a). Saponins are thought to be the main bioactive factors in Chinese traditional medicine for the treatment of anxiety and insomnia because of its effect of decreasing monoaminergic system activity. Animal studies conducted to investigate sedative and hypnotic effects of jujube saponins showed that two saponin compounds from *Z. jujuba* seeds

exerted a significant effect on walking time compared with that of the control group (Jiang et al. 2007a). Compound I had a significant effect on coordinated movement. Both compounds prolonged the suprathreshold barbiturate induced sleeping time. The number of sleeping animals increased by 30 and 20% for compounds I and II, respectively, under the subthreshold dose of sodium barbital. In further animal studies flavonoids and saponins from *Z. jujuba* seeds caused a significant reduction of walking time and coordinated movement ability of mouse, and significantly prolonged its sleeping time at 40 mg/kg, ip, subthreshold dose and increased the sleeping number of animals at 50 mg /kg, ip, superthreshold dose induced by coeliac injection of sodium barbital (Jiang et al. 2007b). Comparative analysis showed that saponins had a more effective sedative and hypnotic function than that of flavonoids while polysaccharides did not show any sedative and hypnotic effect.

Sedative principles of the seeds of *Zizyphus vulgaris* var. *spinosus* were characterized as sanjoinine-A (frangufoline), nuciferine and their congeners (Han and Park 1987a). Heat treatment of sanjoinine-A produced a more active artifact sanjoinine-Ahl. Sedative activity of Zizyphi fructus was determined by potentiation of hexobarbital-induced hypnosis test and its active principles were characterized as nornuciferine and lysicamine (Han and Park 1987b). A new cyclopeptide alkaloid, daechucyclopeptide-1 was isolated together with zizyphusine. Sedative alkaloids in two varieties of *Z. jujuba* were extensively studied by Han et al. (1989b) in Korea. Alkaloids found in the seeds of *Z. vulgaris* var. *spinosus* (Sanjoin) include: sanjoinine-A, sanjoinine-B, sanjoinine-D, sanjoinine-F, sanjoinine-G1 and sanjoinenine cyclopeptide alkaloids and sanjoinine-G2 as open chain peptide alkaloid. Other sanjoinine alkaloids were identified as sanjoinine-E (nuciferine), sanjoinine-I_a (nornuciferine), sanjoinine-I_b (norisocorydine), N-methylasimolobin, caaverine which are aporphine alkaloids. sanjoinine-K was identified a + coclaurine, a benzylisoquinoline alkaloid. Zizyphusine was identified as a quaternary aporphine alkaloid. Alkaloids found in the fruit of daechu, *Z. jujuba* var. *inermis* included daechualkaloid-A, daechualkaloid-C (lyscimine), daechualkaloid-E (nornuciferine), daechucyclopeptide-I, and zizyphusine. Twelve cyclopeptide alkaloids from Daechu stem-bark: daechuine-S1 (frangufoline), daechuine- S2, (frangulanine), daechuine-S4 (franganine), daechuine-S5, daechuine-S3, daechuine-S6, daechuine-S7, daechuine-S8-1, daechuine –S9 (mucronin-D), daechuine-S10, daechuine-S26, daechuine-S27 (Nummularin-B). Oral administration of the methanol extract (1 g/kg) of sanjoin fruit in mice prolonged the hexobarbital sleeping time by >67% compared to the control group. The butanol fraction of the extract showed more potent sedative activity. Sanjoine-A and nuciferine showed strong sedative activity whereas zizyphusine and + coclaurine did not. It was highly probable that some of the sedative activity of the butanol fraction may be attributable to the minor alkaloids.

Sanjoinine-A (frangufoline) was bound to Calmodulin protein at two sets of binding sites in the calcium ion-dependent manner in rat brain cytoplasm (Han et al. 1993). The inhibitory activity of the various cyclopeptides and peptide alkaloids from *Zizyphus* species on Ca^{2+}-ATPase was found to correlate well with their sedative activity (Hwang et al. 2001). Calmodulin-induced activation of Ca^{2+}-ATPase was strongly inhibited by sanjoinine-A dialdehyde (IC_{50}, 2.3 μM), -Ah1 (IC_{50}, 4.0 μM), -A (IC_{50}, 4.6 μM), and -G2 (IC_{50}, 7.2 μM), while calmodulin-induced activation of phosphodiesterase was strongly inhibited by both deachuine S10 (IC_{50}, 4.9 μM) and sanjoinine-D (IC_{50}, 9.0 μM). The sedative peptide alkaloids from *Zizyphus* species inhibited calmodulin-dependent protein kinase II (Han et al. 2005). All 13 alkaloids tested were stronger inhibitors than chlorpromazine (IC_{50}, 98 μM) on calmodulin-dependent protein kinase II. Among them, the most potent inhibitor was daechuine S27 (IC_{50} 2.95 μM), which was stronger than pimozide (IC_{50} 15.0 μM). A study of five men and ten women suffering general malaise showed that administration of jujube extract had a sedative and adaptogenic effect (Goetz 2009)

Studies showed that the water extract of Suanzaoren (jujube seed, SWE) (400 and 800 mg/

kg body wt.) and the ether extract of Danshen (DTT) (300 and 600 mg/kg body wt.) decreased sleep latency significantly, increased sleeping time and prolonged movement convalescence time induced by sodium pentobarbital (55 mg/kg body wt.) administration in mice (Fang et al 2010). Further, the combination of SWE and DTT showed significant synergistic effect in decreasing sleep latency and increasing sleeping time, but not in prolonging the movement convalescence time, which might be helpful for energy recovery in the treatment of insomnia. The results suggested that SWE, DTT, and their combination possessed significant sedative-hypnotic activity, which supported the popular use of Suanzaoren and Danshen for treatment of insomnia.

These results of studies suggested that the hypnotic effect of jujubosides on normal rats may be influenced by circadian rhythm and the serotonergic system may be involved in the hypnotic effect of jujubosides (Cao et al. 2010). During daytime (9:00–15:00), jujubosides significantly increased the total sleep and rapid eye movement (REM) sleep without significant influence on non-REM (NREM) sleep. During nighttime (21:00–3:00), jujubosides significantly increased total sleep and NREM sleep especially the light sleep and showed no significant effect on REM sleep and slow wave sleep (SWS). In pentobarbital-treated mice, jujubosides significantly augmented the hypnotic effect of pentobarbital evidenced by increasing sleep time and this augmentative effect was potentiated by 5-hydroxytryptophan. Further, jujubosides inhibited the para-chlorophenylalanine-induced suppression of pentobarbital-induced hypnosis.

Hypoglycaemic Activity

Adminstration of single (100–400 mg/kg) oral doses of jujube alcoholic leaf extract to normal rats showed a dose-dependent statistically significant lowering of blood glucose 2, 4 and 6 h later (Anand et al. 1989). The effect was most pronounced at 6 h with blood glucose returning to control values at 24 h. In alloxan-diabetic rats, no significant effect was observed with the extract and tolbutamide. The minimum lethal dose was greater than 3,000 mg/kg, orally in mice. In alloxan diabetic rats both methanol extracts of *Zizyphus spina christi* (ZSC) and *Zizyphus jujuba* (ZJ) roots significantly reduced fasting serum glucose level and markedly increased serum insulin level (Said et al. 2006). ZJ significantly reduced serum total lipids (TL), triglycerides (TG), total cholesterol (TC) and lipid peroxides (LP), low density lipoprotein cholesterol (LDL-C), but no significant difference on high density lipoprotein cholesterol (HDL-C). Meanwhile, ZSC caused a noticeable decrease in TC, TG and LP compared with the untreated diabetic rats. ZJ significantly decreased alanine transaminase (ALT), aspartate transaminase (AST) and total bilirubin (TB) in diabetic rats. Serum creatinine and urea showed significant reduction in diabetic rats treated with ZSC extract. Both extracts produced no significant changes in all studied parameters except for a significant reduction of serum lipid peroxides and urea by ZJ extract as compared to untreated diabetic control. The data revealed that both extracts of ZSC and ZJ had beneficial effects on diabetic rats. They reduced hyperglycemia, hyperlipidemia and lipid peroxides associated with diabetes. Besides, they were safe towards liver and kidney functions. The effect of *Z. jujube* roots was more pronounced than that of *Zizyphus spina Christi* roots. In a recent study, hydro-alcoholic extract of *Z. jujuba* leaves was found to have hypoglycaemic effect in alloxan- induced diabetic rats (Shirdel et al. 2009). In diabetic rats treated with the extract, significant reduction of glucose–triglyceride-cholesterol, LDL and VLDL levels resulted. *Z. jujuba* also increased HDL levels significantly. Both studies confirmed findings of earlier studies conducted by Iganacimuthu and Amalraj (1998) on alloxan-induced diabetic rats.

Antiatherosclerotic Activity

Crude *Z. jujuba* fruit and seed extracts significantly inhibited the foam cell formation induced by acetylated low density lipoprotein (Fujiwara et al. 2011).Further thery found that triterpenoids such

as oleanonic acid, pomolic acid, and pomonic acid were the major active compounds, and triterpenoids containing a carboxylic acid at C-28 played an important role in the inhibitory effect on foam cell formation in human macrophages. Their data suggest that triterpenoids in *Zizyphus jujuba* fruits and seeds, may therefore be useful for the prevention of atherosclerosis.

Antiplatelet Activity

A neo-lignan isolated from *Z. jujuba* leaves was found to increase the release of endogenous prostaglandin I2 from the rat aorta by up to 25.3% at 3 μg/mL (Fukuyama et al. 1986). Prostaglandin I2 or prostacyclin had been reported to be both a potent inhibitor of platelet aggregation and a powerful vasodilator (Kelton and Blajchman 1980). It may play an important role in limiting platelet-mediated thrombosis.

Neuroprotective and Central Nervous System Activity

Methanol extract of seeds of *Zizyphus jujuba* var. *spinosa*, at a concentration range of 0.05–5 μg/mL, inhibited N-methyl-D-aspartate (NMDA) (1 mM)-induced neuronal cell death in cultured rat cerebellar granule neuron (Park et al. 2004). The extract (0.5 μg/mL) inhibited glutamate release into medium induced by NMDA (1 mM). Pretreatment of the extract (0.5 μg/mL) inhibited NMDA (1 mM)-induced elevation of cytosolic calcium concentration. In another study, jujube fruit extract exerted neuroprotective effects against ischemic damage in gerbil hippocampus after repeated oral supplementation (Yoo et al. 2010). The treatment significantly decreased the reactive gliosis of astrocytes and microglia in the CA1 region compared to that in the vehicle-treated group. Immunoreactivities of Cu,Zn-superoxide dismutase (SOD1) and brain-derived neurotrophic factor in the jujube-treated ischemia group were higher those in the vehicle-treated ischemia group 4 days after ischemia/reperfusion. In addition, in the jujube-treated ischemia group, levels of hydroxynonenal, an indicator of lipid peroxidation, were much lower than those in the vehicle-treated ischemia group after ischemia/reperfusion. The results suggested that the repeated supplements of jujube could protect neurons from ischemic damage via up-regulation of SOD1 and reduction of lipid peroxidation in the ischemic hippocampal CA1 region. Hwang et al. (2011) found that administration of *Z. jujuba* methanol extract significantly increased the number of Ki67 (a marker for cell proliferation)-positive cells in the subgranular zone of the dentate gyrus of middle-aged mice. Further, the extract significantly increased doublecortin (a marker for neuroblast differentiation)-immunoreactive neuroblasts with tertiary dendrites, but not those without tertiary dendrites, in the dentate gyrus. Also, doublecortin protein levels in the extract-treated groups tended to increase dose-dependently. The results suggested that the repeated supplement of *Z. jujuba* methanol extract may increase the hippocampal plasticity in middle-aged mice.

Analgesic and Antipyretic Activities

Ethanolic jujube fruit extract exhibited significant analgesic activity (Shah et al. 1989a). Jujube fruit extract also exhibited antipyretic activity, it did not produce any significant effect on body temperature and isolated guinea pig tracheal chain (Shah et al. 1989a). Pharmacological studies demonstrated that the compound prescription Huangqin Tang and its component drugs, roots of *Paeonia lactiflora, Scutellaria baicalensis* and *Glycyrrhiza uralensis*, and the fruit of *Ziziphus jujuba* exhibited antipyretic, analgesic and sedative effects (Huang et al. 1990).

Antispasmodic Activity

Studies demonstrated that the compound prescription Huangqin Tang and its component drugs, *Scutellaria baicalensis* and *Glycyrrhiza uralensis*, and the fruit of *Ziziphus jujuba* except the peony root also possessed significant antispasmodic activity (Huang et al. 1990).

Antimicrobial Activity

Ethanolic jujube fruit extract inhibited the growth of *Bacillus subtilis* (Shah et al. 1989a). Active principles in jujube fruit inhibited insoluble glucan formation by the cariogenic bacterium, *Streptococcus mutans* (Kohda et al. 1986). Hydrodistilled volatile oil from the seeds of *Zizyphus jujuba* exhibited strong detrimental effect against all five strains of *Listeria monocytogenes* (Al-Reza et al. 2009) The oil also had potent antioxidant activity. Using 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay, the IC_{50} value of the *Z. jujuba* essential oil was determined to be 5.21 μg/mL. Among the extracts, the strongest activity was exhibited by the methanol extract with an IC_{50} value of 20.44 μg/mL. In the superoxide radicals scavenging activities assay, methanol extract was superior to all other extracts (IC_{50} = 18.60 μg/mL). The results indicated that the essential oil and extracts of *Z. jujuba* could serve as natural antimicrobial and antioxidant agents for the food industry. Low activity was shown by the crude methanolic extract (12%) of *Z. jujuba*, n-hexane (9%), chloroform (20%) and ethyl acetate (14%) fraction against *Penicillium notatum* (Ahmad et al. 2011). Low activity was shown by the n-hexane fraction against *Aspergillus niger* (10%) and *Trichoderma harzianum* (13%) and inactive against *Aspergillus flavus, Fusarium oxysporum* and *Rhizopus stolonifer.* The chloroform fraction exhibited low activity of 10% against *F. oxysporum* while showing no activity against the rest of the test fungi. All the test samples were inactive against *Rhizopus stolonifer.*

Hypotensive and Antinephritic Activity

Kim and Han (1996) found that *Ziziphus jujuba* stimulated nitric oxide release in-vitro, in cultured endothelial cells and in-vivo, in the kidney tissues of rats. They suggested that *Z. jujuba may* possess hypotensive (reduction of blood pressure) and antinephritic (reduction of inflammation of the kidney) action, possibly by increasing renal blood flow.

Antifertility Activity

Ethyl acetate extract of *Zizyphus jujuba* bark arrested the normal estrus cycle of adult female mouse at diestrus stage and reduced the wet weight of ovaries significantly (Gupta et al. 2004). Cholesterol and ascorbic acid content in ovaries of crude extract-treated mice were significantly elevated. The significant inhibition of δ(5)-3β-hydroxysteroid dehydrogenase (δ(5)-3β-HSD) and glucose-6-phosphate dehydrogenase (G-6-PDH), the two key enzymes involved in ovarian steroidogenisis, were also observed in mouse after 18 days of treatment. Normal oestrus cycle and ovarian steroidogenisis were restored after withdrawal of treatment with the bark extract on average 32 days. Antifertility activities of crude bark extracts were found to be reversible.

Hepatoprotective Activity

Methanolic extract of *Zizyphus jujuba* fruits was found to possess hepatoprotective activity probably due to its antioxidant effect (Kumar et al. 2009). The low and medium doses of the extract significantly inhibited the acute elevation of biomarkers in serum and elevated the fall of biomarkers in the rat liver tissue homogenate with paracetamol and thioacetamide induced hepatic damage. The activities of antioxidants enzymes were significantly increased in liver tissue homogenate of rats pretreated with low and medium doses of the extract. Results of histopathological studies supported the biochemical findings. However, high dose of the extract was less effective than low and medium doses.

Cardioprotective and Cerebral-Protective Activity

The increases of lactate dehydrogenase release from damaged myocardial cells induced by deprivation of oxygen and glucose or treatment with chlorpromazine and mitomycin C were attenuated by *Z. jujuba* seed (33 μg/mL) except 11 μg/mL which showed no effect on mitomycin C (24 h)

and chlorpromazine (9 h)-induced injuries (Chen et al. 1990). These data suggested that *Z. jujuba* seed could be an effective protective drug for myocardial cells. Studies showed that *Z. jujuba* seed possessed protective effects on cerebral ischemic injuries (Bai et al. 1996). Total saponins of seeds of Chinese jujube reduced the contents of water and malondialdehyde in ischemic rat's brain tissues, elevated the activity of superoxide dismutase, creatine kinase and lactate dehydrogenase, decreased the content of lactate and alleviated the damages of nerve cells in the brain.

Antidiarrhoeal Activity

In an ethnobotanical survey of antidiarrhoeal plants of Parinche valley, Pune district, Maharashtra, India, *Z. jujuba* was identified as one of the 28 plants with antidiarrhoeal activity (Tetali et al. 2009).

Permeability Enhancing Activity

To assess the permeability enhancing activity of *Ziziphus jujuba*, an aqueous extract of seeds was compared to two members of a known series of permeability enhancement agents belonging to the alkylglycosides (Elery and Dovlatabadi 2001). The *Z. jujuba* extract lowered cell monolayer resistance more rapidly in a given time period than the alkylglycosides and allowed full recovery of cells in a relatively short time period. The extract of *Z. jujuba* appeared to be more efficient as a permeability enhancer than the two alkylglycosides.

Immunobiological/Anticomplementary Activity

Protojujubosides A and jujubosides A, B, and C isolated from *Zizyphus jujuba* var. *spinosa* seeds were found to show potent immunological adjuvant activity (Matsuda et al. 1999). *Z. jujuba* hydroalcoholic leaf extract at 5–50 μg/mL was found to stimulate in-vitro chemotactic, phagocytic and intracellular killing potency of human neutrophils (Ganachari et al. 2004). Pectic polysaccharides were the major components in all water-soluble polysaccharides in Chinese jujube leaves, fruits and flowers (Zhao et al. 2008). All the extracts were very rich in sugars such as uronic acid, arabinose and galactose. Polymers extracted with hot water from different pant parts were different in the degree of branching and degree of esterification. All water-soluble polysaccharides exhibited immunobiological activities especially from the fruits and flowers. Separate studies showed that the crude extract of polysaccharide from *Z. jujuba* cv. Jinsixiaozao, a major Chinese cultivar, to have potential anti-complementary activity (Li et al. 2011b). The polysaccharide extract dramatically increased thymus and spleen indices in mice and enhanced proliferation of splenocytes and peritoneal macrophages. Immunobiological tests indicated that two fractions, coded ZSP3c and ZSP4b, were the main active components. ZSP3c was rich in pectin with a degree of esterification (DE) of 49%, which may be related to its stronger immunological activity.

Among 11 triterpenoides isolated from the fruit, compounds 3-*O*-*cis*-*p*-coumaroyl maslinic acid (5), 3-*O*-*trans*-*p*-coumaroyl maslinic acid (6), and oleanolic acid (8), exhibited significant anticomplementary activity with IC_{50} values of 101.4, 143.9, and 163.4 μM, respectively, whereas the ceanothane-type and the lupane-type triterpenes were inactive (Lee et al. 2004b). This suggested that the oleanane-structure played an important role in inhibiting the haemolytic activity of human serum against erythrocytes.

Antiallergic Activity

Jujubosides A1 and C and acetyljujuboside B isolated from *Zizyphus jujuba* var. *spinosa* seeds were found to inhibit the histamine release from rat peritoneal exudate cells induced by antigen-antibody-reaction (Yoshikawa et al. 1997).

Antigenotxic Activity

Animal studies showed that *Z. jujuba* and *Origanum majorana* extracts exhibited protection against hydroquinone-induced clastogenetic effects and histological changes when treated

alone or combination with hydroquinone (Ghaly et al. 2008). *Z. jujuba* extract was more effective than *O. majorana* extract. Hydroquinone is a myelotoxin that is found in many foods and formed through the metabolism of benzene. The scientists concluded both extracts to be useful especially for people who are occupationally exposed to benzene or its metabolites.

Hair Promoting Activity

Z. jujuba essential oil was found to possess hair growth promoting activity (Yoon et al. 2010). After 21 days, mice treated with 1 and 10% of oil produced a greater effect on the length of hair which were measured to be 9.96 and 10.02 mm, respectively, as compared to the control (8.94 mm). Based on the weight of hair/cm^2 area of dorsal skin, hair thickness and hair follicles, it was found the best results was for 1% of essential oil treated mice.

Toxicity Studies

Ethanolic jujube fruit extract was found to be devoid of any significant toxic effects as evaluated by acute toxicity test observations made for 24 h and chronic treatment of animals for 3 months (Shah et al. 1989a). During acute toxicity, test observations were made for 24 h while the animals were treated for 3 months in chronic treatment. No significant changes in external morphological changes, visceral toxicity, haematological changes, spermatogenic dysfunction, besides effects on average body weight and vital organ weight were recorded.

Traditional Medicinal Uses

Various parts of the tree are used in traditional medicine for a variety of diseases and disorders in many Asian countries (Burkill 1966; CSIR 1976; Zeng et al. 1987; Natural Products Research Institute 1998; Azam-Ali et al. 2006; Mahajan and Chopda 2009). Chinese jujube has been used since ancient times as a nutrient tonic, a blood cleanser, and as an important adjunctive herb to other tonics, especially in combination with ginseng (*Tang Kue)* in China and Korea. Chinese jujube is universally believed in the Asia to build strength, remove obstruction to energy flow, *Qi* and enhance longevity. The fruits are widely used in Chinese and Korean traditional medicine, where they are believed to alleviate stress, for the treatment of various diseases such as chronic fatigue, loss of appetite, diarrhoea, anaemia, pain, cough, irritability, hysteria pharyngitis, bronchitis, anorexia, dysosmia, chalelithiasis, sedative, corn of foot. The fruits are also believed to possess activities such as anodyne, anticancer, refrigerant, sedative, antifungal, antibacterial, antiulcer, antiinflammatory, antispasmodic, sedative, antifertility, hypotensive, antinephritic, stomachic, antiallergic, pectoral, expectorant, styptic, laxative, and tonic. In India, the fruit is believed to purify the blood and to aid in digestion. In China, the seeds are used traditionally for insomnia, irritability, neurasthermia, physical emaciation, and as a remedy for diarrhoea.

The leaves are an ingredient used by some Benue tribes in prescription for gonorrhea. The pounded leaves are applied as a dressing to wounds. The leaves, in plaster form are used in strangury. A paste made from the tender leaves and twigs is applied to boils, abscesses, and carbuncles to promote suppuration. In the Philippines, a decoction of the bark and leaves has been employed as an effective astringent in dysentery and diarrhea and is used in bowel trouble of all kinds.

The bark has been used for diarrhoea in India, as a tonic for digestion in Java and as a tonic for digestion in Malaysia.

The root has some purgative effect, and is said to be drastic if taken in excess. In Angola, it is taken to promote menstruation. A root decoction is used for fevers. In India, the powdered root is applied to ulcers and wounds. The juice of the root bark is used as a purgative, and, externally, in gout and rheumatism. The bark is bitter and is sometimes used for colic; it is probably emetic in larger doses. It is also used for tanning in India. The bark in powdered form, or in decoction, is astringent and a simple remedy for diarrhoea. The powdered bark is a domestic dressing for old wounds and ulcers. In Cambodia, the bark is prescribed in dysentery and gingivitis.

Other Uses

In India, jujube is also grown as a host plant for the lac insect, *Laccifer lacca*. The wood is durable and hard, used in turnery and suitable for wood floor, furniture and construction. In Korea the wood to make the body of the *taepyeongso*, a double-reed wind instrument and for making Go bowls. In Bhutan, the leaves are used as a potpourri to help keep the houses of the inhabitants smelling fresh and clean. It is also said to keep bugs and other insects out of the house and free of infestation. In the traditional Chinese wedding ceremony, jujube and walnut were often placed in the newlyweds' bedroom as a sign of fertility. The fragrance of the flowers are said to make teenagers fall in love, consequently young men will take a flowering shoot and put it on their hats to woo the opposite sex in the Himalaya and Karakoram regions. In Japan, the natsume has given its name to a style of tea caddy used in the Japanese tea ceremony. In Abyssinia, the fruit is used to stupefy fish.

The crude methanolic extract of *Zizyphus jujuba* showed significant antitermite activity against *Heterotermes indicola*, among the test samples (Ahmad et al. 2011). All the test samples except n-hexane showed low activity (20%) against *Tribolium castaneum*. The n-hexane fraction showed low activity (20%) against *Rhizopertha dominica* while the rest of the fractions were inactive against it. Low activity of 40 and 20% was shown by the chloroform and n-hexane fraction respectively against *Callosbruchus analis*.

Comments

Kirkbride et al. (2006) proposed the name *Ziziphus jujuba* as the correct scientific name of the species for conservation against the paratautonym *Ziziphus zizyphus* (L.) H. Karsten.

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Ziziphus mauritiana

Scientific Name

***Ziziphus mauritiana* Lamarck.**

Synonyms

Mansana arborea J.F. Gmel., *Paliurus mairei* H. Léveillé, *Rhamnus jujuba* L., *Sarcomphalus mauritianus* (Lam.) Raf., *Ziziphus abyssinicus* Hochst., *Ziziphus agrestis* Roem. & Schult, *Ziziphus jujuba* (L.) Gaertn., *Ziziphus jujuba* (L.) Lam. not Miller, *Ziziphus mairei* (H. Léveillé) Browicz & Lauener, not Dode, *Ziziphus orthacantha* DC., *Ziziphus rotundata* DC., *Ziziphus rotundifolia* Lam., *Ziziphus sororia* Roem. & Schult., *Ziziphus trinervia* Roth.

Family

Rhamnaceae

Common/English Names

Bear Tree, Ber, Chinee Apple, Common Jujube, Cottony Jujube, Desert Apple, Dunks, Indian Cherry, Indian Jujube, Indian Plum, Jujube, Sour Jujube, Yunnan Jujube, Yunnan Spiny Jujube.

Vernacular Names

Amharic: Kurkura;
Arabic: Beri, Bor, Nabak, Nabbak-El-Fil, Nobig, Sidr;
Bambara: Ntomono, Ntomoro;
Burmese: Eng-Si, Zee-Pen, Zizidaw;
Chamorro: Manzanas, Manzanita;
Chinese: Dian Ci Zao;
Czech: Cicimek Mauricijský;
Danish: Kinesisk Dadel;
Eastonia: India Kreektürn;
Eritea: Geva (Tigrigna)
Ethiopia: Gusura (Afargna);
Fijian: Baere;
French: Jujube, Jujubier, Jujubier Commun, Le Jujubier, Le Jujubier Sauvage, Liane Croc-Chien;
German: Filzblättrige Jujube;
India: Bogori (Assamese), Ber, Ber Boroi, Boroi, Kool, Kul (Bengali), Theng Khi (Garo), Badara, Baer, Bahir, Bara-Bor, Ber, Beri, Bor, Bordi, Borti, Karkandhu, Kath Ber, Kuvala, Pamji-Bor, Pemdiber (Hindu), Bore, Elachi, Elanji, Yalaci (Kannada), Ilanta, Ilantappalam, Lantappalam, Perin-Toddah, Peruntutali (Malayalam), Boroi (Manipuri), Ber, Baher, Bera, Bhor, Bor, Bora (Marathi), Kawrsinhlo (Mizoram), Barkoli (Oriya), Ajapriya, Badara, Badarah, Badri, Karkandhu,Kola, Kolah, Koli, Kuvala,

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Madhuraphala, Sauvira, Sincitikaphala (Sanskrit), Arulatotikacceti, Arulatotiyam, Atitarakamaram, Atitaram, Attiram, Cancarikai, Cancikai, Cannirotayam, Cannirotayamaram, Cattiracamam, Cimaiyilantai, Cinailantai, Civakam,Cuviriyam,Cuviriyam,Cuviriyamaram, Elandai, Iccatti, Ilandai, Ilantai, Ilantappalam, Ilanthei, Ilantha, Ilatai, Inippilantai, Inturu, Inturukam, Inturukamaram, Iracatuntu, Iram, Irantuntu, Irantuntukam, Irantuntukamaram, Irati, Irisipakam, Iruntunar, Irutu, Kamanalatti, Karkkantu, Katturekam, Katturekamaram, Kauvalam, Ko, Kokilam, Kokkumpatari, Kolikam, Kolikamaram, Kolmuli, Kontai, Korkoti, Korkotimaram, Kotali, Kottakkoti, Kottakoti, Kulatti, Kulavali, Kulavalli, Kulavallimaram, Kullari, Kulvali, Kutapalai, Kutapalam, Kuvalam, Miruttiyupalam, Mulatti, Muliyeru, Munnatimatu, Murukatantai, Nalampalam,Nattilantai,Nilailantai,Nilavilantai, Pallavaparuni, Pallavaparunicceti, Pancamiyam, Patari, Patarikam, Patarikamaram, Pulippilantai, Pulippilantaicceti, Ratti, Ratticceti, Tammalai, Tampalai, Tampalam, Tanupicam, Tiritapicam, Tittipilantaimaram, Tittippilantai, Utirumpalam, Uyastavam, Vaccirakantam, Vakkirakantam, Valarotayam, Varuvaluntimuli, Vataram, Vatuputpakam, Vetirimaram, Vettiracceti, Vettiram, Veyam, Yellande, (Tamil), Badari, Ganga Regi, Gangaregu, Regu, Reni (Telugu);
Indonesian: Bidara, Dara, Widara;
Japanese: Indo Natsume;
Khmer: Putrea;
Lithuanian: Manzanita;
Laotian: Than;
Malaysia: Bidara, Epal Siam, Jujub;
Mauritania: Nabagaya, Neggaïe, Sde,Sidar, Sider (Arabic);
Mozambique: N'sao (Se);
Nepali: Bayer;
Niger: Darey (Zarma);
Nigeria: Magarya (Hausa), Huya (Kilba);
Persian: Zizafun, Zizfum;
Philippines: Manzanitas (Taglalog);
Pakistan: Jujube, Ker;
Portuguese: Acuteifa; Anáfega;
Senegal: Nabagaya, Neggaï, Sidar, Sider (Arabic), Â-Ginginô (Basari), Ga-Ngɛ́ngɛ̀ (Bedik);
Somali: Geb, Gub;
Spanish: Azufaifo Africano, Perita Haitiana, Ponseré, Yuyuba;
Sri Lanka: Yellande;
Sudan: N' Domo (Bambara), Tomboro (Malinke, Kasombe), Fâ (Sominke)
Swahili: Mkunazi;
Thai: Ma Tan, Ma Thong, Phut-Saa;
Vietnamese: Tao, Tao-Nhue;
West Africa: Toboro, Tomboron Moussana, Tomborongo (Mandinka);
Zimbawe: Jujube (English), Masau, Musawu (Shona).

Origin/Distribution

Ziziphus mauritiana is native to southern Asia and eastern Africa and is now widely naturalized from tropical Africa to Afghanistan and China, and also through Malaysia and into Australia and some Pacific archipelagos and elsewhere.

Agroecology

Indian jujube occurs in forests, thickets along river banks, hills and slopes in it native habitats in the tropical and subtropical regions. It grows in areas with mean annual temperature: minimum of 7–13 to maximum of 37–48°C, mean annual rainfall: 15–225 mm from sea level to 1,500 m elevation. Beyond the 1,000 m elevation trees do not perform well, and cultivation becomes less economical. Fruit quality is best under hot, sunny and dry conditions, but there should be a rainy season to support extension growth and flowering, ideally leaving enough residual soil moisture to carry the fruit to maturity. It is a hardy and robust tree that copes with extreme temperatures and thrives under rather dry conditions. It is known for its ability to withstand adverse conditions, such as salinity, drought and waterlogged conditions. It prefers neutral to slightly alkaline sandy-loams but can grow on a wide variety of soils including laterite, black cotton and oolithic limestone.

Edible Plant Parts and Uses

Fresh Indian jujube has a mild sub-acid flavour and crisp firm flesh. The fruit is eaten fresh both flesh and peel or can be made into refreshing drink by macerating fruits in water. It can also be eaten boiled, as an addition to rice or millet, stewed or baked. Unripe fruits eaten with chilli, salt and sugar or pickle or made into chutney. The fruits can be made into fritters, jams or candied fruits. The fruit can be dried and processed into a floury meal, beer butter, or a cheese-like paste, used as a condiment. Fermented pulp is pressed into cakes resembling gingerbread. In Venezuela, a jujube liqueur is made and sold as *Crema de ponsigue.* Seed kernels are eaten in times of famine The fruit is a good source of carotene, vitamins A and C, and fatty oils. In Indonesia, young leaves are cooked as a vegetable.

In Zimbawe, surplus fruits are sun dried transformed into various products such as porridge, traditional cakes, *mahewu* (fermented liquid mealie-meal porridge), and also fermented to produce a spirit called *Kachasu* (Nyanga et al. 2008). The ethanol content of the fermented fruit pulp ranged from 2.1 to 3.7 mL/100 mL, whereas the traditionally made distillate contained 23.8–45.6 m/100 mL.

Plate 1 Alternate, ovate leaves with serrulate margins

Plate 2 Young plant with drooping fruiting branch

Botany

A spiny, evergreen shrub or small tree 3–15 m high, with trunk diameter of 40 cm or more, spreading crown, stipular spines and many drooping tomentose branches (Plate 2). Its bark is dark grey or dull black and irregularly fissured. Leaves are simple, alternate, in two rows, on 5–13 mm tomentose petioles. Lamina ovate- or oblong-elliptic, 2.5–6 × 1.5–5 cm, with rounded tip and subrounded, slightly oblique base, serrulate margin, abaxially yellow or gray-white tomentose, adaxially shiny green, glabrous, with 3 conspicuous, depressed, longitudinal veins (Plates 1, 2, 3, and 4). Inflorescence axillary cymes, 1–2 cm long, with 7–20 flowers; peduncles 2–3 mm long. Flowers 2–3 mm across, greenish-yellow, faintly fragrant, male or bisexual, on 3–8 mm long pedicels; calyx with 5 deltoid lobes, hairy outside, glabrous within; petals 5, subspathulate, concave and reflexed; stamens subequaling petals; disc thick, fleshy, 10-lobed, concave at middle; ovary globose, glabrous; style 2-fid. Fruit is a drupe, globose, oblong to ovoid, up to 6 × 4 cm in cultivation, usually much smaller when wild; the skin smooth or rough, glossy, thin but tough, turns from light-green to yellow (Plates 2, 3, 4, and 5), later becomes partially or wholly burnt-orange or red-

Plate 3 Ripe Indian jujube

Plate 4 Close-up of leaves and ripening fruits

Plate 5 Whole and halved ripe Indian jujube

brown or red or blackish; flesh white, crisp (Plate 5), juicy, subacid to sweet, becoming mealy in fully ripe fruits. Seed a tuberculate and irregularly furrowed stone, containing 1–2 elliptic red-brown kernels each 6 mm long.

Nutritive/Medicinal Properties

Nutrient composition of Indian jujube fruit per 100 g edible portion was reported as: moisture 81.6 g, energy 74 kcal, protein 0.8 g, fat 0.3 g, carbohydrate 17 g, ash 0.3 g, total carotene 21 μg, vitamin C 76 mg, Fe 0.5 mg and Ca 4 mg (Gopalan et al. 2002).

Analyses conducted in Honduras (Morton 1987) reported the following food value for the fresh fruit based on 100 g edible portion: moisture 81.6–83.0 g, protein 0.8 g, fat 0.07 g, fiber 0.60 g, carbohydrates 17.0 g, total sugars 5.4–10.5 g, reducing sugars 1.4–6.2 g, non-reducing sugars 3.2–8.0 g, ash 0.3–0.59 g, calcium 25.6 mg, phosphorus 26.8 mg, iron 0.76–1.8 mg, carotene 0.021 mg, thiamine 0.02–0.024 mg, riboflavin 0.02–0.038 mg, niacin 0.7–0.873 mg, citric acid 0.2–1.1 mg, ascorbic acid 65.8–76.0 mg, fluoride 0.1–0.2 ppm and pectin (dry basis) 2.2–3.4%.

Ziziphus mauritiana fruit was found to contain sugars galactose, fructose and glucose; and organic acid citric acid, malonic acid and malic acid (Muchuweti et al. 2005). Phenolic compounds such as *p*-hydroxybenzoic acid, caffeic, ferulic acid and *p*-coumaric acid were found to be the most abundant with concentrations of 365.94,

30.76, 19.64 and 19.28 mg/kg dry mass respectively, whereas vanillic acid was the least abundant with a concentration of 2.52 mg/kg.

Functional properties analysis of mucilage powder from *Z. mauritania* fruit pulp showed that it had brightness in similar value with xanthan gum but higher than guar gum and oil absorption value were 9 and 6 times higher than guar gum and xanthan gum, respectively (Thanatcha and Pranee 2011). It exhibited pseudoplastic property as guar gum and its water holding capacity was 11.77 g dry weight.

Two 14- and 13-membered cyclic alkaloids, mauritine L and mauritine M, and three known cyclopeptide alkaloids, nummularine H, nummularine B and hemsine A were isolated from the methanol extract of *Z. mauritiana* roots (Panseeta et al. 2011).

Scientific investigations revealed that various parts of the plant have various pharmacological activities such as antioxidant, hepatoprotective, antidiarrhoeal, anti microbial, antihyperglycemic/hypoglycemic and antiplasmodial activities.

Antioxidant Activity

Studies indicated that the seed extract of *Ziziphus mauritiana* potentially scavenged the free radicals in a concentration-dependent manner using DPPH assay and Fenton reaction system (Bhatia and Mishra 2009) The pretreatment of Swiss albino mice with *Ziziphus mauritiana* seed extract inhibited lipid peroxidation significantly, and increased the levels of reduced glutathione, catalase activity and superoxide dismutase in all extract treated groups as compared to alcohol treated groups. The extract provided protection against the induction of oxidative stress by alcohol either by converting free radicals into stable products or by strengthening the antioxidant system.

Enzyme assisted processing significantly improved the fruit juice yield, total soluble solids, total phenolics and total antioxidant activity (AOX) (Koley et al. 2011). Using viscozyme, there was significant increase in recovery of antioxidants, to 70.51, 66, and 45% respectively in ascorbic acid, total phenolics and total flavonoids. The in-vitro total AOX of juice extracted via enzyme-assisted processing was 20.9 and 15.59 μmol Trolox/mL in ferric-reducing antioxidant power and cupric-reducing antioxidant capacity assays, respectively. There was 41% increase in AOX of juice extracted with enzyme over straight pressed juice. Results indicated that enzyme-assisted processing could significantly improve the functional properties of the *Ziziphus* juice.

Anticancer Activity

Oral administration of crude *Z. mauritiana* extract increased the survival time and decreased the peritoneal ascitic fluid content significantly in Swiss Albino mice bearing Dalton lymphoma ascites (DLA) tumour (Adhvaryu et al. 2008). Haemoglobin, RBCs and total WBC which were altered by DLA inoculation were restored significantly by the extract. The extract showed in-vitro cytotoxic activity against DLA cell-line. In a recent study, *Z. mauritiana* seed extract was found to markedly inhibit the proliferation of HL-60 (human promyelocytic leukemia) cells (Mishra et al. 2011). The extract dose-dependently induced apoptosis of treated HL-60 cells. DNA fragmentation occurred in HL-60 cells after 3 h incubation with extract. The extract also exhibited potent anticancer potential in-vivo. Treatment of Ehrlich ascites carcinoma bearing Swiss albino mice with varied doses (100–800 mg/kg b.w.) of the extract significantly reduced tumour volume and viable tumour cell count and improved haemoglobin content, RBC count, mean survival time, tumour inhibition, and percentage life span. The enhanced antioxidant status in extract-treated animals was evident from decline in levels of lipid peroxidation and increased levels of glutathione, catalase, and superoxide dismutase.

Antidiabetic Activity

The aqueous extract and the non-polysaccharide fraction of the aqueous extract of fruits of *Z.*

mauritiana were found to exhibit significant antihyperglycemic and hypoglycemic activities (Jarald et al. 2009). The petroleum ether extract was found to exhibit only an antihyperglycemic effect. Treatment of diabetic rats with petroleum ether extract, aqueous extract, and non-polysaccharide fraction of this plant restored the elevated biochemical parameters, glucose, urea, creatinine, serum cholesterol, serum triglyceride, HDL, LDL, hemoglobin, and glycosylated hemoglobin significantly to the near normal level. Comparatively, the non-polysaccharide fraction of the aqueous extract was found to be more effective, followed by the aqueous extract, and the petroleum ether extract. The activity of the non-polysaccharide fraction was comparable to that of the standard drug glibenclamide. Oral administration of *Z. mauritiana* seed extract alone or in combination with glyburide reduced the blood glucose level in all the alloxan diabetic mice after acute and sub-acute (28 days) administration (Bhatia and Mishra 2010). Administration of the extract reduced the weight loss and mortality rate during the sub-acute study. The results of blood glucose level, loss in body weight, and mortality rate were more pronounced in the group treated with the combination (800 mg/kg seed extract and 10 mg/kg glyburide). The extract also augmented the glucose tolerance in both normal and diabetic mice. The results suggested that the extract had synergistic hypoglycemic activity.

Antidiarrheal Activity

The methanolic extract of *Z. mauritiana* roots exhibited anti diarrhoeal effect with a concentration dependent inhibition of the spontaneous pendular movement of the isolated rabbit jejunum and inhibited acetylcholine induced contraction of rat ileum (Dahiru et al. 2006). A dose dependent decrease of gastrointestinal transit was observed with extracts (25 and 50 mg/kg) which also protected mice against castor oil induced diarrhoea and castor oil induced fluid accumulation, respectively. The presence of some of the phytochemicals (alkaloids, flavonoids, glycosides, saponins and volatile oil) in the root extract may be responsible for the observed effects, and also the basis for its use in traditional medicine as antidiarrhoeal drug.

Hepatoprotective Activity

Studies indicated that the aqueous extract of *Ziziphus mauritiana* leaf may prevent chronic alcohol-induced liver injury by enhancing the levels of total antioxidant status and inhibiting hepatic lipid peroxidation (Dahiru et al. 2005; Dahiru and Obidoa 2007a; 2007b). Rats that received alcohol only showed significantly elevated levels of Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, and hepatic lipid peroxidation while reduced glutathione, total antioxidant status and body weight significantly decreased compared to control rats. Pretreatment of rats with 200, 400 mg/kg body weight of aqueous leaf extract of *Ziziphus mauritiana* or 100 mg/kg silymarin resulted in a significant decreased levels of ALT, AST, ALP, and TB with levels of catalase, glutathione peroxidase, glutathione reductase and superoxide dismutase showing a significant increase compared to group administered alcohol only. Histopathology of rat liver administered with alcohol only resulted in severe necrosis, mononuclear cell aggregation and fatty degeneration in the central and mid zonal areas which was a characteristic of a damaged liver. Pre-treatment with the aqueous extract of *Ziziphus mauritiana* or silymarin reduced the morphological changes that are associated with chronic alcohol administration. The presence of tannins, saponins and phenolic compounds observed in the plant extract could be responsible for the observed effects of decreasing the levels of injured tissue marker and lipid peroxidation.

Animal studies showed that *Z. mauritiana* extract showed hepatoprotective potential and prevented immunosuppression (Adhvaryu et al. 2007). The jujube extract treated animals showed normal liver histology and enzyme levels, increased phagocytic % and enhanced chemotactic index. Animals induced with isoniazid, rifampicin, pyrazinamide and treated with jujube extract showed nearly normal histology with

minimal inflammation and microvesicular steatosis. Hepatotoxicity was prevented by restricting the rise of aspartate aminotransferase by 3-fold, aspartate aminotransferase/alanine aminotransferase by 2-fold and alkaline Phosphatase to normal levels. Neutrophil function were normalised or enhanced. The extract showed strong immunostimulatory activity.

Antimicrobial Activity

The methanol leaf extract of *Ziziphus mauritiana* showed significant antibacterial activity against *Bacillus subtilis, Escherichia coli, Pseudomonas fluorescens, Staphylococcus aureus* and *Xanthomonas axonopodis* pv. *malvacearum* and antifungal activity against *Aspergillus flavus, Dreschlera turcica and Fusarium verticillioides* when compared to root/ bark extracts (Mahesh and Satish 2008). *Z. mauritiana* leaf extract showed significant activity against *Xanthomonas axonopodis* pv. *malvacearum* and recorded significant antifungal activity against *Dreschlera turcica.* Alkaloids mauritine M and nummularine H isolated from *Z. mauritiana* roots demonstrated antimycobacterial activity against *Mycobacterium tuberculosis* with the MIC of 72.8 and 4.5 μM, respectively (Panseeta et al. 2011).

Immunomodulatory Activity

Z. mauritiana seed extract demonstrated significant up-regulation of cell-mediated, humoral (sheep red blood cells) immune response and Th-1 mediated cytokine IFN-gamma and decline in Th-2 mediated cytokine IL-4 (Mishra and Bhatia 2010). At higher dose of extract the results were comparable to that of the standard drug levamisole.

Antiplasmodial Activity

The alkaloids from *Z. mauritiana* roots namely mauritine L, mauritine M, nummularine H, nummularine B and hemsine A exhibited potent antiplasmodial activity against the parasite *Plasmodium falciparum* with the inhibitory concentration (IC_{50}) ranging from 3.7 to 10.3 μM (Panseeta et al. 2011).

Allergenic Activity

Studies on skin test responses in patients and specific IgE assays showed that Indian jujube (*Zizyphus mauritiana*) had allergenic components that showed IgE cross-reactivity with natural rubber latex allergen (Lee et al. 2004). Ziz m 1 was found to be a major Indian jujube allergen involved in latex-fruit syndrome (Lee et al. 2008). The researchers identified immunoglobulin E (IgE)-binding epitopes and recombinant IgE reactivities of the rubber latex cross-reacting Indian jujube Ziz m 1 allergen (Lee et al. 2008).

Traditional Medicinal Uses

In India, the fruit is believed to purify the blood and aid in weak digestion. The fruits mixed with salt and chili peppers, are given in indigestion and biliousness and employed in pulmonary ailments and fevers. Fruits sliced or crushed are applied on cuts and ulcers. The dried ripe fruit is a mild laxative. The seeds are sedative and are taken, sometimes with buttermilk, to halt nausea, vomiting, and abdominal pains in pregnancy. They check diarrhea, and are poulticed on wounds; mixed with oil, they are rubbed on rheumatic areas.

The leaves are applied as poultices and are helpful in liver troubles, asthma and fever and, together with catechu, are administered when an astringent is needed, as on wounds. Decoction of the bark and leaves is an effective astringent in dysentery and diarrhea and is sued in the Philippines in bowel ailments. The bitter, astringent bark decoction is taken to halt diarrhea and dysentery and relieve gingivitis. The bark paste is applied on sores. In Java, the bark is regarded as a tonic for indigestion. In Peninsular Malaysia a poultice of the bark has been used for

stomach-ache. The root is purgative. A root decoction is given as a febrifuge, taenicide and emmenagogue, and the powdered root is dusted on wounds. Juice of the root bark is said to alleviate gout and rheumatism. Strong doses of the bark or root may be toxic. An infusion of the flowers serves as an eye lotion.

Other Uses

The tree provides a medium-weight to heavy hardwood that is close-grained, fine-textured, hard, tough and that seasons well. The wood is used for general construction, furniture and cabinet work, tool handles, agricultural implements, tent pegs, golf clubs, gun stocks, sandals, yokes, harrows, toys, turnery, hose-poles, household utensils, legs for bedsteads, bowling pins, baseball bats, boat ribs, chisels and packaging. It is also suitable for the production of veneer and plywood. It yields excellent charcoal and activated carbon; and the timber together with the branches provides a good source of firewood. The bark, including the root bark, has been employed in tanning; when pounded and mashed in water, it yields brown and grey or reddish dyes. In Kenya, the bark yields a non-fading, cinnamon-coloured dye. The leaves provides a ready source of nutritious fodder for cattle, goats, sheep and camels and feed for tasar silkworms which provides the highly prized tasar silk. In Burma, the fruit is used in dyeing silk. The flowers provide minor source of pollens for bees.

Z. mauritiana is a good host tree for the lac insects, *Kerria lacca* in India. The insect feeds on its leaves and produces an orange-red resinous substance. When purified the resin yields a high-quality ber shellac that is used in fine lacquer work and to produce sealing wax and varnish. It is also a suitable tree to used in fixation of coastal dune sand and is used as a living fence; its spiny stems and branches deter livestock. The tree has also been planted for shade and as windbreaks.

Comments

In Queensland, the species has been declared an invasive noxious weed as it forms impenetrable thickets, hampering livestock management and reducing pasture production and accessibility.

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Coffea arabica

Scientific Name

***Coffea arabica* L.**

Synonyms

Coffea arabica f. *abyssinica* A.Chev. nom. inval., *Coffea arabica* var. *amarella* A.Froehner, *Coffea arabica* var. *angustifolia* Cramer, *Coffea arabica* var. *bourbon* Rodr. ex Choussy, *Coffea arabica* var. *brevistipulata* Cif., *Coffea arabica* var. *bullata* Cramer, *Coffea arabica* var. *columnaris* Ottol. ex Cramer, *Coffea arabica* var. *culta* A. Chev. nom. inval., *Coffea arabica* var. *cultoides* A.Chev. nom. inval., *Coffea arabica* var. *erecta* Ottol. ex Cramer, *Coffea arabica* var. *latifolia* A.Chev. nom. inval., *Coffea arabica* var. *longistipulata* Cif., *Coffea arabica* var. *maragogype* A.Froehner, *Coffea arabica* var. *mokka* Cramer, *Coffea arabica* var. *monosperma* Ottol. & Cramer, *Coffea arabica* var. *murta* Lalière, *Coffea arabica* var. *myrtifolia* A.Chev. nom. inval., *Coffea arabica* var. *pendula* Cramer, *Coffea arabica* var. *polysperma* Burck, *Coffea arabica* var. *pubescens* Cif., *Coffea arabica* var. *purpurascens* Cramer, *Coffea arabica* var. *rotundifolia* Ottol. ex Cramer, *Coffea arabica* var. *straminea* Miq. ex A.Froehner, *Coffea arabica* var. *sundana* (Miq.) A.Chev., *Coffea arabica* var. *typica* Cramer nom. inval., *Coffea arabica* var. *variegata* Ottol. ex Cramer, *Coffea bourbonica* Pharm. ex Wehmer nom. nud., *Coffea corymbulosa* Bertol., *Coffea laurifolia* Salisb., *Coffea moka* Heynh., *Coffea sundana* Miq., *Coffea vulgaris* Moench.

Family

Rubiaceae

Common/English Names

Abyssinian Coffee, Arabica Coffee, Arabian Coffee, Brazilian Coffee, Coffea Arabica, Coffee, Coffeetree, Common Coffee, Green Coffee.

Vernacular Names

Afaan Oromo: Bunna;
Afrikaans: Koffie, Koffieboom;
Amharic: Buna;
Arabic: Bun, Kahwa, Kassent, Kawa, Kuehwa, Qahva, Quahwah;
Brazil: Café, Cafeeiro, Cafeiro;
Bulgarian: Arabsko Kafe;
Burmese: Ka-Phi;
Burundi: Akawa (Kirundi);
Chamorro: Cafe, Kafé;

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Chinese: Ka Fei, Ka Fei Dou (Bean), Ka Fei Shu (Tree), Xiao Guo Ka Fei, Xiao Li Ka Fei;
Cook Islands: Kaope, Kaope Maori (Maori);
Croatian: Kava;
Creole: Kafe;
Czech: Kávovník Arabský;
Danish: Ægte Kaffe**,** Ægte Kaffetræ, Kaffetræ;
Democratic Republic Of Congo: Kawa (Kinyarwanda);
Dutch: Arabicakoffie, Arabische Koffieboom, Groene Koffie, Koffie, ,Koffieboom, Koffiestruik;
Egypt: Elive (Arabic);
Eastonian: Araabia Kohvipuu;
Fijian: Kofe, Kove;
Finnish: Arabiankahvi;
French: Café, Cafeier, Caféier Commun, Caféier D' Arabie;
German: Arabicakaffee, Arabischer Kaffeebaum, Arabischer Kaffeestrauch, Bergkaffee, Kaffee, Kaffeestrauch, Kaffeebohne, Kaffeestrauch;
Greek: Kafes;
Hungarian: Arab Kávé, Kávé;
Icelandic: Kaffirunni, Java Kaffi;
India: Bun, Caphi, Kafi, Pilu (Hindi), Bannu Gida, Bonda, Bonda-Bija, Bundu, Bunnu, Bunu, Coffee Gida, Kaaphi, Kaphi, Kapi, Kapi-Bija, Kappi (Kannada), Bannu, Bunnu, Kapi, Kappi, Kappi-Karu, Kuppu (Malayalam), Cofi (Manipuri), Bund, Kaaphe, Kaphe (Marathi), Kawfi (Mizoram), Kaphi, Mlechca-Phala, Rajapiluh (Sanskrit), Capie Cottay, Cilapakakkottai, Cilapakam, Kapi, Kapi-Kottai, Kapikottai, Kappi, Kappikkottai, Kappikkottaicceti, Kopi , Koppi, Koppicceti, Patakari,Patakarikkottai,Ticaipari,Ticaiparikkottai, Tumpavakakkottai, Tumpavakam (Tamil), Kaapivittulu, Kafi, Kapi, Kapi-Vittulu, Kapivittulu, Kappi (Telugu);
Indonesia: Kopi;
Italian: Albero Del Caffè, Arbusto Del Caffè, Caffee, Caffè;
Japanese: Arabika Koohii, Koohii Noki;
Jordan: Qahwa (Arabic);
Kenya: Kahûa, Mûhûa (Kikuyu), Buna (Ormaland);
Khmer: Kafae;
Kirundi: Akawa;
Korean: K'eo P'i Na Mu;
Malaysia: Kopi;
Marquesan: Kafe;
Niuean: Kofe;
Norwegian: Kaffe, Kaffeplante;
Papua New Guinea: Kopi;
Palauan: Kohi;
Persian: Bun, Cahwa, Gehve, Kahwa, Qahva, Tochem Keweh;
Philippines: Kapi (Ifugao), Kapi (Iloko), Kahana (Sulu), Kapé, Kapi (Tagalog);
Polish: Kawa, Kawa Arabska;
Portuguese: Cafe, Café, Caféeiro;
Runyankore: Mwani;
Russian: Kofe Arabica;
Rwanda: Ikawa;
Samoan: Kofe;
Serbian: Domaća Kafa, Kafa;
Shona: Muhubva;
Slovašcina: Kava;
Spanish: Arbol Del Café, Café, Cafeto, Cafeto Arábico, Cafeto De Arabia;
Swahili: Kahawa;
Swedish: Arabiskt Kaffe, Kaffe;
Tahitian: Taofe;
Thai: Kafae;
Tongan: Kofi;
Turkish: Kahvé Oghadji;
Vietnamese: Càphê Arabica;
Zulu: Ikhofi, Ilikhofi.

Origin/Distribution

Coffea arabica is the most widely cultivated species of *Coffea* and the only tetraploid species (2×=44) in the genus. It has its primary centre of genetic diversity in the highlands of South West Ethiopia and the Boma Plateau of Sudan (Lashermes et al. 1995) and disjunct populations of *C. arabica* have been also reported in Mount Imatong (Sudan) and Mount Marsabit (Kenya) (Berthaud and Charrier 1988). DNA molecular studies using restriction fragment length polymorphism (RFLP) markers confirmed that *C. arabica* is an amphidiploid formed by hybridisation between *Coffea eugenioides* and *Coffea canephora*, or ecotypes related to these diploid

species (Lashermes et al. 1995, 1999). Further molecular marker studies found that the cultivated coffee derived from the genetic populations Typica and Bourbon appeared little differentiated from wild coffee growing in the southwest of Ethiopia (Anthony et al. 2001). The results supported the hypothesis that southwestern Ethiopian coffee trees could have been introduced recently in the south and southeast Ethiopia.

Coffee was first cultivated by Arabs during the fourteenth century and introduced into the New World and much of the rest of the tropics during the seventeenth century (Smith 1985; Wrigley 1988). Today, *Coffea arabica* represent the most commonly cultivated species yielding 74% of the world production of coffee. It is cultivated throughout the moist subtropics and high-altitude, moist tropics. Main areas of cultivation are Brazil, Colombia, Mexico, Ethiopia, El Salvador, Costa Rica, Honduras, Indonesia, Guatemala, Ivory Coast, Angola, Jamaica, Uganda, India, Philippines, Cameroon and Vietnam. It is also cultivated in Angola, Cambodia, China Puerto Rico, the Virgin Islands, Papua New Guinea, Guam, Samoa and Australia.

The world's top 10 leading green coffee producing countries in 2010 were: Brazil 2,874,310 tonnes, Vietnam 1,105,700 tonnes, Indonesia 801,000 tonnes, Columbia 514,128 tonnes, India 289,600 tonnes, Ethiopia 270,000 tonnes, Peru 264,605 tonnes, Guatemala 257,000 tonnes Mexico 253,800 tonnes, and Honduras 229,368 tonnes (FAOSTAT 2012).

Agroecology

Coffea arabica prefers a cool, mildly humid climate and is usually grown at altitudes of 1,300–1,500 m in the tropics and subtropics. Arabica coffee can tolerate low temperatures, but not frost, and it thrives best in areas with mean annual temperatures of 15–25°C and with mean annual rainfall of 1,500–2,000 mm. Temperatures close to 30°C or above are detrimental to growth and fruit production.

Coffea arabica is shade tolerant and prefers to be grown under light shade provided by shade tree species such *Albizia* spp, *Erythrina* spp., *Inga* spp and *Leucaena* spp or grown as an understorey in thinned forests. Some Arabica cultivars are also grown without shade. However, studies in Costa Rica showed shade improved bean yield, characteristics and beverage quality of Arabica grown under optimal and sub-optimal conditions. Muschler (2001) found that fruit weight and bean size of *C. arabica* increased significantly when shade intensity was increased from 0% to more than 80% under unpruned *Erythrina poeppigiana*. While large beans (diameter > 6.7 mm) accounted for 49 and 43% of the coffee from unshaded Caturra and Catimor cultivars, respectively, these proportions increased to 69 and 72% under dense permanent shade. This suggested a stronger shade benefit for Catimor than for Caturra. Vaast et al. (2006) reported with fruit loads combined and unthinned, coffee production was 18% lower in shade than in full sun but alternate bearing was reduced. Shade positively affected bean size and composition as well as beverage quality by delaying berry flesh ripening by up to 1 month. They found that caffeine and fat contents were highest in beans of shade-grown plants, whereas sucrose, chlorogenic acid and trigonelline contents were highest in beans of sun-grown plants. Higher sucrose, chlorogenic acid and trigonelline contents in sun-grown beans pointed towards incomplete bean maturation and explained the higher bitterness and astringency of the coffee beverage. They also found that fruit thinning enhanced bean size and hastened the maturation process. Higher fruit loads reduced bean size owing to carbohydrate competition among berries during bean filling. They also found that in full sun, the dwarf coffee cultivar 'Costa Rica 95' poorly self-regulated its productivity, produced beans of lower quality and experienced stronger alternate bearing than in shade.

Bean weight and bean size of *Coffea arabica* cv. Catimor increased significantly when the shade level was progressively increased (Somporn et al. 2012). The coffee beans grown under lychee shade exhibited superior bean yield, 1,000-bean weight, total phenolic content

and antioxidant activity compared to all other beans. The content of total sugar (fructose, glucose and sucrose) was found highest in coffee beans grown in 60% shade, with fructose the predominant sugar. Chlorogenic acid was the most predominant phenolic acid in all samples studied, being the highest in the beans grown under lychee shade, followed by 60% shade, 70% shade, 50% shade and full sun, respectively. In contrast, bean grown under full sun had the highest amount of vanillic acid and caffeic acid. Antioxidant activity was highly positively associated with chlorogenic acid content.

Arabica coffee is more fastidious to grow than robusta coffee and are more susceptible to pests and diseases, strong winds and takes a longer time to fully mature than robusta coffee. Arabica coffee prefers deep, well-drained, friable, fertile loamy soils rich in organic matter and exchangeable bases in particular, potassium. It prefers soils with mildly acidic to neutral or mildly alkaline pH. It abhors heavy clays, sandy soils and is intolerant of acid soils.

Edible Plant Parts and Uses

Coffee berries, edible and slightly sweet, are eaten occasionally by children and field workers. Coffee seeds have been chewed as a masticatory stimulant in its native Ethiopia since ancient times. Dried coffee beans (seeds) are roasted and ground and brewed to make the coffee, the most popular and widely consumed beverage in the world. Probably the principal reason for its popularity is the addictive stimulant alkaloid, caffeine in the beans. Coffee is widely used as flavouring in ice cream, cakes, pastries, candies, and liqueurs. In Arabia, a fermented drink from the pulp is consumed. The fruits and seeds have been used for vitamins, minerals. As a food additive, the seeds have been used for condiment/seasoning.

Seventy-five to eighty percent of the world's coffee is from Arabica coffee.

Botany

Evergreen, glabrous shrub or small tree, up to 5 m tall when unpruned with an open-branching system; leaves opposite, dark green, glossy, oblong elliptic to broadly elliptic, 7–20 cm long by 2.5–6.5 cm wide with 7–10 pairs of lateral veins, acuminate or acute apex, acute base, simple, entire, slightly undulating margin (Plates 1 and 2). Petioles short and stipules deltoid and acute. Flowers white fragrant, stellate in outline, in axillary clusters of 2–9 flowers (Plate 1). Flower 1.0–1.5 cm across, clayx small, cupulate, corolla tubular 10 mm long with 5 segments 5–7 mm long, 5 stamens with 7–8 mm

Plate 1 Berries, flowers and leaves of *Coffea arabica*

Plate 2 Large, glossy dark green opposite leaves

Plate 3 Heavy fruit bearing branch

Plate 4 Ripe red and unripe green berries

long anthers and ovary usually 2-loculed with bicleft stigma. Fruit a berry ovoid, ellipsoid to oblong, 10–18 mm long, green maturing to red (Plates 3, and 4), black on drying, fleshy, usually containing two seeds. Seeds ellipsoidal, 8–12.5 mm long, flattened on one side with a medial straight or s-shaped groove and enclosed in two membranes, the outer one is called the 'parchment' and the inner one is called the 'silver skin'.

Nutritive/Medicinal Properties

Refer also to notes under *Coffea canephora* and *C. liberica.*

Phytochemicals in Coffee Fruit, Pulp, Skin

Camargo (1924) reported green immature Arabica coffee berries to contain adenine, hypoxanthine, xanthine and vernine (guanosine). Dry coffee pulp was found to contain about 10% of crude protein, 21% of crude fibre, 45% of nitrogen-free extract and 1.2% of caffeine whereas coffee hulls were much poorer in nutritive value, containing less than 3% of crude protein, 70% of crude fibre and 19% of nitrogen-free extract on a dry basis (Bressani et al. 1975). The essential amino acid content/g N of coffee pulp was similar to that of soya protein.

Tannins, which are the main phenolic compounds found in the skin and pulp the coffee fruit, have received a special attention because they are considered as anti-nutrients for ruminants (Clifford and Ramirez-Martinez 1991b; Barcelos et al. 2001; Ulloa Rojas et al. 2002, 2003). Caffeine content in the pulp and hull of *C. arabica* cultivars Catuaí, Rubi, Mundo Novo were found to increase during 1 year storage but the contents of tannins, lignin and silica tended to decrease during 1 year storage (Barcelos et al. 2001). The high caffeine contents posed a major limiting factor to the use of the pulp as animal feed. Soluble tannins may account for 0.8–2.8% of *C. arabica* and *C. canephora* skin and pulp, with higher contents observed in *C. canephora*, and with prodelphinidins exceeding procyanidins (Clifford and Ramirez-Martinez 1991a; Barcelos et al. 2001; Ulloa Rojas et al. 2003). Small amounts of insoluble condensed tannins may be also found in the pulp (Clifford and Ramirez-Martinez 1991a).

Four major classes of polyphenols were identified in fresh and 3-day old coffee pulp of the Arabica variety: flavan-3-ols (monomers and procyanidins), hydroxycinnamic acids, flavonols, and anthocyanidins (Ramirez-Coronel et al. 2004). Differences in concentration of procyanidins were observed between fresh and 3-day-old coffee pulp. Constitutive units were mainly epicatechin, accounting for >90% of the proanthocyanidin units, with average degrees of polymerization in the range of 3.8 – 9.1. Monomer to hexamer units of flavan-3-ols from fresh coffee

pulp were separated and the presence of oligomers of the flavan-3-ol (−)-epicatechin confirmed.

The following chlorogenic acids were detected in whole fruits (stage I – rapid expansion and pericarp growth), pericarps and seeds of *Coffea arabica* cv. Tall Mokka and *Coffea canephora*: monocaffeoylquinic acids (3CQA, 4CQA and 5CQA), dicaffeoylquinic acids (3,4diCQA, 3,5diCQA and 4,5diCQA) and a monoferuloylquinic acid (5FQA) (Koshiro et al. 2007). The most abundant chlorogenic acid was 5CQA, which comprised 50–60% of the total of *C. arabica* and 45–50% of *C. canephora* seeds. The content of dicaffeoylquinic acid, mainly 3,5-diCQA, was high in *C. canephor*a. A high content of 5FQA was found in seeds of stages (III) mature (green), (IV) ripening (pink), and (V) fully ripened (red), especially in *C. canephora*. Total chlorogenic acids amounted to 14 mg per fruit in *C. arabica* and 17 mg in *C. canephora*. In contrast, free quinic acid varied from 0.4 to 2.0 mg (*C. arabica*) and 0.2 to 4.0 mg (*C. canephora*) per fruit during growth. High biosynthetic activity of 5CQA, which was estimated via the incorporation of [U-14C]phenylalanine into chlorogenic acids, was found in young fruits (perisperm and pericarp) in stage I, and in developing seeds (endosperm) in stages II and III.

Phytochemicals in Coffee Seeds (Beans)

Green coffee beans could contain up to 14% (dm) chlorogenic acids (CGA) and related compounds as the main components of the phenolic fraction of green coffee beans (Farah and Donangelo 2006). Chlorogenic acids are a family of esters formed between quinic acid and certain trans-cinnamic acids, most commonly caffeic, *p*-coumaric and frolic acid. Coffee beans are remarkably rich in CGAs, containing at least 18CGAs that are not acylated at the C1. The main groups of CGAs found in green coffee beans include: caffeoylquinic acids (CQA), with 3 isomers (3-, 4- and 5-CQA); dicaffeoylquinic acids (diCQA),with 3 isomers (3,4-diCQA; 3,5-diCQA; 4,5-diCQA); feruloylquinic acids (FQA), with 3 isomers (3-, 4- and 5- FQA); *p*-coumaroylquinic acids (*p*CoQA), with 3 isomers (3-, 4- and 5- *p*CoQA), and six mixed diesters of caffeoylferuloyl-quinic acids (CFAQ) (Clifford 2003). Among these compounds, 5-CQA alone accounted for ~ 35% of total CGA in roasted coffee, with all CQA and diCQA isomers being together responsible for 92–95% of CGA (Farah and Donangelo 2006; Monteiro and Trugo 2005).

The most common hydrocinnamic acids in coffee beans had been reported to be caffeic acid (3,4-dihydroxy-cinnamic acid) followed by ferulic acid (3-metoxy, 4-hydroxy-cinnamic acid) and *p*-coumaric acid (4-hydroxy-cinnamic acid) and to a lesser extent sinapic acid (3,5-Dimethoxy-4-hydroxycinnamic acid) (Clifford 1999, 2000, 2003). Other phenolic compounds, such as tannins, lignans and anthocyanins are also present in coffee seeds although in minor amounts (Farah and Donangelo 2006).

Coffee from 17 Brazilian arabica cultivars processed by wet method showed higher contents of nine chlorogenic and trigonelline, and lower content of sucrose compared to those produced by a semi-dry method (Duarte et al. 2010). No difference was observed in caffeine level between both methods.

Non-decaffeinated instant was found to have 5.28% CQA, 1.16% FQA, 0.53% di CQA, 6.97% total CGA DW basis (Trugo and Macrae 1984). Different isomers of chlorogenic acid (CGA) in the groups of caffeoylquinic acids (CQA), dicaffeoylquinic acids (DICQA) and feruloylquinic acids (FQA) were found in nine Brazilian instant coffee (Nogueira and Trugo 2003). The isomers of CQA were predominant in all samples with 5-CQA being the most abundant. Total CGA levels varied from 0.6 to 5.9 g%. The samples with lowest CGA content were obtained from dark roasted coffee beans. The trigonelline levels varied between 0.3 and 1.0 g%. The decaffeinated coffee retained about 0.065 g% of caffeine and the majority of the other samples showed levels around 2.7 g%.

C. robusta was found to have the highest caffeine concentration, 2.26 g/100 g, followed by *C. arabica* with a caffeine concentration of 1.61 g/100 g and *C. liberica* had the lowest caffeine concentration at 1.23 g/100 g (Liew et al.

2001). Arabica and robusta green coffee differed respectively in the content of caffeine 1.2%, 2.4 (>4)%; trigonelline 1.0, 0.7%; amino acids 0.5, 0.8%; chlorogenic acids 7.1, 10.3%; total lipids 16% (range13–17%); 10% (range7–11%); oleic acid 6.7–8.2%, 9.7–14.2%; diterpene: cafestol 0.5–0.95, 0.2%; kahweol 0.3%, nil; 16-0-methyl cafestol nil, 0.07–0.15% respectively (Illy and Viani 1995). In addition to 19 previously identified chlorogenic acids (CGA) and chlorogenic acid lactones, 1-feruloylquinic acid, 1-feruloylquinic lactone and 3,4-diferuloylquinic acid were quantified in *C. arabica* and *C. canephora*, the contents of 3,4-di-*p*-coumaroylquinic acid was also identified in *C. arabica* (Perrone et al. 2008).

The following polyphenols and methylxanthines were detected in green coffee beans: three phenolic acids (caffeic acid, ferulic acid and dimethoxycinnamic acid), three isomeric caffeoylquinic acids, three feruloylquinic acids, one *p*-coumaroylquinic acid, three dicaffeoylquinic acids, three feruloyl-caffeoylquinic acids, four *p*-coumaroyl-caffeoylquinic acids, three diferuloylquinic acids, six dimethoxycinnamoyl-caffeoylquinic acids, three dimethoxycinn amoyl-feruloylquinic acids, six cinnamoyl-amino acid conjugates, three cinnamoyl glycosides, and three methylxanthines (caffeine, theobromine and theophylline) (Alonso-Salces et al. 2009a). Dimethoxycinnamic acid, three isomers of dimethoxycinnamoyl-caffeoylquinic acids and another three of dimethoxycinnamoyl-feruloylquinic acids, as well as the three cinnamoyl glycosides, had not previously been reported in coffee beans. The analysis of caffeic acid, 3-feruloylquinic acid, 5-feruloylquinic acid, 4-feruloylquinic acid, 3,4-dicaffeoylquinic acid, 3-caffeoyl-5-feruloylquinic acid, 3-caffeoyl-4-feruloylquinic acid, 3-*p*-coumaroyl-4-caffeoylquinic acid, 3-caffeoyl-4-dimethoxycinnamoylquinic acid, 3-caffeoyl-5-dimethoxycinnamoylquinic acid, *p*-coumaroyl-N-tryptophan, feruloyl-N-tryptophan, caffeoyl-N-tryptophan, and caffeine enabled the unequivocal botanical characterization of green coffee beans of the two main commercial coffee varieties, *Coffea arabica* (Arabica) and *Coffea canephora* (Robusta) (Alonso-Salces et al. 2009b). Green beans of *C. arabica* cv Catimor were found to have a moisture content of 10.28%, pH 5.53, and total phenolic content 34.32 mg GAE/g fresh sample (Somporn et al. 2011). The phenolic acid content (mg GAE/g fresh sample) of green *C. Arabica* beans was reported as chlorogenic acid 125.39 mg, syringic acid 2.46 g, gallic acid 2.75 mg, sinapic acid 10.34 mg, caffeic acid 6.34 mg, *p*-hydroxybenzoic acid 5.77 mg, protocatechuic acid 2.56 mg, vanillic acid 6.30 mg and total phenolic acids 162.51 mg (Somporn et al. 2011).

Three 3-methylbutanoyl and 3-methylbut-2-enoyl disaccharides isolated from green coffee beans (*Coffea arabica*) were identified as 3-methylbutanoyl-1-*O*-β-D-glucopyranosyl-β-D-apiofuranoside, 3-methylbutanoyl-6-*O*-α-D-glucopyranosyl-β-D-fructofuranoside, and 3-methylbut-2-enoyl-1-*O*-β-D-glucopyranosyl-β-D-apiofuranoside (Weckerle et al. 2002). Hydroxycinnamic acids, *p* -coumaric, *o*-coumaric and 3,4-dimethoxycinnamic acids were detected in the majority of samples: 13 green *Coffea canephora* var. *robusta* and seven green *Coffea arabica* coffee beans from different geographical origins (Andrade et al. 1998). Caffeic and ferulic acids were present in all of them while sinapic and 4-methoxycinnamic acids were found in only one sample from Mexico and Honduras. it appeared that the relative amount of the hydroxycinnamic acids could be related to the botanical origin of coffee. *Coffea canephora* var. *robusta* contained a higher level of 3,4-dimethoxycinnamic (mean = 0.433, ranging from 0.237 to 0.691 g/kg) than the *Coffea arabica* samples (mean = 0.059, ranging from 0.016 to 0.095 g/kg).

Free amino acids ornithine, β-alanine and pipecolic acid were found in Arabica and Robusta coffees as well as hydroxyproline in Arabica coffees (Arnold et al. 1994). In general, Arabica and Robusta coffees contained the same main and minor amino acids. Sucrose was found to be the dominant carbohydrate in green coffee with a concentration of up to 90 mg/g (mean = 73 mg/g) in arabica beans and significantly lower amounts in robusta beans (mean = 45 mg/g) (Murkovic and Derler 2006). Alanine was found to be the amino acid with the highest concentration

(mean = 1200 μg/g) followed by asparagine (mean = 680 μg/g) in robusta and 800 μg/g and 360 μg/g in arabica respectively. In general, the concentration of amino acids is higher in Robusta than in Arabica. Carbohydrates constituted the major constituents of coffee beans, serving various functions like aroma binding, foam stabilization, sedimentation formation, and increased viscosity of coffee extract (Arya and Rao 2007). The principal low molecular weight carbohydrate was sucrose, and the polysaccharide fraction from green coffee dominantly comprised arabinogalactan, galactomannan, and cellulose. The polysaccharide content was reported to be reduced and degraded during roasting to low molecular weight carbohydrates (mono and oligosaccharide) and becoming more extractable.

Most of the free sugar in the mature coffee seed of *Coffea arabica* and *C. canephora* var. *robusta* was accounted for by sucrose, fructose and glucose were both at higher concentrations in the perisperm (Rogers et al. 1999). Considerable amounts of myo-inositol (3–4% dry weight (DW)) were found in young seeds, while only the phosphorylated form phytic acid occurred in mature seeds (0.3–0.6% DW). Quinic acid, which was present in very low amounts in mature endosperm, represented between 6 and 16% DW in young seeds, this possibly being the major precursor pool for the high amounts of chlorogenic acids (5–10% DW) a characteristic of mature coffee beans. Of the other organic acids analysed, citric and malic acids were dominant in the mature seed, with higher concentrations in Arabica than Robusta. Robusta green coffee was found to have higher total and protein tryptophan, whereas Arabica had higher free tryptophan levels (Martins and Gloria 2010). 5-HTP (5-hydroxytryptophan) was not detected in the samples before and after roasting. Free tryptophan was completely degraded during roasting. Roasting significantly affected protein tryptophan. The rate of loss was smaller in Arabica compared to Robusta at every roasting degree. A beverage prepared the Brazilian way with a medium-roasted coffee provided 1.4–2.5 mg tryptophan/50 mL cup.

Coffea arabica var. Caturra and *Coffea canephora* var. ROM green coffee beans contained identical amounts of polysaccharide (Fischer et al. 2001). The monosaccharide compositions of the cell wall material (CWM) were similar, although Arabica beans contained slightly more mannose than Robusta. In the latter, more arabinogalactan was solubilised during preparation of the CWM and the water-soluble fraction of the CWM contained higher amounts of galactomannan than in Arabica. Linkage analysis indicated that the galactomannans possessed unbranched to branched mannose ratios between 14:1 and 30:1. Compared to Arabica, Robusta appeared to contain greater amounts of arabinogalactans with longer side chains. Nunes and Coimbra (2002b) found that the total polysaccharide content and the structures of the galactomannans and arabinogalactans in robusta and arabica coffee varieties were very similar. The content of arabinogalactans extracted from robusta green coffee was higher than that extracted from Arabica. For roasted coffees, the amount of galactomannans extracted ranged from 0.66 to 0.92% (w/w). Arabinose residues, as side chains, were also found as structural features of hot water soluble green (2%) and roasted (<0.9 mol) coffee galactomannans. β-(1 → 4)-linked glucose residues were found as structural features of green and roasted coffee galactomannans. In hot water soluble green coffee mannans, glucose residues were found as a constituent of the mannan backbone, and in the roasted coffee they were detected only at the reducing end of the mannan backbone. The polysaccharides present in the Arabica green coffees high molecular weight material were arabinogalactans (62%), galactomannans (24%), and glucans, and those found in roasted arabica coffees were galactomannans (69%) and arabinogalactans (28%) (Nunes and Coimbra 2001). The polysaccharides of the high molecular weight material of the roasted coffees were less branched than those of the green coffees. The major green coffee proteins had molecular weights of 58 and 38 kDa, and the 58 kDa protein had two subunits, of 38 and 20 kDa, possibly linked by disulfide bonds. The protein fraction obtained from roasted

coffees had only a defined band with < or = 14 kDa and a diffuse band with >200 kDa. The majority of the galactomannans of the roasted fractions showed the presence of polysaccharides, proteins, phenolics, and brown compounds.

Large amounts of diterpene mono-and di-alcohols were found in both Arabica and Robusta varieties; cafestol, kahweol and 16-*O*-methylcafestol were identified (Lercker et al. 1995). Other components that were partly generated during roasting were also identified; these compounds appeared to arise from the dehydration of cafestol and dehydrocafestol. Total sterol and triterpenic alcohol of the unsaponifiable matter from coffee lipids from 10 Arabica samples was 87.1–165 mg/100gm lipids, cholesterol trace –2.0%, unidentified B 2.0–4.4%, campesterol 9.0–14%, 24-methylencholesterol 0.1–0.4%, stigmasterol 16.9–19.4%, β-sitosterol 39.1–45.3%, Δ^5-avenasterol 2.0–4.2%, component H 1.4–3.6%, cycloartenol 4.7–7.1%, 24-mehtylenecycloartenol 7.4–10.1%, unidentified component N 0.8–1.9% (Lercker et al. 1995). Green and roasted coffees of *Coffea arabica* (Arabica) and *Coffea canephora* (Robusta) can be differentiated on their differences in their lipid fraction, especially in the content of the diterpene kahweol, which was present at 0.1–0.3% dry matter basis in arabica beans and only in traces (<0.01%) in robusta (Rubayiza and Meurens 2005). The reverse phase high-performance liquid chromatography method was effective in quantifying these diterpenes kahweol and cafestol in fresh fruits, leaves, and roasted coffee beans (Dias et al. 2010). Good recovery (average of 99% for kahweol and 94% for cafestol), repeatability, and linearity were obtained. Detection limits of 2.3 and 3.0 mg/100 g were observed for kahweol and cafestol. The endosperm and perisperm of *Coffea arabica* cv. IAPAR 59 showed elevated amounts of kahweol as compared to the pericarp and leaves.

Free and conjugated biogenic amines (putrescine, cadaverine, serotonin, tyramine, spermidine, and spermine) were found in green and roasted arabica and robusta coffee beans (Casal et al. 2004). Putrescine was the main biogenic amine present in the green beans either free or conjugated. Free putrescine could be used in the discrimination of arabica and robusta green beans with high statistical significance. Tyramine could be considered a chemical marker for Angolan robustas. With roasting, a significant loss in the free and conjugated biogenic amines levels was observed, especially the free ones. Seven bioactive amines were quantified in Arabica coffee beans: putrescine, spermine, spermidine, serotonin, cadaverine, histamine, and tyramine, with amounts ranging from 71.8 to 80.3 mg/kg (Dias et al. 2012). The levels of spermine and spermidine were lower in the unripe depulped coffee than in the natural coffee. The specific conditions of dry and wet processing also influenced cadaverine levels, and histamine was reduced in unripe depulped coffee. The results confirmed that peeling immature coffee could decrease fermentation processes while providing more uniform drying, thus reducing the number of defects and potentially increasing beverage quality.

Phytochemicals/Nutrients in Roasted, Brewed and Powdered Coffee

Proximate nutrient composition of regular, instant coffee powder per 100 g edible portion had been reported as: water 3.10 g, energy 241 Kcal (1008 kJ), protein 12.20 g, total lipid 0.50 g, ash 8.80 g, carbohydrate 41.10 g, Ca 141 mg, Fe 4.41 mg, Mg 327 mg, P 303 mg, K 3535 mg, Na 37 mg, Zn 0.35 mg, Cu 0.139 mg, Mn 1.712 mg, Se 12.6 μg, thiamine 0.008 mg, riboflavin 0.074 mg, biacin 28.173 mg, pantothenic acid 0.097 mg, vitamin B-6 0.029 mg, total choline 101.9 mg, vitamin K (phylloquinone) 1.9 μg, total saturated fatty acids 0.197 g, 16:0 (palintic acid) 0.146 g, 19:0 (stearic acid) 0.035 g, total monounsaturated fatty acids 0.041 g, 18:01oleic acid 0.040 g, 20:1 0.001 g, total polyunsaturated fatty acids 0.196 g, 18:2 undifferentiated (linoleic acid) 0.180 g, 18:3 undifferentiated (linolenic acid) 0/015 g, tryptophan 0.030 g, threonine 0.142 g, isoleucine 0.172 g, leucine 0.478 g, lysine 0.096 g, methionine 0.023 g, cystine 0.202 g, phenylalanine 0.262 g, tyrosine 0.165 g,

valine 0.276 g, arginine 0.053 g, histidine 0.165 g, alanine 0.335 g, aspartic acid 0.478 g, glutamic acid 2.030 g, glycine 0.441 g, proline 0.351 g, serine 0.126 g, and caffeine 3142 mg (USDA 2012).

Extracts from roasted Arabica and Robusta coffees were found to contain 20–36% carbohydrates, depending on the degree of extraction (Thaler 1979). They were composed predominantly of mannan and galactan in about the same proportions, the share of glucan and araban constituting 1–3% of the extracts. With dialysis a group of polysaccharides with a molecular weight of more than 10,000 was separated, constituting about half of the carbohydrates of the extracts. In addition, another group of almost intact high polymeric carbohydrates as copper complexes was found, consisting only of mannan and galactan, mannan predominating significantly. Arabica and Robusta coffees showed differences in this respect. Whereas Arabica coffee was able to release only a certain amount of these very high-polymeric carbohydrates, Robusta coffee delivered even greater amounts of these polysaccharides with increasing extract yields. Galactomannans and arabinogalactans comprised almost exclusively the polysaccharide fraction of roasted coffee infusions (Nunes and Coimbra 2002a). In Arabica coffee, the degree of polymerization and the degree of branching of the high molecular weight galactomannans decreased with the increase of the degree of roast. As the degree of roast increased, less branched arabinogalactans were extracted. Doubly acetylated and contiguously acetylated hexose residues were found in mannans from green and roasted coffee infusions (Nunes et al. 2005). Specific enzymatic hydrolysis of the β-(1 → 4)-D-mannan backbone revealed the galactomannans of roasted coffee infusions to be high molecular weight supports of low molecular weight brown compounds (Nunes et al. 2006). The molecular weight of the brown compounds linked to the galactomannan increases with the increase of the coffee degree of roast. The reaction pathways of galactomannans during the coffee roasting process involved Maillard reaction, caramelization, isomerization, oxidation, and decarboxylation pathways which were identified by detection of Amadori compounds, 1,6-β-anhydromannose, fructose, glucose, mannonic acid, 2-ketogluconic acid, and arabinonic acid in the reducing end of the obtained oligosaccharides. Mild acidic hydrolysis arabinogalactan-protein of *Coffea arabica* instant coffee powder afforded oligosaccharides without any αAraf substituent while after enzymatic hydrolysis αAraf was found in di-, tri-, and tetrasaccharides (Matulová et al. 2011). In all cases αAraf was a terminal substituent linked separately to O3, O6, and to both, O3 and O6, of βGal residues.

During the roasting of coffee beans of *Coffea arabica* cv. Bourbon, *C. arabica* cv. Longberry, and *C. canephora* cv. Robusta, seven chlorogenic acid lactones (CGL) were identified: 3-caffeoylquinic-1,5-lactone (3-CQL), 4-caffeoylquinic-1,5-lactone(4-CQL),3-coumaroylquinic-1,5-lactone(3-pCoQL),4-coumaroylquinic-1,5-lactone (4-pCoQL), 3-feruloylquinic-1,5-lactone (3-FQL), 4-feruloylquinic-1,5-lactone (4-FQL), and 3,4-dicaffeoylquinic-1,5-lactone (3,4-diCQL) (Farah et al. 2005). 3-CQL was the most abundant lactone in *C. arabica* and *C. canephora*, reaching peak values of 230 and 254 mg/100 g (dry weight), respectively, at light medium roast (approximately 14% weight loss). 4-CQL was the second most abundant lactone (116 and 139 mg/100 g, respectively). The maximum amount of CGL represents approximately 30% of the available precursors. The relative levels of 3-CQL and 4-CQL in roasted coffee were reverse to those of their precursors in green coffee. This suggested that roasting caused isomerization of chlorogenic acids prior to the formation of lactones and that the levels of lactones in roasted coffee did not reflect the levels of precursors in green coffee. Decaffeination produced a 16% average increase in the levels of total chlorogenic acids (CGA) in green arabica coffee (dry matter), along with a 237% increase in 1,5-γ-quinolactones (CGL) direct precursors (Farah et al. 2006). Different degrees of roasting elicited average increments of 5.5 − 18% in CGL levels of decaffeinated coffee, compared to regular. Conversely, CGA levels in roasted coffee were 3 − 9% lower in decaffeinated coffee compared to regular coffee.

Cherry coffee, a variety of *C. canephora* exhibited the highest overall content of total phenols (42.37 mg GAE/g), followed by Minas coffee (*C. arabica*), while Cioccolatato coffee (*C. arabica*) contained the lowest TPC (33.12 mg GAE/g) (Hečimović et al. 2011). Cherry coffee also exhibited the highest content of individual classes of polyphenols (flavan-3-ols, procyanidins and tannins), while the highest content of chlorogenic acid (CQA) derivatives was found in Minas and Cioccolatato coffees. The highest content of total and individual polyphenolic compounds was determined in all coffees roasted in both light and medium roasting conditions, which was also observed for the content of CQA derivatives and antioxidant capacity of roasted coffees. The highest caffeine content in the coffee samples was 0.06–2.55%. Light roasted Cherry coffee contained the highest overall content of caffeine among all coffees, which exhibited a decrease with intensified roasting.

The phenolic acid content (mg/100 g fresh sample) of light roasted *C. arabica* cv Catimor beans was reported as chlorogenic acid 67.44 mg, syringic acid 2.64 g, *p*-coumaric acid 15.46 mg, gallic acid 10.90 mg, sinapic acid 10.89 mg, caffeic acid 3.19 mg, *p*-hydroxybenzoic acid 8.58 mg, protocatechuic acid 3.86 mg, vanillic acid 6.39 mg, ferulic acid 3.63 mg, and total phenolic acids 132.98 mg (Somporn et al. 2011). The phenolic acid content (mg/100 g fresh sample) of medium roasted beans was reported as chlorogenic acid 22.29 mg, syringic acid 2.61 g, *p*-coumaric acid 7.36 mg, gallic acid 3.58 mg, sinapic acid 2.88 mg, caffeic acid 9.50 mg, *p*-hydroxybenzoic acid 42.23 mg, protocatechuic acid 13.00 mg, vanillic acid 14.42 mg, ferulic acid 4.10 mg, and total phenolic acids 121.97 mg. The phenolic acid content (mg/100 g fresh sample) of dark roasted beans was reported as chlorogenic acid 37.94 mg, syringic acid 2.62 g, *p*-coumaric acid 4.53 mg, gallic acid 4.04 mg, sinapic acid 5.27 mg, caffeic acid 6.84 mg, *p*-hydroxybenzoic acid 30.18 mg, protocatechuic acid 13.29 mg, vanillic acid 11.38 mg, ferulic acid 11.09 mg, and total phenolic acids 127.17 mg. Chlorogenic acid was the most predominant phenolic compound of all the coffee beans. It decreased with increase in roasting intensity. Total phenolic acid content increased with roasting degree with the highest in fresh green beans and the lowest in medium roasted beans. Syringic acid, *p*-coumaric acid, gallic acid and sinapic acid content was higher with roasting with the highest values found with light roasted beans (Somporn et al. 2011).

Furan was not detected in green coffees of *Coffea arabica* and *Coffea canephora* whereas levels between 911 and 5,852 μg/kg were found in the roasted samples (Arisseto et al. 2011). Higher concentrations were found in *Coffea canephora* and darker ground coffees. Some of the potential furan precursors were observed in significant amounts in green coffee, especially sucrose and linoleic acid, but their concentrations could not be correlated to furan formation. Furan levels in coffee brews prepared from roasted ground coffees varied from <10 to 288 μg/kg. The factor that most influenced the furan content in coffee brew was the brewing procedure.

The lipid content of boiled, filtered, dripped, Turkish and espresso coffees prepared from roasted beans *of Coffea arabica* and *Coffea robusta*, and of coffees prepared from different brands of instant coffee was found to be different (Ratnayake et al. 1993). Coffee brews filtered through filter paper contained less than 7 mg lipids, those prepared by boiling without filtering and espresso coffee reached 60–160 mg lipids/150-mL cup. Coffee brew filtered through a metal screener contained 50 mg lipids/150-mL cup. Although the lipid content varied, the method of preparation of the brew and filtration had no important influence on the lipid composition. Triglycerides and diterpene alcohol esters were the major lipid classes in coffee brewed from ground coffee beans, and ranged from 86.6 to 92.9 and 6.5 to 12.5% of total lipids, respectively. For coffee brews made from instant coffee, the levels of these two lipid classes were 96.4–98.5 and 1.6–3.6%, respectively. The lipid contents of both regular and decaffeinated instant coffees varied slightly from one brand to the other, and ranged from 1.8 to 6.6 mg/150-mL cup.

Bagdonaite et al. (2008) reported that the potential precursors of acrylamide were 3-aminopropionamide, carbohydrates, and amino acids.

The highest amounts of acrylamide formed in coffee were during the first min of the roasting process [3,800 ng/g in Robusta (*Coffea canephora* robusta) and 500 ng/g in Arabica (*Coffea arabica*)]. With increase in roasting time the concentration of acrylamide decreased. Robusta coffee contained significantly larger amounts of acrylamide (mean = 708 ng/g) than Arabica coffee (mean = 374 ng/g). Asparagine was the limiting factor for acrylamide formation in coffee. Thermal decarboxylation and elimination of the α-amino group of asparagine at high temperatures (>220°C) led to a measurable but low formation of acrylamide.

A comparative study of laboratory scale roasting with industrial roasting showed that 5-hydroxymethyl- 2-furfural decreased with a higher degree of roasting whereas 5-hydroxymethyl-2-furoic acid (HMFA) did not change (Murkovic and Bornik 2007). In the laboratory scale experiments, the highest concentration of 5-hydroxymethyl-2-furfural in coffee (909 μg/g) was obtained after 3 min and the maximum concentration of HMFA after 4 min (150 μg/g). Industrially roasted coffee contained up to 350 μg/g 5-hydroxymethyl-2-furfural and 140 μg/g HMFA. It was shown that HMFA was produced from different precursors than 5-hydroxymethyl-2-furfural namely glyceraldehyde and pyruvate.

The lipid content of boiled, filtered, dripped, Turkish and espresso coffees prepared from roasted beans of *Coffea arabica* and *Coffea robusta*, and of coffees prepared from different brands of instant coffee was found to be different (Ratnayake et al. 1993). Coffee brews filtered through filter paper contained less than 7 mg lipids, those prepared by boiling without filtering and espresso coffee reached 60–160 mg lipids/150-mL cup. Coffee brew filtered through a metal screener contained 50 mg lipids/150-mL cup. Although the lipid content varied, the method of preparation of the brew and filtration had no important influence on the lipid composition. Triglycerides and diterpene alcohol esters were the major lipid classes in coffee brewed from ground coffee beans, and ranged from 86.6 to 92.9 and 6.5 to 12.5% of total lipids, respectively. For coffee brews made from instant coffee, the levels of these two lipid classes were 96.4–98.5 and 1.6–3.6%, respectively. The lipid contents of both regular and decaffeinated instant coffees varied slightly from one brand to the other, and ranged from 1.8 to 6.6 mg/150-mL cup.

Triacylglycerols were found to be the major lipid constituents of *Coffea arabica* coffee oil along with sterol esters, sterols/triterpene alcohol, hydrocarbons and the hydrolyzed products of triacylglycerols as the minor components (Al Kanhal 1997). Fatty acid composition of total oil, neutral lipids, polar lipids and pure triacylglycerols showed the presence of fatty acids of C14, C16, C18, and C20 carbon chains. Palmitic and linoleic acids were the major fatty acids and comprised about 38.7 and 35.9% respectively. Pancreatic lipase hydrolysis revealed that the linoleoyl and palmitoyl moieties were preferentially esterified at the Sn-2 and Sn-1,3 positions of triacylglycerols respectively.

The chlorogenic acids (CGA) identified in 12 commercial brewed coffees (seven regular and five decaffeinated) were three caffeolylquinic acids (3-CQA, 4-CQA, and 5-CQA), three feruloylquinic acids (3-FQA, 4-FQA, and 5-FQA), and three dicaffeoylquinic acids (3,4-diCQA, 3,5-diCQA, and 4,5-diCQA) (Fujioka and Shibamoto 2008). The total CGAs ranged from 5.26 mg/g to 17.1 mg/g in regular coffees and from 2.10 mg/g to 16.1 mg/g in decaffeinated coffees. Among CGA, 5-CQA was present at the highest level, ranging from 2.13 mg/g to 7.06 mg/g coffee, and comprising 36–42% and 37–39% of the total CGA in the regular and decaffeinated coffees, respectively. CGA isomer contents were, in decreasing order, 5-CQA > 4-CQA > 3-CQA > 5-FQA > 4-FQA > 3-FQA > 3,4-diCQA > 4,5-diCQA, 3,5-diCQA. The caffeine content in regular and decaffeinated coffees ranged from 10.9 mg/g to 16.5 mg/g and from 0.34 mg/g to 0.47 mg/g, respectively. The pH of regular and decaffeinated coffees ranged from 4.95 to 5.99 and from 5.14 to 5.80, respectively. Total chlorogenic acids of nine isomers from seven commercial green and roasted coffee beans was found to range from 34.43 to 41.64 mg/g and from 2.05 to 7.07 mg/g,

respectively (Moon et al. 2009). The total chlorogenic acid found in green coffee beans ranged from 86.42 to 61.15 mg/g. Total chlorogenic acids were reduced with intensity of roasting conditions. When green beans were roasted at 230°C for 12 min and at 250°C for 21 min, total chlorogenic acid content was reduced to nearly 50% and to almost trace levels, respectively. The results indicated that roasting conditions played an important role in chlorogenic acid content in roasted coffee beans. A general correlation between total caffeoylquinic acids and pH was observed. Trigonelline and chlorogenic acids contents in Arabica and robusta coffee beans roasted at 220°C decreased with roasting intensity (time) (Bicho et al. 2011). Trigonelline level decreased from 1.274% at 7 min roasting to 0.566% at 11 min for Arabica and for Robutsa from 0.912 at 7 min roasting to 0.485% at 11 min roasting. Total caffeoylquinic acid (comprising 3-CQA, 4-CQA and 5CQA) decreased from 0.274 mg/cm^3 at 7 min roasting to 0.017 mg/cm^3 at 11 min for Arabica coffee and from 3.997 mg/cm^3 at 7 min to 1.004 mg/cm^3 at 11 min for robusta. Total dicaffeoylquinic (comprising 3,4-diCQA, 3,5-diCQA, 4,5-diCQA) decreased from 3.939 mg/cm^3 at 7 min roasting to 0.794 mg/cm^3 at 11 min for Arabica coffee and from 0.497 mg/cm^3 at 7 min to 0.050 mg/cm^3 at 11 min for robusta. Total feruolilquínic acids (comprising 3-FQA, 4-FQA, 5-FQA) decreased from 0.0.194 mg/cm^3 at 7 min roasting to 0.060 mg/cm^3 at 11 min for Arabica coffee and from 0.465 mg/cm^3 at 7 min to 0.158 mg/cm^3 at 11 min for robusta. Soluble solid and caffeine contents and pH levels for both coffees were lowest at medium roasting (9 min). Arabica coffee contained higher levels of trigonelline and soluble solids than robusta but the latter was higher in caffeine content and pH.

Melanoidin fractions isolated from different high-molecular-weight fractions of coffee brews showed an intense brown colour and contained less than 6% each of releasable carbohydrates and amino acids (Gniechwitz et al. 2008). The molecular masses of the melanoidins were estimated to be between 3 and 22 kDa and they contribute to the colour and flavour of coffee brews. Phenolic constituents were postulated to be more likely integrated into melanoidins as condensed phenolics than as intact hydroxycinnamates from chlorogenic acids. Melanoidin fractions isolated by hydrophobic interaction chromatography showed three- to fourfold higher antioxidant activities than the remaining high-molecular-weight material in the ultrafiltration fractions.

Polycyclic aromatic hydrocarbons fluoranthene, pyrene and benz(a)anthracene were found in infusions of unfiltered natural coffee (2002). The presence of undesirable polycyclic aromatic hydrocarbons (PAHs) in coffee had been attributed to the degradation of coffee compounds during the roasting step (Houessou et al. 2005). However, due to the low solubility of these compounds, their concentrations in coffee brews are expected to be rather low. Levels of benzo[b]fluoranthene and benzo[a]pyrene in coffee brews were found to range from 0 to 100 ng/L. Polycyclic aromatic hydrocarbons such as pyrene, benz[a]anthracene, chrysene, and anthracene were found in roasted Arabica coffee samples (Houessou et al. 2008). Formation of phenanthrene, anthracene, and benzo[a]anthracene in Arabica coffee beans was observed at temperatures above 220°C, whereas formation of pyrene and chrysene required 260°C (Houessou et al. 2007). Low levels of benzo[g,h,i]perylene were also noted for dark roasting under 260°C, with simultaneous partial degradation of three-cycle PAHs, suggesting that transformation of low molecular PAHs to high molecular PAHs occurred as the roasting degree was increased. The PAH transfer to the infusion was quite moderate (<35%), with a slightly lower extractability for dark-roasted coffee as compared to light-roasted coffee. The total concentration of the 28 as polycyclic aromatic hydrocarbon(PAH) compounds, expressed as the sum of concentrations (ΣPAH), in coffee brew varies from 0.52 to 1.8 μg/l (Orecchio et al. 2009). Carcinogenic PAHs, expressed as B[a]Peq ranged from 0.008 to 0.060 μg/l. The results indicate that coffee contributes with very insignificant quantities to the daily human intake of carcinogenic PAHs.

Melatonin (3.0 μg/50 mL) and 5-HT (4.0 μg/50 mL) were detected in coffee brew.

In *C. arabica*, serotin 5-HT (5-hydroxytryptamine) was higher in green beans (12.5 μg/g DW) compared with roasted beans (8.75 μg/g DW) (Ramakrishna et al. 2012). The levels of melatonin were higher (9.6 μg/g DW) in roasted beans compared with green beans (6.8 μg/g DW). Both melatonin (3.9 μg/50 mL) and 5-HT (7.3 μg/50 mL) were detected in coffee brew.

Studies showed that the content of β-carboline (norharman and harman) contents in espresso coffee was dependent primarily on the coffee species, followed by brew length (Alves et al. 2007). Roasting degree had only a minor influence on the final content of norharman and harman in espresso coffee. The content of β-carbolines (μg/L) in espresso coffee was similar to that of mocha coffee, both being more concentrated than filter and press-pot coffees. For the caffeinated 30 mL of espresso coffee, the arabica coffees contained about 4.08 μg of norharman and 1.54 μg of harman. Commercial blends (usually with a maximum of 30% robusta) ranged from the cited arabica values to 10.37 μg of norharman and 4.35 μg of harman. Total isoflavone level was found to be sixfold higher in robusta coffees than in arabica ones, mainly due to formononetin. During roasting, the content of isoflavones decreased, whereas their extractability increased (especially for formononetin). (Alves et al. 2010) Total isoflavones in espresso coffee (30 mL) varied from 40 μg (100% arabica) to 285 μg (100% robusta), with long espressos (70 mL) attaining more than double isoflavones of short ones (20 mL). Espressos (30 mL) prepared from commercial blends contained average amounts of 6, 17, and 78 μg of genistein, daidzein, and formononetin, respectively. Comparison of different brewing methods revealed that espresso contained more isoflavones (170 μg/30 mL) than a cup of press-pot coffee (130 μg/60 mL), less than a mocha coffee (360 μg/60 mL), and amounts similar to those of a filtered coffee cup (180 μg/120 mL).

Volatile and Odour Compounds

The major volatile compounds in green beans were aldehydes (hexanal and benzaldehyde) and alkanes (tetradecane, *cis*-cyclotetrasiloxane, octamethyl-), furans (2-pentyl furan,, 2-furanmethanol) , whereas the major volatiles compounds in roasted beans were furans, pyrazines and pyridines (Somporn et al. 2011). After roasting, the levels of furans, pyrazines and pyridines and acetic acid increased appreciably. The contents of cyclopentasiloxane, decathyyl-, 2-cyclopenten-1-one, 3-ethyl-2-hydroxy, 2,5-furandione, 3-ethyl-4-mehtyl- and pyrazines increased in light roasted beans and they were not found in medium and dark roasted beans.

The mass of total volatile components recovered from 200 g Hawaiian green coffee beans (*Coffea arabica)* beans was 2.7 mg. The 23 volatile components identified in the coffee extract were: ten alcohols, four aldehydes, one ketone, one lactone, three heterocyclic compounds, two hydrocarbons, and two miscellaneous compounds (Lee and Shibamoto 2002). The major constituents were 3-methyl butanoic acid 32.8%, phenyl ethyl alcohol 17.3%, 1-hexanol 7.2%, 4-hydroxy-3-methylacetophenone 3.7%, 3-methyl butanol 3.6%, 1-butoxy-2-propanol 3.3%, pentanol 3.2%, and octadecane 3.2%. Other compounds include hexanal 2.35%, benzyl alcohol 2.3%, methyl salicylate 2.1%, γ-butyrolactone 1.7%, hexadecane 1.6%, benzene acetaldehyde 1.3%,2-methyl propenol 1.3%, dimethyl sulphide 1.3%, 3-methyl butanal 1.1%, 2-methoxy-3-(2-methylpropyl)-pyrazine 1.0%, (E)-2-pentenal 0.9%, N,N-dimethyl acetamide 0.6%, 1-octen-3-ol 0.6% and eicosanol 0.6%. Heterocyclic compounds, important components in providing coffee with their characteristic flavours, were not found in the extract from green coffee beans, except for 2-methoxy-3-(2-methylpropyl)-pyrazine.

Aroma extract dilution analysis (AEDA) of an extract containing the volatiles isolated from the freshly filtered coffee brew revealed 40 odour active compounds in the FD (Flavour dilution) -factor range of 32 to 4,096 (Sanz et al. 2002). The highest flavour dilution factors were found for 5-ethyl-3-hydroxy-4-methyl-2(5*H*)-furanone (abhexone; spicy), 4-vinyl-2-methoxyphenol (clove-like), 2-methoxyphenol (phenolic) and (*E*)-β-damascenone (boiled apple-like). Seven other compounds, namely 4-ethyl-2-methoxyphenol

(phenolic), 4-hydroxy-2,5-dimethyl-3(2*H*)-furanone (furaneol; caramel-like), methional (cooked potato), 3-mercapto-3-methylbutyl formate (catty), 3-hydroxy-4,5-dimethyl-2(5*H*) furanone (sotolon; spicy), vanillin (vanilla-like), and 2(5)-ethyl-4-hydroxy-5(2)-methyl-3(2*H*)-furanone (ethylfuraneol; caramel-like) were identified as further contributors to the aroma of the freshly prepared coffee brew. In the extract prepared from instant coffee, the three seasoning-like (spicy) and caramel-like smelling furanones 3-hydroxy-5-ethyl-4-methyl-, 3-hydroxy-4,5-dimethyl-2(5*H*)furanone and 4-hydroxy-2,5-dimethyl-3(2*H*)furanone clearly showed the highest FD factors. Most of the other odorants with low FD factors identified in the filtered coffee were also present in instant coffee such as 2,3-butanedione (buttery); 1-octen-3-one (mushroom-like); 2-methyl-3-furanthiol (meaty); 2-furfurylthiole (roasty); 3-isopropyl-2-methoxypyrazine (earthy); 3-ethyl-2,5-dimethylpyrazine (earthy); 2-ethyl-3,5-dimethylpyrazine; 2,3-diethyl-5-methylpyrazine (earthy); 3-isobutyl-2-methoxy-pyrazine(earthy);2-ethenyl-3,5-dimethylpyrazine (earthy); 2-ethenyl-3-ethyl-5-methylpyrazine (earthy); 2-3-methylbutanoic acid (sweaty); 4-methoxyphenol (phenolic burnt); and 11 unknown compounds. Exceptions were 2-acetyl-2-thiazoline (roasty), 3-methylindole (mothball-like), dimethyl trisulfide (sulfurous) and 2 unknown compounds with clove-like or sweet odour notes which were found in filtered coffee.

One hundred and twenty volatile compounds of roasted coffee, isolated by normal-pressure steam distillation were identified, of which 26 new compounds identified for the first time in roasted coffee include 15 furans, 6 pyrroles, 3 thiophenes, and 2 ketones (Vitzthum and Werkhoff 1976). Of the 15 furans eight methylvinylfurans, dimethylvinylfurans and alkenylfurans were found such as N-acetyl-2-methylpyrrole, N-furfuryl-2-methylpyrrole, 2-vinyl-3-methylfuran and 2-vinyl-3,5-dimethylfuran. Thirteen compounds were found as important contributors to the aroma of roasted Arabica coffee (powder): 2-methyl-3-furanthiol (I), 2-furfurylthiol (II), methional (III), 3-mercapto-3-methylbutylformate (IV), 3-isopropyl-2-methoxypyrazine (V), 2-ethyl-3,5-dimethylpyrazine (VI), 2,3-diethyl-5-methylpyrazine (VII), 3-isobutyl-2-methoxy-pyrazine (VIII), 3-hydroxy-4,5-dimethyl-2(5 H)-furanone (sotolon, IX), 4-ethylguaiacol (X), 5-ethyl-3-hydroxy-4-methyl-2(5 H)-furanone (XI), 4-vinylguaiacol (XII), and (E)-β-damascenone (XIII) (Blank et al. 1992). A comparative aroma extract dilution analysis of the coffee powder and brew showed in the brew an increase of III, IX, vanillin and 4-hydroxy-2,5-dimethyl-3(2 H)-furanone and a decrease of I, II, IV, V, VII. One hundred and twenty-two volatile compounds were identified from ground roasted Arabica coffee, including 26 furans, 20 ketones, 20 pyrazines, 9 alcohols, 9 aldehydes, 8 esters, 6 pyrroles, 6 thiophenes, 4 sulfur compounds, 3 benzenic compounds, 2 phenolic compounds, 2 pyridines, 2 thiazoles, 1 oxazole, 1 lactone, 1 alkane, 1 alkene, and 1 acid (Sanz et al. 2001).

Among the 52 volatile compounds identified in green coffee beans roasted at 230°C for 12 min (light), at 240°C for 14 min (medium), at 250°C for 17 min (city), or at 250°C for 21 min (French), the major compounds were 5-hydroxymethylfurfural, furfuryl alcohol, and 6-methyl-3,5-dihydroxy-4 H-pyran-4-one in light-roasted beans; furfuryl alcohol, 5-hydroxymethylfurfural, and γ-butyrolactone in medium-roasted beans; furfuryl alcohol, γ-butyrolactone, and 2-acetylpyrrole in city-roasted beans; and γ-butyrolactone, furfuryl alcohol, and catechol in French-roasted beans (Moon and Shibamoto 2009). Furfural derivatives and furanones were yielded in relatively high concentrations under mild roasting conditions and then reduced at higher roasting intensities. More pyridines and pyrroles were formed by high roasting intensities than by mild roasting intensities. Chlorogenic acid degradation products, phenols, and a lactone were produced more by high roasting intensities than by low roasting intensities. Thermal degradation of less volatile coffee components: quinic acid, caffeic acid, and chlorogenic acid yielded many volatile chemicals (Moon and Shibamoto 2010). Caffeic acid produced the greatest amount of total volatiles. Quinic acid and chlorogenic acid produced a greater number of volatiles under the nitrogen stream than under the air stream. 2,5-dimethylfuran formed in relatively large

amounts (59.8–2,231.0 μg/g) in the samples obtained from quinic acid and chlorogenic acid but was not found in the samples from caffeic acid. Furfuryl alcohol was found in the quinic acid (259.9 μg/g) and caffeic acid (174.4 μg/g) samples roasted under a nitrogen stream but not in the chlorogenic sample. Heterocyclic compounds, pyridine, pyrrole, and pyrazines, were recovered. Phenol and its derivatives were identified in the largest quantities. The amounts of total phenols ranged from 60.6 μg/g (quinic acid under helium) to 89,893.7 μg/g (caffeic acid under helium). It was proposed that phenol was formed mainly from quinic acid and that catechols were formed from caffeic acid.

Dark roasted coffee brew was slightly more reactive toward thiols, sulfides, pyrroles, and diketones compounds than the light roasted coffee brew (Charles-Bernard et al. 2005). Selected pure coffee constituents, such as caffeine, trigonelline, arabinogalactans, chlorogenic acid, and caffeic acid, showed few interactions with the coffee volatiles. The following interactions were found: low molecular weight and positively charged melanoidins present significant interactions; strong correlations were shown between the melanoidin and protein/peptide content and the extent of interactions depended on the volatile compound; and chlorogenic acids and carbohydrates played a secondary role, because only weak correlations with the interactions were found in complex matrixes.

Twenty-two odorant compound were identified in brewed Arabica and Robusta coffees (Semmelroch and Grosch 1996). Based on odor activity values (ratio of concentration to odor threshold) 2-furfurylthiol, 3-mercapto-3-methylbutyl formate, methanethiol, β-damascenone, methylpropanal, and 3-methylbutanal were determined as the most potent odorants, though their rankings varied in both coffee brews. Polar compounds (e.g. guaiacol, 4-hydroxy-2,5-dimethyl-3(2*H*)-furanone, 3-hydroxy-4,5-dimethyl-2(5*H*)-furanone, 2,3-butanedione) were extracted with higher yields (75–100%); nonpolar compounds (e.g. β-damascenone, 2-isobutyl-3-methoxypyrazine) gave yields of only 10–25%. The following odorants were found to be essential for the flavor of roasted coffee: 2-furfurylthiol, acetaldehyde, propanal, methylpropanal, 2- and 3-methylbutanal, 2-ethyl-3,5-dimethylpyrazine, 2-ethenyl-3,5-dimethylpyrazine, 2,3-diethyl-5-methylpyrazine and 4-vinylguaiacol (Grosch et al. 2000). Further, 2-furfuryithiol, the outstanding odorant in the class of sulfur compounds, was formed during roasting by reactions of cysteine with arabinose. The latter was released from polysaccharides. In raw Arabica coffee revealed 3-isobutyl-2-methoxypyrazine (I), 2-methoxy-3,5-dimethylpyrazine (II), ethyl 2-methylbutyrate (III), ethyl 3-methylbutyrate (IV), and 3-isopropyl-2-methoxypyrazine (V) were identified as potent odorants (Czerny and Grosch 2000). The highest odour activity value was found for I followed by II, IV, and V. They concluded that compound I was responsible for the characteristic, peasy odour note of raw coffee. Twelve odorants occurring in raw coffee and (E)-β-damascenone were also quantified after roasting. The concentration of I did not change, whereas methional, 3-hydroxy-4, 5-dimethyl-2(5 H)-furanone, vanillin, (E)-β-damascenone, and 4-vinyl- and 4-ethylguaiacol increased strongly during the roasting process.

Twenty-two potent odorants from roasted Arabica coffee were released during grinding (Grosch and Mayer 2000). Within 5 min of grinding, 32% of methanethiol present in the coffee sample as well as 15–20% of acetaldehyde, methylpropanal, 2- and 3-methylbutanal were lost by volatilization. Within 30 min, 20–30% of 2-furfurylthiol, methional, vanillin and 2-isobutyl-3-methoxypyrazine, approximately 10% of four alkylpyrazines and only 1% of three furanones were lost from ground coffee. In contrast, after a storage period of 15 min, the losses of these odorants amounted only to 2–12% in whole beans. The different evaporation rates of the odorants caused changes in the odor profile of the coffee sample.

Eight potent odorants were identified in coffee sample; among the components, methanethiol (putrid), acetic acid (sour), 3-methylbutanoic acid (sour), 2-furfuryl methyl disulfide (meaty), and 4-hydroxy-2,5-dimethyl-3(2 H)-furanone

(caramel-like) increased after heating of the coffee sample, whereas 2-furfurylthiol (roasty), methional (potato-like), and 3-mercapto-3-methylbutyl formate (roasty) decreased compared with the coffee sample before heat treatment (Kumazawa and Masuda 2003b). In a roasted Arabica coffee brew, the potent roasty odour quality compound was identified as 3-mercapto-3-methylbutyl acetate (Kumazawa and Masuda 2003a). The concentration of this compound in the coffee brews as with 3-mercapto-3-methylbutyl formate increased with an increase in the degree of roasting.

Scheidig et al. (2007) conducted a comparative aroma extract dilution analysis on unstored, raw Arabica coffee beans (water content = 11.75%) and on the same beans with a water content of 13.5%, stored for 9 months at 40°C. Strong increases in (E)-β-damascenone (cooked apple-like), 2-methoxy-4-vinylphenol (clove-like), and methyl 2-methyl- and methyl 3-methylbutanoate (fruity) were found whereas others, such as the earthy smelling 3-isopropyl-2-methoxypyrazine as well as 2-phenylethanol and 3-methoxyphenol, remained unchanged during storage. Additionally, the previously unknown coffee odorant, 2-methoxy-5-vinylphenol (intense smoky odour) increased significantly during storage. Significant increase of the methyl esters of 2- and 3-methylbutanoic acid were responsible for the pronounced and fruity odour quality perceived in the stored green coffee, whereas the higher concentrations of 2-methoxy-4-vinylphenol and 2-methoxy-5-vinylphenol led to the more pronounced smoky, clove-like odour quality. The aroma profile of Ethiopian Arabica coffee was discriminately different from those of Tanzanian coffee and Guatemalan Arabica coffee (Akiyama et al. 2008). The results of principal component analysis suggested that 4-(4′-hydroxyphenyl)-2-butanone (raspberry ketone; sweet-fruity odor) characterized the aroma profile of freshly brewed Ethiopian coffee. Ethiopian coffee extract of the lightly roasted degree contained the highest amount of this component.

Analysis of the aroma staling compounds of coffee brew revealed a marked decrease in the levels of the odorous thiols 2-furfurylthiol, 3-methyl-2-butenthiol, 3-mercapto-3-methylbutyl formate, 2-methyl-3-furanthiol, and methanethiol when melanoidins were present with 2-furfurylthiol the most affected (Hofmann and Schieberle 2002). This was accompanied by a decrease in the overall roasty-sulfury aroma. The thiols were covalently bound to the coffee melanoidins via Maillard-derived pyrazinium compounds formed as oxidation products of 1,4-bis-(5-amino-5-carboxy-1-pentyl)pyrazinium radical cations (CROSSPY). It was shown that 2-(2-furyl) methylthio-1,4-dihydro-pyrazines, bis[2-(2-furyl)methylthio]-1,4-dihydro-pyrazines, and 2-(2-furyl)methylthio-hydroxy-1,4-dihydro-pyrazines were formed as the primary reaction products. Similar results were obtained for models in which either 1,4-diethyl diquaternary pyrazinium ions were substituted by Nalpha-acetyl-L-lysine/glycolaldehyde, or the 2-furfurylthiol by 2-methyl-3-furanthiol and 3-mercapto-3-methylbutyl formate. They concluded that the CROSSPY-derived pyrazinium intermediates were involved in the rapid covalent binding of odorous thiols to melanoidins, and, consequently, were responsible for the decrease in the sulfury-roasty odor quality observed shortly after preparation of the coffee brew.

Phytochemicals in Flowers/Leaves

Coffea arabica flowers have been found to contain a significant number of nitrogen-containing aromatic volatile compounds as well as phenylethane derivatives (Emura et al. 1997). The epoxygeraniols (2,3-epoxygeraniol and 6,7-epoxygeraniol) were also detected as minor components and were found to possess rosy and muguet-like aromas reminiscent of the living flower. The levels of endogenous caffeine and theobromine were much higher in buds and young leaves of *Coffea arabica* cv Kent than in fully developed leaves (Ashihara et al. 1996). The pathway of caffeine biosynthesis in young leaves was found to be: adenosine monophosphate → inosine monophosphate → xanthosine 5[prime]-monophosphate (or guanosine

monophosphate → guanosine) → xanthosine → 7-methylxanthosine → 7-methylxanthine → theobromine → caffeine.

Coffee Consumption and Health

Epidemiological and experimental studies had shown positive effects of regular coffee-drinking on various aspects of health, such as psychoactive responses (alertness, mood change), neurological (infant hyperactivity, dementia, Alzheimer's and Parkinson's diseases) and metabolic disorders (diabetes, gallstones), liver diseases (cirrhosis and hepatocelluar carcinoma), and gonad and liver function (Dórea and da Costa 2005; Higdon and Frei 2006). Moderate amounts of caffeine intake may increase alertness, reduce fatigue and improve cognitive vigilant performance (Smith 2002). Epidemiological studies had also reported coffee consumption to be associated with lower risk of colorectal cancer (Giovannucci 1998; Woolcott et al. 2002; Larsson et al. 2006; Lee et al. 2007); hepatocelluar carcinoma and steatohepatitis (Inoue et al. 2005; Montella et al. 2007; Larsson and Wolk 2007; Nkondjock 2009; Molloy et al. 2012); prostate cancer (Wilson et al. 2011); gliomas (Michaud et al. 201; Holick et al. 2011); endometrial cancer (Gunter et al. 2011; Je et al. 2012; Giri et al. 2011) and other cancers (Yu et al. 2011). Coffee because of its content of a diverse range of phytochemicals such as caffeine, diterpenes, cafeic acid, chlorogenic acids and other polyphenolic compounds such as tannins, lignans and anthocyanin and volatile and heterocyclic compounds (Farah and Donangelo 2006; Nkondjock 2009) also possesses an array of beneficial pharmacological properties that include antioxidant, hepatoprotective, neuroprotective, hypoglycaemic, antiviral, antihypertensive, antihyperlipidemic, antiobesity, antimicrobial, prebitoic, anti-photoaging, antitussive and immunomodulatory activities that are elaborated below and in the chapter on *C. robusta*. However, high doses of coffee/caffeine consumption may produce negative effects in some sensitive individuals, including anxiety, palpitations, tachycardia, arrhythmia, increase risk of infarction and insomnia (Chou and Benowitz 1994; El Yacoubi et al. 2000; Smith 2002; Ogita et al. 2003; Farah et al. 2006; Cornelis et al. 2006). Epidemiological studies had suggested consumption of boiled coffee to be associated with elevated risk for cardiovascular disease due to the cholesterol elevating effects of two diterpenes identified in the lipid fraction of coffee grounds, cafestol and kahweol (Ranheim and Halvorsen 2005). In psychiatric in-patients, caffeine had been found to increase anxiety, hostility and psychotic symptoms (Winston et al. 2005). Caffeine had been reported to antagonise adenosine receptors, which may potentiate dopaminergic activity and exacerbate psychosis. For adults consuming moderate amounts of coffee (3–4 cups/days providing 300–400 mg/day of caffeine), there is little evidence of health risks and some evidence of health benefits (Pollak and Bright 2003; Higdon and Frei 2006). Currently available evidence suggests that it may be prudent for pregnant women to limit coffee consumption to three cups/day providing no more than 300 mg/day of caffeine to exclude any increased probability of spontaneous abortion or impaired fetal growth. For the elderly, moderate amounts of coffee (50–100 mg of caffeine or 5–10 g of coffee powder a day) or decaffeinated coffee is recommended if their stomach is healthy (Zivković 2000).

Antioxidant Activity

Coffee Beans, Roasted Coffee and Coffee Brews

Green beans of *C. arabica* were found to have a moisture content of 10.28%, pH 5.53, total phenolic content 34.32 mg GAE/g fresh sample and % DPPH inhibition of 92.52% (Somporn et al. 2011). Increasing roasting degrees led to a decrease total phenolic content and in DPPH radical-scavenging activity. Total phenolic content (mg GAE/g fresh sample) in light, medium and dark roasted coffee was 31.55, 24.98 and 22.31 mg respectively. DPPH radical scavenging inhibition for light, medium and dark roasted coffee was 92.63, 88.87, and 86.98% respectively. They found that light-roasted coffee gave the most desirable quality of roasted

coffee with respect to phenolic content and radical-scavenging activities. A progressive decrease in antioxidant activity of Columbian Arabica coffee (associated mainly with chlorogenic acids in the green beans) with degree of roasting was observed with the simultaneous generation of high (HMM) and low molecular mass (LMM) compounds possessing antioxidant activity (Del Castillo et al. 2002). Maximum antioxidant activity was observed for the medium-roasted coffee; the dark coffee had a lower antioxidant activity despite the increase in colour. The LMM fraction contributed more to total antioxidant activity than the HMM components.

The order of ferric reducing power (FRAP) per gram of dry matter (dm) of the different brewed coffees tested, in terms of the coffee-making procedure used, was freeze-dried > filter ≈ espresso ≈ Italian (Sánchez-González et al. 2005). The order of ferric reducing ability per serving was filter > espresso > freeze-dried ≈ Italia n. For ABTS scavenging activity the order was similar to that described for the FRAP assay. There was a high correlation between the estimated polyphenol contents and the FRAP, or the ABTS values ($R^2 = 0.98$, $R^2 = 0.99$ respectively). In the FRAP and ABTS assays; a serving of filtered coffee was equivalent to 2,653 and 1,295 μg trolox, respectively. They found that antioxidant activity increased significantly (by 34%) after 4 h of heating (85°C). The cause of this increase would seem to be the formation of Maillard products, due to the heat process. These compounds also appeared to be responsible for the fact that antioxidant capacity was higher in dark-roast than in other brewed coffees tested. Antioxidant activity decreased when milk was added to the espresso coffee. Under the standard cup serving conditions and using in-vitro low-density lipoprotein oxidation model, the antioxidant activity as determined by the lag time was in the range of 292–948 min for coffee (Richelle et al. 2001). Addition of milk did not alter the antioxidant activity. Green coffee beans of Robusta coffee exhibited a twofold higher antioxidant activity than Arabica coffee, but after roasting this difference was no longer significant.

The antioxidant activity of coffee brews were concentration-dependent (Duarte et al. 2005). A progressive antioxidant activity and polyphenols content was observed decreasing with roasting. The light roasted coffee showed the highest antioxidant activity and dark roasted coffee showed the lowest antioxidant activity. The results indicated that the ingestion of coffee brews prepared with light and medium roasted coffees might protect cells from oxidative stress damages. Beverages prepared with ground coffee, had, on average, 27% higher FRAP values than those prepared with soluble coffee (Moreira et al. 2005). In the former beverages, FRAP of *C. robusta* samples was significantly higher (on average, 50.3%) when compared to that of *C. arabica* samples, and FRAP values decreased with increasing degree of roasting. A strong correlation ($R^2 > 0.91$) was found between FRAP and the total content of chlorogenic acids, particularly that of the caffeoylquinic acid isomers. The iron-reducing activity of coffee beverages was not influenced by caffeine. Only moderate differences were found in the antioxidant capacities of ground and instant coffee samples as determined by the ABTS assay, 0.22 mmol/g TEAC for ground and 0.71 mmol/g TEAC for instant coffee (Brezová et al. 2009). Caffeic acid (coffee component) was effective in all oxidant systems, whereas caffeine was inert to ABTS and DPPh oxidants but effective in scavenging OH radicals. Good correlation $R^2 = 0.859$ was found between $TEAC_{ABTS}$ and $TEAC_{DPPH}$ and also between phenolic contents (GAE) and TEAC antioxidant capacities ($R^2 = 0.729$ for ABTS and $R^2 = 0.922$ for DPPH).

All of the coffee brews (light, medium and dark roasting) presented concentration-dependent antioxidant activity (Santos et al. 2007). The light coffee samples presented the higher reducing power and DPPH scavenging activity. Its ion chelating capacity was similar to the medium samples, but was less than the green coffee chelating capacity. The semi-dry processing was more efficient than the dry processing only for the reducing power. All of the samples presented high lipid peroxidation inhibition activity. Based on the results the degree of coffee roasting

appeared to be more important than the processing to determine the antioxidant activity of brews. The addition of sugar at the end of the torrefacto roasting process may influence the antioxidant and pro-oxidant properties of coffee because sugar is one of the main precursors of the Maillard reaction (López-Galilea et al. 2006). Higher antioxidant activity was observed in Colombian coffees than in conventional roasted arabica/robusta coffee blends. In contrast, when the percentage of torrefacto roasted coffee was increased, an increase of antioxidant activity and a slight decrease in pro-oxidant activity were observed.

Brews extracted from medium roasted coffee showed a higher radical scavenging activity than those from green coffee due to an increase of the radical scavenging activity of the non-phenolic fraction (NPF) upon roasting (Sacchetti et al. 2009). The radical scavenging activity of the NPF increased with increasing roasting degree together with the accumulation of brown coloured Maillard reaction products (MRPs). Brews from dark coffee showed lower radical scavenging activity than those from medium roasted coffee due to polyphenols degradation which, in turn, caused a radical scavenging activity depletion not counterbalanced by an increase of the radical scavenging activity of NPF. The relative contribution of NPF to the overall radical scavenging activity of the brew was in fact much lower than that of the phenolic fraction.

Studies showed that, depending on the roasting degree as well as on the packaging conditions adopted, redox reactions, which could occur during storage, were responsible for significant changes in the overall antioxidant capacity of ready-to-drink coffee brews (Anese and Nicoli 2003). The redox potential of air-packaged coffee brews, obtained from light- and medium-roasted beans, showed maximum values after 2 days of storage, which corresponded to a minimum in the chain-breaking activity, while, in the case of the dark-roasted sample packaged under ordinary atmosphere, both the redox potential and the chain-breaking activity showed a maximum around 2–3 days of storage. Contrariwise, in the absence of oxygen, the coffee brews maintained the initial reducing properties over all the storage time, although the radical-scavenging activity values changed in a way very similar to that of the air-packaged sample. The results suggested that the changes in the antioxidant properties of the coffee brews may be attributed to a further development of the Maillard reaction during storage.

Coffee Constituents and Antioxidant Activity

Caffeine was found to be an effective inhibitor of lipid peroxidation, at millimolar concentrations, against all the three reactive species, hydroxyl radical (.OH), peroxyl radical (ROO.) and singlet oxygen ($^1O_2$) in rat liver microsomes (Devasagayam et al. 1996). The extent of inhibition was high against peroxidation induced by hydroxyl, medium against singlet oxygen and low against peroxyl radical. In general, the antioxidant ability of caffeine was similar to that of the established biological antioxidant glutathione and significantly higher than ascorbic acid.

Reducing substances of *C. robusta* coffee samples were found to be significantly higher when compared to those of *C. arabica* samples (Daglia et al. 2000). Antioxidant activity (using β-carotene-linoleic acid) for green coffee samples were slightly higher than for the corresponding roasted samples while protective activity against rat liver cell microsome lipid peroxidation was significantly lower in green coffee compared to that of all roasted samples. Extraction with three different organic solvents (ethyl acetate, ethyl ether, and dichloromethane) showed that the most protective compounds were extracted from acidified dark roasted coffee solutions with ethyl acetate. The analysis of acidic extract yielded five fractions. Higher molecular mass fractions were found to possess antioxidant activity while the lower molecular mass fractions showed protective activity. The small amounts of these acidic, low molecular mass protective fractions isolated indicated that they contained very strong protective compounds. In-vitro (chemical deoxiribose assay) and ex-vivo (in IMR32 cells) antihydroxyl radical activity showed that both green and roasted *Coffea arabica* and *Coffea robusta* coffee samples possessed antiradical activity and their more active component was

5-O-caffeoyl-quinic acid (Daglia et al. 2004). The highest antioxidant activity obtained by the MA-GC assay (malonaldehyde formation from oxidized cod liver oil using a gas chromatographic method) was from regular whole brewed coffee (97.8%) at a level of 20%, and the highest antioxidant activity obtained by the TBA (thiobarbituric acid) assay was from decaffeinated whole brewed coffee (96.6%) at a level of 5% (Fujioka and Shibamoto 2006). Among 31 coffee chemicals identified in a dichloromethane extract, guaiacol, ethylguaiacol, and vinylguaiacol exhibited antioxidant activities, which were comparable to that of α-tocopherol. Among nine chlorogenic acids (three caffeoylquinic acids, three feruloylquinic acids, and three dicaffeoylquinic acids) identified, 5-caffeoylquinic acid contained the greatest amount both in regular (883.5 μg/mL) and in decaffeinated (1032.6 μg/mL) coffees; it exhibited 24.5% activity by the MA-GC assay and 45.3% activity by the TBA assay at a level of 10 μg/mL. Caffeic and ferulic acids showed moderate antioxidant activities in both assays.

The brown polymers (foaming fractions) of freshly prepared espresso coffee on sub-fractionation yielded an insoluble fraction (foaming fraction A, FFA) and a soluble fraction (foaming fraction B, FFB) (D`Agostina et al. 2004). The former almost colorless, had a higher molecular weight and a lower nitrogen content, and contained mostly polysaccharides, whereas the latter had a lower molecular weight and a higher protein/melanoidin content, which resulted in a darker colour. FFB showed greater foaming capability, but FFA contributed to the stability of the foam. All of the melanoidin-rich fractions showed antioxidant properties with the 2,2-diphenyl-1-picrylhydrazyl hydrate assay.

Roasting process induced high molecular weight components (later Maillard reaction products, i.e., melanoidins) that also possessed antiradical activity in coffee. Roasting resulted in the degradation of chlorogenic acid (5-CQA) and formation of melanoidins, while antioxidant activity was largely unaffected by roasting (Vignoli et al. 2011). The extraction of soluble coffee more prominently affected the antioxidant activity of light-roasted coffee, mainly because it favoured the extraction of 5-CQA. The larger caffeine content in robusta coffee resulted in greater antioxidant activity. All of soluble coffees extracted by various methods from light, medium and dark-roasted arabica and robusta beans possessed antioxidant potential, which was conferred by their concentrations of phenolic compounds, caffeine and melanoidins. Studies showed high molecular weight melanoidins extracted from coffee, barley coffee, and dark beer decreased the synthesis of lipid hydroperoxides and secondary lipoxidation products during simulated gastric digestion of turkey meat (Tagliazucchi et al. 2010). Coffee melanoidins at 3 mg/mL reversed the reaction and broke down hydroperoxides to concentrations lower than the initial value. Barley coffee and dark beer melanoidins were less effective, and even at 12 mg/mL did not reverse the reaction. Coffee melanoidins, which contained more phenolics and proteins with respect to the other melanoidins, showed greater antioxidant activity with respect to the other melanoidins tested.

Among the volatile heterocylcic compounds found in brewed coffee extracts- pyrroles, furans, thiophenes, and thiazoles, 2-acetylpyrrole, 1-methylpyrrole, and pyrrole inhibited hexanal oxidation by 98, 87, and 78%, respectively, at a concentration of 500 μg/mL over a period of 30 days (Fuster et al. 2000). 2-Methylfuran, which inhibited hexanal oxidation by 90% at all concentrations tested (500, 200, and 100 μg/mL) for a 30-day period, exhibited the greatest activity among furans tested. Similarly, 2-methylthiophene, which inhibited hexanal oxidation by almost 100% at a concentration of 500 μg/mL over 30 days, exhibited the greatest activity among the thiophenes tested. In general, thiazoles were ineffective antioxidants at all concentrations tested. However, 4,5-dimethylthiazole was able to inhibit hexanal oxidation by 50% at the highest level tested (500 μg/mL). 2-Acetylpyrrole, 2-methylfuran, and 2-methylthiophene at concentrations of 500, 200, and 100 μg/mL and furan at a concentration of 500 μg/mL exhibited antioxidative activities comparable to that of the synthetic antioxidant butylated hydroxytoluene at a concentration of 50 μg/mL.

Among heterocyclic compounds found in coffee volatiles produced by Maillard reaction, pyrroles exhibited the greatest antioxidant activity (Yanagimoto et al. 2002). All pyrroles inhibited hexanal oxidation by almost 100% at a concentration of 50 μg/mL over 40 days. Addition of formyl and acetyl groups to a pyrrole ring markedly enhanced antioxidative activity. Pyrrole-2-carboxaldehyde, 2-acetylpyrrole, 1-methyl-2-pyrrolecarboxaldehyde, and 2-acetyl-1-methylpyrrole inhibited hexanal oxidation by >80% at 10 μg/mL. Unsubstituted furan exhibited the greatest antioxidant activity among furans tested. Addition of all functional groups used in the study to furan decreased antioxidative activity. The antioxidant activity of thiophene increased with the addition of methyl and ethyl groups, but the addition of formyl or acetyl groups to thiophene decreased antioxidant activity. Thiazoles and pyrazines were ineffective antioxidants at all concentrations tested. Reaction of all heterocyclic compounds with hydrogen peroxide resulted in the formation of various oxidized products. In a subsequent study, they found the dichloromethane extract of brewed coffee inhibited hexanal oxidation by 100 and 50% for 15 and 30 days, respectively, at the level of 5 μg/mL (Yanagimoto et al. 2004). The presence of antioxidative heterocyclic compounds including furans, pyrroles, and maltol were detected. The residual aqueous solution exhibited weak antioxidative activity. The inhibitory activity (%) of the seven fractions from an aqueous solution toward malonaldehyde formation from lipid oxidation ranged from 10 to 90 at a level of 300 μg/mL. The results indicated brewed coffee to contain many antioxidants and consumption of antioxidant-rich brewed coffee may inhibit diseases caused by oxidative damages.

Polar coffee compounds with molecular weights below 1 kDa exhibited major inhibitory effect on the in-vitro peroxidation of linoleic acid as well as the predominant chemopreventive enzyme modulating activity on the NADPH-cytochrome c reductase (CCR) and glutathione S-transferase (GST) in human intestinal Caco-2 cells (Somoza et al. 2003). Coffee component 5-chlorogenic acid was found to be the most powerful antioxidant in-vitro, whereas, chemopreventive effects on the GST activity were found for the N-methylpyridinium ion. A strong in vitro antioxidant activity for coffee and N-methylpyridinium was confirmed by feeding study in rats. Plasma total antioxidant capacity and plasma tocopherol were elevated in animals fed the coffee beverage and the N-methylpyridinium-containing diet.

Melanoidins, the brown polymers formed through Maillard reaction during coffee roasting, constituted up to 25% of the coffee beverages' dry matter (Borrelli et al. 2002). Melanoidins antiradical activity determined by $ABTS^{+}$ and N , N-dimethyl-*p*-phenylendiamine assay (DMPD) assays decreased as the intensity of roasting increased, but the ability to prevent linoleic acid peroxidation was higher in the dark-roasted samples. Roasted coffee silverskin was found to have 60% total dietary fibre with 14% soluble dietary fibre component and small level of free phenols (Borrelli et al. 2004). Silverskin was found to have marked antioxidative activity, attributable to the large amount of Maillard reaction products, the melanoidins.

The effect of roasting on ApV a brownish polymer with zinc-chelating activity in brewed coffee was investigated by Wen et al. (2005). They found as the intensity of roasting increased, the yield of ApV increased, and the brown colour and molecular weight of ApV respectively became darker and higher. Increasing the degree of roasting also decreased the zinc-chelating activity of ApV. The reducing activities of ApVs estimated by the indophenol method were stronger than those of ascorbic acid. Both the antioxidative activity estimated by the ABTS assay and the reducing activity of ApV increased with roasting. When milk was added to instant coffee and, the zinc-chelating activity of ApV was not changed. Yen et al. (2005) reported that HPLC analyses showed that phenolic acids (chlorogenic acid and caffeic acid) and nonphenolic compounds [caffeine, trigonelline, nicotinic acid, and 5-(hydroxymethyl)furfuraldehyde] remained in roasted coffee residues. These compounds showed a protective effect on a liposome model

system. The concentrations of flavonoids and polyphenolic compounds in roasted coffee residues were 8,400 and 20,400 ppm, respectively. Further, the Maillard reaction products (MRPs) remaining in roasted coffee residues were believed to show antioxidant activity. The data indicated roasted coffee residues to have excellent potential for use as a natural antioxidant source because the antioxidant compounds remained in roasted coffee residues.

Three caffeoylquinic acids, three feruloylquinic acids, three dicaffeoylquinic acids, one *p*-coumaroylquinic acid, two caffeoylferuloylquinic acids and three putative chlorogenic lactones were quantified in whole coffee fruit extracts and powder samples , along with a methyl ester of 5-caffeoylquinic acid (Mullen et al. 2011). Multistep whole coffee fruit extracts displayed higher CGA content than single-step extracts, freeze-dried, or air-dried whole raw fruits. Caffeine in multistep extracts was lower than in the single-step extracts and powders. Antioxidant activity in whole coffee fruit extracts was up to 25-fold higher than in powders dependent upon the radical. Total antioxidant activity of samples displayed strong correlation to CGA content.

In-Vivo Antioxidant Studies

In a study of ten volunteers, ingestion of 200 mL (one cup) coffee induced an increase in the resistance of LDL (Low density lipoproteins) to oxidative modification but the LDL concentration did not increase (Natella et al. 2007). The incorporation into LDL of conjugated forms of caffeic, *p*-coumaric, and ferulic acids increased significantly after coffee drinking. The organic *Coffea arabica* coffee showed higher levels of chlorogenic acid, caffeine and trigonelline than conventional coffee, however, this difference did not significantly affect behavior of rats (Carvalho Ddo et al. 2011). The coffee infusions exerted an antioxidant effect, reducing the levels of malondialdehyde; however, the biochemical parameters of the serum were not altered, and there was neither induction nor prevention of preneoplasic lesions.

Hepatoprotective Activity

Diet supplementation of a coffee extract for 14 days significantly suppressed lipopolysaccharide (LPS)-induced hepatitis in D-galactosamine-sensitized rats (He et al. 2001). Its effect was as strong as that of a green tea extract. The coffee extract suppressed LPS-induced hepatitis when singly force-fed (1.2 g/kg) 1.5 h prior to the injection of the drugs, whereas a decaffeinated coffee extract had no significant effect. The hepatoprotective effect of caffeine was stronger than that of theobromine. Separate studies in rats suggested that caffeine, nicotinic acid, non-substituted pyrazinoic acid and 5-methylpyrazinoic acid could protect against lipopolysaccharide/D-galactosamine (LPS/D-GalN) induced acute liver injury, which may be mediated by the reduction of TNF-α production and/or increasing interleukin, IL-10 production (Akashi et al. 2009). Plasma aspartate aminotransferase and alanine aminotransferase levels were significantly increased after LPS/D-GalN-treatment, but were suppressed by pretreatment with caffeine, nicotinic acid, non-substituted pyrazinoic acid or 5-methylpyrazinoic acid 12 h after LPS/D-GalN-treatment. Additionally, rats pretreated with these test compounds showed significantly higher survival rates (83–100%) compared with the control (23%).

Gressner et al. (2008) showed that caffeine significantly suppressed transforming growth factor (TGF)-β dependent and -independent CTGF (connective tissue growth factor) expression in hepatocytes in- vitro and in- vivo, thus suggesting this xanthine-alkaloid as a potential therapeutic agent. In subsequent study they provided evidence that suggested caffeine-derived primary metabolite paraxanthine to be a potentially powerful antifibrotic drug by its inhibitory effect on (hepatocellular) CTGF synthesis (Gressner et al. 2009). Paraxanthine inhibitory dosage (ID)50 of 1.15 mM, i.e. 3.84-fold lower than what is observed for caffeine. In addition, paraxanthine displayed the least cell toxicity as proven by the water-soluble tetrazolium-1 cell vitality assay. However, caffeine or any of the

metabolites (theophylline or theobromine) did not inhibit CTGF expression in hepatic stellate cells. Vitaglione et al. (2010) demonstrated in rats that coffee consumption protected the liver from damage caused by a high-fat diet. This effect was mediated by a reduction in hepatic fat accumulation (through increased fatty acid β-oxidation), systemic and liver oxidative stress (through the glutathione system); liver inflammation (through modulation of genes), and expression and concentrations of proteins and cytokines related to inflammation

In a study of 245 patients, 137 with non-alcoholic fatty liver disease (NAFLD) and 108 controls, Catalano et al. (2010) found an inverse association between coffee intake and fatty liver. Coffee consumption was also inversely associated with the degree of bright liver score, along with insulin resistance and obesity, which, to the contrary, were directly associated with greater likelihood and severity of bright liver appearance.

In the cohort study of 125 580 multiethnic members of a comprehensive prepaid health care plan without known liver disease, Klatsky et al. (2006) found an inverse association between coffee consumption and risks of alcoholic cirrhosis as well as non-alcoholic cirrhosis. Tea drinking was unrelated to alcoholic or nonalcoholic cirrhosis. In the cross-sectional analyses, coffee drinking was related to lower prevalence of high aspartate aminotransferase and alanine aminotransferase levels, with stronger inverse relations in those who drink large quantities of alcohol. Using data from four continuous cycles of the National Health and Nutrition Examination Surveys (NHANES 2001–2008) Birerdinc et al. (2012) found caffeine intake to be independently associated with a lower risk for non-alcoholic fatty liver disease suggesting a potential protective effect.

Antimicrobial Activity

Three peak fractions of brewed coffee exhibited strong antibacterial action against a strain of *Legionella pneumophila* (Dogasaki et al. 2002). On analysis the antibacterial substances were found to be protocatechuic acid (3,4-dihydroxy benzoic acid), chlorogenic acid, and caffeic acid.

All solutions of *Coffea arabica, Coffea robusta* green and roasted and several commercial coffee samples significantly reduced *Streptococcus mutans*' adhesive properties (Daglia et al. 2002). The inhibition of *S. mutans'* adsorption to saliva-coated hydroxyapatite beads was observed both when coffee was present in the adsorption mixture and when it was used to pretreat the beads, suggesting that coffee active molecules may adsorb to a host surface, preventing the tooth receptor from interacting with any bacterial adhesions. Among the known tested coffee components, trigonelline and nicotinic and chlorogenic acids were found to be very active. Dialysis separation of roasted coffee components also showed that a coffee component fraction with 1000 Da < MW < 3,500 Da, commonly considered as low MW coffee melanoidins, may also contribute to the roasted coffee's antiadhesive properties. In subsequent studies, they found that whole high molecular weight coffee fraction (cHMW) and each of its melanoidin and non-melanoidin components (GFC1-5) inhibited *Streptococcus mutans*' adhesion, the strongest effect being exerted by cHMW (91%) and GFC1 (88%) (Stauder et al. 2010). *S. mutans* detachment from saliva-coated hydroxyapatite beads was four times greater (~20%) with cHMW and the GFC1 and GFC4 melanoidins than with controls. Biofilm production by *S. mutans* was completely abolished by cHMW and was reduced by 20% by the melanoidin components GFC2 and GFC4 and by the non-melanoidin component GFC5 compared with controls.

Roasted coffee extract was found to possess antibacterial activity against a wide range of microorganisms, including *Staphylococcus aureus* and *Streptococcus mutans*, whereas green coffee extract exhibited no such activity, thus the naturally occurring coffee compounds, such as chlorogenic acids and caffeine, could not therefore be responsible for the significant antibacterial activity exerted by coffee beverages against both bacteria (Daglia et al. 2007b). The very low minimum inhibitory concentration (MIC) found for standard glyoxal, methylglyoxal, and diacetyl

compounds formed during the roasting process impacted these α-dicarbonyl compounds to be the main agents responsible for the antibacterial activity of brewed coffee against both bacteria. However, their low concentrations determined in the beverage account for only 50% of its antibacterial activity. The addition of caffeine, with weak intrinsic antibacterial activity, to a mixture of α-dicarbonyl compounds at the concentrations found in coffee demonstrated that caffeine synergistically enhanced the antibacterial activity of α-dicarbonyl compounds and that glyoxal, methylglyoxal, and diacetyl in the presence of caffeine accounted for the whole antibacterial activity of roasted coffee.

Polyphenols trigonelline, caffeine and chlorogenic acid occurring in green and roasted coffee was found to interfere with *Streptococcus mutans* adsorption to saliva-coated hydroxyapatite beads (Ferrazzano et al. 2009). Minimum inhibitory concentration (MIC), biofilm inhibition and biofilm reduction of *Streptococcus mutans*, results were correlated with the concentration of coffee compounds and aqueous extracts of green and roasted regular and decaffeinated *Coffea arabica* and *Coffea canephora* beans (Antonio et al. 2010). 5-Caffeoylquinic acid, trigonelline and caffeic acid solutions showed bacteriostatic activity (MIC = 0.8 mg/mL). Lighter and regular extracts showed higher inhibitory activity than darker and decaffeinated extracts, with an inverse correlation between bacterial colony-forming units and roasting degree. Only regular *C. canephora* extracts showed biofilm formation inhibition. The joint effect of chlorogenic acids, trigonelline and caffeine or other compounds removed by decaffeination appeared to be one of the causes for coffee antibacterial activity against *S. mutans*.

Depending on concentration, roasted, but not raw coffee brew inhibited the growth of *Escherichia coli* and *Listeria innocua* (Mueller et al. 2011). Several coffee ingredients in natural concentration, caffeine, ferulic acid and a mixture of all test compounds showed very weak, but significant activity, whereas trigonelline, 5-(hydroxymethyl) furfural, chlorogenic acid, nicotinic acid, caffeic acid, and methylglyoxal were not active. Antimicrobial activity, however, was completely abolished by addition of catalase indicating that hydrogen peroxide was a major antimicrobial coffee component. In accordance with this assumption, bacterial counts during 16 houes of incubation were inversely related to the hydrogen peroxide concentration in the incubation solution. Pure hydrogen peroxide showed slightly weaker activity. Hydrogen peroxide was found to be generated in the coffee brew by Maillard reaction products.

The high-molecular-weight fraction of water-soluble coffee melanoidins (>10 kDa) exerted the highest antimicrobial activity against *Escherichia coli* (Rufián-Henares and Morales 2008). At the minimum inhibitory concentration, melanoidins caused irreversible cell membrane disruption of both the inner and outer membranes, which was independent of the bacterial transmembrane potential. The antimicrobial activity of coffee melanoidins against different pathogenic bacteria was found to be due to their metal-chelating properties (Rufián-Henares and de la Cueva 2009). Three different mechanisms were observed: at low concentrations melanoidins exerted a bacteriostatic activity mediated by iron chelation from the culture medium; in the case of bacterial strains that were able to produce siderophores for iron acquisition, melanoidins chelated the siderophore-Fe3+ complex, which then decreased the virulence of such pathogenic bacteria; and, finally, coffee melanoidins also exerted a bactericide activity at high concentrations by removing Mg2+ cations from the outer membrane, promoting the disruption of the cell membrane and allowing the release of intracellular molecules. In a study of 1000 individuals, of both sexes, who consumed only coffee as a beverage, Anila Namboodiripad and Kpori (2009) found that that coffee if consumed alone had anticaries action, but in the presence of additives (milk, sugar) the antibacterial and anticaries action was totally minimized.

Antitussive and Immunomodulatory Activities

A low molecular mass arabinogalactan-protein (AGP) composed of galactose and arabinose with a low protein content, isolated from the instant

coffee powder of *Coffea arabica* beans, was found to exhibit a significant dose dependant cough-suppressive effect (Nosáľová et al. 2011). Coffee AGP was found to be a good inductor of both pro-inflammatory cytokines TNF-α and IFN-γ cytokines, but was less potent in TNF-α induction in comparison with that of β-D-glucan. Evident induction of TNF-α, IL-2 and IFN-γ cytokines, pro-TH1 polarization confirmed their conclusion about bio-immunological efficacy of AGP with an emphasis on the cellular immunity.

Phytoestrogen Activity

Using proliferation of estrogen-dependent human breast cancer (MCF-7) cells as a model system, Allred et al. (2009) found that when the cells were cotreated with suboptimal doses of estradiol (10 pmol/l) and trigonelline (100 pmol/l) a coffee bean component, an additive enhancement of MCF-7 growth was observed. In the absence of estradiol, trigonelline stimulated MCF-7 cell proliferation in a dose-responsive manner and significantly enhanced cell growth at concentrations as low as 100 pmol/l. This effect was found to be mediated through estrogen receptor expression indicating trigonelline to be a novel phytoestrogen.

Antihypertensive and Hypertensive Activities

Coffee melanoidins formed at the last stage of the Maillard reaction was found to have antihypertensive activity (Rufian-Henares and Morales 2007). They showed in-vitro angiotensin-I converting enzyme (ACE) inhibitory activity which was significantly higher at more severe heating conditions.

Animal studies showed that caffeine reversed insulin resistance and hypertension induced by both high-fat (HF) and the high-sucrose (Hush) in rats (Conde et al. 2012). In the HF-fed animals caffeine treatment restored fasting insulin levels to control values and reversed increased weight gain and visceral fat mass. In the HSu group, caffeine reversed fasting hyperglycaemia and restored non-esterified fatty acids to control values. There were no changes either in plasma NO or in hepatic glutathione levels but caffeine totally prevented the increase in serum catecholamines induced by HF and HSu diets. They concluded that long-term caffeine intake prevented the development of insulin resistance and hypertension in HF and HSu models and that this effect was related to a decrease in circulating catecholamines.

In a study of ten trained, caffeine-naive cyclists (7 women and 3 men), Daniels et al. (1998) found that caffeine could alter the cardiovascular response to dynamic exercise in a manner that may modify regional blood flow and conductance. Before exercise, caffeine increased both systolic blood pressure (17%) and mean arterial pressure (11%) without affecting forearm blood flow (FBF) and forearm vascular conductance (FVC). During dynamic exercise, caffeine attenuated the increase in FBF (53%) and FVC (50%) and accentuated exercise-induced increases in plasma angiotensin lI (44%). Systolic blood pressure and mean arterial pressure were also higher during exercise plus caffeine. No significant differences were observed in heart rate, skin temperature, or rectal temperature.

Antihyperlipidemic Activity

Several animal, human and meta-analysis studies had suggested that coffee consumption could reduce weight gain and obesity. Studies in ddy mice suggested green coffee bean extract to be effective against weight gain and fat accumulation by inhibition of fat absorption and activation of fat metabolism in the liver (Shimoda et al. 2006). Caffeine and chlorogenic acid was found to reduce visceral fat and body weight while chlorogenic acid also reduced hepatic triglyceride level. Neither caffeine nor chlorogenic acid alone was found to enhance hepatic carnitine palmitoyltransferase activity but other phenolic compounds such as neochlorogenic acid and feruloylquinic acid mixture could do so. Cho et al. (2010) found in high-fat diet-induced-obese mice

that supplementation of the diet with caffeic acid and chlorogenic acid significantly lowered body weight, visceral fat mass and plasma leptin and insulin levels compared to the high-fat control group. They also lowered triglyceride (in plasma, liver and heart) and cholesterol (in plasma, adipose tissue and heart) concentrations. Triglyceride content in adipose tissue was significantly lowered, whereas the plasma adiponectin level was elevated by chlorogenic acid supplementation compared to the high-fat control group. Body weight was significantly correlated with plasma leptin ($R^2 = 0.894$) and insulin ($R^2 = 0.496$) levels, respectively. Caffeic acid and chlorogenic acid significantly inhibited fatty acid synthase, 3-hydroxy-3-methylglutaryl CoA reductase and acyl-CoA:cholesterol acyltransferase activities, while they increased fatty acid β-oxidation activity and peroxisome proliferator-activated receptors α expression in the liver compared to the high-fat group. Their results suggested that caffeic acid and chlorogenic acid improved body weight, lipid metabolism and obesity-related hormones levels in high-fat fed mice. Chlorogenic acid appeared to be more potent for body weight reduction and regulation of lipid metabolism than caffeic acid.

Murase et al. (2011) found that supplementation of C57BL/6 J mice diet with coffee polyphenols (CPP), significantly reduced body weight gain, abdominal and liver fat accumulation, and infiltration of macrophages into adipose tissues. Energy expenditure was significantly increased in CPP-fed mice. They found that CPP enhanced energy metabolism and reduced lipogenesis by downregulating sterol regulatory element-binding protein (SREBP)-1c, acetyl-CoA carboxylase-1 and -2, stearoyl-CoA desaturase-1, and pyruvate dehydrogenase kinase-4 in the liver, which led to the suppression of body fat accumulation.

In a study of 50 volunteers with body mass index higher than 25, after 60 days of treatment, a mean reduction in body weight of 4.97 kg (5.7%) and body mass index was observed in the group treated with Svetol®, a green coffee extract rich in chlorogenic acids (5-caffeoylquinic acid and others caffeoylquinic acid isomers) compared with placebo (Dellalibera et al. 2006). The significant decrease in weight, body mass index and fat mass with Svetol® in overweight subjects could be explained by increasing the metabolism of fatty deposits, as shown by change in the muscle mass/fat mass ratio. The results of a 22 week cross-over study of 16 overweight adult suggested that a commercial green coffee extract product GCA may be an effective nutraceutical in reducing weight in preobese adults, and may be an inexpensive means of preventing obesity in overweight adults (Vinson et al. 2012). Significant reductions were observed in body weight and percent body fat as well as a small decrease in heart rate in subjects taking GCA.

Lopez-Garcia et al. (2006) conducted a prospective study of 18,417 men and 39,740 women, with no chronic diseases at baseline, from 1986 to 1998 to assess the relation between caffeine intake and 12-years weight change. Age-adjusted models showed a lower mean weight gain in participants who increased their caffeine consumption than in those who decreased their consumption. An increase in coffee and tea consumption was also associated with less weight gain. In men, the association between caffeine intake and weight was stronger in younger participants; in women, the association was stronger in those who had a body mass index (in kg/m^2) > or = 25, who were less physically active, or who were current smokers. They concluded that increases in caffeine intake may lead to a small reduction in long-term weight gain. Onakpoya et al. (2011) conducted a meta-analysis of five eligible studies and found that coffee green extract caused a significant reduction in body weight compared to placebo. However, they advocated more rigorous studies to be conducted because of heterogeneity amongst the studies and methodological quality.

Antiviral Activity

In HepG2.2.15 cells, chlorogenic acid, quinic acid and caffeic acid inhibited hepatitis virus B (HVB) DNA replication as well as HBsAg production (Wang et al. 2009). Chlorogenic acid and

caffeic acid also reduced serum DHBV level in DHBV-infected duckling model. Also extracts of regular coffee and that of decaffeinated coffee also showed inhibitory effect on HBV replication.

Both hot water extracts of coffee grinds and instant coffee solutions inhibited the multiplication of herpes simplex virus type 1 (HSV-1) a representative enveloped DNA virus (Utsunomiya et al. 2008). The antiherpetic activity the coffee extracts may possibly involve two different mechanisms, (1) a direct inactivation of the infectivity of virus particle (i.e., a virucidal activity) and (2) the inhibition of progeny infectious virus formation at the late stage of viral multiplication in the infected cells. Caffeine, but not quinic acid and chlorogenic acid, was found to inhibit virus multiplication to some extent, but none of them showed virucidal activity, suggesting that other component(s) in the coffee extracts my be involved in the observed antiviral activity. Additionally, the coffee extracts inhibited the multiplication of poliovirus, a non-enveloped RNA virus, but showed no virucidal effect on this virus. In subsequent studies, they found that caffeic acid inhibited the multiplication of HSV-1 in-vitro, mainly before the completion of viral DNA replication, but not thereafter (Ikeda et al. 2011). Chlorogenic acid, a caffeic acid ester with quinic acid, did not. These reagents did not have a direct virucidal effect. N-methyl-pyridinium formate, a novel component of coffee extracts, inhibited the multiplication of both DNA and RNA viruses (Tsujimoto et al. 2010). In the presence of the compound, the progeny viral yields of both herpes simplex virus type 1 (HSV-1) and poliovirus in HEp-2 cells and those of influenza virus type A in MDCK cells decreased with increasing concentrations of the compound, although the degree of viral sensitivity to this compound differed. Characterization of the mode of action of this compound against HSV-1 multiplication revealed that it inhibited the viral growth primarily at the initial step of virus multiplication. In addition, this compound showed a significant cytotoxic effect, although the observed antiviral effect was unlikely to be attributed to the cytotoxic effect.

In a large prospective study (Hepatitis C Antiviral Long-Term Treatment against Cirrhosis (HALT-C)) lasting 3.8 years of 766 participants with advanced hepatitis C-related liver disease, 230 participants had outcomes indicating regular coffee consumption to be associated with lower rates of disease progression (Freedman et al. 2009). In a subsequent study of 885 patients in the Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis Trial, high-level consumption of coffee (more than three cups per day) was found to be an independent predictor of improved virologic response to peginterferon plus ribavirin retreatment in patients with hepatitis C (Freedman et al. 2011).

Anticancer Activity

Several epidemiological case-controlled studies had indicated coffee drinkers to be at a lower risk of developing cancers of the colon and the liver and possibly of several other organs (Cavin et al. 2002; Huber and Parzefall 2005; Yu et al. 2011). Yu et al. (2011) conducted a meta-analysis of 59 studies, consisting of 40 independent cohorts that met the inclusion criteria and found that overall an increase in consumption of one cup of coffee per day was associated with a 3% reduced risk of cancers (RR 0.97). In subgroup analyses, they noted that, coffee drinking was associated with a reduced risk of bladder, breast, buccal and pharyngeal, colorectal, endometrial, esophageal, hepatocellular, leukemic, pancreatic, and prostate cancers.

The chemoprotective effect of coffee diterpenes, cafestol and kahweol in several cancers, had been reported to involved different mechanisms such as modifications of xenobiotic metabolism resulting in a reduction of the genotoxicity of carcinogens (Cavin et al. 2002; Huber and Parzefall 2005), induction of conjugating enzymes (e.g. glutathione S-transferases, glucuronosyl S-transferases), an increased expression of proteins involved in cellular antioxidant defense (e.g. γ-glutamyl cysteine synthetase and heme oxygenase-1) and an inhibition of the expression and/or activity of

cytochromes P450 involved in carcinogen activation (e.g. CYP2C11, CYP3A2) (Cavin et al. 2002). In in–vitro and rodent studies, several individual chemoprotectants out of the >1,000 constituents of coffee were identified as well as some strongly metabolized individual carcinogens against which they specifically protected. In human liver epithelial cell lines transfected to express AFB(1)-activating P450s, cafestol and kahweol treatment resulted in a reduction of aflatoxin AFB(1)-DNA binding. This protection was correlated with an induction of GST-mu, an enzyme known to be involved in AFB(1) detoxification (Cavin et al. 2002). Studies in male Sprague-Dawley rats, showed that treatment of a mixture of cafestol and kahweol in the diet significantly inhibited aflatoxin B1 (AFB1) binding to DNA (Cavin et al. 1998). Two complementary mechanisms may account for the chemopreventive action of cafestol and kahweol against aflatoxin B1 in rats. A decrease in the expression of the rat activating cytochrome P450s (CYP2C11 and CYP3A2) was observed, as well as a strong induction of the expression of the glutathione-S-transferase (GST) subunit GST Yc2, which is known to detoxify highly the most genotoxic metabolite of AFB1. Studies in male Fisher F344 rats exposed to the carcinogen2-amino-1-methyl-6-phenylimidazo-[4,5-b]pyridine (PhIP), showed that kahweol and cafestol palmitates (K/C), two components of unfiltered coffee reduced colorectal cancer PhIP-DNA adducts by>50% (Huber et al. 2004). K/C decreased hepatic NAT-dependent PhIP activation by up to 80% in a dose-dependent manner but increased hepatic glutathione S-transferase (GST) activity/expression. The data suggested the unique potential of K/C to convert rapid acetylators to a slow acetylator phenotype, accompanied by GST induction, and might contribute to chemoprevention against cancers associated with heterocyclic amines. Other coffee components such as polyphenols and K/C-free coffee were also capable of increasing GST and partially of inhibiting NAT, although to a somewhat lesser extent (Huber and Parzefall 2005).

Glei et al. (2006) found that supplementation of bread with green coffee antioxidants improved the chemoprotective property of normal bread under in-vitro cell culture conditions, chlorogenic acid (CGA) content and antioxidative capacity. Green coffee antioxidants and supplemented bread contained 7- and 880-fold more CGA than normal bread and were significantly more antioxidative (ferric reducing ability of plasma assay, 2.9- and 265-fold; Trolox equivalent antioxidant capacity assay, 1.3- and 24-fold, respectively). The treatment of human colon (HT29) and liver (HepG2) cells with supplemented bread extract increased resistance of colon and liver cells against H_2O_2-induced oxidative stress.

Colonic and Colorectal Cancer

A meta-analysis of the combined results from 12 case-control studies showed an inverse association between coffee consumption and risk of colorectal cancer risk (Giovannucci 1998). The lower risk of colorectal cancer among substantial coffee drinkers was observed in studies from Asia, Northern and Southern Europe, and North America. However they were inconclusive because of inconsistencies between case-control and prospective studies, the lack of control for important covariates in many of the studies, and the possibility that individuals at high risk of colorectal cancer avoided coffee consumption. Larsson et al. (2006) analysed the association of coffee consumption with colorectal cancer risk among participants from two population-based cohort studies: 61,433 women in the Swedish Mammography Cohort and 45,306 men in the Cohort of Swedish Men. They found coffee consumption was not associated with risk of colorectal cancer, colon cancer, or rectal cancer in either women or men. The results of this meta-analysis indicated a lower risk of colorectal cancer associated with substantial consumption of coffee, but they were inconclusive because of inconsistencies between case-control and prospective studies. Naganuma et al. (2007) used data from the prospective Miyagi Cohort Study of 22,836 men and 24,769 women, aged 40–64 years, with no previous history of cancer to clarify the association between coffee consumption and the risk of colorectal cancer. They found

coffee consumption was not associated with the incidence of colorectal, colon or rectal cancers.

Je and Giovannucci (2009) conducted a systematic meta-analysis of 12 eligible prospective cohort studies on coffee consumption and colorectal cancer published up to June 2008. The summarized result of the meta-analysis comparing high- vs. low-consumption categories showed no significant effect of coffee consumption on colorectal cancer risk when considering four studies conducted in the United States of America, five studies from Europe, and three Japanese studies. No significant differences by sex and cancer-site were found, but there was a slight suggestion of an inverse association between coffee consumption and colon cancer in women, especially Japanese women. The suggestive inverse associations were slightly stronger in studies that controlled for smoking and alcohol, and in studies with shorter follow-up times.

In a crossover design of 64 healthy volunteers unfiltered coffee did not influence the colorectal cancer proliferation rate, but might increase the detoxification capacity and anti-mutagenic properties in the colorectal mucosa through an increase in glutathione concentration (Grubben et al. 2000). In a single case-control study conducted in Ontario, Canada from 1992 to 1994, Woolcott et al. (2002) found that colon cancer risk was inversely associated with coffee consumption. The reduced risk estimates were more pronounced with cancer of the proximal colon than the distal colon. Rectal cancer risk was not associated with either coffee or tea.

Using data from the Nurses' Health Study (women) and the Health Professionals' Follow-up Study (men) Michels et al. (2005) found that consumption of caffeinated coffee, tea with caffeine, or caffeine was not associated with incidence of colon of rectal cancer, whereas regular consumption of decaffeinated coffee was associated with a reduced incidence of rectal cancer. Using data from the Singapore Chinese Health Study, Peterson et al. (2010) found no overall association between coffee intake and colorectal cancer but found that coffee may protect against smoking related advanced colon cancer. In study of a total of 60 041 Finnish men and women who were 26–74 years of age and without history of any cancer at baseline, Bidel et al. (2010) found no association between coffee consumption and the risk of colorectal, colon and rectal cancer.

Lee et al. (2007) analysed data from a population-based cohort of 96,162 subjects (46,023 men and 50,139 women) in Japan Public Health Center-based Prospective Study(JPHC Study). They found a significant inverse association between coffee consumption and the risk of developing invasive colon cancer among women. Compared with those who almost never consumed coffee, women who regularly consumed three or more cups of coffee per day had a RR (relative risk) of 0.44 after adjustment for potential confounding factors. However, no significant association was found for rectal cancer in women. In men, no significant decrease was observed in any colorectal cancer site. Galeone et al. (2010) conducted a meta-analysis of case-control studies on coffee consumption and colorectal cancer risk involving a total of 14,846 cases of colorectal, colon or rectal cancer in Italy. Their results suggested a moderate favorable effect of coffee consumption on colorectal cancer risk. The reduced risk was consistent across study design (hospital vs. population based), geographic area, and various confounding factors considered

Um et al. (2010) found that kahweol, a coffee-specific diterpene, found in *Coffea arabica* beans sensitizes human renal carcinoma Caki cells, but not normal human mesangial cells, to TRAIL (anticancer compound)-mediated apoptosis. They demonstrated down-regulation of Bcl-2 and c-FLIP contributed to the sensitizing effect of kahweol on TRAIL-mediated apoptosis in cancer cells.

Liver Cancer

Studies by Schilter et al. (1996) showed that A dose-dependent increase in general glutathione S-transferases was observed in male and female Sprague-Dawley rats following 28 or 90 days of treatment a mixture of coffee diterpenes cafestol and kahweol. Immunohistochemical examination of liver slices revealed a strong even distribution of placental glutathione S-transferase

(GST-P) expression throughout the acinus at the highest dose of C + K, while at lower doses the induction of GST-P occurred predominantly in periportal hepatocytes. There was no indication of the presence of preneoplastic foci. The findings indicated that the anticarcinogenic mechanism of cafestol and kahweol may involve a specific induction of GST-P and suggest a potential role for GST-P in detoxifying carcinogenic compounds. In rat primary hepatocytes, cafestol and kahweol reduced the expression of cytochrome P450 CYP 2C11 and CYP 3A2, the key enzymes responsible for aflatoxin B(1) (AFB1) activation to the genotoxic metabolite aflatoxin B1-8,9 epoxide (AFBO) (Cavin et al. 2001). In addition, these diterpenes induced significantly glutathione S-transferase Yc2, the most efficient rat glutathione S-transferase subunit involved in AFBO detoxification. In humans liver epithelial cell lines stably transfected to express AFB1 metabolising cytochrome P450s, cafestol and kahweol also produced a significant inhibition of AFB1-DNA adducts formation linked with an induction of the human glutathione S-transferase GST-mu. Together, these results suggested that cafestol and kahweol may have chemoprotective. Huber et al. (2002) found that kahweol and cafestol fed to male F344 rats in the chow for 10 days, increased a wide spectrum of increases in phase II detoxification enzymes namely overall glutathione transferase (GST) and GST classes α, mu, and pi but also enhanced UDP-glucuronosyl transferase (UDPGT) and GST-theta. All investigated kahweol and cafestol effects were strongest in liver and kidney, and some response was seen in lung and colon but none in the other organs. The data suggested that the effects occurred preferentially in the well perfused organs liver and kidney, which may thus not only contribute to local protection but also to anti-carcinogenesis in distant, less stimulated organs such as the colon.

Coffee diterpenes, namely cafestol palmitate and a mix of cafestol and kahweol (C + K) was found to prevent the genotoxic effects of the dietary carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) and N-nitrosodimethylamine in a human derived liver cell line (HepG2) (Majer et al. 2005). Marked inhibition of PhIP-induced micronucleus formation was observed with C + K and cafestol palmitate at dose levels > or = 0.9 and 1.7 μg/mL, respectively. This was accompanied by significant increase of glutathione-S-transferase but level of N-acetyltransferase 1 was not altered. Also in combination experiments with C + K and N-nitrosodimethylamine (NDMA), strong protective effects (50% reduction of genotoxicity) were seen at low dose levels (> or = 0.3 μg/mL). Cavin et al. (2008) observed, a coffee-dependent induction of enzymes involved in xenobiotic detoxification processes in rat liver and primary hepatocytes. Additionally, coffee was found to induce the mRNA and protein expression of enzymes involved in cellular antioxidant defenses. These inductions were correlated with the activation of the Nrf2 transcription factor. The induction of detoxifying enzymes glutathione S-transferases (GSTd) and aldo-keto reductase (AKR) was compatible with a protection against both genotoxicity and cytotoxicity of aflatoxin B1 (AFB1), wherein coffee reduced both AFB1-DNA and protein adducts. Coffee was also found to inhibit cytochrome CYP1A1/2, indicating that other mechanisms different from a stimulation of detoxification may also play a significant role in the chemoprotective effects of coffee.

Using data from a 10-year follow-up of the Japan Public Health Center-based Prospective Study, comprising 90,452 middle-aged and elderly Japanese subjects (43,109 men and 47,343 women), Inoue et al. (2005) found that subjects (men and women combined) who consumed coffee on a daily or almost daily basis had a lower hepatocellular carcinoma risk than those who almost never drank coffee; risk decreased with the amount of coffee consumed. The inverse association persisted when the participants were stratified by lifestyle factors. Similar associations were observed when the analysis was restricted to hepatitis C virus-positive patients, to hepatitis B virus-positive patients and to subjects with no past history of chronic liver disease. Based on the current available literature, three major components, i.e. coffee diterpenes cafestol and kahweol (C + K), caffeine and chlorogenic acid were

reported to contribute to the chemopreventive effect of coffee in liver cancer (Tao et al. 2008). These components induced phase II detoxifying and antioxidant enzymes as well as inhibit the expression or decrease the activity of phase I activating enzymes thus preventing carcinogenesis. Muriel and Arauz (2010) in their review stated that animal models and cell culture studies had shown that kahweol, diterpenes and cafestol (some coffee compounds) could function as blocking agents by modulating multiple enzymes involved in carcinogenic detoxification; these molecules also altered the xenotoxic metabolism by inducing the enzymes glutathione-S-transferase and inhibiting N-acetyltransferase. Drinking coffee had been reported to be associated with reduced risk of hepatic injury and cirrhosis, a major pathogenic step in the process of hepatocarcinogenesis.

In a hospital-based case-control study conducted in Italy in 1999–2002, of 185 incidents of hepatocellular carcinoma, including 412 controls subjects with acute, non-neoplastic diseases unrelated to diet, Montella et al. (2007) found that compared to people who drunk <14 cups/week of coffee, the risk of hepatocellular carcinoma decreased for increasing levels of consumption. No significant association emerged with consumption of decaffeinated coffee. Larsson and Wolk (2007) conducted a meta-analysis of four cohort and five case-control studies, involving 2,260 cases and 239,146 non-cases, and found that an increased consumption of coffee may reduce the risk of liver cancer. Overall, an increase in consumption of two cups of coffee per day was associated with a 43% reduced risk of liver cancer. Using data from 306 patients in the Brooke Army Medical Center Hepatology Clinic, Molloy et al. (2012) found that coffee caffeine consumption was associated with a significant reduction in risk of fibrosis among non-alcoholic steatohepatitis patients. Using data from the Singapore Chinese Health Study, Johnson et al. (2011) found that coffee consumption may reduce the risk of developing hepatocellular carcinoma among Chinese population in Singapore.

Breast Cancer

A hospital-based, case-control study of 1932 cases with primary, incident breast cancer and 1895 hospital controls with nonneoplastic conditions, Baker et al. (2006) found among premenopausal women, consumption of regular coffee was associated with linear declines in breast cancer risk; consumers of > or = 4 cups/day experienced a 40% risk reduction. No clear associations between intake of black tea or decaffeinated coffee and breast cancer risk were observed among premenopausal women. Among postmenopausal women, breast cancer risk was not associated with consumption of coffee, tea, or decaffeinated coffee.

Pancreatic Cancer

Luo et al. (2007) examined the association between the drinking of green tea or coffee and the risk of pancreatic cancer in a large population-based cohort study in Japan (JPHC study). They found that overall, the risk of pancreatic cancer was not associated with either green tea or coffee consumption in their population.

Prostate Cancer

In a prospective analysis of 47,911 men in the Health Professionals Follow-up Study, Wilson et al. (2011) observed a strong inverse association between coffee consumption and risk of lethal prostate cancer. Men who consumed the most coffee (six or more cups daily) had nearly a 20% lower risk of developing any form of prostate cancer. Even drinking one to three cups of coffee per day was associated with a 30% lower risk of lethal prostate cancer. The inverse association with coffee was even stronger for aggressive prostate cancer. Men who drank the most coffee had a 60% lower risk of developing lethal prostate cancer. The reduction in risk was seen whether the men drank decaffeinated or regular coffee, suggesting that the association appeared to be related to non-caffeine components of coffee. In a population-based study of 1,049 African-American (AA) and 1,083 Caucasian-American (CA), Arab et al. (2012) found that the biracial population with differing risks of prostate cancer did not demonstrate a protective relationship

between high coffee consumption and risk of high aggressive prostate cancer. No significant associations were found between prostate cancer aggressiveness and consumption of either caffeinated or decaffeinated coffee.

Gliomas

Caffeine, a well-known behavior stimulant, was found to activate the fatty acid release mechanism in glioblastoma cells (Jeng and Klemm 1984). Caffeine preferentially stimulated the mobilization of unsaturated fatty acids and may alter membrane structure and enhance eicosanoid biosynthesis. Caffeine was found to inhibit Ca(2+) increase by inositol 1,4,5-trisphospate receptor subtype 3 (IP(3)R3), the expression of which was increased in glioblastoma cells (Kang et al. 2010). Consequently, by inhibiting IP(3) R3-mediated Ca(2+) release, caffeine inhibited migration of glioblastoma cells in various in-vitro assays. Caffeine greatly increased mean survival in a mouse xenograft model of glioblastoma. The results suggested IP(3)R3 as a novel therapeutic target and identified caffeine as a possible adjunct therapy to slow invasive growth of glioblastoma by disturbing Ca(2+) signalling pathways. Using data from the large European cohort study, the European Prospective Investigation into Cancer and Nutrition (EPIC), Michaud et al. (2010) significant inverse association was observed for glioma risk among those consuming ≥100 mL coffee and tea per day compared with those consuming <100 mL/day. The association was slightly stronger in men than in women. Using data of 335 incident cases of gliomas (men = 133, women = 202) from three independent cohort studies, Holick et al. (2011) found consumption of five or more cups of coffee and tea a day compared to no consumption was associated with a decrease risk of glioma. Inverse, although weaker, associations were also observed between coffee, caffeinated coffee, tea, carbonated beverages and glioma risk. No association was observed between decaffeinated coffee and glioma risk. Among men, a statistically significant inverse association was observed between caffeine consumption and risk of glioma; the association was weaker among women.

Endometrial and Ovarian Cancers

Using data from 226,732 women, aged 50–71, enrolled in the NIH-AARP Diet and Health Study, Gunter et al. (2011) found that coffee consumption (>3 cups per day) was inversely related to incidence of endometrial cancer. The association of coffee with endometrial cancer risk was apparent for consumption of both regular and decaffeinated coffee. Endometrial cancer incidence appeared to be reduced among women that habitually drank coffee, an association that did not differ according to caffeine content. Using data from Nurses' Health Study (NHS) with 67,470 female participants aged 34 to 59, Je et al. (2012) found that women who consumed four or more cups of coffee had 25% lower risk of endometrial cancer than those who consumed less than one cup per day. A similar association was found with caffeinated coffee consumption. However, addition of substantial sugar and cream to coffee could offset any potential benefits. Tea consumption was not associated with endometrial cancer risk. Using data from using the Women's Health Initiative Observational Study Research Materials obtained from the National Heart, Lung, and Blood Institute Biological Specimen and Data Repository Coordinating Center, Giri et al. (2011) found that caffeinated coffee consumption may be associated with lower endometrial cancer risk among obese postmenopausal women, but the association with decaffeinated coffee remains unclear. Braem et al. (2012) using data from 330,849 women in the European Prospective Investigation into Cancer and Nutrition (EPIC) study, found no association between coffee and tea consumption with the risk of ovarian cancers. This lack of association between coffee and tea intake and EOC (endometrial ovarian cancer) risk was confirmed by the results of their meta-analysis.

Fibrosarcoma

Caffeic acid was found to exhibit potent anticancer effect in human fibrosarcoma HT-1080 cell line (Prasad et al. 2011). Caffeic acid enhanced

lipid peroxidative markers such as TBARS, CD, and LHP in HT-1080 cell line. Further, caffeic acid treatment altered the mitochondrial membrane potential in HT-1080 cells. Similarly, the authors observed increased oxidative DNA damage (% tail DNA, % tail length, tail moment, and olive tail moment), and apoptotic morphological changes in caffeic acid-treated groups.

Bladder Cancer

Epidemiological studies on coffee, alcohol and bladder cancer risk published up to 2007 were reviewed by Pelucchi et al. (2008). The absence of dose and duration-risk relations weighs against the presence of a causal association between coffee consumption and bladder cancer risk. Most studies of alcohol and bladder cancer found no association, with some studies finding a direct and other an inverse one. This again may be due to differential confounding effect of tobacco smoking-the major risk factor for bladder cancer-in various populations. Thus they asserted that epidemiological findings on the relation between alcohol drinking and bladder cancer remained unclear and inconclusive.

Antiphotoaging Activity

In as 12-week, double-blinded, randomized, controlled clinical trial on 40 Caucasian female participants, the phenolic antioxidant skin care system containing *Coffea arabica* and concentrated fruit and vegetable extracts produced statistically significant improvements in the appearance of photodamaged skin (Palmer and Kitchin 2010). The results demonstrated that the high total ORACsc scoring antioxidant skin care system was well tolerated, with no adverse events reported by the participants during the course of the study, and improved, significantly greater than a control regimen, the appearance of wrinkles, firmness, hyperpigmentation, blotchy redness, tactile roughness and clarity in photodamaged skin. Chiang et al. (2011) found that *Coffea arabica* leaves extract, its hydrolysates, chlorogenic acid and caffeic acid, could prevent photo-damage in skin through inhibiting metalloproteinase (MMP) expression and MAP kinase pathway. The leaf extract extract stimulated type I procollagen expression, inhibited MMP-1, -3, -9 expression and inhibited the phosphorylation of JNK, ERK and p38.

Anxiogenic Activity

El Yacoubi et al. (2000) used the elevated plus-maze and the light/dark box tests in mice, to evaluate the putative anxiogenic effects of caffeine. They found that adaptative mechanisms following mutation in A(2A) receptors or their long-term blockade after chronic ingestion of caffeine may be responsible for increase proneness to anxiety. However, the short-term anxiety-like effect of caffeine in mice might not be related solely to the blockade of adenosine A(2A) receptors, since it was not shared by A(2A) selective antagonists.

Prebiotic Activity

Static batch culture fermentation experiments showed that coffee silverskin induces preferential growth of bifidobacteria rather than *Clostridia* and *Bacteroides* spp (Borrelli et al. 2004). Coffee silverskin can be proposed as a new potential functional ingredient in consideration of the high content of soluble dietary fibre, the marked antioxidant activity, and the potential prebiotic activity.

Neuroprotective Activity

Oxidative stress is involved in many neurodegenerative processes leading to age-related cognitive decline. Coffee, a widely consumed beverage, is rich in many bioactive components, including polyphenols with antioxidant potential. In primary neuronal cell culture, pretreatment with green and roasted coffees (regular and decaffeinated) protected against subsequent H_2O_2-induced oxidative stress and improved neuronal cell survival (green coffees increased neuron survival by

78%, compared to 203% by roasted coffees) (Chu et al. 2009). Regular and decaffeinated samples of both roasted and green coffee all showed high hydrophilic antioxidant activity in-vitro, whereas lipophilic antioxidant activities were on average 30-fold higher in roasted than in green coffee samples. Roasted coffees also contained high levels of chlorogenic acid lactones. All coffee extracts inhibited ERK1/2 activation, indicating a potential attenuating effect in stress-induced neuronal cell death and only roasted coffee extracts inhibited JNK activation, evidencing a distinctive neuroprotective benefit. The study showed roasted coffees to be high in lipophilic antioxidants and chlorogenic acid lactones, and could protect neuronal cells against oxidative stress, by modulation of the ERK1/2 and JNK signaling pathways. Cho et al. (2009) found that instant decaffeinated coffee and coffee phenolic chlorogenic acid protected PC12 neuronal cell from hydrogen peroxide-induced apoptosis by blocking the accumulation of intracellular reactive oxygen species (ROS) and the activation of c-Jun N-terminal protein kinase (JNK) and p38 mitogen-activated protein kinase (MAPK).

Chlorogenic acid significantly improved the impairment of short-term or working memory induced by scopolamine, a muscarinic antagonist, in the Y-maze test, and significantly reversed cognitive impairments in mice as measured by the passive avoidance test (Kwon et al. 2010). Additionally, chlorogenic acid decreased escape latencies in the Morris water maze test. In a probe trial session, chlorogenic acid increased the latency time in the target quadrant in a dose-dependent manner. Ex-vivo, chlorogenic acid inhibited acetylcholinesterase activity and decreased malondialdehyde levels in the hippocampus and frontal cortex. In-vitro, chlorogenic acid was found to inhibit acetylcholinesterase activity (IC_{50} = 98.17 μg/mL) and free radical scavenging activity (IC_{50} = 3.09 μg/mL) in a dose-dependent manner. The results indicated that chlorogenic acid may exert anti-amnesic activity via inhibition of acetylcholinesterase and malondialdehyde in the hippocampus and frontal cortex. Chlorogenic acid derivatives from coffee were found to inhibit DNA methyltransferase 3a which had been associated with development, cancer and brain function (Rajavelu et al. 2011). The data suggested a biochemical mechanism for the beneficial health effect of black tea and coffee and a possible molecular mechanism for the improvement of brain performance and mental health by dietary polyphenols.

Coffee/Caffeine Consumption and Alzheimer's Disease

Retrospective, prospective epidemiologic and experimental studies suggested that enhanced coffee/caffeine intake during aging reduced risk of Alzheimer's disease.

In both behaviorally-tested and aged transgenic mice, long-term caffeine administration resulted in lower hippocampal β-amyloid (Abeta) levels (Arendash et al. 2006). Expression of both Presenilin 1 (PS1) and β-secretase (BACE) was reduced in caffeine-treated Tg mice, indicating decreased Abeta production as a likely mechanism of caffeine's cognitive protection. The ability of caffeine to reduce Abeta production was confirmed in SweAPP N2a neuronal cultures, wherein concentration-dependent decreases in both Abeta1-40 and Abeta1-42 were observed. Their data demonstrated that moderate daily intake of caffeine (the human equivalent of five cups of coffee per day) may delay or reduce the risk of Alzheimer's disease. In subsequent studies they found that even with pre-existing and substantial Abeta burden, aged APPsw mice with cognitive impairment exhibited memory restoration and reversal of Alzheimer's disease pathology with intake of caffeine, suggesting a treatment potential of caffeine in cases of established Alzheimer's disease (Arendash et al. 2009). Cao et al. (2009) reported that acute caffeine administration to both young adult and aged Alzheimer's disease transgenic mice rapidly reduces Abeta levels in both brain interstitial fluid and plasma without affecting Abeta elimination. Long-term oral caffeine treatment to aged Alzheimer's disease mice provided not only sustained reductions in plasma Abeta, but also decreases in both soluble and deposited Abeta in hippocampus and

cortex. Irrespective of caffeine treatment, plasma Abeta levels did not correlate with brain Abeta levels or with cognitive performance in individual aged Alzheimer's disease mice. Plasma caffeine and theophylline levels were tightly correlated, both being associated with reduced inflammatory cytokine levels in hippocampus. They concluded firstly, that both plasma and brain Abeta levels were reduced by acute or chronic caffeine administration in several Alzheimer's disease transgenic lines and ages, indicating a therapeutic value of caffeine against Alzheimer's disease; and secondly, that plasma Abeta levels were not an accurate index of brain Abeta levels/deposition or cognitive performance in aged Alzheimer's disease mice.

One mechanism implicated in the pathogenesis of Alzheimer's disease and Parkinson's disease is blood-brain barrier (BBB) dysfunction (Chen et al. 2010). Using a rabbit model of Alzheimer's disease, Chen et al. (2008) found that chronic ingestion of caffeine protected against high cholesterol diet-induced increases in disruptions (leakages) of the blood-brain barrier, and caffeine and drugs similar to caffeine might be useful in the treatment of Alzheimer's disease. Caffeine inhibited high cholesterol diet-induced increases in extravasation of immunoglobin G (IgG) and fibrinogen, increases in leakage of Evan's blue dye, decreases in levels of the tight junction proteins occludin and ZO-1, increases in astrocytes activation and microglia density where IgG extravasation was present.

Studies in Alzheimer's disease transgenic mice showed that long-term caffeine administration protected against cognitive impairment and reduced brain amyloid-β levels/deposition through suppression of both β- and γ-secretase (Cao et al. 2011). In both AβPPsw + PS1 transgenic mice and non-transgenic littermates, acute i.p. treatment with caffeinated coffee greatly and specifically increased plasma levels of granulocyte-colony stimulating factor (GCSF), interleukins IL-10, and IL-6. Neither caffeine solution alone (which provided high plasma caffeine levels) or decaffeinated coffee provided this effect, indicating that caffeine synergized with some as yet unidentified component of coffee to selectively elevate these three plasma cytokines. The increase in GCSF was particularly important because long-term treatment with coffee (but not decaffeinated coffee) enhanced working memory in a fashion that was associated only with increased plasma GCSF levels among all cytokines. They concluded that coffee may be the best source of caffeine to protect against Alzheimer's disease because of a component in coffee that synergized with caffeine to enhance plasma GCSF levels, resulting in multiple therapeutic actions against Alzheimer's disease. Earlier, they reported that long-term GCSF treatment decreased brain amyloid burden and reversed cognitive impairment in Alzheimer's disease mice through three possible mechanisms (e.g., recruitment of microglia from bone marrow, synaptogenesis, and neurogenesis) (Sanchez-Ramos et al. 2009), the same mechanisms could be complimentary to caffeine's established ability to suppress Aβ. They also reported that APP + PS1 double transgenic (Tg) mice administered melatonin were protected from cognitive impairment in a variety of tasks of working memory, spatial reference learning/memory, and basic mnemonic function Tg control mice remained impaired in all of these cognitive tasks/domains (Olcese et al. 2009). Immunoreactive Abeta deposition was significantly reduced in hippocampus (43%) and entorhinal cortex (37%) of melatonin-treated Tg mice. Inflammatory cytokines such as tumor necrosis factor (TNF)-α were decreased in hippocampus (but not plasma) of Tg + melatonin mice. Thus, melatonin's cognitive benefits could involve its anti-Abeta aggregation, anti-inflammatory, and/or antioxidant properties. Their findings provided support for long-term melatonin therapy as a primary or complementary strategy for abating the progression of Alzheimer disease. In acute studies involving Alzheimer's disease mice, one oral caffeine treatment quickly reduced both brain and plasma Abeta levels - similarly rapid alterations in plasma Abeta levels were seen in humans following acute caffeine administration (Arendash and Cao 2010). "Caffeinated" coffee administered to Alzheimer's disease mice also quickly decreased plasma Abeta levels, but not "decaffeinated"

coffee, suggesting that caffeine was critical to decreasing blood Abeta levels. Caffeine appeared to provide its disease-modifying effects through multiple mechanisms, including a direct reduction of Abeta production through suppression of both β- and γ-secretase levels.

Rifampicin and caffeine are widely used drugs with reported protective effect against Alzheimer's disease. Expression studies of low-density lipoprotein receptor related protein-1 (LRP1) and/or P-glycoprotein (P-gp) in brain endothelial cells and isolated mice brain microvessels following treatment with rifampicin or caffeine demonstrated both drugs as P-gp inducers, and only rifampicin as an LRP1 inducer (Qosa et al. 2012). Also, brain efflux index (BEI%) studies conducted on C57BL/6 mice treated with either drug to study alterations in Aβ clearance demonstrated the BEI% of Aβ in rifampicin (82.4%) and caffeine (80.4%) treated mice were significantly higher than those of control mice (62.4%). Further, the results demonstrated the upregulation of LRP1 and P-gp at the blood-brain barrier by rifampicin and caffeine enhanced brain Aβ clearance, and this effect could explain, at least in part, the protective effect of rifampicin and caffeine against Alzheimer's disease.

In a prospective analysis of risk factors for Alzheimer's disease of 6,434 eligible subjects aged 65 years or older in 1991, 4,615 were alive in 1996 and participated in the follow-up study in the Canadian Study of Health and Aging (Lindsay et al. 2002). Use of nonsteroidal anti inflammatory drugs, wine consumption, coffee consumption, and regular physical activity were associated with a reduced risk of Alzheimer's disease. In the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study in Finland, Eskelinen et al. (2009) and Eskelinen and Kivipelto (2010) found that coffee drinking of 3–5 cups per day at midlife was associated with a decreased risk of dementia/ Alzheimer's disease by about 65% at late-life. Tea drinking was relatively uncommon and was not associated with dementia/ Alzheimer's disease. They also found that most longitudinal epidemiological studies (three out of five) supported coffee's favourable effects against cognitive decline, dementia or Alzheimer's disease. Using data from 3,494 men in the Honolulu-Asia Aging Study, Gelber et al. (2011) found that coffee and caffeine intake in midlife were not associated with cognitive impairment, Alzheimer's disease, vascular dementia, or individual neuropathologic lesions (Alzheimer lesions, microvascular ischemic lesions, cortical Lewy bodies, hippocampal sclerosis, generalized atrophy), although higher caffeine intake was associated with a lower odds of having any of the lesion types at autopsy.

The case-control study of Cao et al. (2012) provided the first direct evidence that caffeine/ coffee intake was associated with a reduced risk of dementia or delayed onset, particularly for those with mild cognitive impairment (MCI). They found plasma caffeine levels at study onset were substantially lower (−51%) in mild cognitive impairment (MCI) subjects who later progressed to dementia (MCI → DEM) compared to levels in stable MCI subjects (MCI → MCI). none of the MCI → DEM subjects had initial blood caffeine levels that were above a critical level of 1200 ng/mL, while half of stable MCI → MCI subjects had blood caffeine levels higher than that critical level. Among the 11 cytokines measured in plasma, three of them (GCSF, IL-10, and IL-6) were decreased in MCI → DEM subjects, but not in stable MCI → MCI subjects with high plasma caffeine levels. Thus, coffee would appear to be the major or perhaps only source of caffeine for such stable MCI patients.

Coffee Consumption and Parkinson's Disease

Parkinson's disease is neurodegenerative disease characterized by set of cardinal motor signs (rigidity, akinesia, bradykinesia, rest tremor) that are consequence of a pronounced death of dopaminergic neurons in the pars compacta of the substantia nigra (Prediger 2010). Other nonmotor symptoms include disturbances to posture, fatigue, sleep abnormalities, and depression. Parkinson's disease (PD) is the second most common neurodegenerative disorder affecting approximately 1% of the population older than 60 years. Chen et al. (2001) reported that caffeine,

at doses comparable to those of typical human exposure, attenuated neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced loss of striatal dopamine and dopamine transporter binding sites. The effects of caffeine were mimicked by several A(2A) adenosine receptor antagonists (7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-[4,3-e]-1,2,4-triazolo[1,5-c] pyrimidine (SCH 58261), 3,7-dimethyl-1-propargylxanthine, and (E)-1,3-diethyl-8 (KW-6002)-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1 H-purine-2,6-dione) (KW-6002) and by genetic inactivation of the A(2A) receptor, but not by A(1) receptor blockade with 8-cyclopentyl-1,3-dipropylxanthine, suggesting that caffeine attenuated MPTP toxicity by A(2A) receptor blockade. The data established a potential neural basis for the inverse association of caffeine with the development of Parkinson's disease, and enhanced the potential of A(2A) antagonists as a novel treatment for this neurodegenerative disease. The adenosine A(2A) receptor had recently emerged as a leading non-dopaminergic therapeutic target for Parkinson's disease, largely due to the restricted distribution of the receptor in the striatum and the profound interaction between adenosine and dopamine receptors in brain (Kalda et al. 2006). They stated that two lines of research in particular had demonstrated the promise of the A(2A) receptor antagonists as novel anti-parkinsonian drugs. First, building on extensive preclinical animal studies, the A(2A) receptor antagonist KW6002 had demonstrated its potential to increase motor activity in Parkinson's disease patients of the advanced stage in a recent clinical phase IIB trial. Second, recently two prospective epidemiological studies of large cohorts had firmly established the inverse relationship between the consumption of caffeine (a non-specific adenosine antagonist) and the risk of developing Parkinson's disease. The potential neuroprotective effect of caffeine and A(2A) receptor antagonists in Parkinson's disease was further substantiated by the demonstration that pharmacological blockade (by caffeine or specific A(2A) antagonists) or genetic depletion of the A(2A) receptor attenuated dopaminergic neurotoxicity and neurodegeneration in animal models of Parkinson's disease (Chen et al. 2001). Moreover, A(2A) receptor antagonism-mediated neuroprotection goes beyond Parkinson's disease models and could be extended to a variety of other brain injuries induced by stroke, excitotoxicity and mitochondrial toxins (Kalda et al. 2006).

Neuroinflammation plays a role in the etiology of Alzheimer's and Parkinson's diseases and caffeine may provide protection through the modulation of inflammation. Studies by Brothers et al. (2010) showed that attenuated the number of activated microglia within the hippocampus of rats with of lipopolysaccharide -induced and age-related inflammation. Chronic neuroinflammation had been reported to be associated with an increase in extracellular levels of glutamate and drugs that limit the effects of glutamate at neuronal receptors had been shown to indirectly reduce the neuroinflammatory response of microglia cells. A1 and A2A receptors hadbeen shown to regulate the pre-synaptic release of glutamate, therefore, caffeine may also reduce neuroinflammation via its ability to regulate glutamate release. The prominent role of A2A receptors in preventing memory deterioration was probably related to the synaptic localization of this receptor in limbic areas and its ability to control glutamatergic transmission, especially N-methyl-D-aspartate (NMDA) receptor-dependent plasticity, and to control apoptosis, brain metabolism, and the burden of neuroinflammation (Cunha and Agostinho 2010).

Lyophilized coffee beverages prepared from either *Coffea arabica* or *Coffea canephora* var. *robusta* beans and constituents were found to stimulate dopamine release from pheochromocytoma cells (PC-12) (Walker et al. 2012). Both coffee lyophilizates showed effects in dilutions between 1:100 and 1:10,000. Caffeine, trigonelline, N-methylpyridinium, chlorogenic acid, catechol, pyrogallol and 5-hydroxytryptamides increased calcium signaling and dopamine release, although with different efficacies. In contrast, no effect was seen for the reconstituted biomimetic mixture. They concluded that each of the coffee constituents tested stimulated the dopamine release in PC-12 cells but since no effect

was found for their biomimetic mixture, other coffee constituents could be responsible for the dopamine release demonstrated for Arabica and robusta coffee brews. Xu et al. (2010) demonstrated that caffeine pre-treatment (30 mg/kg ip) of mice significantly attenuated 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced striatal dopamine depletion. Similarly, pre-treatment of theophylline (10 or 20 mg/kg), paraxanthine (10 or 30 mg/kg) and caffeine (10 mg/kg) significantly attenuated MPTP-induced dopamine depletion in mice. The data suggested that caffeine and its metabolites could protect against putative toxin-induced dopaminergic neuron injury in Parkinson's disease in humans.

In a pilot preliminary, open-label, 6-week dose-escalation study of 25 subjects, Altman et al. (2011) provided evidence that caffeine may improve some motor and non-motor aspects of Parkinson's disease. Maximum dose tolerability for caffeine in Parkinson's disease appears to be 100 to 200 mg BID (twice a day).

Sonsalla et al. (2012) showed that a chronic unilateral intra-cerebroventricular infusion of 1-methyl-4-phenylpyridinium in the rat brain for 28 days produced a progressive loss of dopamine and tyrosine hydroxylase in the ipsilateral striatum and a loss of dopamine cell bodies and microglial activation in the ipsilateral substantia nigra. Chronic caffeine consumption prevented the degeneration of dopamine cell bodies in the substantia nigra. Importantly, neuroprotection was still apparent when caffeine was introduced after the onset of the neurodegenerative process. The results further substantiated the clinical relevance for adenosine receptors as a disease-modifying drug target for Parkinson's disease. Studies by Singh et al. (2009) showed that caffeine partially protected 1-methyl 4-phenyl 1, 2, 3, 6-tetrahydropyridine (MPTP)-induced neurodegenerative changes and modulated MPTP-mediated alterations in the expression and catalytic activity of cytochrome CYP1A2, expression of adenosine A(2A) receptor and dopamine transporter. The results also demonstrated that caffeine altered the striatal CYP1A2, adenosine A(2A) receptor and dopamine transporter expressions in mice exposed to MPTP. In the Parkinson's Epidemiology and Genetic Associations Studies in the United States (PEGASUS) study, two adenosine receptor A2A (ADORA2A) polymorphisms were inversely associated with Parkinson's disease risk, but there was weak evidence of interaction with coffee consumption (Popat et al. 2011). In contrast, the coffee-Parkinson's disease association was strongest among slow metabolizers of caffeine who were homozygous carriers of the cytochrome P450 1A2 (CYP1A2) polymorphisms.

Studies by Nakaso et al. (2008) suggested that caffeine had a cytoprotective effect against developing Parkinson's disease due to the activation of the PI3K/Akt pathways in human dopaminergic neuroblastoma SH-SY5Y cells.

Trinh et al. (2010) reported coffee and tobacco, but not caffeine or nicotine, to be neuroprotective in *Drosophila* fly Parkinson's disease models. They reported that decaffeinated coffee and nicotine-free tobacco were as neuroprotective as their caffeine and nicotine-containing counterparts and that the neuroprotective effects of decaffeinated coffee and nicotine-free tobacco were also evident in *Drosophila* models of Alzheimer's disease and polyglutamine disease. They asserted that the neuroprotective effects of decaffeinated coffee and nicotine-free tobacco required the cytoprotective transcription factor Nrf2 and that a known Nrf2 activator in coffee, cafestol, that was able to confer neuroprotection in their fly models of Parkinson's disease. Their findings indicated coffee and tobacco to contain Nrf2-activating compounds that may account for the reduced risk of Parkinson's disease among coffee and tobacco users and represented attractive candidates for therapeutic intervention in Parkinson's disease and perhaps other neurodegenerative diseases.

Using data from 30 years of follow-up of 8,004 Japanese-American men (aged 45–68 years) enrolled in the prospective longitudinal Honolulu Heart Program between 1965 and 1968, Ross et al. (2000) found higher coffee and caffeine intake to be associated with a significantly lower incidence of Parkinson disease. This effect appeared to be independent of smoking. Ascherio et al. (2001) examined the relationship of coffee and caffeine consumption to the risk of this disease among participants in two ongoing cohorts,

the Health Professionals' Follow-Up Study (HPFS) and the Nurses' Health Study (NHS). The study population comprised 47,351 men and 88,565 women who were free of Parkinson's disease, stroke, or cancer at baseline. In men they found an inverse association of Parkinson's disease with consumption of coffee, caffeine from non-coffee sources and tea but not decaffeinated coffee Among women, the relationship between caffeine or coffee intake and risk of Parkinson's disease was U-shaped, with the lowest risk observed at moderate intakes (1–3 cups of coffee/day, or the third quintile of caffeine consumption). The results supported a possible protective effect of moderate doses of caffeine on risk of Parkinson' disease. Tan et al. (2003) conducted a case control study to examine the relationship between coffee and tea drinking, cigarette smoking, and other environmental factors and risk of Parkinson's disease among ethnic Chinese in our population. Of 300 PD and 500 population controls screened, 200 case control pairs matched for age, gender, and race were finally included in the analysis. They found a dose-dependent protective effect of Parkinson's disease in coffee and tea drinkers and smokers in an ethnic Chinese population. A history of exposure to heavy metals increased the risk of Parkinson's disease, supporting the multifactorial etiologies of the disease. In another case-control study, out of 1000 participants who were initially screened, 886 consisting of 418 Parkinson's disease and 468 race, sex and age matched controls were included (Tan et al. 2007). The association between caffeine intake and risk of Parkinson's disease was similarly observed in both fast and slow caffeine metabolizers, supporting experimental evidence in animal models that both caffeine and its major metabolite, paraxanthine, were neuroprotective.

Costa et al. (2010) conducted a systematic review and meta-analysis of published epidemiological studies to better ascertain the effect of caffeine exposure on the incidence of Parkinson's disease. Twenty-six studies were included: 7 cohort, 2 nested case-control, 16 case-control, and 1 cross-sectional study. Overall their study confirmed an inverse association between caffeine intake and the risk of Parkinson's disease, which could hardly be elucidated by bias or uncontrolled confounding. Liu et al. (2012) conducted a meta-analysis of prospective studies in both men and women among 304,980 participants in the National Institutes of Health-AARP Diet and Health Study and confirmed that caffeine intake was inversely associated with Parkinson disease risk in both men and women. A joint analysis with smoking suggested that smoking and caffeine may act independently in relation to Parkinson disease risk.

Facheris et al. (2008) utilised data from 1,208 subjects (446 case-unaffected sibling pairs and 158 case-unrelated control pairs) recruited from an ongoing study of the molecular epidemiology of Parkinson's disease in the Upper Midwest (USA). They did not observe significant associations of coffee drinking or of the genetic variants with Parkinson's disease susceptibility, either independently or jointly, in the sample overall and in most strata. Their study neither supported the hypothesis that coffee protected against PD nor provided evidence for a pharmacogenetic effect.

Coffee Consumption and Cardiovascular Diseases

Published literature provided little evidence that coffee and/or caffeine in typical dosages increased the risk of infarction, sudden death or arrhythmia (Chou and Benowitz 1994). Initial investigations, showing an association between coffee and coronary heart disease, suffered from confounding variables and had been difficult to replicate. Cornelius et al. (2006) in their study of 2,014 cases with acute nonfatal myocardial infarction and 2,014 population-based controls, found intake of coffee was associated with an increased risk of nonfatal myocardial infarction only among individuals (having CYP1A2 *1 F genotype) with slow caffeine metabolism, suggesting that caffeine plays a role in this association. Cornelis and El-Sohemy (2007) in their review stated that diterpenes present in unfiltered coffee and caffeine each appeared to increase risk of coronary heart disease by raising cholesterol levels. Several

studies had reported a protective effect of moderate coffee consumption, which suggested that coffee contained other antioxidant compounds that may be beneficial. A lower risk of coronary heart disease among moderate coffee drinkers might be due to antioxidants found in coffee.

In a randomized, cross-over trial of 11 healthy, normolipidemic volunteers, administration of both Arabica and Robusta oil to the volunteers elevated serum cholesterol and triglycerides levels (Mensink et al. 1995). None of the effects on serum lipids or lipoprotein cholesterol levels was significantly different between Arabica and Robusta oil. It was postulated that both cafestol and kahweol were involved in raising cholesterol. The mode of action of coffee diterpenes did not involve induction of hypothyroidism. Ratnayake et al. (1995) found that administration of coffee total lipids, coffee non-saponifiable matter and coffee diterpene alcohols extracted from *Coffea arabica* beans, tended to increase serum total cholesterol and high density lipoprotein-cholesterol in adult male Syrian hamsters. In another study they found no significant differences in serum lipid levels between control and coffee lipid-treated groups across time. In either study, total serum cholesterol levels of the three coffee lipid groups were not significantly different from each other. The results supported the concept that coffee lipids may be hypercholesterolaemic and indicated that diterpenes could be the lipid component responsible for such an effect. However, it appeared that this hypercholesterolaemic effect was apparent only when the background diet was low in saturated fat and cholesterol. A high saturated fat/high cholesterol diet may mask the hypercholesterolaemic effect of coffee lipids.

The presence of high amounts of palmitic acid at Sn-1,3 position *in C. arabica* coffee oil may be partly responsible for its hypercholesterolemic effects (Al Kanhal 1997). The diterpenes cafestol and kahweol had been implicated as the components in boiled coffee responsible for its hypercholesterolaemic effects. Scandinavian-style boiled coffee and Turkish-style coffee contained the highest amounts, equivalent to 7.2 and 5.3 mg cafestol per cup and 7.2 and 5.4 mg kahweol per cup, respectively (Gross et al. 1997). In contrast, instant and drip-filtered coffee brews contained negligible amounts of these diterpenes, and espresso coffee contained intermediate amounts, about 1 mg cafestol and 1 mg kahweol per cup. These findings provide an explanation for the hypercholesterolaemic effect previously observed for boiled coffee and Turkish-style coffee, and the lack of effect of instant or drip-filtered coffee brews.

Using a randomized placebo controlled, double-blind study design, ten adults performed two graded maximal cycle ergometry tests with and without caffeine (5 mg/kg1). Karapetian et al. (2012) found that at rest caffeine increased blood lactate, oxygen consumption, carbon dioxide production, heart rate and minute ventilation. During progressive exercise, minute ventilation volumes were higher in caffeine trials but no other parameters were significantly different compared to placebo tests. These data demonstrated the robustness of the lactate, ventilatory and heart rate variability thresholds when challenged by a physiological dose of caffeine.

In a double-blind crossover study of seven healthy subjects, Mahmud and Feely (2001) found that caffeine significantly increased arterial stiffness and aortic pressure wavefrom. Compared with baseline, arterial stiffness measured by carotid femoral pulse wave velocity increased progressively from 7.2 to 8.0 m/s at 90 min after caffeine intake, an effect that may be independent of changes in blood pressure. In addition, arterial wave reflection, measured by applanation tonometry from the aortic pressure waveform, also increased from −5.7 to 5.28%. No such changes were seen with decaffeinated coffee intake. Caffeinated coffee had a more pronounced effect on aortic systolic and diastolic blood pressures than on brachial artery. Trovato et al. (2010) conducted a study with 221 consecutive patients, without diabetes, cancer, liver, renal, and heart disease to assess coffee consumption with renal resistive index (RRI), a hallmark of arterial stiffness. They found coffee consumption was inversely associated with renal resistive index. Habitual coffee users had risk protection against higher RRI; lower serum albumin, insulin

resistance, and renal insufficiency were associated with greater RRI.

Wu et al. (2009) conducted a meta-analysis of 21 prospective cohort studies involving 15,599 cases from 407,806 participants and found that coffee consumption did not increase the long-term risk of coronary heart disease. Habitual moderate coffee drinking was associated with a lower risk of coronary heart disease in women. A prospective, observational study of 34,551 participants of the Swedish Mammography Cohort who were 48–83 years old and did not have heart failure, diabetes, or myocardial infarction at baseline was studied for the association between coffee consumption and heart failure hospitalization or mortality in women (Levitan et al. 2011). They found that women who consumed ≥5 cups of coffee per day did not have higher rates of heart failure events than those who consumed <5 cups per day. Compared with women who consumed ≤1 cup of coffee per day, hazard ratios were 1.01, 0.82, 0.94, and 0.87 for women who consumed 2, 3, 4, and ≥5 cups per day, respectively. They concluded that in the population of middle-aged and older women, there was no association between coffee consumption and incidence of heart failure events.

Using data from 42,659 participants in the large European Prospective Investigation into Cancer and Nutrition (EPIC)-Germany study, Floegel et al. (2012) found that coffee consumption (≥4 cups/day compared with <1 cup/day; 1 cup was defined as 150 mL) was not associated with the overall risk of chronic disease. A lower risk of Type 2 diabetes was associated with caffeinated and decaffeinated coffee consumption (≥4 cups/day compared with <1 cup/day), but cardiovascular disease and cancer risk were not.

Coffee Consumption and Diabetes

Prospective epidemiological and experimental studies had reported that regular coffee consumption could significantly lower the risk of type 2 diabetes. Pimentel et al. (2009) in their review stated that 14 out of 18 cohort studies revealed a substantially lower risk of type 2 diabetes mellitus with frequent coffee intake. Moderate coffee intake (≥4 cups of coffee/day of 150 mL or ≥400 mg of caffeine/day) had generally been associated with a decrease in the risk of type 2 diabetes mellitus. Besides, results of most studies suggested a dose-response relation, with greater reductions in type 2 diabetes mellitus risk with higher levels of coffee consumption. They advocated for more population-based surveys to clarify the long-term effects of decaffeinated and caffeinated coffee intake on the risk of type 2 diabetes mellitus.

Recent evidence suggested that coffee increased production of the incretin hormone glucagon-like peptide-1 (GLP-1), possibly owing to an inhibitory effect of chlorogenic acid (CGA -the chief polyphenol in coffee) on glucose absorption (Johnston et al. 2003; McCarty 2005; Rafferty et al. 2011; Tunnicliffe et al. 2011); GLP-1 acts on β-cells, via cAMP-dependent mechanisms, to promote the synthesis and activity of the transcription factor IDX-1, crucial for maintaining the responsiveness of β-cells to an increase in plasma glucose (McCarty 2005). This transcription factor can be suppressed by glucolipotoxicity in β-cell dysfunction in diabetics. The increased production of GLP-1 associated with frequent coffee consumption could thus be expected to counteract the adverse impact of chronic free fatty acid overexposure on β-cell function in overweight insulin resistant subjects. Further, CGA's putative impact on glucose absorption may reflect the ability of this compound to inhibit glucose-6-phosphate translocase 1, now known to play a role in intestinal glucose transport. Delayed glucose absorption may itself protect β-cells by limiting postprandial hyperglycemia. McCarty (2005) stated that diets high in "lente carbohydrate", or administration of nutraceuticals/pharmaceuticals which slow the absorption of dietary carbohydrate, should help preserve efficient β-cell function by boosting GLP-1 production, as well as by blunting the glucotoxic impact of postprandial hyperglycemia on β-cell function.

In a 3-way, randomized, crossover study of nine healthy fasted volunteers Johnston et al. (2003) found that glucose and insulin concentrations

tended to be higher in the first 30 min after 400 mL caffeinated coffee consumption than after consumption of decaffeinated coffee (equivalent to 2.5 mmol chlorogenic acid/L) or the control. Glucose-dependent insulinotropic polypeptide secretion decreased throughout the experimental period, and glucagon-like peptide 1 secretion increased 0–120 min postprandially after decaffeinated coffee consumption compared with the control. Glucose and insulin profiles were consistent with the known metabolic effects of caffeine. However, the gastrointestinal hormone profiles were consistent with delayed intestinal glucose absorption. The results confirmed the potent biological action of caffeine and suggested that chlorogenic acid might have an antagonistic effect on glucose transport and may attenuate intestinal glucose absorption rates and shift the site of glucose absorption to more distal parts of the intestine. Battram et al. (2006) in 4 double-blinded randomized trials of 11 healthy men found that the effects of acute alkaloid caffeine ingestion chronic coffee ingestion were not identical. They found acute alkaloid caffeine ingestion impaired glucose tolerance while chronic coffee ingestion protected against type 2 diabetes. Also decaffeinated coffee ingestion resulted in a 50% lower glucose response than placebo.

Tunnicliffe et al. (2011) reported that chlorogenic acids (CGA) found in brewed coffee inhibited intestinal glucose uptake in-vitro and in-vivo. In a randomized crossover design separated by a 3-day washout period, plasma glucose-dependent insulinotropic peptide (GIP) response was blunted in rats fed CGA, with a lower peak concentration and AUC up to 180 min postprandially. There were no changes in incretin glucagon-like peptide-1 (GLP-1) secretion in either the in-vivo or in-vitro study. They concluded that CGA treatment resulted in beneficial effects on blood glucose response, with alterations seen in GIP concentrations idcianting it to be a viable prevention tool for type 2 diabetes. Rafferty et al. (2011) reported that olive leaf extract, glutamine, β-casein and chlorogenic acid significantly increased acute in-vitro glucagon-like peptide-1 (GLP-1) secretion (66–386%) in STC-1 cells. GLP-1 is an intestinal hormone with well-established glucose-lowering activity. Olthof et al. (2001) conducted a randomized cross-over trial of the effects of 12 g decaffeinated coffee, 1 g chlorogenic acid, 500 mg trigonelline, and placebo on total and intact glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) concentrations during an oral glucose tolerance test (OGTT) in 15 overweight men. They found no treatment significantly affected the overall GLP-1 or GIP secretion pattern following an OGTT relative to placebo. Decaffeinated coffee slightly increased total GLP-1 concentration 30 min after ingestion (before the OGTT) relative to placebo, but this change did not correspond with changes in glucose or insulin secretion. Their findings did not support the hypothesis that coffee acutely improved glucose tolerance through effects on the secretion of incretin hormones.

Svetol, a standardized decaffeinated green coffee extract, significantly inhibited Glc-6-P hydrolysis in intact human liver microsomes in a competitive manner, and it was determined that chlorogenic acids (caffeoylquinic acids and dicaffeoylquinic acids) were the chief compounds mediating this activity (Henry-Vitrac et al. 2010). This inhibition by Svetol contributed to its antidiabetic, glucose-lowering effects by reducing hepatic glucose production. Results of studies by Cheng et al. (2011) suggested that caffeine, caffeic acid and chlorogenic acid (CGA), major coffee components, as well as dihydrocaffeic acid (a major metabolite of CGA and CA), exhibited varied inhibitory effects on the formation of toxic human islet amyloid polypeptide (hIAPP) amyloids. Caffeic acid showed the highest potency in delaying the conformational transition of the hIAPP molecule with the most prolonged lag time, whereas caffeine exhibited the lowest potency. Their studies suggested that the beneficial effects of coffee consumption on type 2 diabetes mellitus may be partly due to the ability of these major coffee components and metabolites to inhibit the toxic aggregation of hIAPP.

Results of separate studies suggested that coffee ingestion exerted a suppressive effect on hyperglycemia by improving insulin sensitivity, partly

due to reducing inflammatory cytokines (MCP-1, IL-6, and TNFα) expression and improving fatty liver in spontaneously diabetic KK-A(y) mice (Yamauchi et al. 2010). Caffeine ingestion as drinking water also caused an amelioration of hyperglycemia and an improvement of fatty liver suggesting that caffeine may be one of the effective antidiabetic compounds in coffee. Studies in C57BL/6 J mice showed coffee and caffeine exerted an ameliorative effect on high-fat-diet-induced impaired glucose tolerance by improving insulin sensitivity, glucose tolerance and and hyperinsulinemia (Matsuda et al. 2012). The adipose tissue mRNA levels of inflammatory adipocytokines (MCP-1 and IL-6) and the liver mRNA levels of genes related to fatty acid synthesis were lower in the coffee and caffeine groups than those in the control group.

van Dam et al. (2004) conducted an oral glucose tolerance test (OGTT) of Dutch men and women aged 50–74 years in the population-based Hoorn Study and found that habitual coffee consumption could reduce the risk of impaired glucose tolerance (IGT), and affected post-load rather than fasting glucose metabolism. At baseline, a five cup per day higher coffee consumption was significantly associated with lower fasting insulin concentrations and 2-h glucose concentrations but was not associated with lower fasting glucose concentrations. In the prospective analyses, the odds ratio (OR) for IGT was 0.59 for 3–4 cups per day, 0.46 for 5–6 cups per day, and 0.37 for 7 or more cups per day, as compared with the corresponding values for the consumption of two or fewer cups of coffee per day. Higher coffee consumption also tended to be associated with a lower incidence of type 2 diabetes but was not associated with the incidence of impaired fasting glucose. Caffeine could acutely lower insulin sensitivity (van Dam 2006). Intake of the coffee components chlorogenic acid, quinides, lignans, and trigonelline had been shown to improve glucose metabolism in animal studies. Habitual coffee consumption had been studied in relation to the risk of diabetes mellitus type 2 in 12 cohort studies in Europe, the USA, and Japan. Generally, high coffee consumption was associated with a substantially lower risk of type-2 diabetes. The findings were similar for caffeinated and decaffeinated coffee, suggesting that the non-caffeine components of coffee may be responsible. In a randomized crossover trial in 15 overweight men, chlorogenic acid and trigonelline, major coffee components, significantly reduced glucose and insulin concentrations 15 min following oral glucose tolerance test (OGTT) compared with placebo (van Dijk et al. 2009). None of the treatments affected insulin or glucose area under the curve values during the OGTT compared with placebo.

In a prospective cohort study, Salazar-Martinez et al. (2004) followed 41,934 men from 1986 to 1998 and 84,276 women who did not have diabetes, cancer, or cardiovascular disease at baseline, from 1980 to 1998 in the Nurses' Health Study and Health Professionals' Follow-up Study. They found long-term coffee consumption to be associated with a statistically significantly lower risk for type 2 diabetes in both men and women. Wu et al. (2005) in a cross-sectional analysis study among 2,112 healthy women from the Nurses' Health Study I in 1989–1990, found that coffee consumption tend to reduce insulin secretion in women. Intakes of caffeinated and decaffeinated coffee and caffeine were inversely associated with C-peptide concentration in age-adjusted, body mass index-adjusted, and multivariable-adjusted analyses. In multivariable analysis, concentrations of C-peptide were 16% less in women who drank >4 cups/day of caffeinated or decaffeinated coffee compared with non-drinkers. The inverse association between caffeinated coffee and C-peptide was considerably stronger in obese (27% reduction) and overweight women (20% reduction) than in normal weight women (11% reduction). This reduction may be related to other components in coffee rather than caffeine. In a separate cross-sectional analysis of a subsample of subjects aged 45–64 years in 1987 and in 1992 from the population-based FINRISK study (12,287 individuals), coffee showed positive effects on several glycemia markers. Coffee consumption was significantly and inversely associated with fasting glucose, 2-h plasma glucose, and fasting insulin in both men and women (Bidel et al. 2006). Coffee consumption was also significantly and inversely associated

with impaired fasting glucose, impaired glucose regulation, and hyperinsulinemia among both men and women and with isolated impaired glucose tolerance among women. In an 11-year prospective study of the Iowa Women's Health Study (1986–1997) involving 28,812 postmenopausal women free of diabetes and cardiovascular diseases, Pereira et al. (2006) found coffee consumption especially decaffeinated, was inversely associated with risk of type 2 diabetes mellitus in this cohort of postmenopausal women.

Studies by Tsuda et al. (2012) suggested that caffeic acid but not chlorogenic acid (CGA) acutely stimulated 5′-adenosine monophosphate-activated protein kinase (AMPK) activity and increased rate of insulin-independent3-*O*-methyl-d-glucose transport activity in rat skeletal (epitrochlearis) muscles with a reduction of the intracellular energy status. Conversely, Ong et al. (2012) demonstrated that CGA stimulated glucose transport in skeletal muscle via the activation of AMPK suggesting that CGA may contribute to the beneficial effects of coffee on Type 2 diabetes mellitus. They observed in db/db mice, a significant decrease in fasting blood sugar 10 min after the intraperitoneal administration of 250 mg/kg CGA and the effect persisted for another 30 min after the glucose challenge. Besides, CGA stimulated and enhanced both basal and insulin-mediated 2-deoxyglucose transports in soleus muscle. In L6 myotubes, CGA caused a dose- and time-dependent increase in glucose transport. CGA was found to phosphorylate AMPK and acetyl-CoA carboxylase (ACC), consistent with the result of increased AMPK activities. They also observed activation of Akt by CGA. These parallel activations in turn increased translocation of glucose transporter type 4 (GLUT 4) to plasma membrane.

Some studies found that coffee consumption did not contribute to risk reduction of type 2 diabetes. In a study of 814 caffeine-drug users and 623 non-users identified from the German National Health Surveys, Du et al. (2007) found acute intake of caffeine-drugs may impair glucose metabolism, chronic intake of caffeine exclusively from diet had little effects on glucose metabolism and therefore may not contribute to the risk reduction of type 2 diabetes that was found in recent coffee consumption studies. No associations of caffeine concentrations with serum glucose levels were found in any groups of caffeine-drug non-users in their study. In a double-blind, randomized, placebo-controlled crossover study of 16 healthy adult coffee drinkers aged 18–22 years, Mackenzie et al. (2007) found that insulin levels were significantly higher after caffeine intake than after placebo. The homeostasis model assessment index of insulin sensitivity was reduced by 35% by caffeine. The effect persists for at least a week and was evident up to 12 h after administration. Similarly, in four randomized trials of ten healthy men, the ingestion of caffeinated coffee with either a high or low glycemic index (GI) meal significantly impaired acute blood glucose management and insulin sensitivity compared with ingestion of decaffeinated coffee (Moisey et al. 2008). In a subsequent randomised, crossover design of ten healthy males, they found that co-ingestion of caffeinated coffee with one meal resulted in insulin insensitivity during the postprandial phase of a second meal in the absence of further caffeinated coffee ingestion (Moisey et al. 2010).

In a randomized, cross-over, placebo-controlled trial in 11 young men, glucose and insulin were higher for decaffeinated coffee than for placebo within the first hour of the oral glucose tolerance test (OGTT) (Greenberg et al. 2010). Decaffeinated coffee yielded higher insulin than placebo and lower glucose and a higher insulin sensitivity index than caffeine during the whole OGTT. The results indicated that some decaffeinated coffee may acutely impair glucose metabolism but less than caffeine. In five trials of a randomized, cross-over design of ten healthy young men, oral consumption of lipids and caffeinated coffee was found to independently and additively decrease glucose tolerance (Beaudoin et al. 2011). The increase of incretin hormones glucagon-like peptide-1 active (GLP-1a) and glucose-dependent insulinotropic polypeptide (GIP) elicited, could partly explained the impaired glucose homeostasis. In a within-subject, double-blind, placebo-controlled study of 21 adult habitual coffee drinkers (11 women and 9 men) with type 2 diabetes, Lane et al. (2007) found that repeated administration of caffeine in decaffeinated coffee

on a daily basis increased postprandial glucose and insulin responses compared to administration of placebo.

Coffee Consumption and Reproductive Hormone Levels

From a Danish pregnancy cohort established in 1984–1987, 347 sons out of 5,109 were selected for a follow-up study conducted 2005–2006 to study the association between prenatal coffee and current caffeine exposure and semen quality and levels of reproductive hormones (Ramlau-Hansen et al. 2008). They found a tendency toward decreasing crude median semen volume and adjusted mean testosterone and inhibin B concentrations with increasing maternal coffee consumption during pregnancy. Sons of mothers drinking 4–7 cups/day had lower testosterone levels than sons of mothers drinking 0–3 cups/day. Men with a high caffeine intake had ~ 14% higher concentration of testosterone than those with a low caffeine intake. Their findings revealed a small to moderate effect of prenatal coffee exposure on semen volume and levels of reproductive hormones and that adult caffeine intake did not show any clear associations with semen quality, but high caffeine intake was associated with a higher testosterone concentration.

Coffee Consumption and Miscarriage

Pollack et al. (2010) analyzed data on daily caffeine consumption and pregnancy through 12 menstrual cycles at risk for pregnancy and found that caffeine consumption did not increase the risk or hazard of miscarriage, even after adjusting for relevant covariates.

Coffee Consumption and Children Behaviour/Health

Coffee is widely consumed among children in Guatemala and is even one of the first liquids given to infants, beginning as early as 2 months of age (Dewey et al. 1997a, b). In their randomised intervention study on the effects of discontinuing coffee intake on growth, morbidity and iron-status, a total of 139 toddlers (12–24 months) completed the study: 45 coffee, non-anemic; 56 sugar substitute, non-anemic; 19 coffee, anemic; and 19 sugar-substitute, anemic coffee. Children in the control group continued to receive coffee, while children in the intervention group were instead given a substitute consisting of sugar and colouring. They found that the discontinuation had no effect upon weight or length gain. However, a modest increase in growth was associated with the discontinuation of coffee consumption by toddlers with initial intakes of more than 100 mL/day. There was no significant effect of discontinuing coffee consumption on changes in hemoglobin, hematocrit, ratio of zinc protoporphyrin to heme or plasma iron, zinc or copper in either nonanemic or anemic children, or plasma ferritin in children who did not take iron supplements. In children who took iron supplements, change in plasma ferritin was significantly greater in the sugar substitute group than in the coffee group (106% compared with 1%). This implied that coffee interfered with the utilization of supplemental iron. They stated that the amount and strength of coffee consumed by Guatemalan toddlers were too low to significantly affect the other indices of iron status. In another subsequent paper, they reported that the effects of postnatal coffee ingestion in toddlers were seen for sleep duration (shorter), but not for cognitive development (Engle et al. 1999). Prenatal coffee ingestion was negatively associated with Behavior Rating Scales. Muñoz et al. (1988) found coffee consumption to be a factor in iron deficiency anemia among pregnant women and their infants in Costa Rica. Maternal hemoglobin (Hb) and hematocrit (Hct) at 8 months gestation, cord blood Hb and Hct, infant birth weight and Hb and Hct at 1 month of age, and breast-milk Fe concentration were significantly lower in the coffee group than in the non-coffee group. The association of coffee with infant Hb and Hct was independent of maternal Fe status and birth weight.

A 2-week double-blind, cross-over study of hyperactive children showed that caffeine did not significantly improved reaction times and psychological test scores (Firestone et al. 1978) However, impulsivity and general behaviour as measured by parent and teacher rating scales showed some marked improvements due to caffeine. Hugh and Hale (1998) in studying computerised searches found that high doses (>3 mg/kg) of caffeine in children who consumed little caffeine produced negative subjective effects such as nervousness, jitteriness, stomach aches, and nausea. Caffeine appeared to slightly improve vigilance performance and decrease reaction time in healthy children who habitually consumed caffeine but did not consistently improve performance in children with attention deficit-hyperactivity disorder. Castellanos, and Rapoport (2002) in their review of Medline literature, found that overall, the effects of caffeine in children appeared to be modest and typically innocuous.

Pollak and Bright (2003) found in their study of 191 students (US seventh-, eighth-, and ninth-graders) regardless of whether caffeine use disturbed sleep or was consumed to counteract the daytime effect of interrupted sleep, caffeinated beverages had detectable pharmacologic effects. Higher caffeine intake in general was associated with shorter nocturnal sleep duration, increased wake time after sleep onset, and increased daytime sleep. In a double-blind, placebo-controlled study of 26 children aged between 9 and 11 years comprising of habitual caffeine consumers (mean daily caffeine intake = 109 mg) and non/low-consumers (12 mg), caffeine administration improved habitual consumers' accuracy on the cognitive test (to near the level displayed by the non/low-consumers at baseline) (Heatherley et al. 2006). However, caffeine had no significant effect on the non/low-consumers' performance. In habitual consumers, caffeine prevented an increase in headache that occurred after placebo, and it increased alertness relative to placebo. Again, however, caffeine did not significantly affect levels of headache or alertness in the non/low-consumers.

Coffee Consumption and Urinary Incontinence

Using data from a prospective cohort study in 65,176 women 37–79 years old without incontinence in the Nurses' Health Study and the Nurses' Health Study II, Jura et al. (2011) found that high but not lower caffeine intake in women was associated with a modest increase in the incidence of frequent urinary incontinence. In another study, Townsend et al. (2012) using data from a prospective cohort study in 21,564 women with moderate urinary incontinence enrolled in the Nurses' Health Study and Nurses' Health Study II found that long-term caffeine intake over 1 year was not associated with risk of urinary incontinence progression over 2 years among women with moderate incontinence, although acute effects of caffeine could not be examined.

Coffee Consumption and Gastric Irritation

Treatment of human gastric cancer cells (HGT-1) with mild bean coffee did not result in a proton secretory activity (PSA) different from regular coffee treatment, whereas cells treated with stomach friendly coffee or stomach friendly decaffeinated coffee showed a significantly lower PSA than those treated with regular coffee (Weiss et al. 2010). Quantitative and principle component analysis of putative stomach irritating compounds revealed significantly reduced contents of βN-alkanoyl-5-hydroxytryptamides, caffeine, N-methylpyridinium, and catechol in stomach friendly decaffeinated coffee compared to regular coffee. However, none of these compounds appeared to act as the sole key bioactive reducing the PSA of stomach friendly decaffeinated coffee, since their contents in mild bean coffee and stomach friendly coffee samples were not different from those in regular coffee samples, although the PSA of these beverages was significantly lower than that of reconstituted freeze-dried regular coffee beverage. In another study, they fractionated regular coffee beverage by using solvents of different polarity: water, ethylacetate,

dichloromethane, and pentane (Rubach et al. 2010). Functional assays on the proton secretory activity (PSA) of these solvent fractions revealed the least pronounced effect for the water fraction, which demonstrated the highest distribution of chlorogenic acid (95%), βN-alkanoyl-5-hydroxytryptamides (55%), and N-methylpyridinium (N-MP, >99%) among all fractions. Human gastric cells (HGT-1) treated with regular coffee fortified with N-MP at a concentration of about 20 mg/mL N-MP showed a significantly decreased PSA as compared to cells which were exposed to coffee beverages containing higher (32 – 34 mg/l) or lower (5 mg/l) N-MP concentrations. The antisecretory activity of N-MP in coffee beverages was further confirmed by results from cellular pathway analyses of transcription (ATF-1 and Akt1) and signaling (cAMP and EGFr) factors and kinases (ERK1/2), and experiments on the gene expression of pro (histamine-HRH2 and acetylcholine-CHRM3)- and anti (somatostatin-SSTR1)-secretory receptors and H+,K+-ATPase.

Bioavailability of Coffee Phenolics

Caffeine is metabolised to paraxanthine substances, partially to theobromine and theophylline, and a small amount of unchanged caffeine is excreted by urine (Zivković 2000). Chlorogenic acid (5′-caffeoylquinic acid), a bound form of caffeic acid, was present in brewed coffee at high levels, while free phenolic acids were undetectable (Nardini et al. 2002). After alkaline hydrolysis, which released bound phenolic acids, ferulic acid, *p*-coumaric acid, and high levels of caffeic acid were detected. Coffee administration resulted in increased total plasma caffeic acid concentration, with an absorption peak at 1 h. Caffeic acid was the only phenolic acid found in plasma samples after coffee administration, while chlorogenic acid was undetectable. Most of caffeic acid was present in plasma in bound form, mainly in the glucuronate/sulfate forms. Due to the absence of free caffeic acid in coffee, plasma caffeic acid is likely to be derived from hydrolysis of chlorogenic acid in the gastrointestinal tract.

Lafay et al. (2006), using an in-situ intestinal perfusion rat model, found that the net absorption (influent flux minus effluent flux of phenolic acids and their metabolites) accounted for 19.5 and 8% of the perfused caffeic and chlorogenic acids, respectively. Part of the chlorogenic acid (1.2% of the perfused flux) was recovered in the gut effluent as caffeic acid. No chlorogenic acid was detected in either plasma or bile, and only low amounts of phenolic acids (less than 0.4%) were secreted in the bile. The results showed chlorogenic acid to be absorbed and hydrolysed in the small intestine. Three caffeoylquinic acids 3 diCQA, and caffeic, ferulic, isoferulic, and *p*-coumaric acids were identified in plasma of 10 subjects 8 h after the consumption of a decaffeinated green coffee extract containing 170 mg of CGA (Farah et al. 2008). Over 30% (33.1%) of the ingested cinnamic acid moieties were recovered in plasma, including metabolites, with peak levels from 0.5 to 8 h after treatment. CGA and metabolites identified in urine after treatment were 4-CQA, 5-CQA, and sinapic, *p*-hydroxybenzoic, gallic, vanillic, dihydrocaffeic, caffeic, ferulic, isoferulic, and *p*-coumaric acids, totaling 5.5% urinary recovery of the ingested cinnamic and quinic acid moiteties. The study showed that the major CGA compounds present in green coffee were highly absorbed and metabolized in humans.

One hour after coffee ingestion, some of the components in the coffee reached nanomole peak plasma concentrations (C(max)), whereas chlorogenic acid metabolites, including caffeic acid-3-*O*-sulfate and ferulic acid-4-*O*-sulfate and sulfates of 3- and 4-caffeoylquinic acid lactones, had higher C(max) values indicating absorption in the small intestine (Stalmach et al. 2009). In excess of 4 h, dihydroferulic acid, its 4-*O*-sulfate, and dihydrocaffeic acid-3-*O*-sulfate exhibited much higher C(max) values indicating absorption in the large intestine and the probable involvement of catabolism by colonic bacteria. These three compounds, along with ferulic acid-4-*O*-sulfate and dihydroferulic acid-4-*O*-glucuronide, were also major components excreted in urine (8.4–37.1 μmol) after coffee intake. Feruloylglycine, which was not detected

in plasma, was also a major urinary component excreted. Other compounds, not accumulating in plasma but excreted in smaller quantities, included the 3-*O*-sulfate and 3-*O*-glucuronide of isoferulic acid, dihydro(iso)ferulic acid-3-*O*-glucuronide, and dihydrocaffeic acid-3-*O*-glucuronide. Overall, the 119.9 mumol excretion of the chlorogenic acid metabolites corresponded to 29.1% of intake, indicating that as well as being subject to extensive metabolism, chlorogenic acids in coffee are well absorbed. In a subsequent study on human volunteers with an ileostomy, Stalmach et al. (2010) reported that over a 24 h period after coffee intake , excretion of chlorogenic acid metabolites in urine accounted for 8% of intake, the main compounds being ferulic acid-4-*O*-sulfate, caffeic acid-3-*O*-sulfate, isoferulic acid-3-*O*-glucuronide and dihydrocaffeic acid-3-*O*-sulfate. In contrast, after coffee ingestion, urinary excretion by humans with an intact colon corresponded to 29% of chlorogenic acid intake. This difference was due to the excretion of higher levels of dihydroferulic acid and feruloylglycine together with sulfate and glucuronide conjugates of dihydrocaffeic and dihydroferulic acids associated with colonic metabolism. Much earlier, Olthof et al. (2001) in a cross-over study with 4 female and 3 male healthy ileostomy subjects, found after ingestion of chlorogenic acid and caffeic, absorption of chlorogenic acid was 33% and of caffeic acid 95%. Traces of the ingested chlorogenic acid and 11% of the ingested caffeic acid were excreted in urine indicating that one third of chlorogenic acid and almost all of the caffeic acid were absorbed in the small intestine of humans. This implied that part of chlorogenic acid from foods will enter into the blood circulation, but most will reach the colon.

Both chlorogenic and caffeic acids were found to exhibit nonsaturable transport in Caco-2 cells, whereas caffeic acid also showed proton-coupled polarized absorption (Konishi and Kobayashi 2004). Thus, the absorption efficiency of caffeic acid was greater than that of chlorogenic acid. They found that that transport was mainly via paracellular diffusion, although caffeic acid was absorbed to a lesser extent by the monocarboxylic acid transporter (MCT).

Cholesterol Enhancing Activity

Coffee diterpenes cafestol and kahweol, present in both robusta and arabica coffee beans had been found to raise serum concentrations of cholesterol, triacylglycerols, and alanine aminotransferase (ALT) in humans (Van Dusseldorp et al. 1991; Urgert et al. 1995a, b, 1997; Urgert and Katan 1996; Gross et al. 1997; Post et al. 1997) and appeared to mildly affect the integrity of liver cells (Urgert and Katan 1996). Each 10 mg of cafestol consumed per day was reported to elevate cholesterol by 5 mg/dL (0.13 mmol/L) (Urgert et al. 1995b). Scandinavian boiled coffee contained 3 mg, French press coffee 3.5 mg, Italian espresso coffee 1.5 mg, and Turkish/Greek coffee 3.9 mg of cafestol per cup. Consumption of five cups of coffee per day of any of these coffee types could raise serum cholesterol by 4–10 mg/dL. Brewing strength increased diterpenes in boiled, French press and espresso coffee but not in Turkish/Greek coffee. Diterpenes in instant, drip filtered and percolated brews were negligible. Regular and decaffeinated coffees had similar diterpene contents. The two diterpenes were also found in unfiltered coffee in oil droplets and floating fines (Urgert et al. 1995a). Turkish or Scandinavian boiled coffee contained 2–5 g fines/L and French press coffee contained 1.5 g fines/L. Floating fines could contribute substantially to the hyperlipidemic and ALT-elevating effect of unfiltered coffee. Further Urgert et al. (1997) found that the effect of cafestol on serum lipid concentrations was much larger than the additional effect of kahweol, and the hyperlipidemic potential of unfiltered coffee mainly depended on its cafestol content. Both cafestol and kahweol raised alanine aminotransferase concentrations, and their hyperlipidemic effect thus appeared not to be coupled with their effect on liver cells. Patients at increased risk of heart disease who drink large amounts of coffee should be advised to select brews low in diterpenes (Urgert and Katan 1996). The diterpenes cafestol and kahweol had been implicated as the components in boiled coffee responsible for its hypercholesterolaemic effects. Post et al. (1997) found that cafestol suppressed bile acid synthesis by

downregulation of cholesterol 7α-hydroxylase and of, to a lesser extent, sterol 27-hydroxylase in cultured rat hepatocytes, whereas kahweol and isokahweol were less active. They suggested that suppression of bile acid synthesis may provide an explanation for the cholesterol-raising effect of cafestol in humans.

Scandinavian-style boiled coffee and Turkish-style coffee contained the highest amounts, equivalent to 7.2 and 5.3 mg cafestol per cup and 7.2 and 5.4 mg kahweol per cup, respectively (Gross et al. 1997). In contrast, instant and drip-filtered coffee brews contained negligible amounts of these diterpenes, and espresso coffee contained intermediate amounts, about 1 mg cafestol and 1 mg kahweol per cup. These findings provide an explanation for the hypercholesterolaemic effect previously observed for boiled coffee and Turkish-style coffee, and the lack of effect of instant or drip-filtered coffee brews.

In a study of sixty-four healthy volunteers who consumed six cups per day of boiled and filtered coffee for 17 days and then divided randomly divided into three groups, which, for the next 79 days, received either unfiltered boiled coffee (lipid content, 1.0 g/l), boiled and filtered coffee (0.02 g lipid/l), or no coffee (Van Dusseldorp et al. 1991). Serum total cholesterol levels rose by 0.42 mmol/l (16 mg/dl), LDL cholesterol levels by 0.41 mmol/l (16 mg/dl), and apolipoprotein B levels by 8.6 mg/dl in those who consumed boiled coffee relative to those who consumed boiled and filtered coffee. Responses of triglycerides, high density lipoprotein cholesterol, and apolipoprotein A-I did not differ significantly among these groups. No significant effects on serum lipid levels were found in the boiled and filtered coffee-consuming group compared with those who drank no coffee. In subjects who drank boiled coffee, serum campesterol level, an indicator of cholesterol absorption, remained constant; the serum lathosterol level, an indicator of cholesterol synthesis, increased by 11%, but the lathosterol to cholesterol ratio did not change. Their results suggested that drip filtered coffee did not contain cafestol or kahweol, as the diterpenes were retained by the paper filter.

Mutagenic, Genotoxic and Teratogenic Activities

Of 4 coffee flavour ingredients tested for mutagenicity, caffeic acid and chlorogenic acid, were positive in the mouse lymphoma assay but negative in the *Salmonella* assay (Fung et al. 1988). Two of the compounds, pyrazine and trigonelline, were negative in both assays.

The results of bacteria mutation assays (*Salmonella typhimurium* strains TA 98, YG 1024 and YG 1029) showed that trigonelline, alone or in combination with most of the single amino acids and mixtures of amino acids (all natural components in green coffee beans) when heated elicited potent mutagenic activity (Wu et al. 1997). Of the singly heated compounds, the highest mutagenic activity was found for trigonelline. The mutagenic activity detected with metabolic activation of the heated trigonelline samples indicated that the mutagenic compounds might be amines; however, higher mutagenic activity was found for trigonelline and its combinations without metabolic activation, which suggests that other types of mutagens (direct-acting) were predominant. Glyoxal, methylglyoxal, and diacetyl formed as Maillard reaction products in heat-treated food were determined in coffee extracts (coffee brews) obtained from green beans and beans with different degrees of roast (Daglia et al. 2007a). The compounds had been reported to be mutagenic in several in-vitro and genotoxic studies in experimental animals. Daglia et al. (2007a) found that small amounts of glyoxal and methylglyoxal occurred naturally in green coffee beans. Conversely, diacetyl was not found in green beans and was formed later in the roasting process. Therefore, light and medium roasted coffees had the highest glyoxal and methylglyoxal content, whereas dark roasted coffee contained smaller amounts of glyoxal, methylglyoxal, and diacetyl.

Instant coffee was found to exhibit direct genotoxic activity in the *Salmonella typhimurium* tester strains TA 98, 100, 102, 104 and YG 1024 (Duarte et al. 1999). In the Ames tester strain TA 100, the presence of S9 mix, S100 mix, S9 mix without cofactors led to a significant

decrease of the genotoxicity observed. The genotoxicity of instant coffee detected in strain TA 100 was dependent on the pH, with higher genotoxic effects at pH values above neutrality. Also, dependent on the pH was the ability of some phenolic molecules present in coffee promoting the degradation of deoxyribose in the presence of Fe3+/EDTA. The results suggested that apart from other molecules present in instant coffee responsible for their genotoxicity in several short term assays, phenolic molecules could also be implicated in the genotoxicity of coffee, via reactive oxygen species arising from its auto-oxidation.

Nishimura and Nakai (1960) were the first to describe the teratogenic effect of caffeine, reporting that caffeine injected intraperitoneally to mice at a dose of 250 mg/kg at selected times during organogenesis resulted in 43% of the offspring with cleft palate and digital defects. This dose is extremely high and equivalent to a blood level of 250,000 mg/mL (80 mg/mL is the approximate blood level producing terata in rats) (Christian and Brent 2001). The teratogenic effect of caffeine was demonstrated in rodents with variable sensitivity in different animals species (Nehlig and Debry 1994b). Malformations had been demonstrated in mice at 50–75 mg/kg of caffeine, whereas the lowest dose usually needed to induce malformations was 80 mg/kg in rats. However, when caffeine was administered in fractioned amounts during the day, 330 mg/kg/day were necessary to reach teratogenicity in rats. In rodents, the most frequently observed malformations were those of the limbs and digits, ectrodactyly, craniofacial malformations (labial and palatal clefts) and delays in ossification of limbs, jaw and sternum. Nevertheless, even in rodents, caffeine could be considered as a weak teratogenic agent, given the quite large quantities of caffeine necessary to induce malformations and the small number of animals affected. They added that in humans, caffeine did not present any teratogenic risk. The increased risk of the most common congenital malformations entailed by moderate consumption of caffeine was very slight.

In a case-control study of 2,030 malformed infants, six selected birth defects were evaluated in relation to maternal ingestion, during pregnancy, of caffeine from tea, coffee, and cola: 380 infants with inguinal hernia, 299 with cleft lip with or without cleft palate, 277 with cardiac defects, 194 with pyloric stenosis, 120 with isolated cleft palate, and 101 with neural tube fusion defects were compared with 712 other malformed infants who served as controls (Rosenberg et al. 1982). None of the point estimates of relative risk was significantly greater than unity. Their findings suggested that caffeine was not a major teratogen with regard to the six defects evaluated. Narod et al. (1991) also reported that several human studies on birth defects had been conducted and the overall results did not implicate coffee as a likely human teratogen, although some evidence suggested that consumption of three or more cups of coffee per day may have a modest effect on lowering infant birth weight. A review of seven out of 25 scientific papers that met initial criteria for inclusion, yielded no evidence to support a teratogenic effect of caffeine in humans (Browne 2006). Current epidemiologic evidence was not adequate to assess the possibility of a small change in risk of congenital anomalies resulting from maternal caffeine consumption.

Nehlig and Debry (1994a) in their review stated that coffee ingested during gestation induced a dose-dependent decrease in birth weight, but usually only when ingested amounts were high (i.e. more than seven cups/day), whereas coffee had no effect at moderate doses. Caffeine consumption during gestation affected hematologic parameters of the new-born infant or rat. In animals, caffeine induced long-term consequences on sleep, locomotion, learning abilities, emotivity and anxiety, whereas, in children, the effects of early exposure to coffee and caffeine on behavior were not clearly established. They advocated for more studies in humans to ascertain long-term behavioral effects of caffeine ingestion by pregnant mothers. However, caffeine could potentiate the teratogenic effect of other substances, such as tobacco, alcohol, and act synergistically with ergotamine and propranolol to induce materno-fetal

vasoconstrictions leading to malformations induced by ischemia (Nehlig and Debry 1994b). Therefore, even though caffeine does not seem to be harmful to the human fetus when taken in moderation throughout the day, some associations, especially with alcohol, tobacco, and vasoconstrictive or anti-migraine medications should be avoided. Maternal consumption of caffeine had been reported to affect brain composition, especially in case of a low-protein diet and also reported to interfere with zinc fixation in brain. They advised that pregnant mothers should limit their coffee and caffeine intake to 300 mg caffeine/day (i.e. 2–3 cups of coffee or 2.5–3 l of coke) especially because of the increase of caffeine half-life during the third trimester of pregnancy and in the neonate. Using data from the National Birth Defects Prevention Study, Browne et al. (2007) found no evidence for an appreciable teratogenic effect of maternal caffeine consumption with regard to cardiovascular malformation. Risk estimates for both smoking and consuming caffeine were less than the sum of the excess risks for each exposure. Using data from the National Birth Defects Prevention Study, positive associations were observed between spina bifida and total caffeine consumption (Schmidt et al. 2009). Associations with modestly increased risk of neural tube defects (NTDs) and encephalocele were also observed. The association between caffeine consumption and anencephaly differed by maternal race/ethnicity. No dose effects were found. They asserted that additional studies should confirm whether women who consume caffeine are at increased risk for pregnancies complicated by NTDs. Further they found that mothers who consumed caffeine, oxidized CYP1A2*1 F quickly, and acetylized N-acetyltransferase 2 slowly had a non-significantly elevated estimated risk for an NTD-affected pregnancy (Schmidt et al. 2010). Multiplicative interaction effects were observed between maternal caffeine and infant CYP1A2*1 F fast oxidizer status. They advocated that the association identified between maternal CYP1A2*1 F fast oxidation status and NTDs should be examined further in the context of the other substrates of CYP1A2. Maternal caffeine and its metabolites may be associated with increased risk for NTD-affected pregnancies in genetically susceptible subgroups. Studies in rats indicated that even at moderate doses, maternal caffeine ingestion during gestation and lactation may induce a series of subtle developmental alterations that may affect modulation of breathing control in the neonate in pathological situations such hypoxia (Picard et al. 2008).

According to Christian and Brent (2001) the sum of scientific evidence did not indicate caffeine to be a reproductive toxicant, even at very high dosages that produce pharmacological and mild toxic effects in the parental animals. The NOEL (no observable effect level) for reproductive effects of caffeine reported in animals had been reported in the 80–120 mg/kg per day dosage range. The threshold dose for malformation appeared to be within the range of 80–100 mg/kg per day, depending on the method of administration and the species tested. The developmental NOEL in rodents appeared to be approximately 30 mg/kg per day. The most recent review on caffeine and reproductive and development risk by Brent et al. (2011) found that spontaneous abortion epidemiology studies were inconsistent and the majority did not consider the confounding introduced by not considering the pregnancy signal. Animal studies did not support the premise of caffeine being an abortafacient for the wide range of human caffeine exposures. Almost all the congenital malformation epidemiology studies were negative. Animal pharmacokinetic studies indicated that the teratogenic plasma level of caffeine had to reach or exceed 60 μg/mL, which was not attainable from ingesting large amounts of caffeine in foods and beverages. No epidemiological study described the "caffeine teratogenic syndrome." Six of the 17 recent epidemiology studies dealing with the risk of caffeine and fetal weight reduction were negative. Seven of the positive studies had growth reductions that were clinically insignificant. They concluded that moderate or even high amounts of beverages and foods containing caffeine did not increase the risks of congenital malformations, miscarriage or growth retardation

Traditional Medicinal Uses

Coffee is considered to be analgesic, an aphrodisiac, anorexic, antidotal, cardiotonic, stimulant, counterirritant, diuretic, hypnotic, lactagogue and nervine. It is commonly used in folk medicine as a remedy for headache, asthma, flu, tropine poisoning, jaundice, migraine, narcosis, nephrosis, malaria, sores, opium toxicity, snake-bite and vertigo (Grieve 1971; Duke 1983; Burkill 1998; DeFilipps et al. 2004). In Trinidad, leaf poultices are used to treat sores in and root sap or root infusions are drunk to relieve scorpion stings. In French Guiana, infusion of green beans is drunk for migraine headaches. Infusion contains tannins which is useful for gout andas a febrifuge.

Other Uses

Coffee plants have been used in agroforestry. A light coloured, distinctive honey can be obtained from honeybees rhat collect nectar and pollen from the flowers. The trunk provides a hard, dense, durable timber that is suitable for tables, chairs and turnery, and is also used as fuel wood.

Fruit pulp and parchment removed during processing are occasionally fed to cattle in India. Dry coffee pulp was found to contain about 10% of crude protein, 21% of crude fibre, 45% of nitrogen-free extract and 1.2% of caffeine whereas coffee hulls were much poorer in nutritive value, containing less than 3% of crude protein, 70% of crude fibre and 19% of nitrogen-free extract on a dry basis (Bressani et al. 1975). The essential amino acid content/g N of coffee pulp was similar to that of soya protein. Dry coffee pulp should not be used at levels exceeding 20% of the total ration in animal feed owing to the harmful caffeine component. The fruits have been used as a source for dye/tannin. *C. Arabica* beans (seeds) which contained caffeine has been described as a natural herbicide, selectively inhibiting germination of seeds of the weed, *Amaranthus spinosus*. Coffelite, a type of plastic, is made from coffee beans. Coffee with iodine is used as a deodorant.

Coffee husk and spent coffee grounds can be used as substrates without any pre-treatment for the cultivation of edible fungi substrates in solid state fermentation (SSF) to cultivate edible mushrooms *Pleurotus ostreatus* and *Pleurotus sajor-caju* (Fan et al. 2000). Coffee ground can be put in ant hills to get rid of ants and also used to clean stain resistant surfaces such as ash trays and greasy surfaces.

Fruit pulp, leaves and soft stems are often composted for fertilizer and mulch and used as soil improvers. The top-dressing application of coffee ground and tea leaves was found to be an excellent method to recycle coffee grounds and tea wastes from coffee shops (Morikawa and Saigusa 2011). Use of these materials would not only reduce the waste going to landfill but would also benefit the mineral nutrition of rice consumers at low cost by increasing Fe and Zn levels of rice grains as well as grain yield.

Comments

Restriction fragment length polymorphism (RFLP) studies clearly suggested *C. arabica* to be an amphidiploid formed by hybridisation between *C. eugenioides* and *C. canephora*, or ecotypes related to these diploid species (Lashermes et al. 2009).

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Coffea canephora

Scientific Name

***Coffea canephora* Peirre ex Froehner.**

Synonyms

Coffea arabica var. *stuhlmannii* A.Froehner, *Coffea bukobensis* A.Zimm., *Coffea canephora* f. *sankuruensis* De Wild., *Coffea canephora* subvar. *robusta* (L.Linden) A.Chev., *Coffea canephora* var. *crassifolia* Lautent ex De Wild., *Coffea canephora* var. *gossweileri* A.Chev., *Coffea canephora* var. *hiernii* Pierre ex De Wild., *Coffea canephora* var. *hinaultii* Pierre ex De Wild., *Coffea canephora* var. *kouilouensis* De Wild., *Coffea canephora* var. *laurentii* (De Wild.) A.Chev., *Coffea canephora* var. *maclaudii* (A.Chev.) A.Chev., *Coffea canephora* var. *muniensis* Pierre ex De Wild., *Coffea canephora* var. *nganda* Haarer nom. illeg., *Coffea canephora* var. *oka* A.Chev. nom. inval., *Coffea canephora* var. *oligoneura* Pierre ex De Wild., *Coffea canephora* var. *opaca* Pierre ex De Wild., *Coffea canephora* var. *sankuruensis* (De Wild.) De Wild., *Coffea canephora* var. *stuhlmannii* (A.Froehner) A.Chev., *Coffea canephora* var. *trillesii* De Wild., *Coffea canephora* var. *ugandae* (Cramer) A.Chev., *Coffea canephora* var. *welwitschii* (Pierre ex De Wild.) A.Chev., *Coffea canephora* var. *wildemanii* Pierre ex De Wild., *Coffea laurentii* De Wild., *Coffea maclaudii* A.Chev., *Coffea robusta* L.Linden, *Coffea ugandae* Cramer, *Coffea welwitschii* Pierre ex De Wild.

Family

Rubiaceae

Common/English Names

Congo Coffee, Congo Coffee Tree, Robusta Coffee.

Vernacular Names

Brazil: Café, Cafeiro;
Chinese: Zhong Guo Ka Fei;
Czech: Kávovník Statný;
Danish: Robustakaffe;
Eastonian: Kongo Kohvipuu;
French: Café Robusta, Caféier Robuste, Caféier Canéphore;
German: Robusta-Kaffee, Robustakaffeebaum, Robustakaffeestrauch;
Hungarian: Kongói Kávé;
India: Kaphi (Assamese), Kaphi (Bengali), Kophi (Gujarati), Kophi (Hindu), kaaphi (Kannada), Kawphi (Konkani), Kappicceti (Malayalam), kophi (Manipuri), kava, kophi,

T.K. Lim, *Edible Medicinal and Non-Medicinal Plants: Volume 5, Fruits*,
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(*Marathi*), kaw-fi (Mizoram), kapi (Tamil), kaaphi (Telugu);*
Italian: Caffe Di Congo;
Japanese: Robusuta Koohiii;
Polish: Kawa Kongolijska;
Portuguese: Café-Robusta;
Russian: Kofe Robusta;
Spanish: Cafeto Robust;
Thai: Kafae;
Turkish: Kahvesi Kongo;
Vietnamese: Càphê Robusta;
*May also refers to coffee in general.

Origin/Distribution

Coffea canephora is indigenous to tropical West Africa (Benin, Burkina Faso, Cote d'Ivoire, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, Togo), eastwards to Uganda and north to south from Cameroon to northern Angola (Davis et al. 2006; Gomez et al. 2009). *C. canephora* together with *Coffea liberica* have the widest distribution of the genus; both are closely related, diploid, allogamous (self-incompatible) and share the same phylogenetic clade (Maurin et al. 2007; Gomez et al. 2009). Wild distributions of *C. canephora* were found in Côte d'Ivoire, Cameroon, Guinea, Central African Republic and Congo (Gomez et al. 2009). Robusta coffee together with Arabica coffee are the two most commonly and widely cultivated *Coffea* species and Robusta coffee (*Coffea canephora var. robusta*) represents a third of the global coffee production (Bombarely et al. 2011). In recent years Vietnam, which produces mostly robusta, has surpassed Brazil, India, and Indonesia to become the world's single largest exporter of robusta coffee.

Agroecology

Coffea canephora or robusta coffee is a hardier and more robust plant than *C. arabica* as it tolerates less favourable soil and climatic conditions. It is grown at much lower and warmer altitudes, from sea level to 800 m in areas 10°N and 10°S of the equator. It thrives in area with mean annual temperatures of 18–36°c and with mean annual rainfall of 2,000–3,000 mm/year. Robusta coffee is also less susceptible to pest ravages and rough handling than Arabica coffee. Robusta coffee thrives on a wide range of soil types but prefers well-drained, deep, fertile soil rich in organic matter. It prefers slightly acid to neutral soils and grows well on forest soils. It is shade tolerant and cultivated under light shade.

Edible Plant Parts and Uses

The pulp of ripe coffee berry is edible and slightly sweet. The seeds or beans are dried, roasted, ground and brewed to make coffee. Besides being the world's most popular and widely consumed beverage, coffee is also used as flavouring in cakes, pastries, candies, ice cream, sorbets and liqueurs.

Robusta coffee contains twice more caffeine than Arabica coffee and is widely used in instant coffees and in espresso blends as fillers to provide the formation of 'crema' and enhance the body of espresso. It has minor significance in the coffee gourmet market.

Botany

A small perennial tree or bush, 3–6.5 m high, multistemmed with long and flexible branches (Plate 1). The leaves are oblong-elliptic to broadly elliptic, 20–35 cm long by 6–15 cm wide, with acuminate apex, obtuse to broadly cuneate base, wavy (undulating) or corrugated margin and 8–16 pairs of lateral veins and borne on 8–20 mm long petioles (Plates 2, 3, 4, and 5). The interpetiolar stipules are wide, deltoid and semi-persistent. Flowers white, scented, in axillary cymose clusters of 8–30(−50) flowers (Plates 2 and 3). Flowers with small annular, dentate calyx; corolla tubular with 5–7 segments, the tube is shorter than the lobes; stamens five protruding from the top of the

Plate 1 Robusta coffee bush (cv Kopi Talisap No 2 from Thailand)

Plate 2 Axillary clusters of flower and coffee berries (cv. kopi Talisap)

Plate 3 Close-up of flower cluster (cv. kopi Talisap)

Plate 4 Glossy bright green foliage with wavy margins and clusters of green berries

Plate 5 Ripening and unripe Robusta coffee berries

corolla tube together with a single ovary and bifid stigma. Fruits broadly oblong-ellipsoid, 10–16 mm by 5–12 mm, green (Plates 2, 3, 4, and 5) turning red when ripe (Plate 6), usually containing two seeds. Seeds (beans) ovoid, size variable, much smaller than Arabica and with a straight-line groove on the flat side (Plate 7).

Plate 6 Ripe, bright red Robusta coffee berries

Plate 7 Processed robusta coffee beans

Nutritive/Medicinal Properties

Refer also to notes under *Coffea arabica* and *C. liberica*.

Phytochemicals in Coffee Fruit/Beans

Sucrose was found to be the dominant carbohydrate in green coffee with a concentration of up to 90 mg/g (mean = 73 mg/g) in arabica beans and significantly lower amounts in robusta beans (mean = 45 mg/g) (Murkovic and Derler 2006). Alanine was found to be the amino acid with the highest concentration (mean = 1,200 μg/g) followed by asparagine (mean = 680 μg/g) in robusta and 800 μg/g and 360 μg/g in arabica respectively. In general, the concentration of amino acids is higher in robusta than in arabica. Free amino acids ornithine, β-alanine and pipecolic acid were found in Arabica and Robusta coffees as well as hydroxyproline in Arabica coffees (Arnold et al. 1994). In general, Arabica and Robusta coffees contained the same main and minor amino acids. Most of the free sugar in the mature coffee seed of *Coffea arabica* and *C. canephora* var. *Robusta* was accounted for by sucrose, fructose and glucose were both at higher concentrations in the perisperm (Rogers et al. 1999). Considerable amounts of myo-inositol (3–4% dry weight (DW)) were found in young seeds, while only the phosphorylated form phytic acid occurred in mature seeds (0.3–0.6% DW). Quinic acid, which was present in very low amounts in mature endosperm, represented between 6 and 16% DW in young seeds, this possibly being the major precursor pool for the high amounts of chlorogenic acids (5–10% DW) a characteristic of mature coffee beans. Of the other organic acids analysed, citric and malic acids were dominant in the mature seed, with higher concentrations in Arabica than Robusta.

The triacylglycerol found in *Coffea canephora* coffee beans was found to comprise trilinoleyl-glycerol (LLL, 11.76%), dilinolenoyl-palmitoyl-glycerol(PLnLn,2.94%),dilinoleyl-oleyl-glycerol (OLL, 7.77%), dilinoleyl-palmitoyl-glycerol (PLL, 25.90%), dipalmitoyl-linolenoyl-glycerol (PPLn, 1.66%), dioleoyl-linoleyl-glycerol (OOL, 1.68%), dilinoleyl-stearyl-glycerol (SLL, 8.28%), palmitoyl-oleyl-linoleyl-glycerol (POL, 8.76%), dipalmitoyl-linoleyl-glycerol (PPL, 13.74%), dilinoleyl-arachidyl-glycerol (ALL, 3.51%), trioleoyl-glycerol (OOO, 2.33%), palmitoyl-linoleyl-stearyl-glycerol (PLS, 8.73%), and distearoyl-linolenonyl-glycerol (SSLn, 2.91%) (Segall et al. 2005).

Coffea arabica var. Caturra and *Coffea canephora* var. ROM green coffee beans contained identical amounts of polysaccharide (Fischer et al. 2001). The monosaccharide compositions of the cell wall material (CWM) were similar, although Arabica beans contained slightly more mannose than Robusta. In the latter, more arabinogalactan was solubilised during preparation of the CWM and the water-soluble fraction of the CWM

contained higher amounts of galactomannan than in Arabica. Linkage analysis indicated that the galactomannans possessed unbranched to branched mannose ratios between 14:1 and 30:1. No major difference in the structural features of the galactomannans between species was found. The arabinogalactans were heterogeneous both with regard to the degree of branching and the degree of polymerisation of their arabinan side-chains. Compared to Arabica, Robusta appeared to contain greater amounts of arabinogalactans with longer side chains. Similarly, Nunes and Coimbra (2002) found that the total polysaccharide content and the structures of the galactomannans and arabinogalactans in robusta and arabica coffee varieties were very similar. The content of arabinogalactans extracted from robusta green coffee was higher than that extracted from Arabica. For roasted coffees, the amount of galactomannans extracted ranged from 0.66 to 0.92% (w/w).

A phenolic ester of caffeic acid and ferulic acid with quinic acid, identified as 3-*O*-feruloyl-4-*O*-caffeoylquinic acid was isolated from unroasted robusta coffee beans (*Coffea canephora*) (Iwahashi et al. 1985). A quinyl ester of hydroxycinnamic acid identified as 4-*O*-feruloylquinic acid (Morishita et al. 1986b); 3-*O*-caffeoyl-4-*O*-feruloylquinic acid (Morishita et al. 1986a) and caffeoyltryptophan (Morishita et al. 1987) were isolated from unroasted robusta coffee beans (*Coffea canephora var. robusta*). A component found in commercial green robusta coffee beans from many origins, but particularly characteristic of those from Angola, was characterised as N-caffeoyltyrosine (Clifford et al. 1989a).

C. robusta was found to have the highest caffeine concentration, 2.26 g/100 g, followed by *C. arabica* with a caffeine concentration of 1.61 g/100 g and *C. liberica* had the lowest caffeine concentration at 1.23 g/100 g (Liew et al. 2001). Arabica and robusta green coffee differed respectively in the content of caffeine 1.2%, 2.4 (>4)%; trigonelline 1.0%, 0.7%; amino acids 0.5%, 0.8%; chlorogenic acids 7.1%, 10.3%; total lipids 16% (range 13–17)%; 10% (range 7–11)%; oleic acid 6.7–8.2%, 9.7–14.2%; diterpene: cafestol 0.5–0.95, 0.2%; kahweol 0.3%, nil; 16-0-methyl cafestol nil, 0.07–0.15% respectively (Illy and Viani 1995).

Coffee pulp was found to contain smaller quantities of chlorogenic acids (CGA) namely caffeoylquinic acids, feruloylquinic acids and dicaffeoylquinic acids than the beans (Clifford and Ramirez-Martinez 1991a). Caffeoylferuloylquinic acids were not found even in the pulp from a robusta coffee. Pulp from a robusta coffee had lower caffeine content than the pulp from two arabica cultivars, the reverse of the situation existing in the beans. Protocatechuic acid was also identified as a significant component in coffee pulp (Clifford and Ramirez-Martinez 1991a). During coffee fruit maturity, there was a sigmoidal increase in total caffeoylquinic acid essentially in parallel with the total dry matter gain (Clifford and Kasi 1987). The ratio CQA/diCQA appeared to increase with maturation until ripeness of the fruit. The corresponding changes in the contents of several other chlorogenic acids, caffeine and trigonelline were small on a 100 beans mass basis. The following chlorogenic acids were detected in whole fruits (stage I - rapid expansion and pericarp growth), pericarps and seeds of *Coffea arabica* cv. Tall Mokka and *Coffea canephora*: monocaffeoylquinic acids (3CQA, 4CQA and 5CQA), dicaffeoylquinic acids (3,4diCQA, 3,5diCQA and 4,5diCQA) and a monoferuloylquinic acid (5FQA) (Koshiro et al. 2007). The most abundant chlorogenic acid was 5CQA, which comprised 50–60% of the total of *C. arabica* and 45–50% of *C. canephora* seeds. The content of dicaffeoylquinic acid, mainly 3,5-diCQA, was high in *C. canephor*a. A high content of 5FQA was found in seeds of stages (III) mature (green), (IV) ripening (pink), and (V) fully ripened (red), especially in *C. canephora*. Total chlorogenic acids amounted to 14 mg per fruit in *C. arabica* and 17 mg in *C. canephora*. In contrast, free quinic acid varied from 0.4–2.0 mg (*C. arabica*) and 0.2–4.0 mg (*C. canephora*) per fruit during growth. High biosynthetic activity of 5CQA, which was estimated via the incorporation of [U-14C]phenylalanine into chlorogenic acids, was found in young fruits (perisperm and pericarp) in stage I, and in developing seeds (endosperm) in stages II and III. The biosynthetic

activity of chlorogenic acids was markedly reduced in ripening and ripe seeds, especially in *C. canephora*. Caffeoylquinic acids, and particularly 5-CQA, found in high levels in *C. canephora* beans were also found in leaves, occurring 10-fold lower in nature old leaves than in juvenile leaves; feruloylquinic acids were also present (Mondolot et al. 2006). In coffee bean they formed vacuolar complexes with caffeine, in leaves caffeoylquinic acids (mono- and di-esters) were found closely associated with chloroplasts in very young leaves. During leaf ageing, they were found to first accumulate intensively in specific chlorenchymatous bundle sheath cells and then in phloem sclerenchyma cells. In older tissues, their presence in the leaf vascular system indicated that they were transported via phloem and confirmed their involvement in lignification processes.

The most common hydrocinnamic acids in coffee beans had been reported to be caffeic acid (3,4-dihydroxy-cinnamic acid) followed by ferulic acid (3-methoxy, 4-hydroxy-cinnamic acid) and *p*-coumaric acid (4-hydroxy-cinnamic acid) and to a lesser extent sinapic acid (3,5-dimethoxy-4-hydroxycinnamic acid) (Clifford 1999, 2000, 2003). Green coffee beans could contain up to 14% (dm) chlorogenic acids (CGA) and related compounds as the main components of the phenolic fraction of green coffee beans (Farah and Donangelo 2006). They can be subdivided into the classic chlorogenic acids and mixed diesters of caffeic and ferulic acids with quinic acid; other esters, amides and glycosides and transformation products formed during processing. During coffee processing, CGA may be isomerized, hydrolyzed or degraded into low molecular weight compounds. The high temperatures of roasting also produce transformation of part of CGA into quinolactones and, along with other compounds, melanoidins. Chlorogenic acids are a family of esters formed between quinic acid and certain *trans*-cinnamic acids, most commonly caffeic, *p*-coumaric and frolic acid. Coffee beans are remarkably rich in CGAs, containing at least 18CGAs that are not acylated at the C1. The main groups of CGAs found in green coffee beans include: caffeoylquinic acids (CQA), with three isomers (3-, 4- and 5-CQA); dicaffeoylquinic acids (diCQA),with three isomers (3,4-diCQA; 3,5-diCQA; 4,5-diCQA); feruloylquinic acids (FQA), with three isomers (3-, 4- and 5- FQA); *p*-coumaroylquinic acids (*p*CoQA), with three isomers (3-, 4- and 5- *p*CoQA), and six mixed diesters of caffeoylferuloyl-quinic acids (CFAQ) (Clifford 2003). Clifford and Ramirez-Martinez (1991a) reported green coffee beans of *C. canephora* cv *Robusta* to have 7.17 g% total CGA, 5.33% CQA, 0.79% FQA, 1.05% diCQA. Trugo and Macrae (1984) found *C. canephora* cv *robusta* to have 9.80 g% total CGA, 6.82% CQA, 0.60% FQA, 1.37% diCQA. Losses of about 60% of seven TGAs were observed when mild roasting conditions were used and almost 100% after severe roasting in arbica and robusta coffee. *C. canephora* cv *robusta* green coffee beans from two different regions in Angola were found to contain 6.08–7.18 g% total CGA, comprising 3.43–4.97% CQa, 0.54–0.75% FQA and 1.20–1.46% diCQA (Correia et al. 1995). They confirmed the presence of two chlorogenic acid-like components, caffeoyil-tyrosine and Angola II, unique to and characteristic of Angolan robustas, for three of the main Angolan coffee producing regions. Only one of these two components caffeoyl-tyrosine, was found in the sample from Cabinda. Neither could be detected in the coffee samples from Cameroon, Indonesia, Ivory Coast or Zaíre. (Ky et al. 2001) reported green coffee beans of wild *C. canephora* to have 11.3 g% total CGA, 7.66% CQA, 1.43% FQA, 2.31% diCQA. Contents of trigonelline and sucrose, two coffee aroma precursors varied between species from 0.39% to 1.77% dry matter basis (dmb) and from 3.8% to 10.7% dmb, respectively.

Hydroxycinnamic acids, *p*-coumaric, *o*-coumaric and 3,4-dimethoxycinnamic acids were detected in the majority of samples, 13 green *Coffea canephora* var. *robusta* and seven green *Coffea arabica* coffee beans from different geographical origins (Andrade et al. 1998). Caffeic and ferulic acids were present in all of them while sinapic and 4-methoxycinnamic acids were found in only one sample from Mexico and Honduras. it appeared that the relative amount of the hydroxycinnamic acids could be

related to the botanical origin of coffee. *Coffea canephora* var. *robusta* contained a higher level of 3,4-dimethoxycinnamic (mean = 0.433, ranging from 0.237 to 0.691 g/kg) than the *Coffea arabica* samples (mean = 0.059, ranging from 0.016 to 0.095 g/kg). The following cinnamoyl amides *p*-coumaroyl-N-tyrosine, feruloyl-N-tyrosine, feruloyl-N-tryptophan and caffeoyl-N-phenylalanine were found in the methanolic extracts of green robusta coffee beans, in addition to the previously reported *p*-coumaroyl-N-tryptophan, caffeoyl-N-tryptophan and caffeoyl-N-tyrosine (Clifford and Knight 2004). These compounds were found at higher levels in Angolan coffees compared with coffees of other origins.

Twelve chlorogenic acids not previously reported in nature and comprising three isomeric dimethoxycinnamoylquinic acids (7–9), three caffeoyl-dimethoxycinnamoylquinic acids (22, 24, and 26), three diferuloylquinic acids (13–15), and three feruloyl-dimethoxycinnamoylquinic acids (28, 30, and 32) were found in green robusta beans bringing up the total of 45 chlorogenic acids characterized in green robusta coffee beans (Clifford et al. 2006a). Forty-five chlorogenic acids were characterized in green Robusta coffee beans including 15 quantitatively minor *p*-coumaric acid-containing chlorogenic acids not previously reported in nature (Clifford et al. 2006b; 1989b). These comprised 3,4-di-*p*-coumaroylquinic acid; 3,5-di-*p*-coumaroylquinic acid; and 4,5-di-*p*-coumaroylquinic acid; 3-*p*-coumaroyl-4-caffeoylquinic acid; 3-*p*-coumaroyl-5-caffeoylquinic acid; 4-*p*-coumaroyl-5-caffeoylquinic acid; 3-caffeoyl-4-*p*-coumaroyl-quinic acid; 3-caffeoyl-5-*p*-coumaroyl-quinic acid; and 4-caffeoyl-5-*p*-coumaroyl-quinic acid; 3-*p*-coumaroyl-4-feruloylquinic acid; 3-*p*-coumaroyl-5-feruloylquinic acid; and 4-*p*-coumaroyl-5-feruloylquinic acid;and4-dimethoxycinnamoyl-5-*p*-coumaroylquinic acid; and two isomers for which identities could not be assigned unequivocally.

The following polyphenols and methylxanthines were detected in green coffee beans: three phenolic acids (caffeic acid, ferulic acid and dimethoxycinnamic acid), three isomeric caffeoylquinic acids , three feruloylquinic acids, one *p*-coumaroylquinic acid, three dicaffeoylquinic acids, three feruloyl-caffeoylquinic acids, four *p*-coumaroyl-caffeoylquinic acids, three diferuloylquinic acids, six dimethoxycinnamoyl-caffeoylquinic acids, three dimethoxycinnamoyl-feruloylquinic acids, six cinnamoyl-amino acid conjugates, three cinnamoyl glycosides, and three methylxanthines (caffeine, theobromine and theophylline) (Alonso-Salces et al. 2009a). Dimethoxycinnamic acid, three isomers of dimethoxycinnamoyl-caffeoylquinic acids and another three of dimethoxycinnamoyl-feruloylquinic acids, as well as the three cinnamoyl glycosides, had not previously been reported in coffee beans. The contents of chlorogenic acids, cinnamoyl amides, cinnamoyl glycosides, free phenolic acids, and methylxanthines of green coffee beans of *Coffea arabica* (Arabica) and *Coffea canephora* (Robusta), were analyzed to determine their botanical and geographical origins (Alonso-Salces et al. 2009b). The analysis of caffeic acid, 3-feruloylquinic acid, 5-feruloylquinic acid, 4-feruloylquinic acid, 3,4-dicaffeoylquinic acid, 3-caffeoyl-5-feruloylquinic acid, 3-caffeoyl-4-feruloylquinic acid, 3-*p*-coumaroyl-4-caffeoylquinic acid, 3-caffeoyl-4-dimethoxycinnamoylquinic acid, 3-caffeoyl-5-dimethoxycinnamoylquinic acid, *p*-coumaroyl-N-tryptophan, feruloyl-N-tryptophan, caffeoyl-N-tryptophan, and caffeine enabled the unequivocal botanical characterization of green coffee beans. Some free phenolic acids and cinnamate conjugates of green coffee beans also showed great potential as means for the geographical characterization of coffee. Thus, *p*-coumaroyl-N-tyrosine, caffeoyl-N-phenylalanine, caffeoyl-N-tyrosine, 3-dimethoxycinnamoyl-5-feruloylquinic acid, and dimethoxycinnamic acid were found to be characteristic markers for Ugandan Robusta green coffee beans. Linear discriminant analysis (LDA) and partial least-squares discriminant analysis (PLS-DA) provided classification models that correctly identified all authentic Robusta green coffee beans from Cameroon and Vietnam and 94% of those from Indonesia. Further, PLS-DA afforded independent models for Robusta samples from these three countries with sensitivities and specificities of classifications close to 100% and for Arabica samples from America and Africa with

sensitivities of 86 and 70% and specificities to the other class of 90 and 97%, respectively.

Eight quantitatively minor triacyl chlorogenic acids were characterised in green Robusta coffee beans with seven of them not previously reported in nature, making it a total of 52 chlorogenic acids characterized in green Robusta coffee beans (Jaiswal and Kuhnert 2010). These comprised 3,4,5-tricaffeoylquinic acid; 3,5-dicaffeoyl-4-feruloylquinic acid, 3-feruloyl-4,5-dicaffeoylquinic acid and 3,4-dicaffeoyl-5-feruloylquinic acid; 3-caffeoyl-4,5-diferuloylquinic acid and 3,4-diferuloyl-5-caffeoylquinic acid; and 3,4-dicaffeoyl-5-sinapoylquinic acid and 3-sinapoyl-4,5-dicaffeoylquinic acid. Fifteen quantitatively minor sinapic acid and trimethoxycinnamoylquinic acid-containing chlorogenic acids, were characterised in green Robusta coffee beans, with 13 of them not previously reported in nature chalking up the total of CGSs to 69 (Jaiswal et al. 2010). These comprised 3-sinapoylquinic acid, 4-sinapoylquinic acid, and 5-sinapoylquinic acid; 3-sinapoyl-5-caffeoylquinic acid, 3-sinapoyl-4-caffeoylquinic acid, and 4-sinapoyl-3-caffeoylquinic acid; 3-(3,5-dihydroxy-4-methoxy) cinnamoyl-4-feruloylquinic acid; 3-sinapoyl-5-feruloylquinic acid, 3-feruloyl-4-sinapoylquinic acid, and 4-sinapoyl-5-feruloylquinic acid; 4-trimethoxycinnamoyl-5-caffeoylquinic acid, 3-trimethoxycinnamoyl-5-caffeoylquinic acid; and 5-feruloyl-3-trimethoxycinnamoylquinic acid, 3-trimethoxycinnamoyl-4-feruloylquinic acid, and 4-trimethoxycinnamoyl-5-feruloylquinic acid.

Large amounts of diterpene mono-and di-alcohols were found in Arabica and Robusta coffee varieties; cafestol, kahweol and 16-*O*-methylcafestol were identified (Lercker et al. 1995). Total diterpenic alcohol of the unsaponifiable matter from ten arabica samples (mg/100 g lipids) was 851.3–1290.7 mg lipids, made up of kahweol, 414.8–672.7 mg; cafestol 299.4–583.6 mg; 16-*O*-methylcafestol 1.8–14.5 mg; unidentified component 32 0.9–9.2 mg. Other components viz. component17 30–79.2 mg/ and component 18, 46.9–83.3 mg that were partly generated during roasting were also found; these compounds appeared to arise from the dehydration of cafestol and dehydrocafestol. Total diterpenic alcohol of the unsaponifiable matter from seven robusta samples (mg/100 g lipids) was 158.8–361.4 mg, made up of kahweol, 3.6–12.5 mg; cafestol 76.4–190.1 mg; 16-*O*-methylcafestol 45.3–138.9 mg; unidentified component trace-0.4 mg. Other components viz. component17 trace-0.5 mg and component 18, 14.8–32.4 mg that were partly generated during roasting were also found; these compounds appeared to arise from the dehydration of cafestol and dehydrocafestol. Total sterol and triterpenic alcohol of the unsaponifiable matter from coffee lipids from seven robusta samples was 89.8–175.9 mg/100g lipids, cholesterol 0.3–1.3%, unidentified B 2.4–3.6%, campesterol 9.6–13.6%, 24-methylencholesterol 1.7–2.3%, stigmasterol 16.2–20.9%, β-sitosterol 33.1–37.2%, Δ^5-avenasterol 9.6–15.5%, component H 0.2–04%, cycloartenol 4.8–6.4%, 24-methylenecycloartenol 6.0–9.2%, unidentified component N 1.4–2.6% (Lercker et al. 1995).

de Roos et al. (1997) reported the following diterpene level (mg bean mass) in *C. canephora* green beans from Ivory Coast with 239–259 mg cafestol , 5–8 mg kahweol and 16-*O*-methyl cafestol 102–154 mg. Cafestol is universally present in all *Coffea* species and among commercially important *Coffea* species, *C. canephora* had the lowest levels of kahweol. Green and roasted coffees of *Coffea arabica* (arabica) and *Coffea canephora* (robusta) could be differentiated on their differences in their lipid fraction, especially in the content of the diterpene kahweol, which was present at 0.1–0.3% dry matter basis in arabica beans and only in traces (<0.01%) in robusta (Rubayiza and Meurens 2005). The reverse phase high-performance liquid chromatography method was effective in quantifying these diterpenes kahweol and cafestol in fresh fruits, leaves, and roasted coffee beans (Dias et al. 2010). Good recovery (average of 99% for kahweol and 94% for cafestol), repeatability, and linearity were obtained. Detection limits of 2.3 and 3.0 mg/100 g were observed for kahweol and cafestol. The endosperm and perisperm of *Coffea arabica* cv. IAPAR 59 showed elevated amounts of kahweol as compared to the pericarp and leaves. In contrast, cafestol was

detected in all samples except in leaves from *Coffea canephora* cv. Apoatã.

Soluble condensed tannins may comprise 0.8%–2.8% of *C. arabica* and *C. canephora* skin and pulp, with higher levels observed in *C. canephora,* and with prodelphinidins exceeding procyanidinsin the ratio of 2.2 to 6:1 (Clifford and Ramirez-Martinez 1991a; Barcelos et al. 2001; Ulloa Rojas et al. 2003). Small levels of insoluble condensed tannins may be also found in the pulp (Clifford and Ramirez-Martinez 1991a). Ensiled coffee pulp tannin levels together with cellulose and total phenols levels were lower than oven dried coffee pulp (Ulloa Rojas et al. 2003). Storage of dehydrated arabica coffee skin and pulp produced a linear decrease in tannins content, 38.6%/year and also lignin (Barcelos et al. 2001).

Free and conjugated biogenic amines (putrescine, cadaverine, serotonin, tyramine, spermidine, and spermine) were found in green and roasted arabica and robusta coffee beans (Casal et al. 2004). Putrescine was the main biogenic amine present in the green beans either free or conjugated. With roasting, a significant loss in the free and conjugated biogenic amines levels was observed, especially the free ones. Free putrescine could be used in the discrimination of arabica and robusta green beans with high statistical significance. Tyramine could be considered a chemical marker for Angolan robustas.

Phytochemicals in Roasted and Brewed Coffee

Robusta green coffee was found to have higher total and protein tryptophan, whereas Arabica had higher free tryptophan levels (Martins and Gloria 2010). 5-HTP (5-hydroxytryptophan) was not detected in the samples before and after roasting. Free tryptophan was completely degraded during roasting. Roasting significantly affected protein tryptophan. The rate of loss was smaller in Arabica compared to Robusta at every roasting degree. A beverage prepared the Brazilian way with a medium-roasted coffee provided 1.4–2.5 mg tryptophan/50 mL cup. Cherry coffee, a variety of *C. canephora* exhibited the highest overall content of total phenols (42.37 mg GAE/g), followed by Minas coffee (*C. arabica*), while Cioccolatato coffee (*C. arabica*) contained the lowest TPC (33.12 mg GAE/g). Cherry coffee also exhibited the highest content of individual classes of polyphenols (flavan-3-ols, procyanidins and tannins), while the highest content of chlorogenic acid (CQA) derivatives was found in Minas and Cioccolatato coffees. The highest content of total and individual polyphenolic compounds was determined in all coffees roasted in both light and medium roasting conditions, which was also observed for the content of CQA derivatives and antioxidant capacity of roasted coffees. The highest caffeine content in the coffee samples was 0.06–2.55%. Light roasted Cherry coffee contained the highest overall content of caffeine among all coffees, which exhibited a decrease with intensified roasting.

During roasting, some CGA were reported to be isomerized, some transformed into quinolactones (CGL) due to dehydration and formation of an intramolecular bond and some hydrolyzed and degraded into low molecular weight compounds (Trugo and Macrae 1984a; Leloup et al. 1995; Clifford 2000; Farah et al. 2005). Both CGA and CGL are important compounds for flavor and potentially beneficial to human health (Perrone et al. 2008). High levels of CGA had been reported in coffee beans (Leloup et al. 1995). Five of the quinic acids and three of the quinides plus four lactones were detected in roasted Kenyan robusta coffee (Scholz and Maier 1990). The identities of (±)-quinic acid (systematic IUPAC names ID-I(OH),4,5/3- and JL-J(OH),3,4/5-tetrahydroxycyclohexanecarboxylic acids), seyllo-quinic acid (systematic IUPAC name l(OH),3,5/4-tetrahydroxycyclohexanecarboxylic acid) and (±)-epi-quinic acids (systematic IUPAC names JD-l(OH),5/3,4- and 1 h-J(OH),3/4,5-tetrahydroxycyclohexanecarboxylic acids) were confirmed. Three remaining unidentified quinic had a meso structure (5,3,4,5-, 1,4/3,5- and J/3,4,5-tetrahydroxycyclohexanecarboxylic acids) and hence were designated meso-X, meso-Y, and meso-Z; all had not been reported in the literature before. Also, the identities of

(±)-quinide [l,3-7-1actone of (±) quinic acid], and (±)-epi-quinide [l,3-7-1actone of (+)-epi-quinic acid] were positively identified. The two quinides left were referred to as quinide 2 and quinide 4. The amounts of (±)-quinic acid and (±)-quinide decreased at high degrees of roasting. Six stereoisomeric quinic acids (four meso forms and two pairs of enantiomers), four γ-quinides (four pairs of enantiomers), and three δ-quinides (two meso forms and one enantiomeric pair) and their γ-and δ-lactones were formed under the roasting conditions of coffee (Scholz-Bottcher et al. 1991). The existence of neo-quinic acid, its γ- lactone and δ-lactone, of epi-δ-quinide, of two meso-quinic acids, and of another γ-quinide was reported for the first time. Chlorogenic acid lactones, derivatives of caffeic acid namely 3- caffeoylquinic acid-γ-lactone (3-CQL) and 4-caffeoylquinic acid-γ-lactone (4-CQL) were identified in roasted coffee (Bennat et al. 1994). The content of the caffeoylquinides in commercial coffee samples ranged from 1.5 to 3.5 g/kg dry matter. The average contents of mono-caffeoylquinic acids and dicaffeoylquinic acids (CQA and di-CQA), corresponding lactones (CQL) and feruloylquinic acids (FQA) in commercial roasted coffee samples (n = 12) were: 3-CQA, 5·0 g/kg; 4-CQA, 6·2 g/kg; 5-CQA, 11·4 g/kg; 4-FQA, 0·7 g/kg; 5-FQA, 1·4 g/kg; 3-CQL, 2·1 g/kg; 4-CQL, 1·0 g/kg 1; 3,4-di-CQA, 0·7 g/kg; 3,5-di-CQA, 0·4 g/kg and 4,5-di-CQA, 0·8 g/kg dry matter (Schrader et al. 1996). Keeping coffee brews at an elevated temperature (4 h at 80°C) reduced the amounts of CQL to 60% of the initial value. The contents of 3-CQA and 4-CQA increased, whilst that of 5-CQA decreased. The overall contents of CQA decreased. Farah et al. (2005) identified seven CGLs during the roasting of coffee beans in *Coffea arabica* cv. Bourbon, *C. arabica* cv. Longberry, and *C. canephora* cv. Robusta: 3-caffeoylquinic-1,5-lactone (3-CQL), 4-caffeoylquinic-1,5-lactone (4-CQL), 3-coumaroylquinic-1,5-lactone (3-pCoQL), 4-coumaroyquinic-1,5-lactone (4-pCoQL), 3-feruloylquinic-1,5-lactone (3-FQL), 4-feruloylquinic-1,5-lactone (4-FQL), and 3,4-dicaffeoylquinic-1,5-lactone (3,4-diCQL). 3-CQL was the most abundant lactone in *C. arabica* and *C. canephora*, reaching maximum values of 230 mg and 254 mg/100 g (dry weight), respectively, at light medium roast. 4-CQL was the second most abundant lactone (116 mg and 139 mg/100 g), respectively. The relative levels of 3-CQL and 4-CQL in roasted coffee were reverse to those of their precursors in green coffee. Both CGA and CGL are important compounds for flavor and potentially beneficial to human health (Perrone et al. 2008). In addition to 19 previously identified CGA and CGL, 1-feruloylquinic acid, 1-feruloylquinic lactone and 3,4-diferuloylquinic acid were quantified in *C. arabica* and *C. canephora*, the contents of 3-*p*-coumaroylquiniclactone and 4-*p*-coumaroylquinic lactone were found in *C. canephora* and 3,4-di-*p*-coumaroylquinic acid was identified in *C. arabica* (Perrone et al. 2008). The content of total CGA lactones increases until about 14% weight loss, i.e., light medium roast, reaching average levels of 398 and 424 mg/dL (dm) for Arabica and Robusta coffees, respectively, and decreasing gradually thereafter (Farah et al. 2005; Bennat et al. 1994). The degradation of seven chlorogenic acids was followed during roasting of Arabica and Robusta coffee (Trugo and Macrae 1984). Losses of about 60% were observed when mild roasting conditions were used and almost 100% after severe roasting. Trigonelline and chlorogenic acids contents in Arabica and robusta coffee beans roasted at 220ºC decreased with roasting intensity (time) (Bicho et al. 2011). Trigonelline level decreased from 1.274% at 7 min roasting to 0.566% at 11 min for Arabica and for Robutsa from 0.912 at 7 min roasting to 0.485% at 11 min roasting. Total caffeoylquinic acid (comprising 3-CQA, 4-CQA and 5CQA) decreased from 0.274 mg/cm^3 at 7 min roasting to 0.017 mg/cm^3 at 11 min for Arabica coffee and from 3.997 mg/cm^3 at 7 min to 1.004 mg/cm^3 at 11 min for robusta. Total dicaffeoylquinic (comprising 3,4-diCQA, 3,5-diCQA, 4,5-diCQA) decreased from 3.939 mg/cm^3 at 7 min roasting to 0.794 mg/cm^3 at 11 min for Arabica coffee and from 0.497 mg/cm^3 at 7 min to 0.050 mg/cm^3 at 11 min for robusta. Total feruolilquínic acids (comprising 3-FQA, 4-FQA, 5-FQA) decreased from 0.0.194 mg/cm^3 at 7 min roasting to

0.060 mg/cm^3 at 11 min for Arabica coffee and from 0.465 mg/cm^3 at 7 min to 0.158 mg/cm^3 at 11 min for robusta. Soluble solid and caffeine contents and pH levels for both coffees were lowest at medium roasting (9 min). Arabica coffee contained higher levels of trigonelline and soluble solids than robusta but the latter was higher in caffeine content and pH.

A group of ethyl acetate soluble compounds formed from *O*-hydroxycinnamoyl quinic acid derivatives upon coffee roasting was identified as the key compounds contributing to the bitter taste of roasted coffee beverages (Frank et al. 2006). 3-*O*-caffeoyl-γ-quinide (2a), 4-*O*-caffeoyl-γ-quinide (3a), 5-*O*-caffeoyl-epi-δ-quinide (4a), 4-*O*-caffeoyl-muco-γ-quinide (5a), 5-*O*-caffeoyl-muco-γ-quinide (6a), 3-*O*-feruloyl-γ-quinide (2b), and 4-*O*-feruloyl-γ-quinide (3b) were identified as intense coffee bitter tastants. Besides these individual bitter compounds, a highly complex and intensely bitter HPLC fraction 15 was isolated from the ethyl acetate extractables of coffee brew. COSY spectroscopy and alkaline hydrolytic degradation evidence suggested that the bitter taste of that fraction was due to a multiplicity of rather complex quinic acid lactone isomers multiply esterified with *p*-coumaric acid, caffeic acid, ferulic acid, 3,4-dimethoxycinnamic acid, and quinic acid, respectively. As representatives of this fraction, 3,4-*O*-dicaffeoyl-γ-quinide(10),3,5-*O*-dicaffeoyl-*epi*-δ-quinide (11), and 4,5-*O*-dicaffeoyl-*muco*-γ-quinide (12) were isolated, purified, and identified as strongly bitter-tasting compounds in roasted coffee.

Roasting of coffee affected the chlorogenic acids, caffeine and polycyclic aromatic hydrocarbons levels in two *Coffea* cultivars: *Coffea arabica* cv. Catuaí Amarelo and *Coffea canephora* cv. Apoatã (Tfouni et al. 2012). Caffeine levels were higher in *C. canephora* (1,486–1,884 mg/100 g) than in *C. arabica* (1,110–1,255 mg/100 g) and increased up to 21% at darker roasts. Summed CQA levels were higher in green coffee (4,661 and 4,946 mg per 100 g) and decreased at darker roasts (234 and 377 mg per 100 g), showing no difference between the coffee cultivars studied. Polycyclic aromatic hydrocarbons summed levels varied from 0.052 to 0.814 μg/kg (*C. arabica*) and 0.108 to 0.392 μg/kg (*C. canephora*).

Decaffeination produced a 16% average increase in the levels of total CGA in green coffee (dry matter), along with a 237% increase in CGL direct precursors (Farah et al. 2006). Different degrees of roasting showed average increments of 5.5–18% in CGL levels of decaffeinated coffee, compared to regular coffee. In contrast, CGA levels in roasted coffee were 3–9% lower in decaffeinated coffee compared to regular coffee.

Extracts from roasted Arabica and Robusta coffees were found to contain 20–36% carbohydrates, depending on the degree of extraction (Thaler 1979). They were composed predominantly of mannan and galactan in about the same proportions, the share of glucan and araban constituting 1–3% of the extracts. With dialysis a group of polysaccharides with a molecular weight of more than 10,000 was separated, constituting about half of the carbohydrates of the extracts. In addition, another group of almost intact high polymeric carbohydrates as copper complexes was found, consisting only of mannan and galactan, mannan predominating significantly. Arabica and Robusta coffees showed differences in this respect. Whereas Arabica coffee was able to release only a certain amount of these very high-polymeric carbohydrates, Robusta coffee delivered ever greater amounts of these polysaccharides with increasing extract yields. The content of arabinogalactans extracted from robusta green coffee was higher than that extracted from Arabica (Nunes and Coimbra 2002). For roasted coffees, the amount of galactomannans extracted ranged from 0.66% to 0.92% (w/w). These values were near 50% of those obtained from the arabica coffees using the same extraction procedure. However, the amount of arabinogalactans extracted from robusta coffees (0.56–0.72%) was in the range obtained from arabica. The structures of arabinogalactans and galactomannans extracted from green and roasted coffees were not sufficiently different between robusta and arabica coffees to explain the observed differences in extraction yields for the arabinogalactans from

green coffees and for the galactomannans from roasted coffees. The total polysaccharide content and the structures of the galactomannans and arabinogalactans in the two green coffee varieties were also very similar.

Both melatonin and serotonin 5-HT (5-hydroxytryptamine) were detected in green coffee beans (5.8 μg/g dry weight (DW), 10.5 μg/g DW) and also in roasted beans of *C. canephora* (8.0 μg/g DW, 7.3 μg/g DW) (Ramakrishna et al. 2012). Melatonin (3.0 μg/50 mL) and 5-HT (4.0 μg/50 mL) were detected in coffee brew.

Coffee brew fractions differing in molecular weight (Mw) were isolated from green and light-, medium-, and dark-roasted coffee beans (Bekedam et al. 2008a). It was found that the melanoidin level in all fractions correlated with the nitrogen and the protein content and with the phenolic groups' and ester-linked quinic acid levels. They found proteins and chlorogenic acids to be primarily involved in melanoidin formation. Initial roasting, from green to light-roasted beans, especially led to the formation of intermediate Mw (IMw) melanoidins mainly due to Maillard reactions when compared to high Mw (HMw) melanoidins. Additionally, they found that prolonged roasting predominantly led to formation melanoidins with a high Mw and that arabinogalactans appeared to be relatively more involved in melanoidin formation than galactomannans. They concluded that galactomannans were continuously incorporated in arabinogalactan proteins (AGP) -melanoidins upon roasting. Bekedam et al. (2006) found most high molecular weight (HMw) coffee melanoidins to be soluble at high ethanol concentrations. The amino acid composition of the HMw fractions was similar, while 17% (w/w) of the nitrogen was non-protein nitrogen (NPN), probably originating from degraded amino acids/proteins and now part of melanoidins. A strong correlation between the melanoidin content, the NPN, and protein content was found. The majority of the low molecular weight (LMw) melanoidins of coffee brew were found to have an apolar character, whereas most non-melanoidins had a polar character (Bekedam et al. 2008b). The melanoidins isolated showed similar features as high molecular weight coffee melanoidins. All three melanoidin fractions contained approximately 3% nitrogen, indicating the presence of incorporated amino acids or proteins; glucose was the main sugar present in these melanoidins. The LMw melanoidins exposed a negative charge, and this negative charge was inversely proportional to the apolar character of the melanoidins. Phenolic group levels as high as 47% were found, which could be explained by the incorporation of chlorogenic acids in these melanoidins. For all coffee brew melanoidin fractions, it was found that more quinic acid than caffeic acids was released upon saponification (Bekedam et al. 2008c). Quinic acid levels correlated with melanoidin levels, indicating that quinic acid was incorporated in melanoidins. The quinic acid level correlated with the phenolic acid group level, indicating that quinic acid was incorporated to a similar extent as the polyphenolic moiety from chlorogenic acids (CGAs). The quinic acid and caffeic acid released from brew fractions by enzymes confirmed the incorporation of intact CGAs. Intact CGAs were proposed to be incorporated in melanoidins upon roasting via caffeic acid through mainly nonester linkages. Additionally, a total of 12% of quinic acid was identified in coffee brew, whereas only 6% was reported in the literature so far.

Daglia et al. (2007a) found that small amounts of glyoxal and methylglyoxal occurred naturally in green coffee beans. Conversely, diacetyl was not found in green beans and was formed later in the roasting process. Therefore, light and medium roasted coffees had the highest glyoxal and methylglyoxal content, whereas dark roasted coffee contained smaller amounts of glyoxal, methylglyoxal, and diacetyl. More recently, α-dicarbonyl compounds had been implicated in the glycation process. Furan was not detected in green coffees of *Coffea arabica* and *Coffea canephora* whereas levels between 911 and 5,852 μg/kg were found in the roasted samples (Arisseto et al. 2011). Higher concentrations were found in *Coffea canephora* and darker ground coffees. Some of the potential furan precursors were observed in significant amounts in green coffee, especially

sucrose and linoleic acid, but their concentrations could not be correlated to furan formation. Furan levels in coffee brews prepared from roasted ground coffees varied from <10 to 288 μg/kg. The factor that most influenced the furan content in coffee brew was the brewing procedure.

The content of acrylamide in coffee reaches a peak early in the roasting process, reflecting occurrence of both formation and destruction of acrylamide during roasting (Lantz et al. 2006). The main factors affecting the level of acrylamide in roasted coffee appeared to be the Arabica/Robusta ratio, with Robusta giving higher levels; time and degree of roast, with both shorter and lighter roasting at the edges of the normal roasting range giving higher levels; storage condition and time, with clear reduction at ambient storage. In separate studies, Bagdonaite et al. (2008) reported that the potential precursors of acrylamide were 3-aminopropionamide, carbohydrates, and amino acids. The highest amounts of acrylamide formed in coffee were during the first minutes of the roasting process [3,800 ng/g in Robusta (*Coffea canephora* robusta) and 500 ng/g in Arabica (*Coffea arabica*)]. With increase in roasting time the concentration of acrylamide decreased. Robusta coffee contained significantly larger amounts of acrylamide (mean = 708 ng/g) than Arabica coffee (mean = 374 ng/g). Asparagine was the limiting factor for acrylamide formation in coffee. Thermal decarboxylation and elimination of the α-amino group of asparagine at high temperatures (>220°C) led to a measurable but low formation of acrylamide.

The chlorogenic acids (CGA) identified in commercial brewed coffees (seven regular and five decaffeinated) comprised three caffeolylquinic acids (3-CQA, 4-CQA, and 5-CQA), three feruloylquinic acids (3-FQA, 4-FQA, and 5-FQA), and three dicaffeoylquinic acids (3,4-diCQA, 3,5-diCQA, and 4,5-diCQA) (Fujioka and Shibamoto 2008). Total CGAs ranged from 5.26 to 17.1 mg/g in regular coffees and from 2.10 to 16.1 mg/g in decaffeinated coffees. Among CGA, 5-CQA predominated, ranging from 2.13 to 7.06 mg/g coffee, and comprising 36–42% and 37–39% of the total CGA in the regular and decaffeinated coffees, respectively. CGA isomer contents were, in decreasing order, 5-CQA > 4-CQA > 3-CQA > 5-FQA > 4-FQA > 3-FQA > 3,4-diCQA > 4,5-diCQA, 3,5-diCQA. The caffeine content in regular coffee ranged from 10.9 to 16.5 mg/g and in decaffeinated coffees from 0.34 to 0.47 mg/g.. The pH of regular ranged from 4.95 to 5.99 and decaffeinated coffees from 5.14 to 5.80.

Studies showed that the content of β-carboline (norharman and harman) contents in espresso coffee was dependent primarily on the coffee species, followed by brew length (Alves et al. 2007). Roasting degree had only a minor influence on the final content of norharman and harman in espresso coffee. The content of β-carbolines (μg/L) in espresso coffee was similar to that of mocha coffee, both being more concentrated than filter and press-pot coffees. For the caffeinated 30 mL of espresso coffee, the arabica coffees contained about 4.08 μg of norharman and 1.54 μg of harman. Commercial blends (usually with a maximum of 30% robusta) ranged from the cited arabica values to 10.37 μg of norharman and 4.35 μg of harman. Total isoflavone level was found to be 6-fold higher in robusta coffees than in arabica ones, mainly due to formononetin. During roasting, the content of isoflavones decreased, whereas their extractability increased (especially for formononetin). (Alves et al. 2010) Total isoflavones in espresso coffee (30 mL) varied from ~40 μg (100% arabica) to ~285 μg (100% robusta), with long espressos (70 mL) attaining more than double isoflavones of short ones (20 mL). Espressos (30 mL) prepared from commercial blends contained average amounts of 6, 17, and 78 μg of genistein, daidzein, and formononetin, respectively. Comparison of different brewing methods revealed that espresso contained more isoflavones (~170 μg/30 mL) than a cup of press-pot coffee (~130 μg/60 mL), less than a mocha coffee (~360 μg/60 mL), and amounts similar to those of a filtered coffee cup (~180 μg/120 mL).

Chlorogenic acids (CGA) and related compounds had been reported to possess a number of beneficial health properties related to their potent antioxidant activity as well as hepatoprotective, hypoglycaemic, antiviral (Farah and Donangelo

2006) and neuroprotective activities as elaborated below. Coffee also contained other compounds with health benefits such as amylase inhibition and antimicrobial activities. Diterpene cafestol, one of the major components of coffee, had been reported to havebeneficial health through various biological activities such as chemopreventive, antitumorigenic, hepatoprotective, antioxidative and antiinflammatory effects (Shen et al. 2010). On the down-side, coffee also contained diterpenes which had been reported to elevate cholesterol levels.

Antioxidant Activity

Reducing substances of *C. robusta* coffee samples were found to be significantly higher when compared to those of *C. arabica* samples (Daglia et al. 2000). Antioxidant activity (using β-carotene-linoleic acid) for green coffee samples were slightly higher than for the corresponding roasted samples while protective activity against rat liver cell microsome lipid peroxidation was significantly lower in green coffee compared to that of all roasted samples. Extraction with three different organic solvents (ethyl acetate, ethyl ether, and dichloromethane) showed that the most protective compounds were extracted from acidified dark roasted coffee solutions with ethyl acetate. The analysis of acidic extract yielded five fractions. Higher molecular mass fractions were found to possess antioxidant activity while the lower molecular mass fractions showed protective activity. The small amounts of these acidic, low molecular mass protective fractions isolated indicated that they contained very strong protective compounds. In-vitro (chemical deoxiribose assay) and ex-vivo (in IMR32 cells) antihydroxyl radical activity showed that both green and roasted *Coffea arabica* and *Coffea robusta* coffee samples possessed antiradical activity and their more active component was 5-*O*-caffeoyl-quinic acid (Daglia et al. 2004). Roasting process induced high molecular weight components (later Maillard reaction products, i.e., melanoidins) that also possessed antiradical activity in coffee. Delgado-Andrade et al. (2005) found that coffee brews, coffee melanoidins, and bounded melanoidin compounds exerted highest antioxidant activity in aqueous media, whereas pure melanoidins was not dependent on the reaction media. The higher contribution of melanoidins to the total antioxidant activity of coffees was shown to be caused by the low molecular weight compounds linked noncovalently to the melanoidin skeleton. The highest correlation was found between 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing power (FRAP) methods. Perrone et al. (2012) found that changes in the relative content of free chlorogenic acids (CGA), free lactones, and melanoidin-bound phenolic acids during roasting indicated that phenolic compounds were incorporated into melanoidins mainly at early stages of the process, being thereafter partly oxidized to dihydrocaffeic acid, and degraded. Although less than 1% of CGA in green coffee was incorporated into melanoidins during roasting, the relative content of melanoidin-bound phenolic acids increased significantly during this process, reaching up to 29% of total phenolic compounds in brews from dark roasted coffees. Regardless of the antioxidant activity assay used and considering all roasting degrees, the overall contribution of CGA to the antioxidant activity of the whole brews was higher than that of melanoidin-bound phenolic compounds. It was estimated that the melanoidin-bound phenolic compounds contributed to 25–47% of the antioxidant activity, depending on the assay used.

Roasting resulted in the degradation of chlorogenic acid (5-CQA) and formation of melanoidins, while antioxidant activity was largely unaffected by roasting (Vignoli et al. 2011). The extraction of soluble coffee more prominently affected the antioxidant activity of light-roasted coffee, mainly because it favoured the extraction of 5-CQA. The larger caffeine content in robusta coffee resulted in greater antioxidant activity. All of soluble coffees extracted by various methods from light, medium and dark-roasted arabica and robusta beans possessed antioxidant potential, which was conferred by their concentrations of phenolic compounds, caffeine and melanoidins.

All coffee extracts showed marked direct antioxidant activity: medium roasts > light roast AB1 (caffeoylquinic acid (CQA)-rich Arabica Brazil extract) > dark roast AB2 (N-methylpyridinium (NMP)-rich Arabica Brazil extract) (Bakuradze et al. 2010). The coffee extracts reduced t-butylhydroperoxide-induced reactive oxygen species (ROS) level in HT-29 cells (AB2 > medium roasts > AB1). NAD(P)H:quinone oxidoreductase 1 expression and γ-glutamylcysteine ligase expression were markedly induced by AB1 and 5-CQA, but not by AB2 and NMP. Caffeic acid and 5-CQA elicited highest Trolox equivalent antioxidant capacity/oxygen radical absorbing capacity values (5-CQA: 1.3/3.5 mM and caffeic acid: 1.3/3.9 mM trolox). Reactive oxygen species level was markedly reduced by 5-CQA (≥3 μM), catechol (30 μM) and trigonelline (≥30 μM), whereas menadione-induced DNA damage in Caco-2 cells was diminished by NMP compounds (1–30 μM).

Caffeic acid exhibited stronger in-vitro antioxidant activity than chlorogenic acid (Sato et al. 2011). The uptake of chlorogenic acid by Caco-2 cells was much less than that of caffeic acid. In-vivo studies, both chlorogenic acid and caffeic acid had effects on intestinal ischemia–reperfusion injury. Caffeic acid with a stronger antioxidant activity than that of chlorogenic acid and chlorogenic acid being hydrolyzed into caffeic acid in the intestine, they postulated that caffeic acid played a major role in the protective effect of chlorogenic acid against ischemia–reperfusion injury.

Antimicrobial Activity

Minimum inhibitory concentration (MIC), biofilm inhibition and biofilm reduction of *Streptococcus mutans*, results were correlated with the concentration of coffee compounds and aqueous extracts of green and roasted regular and decaffeinated *Coffea arabica* and *Coffea canephora* beans (Antonio et al. 2010). 5-caffeoylquinic acid, trigonelline and caffeic acid solutions showed bacteriostatic activity (MIC = 0.8 mg/mL). Lighter and regular extracts showed higher inhibitory activity than darker and decaffeinated extracts, with an inverse correlation between bacterial colony-forming units and roasting degree. Only regular *C. canephora* extracts showed biofilm formation inhibition. The joint effect of chlorogenic acids, trigonelline and caffeine or other compounds removed by decaffeination appeared to be one of the causes for coffee antibacterial activity against *S. mutans*, a cariogenic bacterium. Light roasted *C. canephora* extract exhibited in-vitro antibacterial activity against cariogenic bacteria *Streptococcus mutans* (Antonio et al. 2011). The MIC and MBC for *S. mutans* were 7 mg/mL and 160 mg/mL, respectively, the extract was inactive against for *Streptococcus sobrinus*. The extract produced a 4-log reduction in the number of colonies of *S. mutans* after 3-h treatment with undiluted extract (20%) and MBC concentration (16%). At depths up to 30 μm from the enamel surface, coffee extract and chlorhexidine promoted higher cross-sectional microhardness values when compared to blank/negative controls. In another study after 30 min contact with unsweetened and sweetened (10% sucrose) brewed light-roasted *Coffea canephora* brews, the average microorganism count in the biofilms formed by non-stimulated saliva from three volunteers, was reduced by 15.2% and 12.4%, respectively, with no statistical difference among them (Antonio et al. 2012). *Coffea canephora* extract reduced the microbial count in oral biofilm, and their data suggested that sucrose concentration in coffee brew could influence its antimicrobial property against the referred biofilm. Antonio et al. (2011) found light roasted *C. canephora* extract to have benefits as an anticariogenic. The extract showed antibacterial activity against *Streptococcus mutans* with MIC and MBC for S. mutans were 7 mg/mL and 160 mg/mL respectively. At depths up to 30 μm from the enamel surface, coffee extract and chlorhexidine promoted higher cross-sectional microhardness values when compared to blank/negative controls.

All solutions of *Coffea arabica, Coffea robusta* green and roasted and several commercial coffee samples significantly reduced *Streptococcus mutans*' adhesive properties

(Daglia et al. 2002). The inhibition of *S. mutans'* adsorption to saliva-coated hydroxyapatite beads was observed both when coffee was present in the adsorption mixture and when it was used to pretreat the beads, suggesting that coffee active molecules may adsorb to a host surface, preventing the tooth receptor from interacting with any bacterial adhesions. Among the known tested coffee components, trigonelline and nicotinic and chlorogenic acids were found to be very active. Dialysis separation of roasted coffee components also showed that a coffee component fraction with 1,000 Da < MW < 3,500 Da, commonly considered as low MW coffee melanoidins, may also contribute to the roasted coffee's antiadhesive properties. In subsequent studies, they found that whole high molecular weight coffee fraction (cHMW) and each of its melanoidin and non-melanoidin components (GFC1-5) inhibited *Streptococcus mutans*' adhesion, the strongest effect being exerted by cHMW (91%) and GFC1 (88%) (Stauder et al. 2010). *S. mutans* detachment from saliva-coated hydroxyapatite beads was four times greater (~20%) with cHMW and the GFC1 and GFC4 melanoidins than with controls. Biofilm production by *S. mutans* was completely abolished by cHMW and was reduced by 20% by the melanoidin components GFC2 and GFC4 and by the non-melanoidin component GFC5 compared with controls.

A lipid transfer protein of 9 kDa isolated from *Coffea canephora* designated Cc-LTP(1) exhibited strong antifungal activity, against *Candida albicans*, and also promoted morphological changes including the formation of pseudohyphae on *Candida tropicalis* (Zottich et al. 2011).

Commercial coffee extracts, caffeic acid and trigonelline showed similar inhibitory effect against the growth of nine strains of enterobacteria (Almeida et al. 2006). Caffeine, chlorogenic acid, and protocatechuic acid showed particularly strong effect against *Serratia marcescens* and *Enterobacter cloacae*. The low IC_{50} and IC_{90} values for trigonelline, caffeine, and protocatechuic acids indicated them to have potential as natural antimicrobial agents against *Salmonella enterica*.

Antihypertensive Activity

Suzuki et al. (2006) reported that when spontaneously hypertensive rats were fed diets containing 0.5% 5-caffeoylquinic acid (CQA), a representative chlorogenic acid, for 8 weeks (approximately 300 mg/kg per day), the development of hypertension was inhibited compared with the control diet group. They found that dietary CQA reduced oxidative stress and improved nitric oxide bioavailability by inhibiting excessive production of reactive oxygen species in the vasculature, leading to the attenuation of endothelial dysfunction, vascular hypertrophy, and hypertension in spontaneously hypertensive rats. Zhao et al. (2012) in their recent review of antihypertensive effects and mechanism of chlorogenic acids stated that the dietary consumption of CGAs may hold promise for providing a non-pharmacological approach for the prevention and treatment of high blood pressure. They asserted that the metabolites of CGAs attenuated oxidative stress (reactive oxygen species), which led to the benefit of blood-pressure reduction through improved endothelial function and nitric oxide bioavailability in the arterial vasculature. Montagnana et al. (2012) stated that chlorogenic acids would be effective in decreasing blood pressure, systemic inflammation, risk of type 2 diabetes, and platelet aggregation, whereas caffeine intake had instead been reported to be associated with decreased body weight, as well as with increased flow-mediated dilatation and fibrinolysis. They added that most benefits were evident in individuals with a rapid caffeine metabolizer genotype and a low baseline cardiovascular risk.

Antiinflammatory Activity

Kahweol and cafestol, coffee specific diterpenes, significantly suppressed the lipopolysaccharide (LPS)-induced production of prostaglandin E(2), COX-2 protein and mRNA expression, and COX-2 promoter activity in a dose-dependent manner in RAW 264.7 macrophages (Kim et al. 2004). Both prostaglandin

E(2), COX-2 protein play key roles in the processes of inflammation and carcinogenesis. Further, kahweol blocked the LPS-induced activation of NF-kappaB by preventing IkappaB degradation and inhibiting IkappaB kinase activity. Studies by Shen et al. (2010) suggested that cafestol, a major diterpene component of coffee may be a novel extracellular signal-regulated kinase inhibitor with AP-1-targeted inhibition of prostaglandin E2 (PGE2) production, a critical factor involved in inflammatory responses. Cafestol inhibited both PGE(2) production and the mRNA expression of cyclooxygenase (COX)-2 from lipopolysaccharide (LPS)-treated RAW264.7 cells.

In a study of 982 diabetic and 1,058 nondiabetic women without cardiovascular disease from the Nurses' Health Study, Williams et al. (2008) found that women with and without diabetes who drank ≥4 cups of coffee per day had significantly higher adiponectin concentrations than those who didn't drink coffee regularly (7.7 vs. 6.1 μg/mL, respectively, in diabetic women,; 15.0 vs. 13.2 μg/mL in nondiabetic women). Similar associations were observed for caffeine intake. They confirmed previously reported inverse associations of coffee consumption with inflammatory markers, C-reactive protein and tumor necrosis factor-α receptor II. Their results confirmed high consumption of caffeine-containing coffee to be associated with higher adiponectin and lower inflammatory marker concentrations.

Kempf et al. (2010) found that coffee consumption appeared to have beneficial effects on subclinical inflammation and HDL cholesterol, whereas no changes in glucose metabolism were found in their study. Significant changes were observed for serum concentrations of interleukin-18, 8-isoprostane, and adiponectin (8 compared with 0 cups coffee/day). Serum concentrations of total cholesterol, HDL cholesterol, and apolipoprotein A-I increased significantly by 12, 7, and 4%, respectively, whereas the ratios of LDL to HDL cholesterol and of apolipoprotein B to apolipoprotein A-I decreased significantly by 8% and 9%, respectively (8 compared with 0 cups coffee/day). Further, coffee consumption led to an increase in coffee-derived compounds, mainly serum caffeine, chlorogenic acid, and caffeic acid metabolites, useful as biomarkers of coffee intake.

During the 26 years of follow-up, Choi and Curhan (2010) documented 896 confirmed incident cases of gout among 89,433 female participants in the Nurses' Health Study and found an inverse association between higher coffee intake and the risk of gout, a common and excruciatingly painful inflammatory arthritis. The multivariate relative risks (RRs) for incident gout according to coffee-consumption categories [ie, 0, 1–237, 238–947, and ≥948 mL coffee/d (237 mL = one 8-ounce cup)] were 1.00, 0.97, 0.78, and 0.43, respectively. For decaffeinated coffee, the multivariate RRs according to consumption categories (0, 1–237, and ≥237 mL decaffeinated coffee/day) were 1.00, 1.02, and 0.77 respectively. There was an inverse association between total caffeine from all sources and the risk of gout; the multivariate RR of the highest quintile compared with the lowest quintile was 0.52.

Hepatoprotective Activity

Methyl 3,4-di-*O*-caffeoyl quinate (1), 3,4-di-*O*-caffeoyl quinic acid (2), methyl 4,5-di-*O*-caffeoyl quinate (3), and 3,5-di-*O*-caffeoyl quinic acid (4) extracted from water extract of propolis were more potent hepatoprotective agents against CCl4-toxicity than glycyrrhizin at a concentration of 10 μg/mL and one was the most potent among the four compounds in the cultured hepatocytes (Basnet et al. 1996a, b). Quinic acid (5) alone did not show hepatoprotective effects in cultured rat hepatocytes against CCl4-toxicity. Further, chlorogenic acid (6) or caffeic acid alone was found to be less potent than the dicaffeoyl quinic acid derivatives.

Studies showed that pre-treatment with chlorogenic acid (CGA) exhibited hepatoprotective effect against acute liver injury caused by lipopolysaccharide (LPS) in mice (Xu et al. 2010). CGA attenuated the infiltration of neutrophil cells and the necrosis of hepatocytes and decreased the elevated plasma levels of alanine aminotransferase and aspartate aminotransferase.

CGA pretreatment also suppressed hepatic mRNA expression of toll-like receptor 4 (TLR4), TNF-α and NF-kappaB p65 subunit. The findings suggested that the marked hepatoprotective effects on LPS-induced liver injury was possibly related to its anti inflammatory action. Coffee bean extract (CBE) reduced hepatic triglycerides in mice and rats fed high fat diets (Shimoda 2012). Among the polyphenolics of CBE, chlorogenic acid suppressed triglyceride accumulation, but did not influence the activity of carnitine palmitoyltransferase (CPT), a key enzyme in mitochondrial β-oxidation, 3-Caffeoyl quinic acid and feruloylquinic acids, in contrast, enhanced CPT activity. These polyphenolics appear to be at least partially involved in the anti-lipid oxidative effect of CBE leading to hepatic lipid reduction.

Chlorogenic acid was found to alleviate ischemia/reperfusion injury-induced liver injury in rats (Yun et al. 2012). Their hepatoporteite activity was suggested to be due to inhibition of inflammatory response and enhancement of antioxidant defense system. Chlorogenic acid attenuated the elevated levels of serum tumour necrosis factor-α, inducible nitric oxide synthase and cyclooxygenase-2 protein and mRNA expressions induced by ischemia/reperfusion. Chlorogenic acid enhanced heme oxygenase-1 expression and nuclear translocation of nuclear factor erythroid 2-related factor 2.

Chlorogenic acid, the main phenolic compound in coffee, was found to be a potent inhibitor of nonhaeme iron absorption (Fleming et al. 1998; Hurrell et al. 1999). Hurrell et al. (1999). found that compared with a water control, beverages including coffee containing 20–50 mg total polyphenols/serving reduced Fe absorption by 50–70%, whereas beverages containing 100–400 mg total polyphenols/serving reduced Fe absorption by 60–90%. Fleming et al. (1998) reported that in the Framingham Heart Study, elderly participants consuming once cup (236 mL) coffee per week had 1% lower serum ferritin. There is increasing evidence suggesting that even mildly increased amounts of iron in the liver can be damaging, particularly if combined with other factors, such as alcohol use, assumption of hepatotoxic drugs, cirrhosis or chronic viral hepatitis (Di Bisceglie et al. 1992; Tsukamoto et al. 1995; Bonkovsky et al. 1996, 2003; Adams 1998; Tsukamoto and Lu 2001). Heavy iron overload as occurs in primary and secondary hemochromatosis can induce fibrosis of various parenchymal organs such as the liver, heart, and pancreas (Alla and Bonkovsky 2005). Lesser degrees of hepatic iron deposition are also risk factors associated with certain nonhemochromatotic liver diseases. Iron overload may suppress functions of the complement system (classic or alternative types) and in various clinical situations may tip the immunoregulatory balance unfavourably to allow enhanced growth rates of cancer cells and infectious organisms, and complicate the clinical management of pre-existing acute and chronic diseases (Walker and Walker 2000). Iron-reduction therapy had been shown to improve liver functions in a variety of pathological conditions (Bonkovsky et al. 2003), hence the increased intake of polyphenol compounds present in beverages like coffee may maintain a relatively lower iron status and therefore reduce the risk of liver injury (Mascitelli et al. 2008). Moreira et al. (2005) demonstrated iron-reducing activity of coffee beverages by using the ferric reducing antioxidant power (FRAP) assay. They found that beverages prepared with ground coffee had, on average, 27% higher FRAP values than those prepared with soluble coffee. In the former beverages, FRAP of *C. robusta* samples was significantly higher (on average, 50.3%) when compared to that of *C. arabica* samples and FRAP values decreased with increasing degree of roasting. A strong correlation ($R^2 > 0.91$) was found between FRAP and the total content of chlorogenic acids, particularly that of the caffeoylquinic acid isomers. The iron-reducing activity of coffee beverages was not influenced by caffeine. A number of studies had reported the beneficial effects of coffee on abnormal liver biochemistry, cirrhosis and hepatocellular carcinoma (Cadden et al. 2007).

The coffee diterpenes kahweol and cafestol exhibited hepatoprotective effects on carbon tetrachloride-induced liver damage in mice (Lee et al. 2007). Pretreatment with kahweol and

cafestol prior to the administration of CCl(4) significantly prevented the increase in the serum levels of hepatic enzyme markers (alanine aminotransferase and aspartate aminotransferase) and reduced oxidative stress, such as reduced glutathione content and lipid peroxidation, in the liver in a dose-dependent manner. Kahweol and cafestol exhibited antioxidant effects on FeCl(2)-ascorbate induced lipid peroxidation in a mouse liver homogenate, and on superoxide radical scavenging activity. The results suggested that the protective effects of kahweol and cafestol against the CCl(4)-induced hepatotoxicity possibly involved mechanisms related to their ability to block the CYP2E1-mediated CCl(4) bioactivation and free radical scavenging effects.

Anticancer Activity

In numerous animal model and in-vitro studies, kahweol/cafestol had been found to protect against the mutagenic/carcinogenic effects of several carcinogens such as heterocylic amines such as 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), aflatoxin B1, alkylating agents and 7,12-dimethylbenz[a]anthracene. Miller et al. (1991) showed that hamsters with cancer of the buccal pouch induced by 7,12-dimethylbenz[a] anthracene (DMBA) and receiving kahweol and cafestol in the diet (2 g/kg of food) exhibited a 35% reduction in tumour burden. Cavin et al. (1998) found that kahweol/cafestol diet significantly inhibited the covalent binding of aflatoxin B1 (AFB1) metabolites to DNA in the rat liver. Significant inhibition was detected at 2,300 p.p.m. and maximal reduction of DNA adduct formation to nearly 50% of the control value was achieved with 6,200 p.p.m. of dietary kahweol/cafestol. Two complementary mechanisms were postulated to account for the chemopreventive action of cafestol and kahweol against aflatoxin B1 in rats. A decrease in the expression of the rat activating cytochrome P450s (CYP2C11 and CYP3A2) was observed, as well as a strong induction of the expression of the glutathione-S-transferase (GST) subunit GST Yc2, which is known to detoxify highly the most genotoxic metabolite of AFB1. Studies also showed that kahweol/cafestol may have chemoprotective activity against AFB1 genotoxicity in both rats and humans In rat primary hepatocytes, kahweol/cafestol reduced the expression of cytochrome P450 CYP 2C11 and CYP 3A2, the key enzymes responsible for AFB1 activation to the genotoxic metabolite aflatoxin B1-8,9 epoxide (AFBO) (Cavin et al. 2001). In human liver epithelial cell lines cells, kahweol/cafestol also produced a significant inhibition of AFB1-DNA adducts formation linked with an induction of the human glutathione S-transferase GST-μ. They found that the protection afforded by kahweol/cafestol in human liver epithelial cell lineswas correlated with an induction of GST-μ, an enzyme known to be involved in AFB(1) detoxification (Cavin et al. 2002). Additionally, kahweol/cafestol K was found to inhibit P450 2B6, one of the human enzymes responsible for AFB(1) activation. Cavin et al. (2003) found that kahweol/cafestol exhibited protective effects against the genotoxicity of benzo[a]pyrene in rat primary hepatocytes and in human bronchial Beas-2B cells. Their data showed that the significant induction kahweol/cafestol of the detoxifying enzyme GST-Yp subunit was the key mechanism of protection against B[a]P DNA-binding in rat liver. In contrast, the phase I-mediated mechanism where kahweol/cafestol produced an inhibition of CYP 1A1 induction by B[a]P was of key significance for the kahweol/cafestol protection in human Beas-2B cells.

Studies by Huber et al. (2002b) found that in the liver of kahweol/cafestol–fed rats a dose-dependent increase of up to 2.4-fold in the activity of γ-glutamylcysteine synthetase (GCS), was observed, and associated with an increase in glutathione (GSH) of up to threefold. Their data showed that kahweol/cafestol increased GSH levels apparently through the induction of the rate limiting enzyme of GSH synthesis, which may be a key factor in the chemopreventive potential of coffee components. Huber et al. (2002a). showed that kahweol/cafestol was not only capable of increasing overall glutathione transferase (GST) and GST classes α, μ, and π but also of enhancing

UDP-glucuronosyltransferase (UDPGT) and GST-theta in the rat. All investigated kahweol/cafestol were strongest in liver and kidney, and some response was seen in lung and colon but none in the other organs. Their results showed that kahweol/cafestol treatment led to a wide spectrum of increases in phase II detoxification enzymes. These effects may not only contribute to local protection but also to anti-carcinogenesis in distant, less stimulated organs such as the colon. Further Huber et al. (2003) found that kahweol/cafestol and cafestol increased hepatic the DNA repair protein O(6)-methylguanine-DNA methyltransferase (MGMT) in a dose-dependent manner up to a maximum of 2.6-fold at 0.122% kahweol/cafestol in the feed in rats. Dose-response studies with kahweol/cafestol revealed that MGMT increased in parallel with GST-related parameters (overall GST, glutathione, γ-glutamylcysteine-synthetase) whereas the dose-response curves of of UDP-glucuronosyltransferase (UDPGT) and glutathione transferase pi (GST-pi) activity displayed a steeper slope. Increased expression level of MGMT may extend the antimutagenic/anticarcinogenic potential of coffee components to protection against DNA alkylating agents. In primary rat hepatocytes, Huber et al. (2004) found that kahweol/cafestol palmitates decreased hepatic N-acetyltransferase- (NAT)- dependent PhIP activity by 80%. The unique potential of kahweol/cafestol to convert rapid acetylators to a slow acetylator phenotype, accompanied by GST induction, might contribute to chemoprevention against cancers associated with heterocyclic amines. In a more recent animal study, Huber et al. (2008) found that kahweol/cafestol decreased potentially carcinogen-activating hepatic cytochrome P450 (CYP450) and sulfotransferase (SULT). Kahweol/cafestol decreased the metabolism of four resorufin derivatives representing CYP1A1, CYP1A2, CYP2B1, and CYP2B2 activities by approximately 50%. In contrast, coffee increased the metabolism of the resorufin derivatives up to sevenfold which was only marginally influenced by filtering. CYP2E1 activity and mRNA remained unchanged by K/C and coffee. K/C but not coffee decreased SULT by approximately 25%. Theri resuls suggested that kahweol/cafestol may contribute to chemoprevention but such protection to drinker with coffees was unlikely. Higgins et al. (2008) showed that mice fed containing 3% or 6% coffee for 5 days had increased levels of mRNA for cancer chemopreventive enzymes NAD(P)H:quinone oxidoreductase 1 (NQO1) and glutathione S-transferase class Alpha 1 (GSTA1) in the liver and small intestine, while at 6% coffee had increased levels of UDP-glucuronosyl transferase 1A6 (UGT1A6) and the glutamate cysteine ligase catalytic (GCLC) in the small intestine. Up-regulation of these mRNAs was significantly greater in mice possessing Nrf2 (NF-E2 p45 subunit-related factor 2) than those lacking the transcription factor. Treatment of mouse embryonic fibroblasts (MEFs) from nrf2(+/+) mice with either coffee or the coffee-specific diterpenes cafestol and kahweol increased NQO1 mRNA. The results showed that priming Priming of nrf2(+/+) MEFs, but not nrf2(-/-) MEFs, with C+K conferred 2-fold resistance towards acrolein.

Cafestol treatment inhibited human renal Caki cells viability a dose-dependent manner by inducing apoptosis, as evidenced by DNA fragmentation and the accumulation of sub-G1 phase (Choi et al. 2011). Cafestol-induced apoptosis was associated with the reduction of mitochondrial membrane potential (MMP), activation of caspase 3, cytochrome c release, and down-regulation of anti-apoptotic proteins (Bcl-2, Bcl-xL, Mcl-1 and cFLIP). Further cafestol inhibited phosphatidylinositol 3-kinase (PI3K)/Akt signal pathway, and PI3K inhibitor LY29004 significantly increased cafestol-induced apoptosis in Caki cells. The results suggested cafestol to have potential as a therapeutic agent for preventing cancers such as renal carcinoma. Cárdenas et al. (2011) using various in-vivo and ex-vivo angiogenesis assays showed kahweol to be an anti-angiogenic compound with inhibitory effects with effects on specific steps of the angiogenic process: endothelial cell proliferation, migration, invasion and tube formation on matrigel. Kahweol inhibited two key molecules involved in the process, matrix metalloproteinase-2 (MMP-2) and

urokinase-type plasminogen activator (uPA). Kahweol demonstrated its antiinflammatory potential by its inhibition of both COX-2 expression and monocyte chemotactic protein-1 (MCP-1) secretion in endothelial cells. The results indicated kahweol to behave as an antiinflammatory and antiangiogenic compound with potential use in antitumoral therapies. Wang et al. (2012) showed that cafestol inhibited angiogenesis (viz. proliferation, migration, and tube formation) of human umbilical vascular endothelial cells by affecting the angiogenic signaling pathway. The inhibitory effects were accompanied by decreasing phosphorylation of FAK and Akt and by a decrease in nitric oxide production.

Kang et al. (2009) found that caffeic acid suppressed UVB-induced skin carcinogenesis by directly inhibiting Fyn kinase activity. They found that Fyn, one of the members of the non-receptor protein tyrosine kinase family, was required for ultraviolet (UV) B-induced cyclooxygenase-2 (COX-2) expression. Caffeic acid more effectively suppressed UVB-induced COX-2 expression and subsequent prostaglandin E(2) production in JB6 P + mouse skin epidermal (JB6 P+) cells compared with chlorogenic acid (5-*O*-caffeoylquinic acid). In-vivo data from mouse skin also supported the idea that caffeic acid suppressed UVB-induced COX-2 expression by blocking Fyn kinase activity. Their results suggested that caffeic acid could act as a potent chemopreventive agent against skin cancer.

Boettler et al. (2011a, b) found that a low-roast coffee rich in 5-O-caffeoylquinic acid (CGA) and a heavy-roast low in CGA but containing high levels of N-methylpyridinium (NMP) induced chemopreventive phase II-enzymes via the Nrf2/ARE pathway in-vitro and in-vivo. Both were identified as potent activators of Nrf2 nuclear translocation and ARE-dependent gene expression of selected antioxidative Phase II enzymes in human colon carcinoma cells (HT29). In contrast, trigonelline was found to interfere with Nrf2 activation, effectively suppressing the NMP-mediated induction of Nrf2/ARE-dependent gene expression. They concluded that several coffee constituents, partly already present in the raw material as well as those generated during the roasting process, contributed to the Nrf2-translocating properties of consumer-relevant coffee. A fine tuning in the degradation/formation of activating and deactivating constituents of the Nrf2/ARE pathway during the roasting process may be critical for the chemopreventive properties of the final coffee product.

Neuroprotective Activity

Chu et al. (2009) found roasted coffees to be rich in lipophilic antioxidants and chlorogenic acid lactones and could protect neuronal cells against oxidative stress, through inhibition of the ERK1/2 and JNK signaling pathways. Lipophilic antioxidant activities were on average 30-fold higher in roasted than in green coffee samples. In primary neuronal cell culture, pretreatment with green and roasted coffees (regular and decaffeinated) protected against subsequent hydrogen peroxide-induced oxidative stress and improved neuronal cell survival (green coffees increased neuron survival by 78%, compared to 203% by roasted coffees).

Coffee constituents namely caffeine, trigonelline, N-methylpyridinium, chlorogenic acid, catechol, pyrogallol and 5-hydroxytryptamides were found to differentially increase calcium signalling and dopamine release pheochromocytoma cells (PC-12 cells) (Walker et al. 2012). While N-methylpyridinium stimulated the Ca(2+)-mobilization most potently (EC_{200}: 0.14 μM), treatment of the cells with pyrogallol (EC_{200}: 48nM) or 5-hydroxytryptamides (EC_{200}: 10nM) led to the most pronounced effect on dopamine release. Conversely, no effect was seen for the reconstituted biomimetic mixture. The researchers concluded that each of the coffee constituents tested stimulated the dopamine release in PC-12 cells and since no effect was found for their biomimetic mixture, they hypothesized other coffee constituents to be responsible for the dopamine release demonstrated for *Coffea arabica* or *Coffea canephora* var. *robusta* coffee brews.

Kim et al. (2012) found that pretreatment with caffeinated coffee, decaffeinated coffee, or

chlorogenic acid strongly inhibited hydrogen peroxide-induced apoptotic nuclear condensation in neuronal cells and inhibited hydrogen peroxide-induced down-regulation of anti-apoptotic proteins Bcl-2 and Bcl-X(L) while blocking hydrogen peroxide -induced pro-apoptotic cleavage of caspase-3 and pro-poly(ADP-ribose) polymerase. Caffeinated coffee, decaffeinated coffee, and chlorogenic acid also induced the expression of NADPH:quinine oxidoreductase 1 (NQO1) in neuronal cells, suggesting that these substances protected neurons from hydrogen peroxide-induced apoptosis by up-regulation of this antioxidant enzyme. The neuroprotective efficacy of caffeinated coffee was similar to that of decaffeinated coffee, indicating that active compounds present in both caffeinated and decaffeinated coffee, such as chlorogenic acid, may be responsible for the effect.

Antidiabetic Activity

A lipid transfer protein of 9 kDa isolated from *Coffea canephora* designated Cc-LTP(1) was found to inhibit mammalian α-amylase activity (Zottich et al 2011). Eight major chlorogenicacids (CGAs) isolated from green coffee beans were found to inhibit porcine pancreas amylase isozyme 1 (PPA-1) in mixed-type inhibition fashion (Narita and Inouye 2011). CGAs with caffeic-acid moiety inhibited stronger than those with feruloic-acid one and CGAs with one caffeic-acid moiety inhibit much more strongly than those with two moieties. The IC_{50} values of CQAs, FQAs, and diCQAs against the PPA-I-catalysed hydrolysis of *p*-nitrophenyl-α-D-maltoside were 0.08–0.23 mM, 1.09–2.55 mM, and 0.02–0.03 mM, respectively. All CQAs and FQAs and 3,5-diCQA showed mixed-type inhibition with binding to the enzyme-substrate complex (ES) being stronger than to the enzyme (E). 3,4-DiCQA and 4,5-diCQA showed mixed-type inhibition, but, conversely were suggested to bind to E stronger than ES. CGAs could have enough potential for therapy of diabetes and obesity.

Antinociceptive Activity

de Paulis et al. (2002) found that dicinnamoylquinide derivatives of chlorogenic acid, formed in the roasting process of coffee, had low micromolar affinity for the human adenosine *es* transporter (hENT1). The potency of these compounds for inhibiting the human adenosine transporter was equal to or higher than that of caffeine for blocking adenosine receptors. DIFEQ (3,4-diferuloyl-1,5-quinolactone), a neutral derivative of the chlorogenic acids, i.e. isomeric mono- and di-substituted coumaroyl-, caffeoyl-, and feruloyl-esters of quinic acid, formed in the roasting process of coffee, displaced the adenosine transporter antagonist [(3)H](S)-(nitrobenzyl)-6-thioinosine binding in cultured U-937 cell preparations, expressing the human adenosine transporter protein (hENT1). Acute administration of a high dose of DIFEQ (100 mg/kg i.p.) reduced open field locomotion in mice for 20 min in correlation with brain levels of DIFEQ. Both 3,4-dicaffeoyl-1,5-quinide and 3,4-dicoumaroyl-1,5-quinide, two close structural analogs of DIFEQ also present in roasted coffee, showed similar affinities for the adenosine transporter, while the corresponding 3- and 4-mono caffeoyl- and feruloyl-quinides were one to two orders of magnitudes less active. The data suggested that 3,4-dicinnamoyl-1,5-quinides in coffee could have the potential to raise extracellular adenosine levels, thereby counteracting the stimulant effect of caffeine. In a subsequent study, de Paulis et al. (2004) found that compounds with a cinnamoyl substituent in the 4-position of the quinide, i.e. 4-caffeoyl-1,5-quinide (4-CQL), 3,4-dicaffeoyl-1,5-quinide (DICAQ), 3,4-diferuloyl-1,5-quinide, and 3,4-dicoumaroyl-1,5-quinide, had affinities for the μ opioid receptor in the low micromolar range. In the hot plate test, coffee extract, containing 0.78% of 4-CQL, reversed the antinociceptive effect of morphine at 10 mg/kg IP. Two cinnamoyl-1,5-quinides found in roasted coffee, DICAQ, and 4-CQL, were active at 1 and 0.1 mg/kg IP, respectively. Their results confirmed that that the previously reported anti-opioid activity

of instant coffee is caused primarily by the presence of 4-CQL, and to lesser extent by other cinnamoyl-1,5-quinides.

Studies showed that administration of cafestol into the hyperalgesic hind paw of male Wistar rats, elicited a peripheral antinociceptive effect that was suggested to be mediated by the release of endogenous opioid peptides (Guzzo et al. 2012).

Cognitive Enhancement Activity

In a randomized, double-blind, crossover study of 39 healthy older participants, caffeinated coffee showed a robust positive effect on higher-level mood and attention processes compared with decaffeinated coffee with regular chlorogenic acid and placebo (Cropley et al. 2012). To a lesser extent, the decaffeinated coffee high in chlorogenic acid also improved some mood and behavioral measures, relative to regular decaffeinated coffee. The results suggested that non-caffeine compounds in coffee such as the chlorogenic acids may be capable of exerting some acute behavioral effects.

Cholesterol Enhancing Activity

Coffee diterpenes cafestol and kahweol, present in both robusta and arabica beans had been found to raise serum concentrations of cholesterol, triacylglycerols, and alanine aminotransferase (ALT) in humans (Weusten-van der Wouw et al. 1994; Mensink et al. 1995; van Rooij et al. 1995; Boekschoten et al. 2004; Rubayiza and Meurens 2005).

In 15 volunteers who ingested 0.75 g/day of a non-triglyceride-fraction from coffee oil for 4 weeks, mean cholesterol increased by 48 mg/dl (1.2 mmol/l) relative to placebo (Weusten-van der Wouw et al. 1994). In contrast, a coffee oil stripped of the non-triglyceride lipids cafestol and kahweol had no effect. In three volunteers, purified cafestol (73 mg/day) plus kahweol (58 mg/day) increased cholesterol by 66 mg/dl (1.7 mmol/l) after 6 weeks. Oil from Robusta beans, containing cafestol but negligible kahweol, also raised serum cholesterol. Coffee oils and brews containing cafestol consistently increased serum triglycerides and alanine amino-transferase, and depressed serum creatinine and γ-glutamyl-transferase (GGT). After withdrawal, GGT activity rose above baseline. Norwegians who habitually consumed 5–9 cups of boiled coffee per day had higher serum cholesterol levels and lower GGT but no higher alanine aminotransferase activity than controls. The results suggested that serum cholesterol was raised by cafestol and possibly also kahweol, both natural components of coffee beans.

In a randomized, cross-over trial of 11 healthy, normolipidemic volunteers, administration of both Arabica and Robusta oil to the volunteers elevated serum cholesterol and triglycerides levels (Mensink et al. 1995). None of the effects on serum lipids or lipoprotein cholesterol levels was significantly different between Arabica and Robusta oil. It was postulated that both cafestol and kahweol were involved in raising cholesterol. The mode of action of coffee diterpenes did not involve induction of hypothyroidism. van Rooij et al. (1995) in a randomized placebo-controlled, double-blind parallel study in 36 subjects found that Arabica coffee elevated serum cholesterol, triglycerides and alanine aminotransferase more than Robusta coffee although this was not significant. This was attributed to the higher content of kahweol and cafestol in Arabica than in Robusta. Robusta coffee was found to contain very low to traces (<0.01%) of kahweol (de Roos et al. 1997; Rubayiza and Meurens 2005). Boekschoten et al. (2004) found that Robusta coffee oil rich and poor in kahweol both gave rise to elevation of liver enzymes, alanine aminotransferase and aspartate aminotransferase. The results suggested that kahweol was not responsible for the elevating enzyme effect. They concluded that otherwise unexplained elevation of liver enzyme levels observed in patients might be caused by a switch from consumption of filtered coffee to unfiltered coffee.

Other Uses

Coffea canephora var. robusta is the main source of disease resistance genes used in coffee breeding (Bombarely et al. 2011; Mueller et al. 2005). The top-dressing application of coffee ground and tea leaves was found to be an excellent method to recycle coffee grounds and tea wastes from coffee shops (Morikawa and Saigusa 2011). Use of these materials would not only reduce the waste going to landfill but would also benefit the mineral nutrition of rice consumers at low cost by increasing Fe and Zn levels of rice grains as well as grain yield.

Some coffee genotypes (*Coffea canephora* and *Coffea racemosa* and its hybrids with *Coffea arabica*) exhibited high pesticidal activity (100% mortality) toward to the leaf miner *Leucoptera coffeella* (Magalhães et al. 2010). However, there was no correlation between this activity and the leaf levels of coffee alkaloids and phenolics.

Traditional Medicinal Uses

Refer to notes under *C. arabica*.

Comments

Restriction fragment length polymorphism (RFLP) studies clearly suggested *C. arabica* to be an amphidiploid formed by hybridisation between *C. eugenioides* and *C. canephora*, or ecotypes related to these diploid species (Lashermes et al. 1999).

Coffea liberica Hiern and *C. canephora* Pierre can be distinguished from each other on the basis of leaf, inflorescence, fruit and seed characters (Amidou et al. 2007). Eight QTLs (quantitative trait loci) were detected, associated with variations in petiole length, leaf area, number of flowers per inflorescence, fruit shape, fruit disc diameter, seed shape and seed length.

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Coffea liberica

Scientific Name

***Coffea liberica* Hiern.**

Synonyms

None recorded.

Family

Rubiaceae

Common/English Names

Liberica Coffee, Liberian Coffee, Monrovia Coffee.

Vernacular Names

Chinese: Da Guo Ka Fei, Da Ka Fei Shu, Da Li Ka Fei;
Cook Islands: Kaope Papa'Ā;
Czech: Kávovník Liberský;
Danish: Liberiakaffe;
Dutch: Liberiakoffie;
Eastonian: Libeeria Kohvipuu;
Finnish: Kahvi;
French: Caféier De Liberia;
German: Liberiakaffee, Liberiakaffeebaum, Liberiakaffeestrauch;
Hungarian: Libériai Kávé;
Indonesia: Kopi Nangka;
Italian: Caffe Liberica;
Malaysia: Kopi Liberika;
Philippines: Kapeng Barako;
Polish: Kawa Liberyjska;
Portuguese: Café-Libérica;
Russian: Kofe Liberika;
Spanish: Cafeto De Liberia;
Swedish: Liberiskt Kaffe;
Thai: Kafae Bai Yai;
Vietnamese: Càphê Libéri.

Origin/Distribution

Coffea liberica is indigenous to tropical West Africa (Benin, Burkina Faso, Cote d'Ivoire, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, Togo), eastwards to Uganda and north to south from Cameroon to northern Angola (Davis et al. 2006; Gomez et al. 2009). *Coffea liberica* together with *C. canephora* have the widest distribution of the genus; both are closely related, diploid, allogamous (self-incompatible) and share the same phylogenetic clade (Maurin et al. 2007; Gomez et al. 2009).

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Today, this species is mainly cultivated in Malaysia, Indonesia, Philippines West Africa, Bioko island (Fernando Po), São Tomé, Surinam, Guyana. It is grown to in a restricted extent in Mauritius, India, Sri Lanka, Thailand, Vietnam, Taiwan and Timor.

Agroecology

Coffea liberica is a warm tropical species occurring in lowland to lower montane rain-forests or open scrub vegetation, and is usually grown in altitudes of 400–600 m but it also grows at altitudes up to 1,200 m. It is adapted to a warm and humid climate. It thrives in areas with mean average temperature of 27–30°C and with mean annual rainfall of 1,500–2,500 mm. It is rather frost sensitive. It grows well in full sun or light shade. It is quite drought tolerant and abhors water-logged conditions. It can be grown or well-drained clayey soil to sandy soil of low to medium fertility.

Edible Plant Parts and Uses

Roasted coffee beans of *C. liberica* is more popularly consumed in southeast Asia where the coffee is brewed and drunk with sugar and milk. Liberica coffee is also consumed in blended powdered coffee mixtures with Arabica and Robusta coffee. The quality of liberica coffee is inferior to that of Arabica and Robusta coffee which accounts for its restricted global popularity and demand.

The Malays have also been reported to steep and brew the leaves like tea.

Botany

An evergreen, robust shrub or tree growing to 20 m high when not pruned and with glabrous branches. Leaves opposite on 1–2 cm petioles, narrowly obovate or broadly elliptic to 38 cm long and up to 15 cm wide, coriaceous, dark glossy green above, base acute, apex obtuse to rounded or with short acumen margin entire, 6–12 pairs lateral veins (Plate 1). Flowers 5-9-merous, borne in tight axillary sessile clusters (Plate 2). Calyx tubular 4 mm; corolla white, tubular, 10–12 mm long with 5–11 glabrous lobes; stamens 7–8 attached to throat of corolla tube, disk annular, ovary inferior with 2-locule each with one ovule (Plate 3). Fruit ellipsoid-oblong drupe, 18–30 mm long, glabrous, green (Plate 4) turning red when ripe (Plate 5) with fleshy, thick mesocarp and fibrous endocarp. Seeds 2 per fruit, 7–15 mm long, greyish-brown and grooved with thin, papery testa.

Plate 1 Large glossy dark green leaves of *Coffea liberica*

Plate 2 Axillary cluster of flowers

Nutritive/Medicinal Properties

The mean nutrient composition per 100 g of *C. liberica* beans was reported as: water 11 g, protein 14 g, sucrose and reducing sugars 8 g,

Plate 3 Close-up of flower

Plate 4 Immature berries of *Coffea liberica*

Plate 5 Ripe berries of *Coffea liberica*

cellulose and polysaccharides 42 g, lipids 12 g, chlorogenic acids 7 g, ash 4 g, caffeine 1.6 g (Sofef and Boer 2000). On a dry basis liberica contained 0.5-1-8% caffeine. *C. robusta* had the highest caffeine concentration, 2.26/100 g, followed by *C. arabica* with a caffeine concentration of 1.61/100 g. *C. liberica* had the lowest caffeine concentration at 1.23/100 g (Liew et al. 2001). *Coffea liberica* 'dewevrei' was found to have low levels of sucrose compared with beans of the wild species *Coffea pseudozanguebariae* (Ky et al. 2000). Chlorogenic acids (CGA), phenolic compounds commonly found in green coffee beans of *Coffea s*pp., comprised three main CGA classes caffeoylquinic acids (CQA), dicaffeoylquinic acids (diCQA), and feruloylquinic acids (FQA) (Ky et al. 1999). The three classes accounted for approximately 98% of the CGA content (Clifford and Staniforth, 1977). Each class comprised three isomers, but one isomer, 5-caffeoylquinic acid (5-CQA), constituted 85% of the CGA content in coffee beans (Clifford et al. 1989; Ky et al. 1999). CGA content varies between and within coffee species. In *C. canephora*, CGA content was11.3% dmb (dry matter basis), with a range from 7.9 to 14.4% dmb (Ky et al. 2001). *C. liberica* var 'dewevrei' was found to have high CGA content (Ky et al. 1999).

Studies showed that predrying of *Coffea liberica* coffee beans caused 15–30% loss of 5-hydroxytryptamides (C-5-HT) of carboxylic acids, depending on the applied drying conditions (Nebesny and Budryn, 2002). A higher C-5-HT loss occurred in the case of beans subjected to two-stage processing, predrying and roasting. Convection roasting caused higher degradation of C-5-HT than microwave roasting.

Methylated uric acids namely *O*(2),1,9-trimethyluric acid and 1,3,7,9-tetramethyluric acid were isolated from young leaves of *Coffea liberica, C. arnoldiana, C. dewevrei* var. *excelsa* and var. *aruwimiensis* (Wanner et al. 1975). Their structures were determined as 2-methoxy-1,9-dimethyl-7.9-dihydro-1 H-purine-6,8-dione and 1,3,7,9-tetramethyl-7,9-dihydro-1 H-purine-2,6,8(3 H)-trione respectively. A new tetramethyluric acid, *O*(2),1,7,9-tetramethyluric acid was isolated from *Coffea liberica* and *C. dewevrei* leaves (Petermann et al. 1977).

Petermann and Baumann (1983) observed in the leaves of seedlings of *Coffea dewevrei var excelsa, Coffea liberica* and *Coffea abeokutae* that theobromine was transformed to caffeine; caffeine and theobromine were metabolized to theacrine (1,3,7,9-tetramethyluric acid), which

was degraded to liberine (*O*(2), 1,9-thrimethyluric acid) and *O*(2),1,7,9-tetramethyluric acid (methyl-liberine). However, these compounds were not detected in cell suspensions of the same coffee species (Baumann and Frischknecht 1988). Leaves of *C. liberica* were found to contain the methyluric acids, theacrine, liberine and methyl-liberine (Wanner et al. 1975; Baumann et al. 1976; Petermann et al. 1977; Petermann and Baumann, 1983). There was also evidence that these compounds occurred in the beans of *C. lberica* and *C. deweveri* (Clifford et al. 1989).

Coffee beans of commercially important *Coffea* species including *C. liberica* were found to contain the diterpene cafestol (de Roos et al. 1997), which was reported to raise serum cholesterol in humans (Weusten-van der Wouw et al. 1994; Urgert et al. 1997). De Roos et al. (1997) reported the following diterpene level (mg bean mass) in *C. liberica* green beans: *C. liberica* var. *liberica* from Ivory Coast with 273–283 mg cafestol, 152–154 kahweol, *C. liberica* var. *dewevrei from* Central African Republic with 334 mg-616 cafestol, 54–95 mg kahweol and 16-*O*-methyl cafestol 19 mg.

For more information on the nutritive value and pharmacological properties of coffee see also notes on *C. arabica* and *C. canephora*.

Traditional Medicinal Uses

Leaves of *C. liberica* have been used to treat headaches and sore-eyes in NW Guyana (DeFilipps et al. 2004).

Other Uses

C. liberica is used also as rootstock for coffee breeding and improvement programs.

Comments

Coffea liberica Hiern and *C. canephora* Pierre can be distinguished from each other on the basis of leaf, inflorescence, fruit and seed characters (Amidou et al. 2007). Eight QTLs (quantitative trait loci) were detected, associated with variations in petiole length, leaf area, number of flowers per inflorescence, fruit shape, fruit disc diameter, seed shape and seed length.

Kape barako, or baraco, is a variety of *C. liberica,* a major crop in the Philippines. The provinces of Batangas and Cavite produce most of the baraco from the Philippines.

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Wrigley G (1988) Coffee. Longman Scientific Technical/Wiley, New York, 639 pp

Morinda citrifolia

Scientific Name

***Morinda citrifolia* L.**

Family

Rubiaceae

Synonyms

Morinda angustifolia Roth nom. illeg., *Morinda aspera* Wight & Arn., *Morinda bracteata* Roxb. nom. illeg., *Morinda chachuca* Buch.-Ham., *Morinda chrysorhiza* (Thonn.) DC., *Morinda citrifolia* f. *potteri* (O.Deg.) H.St.John, *Morinda citrifolia* var. *bracteata* (Roxb.) Kurz, *Morinda citrifolia* var. *elliptica* Hook.f., *Morinda citrifolia* var. *potteri* O.Deg., *Morinda coreia* var. *stenophylla* (Spreng.) Chandrab., *Morinda elliptica* (Hook.f.) Ridl., *Morinda ligulata* Blanco, *Morinda littoralis* Blanco, *Morinda macrophylla* Desf., *Morinda mudia* Buch.-Ham., *Morinda multiflora* Roxb., *Morinda nodosa* Buch.-Ham., *Morinda quadrangularis* G.Don, *Morinda stenophylla* Spreng., *Morinda tinctoria* Noronha, *Morinda tinctoria* var. *aspera* (Wight & Arn.) Hook.f., *Morinda tinctoria* var. *multiflora* (Roxb.) Hook.f., *Morinda tomentosa* B.Heyne ex Roth, *Morinda teysmanniana* Miq., *Morinda zollingeriana* Miq., *Platanocephalus orientalis* Crantz, *Psychotria chrysorhiza* Thonn., *Samama citrifolia* (L.) Kuntze, *Sarcocephalus leichhardtii* F.Muell.

Common/English Names

Awl Tree, Beach Mulberry, Brimstone Tree, Canary Wood, Cheese Fruit, East Indian Mulberry, Forbidden Fruit, Grand Morinda, Great Morinda, Headache Tree, Hog Apple, Indian Mulberry, Large-Leaved Morinda, Leichardt's Tree, Morinda, Limburger Tree, Noni, Noni Berry, Noni Fruit, Pain Bush, Pain Killer Tree, Rotten Cheese Fruit, Tahitian Noni Fruit, Togari Wood, Turkey Red, Wild Pine.

Vernacular Names

American Samoa: Nonu;
Australia: Awl Tree, Canary Wood, Cheesefruit, Great Morinda, Indian Mulberry, Morinda;
Banaban: Te Non;
Barbados: Fobbiden Fruit, Wild Pine;
Borneo: Bamkoro, Bangkudu, Bangkuru, Bengkal Putih, Bingkuduk, Engkudu Hutan, Mengkudu;
Brazil: Noni;

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Burmese: Al, Mhanbin, Neihpahsae, Yaiyae;
Chamorro: Kuti, Ladda;
Chinese: Hai Bin Mu Ba Ji:
Chuuk: Nen, Nin;
Cook Islands: Nono;
Cuba: Mora De La India;
Czech: Rojok Citroníkolistý;
Danish: Indisk Svovltræ, Noni;
Dominican Republic: Baga, Buñuela, Coca, Huevo De Reuma, Nigua, Piña de Puerco, Piñuela;
Dutch: Noni, Kaasvrucht, Stinkend Kaasvrucht;
El Salvador: Rubarbe Caraibe, Ruibarbo Caribe;
***Fijian*:** Kura;
French: Bois Douleur, Bois Tortue, Fromager, Morinde, Morindier, Mûrier De Java, Mûrier Des Indes, Murier Indien, Noni, Nono;
French West Indies: Bilmbi, Pomme macaque, Rubarbe Caribe;
German: Indische Maulbeere, Indischer Maulbeerbaum, Indischer Maulbeerstrauch, Noni, Noni-Baum;
Gilbertese: Te Non;
Guadeloupe: Rubarbe Caraibe, Ruibarbo Caribe;
***Guam*:** Indian Mulberry, Lada, Ladda;
Haiti: Boi Doleur, Doleur, Feuille Froide, Fromagier;
Hawai: Indian Mulberry, Noni;
India: Aal, Ach, Achhu, Aich, Bartundi, Chaili, Huldikunj, Hurdi, Rouch,Surangi (Bengali), Ach, Al, bartundi, Saraoji, Surangi (Gujerati), Ach, Achi, Ak, Al, Barraal, Bartundi, Surangi (Hindu), Ainshi, Anishi, Avishe, Burmanona, , Dodda Thagachi, Haladi Paavate, Haladipaavate, Haladi-Pavate, Haladipavate, Madde, Maddee Mara, Madderbanna, Maddi, Maligi, Mulgul, Mulgul Tagase, Popli, Thakote, Thagache, Tagache, Tagace, Tagatemara, Takote (Kannada), Cada-Pilava, Cadapilava, Kadappilavu, Kattapitalavam, Kadapilva, Karrapitalavam, Katappilavu, Manchapavatta, Manjanatthi, Manjapavattai, Mannapavatta, Mannanarri, Mannanatti, Munjapavittai, Noona (Malayalam), Aal, Al, Alita, Aseti, Baratindiala, Bartondi, Bartutndi, Makadphal, Nagakunda, Nagkura, Surangi (Marathi), Gondhonagi, Pindre (Oriya), Achuka, Achchhuka, Achuka, Ashyuka (Sanskrit), Chayapattai, Mancanaari,Mancanatti, Manjanatti, Manjatbavattai, Manjanathi, Minamaram, Munja Pavattay, Nuna, Nunaa, Nona, Nunavu, Periyanuna, Seyal, Tanakku, Tunaon, Tunavu, Tunnam, Tunnavu, Vellainuna (Tamil), Maddi, Maddi Chettu, Maddichettu, Manajaparvetti, Mogali, Molaga, Molagha, Molugu, Molugu Chettu, Mulugu, Thogaru Chettu, Thogarumogali, Thogoda, Togarumogali, Togara, Togaree, Togareemogilli, Togaru, Togarumaddi, Toghur (Telugu);
Indonesia: Bentis, Kudu, Kemudu, Mengkudu Pache, (Javanese), Bengkudu (Minahasa, Gorontalo), Koddhu, Kodhuk (Madurese), Cangkudu, Kudu (Sundanese), Mekudu (Sumatra);
Khmer: Nhoër Srôk, Nhoër Thôm;
Kiribati: Non;
Kosrae: I, Ee;
Laotian: Nhoo Baanz, Nhor;
Malaysia: Bengkudu, Mengkudu,Mengkudu Besar, Mengkudu Jantan, Mengkudu Laut;
Marquesas: Noni;
Marshall Islands: Nen, Nin;
Nepalese: Hardikath;
Nicaragua: Noni, Yema De Heuvo;
***Niue*:** Non, Nonu Atogi, Gogu Atogi;
Northern Marianas: Lada;
Norwegian: Noni, Nonomorinda;
Pakistan: Achu (Urdu);
Palau: Kesengel, Lel, Ngel;
Philippines: Bancudo, Bangcudo, Bangkudo, Bangkuro, Lino, Nino (Bisaya), Apatot, Apatot-Nga-Basit (Iloko), Bankoro (Maguindanao), Galongog (Subanum), Nino (Sulu), Rukurok (Kuyonon), Bankoro Bangkudo, Bankuro, Bankuru, Lino, Nino, Taeng-Aso, Tumbong-Aso (Tagalog);
Pohnpei: Weipwul;
Portuguese: Pau-Azeitona;
Puerto Rico: Mora De La India Noni, Morinda, Gardenia Hedionda, Noni, Pain Killer;
Rotuman: Ura;
Samoa: Nonu, Non, Nonu, Nonu Atogi, Gogu Atogi;
Seychelles: Mirier De Java;
Singapore: Hai Ba Ji, Wu Ning, Luo Ling (Chinese);

Solomon Islands: Kikiri, Urati;
Spanish: Mora De La India Noni, Huevo De Reuma;
Sri Lanka: Ahugaha, Yhugaha (Sinhalese);
Surinam: Benghoedoe, Mengkoedoe, Morinda, Parja;
Swedish: Noni,
Taiwan: Luo Ling;
Tahitian: Mona, Monii, Nono;
Thailand: Mata Suea (Northern Thailand),Yae Yai (Karen), Yo Ban Yaw, Yor Ban;
Tokelau: Monu;
Tongan: Non, Nonu, Nonu Atogi, Gogu Atogi;
Trinidad & Tobago: Pain bush;
Tuvalu: Nonu;
Uvea/Futuna: Non, Nonu Atogi, Gogu Atogi;
Vanuatu: Nowoi, Yalotri (Bislama);
Vietnam: Nhàu, Cây Nhàu, Trái Nhàu, Nhau Rung, Nhau Nui;
Wallis and Futuna: Nonu;
Yap: *Lol*, Mangal'Wag.

Origin/Distribution

The species is native to southeast Asia and tropical Northern Australia. The species is found distributed from Asia and the Pacific and to the Caribbean region. The species has naturalised in many tropical regions around the world as wild plantings and is also cultivated.

Agroecology

Morinda citrifolia is found from sea level to altitudes of 1,500 m in warm, humid and seasonal climates of the tropical region, with an estimated annual rainfall of 1,500–3,000 mm or more and mean annual temperature of 20–35°C. The plant tolerates mean minimum temperature of 12°C and low rainfall down to 250 mm. It occurs in disturbed forests, dry to mesic forests, grasslands, open areas near the shoreline, pastures and coconut plantations, in littoral forest understories, fallow areas, waste places, stream banks, gulches around villages and home gardens. In northern Australia, the species is common in the littoral vegetation along the coast to pioneer and secondary vegetation after cultivation and bush fires or deforestation activities or in secondary or light forest.

It is adaptable to a wide range of soil types, from dry to wet soils, from infertile, degenerated soils with low water holding capacity or poorly drained to poor, ferralitic soils, from saline or sodic soils to rich, fertile, volcanic soils. It is extremely hardy and survives in harsh environments such as those found on coral atolls or basaltic lava or brackish tide pools. It tolerates water-logging to a certain extent but prefers free, well drained soils. It is also drought tolerant, withstanding drought for 6 months or more. Noni grows well in full sun or partial shade.

Edible Plant Parts and Uses

Fruit is eaten raw or cooked in Asia, Northern Australia and the Pacific. In Indonesia, the young fruits are eaten cooked as lalab while half-ripe and ripe fruits are made into rujak or pounded and eaten with sambal. The ripe fruits devoid of kernels are mashed and drunk with syrup or sugar. In Indo-China and Myanmar, ripe fruit is eaten with salt. In India, the green fruit is used in curries. The young leaves are cooked and eaten as vegetable in Thailand, Vietnam, Indonesia, Hainan Island, China and Papua New Guinea. In Indonesia, the young leaves are cooked or eaten raw as lalab with rice. Mature leaves are used to wrap fish or meat before cooking and then eaten with the cooked fish or meat. In Kiribati, the terminal bud is utilised as food. In Vietnam, the young leaves are used in eel soup. The seeds are edible when roasted.

Botany

This is an erect, glabrous shrub or small tree 3–10 m high with quadrangular, jointed branchlets. The leaves are simple, opposite, broadly elliptic to oblong, large, 10–30 cm by 5–15 cm wide, glabrous, acuminate or acute, base cuneate,

Plate 1 Noni fruit and large glossy leaves

Plate 2 Noni flower and fruit

Plate 3 Immature green fruits

Plate 4 Ripe noni fruit

Plate 5 Mature, unripe noni fruit harvested for sale

glossy green on the upper side and dull green on the lower (Plates 1, 2, 3, and 4). Petioles are 0.5–2.5 cm long; stipules variable in size and shape, broadly deltoid and membranous. Inflorescences are globose terminal capitulum with 20–50 densely packed flowers, 1–4 cm long peduncled, in axils of stipules opposite normally developed leaves. Flowers are bisexual, 5–6-merous, fragrant; ovary crowned by persistent, urceolate, truncate or indistinctly dentate, yellowish-green calyx; corolla funnel-shaped, up to 1.5 cm long, white; stamens 5 inserted, with wooly filaments and exserted anthers; stigma bilobed (Plate 2). Fruit is an ovoid syncarp of 2-seeded, pyramidal drupes, 3–10 cm long by 3–7 cm across, white, greenish white to yellow-white when ripe with numerous protuberances and with a strong putrid odour when ripe (Plates 1, 2, 3, 4, and 5). Seeds are black, albuminous.

Nutritive/Medicinal Properties

Fruit Nutrients and Phytochemicals

Analyses carried out in Australia (Brand Miller et al. 1993) reported fresh *Morinda citrifolia* fruit to have the following proximate composition (per 100 g edible portion): water 86.1 g, energy 46 kJ, protein 0.8, fat 0.3, ash 0.8 g, available carbohydrates 0 g, dietary fibre 2.6 g, Ca 23 mg, Fe 1.1 mg, Mg 25 mg, K 176 mg, Na 30 mg, Cu 0.6 mg, vitamin C 56 mg, thiamin 0.08 mg, riboflavin 0.1 mg and niacin equivalent 0.1 mg.

The physico-chemical composition of noni fruit juice as reported by the European Commission (2002) per 100 g was: pH 3.4–3.6, dry matter 10–11%, protein 0.2–0.5%, lipid 0.1–0.2%, glucose 3–5 g, fructose 3–4 g, K 30–10 mg, Na 15–40 mg, Mg 3–12 mg, Ca 20–25 mg, and vitamin C 3–25 mg.

Most of the essential amino acids were detected as free amino acids (unhydrolysed sample) at the mature green, mature ripe and fermented stages of noni fruit ripening, with threonine presenting the highest value (3.95 mg/100 g) at the fermented stage and histidine showing the lowest value (0.05 mg/100 g) at the mature green stage (Golden and Lindsay 2012). The essential amino acids with the exception of tryptophan (destroyed by acid hydrolysis) were also detected as total amino acids (hydrolyzed sample) albeit at much higher concentrations. Leucine showed the highest value (94.21 mg/100 g) at the mature ripe stage, whereas methionine the lowest value (2.80 mg/100 g) at the mature green stage. In fatty acid content, the short chain caprylic acid (80.69 mg/100 g) showed the highest value at the ripe stage. The essential fatty acids linolenic (8.60 mg/100 g) and linoleic (50.57 mg/100 g) were highest at the green stage. Also present in significant quantities were palmitic acid (44.27 mg/100 g) and stearic acid (4.78 mg/100 g) at the green stage. The amount of fatty acids decreased significantly at the fermented stage. Of the fatty acids detected at the fermented stage 79% of them were below 1.00 mg/100 g fresh weight of the fruit.

Several nonvolatile compounds, including acetyl derivatives of asperuloside and glucose, were identified in noni fruit (Levand and Larson 1979). Elkins (1998) reported the fruit to contain caprioc acid, carprylic acid, alizarin, anthraquinones, damnacanthol and proxeronine. The two organic acids caprioc acid, carprylic acid were identified by Dittmar (1993) and proxeroxine by Heinicke (1985). A trisaccharide fatty acid ester 2, 6-di-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-glucopyranose and two known compounds rutin and asperulosidic acid were isolated from the n-butanol-soluble fraction of noni fruit (Wang et al. 1999). Three glycosides were isolated from noni fruits (Wang et al. 2000). Their structures were determined to be 6-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-glucopyranose (1), 6-*O*-(β-D-glucopyranosyl)-1-*O*-hexanoyl-β-D-glucopyranose (2), and 3-methylbut-3-enyl 6-*O*-β-D-glucopyranosyl-β-D-glucopyranoside (3). Two novel glycosides, 6-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-glucopyranose and asperulosidic acid, were extracted from noni fruit juice (Liu et al. 2001). Four new trisaccharide fatty acid esters named noniosides E–H (4–7) were isolated from noni fruit (Dalsgaard et al. 2006). Their structures were elucidated as 2,6-di- *O*-(β-D-glucopyranosyl)-1-*O*-hexanoyl-β-D-glucopyranose (4), 2,6-di-*O*-(β-D-glucopyranosyl)-1-*O*-decanoyl-β-D-glucopyranose (5), 2-*O*-(6-*O*-octanoyl-β-D-glucopyranosyl)-6-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-glucopyranose (6), and 2-*O*-(6-*O*-hexanoyl-β-D-glucopyranosyl)-6-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-glucopyranose or 2-*O*-(6-*O*-octanoyl-β-D-glucopyranosyl)-6-*O*-(β-D-glucopyranosyl)-1-*O*-hexanoyl-β-D-glucopyranose (7), respectively. In addition, an HPLC-MS analysis of a methanolic extract of the fruit powder revealed the presence of further derivatives including new disaccharide and trisaccharide esters with fatty acid residues of various lengths.

The following chemicals 1-*O*-(3′-methylbut-3′-enyl)-β-D-glucopyranose;1-n-butyl-4-(5′-formyl-2′-furanyl)methyl succinate; and 4-epi-borreria-

genin, together with the known iridoid lycosides asperulosidic acid and deacetylasperulosidic acid and a mixture of 1-n-butyl-4-methyl-2-hydroxysuccinate and 1-n-butyl-4-methyl-3-hydroxysuccinate, as well as a mixture of α-glucopyranose and β-glucopyranose were found in noni fruit juice obtained from Puerto Rico (Samoylenko et al. 2006). Furthermore, samples from fresh-squeezed noni fruit juice from Japan revealed the presence of scopoletin.

An ethanol-insoluble, high molecular weight fraction from noni fruit juice was found to composed primarily of carbohydrate (67% w/w) (Bui et al. 2006). The polysaccharide fraction was found to consist predominantly of GalAp (53.6 mol%), Araf (13.6 mol%), Galp (17.9 mol%) and Rhap (9.5 mol%). Glycosyl linkage analysis suggested the polysaccharide fraction to contain mostly pectic polysaccharides, homogalacturonan (4-GalAp), rhamnogalacturonan I (4-GalAp, 2-Rhap, 2,4-Rhap), arabinan (5-Araf, 3,5-Araf, t-Araf), type I arabinogalactan (4-Galp, 3,4-Galp, t-Araf) and β-glucosyl Yariv-binding type II arabinogalactan (3,6-Galp, t-Araf). Low levels of xyloglucan (4-Glcp, 4,6-Glcp, t-Xylp, t-Fucp), heteroxylan (4-Xylp) and heteromannan (4-Manp) were also present.

In light of the array of commercial noni fruit juice products gaining popularity as dietary supplements, with claims of anticancer and immunostimulant activities studies were conducted to determine markers for noni juice. Three new markers, namely, 1-*O*-(3′-methylbut-3′-enyl)-β-D-glucopyranose (1), 1-n-butyl-4-(5′-formyl-2′-furanyl)methyl succinate (2), and 4-epi-borreriagenin (3), together with the known iridoid glycosides asperulosidic acid (4) and deacetylasperulosidic acid (5) and a mixture of 1-n-butyl-4-methyl-2-hydroxysuccinate (6a) and 1-n-butyl-4-methyl-3-hydroxysuccinate (6b), as well as a mixture of α-glucopyranose and β-glucopyranose were obtained from noni fruit juice from Puerto Rico (Samoylenko et al. 2006). Furthermore, samples from fresh-squeezed noni fruit juice from Japan revealed the presence of scopoletin (7), in addition to compounds 1–6, indicating no significant differences in the marker constituents of noni collected from Atlantic and Pacific regions. Pentanoic, hexanoic and octanoic acid and their ethyl esters were found to be suitable markers of authentication of noni juice (Lachenmeier et al. 2006). Amounts of coumarin derivatives: scopoletin and 7-hydroxycoumarin in noni juices (A–H) ranged from 5.1–231 μg/mL to 0.04–0.45 μg/mL, respectively (Ikeda et al. 2009). No 4-hydroxycoumarin was detected in any noni juice samples examined.

Saludes et al. (2002) isolated the following constituents from the hexane fraction of *M. citrifolia*: E-phytol, cycloartenol, stigmasterol, β-sitosterol, campesta-5,7,22-trien-3β-ol and the ketosteroids stigmasta-4-en-3-one and stigmasta-4-22-dien-3-one. Two new anthraquinones, 1,6-dihydroxy-5-methoxy-2-methoxymethylanthraquinone (1) and 1,5,7-trihydroxy-6-methoxy-2-methoxymethylanthraquinone (2), and one new lignan isoamericanoic acid A (3) were isolated from the fruits of *Morinda citrifolia* along with 11 known compounds scopoletin, luteolin, americanin A, americanin D, 3,3′-bisdemethylpinoresinol, *p*-cresol, *p*-hydroxybenzoic acid, *p*-hydroxybenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde, 4-hydroxy-3-methoxycinnamaldehyde, and 2,5-dihydroxy-4-methoxybenzadehyde (Lin et al. 2007). Six lignans were isolated from the ethyl acetate -soluble phase of noni fruit: 3,3′-bisdemethylpinoresinol (1), americanol A (2), americanin A (3), americanoic acid A (4), morindolin (5), and isoprincepin (6), of which 4 and 5 are novel compounds (Kamiya et al. 2004). From the fruits of *M. citrifolia*, one new anthraquinone, 5,15-*O*-dimethylmorindol, together with five known anthraquinones and one new iridoid, morindacin, together with known iridoids, deacetylasperulosidic acid were isolated (Kamiya et al. 2005). Two new iridoid glucosides, 6α-hydroxyadoxoside and 6β,7β-epoxy-8-epi-splendoside, as well as 17 known compounds, americanin A, narcissoside, asperuloside, asperulosidic acid, borreriagenin, citrifolinin B epimer a, citrifolinin B epimer b, cytidine, deacetylasperuloside, epi-dihydrocornin, dehydromethoxygaertneroside, D-glucose, D-mannitol, methyl α-D-fructofuranoside, methyl β-D-fructofuranoside, nicotifloroside, and β-sitosterol 3-*O*-β-D-glucopyranoside were isolated from the fruit

(Su et al. 2005). 2-methoxy-1,3,6-trihydroxyanthraquinone was isolated from the fruit (Pawlus et al. 2005). The fruits afforded a new constituent, morinaphthalenone, and three known constituents, scopoletin, 1, 3-dimethoxy-anthraquinone and 1, 2-dihydroxy-anthraquinone (Siddiqui et al. 2007a). A new anthraquinone, 1,5,15-tri-*O*-methylmorindol (1), and two new saccharide fatty acid esters, 2-*O*-(β-D-glucopyranosyl)-1-*O*-hexanoyl-β-D-gluropyranose (4) and 2-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-gluropyranose (5), were isolated from a methanol extract of the fruits of *Morinda citrifolia* along with 10 known compounds, namely, two anthraquinones (2, 3), six saccharide fatty acid esters (6–11), an iridoid glycoside (12), and a flavanol glycoside (13) (Akihisa et al. 2007). Deng et al. (2007b) isolated two new lignans, (+)-3,4,3′,4′-tetrahydroxy-9,7′α-epoxylignano-7 α,9′-lactone (1) and (+)-3,3′-bisdemethyltanegool (2), as well as seven known compounds, (−)-pinoresinol (3), (−)-3,3′-bisdemethylpinoresinol (4), quercetin (5), kaempferol (6), scopoletin (7), isoscopoletin (8), and vanillin from noni fruit. Two new compounds, morinaphthalene (=1,3,6,7-tetrahydroxy-2-hydroxymethyl-1,2,3,4-tetrahydronaphthalene, (1); and morindafurone (=5-hydroxy-1,10b-dihydro-6 H-anthra [1,9-bc] furan-6-one, (2); as well as two known constituents, 1,8-dihydroxy-6-methoxy-3-methyl-9-anthrone (3) and 2,4-dimethoxy-9-anthrone (4) were isolated from noni fruit (Siddiqui et al. 2008). Noni fruit was found to contain n-butyl (5-formylfuran-2-yl) methyl succinate, the natural succinate derivative of 5-(hydroxymethyl)furfural (Quiroz-Florentino et al. 2009).

A new iridoid glycoside, 9-epi-6α-methoxy geniposidic acid (4); three new hemiterpene glycosides, 3-methylbut-3-enyl 2′-*O*-(β-D-glucopyranosyl)-β-D-glucopyranoside (nonioside K) (6),3-methylbut-3-enyl6′-*O*-(β-D-xylopyranosyl)-β-D-glucopyranoside (nonioside L) (8), and 3-methylbut-3-enyl 6′-*O*-(β-D-xylofuranosyl)-β-D-glucopyranoside (nonioside M) (9); and two new saccharide fatty acid esters, 6′-*O*-(β-D-glucopyranosyl)-1′-*O*-[(2xi)-2-methylbutanoyl]-β-D-glucopyranose (nonioside N) (16) and 6′-*O*-(β-D-xylopyranosyl)-1′-*O*-[(2xi)-2-methylbutanoyl]-β-D-glucopyranose (nonioside O) (17), were isolated from a methanol extract *Morinda citrifolia* fruits, along with 11 known compounds, namely, three iridoid glycosides asperulosidic acid (1), deacetylasperulosidic acid (2), and scandoside methyl ester (3); two hemiterpene glycosides 3-methylbut-3-enyl β-D-glucopyranoside (5) and 3-methylbut-3-enyl 6′-*O*-(β-D-glucopyranosyl)-β-D-glucopyranoside (nonioside A) (7); and five saccharide fatty acid esters 2′-*O*-(β-D-glucopyranosyl)-1′-*O*-hexanoyl-β-D-glucopyranose (nonioside I) (10), 2′-*O*-(β-D-glucopyranosyl)-1′-*O*-octanoyl-β-D-glucopyranose (nonioside J) (11), 6′-*O*-(β-D-glucopyranosyl)-1′-*O*-hexanoyl-β-D-glucopyranose (nonioside D) (12), 6′-*O*-(β-Dglucopyranosyl)-1′-*O*-octanoyl-β-D-glucopyranose (nonioside C) (13), 6′-*O*-(β-Dglucopyranosyl)-1′-*O*-octanoyl-β-D-glucopyranose (nonioside C) (13) 7,12), 2′,6′-di-*O*-(β-D-glucopyranosyl)-1′-*O*-hexanoyl-β-D-glucopyranose (nonioside E)(14), and 2′,6′-di-*O*-(β-D-glucopyranosyl)-1′-*O*-octanoyl-β-D-glucopyranose(nonioside B) (15) (Akihisa et al. 2010). Five new saccharide fatty acid esters, named nonioside P (3), nonioside Q (4), nonioside R (8), nonioside S (10), and nonioside T (14), and one new succinic acid ester, butyl 2-hydroxysuccinate (=4-butoxy-3-hydroxy-4-oxobutanoic acid) (31), were isolated, along with 26 known compounds, including eight saccharide fatty acid esters, 1, 2, 5, 6, 7, 9, 12, and 13, three hemiterpene glycosides, 15, 17, and 18, six iridoid glycosides, 21–25, and 27, and nine other compounds, 20, 28, 29, and 32–37, from a MeOH extract of the fruit of *Morinda citrifol*ia (noni) (Akihisa et al. 2012). Two new phenylpropanoids, methyl 3-(2,4-dihydroxy-5-methoxyphenyl)propionate and butyl 3-(2,4-dihydroxy-5-methoxyphenyl)propionate, and one unusual propanoate, 5-hydroxyhexyl 2-hydroxypropanoate, were isolated from *M. citrifolia* fruits (Wang et al. 2011a).

Thirty seven volatile compounds were detected in noni fruit pulp, mainly alcohols 7 (63.3%), esters 20 (26.9%), ketones 3 (7.4%), and acids 6 (1.2%) and 1 aldehyde pentanal (trace) (Sousa et al. 2010). The major esters were methyl

hexanoate (13.4%), methyl butanote (8.10%), methyl octanoate (2.19%), methyl 2-methylpropanoate (1.20%); major alcohols: 3-methyl-3-buten-1-ol (54.3%), benzyl alcohol (5.20%), 3-methyl-2-buten-1-ol (2.69%); major acids (octanoic acid (0.27%), butanoic acid (0.35%); and ketone 2-heptanone (6.86%). Ninety-six volatile compounds were identified from ripe and over-ripe noni fruit; octanoic acid (70% of total extract) and hexanoic acid (8% of total extract) were found to be the major constituents (Pino et al. 2010). An abundance of aliphatic esters in over ripe fruits especially alkyl esters of hexanoic and octanoic acids was observed. As noni fruit matured, levels of octanoic acid, decanoic acid and 2E-nonenal decreased, while levels of some esters (methyl hexanoate, methyl octanoate, ethyl octanoate and methyl 4E-decenoate), responsible for fruity odor notes, were augmented while some compounds, mainly acids, decreased or even disappeared during ripening. The over-ripe noni fruit showed significantly higher amounts of methyl hexanoate, methyl octanoate, ethyl octanoate and methyl 4E-decenoate, while octanoic acid and decanoic acid concentrations significantly decreased. The concentration of two unsaturated esters, 3-methyl-3-buten-1-yl hexanoate and 3-methyl-3-buten-1-yl octanoate, significantly decreased in the ripe to over-ripe fruits. In general, although terpenes are present in small quantities in both maturity stages, their contribution to the fruit's flavor could be considerable, as in the case of limonene and linalool, which were found to possess intense citrus and flower-like odors. An unsaturated aldehyde related with lipid-degraded product, 2E-nonenal, decreased during fruit maturation. Three sulphur compounds were found for the first time in noni fruit, e.g. dimethyl disulfide, dimethyl trisulfide and 3-(methylthio)-1-propanol. No nitrogen-containing volatile compounds were found.

Solid phase microextraction (SPME) of noni fruit afforded the following volatiles: 9 acids (predominantly hexanoic acid and octanoic acid); 11 aldehydes and ketones; 6 alcohols (major one was 3-methyl-3-buten-1-o)l; 32 esters, main ones were methyl octanoate, methyl hexanoate, methyl decanoate, ethyl hexanoate; 6 terpenes (all traces) and 6 sulphur compounds viz. methanethiol (I), S-methyl thioacetate (II), dimethyl disulfide (III), methyl 3-methylthiopropanoate (IV), ethyl 3- methylthiopropanoate (V), and 3-methylthiopropanoic acid (VI) (Wei et al. 2011). Two new esters were tentatively identified as 3-methyl-3-buten-1-yl esters of hexanoic acid and octanoic acid.

Potterat et al. (2007) developed and validated a method for the quantification of characteristic noni constituents, such as iridoid glucosides, scopoletin, rutin, fatty acid glucosides, and anthraquinones in commercial juices and capsules. 3-Methyl-1,3-butanediol was identified as a typical marker in noni juices. Sorbic acid (E200) was detected in one juice declared as additive free. Asperulosidic acid, deacetylasperulosidic acid, and rutin were present in varying concentrations all samples analysed. Fatty acid glucosides, noniosides B and C, were present in capsules and most juices. Scopoletin was mainly found in juices. The anthraquinone alizarin, which had been reported from roots and leaves, was not detected in the samples investigated.

Phytochemicals in Seeds

The average oil content of noni seeds was found to be 124.9 g/kg (West et al. 2008a). The mean linoleic acid content of crude noni seed oil was 59.4%. The average β-sitosterol, campesterol, stigmasterol, and α-tocopherol contents of noni seed oil were 4,310, 2,195, 2,020, and 382 mg/kg, respectively. No evidence of acute oral toxicity was observed for noni seed or the oil at 5 g/kg b.w. and 10 mL/kg b.w., respectively. Noni seed oil was not gentoxic in the *Salmonella typhimurium* reverse mutation assay or the in-vitro mammalian chromosomal aberration assay. These results indicate that noni seeds may be a useful new source of vegetable oil. The seed of *M. citrifolia* was found to contain 16.1% oil; the main fatty acid components of the oil were linoleic (55%), oleic (20.5%), palmitic (12.8%), ricinoleic (6.8%) and stearic (4.9%) (Dualatabad et al. 1989; Seidemann 2002).

A lignan, 3,3′-bisdemethylpinoresinol and americanin A (2), quercetin (3) and ursolic acid (4), were isolated from the ethanol extract of *M. citrifolia* seeds (Masuda et al. 2009, 2012b). Twenty chemical constituents were isolated from noni seeds: daucosterol (1), ursolic acid (2), 19-hydroxyl-ursolic acid (3), 1, 5,15-trimethyl-morindol (4), 5, 15-dimethyl-morindol (5), scopoletin (6), 3, 3′-bisdemethylpinoresinol (7), 3, 4, 3′ 4′- tetrahydroxy-9, 7′α-epoxylignano-7α, 9′-lactone (8), americanin D (9), americanin A (10), americanin (11), isoprincepin (12), deacetyl-asperulosidic acid (13), loganic acid (14), asperulosidic acid (15), rhodolatouside (16), quercetin-3-*O*-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside (17), 4-ethyl-2-hydroxyl-succinate (18), 5-hydroxymethyl-2-furancarboxaldehyde (19), and 3-methylbut-3-enyl-6-*O*-β-D-glucopyranosyl-β-D-glucopyranoside (20) (Yang et al. 2009).

Phytochemicals in Flowers

One anthraquinone glycoside and two flavone glycosides were reported in noni blossoms (Singh and Tiwari 1976; Tiwari and Singh 1977). Elkins (1998) reported the flowers to contain acacetin 7-0-D (+)–glucophyranoside; 5,7,-dimethyl apigenin-4-0-8-D(+)-galactophyranoside; and 6,8,-dimethoxy-3-methyl anthroquinone-1-0-8-rhamnosyl glucophyranoside. The major phytochemicals in noni blossoms were: iridoid glycosides, deacetylasperulosidic acid and asperulosidic acid, and flavonoids, quercetin-3-*O*-*α*-L-rhamnopyranosyl-(1 → 6)-*β*-D-glucopyranoside and kaempferol-3-*O*-*α*-L-rhamnopyranosyl-(1 → 6)-*β*-D-glucopyranoside, each present at 3.764, 3.576, 1.513, and 3.096 mg/g, respectively (Deng et al. 2012).

Phytochemicals in Leaves

β-sitosterol and ursolic acid were isolated from the leaves (Ahmad and Bano 1980). The leaves were reported to contain amino acids (alanine, arginine, aspartic acid, cysteine, cystine, glycine, glutamic acid, histidine, leucine, isoleucine, methionine, proline, serine, phenylalanine, threonine, tryptophan, tyrosine, and valine), anthraquinones, glycosides, phenolic compounds, resins, β-sitosterol and ursolic acid (Elkins 1998). An iridoid glucoside, named citrifolinoside A, was isolated from the leaves of *Morinda citrifolia* along with the known iridoids citrifolinin A, asperuloside and asperulosidic acid (Sang et al. 2001c, d). Schripsema et al. (2006) revised the leaf iridoids, citrifolinin A to dehydromethoxy-gaertneroside, citrifolinoside to dehydroepoxymethoxygaertneroside and morindacin to borreriagenin. The leaves of *Morinda citrifolia*, afforded a benzofuran and a bis-nor-isoprenoid, blumenol C, (Siddiqui et al. 1993). Their structures were elucidated as 5-benzofuran carboxylic acid-6-formyl methyl ester (1) and 4-(3′(R)-hydroxybutyl)-3,5,5, trimethyl-cyclohex-2-en-1-one (2) respectively. A new iridoid glycoside, citrifoside and a new anthraquinone, 1,5,15-trimethylmorindol, together with 24 known compounds, were isolated from the leaves of *Morinda citrifolia* (Takashima et al. 2007). West and Zhou (2008) found palmitic acid and *E*-phytol to be the major aroma components in the volatile oil from frozen noni leaves, others included methyl oleate; linoleic acid; octanoic acid; hexanoic acid; 2,6,10,14,18,22-tetracosahexaene; β-ionone; methyl palmitate; geranyl acetone; 6,10,14-trimethyl-2-pentadecanone; benzeneacetaldehyde; and benzaldehyde. 1,2-dihydro-1,1,6-trimethyl-naphthalene and 5-methylfurfural were found only from roasted leaf. West et al. (2007) reported the following from noni leaves: campesterol, stigmasterol, and β-sitosterol, phytic acid (<1 g/kg) in raw leaf, oxalic acid (1 g/kg) and tannin 1.6 and 25.8 g/kg in frozen and dried leaves respectively. No phtyic acid was detected.

Phytochemicals in Stem/Heartwood

Anthraquinones isolated from *Morinda citrifolia* stem included: morindicinone (=2-hydroxy-1,8-dimethoxy-7-methoxymethylanthraquinone;morindicininone (=4-hydroxymethyl-1,

3-dimethoxyanthraquinone; 2-hydroxyanthraquinone; 2-methoxyanthraquinone (Siddiqui et al. 2006); morindicone (9-hydroxy-2-methoxy-4-methyl-3,10-anthracenedione; morinthone (4-methoxy-3-heptadecylxanthone; 1-hydroxy-2-methylanthraquinone; and 2-hydroxymethylanthraquinone (Siddiqui et al. 2007b).

An anthraquinone glycoside, physcion -8-*o*-((α-L-arabinopyranosyl (1→3)) (β-D galactopyranosyl (1→6))-β-D-galactopyranoside) was isolated from noni heartwood together with physcion and morindone (Srivastava and Singh 1993).

Phtyochemical in Root and Root Bark

An anthraquinone compound, damnacanthal, was isolated from the chloroform extract of the root of *Morinda citrifolia* (Hiramatsu et al. 1993). Elkins (1998) reported the following in the root and root bark: carbonate, chlorubin, rubicholric acid, soranjidol, chrysophanol, magnesium, sodium, phosphate, ferric ion, glycosides, morindine, morinadadiol, rubiadin, resins, sterols, glycosides. Three naphthoquinone derivatives and one new anhydride were isolated from noni roots (Sang and Ho 2006). 2-Formyl-1-hydroxyanthraquinone, along with ten other known anthraquinones (1-hydroxy-2-methylanthraquinone, nordamnacanthal, damnacanthal, lucidin-ω-methyl ether, rubiadin, rubiadin-1-methyl ether, soranjidiol, morindone, morindone-5-methyl ether and alizarin-1-methyl ether) were isolated from the roots (Ismail et al. 1997; Ali et al. 2000). Two iridoids deacetylasperulosidic acid and asperulosidic acid and three anthraquinones damnacanthol-3-*O*-β-D-primeveroside, lucidin 3-*O*-β-D-primeveroside and morindone-6-*O*-β-D-primeveroside were isolated from the roots (Kamiya et al. 2008). Six new anthraquinone glycosides: digiferruginol-1-methylether-11-*O*-β-gentiobioside (1); digiferruginol-11-*O*-β-primeveroside (2); damnacanthol-11-*O*-β-primeveroside (3); 1-methoxy-2-primeverosy loxymethyl-anthraquinone-3-olate (4); 1-hydroxy-2-primeverosyloxymethyl-anthraquinone-3-olate (5); and 1-hydroxy-5,6-dimethoxy-2-methyl-7-primeverosyloxyanthraquinone (6) were isolated from noni roots together with four known anthraquinone glycosides (Kamiya et al. 2009). A new anthraquinone, 2-ethoxy-1-hydroxyanthraquinone (1), along with five other known anthraquinones: 1-hydroxy-2-methylanthraquinone (2), damnacanthal (3), nordamnacanthal (4), 2-formyl-1-hydroxyanthraquinone (5) and morindone-6-methyl-ether (6) were isolated from noni roots (Ee et al. 2009). Lv et al. (2011) isolated the following anthraquinones from noni roots: 2-formylanthraquinone; 1-hydroxy-2-methyanthraquinone; 2-formyl -1-hydroxyanthraquinone; 1-methyl-3-hydroxyanthraquinone; alizarin-1-methyl ether; 1-methoxy-3-hydroxyanthraquinone; rubiadin, ibericin, nordamnacanthal; damnacanthal; and 1,3-dimethoxy-2-methoxymethylanthraquinone.

Phytochemicals in Whole Plant/ Cell Suspension Culture

The compound 1,3-dihydroxy-9,10-dioxo-9,10-dihydroanthracene-2-carbaldehyde, also known as nordamnacanthal, was isolated from *Morinda citrifolia* (Awang et al. 2008). A coumarin 7-hydroxy-6-methoxy-2 H-chromen-2-one was found in *Morinda citrifolia* (Beh et al. 2010).

Deacetylasperulosidic acid (DAA) and asperulosidic acid (AA) found in leaf, root, seed and flower of noni plants, were identified as the major components in noni fruit (Deng et al. 2011). In order of predominance, DAA concentrations in different parts of the noni plant were dried noni fruit > fruit juice > seed > flower > leaf > root. The order of predominance for asperulosidic acid (AA) concentration was dried noni fruit > leaf > fl ower > root > fruit juice > seed. DAA and AA contents of methanolic extracts of noni fruits collected from different tropical regions were 13.8–42.9 and 0.7–8.9 mg/g, respectively, with French Polynesia containing the highest total iridoids and the Dominican Republic containing the lowest.

From cell suspension cultures of *Morinda citrifolia*, five known anthraquinones, rubiadin; lucidin; morindone; lucidin-3-β-primeveroside

and morindone-6-β-primeveroside, and seven new anthraquinones were isolated (Inoue et al. 1981). Six of the seven new quinones were characterized as 2-methyl-3,5,6-trihydroxyanthraquinone; 3-hydroxymorindone; 5,6-dihydroxylucidin; 2-methyl-3,5,6-trihydroxyanthraquinone-6-β-primeveroside;3-hydroxymorindone-6-β-primeveroside and 5,6-dihydroxylucidin-3-β-primeveroside, respectively. Six anthraquinones: nordamnacanthal, alizarin-1-methyl ether, rubiadin, soranjidiol, lucidin-ω-methyl ether and morindone were isolated from noni cell suspension culture (Jasril et al. 2003). Quevedo et al. (2010) reported that anthraquinone production could be increased by overexpression of 1-deoxy-D: -xylulose-5-phosphate synthase in transgenic cell suspension cultures of *Morinda citrifolia*.

Contemporary global medicinal application of noni covers a wide range of ailments which include attention deficit disorder, addictions, allergies, arthritis, asthma, brain problems, burns, cancer, cardiovascular disease, chemical sensitivity, chronic fatigue, diabetes, digestive problems, endometriosis, fibromyalgia, gout, hypertension, immune deficiency, infection, inflammation, jet lag, multiple sclerosis, muscle and joint pain, polio, rheumatism, severed fingers, sinus, and veterinary medicine (Wang et al. 2002). Noni seed oil is rich in linoleic acid that may have useful properties when applied topically on skin, e.g., anti-inflammation, acne reduction, moisture retention. Many of these claims are yet to be validated. Over the past two decades extensive studies have been conducted and researches published on Noni's broad range of therapeutic effects, including antioxidant, antibacterial, antiviral, antifungal, antitumor, antihelminthic, analgesic, hypotensive, anti-inflammatory, and immune enhancing effects. Much has been reported on the chemical constituents and phytochemicals of the various parts of Noni and their bioactivities to support some traditional medicinal uses and more research is being conducted to confirm conclusive human health benefits.

Proxeronine, an alkaloid, was first found in noni fruit by Dr. Ralph M. Heinicke (1985). He postulated this pro-enzyme to be a xeronine precursor and to be effective in initiating a series of beneficial cellular reactions through its involvement with the integrity of specific proteins. He pointed out that tissues contain cells which possess certain receptor sites for xeronine. Because the reactions that can occur are so varied, many different therapeutic actions can result when xeronine production escalates, explaining why Hawaiin noni is good for so many seemingly unrelated disorders. He proposed this as the xeronine system (Heinicke 2001). According to his theory, a deficiency of this material can lead to various health issues.

Antioxidant Activity

The study suggested that root, leaf and fruit of *M. citrifolia* might contribute significantly to exogenous antioxidant which is crucial in combating oxidative stress (Mohd Zin et al. 2002, 2006). The fractions from different parts of the plants (fruits, leaves and roots) exhibited considerably high antioxidative activity in the ferric thiocyanate assay and thiobarbituric acid test. The fractions from different parts of the plants were found to contain different amounts of total phenolic compounds, which, interestingly, do not correspond to the antioxidative activity measured. The methanol extract of mengkudu root exhibited high antioxidative activity that was not significantly different from α-tocopherol or butylated hydroxyl toluene (BHT), while the methanol extracts of fruit and leaf showed negligible activities. On the other hand, the ethyl acetate extract of all parts of mengkudu exhibited significant antioxidative activity, which is comparable to that of both α-tocopherol and BHT. Roots showed the highest activity of the parts tested. The results suggest that several compounds contribute to antioxidative activity of different parts of mengkudu. Activity in the roots may be due to both polar and non-polar compounds but, in the leaf and fruit, only to non-polar compounds. Results of a subsequent study (Mohd Zin et al. 2007) showed that all isolated fractions of the fruit demonstrated high antioxidative activity compared to either BHT or α-tocopherol.

The bioactive compounds were found to be flavonoids such as catechin and epicatechin.

Purification of a n-butanol-soluble partition of the methanol extract of *Morinda citrifolia* (noni) fruits led to the isolation of two new iridoid glucosides, 6α-hydroxyadoxoside and 6β,7β-epoxy-8-epi-splendoside, as well as 17 known compounds, americanin A, narcissoside, asperuloside, asperulosidic acid, borreriagenin, citrifolinin B epimer a, citrifolinin B epimer b, cytidine, deacetylasperuloside, dehydromethoxygaertneroside, epi-dihydrocornin, D-glucose, D-mannitol, methyl α-D-fructofuranoside, methyl β-D-fructofuranoside, nicotifloroside, and β-sitosterol 3-*O*-β-D-glucopyranoside (Su et al. 2005). The antioxidant activity was evaluated for all isolates in terms of both DPPH and nitric oxide bioassays. The neolignan, americanin A, was found to be a potent antioxidant in these assays. Wang and Su (2001) found that the superoxide scavenging activity of noni juice was 2.8 times higher than that of vitamin C, 1.4 times that of pycnogenol and equivalent to that of grape seed powder.

In the luminol chemiluminescent assay, both Noni juice samples and coumarin derivatives dose-dependently quenched reactive oxygen species (ROS) such as superoxide, singlet oxygen, hydroxyl radical and peroxynitrite ($ONOO^-$) (Ikeda et al. 2009). The EC_{50} of scopoletin for superoxide, singlet oxygen, hydroxyl and $ONOO^-$ were 1.27 mg/mL, 0.68 mg/mL, >4.00 mg/mL, and 0.042 mg/mL, respectively. Noni juice demonstrated a free radical scavenging capacity in-vitro as evaluated by Oxygen Radical Absorbance Capacity (ORAC) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging methods and was found to contain several polyphenols belonging to coumarin, flavonoid and phenolic acid groups, and two iridoids (Dussossoy et al. 2011). Noni juice was reported to possess antioxidant activity and prevent superoxide-mediated tissue injury in laboratory animals (Berg and Furusawa 2007). A polysaccharide-rich precipitate of noni juice (noni-ppt) also stimulated tumor necrosis factor (TNF) and interleukin 1 (IL-1) in mice. Endotoxin (lipopolysaccharide) stimulated TNF and IL-1 in rats and protected against superoxide-mediated oxygen toxicity. Rats receiving saline, noni-ppt or noni juice exhibited typical signs of oxygen toxicity with hemorrhagic lungs, large pleural effusions and increases in protein concentration in bronchoalveolar lavage fluid (Berg and Furusawa 2007). They also developed heavy lungs with increases in wet/dry weight ratios, hematocrit values and ratios of effusion protein to plasma protein concentration. These results showed that Noni juice and Noni-ppt did not prevent oxygen toxicity in rats when administered according to the protocols used in this study.

A 50% ethanolic extract from noni seeds elicited more potent in-vitro inhibition of elastase and tyrosinase, and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity than leaf or pulp extracts (Masuda et al. 2009). Ursolic acid was isolated as the active constituent of elastase inhibitory activity whilst 3,3′-bisdemethylpinoresinol, americanin A, and quercetin were isolated as active constituents having both tyrosinase inhibitory and radical scavenging activities. Americanin A and quercetin also showed superoxide dismutase (SOD)-like activity.

A new iridoid glucoside (1), named citrifolinin B, together with five known flavonol glycosides, quercetin-3-*O*-β-D-glucopyranoside (2), kaempferol-3-*O*-R-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside (3), quercetin-3-*O*-R-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside (4), quercetin-3-*O*-β-D-glucopyranosyl-(1 → 2)-[R-L-rhamnopyranosyl-(1 → 6)]-β-D-galacopyranoside (5), and kaempferol-3-*O*-β-D-glucopyranosyl-(1 → 2)-[R-L-rhamnopyranosyl-(1 → 6)]-β-D-galacopyranoside (6), isolated *Morinda citrifolia* leaf, all showed DPPH free radical scavenging activity at the concentration of 30 μM with 7.7, 85.8, 4.5, 79.9, 81.3, and 28.6% respectively (Sang et al. 2001b). The aqueous extract from *M. citrifolia* leaves exhibited antioxidant activity against lipid peroxidation, nitric oxide, and hydroxyl radicals (Serafini et al. 2011). The aqueous extract of noni blossoms, at 500 μg/mL, exhibited greater antioxidant activity in the 2,2-diphenylpicrylhydrazyl radical scavenging assay than green tea (88.11% versus 76.60%) (Deng et al. 2012).

In antioxidant assay using ferric thiocyanate (FTC) method, nordamnacanthal and morindone from noni cell suspension culture, showed stronger antioxidant activity than α-tocopherol (Jasril et al. 2003). In 1-diphenyl-2-picrylhydrazyl (DPPH) free radical assay, only morindone was considered to be active as free radical scavenger with 50% inhibition concentration (IC_{50}) of 40.6 μg/mL.

Anticancer Activity

Brown (2012) conducted a thorough review on the anticancer activity of *M. citrifolia* (noni). He found that out of 19 studies actually related to cancer, seven were in-vitro cancer studies, nine were in-vivo animal cancer studies, and three were in-vivo human cancer studies. Among the in-vitro studies, a 'concentrated component' in noni juice and not pure noni juice may (1) stimulate the immune system to 'possibly' assist the body fight the cancer, and (2) kill a small percentage (0–36%) of cancer cells depending on the type. The nine animal studies suggested that a concentrated component in noni juice may stimulate the immune system; but only slightly increased the number (about 1/3; 25–45%) of surviving mice. Other than two case studies, only two human clinical studies were found. The first comprised testing freeze-dried noni fruit, which reduced pain perception, but did not reverse advanced cancer. The second was on smokers ingesting an unknown concentration of noni juice who experienced decreased aromatic DNA adducts, and decreased levels of plasma superoxide anion radicals and lipid hydroperoxide. He also raised the issue of hepatotoxicity but added that there were confounding factors in most of the case reports.

In-Vitro Studies

Methanol noni fruit extract exhibited antiproliferative activity against selected tumour cells (Arpornsuwan and Punjanon 2006). The LC_{50} of the extract in baby hamster kidney (BHK) cells, African green monkey kidney (Vero) cells and human laryngeal carcinoma (Hep2) cells were found to be 2.5, 3 and 5 mg/mL, respectively. The crude extract at a concentration of 0.1 mg/mL exhibited cytotoxic activity against breast cancer (MCF7) and neuroblastoma (LAN5) cell lines at 29 and 36%, respectively. The same concentration of extract showed no toxicity to Vero and very little toxicity to BHK (6%) and Hep2 (13%) cells. The dichloromethane extract of fresh noni leaf exhibited higher inhibitory effect against KB (human epidermoid carcinoma), HeLa (human cervical carcinoma), with IC_{50} values of 21.67 and 68.50 μg/mL, respectively than against MCF-7 (human breast carcinoma) and HepG2 (human hepatocellular carcinoma) cell lines (Thani et al. 2010). The dichloromethane extract of dried leaves revealed cytotoxicity against the KB cell line with an IC_{50} value of 39 μg/mL. Other extracts, as well as rutin and scopoletin, showed lower anti-proliferative effects on all cancer cell lines (IC_{50} 103 to >600 μg/mL). Further, damnacanthal displayed potent cytotoxicity against all cancer cell lines and Vero (African green monkey kidney) cell line. Several non-aqueous extracts from the leaves showed antioxidant properties, giving IC_{50} values of 0.20–0.35 mg/mL. The authors concluded that the leaves of *M. citrifolia* may have benefit as a food supplement for chemoprevention against epidermoid and cervical cancers. The methanol extracts of noni fruits and leaves and the subsequent chloroform fraction of the fruit methanolic extract were found to have potential anti-angiogenic activity and were more potent compared to suramin (Beh et al. 2012). Scopoletin was identified as one of the chemical constituents that may be partly responsible for the anti-angiogenic activity of *M. citrifolia* fruits. The authors concluded that the findings further supported the use of *M. citrifolia* in cancer or other pathological conditions related to angiogenesis.

Noni fruit juice was found to have antiangionenic activity (Hornick et al. 2003). Noni fruit juice in concentrations of 5% (vol/vol) or higher was highly effective in inhibiting the initiation of new vessel sprouts from placental vein explants and also effective in reducing the growth rate and proliferation of newly developing capillary sprouts, compared with initiation in control explants in media supplemented with an equivalent

amount of saline. When used at a concentration of 10% in growth media, noni juice was able to induce vessel degeneration and apoptosis in wells with established capillary networks within a few days of its application. They also found that 10% noni juice in media was an effective inhibitor of capillary initiation in explants from human breast tumours. In tumour explants which did show capillary sprouting, the vessels rapidly degenerated (2–3 days) in those exposed to media supplemented with 10% noni.

Two novel glycosides, 6-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-glucopyranose and asperulosidic acid, extracted from the juice of noni fruits, were effective in suppressing 12-*O*-tedtradecanoylphorbol-13-acetate (TPA)- or epidermal growth factor (EGF)-induced cell transformation and associated AP-1 activity in mouse epidermal JB6 cells (Liu et al. 2001). TPA- or EGF-induced phosphorylation of c-Jun, but not extracellular signal-regulated kinases or p38 kinases, was also blocked by the compounds, indicating that c-Jun N-terminal kinases were critical in mediating TPA- or EGF-induced AP-1 activity and subsequent cell transformation in JB6 cells. *M. citrifolia* (noni) on it own or in combination with, doxorubicin, inhibited the growth and proliferation of Ehrlich ascites tumour grown in female Balb-c mice by induction of apoptosis. (Ta kin et al. 2009). The induction of apoptosis, was confirmed by the positive results from the Terminal Deoxynucleotidyl Transferase dUTP Nick End Labeling (TUNEL) analysis and the active caspase-3 cells in tissues. Apoptosis was also confirmed by caspase-cleaved cytokeratin 18 elevation in serum of the treated groups.

Bioassay-guided fractionation of a dichloromethane-soluble partition of a methanol extract of noni fruits afforded the isolation of an extremely potent quinone reductase inducer, 2-methoxy-1,3,6-trihydroxyanthraquinone (1) (Pawlus et al. 2005) . This new anthraquinone (1) was nearly 40 times more potent than a positive control, l-sulforaphane. Further, compound 1 demonstrated no discernible cytotoxicity at the highest dose tested. Reduction of electrophilic quinones by quinone reductase is an important detoxification pathway in chemoprevention. In another study, two new benzophenones, morintrifolins A and B, together with 14 known anthraquinones and four other known compounds, were isolated from a chloroform-soluble extract of *Morinda citrifolia* roots (Deng et al. 2007a). Of the isolated compounds, four known anthraquinones, namely, 1,2-dihydroxyanthraquinone; 1,3-dihydroxy-2-methylanthraquinone; 2-hydroxy-3-(hydroxymethyl)anthraquinone and 1,3, 6-trihydroxy-2-methylanthraquinone, exhibited quinone reductase (QR)- inducing activity in Hepa lclc7 cells, with concentrations required to double QR activity of 12.0, 8.1, 0.94, and 0.56 μM, respectively.

Jang (2012) demonstrated that noni juice had the ability to strongly downregulate manganese-induced HIF-1α (a tumor angiogenic transcription factor) protein expression in A549 human lung cancer cells in a concentration-dependent manner. HIF-1α protein downregulation appeared to be largely associated with the ability of noni juice to interfere with metal's signalling to activate PKB, ERK-1/2, JNK-1 and S6 in A549 cells. It was further shown that noni juice could repress the induction of HIF-1α protein by desferoxamine or interleukin-1β (IL-1β), another HIF-1α inducer in A549 carcinoma cells. The findings suggest that the noni juice may mediate beneficial effects on lung pathologies in which manganese and HIF-1α overexpression play pathogenic roles.

A new iridoid glycoside, citrifoside and a new anthraquinone, 1,5,15-trimethylmorindol, together with 24 known compounds, were isolated from the leaves of *Morinda citrifolia* (Takashima et al. 2007). 1,5,15-trimethylmorindol did not show significant cytotoxic activity by itself but showed cytotoxicity when combined with tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), while citrifoside did not show any activity even with TRAIL.

The anthraquinone compound, damnacanthal, from noni roots, was found to be an inhibitor of ras function (Hiramatsu et al. 1993). Damnacanthal induced normal morphology and cytoskeletal structure in Kirsten sarcoma virus infected rat kidney (K-rast-NRK) cells without changing the amount and localization of Ras (Hiramatsu et al. 1993).

Ras gene is a transforming oncogene responsible for the cancer-causing activities of the Harvey (the HRAS oncogene) and Kirsten (KRAS) sarcoma viruses. The effect of damnacanthal was reversible, and the compound had no effect on the morphology of RSVts-NRK cells expressing the src oncogene. Ras and ras-related proteins are often deregulated in cancers, leading to increased invasion and metastasis, and decreased apoptosis. In another study, damnacanthal isolated from noni root was reported to have a potent inhibitory activity towards tyrosine kinases such as Lck, Src, Lyn and EGF receptor (Hiwasa et al. 1999). Prior treatment of ultraviolet-resistant human fibroblast UVr-1 cells with damnacanthal before UV irradiation caused more pronounced DNA fragmentation as compared to ultraviolet irradiation alone. The other tyrosine kinase inhibitors, herbimycin A and genistein, also caused similar effects on ultraviolet-induced apoptosis but to a lesser extent. Immunoblot analysis showed that pretreatment with damnacanthal followed by ultraviolet irradiation increased the levels of phosphorylated extracellular signal-regulated kinases and stress-activated protein kinases. Damnacanthal from noni roots was cytotoxic towards the MCF-7 (breast carcinoma) and CEM-SS (T-lymphoblastic leukaemia) cell line (Ali et al. 2000). Nordamnacanthal was very cytotoxic against the CEM-SS cell lines. Other anthraquinones that showed strong cytotoxicity towards the cell lines tested were lucidin-ω-methyl ether (CEM-SS and MCF-7) and rubiadin (CEM-SS).

Treatment of SKHep 1 (human, liver adenocarcinoma) cells with damnacanthal (from *M. citrifolia*) for 24 h elicited a dose-dependent antiproliferative activity (Lin et al. 2011). Damnacanthal appeared to be selective for tumour cell lines, since there was only minimal toxicity against normal hepatocyte cells (FL83B). It was found that damnacanthal-mediated apoptosis involved the sustained activation of the p38 MAPK (mitogen activated protein kinase) and mitochondrion-mediated caspase-dependent pathways through TRAIL/DR5 (TNF-related apoptosis-inducing ligand, death receptor 5) and TNFR1/TNF-α (tumour necrosis factor receptor 1/tumour necrosis factor-α) and p53 pathways. In a separate study, damnacanthal, exhibited cell growth arrest as well as caspase activity induction in colorectal cancer cells (Nualsanit et al. 2012). The proapoptotic protein nonsteroidal anti-inflammatory activated gene-1 (NAG-1) was highly induced by damnacanthal. Damnacanthal also enhanced transcription factor CCAAT/enhancer binding protein β (C/EBPβ). Blocking of C/EBPβ by shRNA resulted in the reduction of NAG-1 expression as well as caspase activity in the presence of damnacanthal. The results indicated that damnacanthal increased antitumorigenic activity in human colorectal cancer cells and that C/EBPβ played a role in damnacanthal-induced NAG-1 expression.

The following anthraquinones isolated from noni roots showed significant inhibitory effects on the proliferation of human lung and colon cancer cells: 2-formylanthraquinone; 1-hydroxy-2-methyanthraquinone and alizarin-1-methyl ether against H1299 non-small lung cancer cells with IC_{50} values of 4.9 μg/mL, 4.1 μg/mL and 4.3 μg/mL respectively; and 2-formylanthraquinone and 1-hydroxy-2-methyanthraquinone against colorectal cancer cell HT116 with IC_{50} values of 5.9 μg/mal and 6.9 μg/m respectively (Lv et al. 2011).

Animal Studies

The fruit juice of noni was found to be therapeutically active against Lewis lung carcinoma (LLC) in syngeneic C57BL/6 mice (Hirazumi et al. 1994). The antitumor principle(s), which was concentrated in the ethanol-precipitable (EtOH-ppt) fraction, increased the survival time of mice by 123%. The EtOH-ppt was non-cytotoxic in KB cell cultures. Concomitant treatment with 2-chloroadenosine or cyclosporine resulted in the abrogation of the antitumor activity of the EtOH-ppt, suggesting the antitumor activity acted via activation of host-immune system. Chemoimmunotherapy of vincristine, 5-fluorouracil, cisplatin, or adriamycin combined with the EtOH-ppt demonstrated beneficial additive or synergistic effects. Preliminary data showed production of interleukin-1, but not interleukin-2, from cell culture supernatant of human peripheral mononuclear cells. Antiviral studies

using Rauscher murine retrovirus, a convenient model for HIV studies, showed inhibition of leukemic splenomegaly in BALB/c mice inoculated with the virus (Hirazumi et al. 1994).

The fruit juice of *Morinda citrifolia* (noni) was found to contain a polysaccharide-rich substance (noni-ppt) with antitumour activity in the Lewis lung (LLC) peritoneal carcinomatosis model (Hirazumi and Furusawa 1999) Therapeutic administration of noni-ppt significantly enhanced the duration of survival of inbred syngeneic LLC tumour bearing mice. It did not exert significant cytotoxic effects in an adapted culture of LLC cells, LLC1, but could activate peritoneal exudate cells to impart profound toxicity when co-cultured with the tumour cells. This suggested the possibility that noni-ppt may suppress tumour growth through activation of the host immune system. Concomitant treatment with the immunosuppressive agent, 2-chloroadenosine or cyclosporin diminished its activity, thereby substantiating an immunomodulatory mechanism. Noni-ppt was also capable of stimulating the release of several mediators from murine effector cells, including tumour necrosis factor-α, interleukin-1beta (IL-1beta), IL-10, IL-12 p70, interferon-γ (IFN-γ) and nitric oxide, but had no effect on IL-2 and suppressed IL-4 release. Improved survival time and curative effects occurred when noni-ppt was combined with sub-optimal doses of the standard chemotherapeutic agents, adriamycin, cisplatin, 5-fluorouracil, and vincristine, suggesting important clinical applications of noni-ppt as a supplemental agent in cancer treatment.

An immunomodulatory polysaccharide-rich substance (Noni-ppt) from the fruit juice of *Morinda citrifolia* was found to possess both prophylactic and therapeutic potentials against the immunomodulator sensitive Sarcoma 180 tumour system (Furusawa et al. 2003). The antitumour activity of Noni-ppt produced a cure rate of 25–45% in allogeneic mice and its activity was completely abolished by the concomitant administration of specific inhibitors of macrophages (2-chloroadenosine), T cells (cyclosporine) or natural killer (NK) cells (anti-asialo GM1 antibody). Noni-ppt showed synergistic or additive beneficial effects when combined with a broad spectrum of chemotherapeutic drugs, including cisplatin, adriamycin, mitomycin-C, bleomycin, etoposide, 5- fluorouracil, vincristine or camptothecin. It was not beneficial when combined with paclitaxel, cytosine arabinoside, or immunosuppressive anticancer drugs such as cyclophosphamide, methotrexate or 6-thioguanine. Noni-ppt also demonstrated beneficial effects when combined with the Th1 cytokine, interferon γ, but its activity was abolished when combined with Th2 cytokines, interleukin-4 or interleukin-10, thereby suggesting that Noni-ppt induces a Th1 dominant immune status in vivo. The combination of Noni-ppt with imexon, a synthetic immunomodulator, also demonstrated beneficial effects, but not when combined with the MVE-2 copolymer, a high molecular weight immunomodulator. It was also not effective when combined with interleukin-2 or interleukin-12.

Preliminary studies indicated that 10% Tahitian Noni Liquid Dietary Supplement or Tahitian Noni Juice (TNJ), made from *Morinda citrifolia* fruit, in drinking water for 1 week was able to prevent dimethylbenz[*a*]anthracene (DMBA)-DNA adduct formation (Wang and Su 2001). The levels of DMBA-DNA adducts were reduced by 30% in the heart, 41% in the lung, 42% in the liver, and 80% in the kidney of female Sprague Dawley rats. Even more dramatic results were obtained in male C57 BL-6 mice: 10% TNJ was able to reduce DMBA-DNA adduct formation by 60% in the heart, 50% in the lung, 70% in the liver, and 90% in the kidney. TNJ showed a dose-dependent inhibition of both LPO (lipid hydroperoxide) and SAR (superoxide anion radicals) in our system. The antioxidant activity of TNJ was compared to the effects of vitamin C, grape seed powder (GSP), and pycnogenol (PYC) at the daily dose per serving level recommended by U.S.RDAs or manufacturers. The results suggested that prevention of carcinogen-DNA adduct formation and the antioxidant activity of TNJ may contribute to the cancer preventive effect of *Morinda citrifolia*. Oral treatment with 50 mg/kg/day of crude methanol leaf extract of *Morinda citrifolia* for 14 days significantly increased the antioxidant enzymes, like catalase, glutathione

peroxidase (GSHPx) and superoxide dismutase (SOD), and antioxidants like glutathione (GSH) and ascorbic acid decreased in lymphoma-bearing mice (Anitha and Mohandass 2006).

Noni juice treatment resulted in significant reductions in HER2/neu breast cancer tumour weight and volume and in longer tumour doubling times in MMTV-neu transgenic mice (Clafshenkel et al. 2012). Noni juice inhibited the growth of this aggressive form of cancer occurred with the mouse equivalent of a recommended dose for humans (<3 oz/day). A 30-day treatment with noni juice also induced significant changes in mammary secondary ductule branching and lobuloalveolar development, serum progesterone levels, and estrous cycling. The authors added that additional studies investigating noni juice-induced tumour growth suppression and modified reproductive responses were needed to characterize its potential as a CAM (complementary and alternative medicine) therapy for women with and without HER2(+) breast cancer.

Clinical Studies

In a study of 203 smokers who completed the trial, the results suggested that drinking 1–4 oz of noni juice daily may reduce the cancer risk in heavy cigarette smokers by blocking carcinogen-DNA binding or excising DNA adducts from genomic DNA (Wang et al. 2009b). Although gender-specific analyses resulted in no significant differences in the 4-oz noni juice groups, the 1-oz noni juice group showed a reduction of 43.1% in females compared with 56.1% in males. In another 30 day, double-blind, and placebo controlled clinical trial with 285 current heavy smokers, they found that plasma superoxide anion radicals (SAR) and lipid hydroperoxide levels decreased in the groups administered 29.5 mL and 118 mL noni juice (Wang et al. 2009a). No significant reductions in SAR or lipid hydroperoxide levels were observed in the placebo group.

Antiinflammatory Activity

Li et al. (2003) reported that noni fruit powder exhibited inhibition of cyclooxygenase-1 (COX-1) with an IC_{50} of 163 μg/mL uspoorting the use of the plant in for the treatment of inflammatory conditions in Australian aboriginal medicine and traditional Chinese medicine. A new anthraquinone, 1,5,15-tri-*O*-methylmorindol (1), and two new saccharide fatty acid esters, 2-*O*-(β-D-glucopyranosyl)-1-*O*-hexanoyl-β-D-gluropyranose (4) and 2-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-gluropyranose (5), have been isolated from a methanol extract of the fruits of *Morinda citrifolia* along with 10 known compounds, namely, two anthraquinones (2, 3), six saccharide fatty acid esters (6–11), an iridoid glycoside (12), and a flavanol glycoside (13) (Akihisa et al. 2007). Upon evaluation of six compounds (5–7, 9, 10, and 13) for inhibitory activity against 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation (1 μg/ear) in mice, four saccharide fatty acid esters, 5–7 and 9, exhibited potent antiinflammatory activity, with ID_{50} values of 0.46–0.79 mg per ear.

Studies by Mckoy et al. (2002) showed that the oral administration of a noni juice extract (200 mg) quite rapidly inhibited the formation of rat paw edema. This effect may have resulted from interference with the B2 receptor-mediated mechanism by which bradykinin induces rat paw edema. Noni juice reduced carrageenan-induced paw oedema, directly inhibited cyclooxygenase COX-1 and COX-2 activities and inhibited the production of nitric oxide (NO) and prostaglandins E(2) (PGE(2)) in activated J774 cells, in a dose dependent manner (Dussossoy et al. 2011).

Noni fruit was found to contain compounds with lipoxygenase inhibitory activities (Deng et al. 2007b). Lipoxygenase belongs to a heterogenous family of lipid peroxidising enzymes and are involved in the biosynthesis of mediators of inflammation. Two new lignans, (+)-3,4,3′,4′-tetrahydroxy-9,7′α-epoxylignano-7 α,9′-lactone (1) and (+)-3,3′-bisdemethyltanegool (2), as well as seven known compounds, (-)-pinoresinol (3), (−)-3,3′-bisdemethylpinoresinol (4), quercetin (5), kaempferol (6), scopoletin (7), isoscopoletin (8), and vanillin were isolated from noni fruit. Compounds 1–8 were shown to inhibit 5- and/or 15-lipoxygenase, with IC_{50} values ranging from

0.43 to 16.5 μM. Compound 5 exhibited weak inhibitory activity toward cyclooxygenase-2.

The methanol extracts of *M. citrifolia* suppressed melittin-induced [(3)H]AA release in a concentration-dependent manner in RAW 264.7 cells, and inhibited cPLA(2)/sPLA(2)-induced hydrolysis of 1-palmitoyl-2-[(14)C]arachidonyl phosphatidylcholine in a concentration- and time-dependent manner (Song et al. 2010). The inhibition by the methanol extracts on cPLA(2) and sPLA(2) appeared to be competitive with inhibition constants (K(i)) of 3.7 μg/mL and 12.6 μg/mL, respectively. The data suggested that methanol extracts of *Morinda citrifolia* inhibited both Ca(2+)-dependent phospholipase A(2) isozyme such as, cPLA(2) and sPLA(2) and may possess antiinflammatory activity secondary to Ca(2+)-dependent phospholipase A(2) inhibition.

The 50% ethanolic extract of *M. citrifolia* seeds (MCS-ext) (10 μg/mL) inhibited matrix metalloproteinase-1 (MMP-1) secretion from UVA-irradiated normal human dermal fibroblasts, without cytotoxic effects, at 48 h after UV exposure (Masuda et al. 2012b). The ethyl acetate-soluble fraction of MCS-ext was the most potent inhibitor of MMP-1 secretion. Among the constituents of the fraction, a lignan, 3,3′-bisdemethylpinoresinol (1), inhibited the MMP-1 secretion at a concentration of 0.3 μM without cytotoxic effects. Further, the lignan1 (0.3 μM) reduced the level of intracellular MMP-1 expression. Other constituents, namely americanin A (2), quercetin (3) and ursolic acid (4), were inactive. Western blot analysis revealed that the lignan (0.3 μM) reduced the phosphorylations of p38 and c-Jun-N-terminal kinase (JNK). The results suggested that the lignan suppressed intracellular MMP-1 expression, and consequent secretion, by down-regulation of MAPKs phosphorylation.

Citrifolinoside, an iridoid isolated from noni leaves, showed significant inhibition of UVB-induced Activator Protein-1 (AP-1) activity in cell cultures (Sang et al. 2001c). A novel iridoid dimer in whose structure the two iridoid units are connected by a rare ether group, together with two new unusual iridoids isolated from noni leaves showed significant inhibition of UVB-induced Activator Protein-1 (AP-1) activity in cell cultures (Sang et al. 2003). Activator Protein-1 (AP-1) is a redox-sensitive transcription factor which is a heterodimeric protein that regulates gene expression in response to a variety of stimuli, including cytokines, growth factors, stress, and bacterial and viral infections. AP-1 is also an important modulator in inflammatory diseases such as rheumatoid arthritis, psoriasis and psoriatic arthritis.

Nualsanit et al. (2011) demonstrated that noni extract and its bioactive component damnacanthal exhibited suppression of inflammation as evidenced by the suppression of paw and ear edema in rats and mice, and down-regulation of lipopolysaccharide-induced nuclear factor-κB (NF-κB) activity, respectively. As a result, the expression of pro-cytokines, cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase (iNOS) were suppressed in the presence of damnacanthal. The chloroform-soluble phase (3 g/kg, per os (p.o.)) of noni root significantly reduced pain-related behavior observed in the formalin test in mice (Okusada et al. 2011). These effects were not suppressed by pretreatment with naloxone (1 mg/kg, intraperitoneally (i.p.)), an opioid receptor antagonist. The chloroform -soluble phase (3 g/kg, p.o.) significantly reduced histamine-induced paw edema. Further, damnacanthal, the main active component at 10–100 mg/kg, p.o. exerted an antinociceptive effect on chemical nociceptive stimuli, and decreased histamine-induced paw edema. Damnacanthal was weakly bound to the histamine H(1) receptor. The data suggested that the chloroform-soluble phase of the Noni root had antinociceptive and antiinflammatory effects. Further, these effects of damnacanthal isolated from the noni root was mediated in part by the histamine H(1) receptor.

Antinociceptive /Analgesic Activity

The aqueous extract of noni root did not exhibit any toxic effects in mice but did show a significant, dose-related, central analgesic activity in the writhing and hotplate tests; this effect was confirmed by the antagonistic action of naloxone

(Younos et al. 1990). Moreover, administration of *M. citrifolia* extract at high dosages decreased all behavioural parameters in the two compartment test, the light/dark choice situation test, and the staircase test; together with the induced sleeping time, these results were suggestive of sedative properties. Studies by Deng et al. (2007c) indicated that the methanol crude extract of noni fruit showed significant affinity to the γ-aminobutyric acid A (GABAa) inhibitory neurotransmitter receptors, and displayed 75% binding inhibition of the agonist radioligand [3 H] muscimol at a concentration of 100 μg/mL. The methanol, butanol and water partitions exhibited IC_{50} values of 22.8, 27.2, and 17.1 μg/mL, respectively, in the GABAa-binding assay. Experimental results with noni fruit indicated the presence of competitive ligand(s), which may bind to the GABAa receptor as an agonist, and thus induce its anxiolytic and sedative effects.

A 10% solution of freeze concentrated noni fruit puree in the drinking water of mice reduced the pain sensitivity comparably to the central analgesic drug tramadol using the hot plate test (Basar et al. 2010). This effect was only partly reversed by the application of the morphine antagonist naloxone. An alcohol extract of noni fruit puree also caused an inhibition of MMP-9 release from human monocytes after stimulation with LPS (lipopolysaccharide). This effect was comparable to hydrocortisone (10^{-5} m). The findings suggested the preparations of noni fruits were effective in decreasing pain and joint destruction caused by arthritis. The aqueous extract from *M. citrifolia* leaves exhibited antinociceptive effect in the acetic acid-induced writhing test at the higher dose of 400 mg/kg (Serafini et al. 2011).

Anti atherosclerotic Activity

Kamiya et al. (2004) found that the methanol extract and ethyl acetate-soluble phase of noni fruits showed 88 and 96% inhibition of copper-induced low-density lipoprotein (LDL) oxidation by the thiobarbituric acid-reactive substances (TBARS) method, respectively. The oxidative modification of low-density lipoprotein (LDL) plays an important role in the genesis of arteriosclerosis. This beneficial effect may be attributed to the presence of lignans, phenylpropanoid dimmers. Six lignans were isolated from the ethyl acetate -soluble phase: 3,3′-bisdemethylpinoresinol (1), americanol A (2), americanin A (3), americanoic acid A (4), morindolin (5), and isoprincepin (6). These compounds inhibited copper-induced LDL oxidation in a dose-dependent manner. Compounds 1, 2, 5, and 6 exhibited remarkably strong activities, which were the same or better than that of the known antioxidant 2,6-di-tert-butyl-*p*-cresol. The IC_{50} values for 1, 2, 5, and 6 were 1.057, 2.447, 2.020, and 1.362 μM, respectively. The present study showed that the fruits of *Morinda citrifolia* may have potential in preventing arteriosclerosis.

Immunomodulatory Activity

Noni juice may exert beneficial immunomodulation effects in conditions involving inadequate immune responses (Palu et al. 2008a). In-vitro, Tahitian noni Juice (TNJ) and noni fruit juice concentrates (NFJC) (1, 5 mg/mL) potently activated cannabinoid 2 (CB2), but inhibited cannabinoid 1 (CB1) receptors in a concentration-dependant manner. In-vivo, oral administration of TNJ ad libitum for 16 days decreased the production of IL-4, but increased the production of IFN-γ. These results suggested that noni modulated the immune system via activation of the CB2 receptors, and suppression of the IL-4, but increasing the production of IFN-γ cytokines.

Li et al. (2008) demonstrated that intraperitoneal injection of fermented noni juice (fNE) significantly increased the percentages of granulocytes and natural killer (NK) cells in the peripheral blood, peritoneum, and spleen. fNE injection induced complete tumor rejection in normal C57BL/6 J mice, partial tumour rejection in C57 nude mice lacking functional lymphocytes, and no tumour rejection in NK cell deficient beige mice. Over 85% of the C57BL/6 J mice that received fNE survived the first tumour injection

and rejected up to 5×10^6 tumor cells when re-challenged. The anti-tumor activity remains in the heat-inactivated and filtrated supernatant of fNE. These data demonstrated that fNE appeared to be able to stimulate the innate immune system and the adaptive immune system to reject tumour cells.

Zhang et al. (2009) demonstrated that dendritic cells treated with fermented noni exudate (fNE) stimulated proliferation of splenocytes especially B cells. The proliferative response of B cells to fNE-treated dendritic cells was cell contact-dependent, CD40L-independent; and the adhesion feature of dendritic cells was enhanced to form large dendritic cells-B conjugation cluster. Moreover, it was demonstrated that fNE-treated dendritic cells promote B cell differentiation and immunoglobulin (Ig) class switching. Nayak and Mengi (2010) found that the hydroalcoholic (0.5 and 1.0 mg/mL) and aqueous extracts (0.5 and 1.0 mg/mL) of noni fruit significantly increased in-vitro splenocyte proliferation to the extent of 43.6, 54.5, 32.7, and 36.4%, respectively. Further, the hydroalcoholic (200 mg/kg) and the aqueous (200 mg/kg) extracts significantly increased the cell-mediated immune response by 33.52 and 18.56%, respectively. The hydroalcoholic extract (200 mg/kg) and fraction F I (40 mg/kg) also significantly increased the humoral response by 33.33 and 35.12%, respectively. The results confirmed the cellular and humoral immunostimulant properties of *M. citrifolia* fruits and rationalised its usage in traditional medicine.

Gastroprotective Activity

Umezawa (1992) reported that noni can help in stomach ulcer through inhibition of the bacterium *Helicobacter pylori*. An aqueous extract of dried mature, unripe noni fruit (0.63–2.50 g/kg) significantly prevented the formation of acid reflux esophagitis, reduced the formation of ethanol-induced acute gastric lesions, suppressed the development of gastric lesions in response to serotonin, and accelerated the healing of acetic acid-induced chronic gastric ulcer in rats with equal potency to those obtained by standard antisecretory agents (ranitidine and lansoprazole) (Mahattanadul et al. 2011). Noni extract also significantly inhibited gastric acid secretion and pepsin activity in pylorus ligated rats and strongly increased the gastrointestinal transit of charcoal meal with a higher potency than cisapride. Pure scopoletin, when compared at the same equivalent dose containing in noni extract, possessed similar antiulcer and antisecretory properties although it exerted a less prokinetic activity than the extract. The findings indicated that the noni extract as well as its biomarker: scopoletin may be beneficial as a potential preventive and therapeutic agent for gastro-esophageal inflammatory diseases, mainly through its antisecretory and prokinetic activities including an inhibitory activity on serotonin, free radicals, and cytokine-mediated inflammation.

Ergogenic Activity

In a placebo-controlled trial involving 40 highly-trained athletes showed that drinking 100 m of Tahitian noni juice (TNJ) twice daily increased endurance (time-to-fatigue) by 21%, and improved antioxidant status as measured by a 25% decrease in blood chemiluminescence (Palu et al. 2008b). Chemical analyses by multiple laboratories and drug-urine screening of human volunteers revealed that TNJ did not contain any illegal drugs or substances prohibited by the World Anti-doping Agency. The collective results indicated that TNJ improved endurance via potent antioxidant effects. Clinical studies had revealed that noni juice consumption improved quality of life scores related to physical functioning and energy levels (Ma et al. 2007). To further evaluate the ergogenic (antifatigue and endurance promoting) potential of noni juice, aged mice were pretreated orally with increasing doses (10, 20 and 40 mL/kg body weight) of Tahitian noni juice (TNJ) and then compared with young and aged controls in the forced swim test and rotarod test. The average times of all TNJ dose groups were significantly longer than the aged controls in both the swim test (36–45%) and the rotarod test (59–128%), and were similar to those of the young controls. This demonstrated not only an improvement in

endurance but also in balance and flexibility. These results confirmed the reported use of noni juice to combat fatigue, improve endurance and increase overall physical performance

Hepatoprotective Activity

Studies on female Sprague Dawley rats with CCl(4)-induced chronic liver damage showed that Tahitian noni juice (TNJ) had hepatoprotective effects (Wang et al. 2008a). Histopathological examination revealed that liver sections from the TNJ + CCl(4) appeared similar to controls, whereas typical hepatic steatosis was observed in the placebo + CCl(4) group. Serum alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine transaminase (ALT), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels were increased in the placebo group compared with the TNJ group. In contrast, high-density lipoprotein (HDL) was increased in the TNJ group and decreased in the placebo group. Thus, TNJ juice appeared to protect the liver from chronic exogenous CCl(4) exposures. In another study, pretreatment with 20% noni juice in drinking water + CCl(4) resulted in markedly decreased hepatotoxic lesions (Wang et al. 2008b). Furthermore, serum alanine aminotransferase and aspartate aminotransferase levels were significantly lower in the noni group than the placebo group. In a correlative time-dependent study, one dose of CCl(4) (0.25 mL/kg in corn oil, p.o.) in female SD rats, pretreated with 10% placebo for 12 days, caused sequential progressive hepatotoxic lesions over a 24 h period, while a protective effect from 10% noni juice pretreatment was observed. From the results they suggested noni juice to be effective in protecting the liver from extrinsic toxin exposure.

Antidiabetic Activity

Results of experiments showed that after an initial hyperglycemia, following alloxan induced diabetes, treatment with noni juice restored reduced blood sugar but euglycaemia was not achieved in male Sprague Dawley rats (Horsfall et al. 2008). At the end of 4 weeks of experimentation, the mean fasting blood sugar level of 8.0 mmol/L following combination therapy, in which insulin treatment was combined with noni juice for 4 weeks, was lower than when either noni juice 15.4 mmol/l or insulin was used alone 12.9 mmol/L. A synergistic action with insulin was demonstrated by noni fruit. Oral administration of n-butanol noni root soluble phase of the methanol extract to streptozotocin (STZ)-induced diabetic mice elicited a significant reduction of the blood glucose levels (Kamiya et al. 2008). Two iridoids and three anthraquinones were isolated as the bioactive constituents. These compounds were identified to be deacetylasperulosidic acid (1), asperulosidic acid (2), damnacanthol-3-*O*-β-D-primeveroside (3), lucidin 3-*O*-β-D-primeveroside (4) and morindone-6-*O*-β-D-primeveroside (5). 3 and 4 exhibited the hypoglycemic effects, which were anthraquinones with no substituents in one aromatic ring.

Studies demonstrated that the juice of *Morinda citrifolia* fruit significantly reduced blood sugar levels and hastened wound healing in diabetic rats%) (Nayak et al. 2007). The wound area of the *Morinda citrifolia*-treated group reduced by 73% when compared with the diabetic controls (63%). Significant increases in the weight of granulation tissue and hydroxyproline content were observed. The protein content was moderately high. Histological studies showed that collagen was laid down faster in the experimental diabetic animals than in the normal control and diabetic control groups. Fasting blood glucose values in the diabetic experimental group was reduced by 29% compared with the diabetic control animals. There was a good correlation between the wound contraction rate and blood glucose values. Owen et al. (2008) reported that noni fruit, noni leaf, commercial noni juice and mangrove bean exhibited insulin-like activity but had little or no effect on insulin action while guava bud extract displayed significant insulin-mimetic and potentiating activity. They suggested that habitual intake of guava and noni offered better protection against type 2 diabetes mellitus

development and/or betel quid diabetogenicity than cooked mangrove bean.

Oral administration of fermented noni fruit juice (2 mL/kg, twice a day) and diabetic standard reference hypoglycemic drug, glibenclamide, to streptozotocin-induced diabetic rats resulted in a significant reduction in blood glucose level compare to untreated diabetic rats (Nayak et al. 2011). Histological study of liver tissue obtained from untreated diabetic animals revealed significant fatty degeneration as compared to other three groups. They concluded that the data confirmed the hypoglycemic and hepatoprotective activity of *M. citrifolia*.

Supplementation of C57BL/6 male mice fed a high-fat diet with fermented noni fruit juice (fNJ) inhibited weight gain and improved glucose and insulin tolerance and fasting glucose (Nerurkar et al. 2012). Hypoglycaemic properties of fNJ were associated with the inhibition of hepatic forkhead box O (FoxO1) mRNA expression, with a concomitant increase in FoxO1 phosphorylation and nuclear expulsion of the proteins. Gluconeogenic genes, phosphoenolpyruvate C kinase (PEPCK) and glucose-6-phosphatase (G6P), were significantly inhibited in mice fed a high fat diet and fNJ. HepG2 cells demonstrated more than 80% inhibition of PEPCK and G6P mRNA expression in cells treated with FoxO1 siRNA and fNJ. These data suggested that fNJ improved glucose metabolism via FoxO1 regulation in high fat diet-fed mice.

Antigout Activity

In-vitro bioassay studies showed that noni fruit juice dose-dependently inhibited xanthine oxidase activity (Palu et al. 2009). Similar inhibitory results were obtained with noni fruit juice concentrate and a methanol extract from the fractionation of noni fruit puree. The results supported the traditional use of noni in the treatment of gout.

Melanogenesis Inhibitory Activity

A new iridoid glycoside, 9-epi-6α-methoxy geniposidic acid (4); three new hemiterpene glycosides, 3-methylbut-3-enyl 2′-*O*-(β-D-glucopyranosyl)-β-D-glucopyranoside (nonioside K) (6), 3-methylbut-3-enyl 6′-*O*-(β-D-xylopyranosyl)-β-D-glucopyranoside (nonioside L) (8), and 3-methylbut-3-enyl 6′-*O*-(β-D-xylofuranosyl)-β-D-glucopyranoside (nonioside M) (9); and two new saccharide fatty acid esters, 6′-*O*-(β-D-glucopyranosyl)-1′-*O*-[(2xi)-2-methylbutanoyl]-β-D-glucopyranose (nonioside N) (16) and 6′-*O*-(β-D-xylopyranosyl)-1′-*O*-[(2xi)-2-methylbutanoyl]-β-D-glucopyranose (nonioside O) (17), were isolated from a methanol extract *Morinda citrifolia* fruits, along with 11 known compounds, namely, three iridoid glycosides asperulosidic acid (1), deacetylasperulosidic acid (2), and scandoside methyl ester (3); two hemiterpene glycosides 3-methylbut-3-enyl β-D-glucopyranoside (5) and 3-methylbut-3-enyl 6′-*O*-(β-D-glucopyranosyl)-β-D-glucopyranoside (nonioside A) (7); and five saccharide fatty acid esters 2′-*O*-(β-D-glucopyranosyl)-1′-*O*-hexanoyl-β-D-glucopyranose (nonioside I) (10), 2′-*O*-(β-D-glucopyranosyl)-1′-*O*-octanoyl-β-D-glucopyranose (nonioside J) (11), 6′-*O*-(β-D-glucopyranosyl)-1′-*O*-hexanoyl-β-D-glucopyranose (nonioside D) (12), 6′-*O*-(β-Dglucopyranosyl)-1′-*O*-octanoyl-β-D-glucopyranose (nonioside C) (13), 6′-*O*-(β-Dglucopyranosyl)-1′-*O*-octanoyl-β-D-glucopyranose (nonioside C) (13) 7,12), 2′,6′-di-*O*-(β-D-glucopyranosyl)-1′-*O*-hexanoyl-β-D-glucopyranose (nonioside E)(14), and 2′,6′-di-*O*-(β-D-glucopyranosyl)-1′-*O*-octanoyl-β-D-glucopyranose(nonioside B) (15) (Akihisa et al. 2010). Upon evaluation of compounds 1–17 on the melanogenesis in the B16 melanoma cells induced with α-melanocyte-stimulating hormone (α-MSH), 13 compounds (1, 3, 4, 6–14, and 17) exhibited marked inhibitory effects with 34–49% reduction of melanin content at 100 μM with no or almost no toxicity to the cells (91–116% of cell viability at 100 μM). Five new saccharide fatty acid esters, named nonioside P (3), nonioside Q (4), nonioside R (8), nonioside S (10), and nonioside T (14), and one new succinic acid ester, butyl 2-hydroxysuccinate (=4-butoxy-3-hydroxy-4-oxobutanoic acid) (31), were isolated, along with 26 known compounds, including eight saccharide fatty acid esters,

1, 2, 5, 6, 7, 9, 12, and 13, three hemiterpene glycosides, 15, 17, and 18, six iridoid glycosides, 21–25, and 27, and nine other compounds, 20, 28, 29, and 32–37, from a MeOH extract of the fruit of *Morinda citrifol*ia (noni) (Akihisa et al. 2012). Most of the saccharide fatty acid esters, hemiterpene glycosides, and iridoid glycosides showed inhibitory effects against melanogenesis in B16 melanoma cells induced with α-melanocyte-stimulating hormone (α-MSH), with no or negligible toxicity to the cells. Americanin A, 3,3′-bisdemethylpinoresinol and quercetin isolated from a 50% ethanolic extract of noni seeds were found to be the active constituents with both tyrosinase inhibitory and radical scavenging activities (Masuda et al. 2009). In a recent study, Masuda et al. (2012a) reported that a 50% ethanolic extract of noni seeds (MCS-ext) showed significant inhibition of melanogenesis with no effect on cell proliferation. The seed extract was more active than noni leaf and fruit pulp extracts. Two lignans, 3,3′-bisdemethylpinoresinol (1) and americanin A (2), were isolated as bioactive constituents. To elucidate the mechanism of melanogenesis inhibition by the lignans, α-MSH-stimulated B16 cells were treated with 1 (5 μM) and 2 (200 μM). Time-dependent increases of intracellular melanin content and tyrosinase activity in α-MSH-stimulated B16 cells, during 24–72 h, were inhibited significantly by treatment with both lignans. The activity of 1 was greater than that of 2. Western blot analysis suggested that the lignans inhibited melanogenesis by down-regulation of the levels of phosphorylation of p38 mitogen-activated protein kinase, resulting in suppression of tyrosinase expression.

Gastric Emptying Activity

Administration of noni at 0.25 mL/kg, but not at 1 mL/kg and 4 mL/kg, for 1 day significantly inhibited gastric emptying (Pu et al. 2004). In contrast, gastric emptying was significantly inhibited by oral noni (0.25, 1, or 4 mL/kg) for 7 days. Intraperitoneal injection of lorglumide (5 or 10 mg/kg), a selective cholecystokinin (CCK)1 receptor antagonist, effectively attenuated the noni-induced inhibition of gastric emptying. The intestinal transit and body weight, food intake, water intake, urine volume as well as feces weight were not altered by the administration of noni either acutely or chronically, but the administration of oral noni (1 mL/kg) for 7 days increased the level of plasma CCK in male rats. These results suggested that oral noni inhibited gastric emptying in male rats via a mechanism involving stimulation of cholecystokinin CCK secretion and CCK1 receptor activation.

Antidyslipidemic Activity

Morinda citrifolia (Noni) fruit, leaves and root extracts were found to possess antidyslipidemic property (Mandukhail et al. 2010). Aqueous-ethanolic extracts of noni fruit, leaves and roots caused reduction in total cholesterol and triglyceride levels in triton-induced dyslipidemic rats. In high fat diet-induced dyslipidemia all three extracts caused significant reduction in total cholesterol, triglyceride, low density lipoprotein-cholesterol (LDL-C), atherogenic index and TC/HDL ratio. Noni root extract also caused increase in high density lipoprotein-cholesterol (HDL-C). Noni root and leaf extracts reduced gain in body weight with a reduction in daily diet consumption but the fruit extract had no effect on body weight and daily diet.

In-vitro studies showed that the highest lipoprotein lipase inhibitory activity was exhibited by noni leaf extract (66%), which was significantly higher than that demonstrated by noni fruit extract (54.5%), green tea extract (54.5%), and catechin (43.6%) (Pak-Dek et al. 2008). The degree of lipoprotein lipase inhibition increased with increasing concentration of the extracts. Both noni extracts contained high levels of (+)-catechin at 63.5 and 53.7 mg/g in leaf and fruit extracts, respectively but not as high as that found in green tea (530.6 mg/g). Appreciable amount of epicatechin was found in all extracts tested, while rutin was only found in noni leaf and fruit extracts. The study suggested that both leaf and fruit of *M. citrifolia* may be used as antiobesity agents in body weight management.

Neuroprotective and CNS Activity

Studies in ddy mice showed that ingestion of 10% noni juice before middle cerebral artery occlusion (MCAO) prevented neuronal damage induced by focal ischemia (Harada et al. 2009). The intake of juice reduced the infarct volume on the 3rd day of MCAO when compared to the control group. In addition, they found that the neurological deficit scores (NDS) were decreased after the reperfusion in the juice-supplied mice. They also found that glucose intolerance observed on the 1st day after MCAO completely disappeared after 10% noni juice administration (Harada et al. 2010). Further noni juice treatment significantly increased serum insulin levels while serum adiponectin levels were not affected. The results suggested noni juice could facilitate insulin secretion after ischemic stress and may attenuate the development of glucose intolerance, thus contributing to the neuronal protective effect of noni juice against ischemic stress.

Results of animal studies suggested that the administration of Noni fruit juice 6 days a week for 6 weeks protected the brain of male ICR mice from stress-induced impairment of cognitive function as measured by the water maze test (Muto et al. 2010). It was also found that the protective effect may be related to improvement in stress-induced decreases in blood vessel density in the hippocampal dentate gyrus. Muralidharan et al. (2010) found noni fruit to have a protective effect on β-amyloid (25–35) induced cognitive dysfunction in mice. In the step-down inhibitory avoidance, ethyl acetate noni fruit extract (EMC) exhibited a significant increase in short-term memory and long-term memory. A significant decrease in escape latency was noticed in mice in the water maze. A significant increase in alteration of behavior was exhibited upon administration of EMC 200 and 400 mg/kg on the Y maze. Exploratory parameters such as line crossings, head dipping and rearing were increased significantly in EMC treated groups in a dose-dependent manner. A significant reduction in level of monoamine oxidase-A and acetyl cholinesterase activity was observed in the EMC 200 and 400 mg/kg treated groups. EMC at a dose of 400 mg/kg exhibited a significant increase in the levels of serotonin and dopamine. Antioxidant enzymes such as superoxide dismutase, glutathione reductase, glutathione peroxidase and ascorbic acid were decreased significantly in the β-amyloid peptide injected group, whose levels were restored significantly by the administration of EMC (400 mg/kg).

Ethanolic extract of noni fruits and its chloroform and ethyl acetate fractions significantly improved memory and cerebral blood flow in scopolamine induced amnesia mice model (Pachauri et al. 2012). However, butanol fraction had no effect. Further, increased oxidative stress and acetylcholinesterase activity following scopolamine was significantly attenuated by ethanolic extract of Noni and its fractions. Also ethanolic extract and its fractions showed dose dependent inhibition of acetylcholinesterase activity in-vitro.

Photoprotective Activity

West et al. (2009b) reported that noni leaf extracts mitigated UVB-induced erythema and was safe for topical use. When the combination of ethanol extract and leaf juice was applied, the UVB dose required to induce erythema was almost 3.5 times greater than with untreated skin in 25 volunteers. There was no evidence of allergenic potential in the repeat-insult patch test in 49 volunteers. In the histamine H-1 receptor-binding assay, the crude ethanol extract of noni leaves inhibited receptor binding by 57%.

Wound Healing Activity

Morinda citrifolia (noni) fruit extract was reported to up-regulate biosynthesis of type I collagen and glycosaminoglycans in primary cultures of normal human fibroblasts (Kim et al. 2005). An active single compound having a type I collagen-stimulating effect was isolated from noni fruit and identified as 1,4-dihydroxy-2-methoxy-7-methylanthraquinone. The anthraquinone showed significantly increased elaboration

of procollagen type I C-terminal peptide and glycosaminoglycans and reduced expression of the collagenase matrix metalloproteinase-1 dose-dependently in human dermal fibroblasts. Further, in a clinical trial, a nano-emulsion containing anthraquinone predominantly increased the dermal type I procollagen in nude mouse skin. These results suggested that anthraquinone derived from Noni extract is a good candidate for use as a new anti-wrinkle agent due to its strong induction of biosynthetic activity of extracellular matrix components. In recent studies, noni leaf extract was demonstrated to have wound healing activity. On day 11 after oral administration of noni juice ethanol extract (150 mg/kg/day) in the drinking water, the extract-treated animals exhibited 71% reduction in the wound area when compared with controls which exhibited 57% (Nayak et al. 2009). The granulation tissue weight and hydroxyproline content in the dead space wounds were also increased significantly in noni-treated animals compared with controls. Enhanced wound contraction, decreased epithelialization time, increased hydroxyproline content and histological characteristics suggested that noni leaf extract may have therapeutic benefits in wound healing. In one recent wound-healing study, there was a significant increase in wound contraction rate, tensile strength, granuloma breaking strength, collagen content, dry granuloma weight and hydroxyproline content with noni leaf extract treatment (Rasal et al. 2008). A significant decrease in epithelialisation period and malondialdehyde (MDA) levels in *Morinda citrifolia* leaf extract treated group were observed when compared to control group. From the results, it was concluded that the *M. citrifolia* aqueous leaves enhanced the wound healing and possessed antioxidant activity

In another recent study, a 50% ethanolic extract (MCS-ext) from seeds of *Morinda citrifolia* (noni seeds) showed more potent in vitro inhibition of elastase and tyrosinase, and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity than extracts of *M. citrifolia* leaves or flesh (Masuda et al. 2009) . Activity-guided fractionation of MCS-ext using in vitro assays led to the isolation of ursolic acid as an active constituent of elastase inhibitory activity. 3,3′-bisdemethylpinoresinol, americanin A, and quercetin were isolated as active constituents having both tyrosinase inhibitory and radical scavenging activities. Americanin A and quercetin also showed superoxide dismutase (SOD)-like activity.

Results of studies by Palu et al. (2010) suggested that noni leaf significantly accelerated wound healing in mice via its ligand binding to the PDGF (platelet-derived growth factor) and A(2A) receptors as its probable mechanisms of wound-healing. Fresh noni leaf juice showed significant affinity to PDGF receptors, and displayed 166% binding inhibition of the ligand binding to its receptors, while at the same concentration, it only had 7% inhibition of the ligand binding to the A(2A) receptors. The ethanol leaf extract and its methanol and hexane fractions showed significant affinity to A(2A) receptors in a dose dependent manner. The methanol fraction significantly increased wound closure and reduced the half closure time in mice with a CT_{50} of 5.4 ± 0.2 days compared with control. The results also supported the traditional use of noni for wound healing.

Antithrombotic Activity

In-vivo studies using the jugular vein thrombosis model induced by ferric chloride in SD rats showed that noni juice had antithrombotic activity (Ayanbule et al. 2011). Noni juice also exhibited an additive effect with heparin which was elucidated by the slight inhibition on aPTT (activated partial thromboplastin time) by noni juice without induction of thrombocytopenia. Heparin is the most common anti-coagulant for venous thromboembolism, but severe allergic reactions, bleeding, and thrombocytopenia limit its use.

Antiviral Activity

A compound isolated from noni roots named 1-methoxy-2-formyl-3-hydroxyanthraquinone suppressed the cytopathic effect of HIV infected

MT-4 cells, without inhibiting cell growth and removal of endothelium (Umezawa 1992). Six anthraquinones: nordamnacanthal, alizarin-1-methyl ether, rubiadin, soranjidiol, lucidin-ω-methyl ether and morindone, isolated from noni cell suspension culture exhibited strong antitumor promoting activity at the concentration of 2.0 μg/mL when assayed using the inhibition test of Epstein Barr Virus (EBV) activation on Raji cells (Jasril et al. 2003). At the concentration of 0.4 μg/mL, only nordamnacanthal exhibited strong antitumor promoting activity with the inhibition rate and the cell viability of 75.0 and 75.8%, respectively, which was stronger than the reference compounds genistein and quercetin. From the screen of 504 bioactive compounds, Kamata et al. (2006) identified damnacanthal, a component of noni root, as an inhibitor of viral protein R (Vpr), one of the human immunodeficiency virus type 1 (HIV-1) accessory proteins, responsible for multiple cytopathic effects, G2 cell cycle arrest and apoptosis.

A new anthraquinone, 1,5,15-tri-*O*-methylmorindol (1), and two new saccharide fatty acid esters, 2-*O*-(β-D-glucopyranosyl)-1-*O*-hexanoyl-β-D-gluropyranose (4) and 2-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-gluropyranose (5), have been isolated from a methanol extract of the fruits of *Morinda citrifolia* along with 10 known compounds, namely, two anthraquinones (2, 3), six saccharide fatty acid esters (6–11), an iridoid glycoside (12), and a flavanol glycoside (13) (Akihisa et al. 2007). All the compounds 1–13 exhibited moderate inhibitory effects (IC_{50} values of 386–578 mol ratio/32 pmol TPA) against the Epstein-Barr virus early antigen (EBV-EA) activation induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA).

Noni fruit juice exhibited antiviral activity (Selvam et al. 2009). Noni juice MC exhibited a maximum protection of 18% of the MT-4 cells against the cytopathic effect of HIV-1(III_B) after acute infection. Noni juice displayed marked cytotoxic activity in lymphocyte (MT-4) cells (CC_{50} 0.19 μg/mL). The 50% effective concentration for inhibition of HCV subgenomic replicon replication in Huh 5–2 cells by noni juice was 0.98 mμg/mL and cytotoxicity was found to be greater than 50 μg/mL.

Antimicrobial Activity

Atkinson (1956) reported phenolic compounds such as acubin, L-asperuloside, alizarin, scopoletin and other anthraquinones to be the bioactive ingredients for the in-vitro growth inhibitory effect of noni extract against the following bacteria: *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus morgaii*, *Bacillus subtilis*, *Escherichia coli*, *Helicobacter pylori*, *Salmonella* sp. and *Shigella* sp. Other studies also reported significant antimicrobial effect of ripe noni fruit on *P. aeruginosa*, *S. pyrogenes*, *E. coli*, *Salmonella typhosa*, *Salmonella montevideo*, *Salmonella schottmuelleri*, and *Shigella paradys* (Bushnell et al. 1950; Dittmar 1993). Leach et al. (1988) reported *M. citrifolia* to have antibacterial activity agsint both Gram positive and negative bacteria. Locher et al. (1995) demonstrated that an acetonitrile extract of the dried fruit inhibited the growth of *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Escherichia coli*, and *Streptococcus pyrogenes*. They found that the antimicrobial effect was highly dependent on the stage of ripeness and on processing, being greater when the fruit was ripe, without drying. Three anthraquinones viz., nordamnacanthal, damnacanthal and morindone from noni roots, were found to have strong antimicrobial activity (Ali et al. 2000).

Methanol extract of *M. citrifolia* exhibited potential antibacterial activities to both gram positive *Staphylococcus aureus* and Methicillin Resistant *Staphylococcus aureus* (MRSA) but were inactive towards Gram negative *Eshcerichia coli and Klebsiella pneumoniae* (Zaidan et al. 2005). In another study, the crude ethanol extract and hexane fraction from *Morinda citrifolia* showed antitubercular activity (Saludes et al. 2002). The major constituents of the hexane fraction were: E-phytol, cycloartenol, stigmasterol, β-sitosterol, campesta-5,7,22-trien-3β-ol and the ketosteroids stigmasta-4-en-3-one and stigmasta-4-22-dien-3-one. E-Phytol, a mixture of the two ketosteroids, and the epidioxysterol derived from campesta-5,7,22-trien-3β-ol all showed pronounced antitubercular activity. The aqueous extract from *M. citrifolia* leaves significantly reduced leukocyte migration in doses of 200 and 400 mg/kg and showed mild antibacterial activity (Serafini et al. 2011).

An aqueous *Morinda citrifolia* extract was shown to interfere with the serum-induced morphological conversion of *Candida albicans* from a cellular yeast to a filamentous form in- vitro (Banerjee et al. 2006). The conversion of from a cellular yeast to a filamentous form in-vivo is associated with pathogenicity. The same extract also inhibited the germination of *Aspergillus nidulans* spores. These results demonstrate that *M. citrifolia* may have potential therapeutic value with regard to candidiasis and aspergillosis. *M. citrifolia* fruit extract exhibited in-vitro antifungal effect on *Candida albicans* and the inhibitory effect varied with concentration and contact time (Jainkittivong et al. 2009).

Schäfer et al. (2008) reported that calves fed noni puree exhibited enhanced bactericidal activity against *Escherichia coli*. Blood samples from noni puree-fed calves displayed significantly more *E. coli* bacterial killing than did controls on day 14. There was no significant difference between the groups for *Staphylococcus epidermidis* mortality.

Endodontic Uses

In-vitro-studies by Murray et al. (2008) showed that *M. citrifolia* juice to be an effective endodontic irrigant. They found the most effective removal of smear layer from the canal walls of endodontically instrumented teeth occurred with noni juice and NaOCl (sodium hypochlorite), both with a rinse of 17% EDTA. Both noni juice and NaOCl treatments were similarly effective with a rinse of 17% EDTA (to completely remove up to 80% of the smear layer from some aspects of the root canal. Noni juice was more effective than chlorhesidine gluconate for removing smear layer and saline as the negative control. The efficacy of noni juice was similar to NaOCl in conjunction with EDTA as an intracanal irrigant. They stated that noni juice appeared to be the first fruit juice to be identified as a possible alternative to the use of NaOCl as an intracanal irrigant. They also compared the effect of 10 different endodontic irrigation and chelating treatments on dental pulp stem cell (DPSC) attachment to root canal surfaces using extracted, cleaned, and shaped human nondiseased single-canal teeth (Ring et al. 2008). The number of attached DPSCs appeared to be correlated with the cytotoxicity of the root canal irrigating solution. The presence or absence of the smear layer had little influence on DPSC activity. Their results suggested that biocompatible irrigants were needed to promote DPSC attachment to root canal dentin, and to accomplish some regenerative endodontic therapies.

Kandaswamy et al. (2010) found that propolis and *M. citrifolia* juice were effective against *Enterococcus faecalis* colonisation in the root canal dentine of extracted teeth. Chlorhexidine gluconate (100%) produced highest antimicrobial efficacy followed by 2% povidone-iodine (87%), propolis (71%), noni juice (69%), and calcium hydroxide (55%). There was no significant difference between propolis and noni juice and no significant difference between data at 200 and 400 μm root canl depth.

Nephroprotective Activity

Supplementation of noni fruit juice may be useful in reducing gentamicin nephrotoxicity in rats (Pai et al. 2011). Co-administration of noni fruit juice with gentamicin dose-dependently decreased the rise in serum urea, serum uric acid, serum creatinine and blood urea nitrogen caused by gentamicin. Noni fruit juice plus gentamicin treated rats revealed insignificant changes in tubular epithelium compared to epithelial loss with intense granular degeneration involving >50% renal cortex in gentamicin treated rats.

Antigenotoxic Activity

Aqueous noni leaf extract was found to have antigenotoxic effect (Sreeranjini and Siril 2011). Hydrogen peroxide-induced chromosomal aberrations such as breaks, bridges, stickiness and polar deviations were reduced in *Allium cepa* root tip meristem cells treated with noni leaf extract (15 g/L). A significant reduction in mitotic index was recorded in treatment groups over negative control. The observations suggested that *M. citrifolia* aqueous leaf extracts had anti-mitotic

and anti-genotoxic effects; consequently oxidative stress induced aberrations due to hydrogen peroxide were efficiently restored in the extract treated *A. cepa* root meristem cells.

Antileishmanial activity

In a double-blind, randomized, clinical trial, out of 40 patients with cutaneous leishmaniasis, 50% showed an excellent response and 30% exhibited good improvement with a topical ointment prepared from noni stem (Sattar et al. 2012). Morindicone and morinthone isolated from the extract exhibited good in-vitro antileishmanial activity.

Antiemetic Activity

Prapaitrakool and Itharat (2010) conducted a preliminary, prospective, randomized double blinded, placebo-controlled trial to evaluate the efficacy of noni for the prevention of postoperative nausea and vomiting (PONV) in 100 patients of ASA (American Society of Anesthesiologists) physical status I or II, aged 18–65 years, considered at risk for PONV after various types of surgery. They found significantly fewer patients who had received the 600 mg noni extract experienced nausea during the first 6 h compared to the placebo group. The incidence of PONV in other time periods was not statistically different for all three noni doses compared to the placebo group. No side effects were reported in all groups. They concluded that noni had antiemtic property and prophylactic noni extract at 600 mg (equivalent to 20 g of dried noni fruit or scopoletin 8.712 μg) effectively reduced the incidence of early postoperative nausea (0–6 h).

Antispasmodic Activity

Noni root extract was found to have antispasmodic activity (Gilani et al. 2010). Ethanol extract of noni roots elicited a concentration-dependent relaxation of spontaneous and high K^+ induced contractions in isolated rabbit jejunum preparations and caused an upward shift in the concentration response curves of Ca^{2+}. In guinea-pig right atria, the extract inhibited both atrial force and rate of spontaneous contractions. In rabbit thoracic aortic preparations, the extract also suppressed contractions induced by phenylephrine (1.0 μM) and by high K^+, similar to that of verapamil. The root extract showed the presence of saponins, flavonoids, anthraquinine coumarines, sterols and phenolic compounds. These results suggested the spasmolytic and vasodilator effects of noni ethanol root extract were mediated possibly through blockade of voltage-dependent calcium channels and release of intracellular calcium, which may explain the medicinal use of *Morinda citrifolia* in diarrhea and hypertension.

Gastrokinetic Activity

Noni fruit extract was reported to have gastrokinetic activity (Nima et al. 2012). In a single-dose, randomized, open-label and 2-period crossover study on 20 Thai healthy volunteers, aqueous noni fruit extract or drinking water was administered orally 30 min prior to a single oral administration of ranitidine, a putative indicator of gastrointestinal motility. Noni extract significantly enhanced of the rate and the extent of ranitidine absorption. Noni extract produced a definite contractile response of a rat gastric fundus strip in a dose dependent manner. Scopoletin at the same equivalent dose present in the extract elicited a concentration-dependent contraction that amounted to 45% of the maximal response to the extract . The contractile response of both noni fruit extract and scopoletin was mediated through the 5-HT(4) receptor.

Insecticidal Activity

The ripe fruit was found to have insecticidal activity and to be highly toxic to *Drosophila melanogaster*, *D. simulans*, and *D. mauritiana* (Legal et al. 1994). Green and rotten fruits are not toxic for all species tested. Short chain fatty acid were

most abundant in the ripe fruit pulp and the most abundant octanoic acid alone appeared to be sufficient to explain the toxic effect of the pulp. It was less abundant in rotten fruit and absent in green fruit. *D. sechellia* was five–six fold more resistant than *D. melanogaster* to octanoic acid. Similar results were obtained by Farine et al. (1996). They found that octanoic acid, among the 51 volatile compounds isolated, to be responsible for the general toxicity of noni fruit to most *Drosophila* species; *D. sechellia* was the only species resistant to this acid. Hexanoic acid elicited a unique effect, causing reversible coma but no mortality while decanoic acid was inactive. A mixture of these three acids in proportions similar to those found in the fruit, mimicked the effects of ripe noni fruits. The anthraquinone, damnacanthal and 1-hydroxy-2-methylanthraquinone from noni roots exhibited promising larvicidal activities against the larvae of *Aedes aegypti* (Ee et al. 2009). *M. citrifolia* leaf extract at 200, 300, 400, 500, and 600 ppm caused a significant mortality of three mosquito species, as malarial vector *Anopheles stephensi*, dengue vector *Aedes aegypti*, and filarial vector *Culex quinquefasciatus* (Kovendan et al. 2012). Hexane, chloroform, acetone, and water extracts caused moderate considerable mortality; however, the highest larval mortality was methanolic extract, observed in three mosquito vectors. The larval mortality was observed after 24-h exposure whilst no mortality was observed in the control.

Anthelmintic Activity

Alcoholic extract of noni leaves showed good in-vitro activity anthelmintic activity against human *Ascaris lumbricoides* (Raj 1975). The chloroform extract of noni fruit exhibited highest in-vitro anthelmintic activity against *Haemonchus contortus* compared to the control based on the ability of the extract to kill the worm and the ability of the extracts to prevent egg development (Murdiatia et al. 2000). Noni fruit extract was found to have anthelmintic activity in-vitro and in chicken naturally infected by *Ascaridia galli* (Brito et al. 2009). At concentrations of 13.48 and 26.96 mg/mL, the aqueous fruit extract demonstrated in-vitro mortality of 46.67 and 50%, respectively, there was a significative difference from the negative control. The ethanolic extract presented statistical difference from the negative control for the concentrations of 33.36 and 66.72 mg/m), expressed by a mortality rate of 66.67 and 76.67%, respectively. In the in-vivo test, the aqueous extract of noni fruit showed 27.08% of elimination, differing statistically from the control group. There was no statistical difference between the ethanolic fruit extract treatments and the control.

Genotoxicity and Toxicity Studies

Morinda citrifolia (noni) being known to contain genotoxic anthraquinones in the roots and because of the widespread use of noni juice, the possible genotoxic risk was examined through a battery of short-term tests (Westendorf et al. 2007). Noni juice extract in the *Salmonella* microsome assay showed a slight mutagenic effect in strain TA1537, due to the presence of flavonoids. No mutagenicity was observed in the mammalian mutagenicity test with V79 Chinese hamster fibroblasts. Rats treated with a noni juice concentrate did not show DNA repair synthesis in primary rat hepatocytes, nor could DNA adducts or DNA strand breaks be observed. HPLC analysis of noni juice for anthraquinones was negative, with a sensitivity of <1 ppm. In summary, chemical analysis and genotoxicity tests revealed that noni juice did not have a genotoxic potential and that genotoxic anthraquinones did not exist in noni juice. A primary DNA damage test in *E. coli* PQ37 (SOS-chromotest) and a 24 h brine shrimp toxicity test did not reveal any genotoxic or cytotoxic activity of aqueous extract of noni blossoms (Deng et al. 2012). Wang et al. (2011b) in their study in ICR mice for 3 generations of offsprings, found that authentic noni juice had no adverse effect on fertility and fetal development. Litter sizes of the noni group in the first (F1), second (F2), and third (F3) generations were, respectively, 29.3, 19.8 and 19.6% larger than corresponding controls. Despite larger litter sizes,

there were no decreases in fetal weight in any generation of the noni group. Further, maternal health and offspring viability in the noni groups were equal to or greater than the controls.

Millonig et al. (2005) reported a case of a 45-year-old patient with highly elevated transaminases and elevated lactate dehydrogenase. Liver biopsy confirmed herbal hepatoxicity and he admitted drinking noni juice for the preceding 3 weeks. After stopping ingestion of noni, transaminase levels normalized quickly and were within normal ranges 1 month after the first presentation. Stadbaeur et al. (2005) reported two cases of hepatotoxicity of noni juice. A 29-year-old man with previous toxic hepatitis associated with small doses of paracetamol developed subacute hepatic failure following consumption of 1.5 L noni juice over 3 weeks necessitating urgent liver transplantation. A 62-year-old woman without evidence of previous liver disease developed an episode of self-limited acute hepatitis following consumption of 2 L noni juice for over 3 months. Routine laboratory tests and transjugular or percutaneous liver biopsy were performed. The first patient underwent successful liver transplantation while the second patient recovered spontaneously after cessation of noni juice. Yuce et al. (2006) reported a 24-year-old female patient mild elevations of serum transaminase and bilirubin levels. After several weeks of investigation, fine-needle aspiration biopsy of the liver ruled out an autoimmune hepatitis but showed signs of drug-induced toxicity. She admitted that for 'general immune system stimulation' she had been drinking noni juice. After cessation of the noni juice ingestion, her transaminase levels normalized quickly and were in the normal range within 1 month.

Measurements of liver function in a human clinical safety study of Tahitian noni juice, as well as subacute and subchronic animal toxicity tests revealed no evidence of adverse liver effects at doses many times higher than those reported in the case studies (West et al. 2006). Additionally, *M. citrifolia* anthraquinones occur in the fruit in quantities too small to be of any toxicological significance. Further, these do not have chemical structures capable of being reduced to reactive anthrone radicals, which were implicated in previous cases of herbal hepatotoxicity. The available data revealed no evidence of liver toxicity. West et al. (2009a) conducted in-vitro hepatotoxicity tests of noni fruit in human liver cells, HepG2 cell line and a subchronic oral toxicity test of noni fruit was also performed in Sprague-Dawley (SD) rats. Freeze-dried filtered noni fruit puree did not decrease HepG2 cell viability or induce neutral lipid accumulation and phospholipidosis. There were no histopathological changes or evidence of dose-responses in hematological and clinical chemistry measurements, including liver function tests. The no-observed-adverse-effect level (NOAEL) for freeze-dried noni fruit puree wais greater than 6.86 g/kg body weight, equivalent to approximately 90 mL of noni fruit juice/kg. Based on these findings they concluded that consumption of noni fruit juice was unlikely to induce adverse liver effects.

In another study, daily administration of freeze- dried noni fruit puree by gastric intubation to pregnant Sprague Dawley rats at 1.72, 3.43, and 6.86 g/kg body weight for 21 days caused no prenatal toxicity in the pregnant dams (West et al. 2008b). There was no difference between the control (given water) and any noni group in the number of live fetuses, resorptions, fetal weight and length, or skeletal abnormalities. No dead fetuses, gross external malformations, or internal organ defects were observed in any group. The authors asserted that the findings do not indicate that toxicity from noni juice to developing embryos and fetuses is expected. However, in another study, exposure of pregnant Wistar rats to aqueous noni fruit extract (7, 30 and 300 mg/kg bw) or commercial noni fruit juice (0.4, 2 and 20 mL/kg bw) during organogenesis period did not induce maternal toxicity but induced delayed ossification in foetuses (Marques et al. 2010). Müller et al. (2009) found that exposure of aqueous *M. citrifolia* extract in Wistar rats induced reproductive toxicity in nonlinear dose-response. The uterotrophic assay indicated presence of in-vivo antiestrogenic activity of extract at doses of 7.5 and 750 mg/kg. The in utero and lactational exposure showed that the treatment with noni extract at the dose of 7.5 mg/kg induced a reduction

of 50% in parturition index and an increase of 74% in post-implantation losses index. The in-vitro test showed that uteri from rats treated with 7.5 mg/kg of the extract presented a 50% reduction on contraction induced by arachidonic acid.

In a 28-day double-blind clinical safety study of Tahitian noni fruit juice conducted with 96 healthy volunteers, West et al. (2009c) found those in the noni groups experienced 20–50% fewer total adverse events than those in the placebo group. No other clinically significant differences between any of the groups were noted in the parameters and measurements of this study, nor was there evidence suggesting any adverse dose-related effects. Based on the results they suggested drinking up to 750 mL Tahitian noni juice per day to be safe.

An article reviewing the current knowledge on the phytochemistry, pharmacology, safety aspects of noni fruit and noni-derived products, and health-related claims and benefits was published in 2007 (Potterat and Hamburger 2007). Products derived from noni fruit (*Morinda citrifolia*) have been commercialised in the USA since the 1990s and are increasingly distributed all over the world. A large number of beneficial health effects have been claimed for noni from in-vitro and in-vivo studies, albeit clinical evidence are essentially lacking. Fruit juice of noni has been approved as a novel food by the European Commission in 2003. Based on a toxicological assessment, noni juice was considered as safe. Due to recent reported cases of hepatotoxicity, the safety issue has been re-examined in Europe. They stated that while the European Food Safety Authority see no link between adverse effects on liver and consumption of noni juice, a continuing monitoring of the situation was deemed desirable and some vigilance advised.

Safety tests and antinutrient analyses of noni leaf revealed no toxicity problems (West et al. 2007). No evidence of toxicity or differences in weight gain were observed in acute, subacute, and subchronic oral toxicity tests of ethanol-water (1:1 v/v) and hot-water extracts of noni leaves in mice at doses of 2000, 200, and 20 mg/kg body weight, respectively. Acute systemic anaphylaxis tests of the ethanol-water (4:1 v/v) and hot-water extracts were negative. Further, leaf proteins were readily digested in simulated gastric fluid. Phytic acid was not detected in the raw leaf (<1 g/kg) and oxalic acid was very low 1 g/kg. Tannic acid concentrations in frozen and dried leaf were 1.6 and 25.8 g/kg, respectively.

Hyperkalemia

Herbal remedies and alternative medicine products may be surreptitious sources of potassium in patients with renal disease. One case of a man with chronic renal insufficiency who self-medicated with noni juice developed hyperkalemia despite claiming adherence to a low-potassium diet (Mueller et al. 2000). The potassium concentration in noni juice samples was determined and found to be 56.3 mEq/l, similar to that in orange juice and tomato juice.

Traditional Medicinal Uses

Morinda citrifolia has been used in traditional folkloric medicine in Asia, Polynesia and elsewhere in the tropics (CSIR 1962; Watt and Breyer-Brandwijk 1962; Burkill 1966; Quisumbing 1978; Morton 1992).

Morinda citrifolia (noni) is one of the most important traditional Polynesian medicinal plants (Dixon et al. 1999; Morton 1992). Remedies from isolated Polynesian cultures, such as that of Rotuma, illustrate traditional indications that focus upon leaves, roots, bark, and green fruit, primarily for topical ailments (McClatchey 2002). Locher et al. (1995) reported that selected plants including *M. citrifolia* have a history of use in Polynesian traditional medicine for the treatment of infectious disease. Anecdotally collected Hawaiian remedies that employ noni fruit illustrate changing usage patterns with shifts in recent times to preparation of juice made of ripe or decaying fruit. Ralph M. Heinicke promoted a wide range of claims about noni, and these appeared to have fueled much of the current commercial interest in the plant. Bushnell et al. (1950) reported that noni was traditionally used to treat

broken bones, deep cuts, bruises, sores and wounds. Recent studies of the proliferation of commercial products have shown that noni product manufacturers are promoting a range of therapeutic claims. These claims are based upon traditional Polynesian uses, Heinicke's ideas, and fragments of recent scientific studies including the activity of noni in the treatment of cancer. One of the common traditional uses of noni is the treatment of painful inflammatory conditions, such as arthritis (Basar et al. 2010).

Most parts of the tree have been widely used in traditional medicine since ancient times. In Vietnam, the fruit is considered stomachic, laxative and emmenagogue. It is used for metrorrhagia, leucorrhoea, dropsy, diabetes and asthma, Roasted fruit is administered orally for dysentery. The young fruit are used in combination with roots of *Costus speciosus* and tubers of *Ipomea digitata* for traumatic injuries, contusions, hyperaemia. The leaves are considered deobstruent and emmenagogue. Leaves are used for dysentery, diarrhoea, fevers, headache and dizziness. Pounded fresh leaves are used as poultices for healing furunculosis. The roots are use for treating hypertension, lumbago, body ache and rheumatoid arthritis.

In India, the roots are considered purgative, cathartic and febrifuge and pounded roots are used as poultice for alleviating gout pains. In Bombay the leaves are used as a healing application to wounds and ulcers and are administered internally as a tonic and febrifuge. The charred leaves made into a decoction with a little mustard are said to be a remedy for infantile diarrhoea; with aromatics, the decoction is given in dysentery. The fruit is used as an emmenagogue and a deobstruent. The charred green fruit is mixed with salt, and applied to spongy gums. The juice of the fruit is made into a syrup and used as a gargle to relieve sore throat.

In Malaysia, a decoction of the bark has been used for ague. Heated leaves were applied to the chest or abdomen for coughs, enlarged spleen, in nausea, colic and fever. The leaves are used in a complex ointment mixture for small-pox. The ripe fruit is used as emmenagogue and was used for leucorrhoea and sapraemia. The fruit is used as a shampoo in against head lice. In Indonesia, the fruit is used internally for swollen spleen, liver diseases, beri-beri, haemorrhage and coughs and as a laxative.

Morinda citrifolia is one of the most important medicinal plant in Polynesia and Micronesia. Noni has been used in traditional folk remedies for over 2,000 years. All parts of the tree has been utilised in various medicinal preparations, healing protocols and home therapies for a wide array of ailments and disorders. various parts of the tree (leaves, flowers, fruits, bark, roots) serve as tonics and to alleviate fever, to treat eye and skin problems, gum and throat problems as well as constipation, stomach pain, or respiratory discomfort. The plant has been used for treating malaria, as a general febrifuge, urinary tract infections, hernia, stings from stone-fish and laxative especially the seed. Juice from mashed immature fruit has been used alone or in combination with coconut oil for sores and scabs around and within the mouth, tooth-ache and used as a purgative on its own or in combination with sugarcane juice or mashed candlenut (*Aleurites moluccana*) fruit. Ripe fruit extract or mash are use as a vermicide to expel intestinal worms, as a poultice on wounds, boils, carbuncles, and pimples for peeling and cracking sole and toes. Fruit juice is used for treating loss of appetite, diabetes, heart discomfort and high blood pressure. Fruit juice is also used to counteract intoxication from kava. Fruit oil is also used for stomach ulcers. Dried leaves and fruit are used to make herbal infusions and teas. Leaves and fruit poultices are used for deep bruising, rheumatism and sprains and extracts of the leaves, fruit and bark used for hypertension, diabetes, tuberculosis. Stem and root bark has been used for jaundice. Leaf poultices have been used as body wrap and for wrapping the skin around fractured bones. Leaf tea is commonly used as analgesic.

Other Uses

The tree has been used in Malaysia and Thailand as a support for pepper plants. In Surinam and some other countries, the tree serves as a windbreak, as support for vines and as shade for coffee trees. In Java, Indonesia, noni is cultivated for a

red dye which is widely used in the production of high quality batik in the batik industry. The basis of the morindone dyeing matter, called Turkish red, is the hydrolysed (red) form of the glycoside morindin. In Hawaii, a yellowish dye is extracted from its root for dyeing cloth and fala (mats). The bark of the roots has been used for cleansing the hair and sometimes for cleaning iron and steel. The wood can be used in light construction, canoe parts and paddles, furniture, toolsaxe handles, crafts, digging sticks, poles and fuel wood. Roots are used for carving in Niue. Leaves are used for feeding silkworms in India and for livestock fodder in India and Niue. The fruit is used for pig feed in Puerto Rico. A fetid oil obtained from seeds is used as scalp insecticide or insect repellent e.g. in Hawaii. In Suriname, the pulp is used for washing hair and the tree lopped for fodder.

M. citrifolia demonstrated moderate antinematodal activity against *Bursaphelenchus xylophilus*, the pine wood nematode (Mackeen et al. 1997).

Comments

M. citrifolia is dwindling in its natural habitat but is unlikely to be endangered by serious genetic erosion as it is being planted in house backyards in the rural areas.

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Nauclea orientalis

Scientific Name

Nauclea orientalis (L.) L.

Synonyms

Adina orientalis (L.) Lindeman ex Bakh.f., *Bancalus cordatus* (Roxb.) Kuntze, *Bancalus grandifolius* (DC) Kuntze, *Bancalus macrophyllus* Kuntze, *Bancalus orientalis* (L.) Kuntze, *Cadamba nocturna* Buch.-Ham., *Cephalanthus orientalis* L., *Nauclea annamensis* (Dub. & Eberh.) Merr., *Nauclea coadunata* Roxb. ex J.E. Smith, *Nauclea cordata* Roxb., *Nauclea elmeri* Merr., *Nauclea glaberrima* Bartl., *Nauclea grandifolia* DC nom. illeg., *Nauclea leichhardtii* F. Muell., *Nauclea lutea* Blanco, *Nauclea macrophylla* Blume nom. illeg., *Nauclea orientalis* var. *pubescens* (Kurz) Craib, *Nauclea ovoidea* (Pierre ex Pit.) N.N. Tran, *Nauclea roxburghii* G. Don., *Nauclea stipulacea* G. Don, *Nauclea undulata* Roxb., *Nauclea wallichiana* R.Br. nom. illeg., *Platanocarpum cordatum* (Roxb.) Korth., *Sarcocephalus annamensis* Dub. & Eberh., *Sarcocephalus bartlirgii* Miq., *Sarcocephalus buruensis* Miq., *Sarcocephalus coadunatus* (Roxb. ex Sm.) Druce, *Sarcocephalus cordatus* (Roxb.) Miq., *Sarcocephalus cordatus* var. *glabra* Kurz, *Sarcocephalus cordatus* var. *pubescens* Kurz, *Sarcocephalus glaberrimus* (Bartl.) Miq., *Sarcocephalus orientalis* (L.) Merr., *Sarcocephalus ovatus* Elmer, *Sarcocephalus ovatus* var. *mollis* Koord. & Valeton, *Sarcocephalus ovoideus* Pierre ex Pit., *Sarcocephalus papagola* Domin., *Sarcocephalus undulatus* (Roxb.) Miq., *Sarcocephalus undulatus* var. *buruensis* (Miq.) Havil.

Family

Rubiaceae also placed in Naucleaceae.

Common/English Names

Burr Tree, Cheesewood, Canary Cheesewood, Canary Wood, Cape York Leichardt, Leichhardt Pine, Leichhardt Tree, Soft Leichhardt, Yellow Cheesewood.

Vernacular Names

Australia: Atulwanyi, Atulganyi, Gadugay, Jirrib, Kaapi, Kalpi, Kabal, Oboy, Opoy, Wowerik (Aboriginal Names);
Borneo: Bankal, Bangkol, Bongkol;
Laos: Karn Luang;
Philippines: Malakabak (Bagobo), Mambog (Bikol), Bulabangkal, Hambabalos, Kabag (Bisaya), Kabak (Cebu Bisaya), Bulala (Ilkoko), Balikakak (Maguindanao), Bangkal (Manobo), Bangkal, Bulubitoan (Panay Bisaya), Bulala (Pangasinan), Bangkal, Malbog (Samar-Leyte Bisaya), Bangkal, Mabalot (Tagalog);
Sri Lanka: Batticaloa (Tamil), Bakmee (Sinhalese);

T.K. Lim, *Edible Medicinal and Non-Medicinal Plants: Volume 5, Fruits*,
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Thailand: Kanluang;
Vietnamese: Gao Vang.

Origin/Distribution

The species is found from Sri Lanka and Indo-China to New Guinea and Australia. In Papua New Guinea it is found in West Sepik, East Sepik, Madang, Morobe, Western, Gulf, Central, Milne Bay, Papuan Islands, New Britain and Bougainville. In Thailand, it is the most common and widely distributed *Nauclea* species and is found in – Northern Thailand: Mae Hong Son, Chiang Mai, Phrae, Phitsanulok, Kamphaeng Phet, Phichit; North-Eastern Thailand : Khon Kaen; Eastern: Chaiyaphum, Ubon Ratchathani; South-Western Thailand: Uthai Thani, Kanchanaburi, Ratchaburi, Phetchaburi; Central Thailand: Krung Thep Maha Nakhon (Bangkok) [cultivated]; South-Eastern Thailand: Sa Kaeo, Chanthaburi and in Peninsular Thailand: Satun. In Australia, the species occurs in northern Western Australia, Top End of the Northern Territory and North East Queensland.

Agroecology

In Australia the yellow cheesewood occurs at 0–500 m altitude, in a variety of soil types and vegetation types from sparse rheophyte shrublands, monsoon vine forests, open vegetation along water ways, edge of swamps, black soil plains to tall well-developed gallery tropical lowland rainforest where it reaches its best development. The mean annual temperature is 25°C and mean annual rainfall, 800–3,800 mm. The species prefers alluvial soils along river and stream banks and along beaches. In continental southeast Asia – it is found scattered in mixed dipterocarp forest, mixed evergreen and deciduous forest, dry evergreen forest or in pine-dipterocarp forest with patches of dry evergreen forest; occasionally in lowland evergreen forest; often near streams (but not rheophytic); sometimes over limestone; also in disturbed, secondary forest at altitude of 50–850 m elevation.

Edible Plant Parts and Uses

The fruit is edible but bitter tasting, eaten by the Aboriginal people of Australia when they are ripe and soft to touch. Its fruit when crushed with water is used as baby food. Fragrant yellow flowers are a source of nectar and pollen.

Botany

A sub-canopy, perennial tree growing to 25 m tall, with a cylindrical bole diameter to 50 cm with rough, furrowed, grey-cream bark and young twigs often lenticellate. Stipules about 25 mm long, tip rounded. Leaves opposite, simple, penni-veined, coriaceous, deep green, glossy, broadly ovate, (10) 15–30 cm by 7–15 cm, base rounded to acute, glabrous above, glabrous to pubescent below; 5–8 pairs of lateral veins; petiole 10–40 mm long; stipules broadly ovate to orbicular or obovate. Inflorescence axillary and/or terminal, usually a single flowering globose head about 2.5–4 cm in diameter (Plate 1). Flowers 4- or 5-merous, sweetly scented, 8 mm diameter. Calyx lobes 3 mm long, clavate to spathulate, pubescent. Corolla pale orange to greenish-yellow, glabrous, tube 6–9 mm long, lobes ovate, 4–5 mm long. Stamens subsessile, anthers c. 1 mm long. Ovaries of a flowering head fused; style white with spindle-shaped protruding prominent, white stigma 1.5–2 cm long. Fruit – a syncarp (fused mass of multiple individual fruits) indehiscent, green turning yellow to brown when ripe (Plate 2), rough-surfaced, globose to slightly ovoid, 3–5 cm across with numerous tiny 1 mm long, bilaterally compressed, ovoid to ellipsoid seeds.

Nutritive/Medicinal Properties

The proximate nutrient composition of *Nauclea orientalis* fruit based on analyses made in Australia (Brand Miller et al. 1993) per 100 g edible portion was reported as: energy 51 kJ, moisture 77.3 g, nitrogen 0.13 g, protein 0.8 g, fat 1.0 g, available carbohydrate 0 g, Ca 105 mg, Cu

Plate 1 Inflorescence head with some flowers removed

Plate 2 Young, immature fruit

0.1 mg, Fe 0.6 mg, Mg 79 mg, P 47 mg, K 363 mg, Na 6 mg, Zn 0.7 mg, thiamin 0.24 mg, riboflavin 0.18 mg, niacin (derived form tryptophan or protein) 0.1 mg and vitamin C 11 mg.

The fruit is rich in Ca, Mg, K and also has vitamin C and vitamin Bs.

Many alkaloids isolated and identified from the leaves of yellow cheesewood, among the 9 angustine-type alkaloids namely 10-hydroxyangustine and the two diastereoisomeric 3,14-dihydroangustolines, were found to exhibit in vitro anti-proliferative activity against the human bladder carcinoma T-24 cell line and against EGF (epidermal growth factor)-dependent mouse epidermal keratinocytes in animal studies (Erdelmeier et al. 1992). The use of ammonia in the extraction process resulted in a significant increase in the formation of angustine-type alkaloids from strictosamide-type precursors. Two indole alkaloid glycosides, 10-hydroxystrictosamide and 6′-*O*-acetylstrictosamide, as well as the known alkaloids strictosamide and vincosamide were isolated from the leaves of *Nauclea orientalis* (Erdelmeier et al. 1991).

Four new alkaloids, nauclealines A and B, and naucleosides A and B, together with six known compounds, strictosamide, vincosamide, pumiloside , kelampayoside A, sitosterol, and sitosteryl β-D-glucoside, were also isolated from the bark (Zhang et al. 2001). Terpenoids including β-sitosterol, noreugenin, palmitic acid, and naucleoside, a new triterpene glycoside, and D-xylose-L-rhamnose-(C-3)-quinovaic acid were also isolated from *Nauclea orientalis* L. (Fujita et al. 1967).

Two new isomeric indole alkaloids, naucleaorals A (1) and B (2) were isolated from the roots of *Nauclea orientalis*. Compound 1 showed significant cytotoxicity to HeLa cells with an IC_{50} value of 4.0 μg/mL, while compound 2 exhibited very modest cytotoxicity to both cell lines with IC_{50} values of 7.8 and 9.5 μg/mL, respectively (Sichaem et al. 2010). Both compounds proved to be inactive in antimalarial assays ($IC_{50} > 10$ μg/mL).

Extract of the dried stem of *Nauclea orientalis* were found to possess compounds which exhibited antimalarial activities (He et al. 2005). The following compounds were isolated: tetrahydro-β-carboline monoterpene alkaloid glucosides,naucleaorine(=(16α,17β)-3,14:15,20-tetradehydro-16-ethenyl-17-(β-D-glucopyranosyl-oxy)-19α-methoxyoxayohimban-21-one; (1) and epimethoxynaucleaorine (2), as well as the known compounds, strictosidine lactam (=(15β,16α,17β)-19,20-didehydro-16-ethenyl-17-(β-D-glucopyranosyloxy)oxayohimhan-21-one; (3), 3,4,5-trimethoxyphenol (4), 3α-hydroxyurs-12-en-28-oic acid methyl ester (5), 3α,23-dihydroxy-urs-12-en-28-oic acid (6), 3α,19α,23-trihydroxyurs-12-en-2S-oic acid methyl ester (7), and oleanolic acid (8). Among the compounds, compounds naucleaorine, epimethoxynaucleaorine, 3α,23-dihydroxy-urs-12-en-28-oic acid and oleanolic acid showed moderate in-vitro activities against *Plasmodium falciparum*. In folkloric medicine, an aqueous

extract of the fruit is drunk to treat coughs, colds, stomach pains and diarrhoea. The leaves and bark are used medicinally to treat abdominal pain, animal bites, boils and wounds.

Other Uses

N. orientalis is used to control soil loss on riverine areas. It is a hardy species with dryland reclamation potential. It provides excellent shade or shelter and is also planted as ornamental tree in gardens. The pale colour wood can be used for framing and internal flooring, venner and plywood, novelties, furniture, musical instruments, carvings and is also used for making canoes and paddles. The wood is used for pulpwood, firewood and charcoal. The wood was shown to be toxic to the termite *Cryptotermes domesticus* under laboratory conditions. The bark is chipped off and use as a poison which can be put into water to stun fish. The bark is also the source of a bright yellow dye.

Comments

Fresh seeds germinate readily and being recalcitrant they cannot be stored for long periods as they lose their viability.

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Dovyalis hebecarpa

Scientific Name

Dovyalis hebecarpa (Gardner) Warb.

Synonyms

Aberia hebecarpa (Gardner) Kuntze, *Aberia gardnerii* Clos, *Roumea hebecarpa* Gardn. (basionym).

Family

Salicaceae, also placed in Flacourtiaceae.

Common/English Names

Ceylon Gooseberry, Ketembilla, Kitembilla.

Vernacular Names

Brazil: Groselha-Do-Ceilao;
Chinese: Xi-Lin-Cu, His-Lu-Ts'u-Li;
Cuba: Aberia;
French: Groseillier De Ceylan, Ketembillier;
German: Kaffernpflaume;
India: Kocu Vetti (Tamil);
Spanish: Quetembilla;
Sri Lanka: Ketembilla, Kitaembilla, Kitembilla, Kithaembilla (Sinhala), Kocu Vetti (Tamil).

Origin/Distribution

The species is native to Sri Lanka and southern India.

Agroecology

The tree thrives from sea-level to 1,200 m. It does well in wet or semi dry areas but requires adequate supply of water during fruit development. It does not tolerate waterlogged conditions. It is extremely drought resistant and also tolerates sea spray. A hardy tree, that thrives on any soil including limestone. In Florida, the tree grows well on sand or limestone, but a rich, friable soil is best for maximum fruit production.

Edible Plant Parts and Uses

The very sour and astringent fruits are almost too acid to eat raw and this is compounded by its velvety hairs which are objectionable in the mouth. The fruits are excellent for making preserves,

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jelly, jam and juice. In Hawaii, there are recipes for juice, spiced jelly, ketembilla-papaya jam, ketembilla-guava jelly, and ketembilla-apple butter. In Israel, ketembilla is esteemed mainly as a source of jelly for export.

Botany

A shrub or small, dioecious perennial tree growing to 4–6 m high with long, slender, arching, wide-spreading branches. The trunk and lower branches have sharp, 4 cm long spines. Leaves are alternate, simple, elliptic to ovate, 7–10 cm long, 2–3.5 cm wide, grey-green, finely velvety, wavy entire margin (Plates 1 and 2), with pinkish woolly, thin petioles. Male, female and hermaphrodite flowers are borne on separate trees. Flowers are greenish-yellow, apetalous, 1.25 cm across and axillary. Fruit is globose, berry up to 2.5 cm diameter, velvety pubescent, turning from green to orangey brown to maroon-purple (Plates 1, 2 and 3). The pulp is very juicy, extremely acid, purple-red, enclosing 9–12 pubescent seeds about 6 mm long.

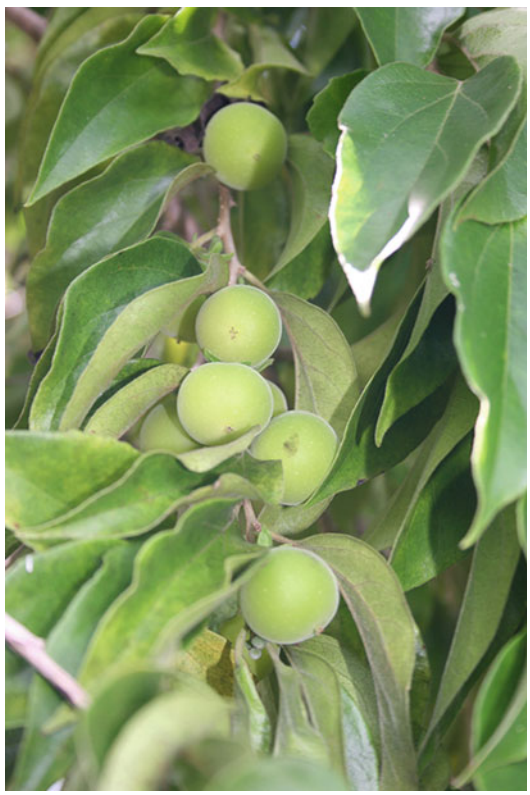

Plate 1 Developing fruits and leaves

Plate 2 Ripening fruit

Plate 3 Ripe, purplish-black fruit

Nutritive/Medicinal Properties

The food value of ketembilla fruit per 100 g edible portion was reported by Leung et al. (1972) as follows: energy 63 Cal, moisture, 82.8%, protein 1.2 g, fat 0.8 g, crude fibre 14.6 g, ash 1.8 g, Ca 13 mg, P 26 mg, Fe 1.2 mg, β-carotene equivalent 210 μg, thiamin 0.02 mg, riboflavin 0.4 mg, niacin 0.3 mg, ascorbic acid 98 mg.

Another study reported that *Dovyalis* fruit had good physical quality for the market with an average of 75% pulp and vitamin C content averaging 120.3 mg/100 g of fresh fruit, characterizing

Dovyalis as a good and rich source of vitamin C (Cavalcante and Martins 2005). Near ripe fruits were also high in pectin.

Dovyalis hebecarpa fruit was found to possess 10 anthocyanins and 26 carotenoids (de Rosso and Mercadante 2007). The anthocyanins from the crude extract of *Dovyalis* peel amounted to a total of 42.0 mg/100 g. The anthocyanin profile showed the preponderance of delphinidin 3-rutinoside (47.9%), followed by cyanidin 3-rutinoside (23.8%), delphinidin 3-glucoside (9.4%), petunidin 3-rutinoside (9.1%), and cyanidin 3-glucoside (5.8%). The other five minor anthocyanins, totaling 4.0% of the total content, were detected in less than 1.0% each. The total carotenoid content found in *Dovyalis* pulp was 6.6 mg/100 g, the major carotenoid being (all-*E*)-β-cryptoxanthin, accounting for 33.5% of the total content, followed by its (9*Z*)+(9′*Z*) isomers (18.7%), (all-*E*)-β-carotene (10.2%), (13-*Z*)-+(13′-*Z*)-β-cryptoxanthin (9.7%), and (9-*Z*)-β-carotene (4.1%).

Dovyalis species including *D. abyssinica, D. hebecarpa*, and *D. macrocalyx* were reported to have spermidine-type alkaloids such as dovyalicin A, dovyalicin B, dovyalicin C, dovyalicin E and dovyalicin F; phenol glucoside, 4-hydroxytremulacin, 1,2-cyclohexanediol glucoside, methyl 1-hydroxy-6-oxocyclohex-2-enecarboxylate and tremulacin (Rasmussen et al. 2006).

Other Uses

Dovyalis hebecarpa is also planted as an ornamental or as wind-break.

Comments

This species was formerly placed in the family Flacourtiaceae now a defunct family of flowering plants whose former members have been scattered to various other families, mostly to Achariaceae, Samydaceae, and Salicaceae (Miller 1975; Chase et al. 2002). Miller (1975) asserted that Flacourtiaceae as a family is a fiction; only the tribes are homogeneous.

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Flacourtia indica

Scientific Name

***Flacourtia indica* (Burm. f.) Merrill.**

Synonyms

Flacourtia afra Pichi-Serm., *Flacourtia balansae* Gagnep., *Flacourtia cataphracta* Rolfr., *Flacourtia frondosa* Clos, *Flacourtia heterophylla* Turcz., *Flacourtia hirtiuscula* Oliv., *Flacourtia lenis* Craib, *Flacourtia obcordata Roxb*., *Flacourtia parvifolia* Merrill, *Flacourtia perrottetiana* Clos, *Flacourtia ramontchi* L'Her., *Flacourtia rotundifolia* Clos, *Flacourtia sapida* Roxb., *Flacourtia sepiaria* Roxb., *Flacourtia thorelii* Gagnep., *Gmelina indica* Burm. f., *Mespilus sylvestris* Burm., *Myroxylon dicline* Blanco, *Rhamnopsis sepiaria* Rchb., *Sideroxylon spinosum* Willd., *Stigmarota africana* Lour., *Stigmarota edulis* Blanco.

Family

Salicaceae also placed in Flacourtiaceae.

Common/English Names

Batoka Plum, Batoko Plum, Botoko Plum, Ceyon Plum, Flacourtia, Governor's Plum, Indian Plum, Madagascar Plum, Many Spiked Flacourtia, Mauritius Plum, Paniala, Ramontchi, Rhodesia Plum.

Vernacular Names

Afrikaans: Goewerneurspruim;
Burmese: Naywe, Nayuwai;
Chinese: Ci Li Mu, Da Guo Ci Li Mu, Ma Jin, Ma Jin Dai, Nuo Nuo Guo;
East Africa: Mchongoma, Nthuzda;
French: Jujume Malgache, Marromse, Grosse Prune-Café, Jujube Malgache, Prune Malgache, Prune Pays, Prune Malgache, Prunier De Madagascar;
German: Batokopflaume, Echte Flacourtie, Madagaskarpflaume, Ramontchi;
Hungarian: Batokószilva, Madagaszkáriszilva, Maronszilva, Kormányzószilva, Ramoncsi;
India: Baichi, Benchi, Katai, Serali, Tambat (Bengali), Baichi, Bhanber, Bilangada, Bilangra, Ghargoogar, Kakein,Kancu, Kandai, Kangu, Kanju, Kankair, Katai,Kattar, Kondai, Kondari, Konkrol, Kukai (Hindi), Ablu, Aturake, Bilehuli, Gajale, Gaajaale, Gekara, Hennusampige, Hettari Mullu, Kaakade, Karre, Kuduvale, Miradi, Mirde, Mullu Thaare, Mulluthotti, Mulluvinda, Naayi Beli, Nakkeharagu (Kannada), Babhuli Tambat (Konkani), Aghori, Courou-Moelli, Karimulli, Mullullakatta (Malayalam), Athruna, Babhuli, Bhekal, Bhekala, Binka, Kaker, Kuki, Kaantera, Paker, Tambut (Marathi), Aghori, Kantaki, Shruvavrikksha, Sruvavrksa, Svadukantaka,

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Vikankata (Sanskrit), Cholhakilai, Cottai-k-kala, Cottai, Kattukala, Katukalai, Kodikarral, Kodumundi, Kotimunti, Kottaikkala, Kotumunti, Kurumulli, Kutukali, Mulanninchil,Malukkarai, Nattukkottaikkala, Sottaikala, Shothukala, Sottaikalai, Sottaikalla (Tamil), Bontakandraegu, Kaanaraegu, Kanaregu, Kandraegu, Kanru, Mulielka, Mulu Tiruman, Nakkanaraegu, Nakkaneraedu, Nelli, Peddakanaraegu, Ptikatada, Pullerika, Pulregu, Pulivelaga, Putikatada (Telugu);
Indonesia: Baga, Ri Rukem, Ri Sisir, Rukem, Duri Rukem (Java), Saradan (Sundanese), Duri Rukem, Ganda Rukem, Kerkup Kechil, Rukam Sepat, Rukem Mincid;
Japanese: Indo Rukamu, Ramonchii;
Laotian: Mak Ken, Mak Keng;
Malaysia: Kerkup Kecil;
Pakistan: Kokoh;
Philippines: Sauasaua (Bisaya), Palutan (Ibanag), Bolong (Mangyan), Bitañgal (Sambali), Bituñgol (Tagalog);
Portuguese: Ameixa De Madagáscar, Ameixa Da Mauricia, Cerezo Del Gobernador;
Spanish: Ciruela Gobernadora, Ciruela De Madagascar, Ciruela Del Gobernador, Ciruela Gobernadora, Ramontchi;
Sri Lanka: Uguressa (Sinhalese);
Swahili: Mchongoma, Mgo, Mkingii, Mkingila, Mkingili, Mugovigovi, Ngovigovi;
Taiwan: Ci Li Mu;
Thailand: Ma Kwen Pa (Northern Thailand), Makwen-Nok , Ta Khop Pa (Central Thailand);
Tibetan: Bi Ka Na Ka, Sa Ba Na Rnam Gcig, Sra Ba Na Rnam Gcig, Sra Sa, Srs Ba;
Vietnam: Ân Do, Muôn Quân;
Zimbabwe: Munhunguru, Mutunguru, Mutudza, Mutombototo(Shona),Umqokolo,Umthunduluka (Ndebele).

Origin/Distribution

The plant is endemic to Africa and Asia – Botswana, Burundi, Cameroon, Democratic Republic of Congo, Eritrea, Ethiopia, India, Kenya, Malawi, Namibia, Nigeria, Rwanda, Sierra Leone, South Africa, Tanzania, Uganda, Zambia, Zanzibar, Zimbabwe, Swaziland, Madagascar; India, Sri Lanka, Indo-china, Indonesia and south China.

Agroecology

In its native range, its habitat is found in tropical dry deciduous and thorn forests, woodland, bushland, thickets, wooded grassland, and often in riparian vegetation from sea level to 2,400 m elevation. It is somewhat drought resistant but frost sensitive. It is adaptable to a wide temperature range of 4–40°C but its normal range is from 13–30°C with mean annual rainfall of 500–1,600 mm in the tropics and subtropics. It grows on a wide variety of soils including limestone, clayey, sandy and calcareous soils. It is heliophilous and prefers full sun and high water table. It will tolerate some light salt spray.

Edible Plant Parts and Uses

The acid to acid-sweet ripe fruits are eaten fresh, stewed or used for preserves, jams, jellies and pies. Ripe fruits are often dried and stored as food. The fruit can be fermented to produce wine.

Botany

An erect, branched, armed, deciduous, dioecious shrub or small tree to 5 m high occasionally to 10 m. Bark is pale grey-brown and flaky, branches pubescent with axillary simple spines. Leaves are alternate, on 2 cm long petioles, greenish abaxially, deep green adaxially (Plates 1 and 2), pink when young, obovate to oblong-obovate, 2–4 cm by 1.5–3 cm, coriaceous, abaxially glabrous or sparsely pubescent, adaxially glabrous, mid-vein raised abaxially, flat adaxially; lateral veins 5–7 pairs; reticulate veins conspicuous; base mostly acute to obtuse; margin serrulate; apex rounded or retuse. Flowers are inconspicuous, greenish-yellow in short axillary or terminal racemes, unisexual, with male and female flowers on separate trees. Male flowers in short, branched, clustered racemes; branches pubescent. Calyx consists of 4–5 pubescent sepals, 1–1.5 mm long. Stamens numerous; filaments long; anthers short, oblong, opening by slits. Female flowers are borne on pubescent pedicels on short, pubescent branches, in pairs or solitary. Sepals are 4–5, 1–1.5 mm

Plate 1 Fruits and obovate leaves

Plate 3 Ripe and immature Ramontchi fruit

Plate 2 Close-view of fruit

Plate 4 Ramontchi fruit sliced to reveal the yellowish-brown flesh

long and pubescent. Petals lacking. Ovary glabrous on a disc; stigmas 5–10. Fruit is globose, up to 2.5 cm across, with persistent styles, green when immature turning to reddish to reddish purple or purple when ripe (Plates 1, 2, 3 and 4), with translucent yellowish-brown flesh, containing 6–10 seeds (Plate 4). Seeds 8–10 mm long, 4–7 mm broad, rugose, pale brown and flattened.

Nutritive/Medicinal Properties

Analyses made in the Philippines reported that the fruit contained: moisture 66.42%, protein 0.69%, fat 1.67%, sugar 7.68%, ash 1.09% and acidity 1.78% (Morton 1987).

The bark of *Flacourtia indica*, yielded a new phenolic glucoside ester, flacourtin, identified as 3-hydroxy-4-hydroxymeth (Bhaumik et al. 1987). Beta-Sitosterol, β-sitosterol-β-D-glucopyranoside and a butyrolactone lignan disaccharide, ramontoside, were isolated from the heartwood (Satyanarayana et al. 1991). The structure of ramontoside was determined as diphyllin-4-*O*-[β-D-glucopyranosyl(1–4)]-β-2,3-di-*O*-methyl-D-xylopyranoside.

Some pharmacological properties of the various plant parts that have been reported are discussed below.

Antioxidant Activity

Flacourtia indica was reported to contain total phenolics 334 μg GAE/g, flavanoids 41 μg catechin/g and condensed tannins 1.4% (Ndhlala et al. 2007). Significant differences were noted in the flavanoids and the condensed tannins between the peels and pulps of the fruit. Ferulic acid, caffeic acid and vanillic acid were the dominant phenolic acids. There were differences between

the phenolic acids in the peels and the pulps of the fruits. The peels of *F. indica* had higher 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging effects, reducing power and superoxide-scavenging effects compared with the pulp (Ndhlala et al. 2008). Phenolic compounds and flavonoids were responsible for its antioxidant and other biological activities.

A new phenolic glucoside, (rel)-2-(4′,6′-dibenzoyl-β-glucopyranosyloxy)-7-(1α-hydroxy-2α-ethoxy-6α-acetyloxy-3-oxocyclohex-4-enoyl)-benzyl alcohol (Flacourticin) (1) and the known, 2-(4′,6′-dibenzoyl-β-glucopyranosyl)-5-hydroxy benzyl alcohol (4′-benzoylpoliothrysoside) (2) together with the new, (2E)-heptyl-3-(3,4-dihydroxyphenyl) acrylate (3), (+)-catechin (4) and sitosterol-β-D-glucoside were isolated from *Flacourtia indica* (Madan et al. 2009). Compound 3 was found to be twofold less potent in α-diphenyl-β-picrylhydrazyl (DPPH) radical scavenging activity with an IC_{50} = 12.01 μg/mL, compared to the positive control, rutin, (IC_{50} = 5.83 μg/mL). A new glucoside ester, named flacourside, 4-oxo-2-cyclopentenylmethyl 6-*O*-(*E*)-*p*-coumaroyl-β-d-glucopyranoside was isolated together with known methyl 6-*O*-(*E*)-*p*-coumaroyl glucopyranoside and 6-*O*-(*E*)-*p*-coumaroyl glucopyranose from the *n*-butanol extract of fruit juice of the *Flacourtia indica* (Amarasinghe et al. 2007).

F. indica fruit was found to have a total phenol content of 3.87 mg GAE/g, total flavonoid content of 4.30 mg RE/g; FRAP (ferric reducing antioxidant power) value of 0.64 mmol $FeSO_4$/g; DPPH value of 59.78% inhibition and AEAC (Ascorbic acid antioxidant capacity) of 0.49 mg ascorbic acid/g respectively (Kubola et al. 2011). *F. indica* fruit was found to contain the following phenolic acids (mg/g): gallic acid 3.09 mg; protocatechuic acid 5.444 mg, *p*-hydroxy benzoic acid 3.35 mg, vallinic acid 7.10 mg, chorogenic acid 19.99 mg, caffeic acid 7.43 mg, syringic acid 16.81, *p*-coumaric acid 9.23 mg, ferulic acid 29.63 mg, sinapicnic acid 32.72 mg, and total phenolic acid content 133.79 mg. *F. indica* fruit was found to contain the following flavonoid contents (mg/g dry sample): rutin 11.56 mg, myricetin 20.45 mg, luteolin 90.35 mg, quercetin nd (not detected), apigenin 60.54 mg, kaempferol nd, total flavonoid content 182.90 mg. *F. indica* also contained the following sugar composition (mg/g dw): D(+) raffinose nd, D(+)sucrose nd, D(+)maltose 0.22 mg, D(+)glucose 203.31 mg, D(+)galactose nd, D(+)fructose 191.33 mg, myo-inositol 1.07 mg, and total sugars 395.93 mg. *F. indica* fruit contained 1.15 mg/g vitamin C and 3.21 g/100 g crude fibre.

Hepatoprotective Activity

Flacourtia indica aerial parts were found to possess hepatoprotective activity (Nazneen et al. 2009). In paracetamol-induced hepatic necrosis in rat models, all extracts viz. petroleum ether, ethyl acetate and methanol extracts of the aerial parts of *Flacourtia indica* were found to reduce serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and serum alkaline phosphatase (SAP). The most significant reduction of the serum level of SGOT and SGPT were exhibited by petroleum ether and ethyl acetate extracts. At a single oral of dose of 1.5 g/kg of body weight a petroleum ether extract caused a reduction in levels of SGOT (29.0%) and SGPT (24.0%) and the ethyl acetate extract caused a reduction in levels of SGOT (10.57%) and (SGPT 96.7%) compared to paracetamol (3 g/kg of body weight) treated animals. Histopathological examination also showed good recovery of paracetamol-induced necrosis by petroleum ether and ethyl acetate extracts. In contrast, the methanol extract did not show any marked effect on paracetamol-induced hepatic necrosis. The hepato protective effects exhibited by petroleum ether and ethyl acetate extract may be mediated through the inhibition of microsomal drug metabolizing enzymes. This was also reported in a separate preliminary study that showed *Flacourtia indica* possessed good hepatoprotective activity (Gnanaprakash et al. 2010). The aqueous extract of the leaves of *Flacourtia indica* protected liver against oxidative damages and could be used as an effective protectant against carbon tetrachloride induced hepatic damage. Treatment of aqueous extract of *Flacourtia indica* leaves (250 and 500 mg/kg) exhibited a significant prophylactic action by

changing the serum levels of Alanine aminotranferease (ALT), aspartate aminotransferase (AST), alkaline phosphatise (ALP), total protein, total bilirubin and liver Thiobarbituric acid reactive substances (TBARS) lipid perooxidation. This was confirmed by histopathological study of liver sections.

Antiplasmodial Activity

Three compounds, pyrocatechol, homaloside D and poliothrysoside were isolated from the decoction of *Flacourtia indica* aerial plant parts (Kaou et al. 2010). Poliothrysoside isolated from the ethyl acetate extract exhibited a strong antiplasmodial activity (IC_{50} = 7.4 μM) against *Plasmodium falciparum* and a good selectivity index (>28) similar to chloroquine. The results supported the traditional use of *F. indica* in treating malarial in the Comoros islands.

Protease Inhibitory Activity

The polar extracts of *F. ramontchi* showed inhibitory activity in different types of proteases, the serinic subtilisin and aspartic pepsin but the apolar extract only inhibited the serinic protease subtilisin (Flausino et al. 2009).

Traditional Medicinal Uses

Flacourtia indica has been used in traditional medicine especially in Ayurvedic system. In India, the fruit is employed for jaundice and enlarged spleens, to relieve nausea and to halt purging. Infusion of roots are used for hoarseness, pneumonia, intestinal worms, inflammations, and as an astringent, diuretic, and pain reliever. The dried leaves are carminative, expectorant, tonic, and astringent. They are useful in asthma, bronchitis, phthisis, and catarrh of the bladder. The juice of the fresh leaves is useful in fevers as an antiperiodic for infants; it is also used in affections of the chest, cough, dysentery, febrifuge, diarrhoea, and indigestion caused during dentition. Leaf decoctions are useful for gynaecological complaints and as an antihelmintic, and treatment for hydrocele, pneumonia and intestinal worms. In Bengal, it is given as a tonic in parturition. The leaves and roots are said to be effective against snakebite and are taken for schistosomiasis, malaria, and diarrhoea.

Filipinos use the bark infusion as a gargle, and a root infusion is taken in cases of pneumonia. In Madagascar, the pulverised bark triturated in sesame oil is used as a liniment in rheumatism. The ashes of the root are considered useful in kidney ailments. The Lobedu tribe of southern Africa take a decoction of the root for the relief of body pains. In Madagascar, the bark, triturated in oil, is used as an anti-rheumatic liniment. A decoction of the stem has been used for scarlet fever and chicken pox in Thailand (Chuakul and Saralamp 2002).

Other Uses

The small tree is also planted as an ornamental boundary and barrier plant. In Puerto Rico, the tree is considered useful as a tall barrier hedge or windbreak. Farmers in India lop the branches and leaves as fodder for cattle. The tree provides timber used for agricultural implements such as ploughs, posts, building poles, rough beams, walking sticks and the manufacture of turnery articles. The wood is used for fuel-wood for firewood and charcoal. The bark furnishes tannin used for tanning materials.

Comments

The taxonomy of *Flacourtia indica* is complex. Some authors have treated the species in a broad sense, and include in synonymy not only *F. ramontchi* but also several other entities found across tropical Asia and Africa as is done in the present account. Several authors have treated *F. ramontchi* as a separate species (Yang and Zmarzty 2007).

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Flacourtia inermis

Scientific Name

***Flacourtia inermis* Roxb.**

Synonyms

None recorded

Family

Salicaceae, also placed in Flacourtiaceae.

Common/English Names

Batoko Plum, Batoko-Plum, Lobi-Lobi, Louvi Plum, Lovi-Lovi, Plum of Martinique, Plum-of-Martinique, Thornless Rukam.

Vernacular Names

Burmese: Nayuwai, Naywe;
French: Prune De La Martinique, Prunier De La Martinique;
German: Lovi-Lovi;
India: Cimaikkottaikkala, Cottaikkala (Tamil);
Indonesia: Kamonju, Mengkoronda (Baree), Balakko, Lubi-Lubi (Batak), Kenilango (Boeol), Tomu-Tomu (South Ceram), Tombi-Tombi (South Halmaheira), Lobi-Lobi (Java), Lobi-Lobi (Lampong), Lobe Lobe (Makassar), Lubi-Lubi (Malay, Singkep), Rukem Belanda (Malay, Lingga), Tome-Tome, Tomi-Tomi (Maluku, Manado), Lubi-Lubi (Minangkabau), Lubilubi (Sumatra), Saradan Kayu (Sundanese);
Malaysia: Lobeh-Lobeh, Tomi-Tomi, Rukam, Rokam Masam, Rukam Masam;
Philippines: Ratiles;
Spanish: Ciruela De Martinica, Louvi Malayo;
Sri Lanka: Looy-Looy, Lowi Lowi;
Thailand: Takhop-Thai.

Origin/Distribution

Its exact origin is uncertain, probably native to the Moluccas (Maluku); now naturalized from India through Malesia to New Britain in Papua New Guinea. It is cultivated in Malaysia, Indonesia, and Sri Lanka for both its fruit and decorative foliage. The cultivated varities are mostly thornless and could have been derived from an ancestral thorny var. *moluccana* Sleumer (Moluccas and New Guinea).

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Agroecology

Lovi-Lovi is adapted to the hot, humid tropical climate. It thrives on well-drained, friable sandy soils from sea level to 1,300 elevation.

Edible Plant Parts and Uses

The attractive cherry red fruit are very sour but can be eaten raw or used to make jam, jelly, pickles, chutney, pies, preserves and confectionary. In Indonesia, the fruit raw or cooked are used in "*rujak*" (mixed fruit, peanut and chilli sauce) and "*asinan*" (mixed fresh vegetable with chilli flavour) (Sumiasri and Indarto 1999). Processed fruits can be found in the local supermarket as syrup, jam and sweets.

Botany

An evergreen shrub or small tree reaching a height of 10 m with a bole of 35 cm with a short trunk and bushy crown (Plate 1). The leaves are alternate, simple, bright-red when young, are glossy green on the upper surface, dull beneath, ovate-oblong to ovate-elliptic, 9–25 cm long by 5–12.5 cm wide, sub-coriaceous with obtuse base, acuminate apex and serrulate to serrate margin (Plates 1 and 2) and pubescent on mid rib. Inflorescences are axillary and consists of a few flowered, finely pubescent racemes. Flowers are yellowish green, scentless, bisexual, apetalous with 3–5 sepals and 15–25 stamens with yellow anthers and borne on pubescent, 4–10 mm pedicel. Fruit sub-globose to globose, 2–2.5 cm diameter, smooth, green to yellow to glossy, bright red when ripe (Plates 3, 4, and 5) with whitish acid, astringent flesh and containing 4–10 or more hard, irregular seeds 6 mm wide.

Nutritive/Medicinal Properties

No information has been published on the nutritive value of the edible fruits.

Plate 1 Lovi-Lovi tree – much branched and with a short trunk

Plate 2 Serrulate to serrate, alternate leaves in various stages of development

Five caffeoylquinic acid derivatives were obtained from the fruit juice of *Flacourtia inermis*: methylchlorogenate(1),methyl5-*O*-caffeoylquinate (2), methyl 4-*O*-caffeoylquinate (3), n-butyl chlorogenate (4), n-butyl 5-*O*-caffeoylquinate (5) and a rare phenolic glucoside (rel)-6α-benzoyloxy-1α,2α-dihydroxy-5-oxocyclohex-3-enecarboxylic

Plate 3 Fruiting branch

Plate 4 Lovi-Lovi fruit with short pedicels

Plate 5 Lovi-Lovi fruit – subglobose to globose and bright red when ripe

acid 2-(6-O-benzoyl-β-D-glucopyranosyloxy)-5-hydroxybenzyl ester (6), together with quinic acid (7) and malic acid (8) (Jayasinghe et al. 2012). Compounds 1, 2, 4, and 5 exhibited strong radical scavenging properties towards the 2,2′-diphenyl-1-picrylhydrazyl radical.

Studies revealed that the acetonic extract of *Flacourtia inermis* potently inhibited the growth of multidrug resistant bacterial strains (George and Benny 2010a). Among the sensitive strains, *Serratia marcescens* showed highest susceptibility followed by *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Escherichia coli.* The acetone fruit extract of *F. inermis* was also found to exhibit highest activity against *Aspergillus fumigatus* with an average inhibition zone of 47 mm (George and Benny 2010b). Least susceptibility was shown by *Aspergillus niger* with a mean zone of inhibition of 30 mm, which also was a promising result for a plant extract. *Aspergillus flavus*, *Mucor ramosissimus*, and *Chrysosporium* sp. were also potently inhibited by the fruit extract.

Recent study showed that *F. inermis* fruit contained a phenolic compound, 2, 3-dihydroxybenzoic acid, which was found to be a potent antiprotozoal agent against fresh water protozoa and rectal ciliates of frog (George et al. 2011).

The filtrate of the fruit has been used in traditional medicine in Indonesia (Sumiasri and Indarto 1999).

Other Uses

The tree is often planted as an ornamental and its wood is similarly used as described for *F. rukam*.

Comments

Lovi-Lovi can be propagated by seeds, air-layering or from budding.

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Flacourtia jangomas

Scientific Name

***Flacourtia jangomas* (Lour.) Raeusch.**

Synonyms

Flacourtia cataphracta Roxb. ex Willd., *Roumea jangomas* Spreng., *Stigmarota jangomas* Lour., *Xylosma borneense* Ridley.

Family

Salicaceae also placed in Flacourtiaceae.

Common/English Names

Coffee Plum, East Indian Plum, Indian Plum, Indian-Plum, Manila Cherry, Paniala, Puneala Plum, Rukam, Runeala-Plum, Spiked Flacourtia.

Vernacular Names

Arabic: Talisfir, Zarnab;
Antilles: Merisier Pays (French);
Brazil: Cereja-De-Cametá;
Burmese: Kyetyo Po, Mak Kyen, Naywe, Sumbrung;
Chinese: Yun Nan Ci Li Mu
Cook Islands: Venevene Pāma (Maori);
Dutch: Babydruif, Babykers;
French: Prunier D'inde, Prunier Malgache;
French Reunion: Prunier D´Inde, Prunier D'Inde;
German: Paniala;
India: Paniyal, Phinel, Polian (Assamese), Bara Baichi, Paniala, Tali (Bengali), Dorichik (Garo),Talispatra (Gujarati), Jamuna, Pachnala, Paniala, Paniamla, Pani Amla, Paniyala, Paniyamalak, Talisapatri, Talispatar, Talispatri (Hindu); Chanchali Mara, Chankali, Charichali, Goraji, Hulumanikc, Kirinelli, Shamper, Tahspatram, Talisapatri (Kannada), Dieng Sohmluh (Khasi), Jagam (Konkani), Thaliru, Vaiyyamkaitha, Vaiyyaṅkata, Vayyaṅkataku (Malayalam), Heitroi (Manipuri), Champeran, Jangam, Jangli-Jagam, Paanaamle, Thambat (Marathi), Baincha (Oriya), Paaniiyaamalaka, Paniaala, Praachinaamalaka, Pracinamalaka, Sruvavrkash, Taala, Taali, Talisapatra, Talisapatraka, Vikankatah (Sanskrit), Acatam, Caralaka, Caralanka, Caralankam, Caralankay, Caralu, Catapattiram, Catapattiri, Ciropattiravicotani, Cukotaram, Curovattiravi, Cuvacakacaki, Cuvatukantakam, Cuvatukantam, Ilavankappattai, Mici, Mullumukanchi, Pattiracciliyam, Pattiraciliyam, Pattirakentam, Pattirakkiyam, Pattiri, Perunkamicam, Perunkamikappattiri, Piracciyamalakam, Piraciyamalakam, Talicai, Talicam, Tamalakam, Tamalakapattiri, Tamalakitalam, Tamalakitalam, Vaiyankarai, Vaiyyankarai, Valankarai, Vayankatucharalu (Tamil), Kuragayi, Kuski, Kusus, Mullumaana, Tahspatram, Talisapatramu, Talisapatri, Thaaleesapathramu (Telugu), Talispatar (Urdu);
Indonesia: Rukem, Situ (Java);

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Khmer: krâkhôp khmaèr;
Malaysia: Akar Temberak, Daun Ekor Serangat, Bebuas Akar, Kelekup, Kerkuh, Kerkup, Kerkup Besar, Kerkup Bakoh, Kerpup, Kerukup, Rokam, Rukam;
Nepalese: Talispatri;
Niuean: Palamu;
Persian: Talispatar;
Portuguese: Ameixa-Da-Índia;
Spanish: Ciruela De Madagascar, Ciruela Forastera, Jagomeira, Kerkup, Mamonga;
Taiwan: Luo Dan Mei, Yin Du Li;
Thai: Makwen Khwai (Northern Thailand), Ta Khop Khwai (Central Thailand), Khrop, Ta Khop Thai;
Vietnamese: Bô Quân, Hông Quân, Muôn Quân.

Origin/Distribution

According to Sleumer (1954), *Flacourtia jangomas* is not known in the wild state. The species is cultivated around villages, and naturalized from them, throughout tropical regions, especially in East Africa and tropical Asia.

Agroecology

The species has naturalized in tropical regions in East Africa and tropical Asia and is found in primary and secondary rain forest up to 1,500 m altitude. It is commonly cultivated throughout Southeast Asia, Eastern Malaya, Southern China and also in the Philippines. It is also grown in East Africa. It thrives in well-drained fertile soils and in full sun. It is sensitive to frost.

Edible Plant Parts and Uses

For eating fresh out-of-hand, the fruit is rolled between the hands to reduce astringency, and is better-liked than that of other species. It is stewed as dessert, made into juice, syrup, jam, marmalade and pickles and also used in chutneys. When slightly under-ripe, it is used to make jelly. The acid young shoots are eaten in Indonesia.

Plate 1 Pinkish-reddish-brown juvenile leaves

Botany

A, large erect deciduous shrub to small tree 5–10 m high with low branches. Trunk and older branches are unarmed, young branches lenticellate and spiny with simple or divaricate spines. Bark light brown to reddish brown and flaky. Leaves simple, alternate, narrow-ovate, ovate-elliptic to ovate-oblong, 7–12 cm by 2.5–5 cm, apex tapering to narrowly acuminate, base cuneate to rounded, margin entire, sinuate or sub-serrate to crenate, membranous to thinly chartaceous, glabrous, shiny above, dull below; juvenile leaves pinkish to reddish-brown (Plates 1, 2, and 3). Inflorescences a few-flowered axillary racemes (Plates 3 and 4). Flowers appearing with or before young leaves, white to greenish, honey-scented on slender pedicels, 1–1.5 cm; sepals 4(–5), ovate-obtuse, greenish, sparingly pubescent. Male flowers glabrous, stamens with 2–3 mm filaments. Female flowers with flask-shaped to subglobose ovary 2–3 mm across, with 4–6 styles, connate into a distinct column, slightly free at the apices, each with a reniform, dilated, recurved stigma. Fruit subglobose 1.7–2.5 cm across, pale green

Plate 2 Maturing buff coloured and deep-green shiny leaves

Plate 3 Axillary greenish-white flowers, some appearing before leaves

Plate 4 Flowers and young fruits

tuning to dull-brownish red or purple, then blackish, crowned by persistent short stylar column (Plates 4, 5, and 6). Pulp greenish-yellow, acid-sweet, enclosing 4–5 (−10) flat, hard, pale-yellow seeds.

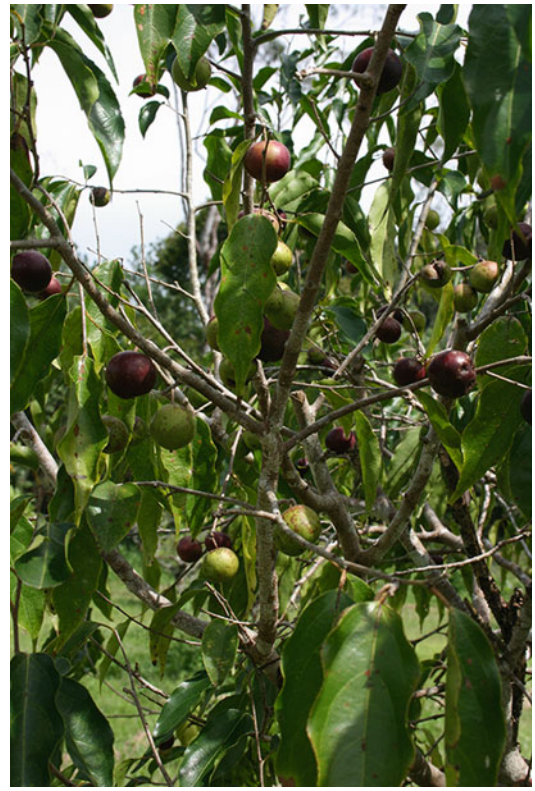

Plate 5 Ripe and immature fruits

Plate 6 Close-up of ripe fruits

Nutritive/Medicinal Properties

The proximate composition of *F. jangomas* fruit was reported as: energy 78 cal, moisture 77.7, protein 0.5 g, fat 0.1 g, carbohydrate 20.9 g, dietary fibre 1.0 g, ash 00.8 g, Ca 43 mg, P 25 mg.

(Leung et al. 1972). Philippine analyses showed the fruit to have: moisture, 78.28%; protein, 0.03%; fat, 0.39%; sugar, 4.86%; ash, 0.94%; acidity, 1.16% in the fruit. The fruit is fairly rich in pectin; contains 9.9% tannin on a dry-weight basis (Morton 1987). Kermasha et al. (1987) reported that *F. jangomas* fruits had the following proximate composition of a dry weight basis: protein 3.9%, vitamin C 218 mg/100 g, total sugars (fructose, α- and β-glucose and sucrose) 21%, and mineral mg/100 g – Ca 175 mg, K 158 mg, P 147 mg, Fe 118 mg, Mg 57 mg. Concentrations of amino acids, Na, Mn, Cu and Zn were also found. Jangomolide, a novel limonoid was isolated, together with limonin, from *Flacourtia jangomas* (Ahmad et al. 1984). Tee et al. (1997) reported the following nutrient composition per 100 g for candied rokam (*F. jangomas*): energy 338 kcal, water 14.8%, protein 0.7 g, fat 0.3 g, carbohydrate 83.1 g, fibre 1 g, ash 0.1 g, Ca 11 mg, Fe 1.4 g, Na 100 mg, K 10 mg, carotenes 37 μg, retinol equivalent 6 μg, vitamin B2 0.06 mg, niacin 0.3 mg and vitamin C 4.6 mg.

Hypoglycemic Activity

Methanolic extract of the leaf and stem of *Flacourtia jangomas* was found to have hypoglycaemic activity (Singh and Singh 2010). Oral administration of the extract to streptozotocin (STZ)-induced diabetic rats for 21 days exhibited highly significant hypoglycemic activity and also significantly restored altered biochemical parameters, namely cholesterol and triglycerides. On the 21st day, glucose and ketone traces were absent in extract- and glibenclamide-treated groups while they were present in diabetic control. Phytochemical analysis of the methanol extract of leaves and stem revealed the presence of flavonoids, saponins, carbohydrates, steroids, tannins, and phenolic compounds. In acute toxicity study, no toxic symptoms were observed for the combined extract up to dose 2,000 mg/kg.

Antimicrobial Activity

Srivastava et al. (2010) reported that the *F. jangomas* fruit extract showed good antimicrobial activity towards *Psuedomonas aeuriginosa, Klebsiella pneumonia* and *E. coli*. An another study, the chloroform fraction of *F. jangomas* root exhibited good activity against Gram positive and negative bacteria with MIC values of 0.325–5 mg/mL (Sarker et al. 2011). The extract at the dose of 250 μg/mL exerted highest inhibition against *Escherichi coli* (34.82%) followed by *Bacillus megaterium* (22.91%) and *Shigella shiga* (20.45%). The chloroform fraction also showed cytotoxic effect using the brine shrimp lethality bioassay with LC_{50} value of 12.58 μg/mL.

Traditional Medicinal Uses

The fruits are eaten to overcome biliousness, nausea and diarrhoea. The leaf decoction is taken to halt diarrhoea. Powdered, dried leaves are employed to relieve bronchitis and coughs. The leaves and bark are applied on bleeding gums and aching teeth, and the bark infusion is gargled to alleviate hoarseness. Pulverized roots are poulticed on sores and skin eruptions and held in the mouth to soothe toothache.

Other Uses

The red to scarlet wood is close-grained, hard, brittle, durable and polishes well. It is used for agricultural implements.

Comments

F. jangomas can be mass propagated by soaking seeds in cold water for 48 h for nursery raising and using 0.4% indole butyric acid treatment of stem cuttings for clonal propagation (Hossain et al. 2011).

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Flacourtia rukam

Scientific Name

***Flacourtia rukam* Zoll. & Moritzi.**

Synonyms

Flacourtia cataphracta sensu Blume, *Flacourtia edulis* Griff., *Flacourtia euphlebia* Merr., *Flacourtia megaphylla* Ridley, *Flacourtia peninsula* Elmer, *Flacourtia sulcata* Elmer, *Hisingera grandifolia* Turcz.

Family

Salicaceae, also placed in Flacourtiaceae.

Common/English Names

Governor's Plum, Indian Plum, Indian Prune, Rukam.

Vernacular Names

Chinese: Da Ye Ci Li Mu;
Dutch: Rockam, Roekem;
Fijian: Filimoto;
French: Prunier Café, Prunier De Chine, Prunier Malgache;
German: Batoka, Madagaskarpflaume;
Indonesia: Rukom, tonggolen (Batak, Sumatra), Rukem Gajah (Bengkoelen, Sumatra), Gandarukem, Landak, Rukam, Saradan (Java), Jukum, Lubi-Lubi Manis (Lampong, Sumatra), Klang Tatah Kutang (Kalimantan), Rokem (Madurese), Lobi-Lobi manis, Rukem (Malay), Rukem (Lingga), Tome-Tome Manis, Tomi-Tomi mansi (Malay, Manado, Sulawesi), Landak, Rokem (Madurese), Tangkulung (Simaloer, Sumatra), Lubi-Lubi Manis (Singkep), Kupa Landak, Rukem (Sudanese);
Kampuchea: kra khop nhi, ko kop;
Laos: Ken;
Malaysia: Rokam, Rukam, Rukam Gajah, Rukam Manis;
Palauan: Chemechong, Emechong;
Philippines: Agasas, Salabagin (Cebu Bisaya), Obieng (Iloko), Kalomiñgas, Kaluñga (Igorot), Kalamasati, Lalamasah (Sambali), Amaiit, Bitoñgol (Tagalog);
Samoan: Filimoto;
Spanish: Ciruela De Madagascar;
Taiwan: Luo Geng Guo;
Thailand: Ma-Kwen-Yai, Takhop-Thai (Central), Khrop-Dong (Pattani);
Tongan: Filimoto;
Vanuatu: Rangrangmarxe;
Vietnamese: Mung Guan Ru'ng.

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Origin/Distribution

The species is found in Madagascar and Malesia, but rare in the Moluccas (Maluku) and New Guinea. It is widely distributed but scattered, both cultivated and wild, all over Malesia. It was introduced into Indo-China, Southern China and Taiwan, Thailand, India and elsewhere in the tropics.

Agroecology

Rukam grows thrives under hot, humid tropical conditions from near sea level up to 2,100 m above sea level. It occurs naturally in primary or secondary forest; often along rivers in partial shade or in full sun. It is adaptable to a range of temperatures, rainfall and soil conditions but is intolerant of frost and saline conditions.

Edible Plant Parts and Uses

The ripe fruit is sweet to acid sweet and is eaten fresh, pickled and used for making preserves, jam, juice, syrup or confectionary. In Java, the fruit is pounded for the preparation of *sambal petis* used in *rujak*, a fruit salad with spicy, chilli sauce. Young, tender, reddish shoots and leaves are eaten in Papua New Guinea and are sold in markets in Java to be eaten raw as *lalab* in side dishes.

Botany

A much-branched, evergreen, perennial tree, 5–20 m with dark brown bark. The tree is armed with forked, woody spines on the trunk and old branches but can be thornless in cultivated forms. Branchlets are terete, glabrous to densely pubescent when young. Juvenile leaves are flaccid, drooping, rose-red to brown (Plate 1). Mature leaves are ovate-oblong, elliptic-oblong, or oblong-lanceolate, 6–16 × 4–7 cm, sub-coriaceous with obtuse to rounded base, acuminate apex and with margin serrulate (Plates 1 and 2), serrate, teeth obtuse. Both leaf surfaces are glabrous or minutely puberulous, midrib raised and sometimes prominent abaxially, impressed adaxially with 5–11 pairs of lateral veins. Inflorescences are axillary and consists of a few to many flowered, finely pubescent racemes. Flowers are yellowish green, scentless, apetalous with four sepals rarely 3–6, usually unisexual and on 3–4 mm puberulous pedicels with 1 mm ovate bracts. Staminate flowers with numerous stamens and eight orange or yellowish, fleshy disk-lobes. Pistillate flowers are usually without stamens, with 4–6 (−8) free styles, free and indistinctly bilobed stigmas. Fruit is a globose, depressed-globose to obovate berry, 2–2.5 cm in diameter, light-green to pink or purplish-green to red to dark purple when ripe with whitish, juicy, acid-sweet pulp, crowned by

Plate 1 Young and old leaves

Plate 2 Immature and ripe fruits

Plate 3 Immature fruit with ring of style pegs

Plate 4 Ripe, dark purple globose rukam fruit

small persistent style pegs 4–6 (–8) spaced in a circle (Plates 2, 3, and 4). Each fruit has 4–7 flat, hard seeds.

Nutritive/Medicinal Properties

Analyses of the edible fruit in the Philippines recorded the following composition per 100 g edible portion: energy 345 kJ, moisture 77 g, protein 1.7 g, fat 1.3 g, carbohydrates 15 g, fibre 3.7 g and ash 0.8 g (Sunarjono 1992).

In Peninsular Malaysia, the astringent juice of the immature fruit has been used as traditional medicine for diarrhea and dysentery. The fruit was prescribed for dysmenorrhoea. The juice of the leaves has been applied to inflamed eyelids. The leaves were also used in a complex medication for smallpox. In Sabah, roots are employed for abdominal colic leaves for headaches. In Java, the leaves were dried and pounded and dusted over wounds. In the Philippines, the root decoction was given internally to women after childbirth. The roots have been employed to treat skin allergies, pneumonia and liver ailments.

Other Uses

The wood is hard and strong and used for making household utensils such as pestles and furniture.

Comments

Large-leaved forms have been described as *Flacourtia megaphylla* Ridley and *Flacourtia euphlebia* Merr., narrow-leafed forms as *Flacourtia peninsula* Elmer.

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Pangium edule

Scientific Name

***Pangium edule Reinwardt*.**

Synonyms

Hydnocarpus polyandra Blanco, *Pangium ceramense* Teijsm. & Binnend. ex Boerl., *Pangium naumannii* Warb., *Pangium rumphii* Voigt.

Family

Silacaceae, previously placed in Flacourtiaceae.

Common/English Names

Football Fruit, Sis Nut.

Vernacular Names

Chamorro: Lasret, Raoel, Rauel;
Chuukese: Durien;
Dutch: Kloewak;
Indonesia: Pucung, Pakem, Pucong (Javanese), Kapayang, Kapenceung, Kapecong, Kepayang, Simuang, Kayu Tuba Buwah (Sumatra), Picung, Pucung Pacung (Sundanese), Kluwak;
Malaysia: Peyang (Bidayuh), Kepayang, Buah Keluak, Payang, Pangi (Malay);
Palauan: Ariaml, Riamel;
Papua New Guinea: Rumrum, Suete (Bismarck Archipelago) Sis Nut, Solomon;
Pohnpeian: Drian, Duhrien, Durien;
Solomon Islands: Rawahn Falaka, Ra;
Yapese: Rowa.

Origin/Distribution

The species occurs throughout Malesia, Melanesia and Micronesia. Wild and cultivated in Malaysia, Indonesia, Papua New Guinea and Vanuatu.

Agroecology

It occurs in the tropical rain forests and secondary forests in the Malay archipelago. In Papua New Guinea, it is found primary forests from sea level up to an elevation of 1,050 m, and occasionally as high as 1,380 m. The tree is shade loving and grows well in a slightly acidic soil. It is also found along riverbanks and inundated areas and on stony and clayey soils.

Edible Plant Parts and Uses

Within Papua New Guinea, the seed kernel is eaten in most provinces after extensive processing to remove a toxic substance, a cyanogenic glycoside. Seed kernels are consumed after processing the seed by washing, fermentation and roasting or cooking in Papua New Guinea

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and Fiji. In Papau, the seed kernel is only eaten after being washed in water, then roasted and fermented seeds cooked with sago in bamboo tubes over fire.

Elsewhere the seeds are boiled for several hours and the hard seed coat removed and the kernels soaked in several changes of water overnight. After soaking the kernels are cut up and used as vegetable (Plate 5). Fried with meat or fish makes a savoury dish, Alternatively the seeds are left in wood ash for several moths to ferment. This results in the kernel becoming dark brown to black, slippery and greasy and the fermented kernel is then spooned and used in fish, meat or chicken curries by Peranakan (Nyonya), Eurasian, Malays and Indonesians. In Malaysia and Singapore, keluak seed kernels are used in the Nyonya speciality cuisine such as *Ayam buah keluak* or *babi buah keluak*. In Sabah, it is used in *Bosou* a signature dish for Kadazan Dusun which include ingredients like raw freshwater fish, pangi, salt, steamed rice and some other optional ingredients such as jackfruits, young pineapple fruits, tahu (bean curd), etc.

In Indonesia, the seed kernels are used as an important basic ingredient for *bumbu rawon* – a mixture of spices: kemiri (candlenut), asam jawa (tamarind), kluwak (sisnut), bawang putih (garlic), kunyit (turmeric), lenguas (galangal), jahe (ginger) and lada (chilli). This spice mixture is use in the following Indonesian cuisine – *sayur kluwak* and *soto rawon*. *Soto Rawon* is a much relished Indonesian soup with beef. This dark beef soup, is served with mung bean sprouts and sambal. Young leaves also are edible after cooking and are cut into small pieces and used in the preparation of preserved meat 'kasam' in Sarawak.

An edible oil obtained from the seeds are used for cooking in places where coconut was unavailable.

Botany

A medium to large, much branched, evergreen perennial tree 18–40 m. Leaves spiral, clustered at twigs on long petioles at the shoot apex (Plate 1). Leaves are entire, broadly ovate, cordate to truncate base, 15–25 cm long, 3-lobed on young trees, acuminate, glossy green, nerves palmate (Plate 2). Flowers mostly unisexual; male flowers occur in racemes, to 5 cm wide; with 2–3 calyx-lobes; 5 or 6 petals with a basal scale and many stamens. Female flowers are solitary, similar to male flowers, but have no stamens but with 5–6 staminodes alternating with the petals, ovary long-ovoid, thick-walled, 1-celled with 2–4 placentae and many ovules and sessile stigma. Fruit is large, subglobose to ovoid-subpyriform (football shaped), indehiscent, rough, brown, generally 15–30 cm long, and about half as thick (Plates 2 and 3). Seeds many, compressed ovate, greyish, 5 cm long, the

Plate 1 Large cordate leaves clustered towards the shoot tip

Plate 2 Subglobose, immature sisnut

Plate 3 Sisnut with rough, scruffy brown skin

Plate 4 Greyish, hard-shelled seeds of sisnut

hard seed coat with prominent raised nerves (Plates 4) and embedded in creamy-white or yellowish pulp.

Nutritive/Medicinal Properties

The proximate nutrient composition of the seed kernel of *Pangium edule* per100 g edible portion based on analyses made in Sarawak (Voon and Kueh 1999) is: water 57.7%, energy 227 kcal, protein 7.3%, fat 20.2%, carbohydrates 4.1%, crude fibre 9.6%, ash 1.1%, P 30 mg, K 401 mg, Ca 42 mg, Mg 97 mg, Fe 2.1 mg, Mn 47 ppm, Cu 3.4 ppm, Zn 14 ppm, vitamin C 19 mg.

The proximate nutrient composition of the leaves per100 g edible portion (Voon and Kueh 1999) is: water 71.2%, energy 106 kcal, protein 6.2%, fat 2.3%, carbohydrates 15%, crude fibre 3.3%, ash 2%, P 66 mg, K 231 mg, Ca 439 mg, Mg 95 mg, Fe 7.3 mg, Mn 19 ppm, Cu 8.9 ppm, Zn 25 ppm, vitamin C 2.3 mg.

Plate 5 Kernels of sisnut on sale in a local market

The oily kernels of Kepayang are rich in calories, protein and has fair amounts of vitamin C. The leaves are also rich in calories, crude fibre and minerals like P, Ca, Mg, and Fe and also has fair amount of potassium.

Pangium edule seeds have been reported to have antioxidant and antibacterial activities.

Antioxidant Activity

During germination of *Pangium edule* seeds, lipid content decreased, whereas the major fatty acids did not change significantly (Andarwulan et al. 1999). The dominant fatty acids were oleic acid (C18:1(n-9)) and linoleic acid (C18:2(n-6)). During germination, oleic acid decreased while linoleic acid increased proportionally. The hypocotyl synthesized chlorophyll and the tocol composition also changed substantially. The antioxidant activity of phenolic extract increased in proportion to the total phenolics. Increase in guaiacol peroxidase and glucose-6-phosphate dehydrogenase activities coincided with increased total phenolics and free proline. The acetone extract of *Pangium edule* seed with higher phenolic content (22.22 mg GAE/g) showed the most potent antioxidative activity in both DPPH radical scavenging and β-carotene bleaching assays

as compared to other extracts (ethyl acetate, water) (Yee et al. 2009).

Antibacterial Activity

The phenolic extract of *Pangium edule* seed was found to have stronger inhibitory against *Listeria monocytogenes* than *Salmonella typhimurium* (Yee et al. 2009). The free phenolic acid extract was found to have the highest Minimum Inhibition Concentration (MIC) among the seed extracts, indicating its weak antibacterial activity against both bacteria. Nevertheless, both tested pathogens were killed at the Minimum Bactericidal Concentration (MBC) of 30.3 and 55.5 mg/mL, respectively, for the phenolic extracts. Significant correlation was observed between the total phenolic content and its antioxidative activity ($R^2 = 0.878$) as well as antibacterial ($R^2 = 0.840$) activity suggesting that phenolics of the seed extract could be potential sources of natural antioxidant and antibacterial.

Traditional Medicinal Uses

Seeds are reported to possess anthelmintic and narcotic properties in traditional medicine. In the Philippines all parts of the tree is considered to be anthelmintic. In Malaysia, fresh crushed seeds have been used for boils and the leaves being anthelmintic were mixed with lime juice and salt and use for itch due to parasite, ulceration, wounds, and scurf. In Sarawak, the Penan consume a decoction of the bark for constipation. A solution made from the seeds is used as shampoo and to remove head lice while oil extracted from the seeds is used as hair cream to produce healthy and shiny hair. The Iban apply sap from the inner bark as antiseptic to treat wounds. Young leaves are rubbed on the skin to treat infections. In Papua New Guinea the fruit is sliced and the fruit juice is applied for sores and cuts. All parts are credited with possessing narcotic attributes and an overdose will result in sleepiness, headache and intoxication leading to delirium and death in extreme cases.

Other Uses

The seeds possess antiseptic property and are pounded and used for preservation of fish and shrimps in Java. The seeds are used to kill rats and wild chickens, and the pounded bark and leaves are used to stupefy fish so they can be scooped up easily. Kepayang oil has been used for making soap and to provide a red dye. The wood has been used for matchsticks.

Comments

The seeds and leaves are poisonous when consumed raw without thorough processing and preparation.

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Santalum acuminatum

Scientific Name

Santalum acuminatum (R. Br.) A. DC.

Synonyms

Eucarya acuminata (R. Br.) Sprague & Summerhayes, *Fusanus acuminatus* R. Br., *Mida acuminata* (R. Br.) Kuntze, *Santalum densiflorum* Gand.

Family

Santalaceae

Common/English Names

Australian Quandong, Australian Sandalwood, Burn-Burn, Desert Quandong, Katunga, Native Peach, Peach Bush, Quandong, Quandong Tree, Sweet Qunadong. Wild Peach

Vernacular Names

Australia: guwandhang (Wiradjuri, New South Wales), gutchu (Wotjobaluk, Western Victoria), mangata, wanjanu (Pitjantjatjara, Uluru, Northern Territory), goorti (Narungga, South Australia)

Kelango, Gutchu, Mangart (1), Pmerlpe (2), Pmwerlpe (2) (3), Mangata (4) (5), Walku (4) (5), Kuuturu (5), Wayanu (5), Witirrpa (5), Mangarda (6), Mangarta (6)

Origin/Distribution

The species is indigenous to Australia. It is found in semiarid areas in the mainland states of Australia. Its distribution extends from Western Australia's north to Carnarvon (24°53′S), reaching inland from the coastal plains, and is found throughout coastal Southwest Australia, across southern Northern Territory, most of South Australia, to New South Wales and south western Queensland. It is widespread in western New South Wales, eastwards to Dubbo and Culcairn but is rare in the northwest of the state.

Agroecology

Quandong has a wide natural distribution range, from arid desert areas to Mediterranean-climate coastal regions. It tolerates temperatures from 3 to 38°C and frost from −5 to 0°C and has an optimum range of 13–28°C. It thrives in areas with mean annual rainfall of 150–750 mm but is drought tolerant and sensitive to water-logged conditions. It tolerates salt-laden coastal winds.

T.K. Lim, *Edible Medicinal and Non-Medicinal Plants: Volume 5, Fruits*,
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It is typically found in dune swales, along creeks, on plains and low rises, and rarely on hills from 10 to 770 m altitudes.

In its native range quandong occurs in areas with free-draining, sandy or loamy soils sometime with limestone or sand-stone shallowly below the surface with soil pH from 6 to 7.5. Quandong, has been found to have relatively high salt tolerance and can be classified as a salt-tolerant non-halophyte (Walker 1989). It prefers full sun.

Quandong is a hemiparaiste, it attaches itself by producing a modified root structure called a haustorium, which attaches to a living plant host and extracts xylem sap for water and nutrients while it is able to photosynthesise using its own leaves. In a natural situation, *Santalum* appears to rely on nitrogen fixing trees such as *Acacia* and *Allocasuarina*, though it has been found to parasitise many other legumes, shrubs, herbs and grasses.

Edible Plant Parts and Uses

Quandong fruits are eaten raw, or more commonly, halved, dried and then reconstituted for use in a range of sweet and savoury products that include preserves, sauces, chutneys, jellies, confit, pie filling or in cordials and liqueur. The ripe fruits are also boiled and used for making jams. The flavour is tart and reminiscent of peach, apricot or rhubarb. The kernels (nuts) are also edible and much sought after by aboriginal people. Quandong has gained popularity as an exotic bush food and is highly prized by gourmands.

Botany

Erect tall shrub or small tree (Plate 1) 3–6 m high and 2–3 m wide with rough, dark gray bark and spreading to pendent braches (Plate 2). Leaves opposite, more or less lanceolate, often falcate, 3–9 cm long by 3–15 cm wide, pale green to olive green, margin entire, apex acute to acuminate with a curved point and pinnately-veined (Plates 2, 3, 4, and 5). Flowers small, creamy white or greenish-white, 2–4 mm across, numerous in mostly terminal panicles (Plate 4), peduncles 5–10 mm long and pedicel 1–2 mm long; with four thick ovate tepals, 1–2 mm long; red shortly-lobed disc; four stamens with anthers that dehisced by longitudinal slits; half-inferior ovary with short style and bilobed papillate stigma. Fruit a globose drupe,

Plate 1 Tree habit (M Hoult)

Plate 2 Sapling with ascending, spreading branches

Plate 3 Slender, lanceolate and falcate leaves

Plate 4 Terminal inflorescence

Plate 5 Ripening quandong fruit (M Hoult)

15–35 mm long, green turning to orangey red to bright, glossy red when ripe, crown by persistent tepal scar (Plate 5), enclosing a succulent or firm edible mesocarp and wrinkled and pitted endocarp.

Nutritive/Medicinal Properties

The food value of quandong fruit was reported by Food Standards Australia New Zealand (2006) and Brand et al. (1983) as: energy 206 kJ, moisture 71.9 g, protein 2.5 g, N 0.4 g, ash 2 g, dietary fibre 4.2 g, total sugars 8.1 g, fructose 4.6 g, glucose 2.3 g, sucrose 1.2 g, available carbohydrates including sugar alcohols 8.1 g, Ca 7 mg, Mg 28 mg. P 11 mg, K 747 mg, Na 116 mg, vitamin C 20 mg, thiamin 0.04 mg, niacin equivalents 0.42 mg, total folate 191 μg, α-carotene 22 μg, β-carotene 45 μg, β-carotene equivalents 62 μg, cryptoxanthin 12 μg and retinol equivalent 10 μg.

Kernels of *S. acuminatum* were found to have high levels of oil (58–67%) and protein (13–19%), although there was significant variation between samples from different sites (Jones et al. 1985). Quandong oil content is typically in the range 45–65% and the fatty acids, oleic acid (*cis*-9-octadecenoic acid) and santalbic acid (*trans*-11-octadecen-9-ynoic acid), predominate in the triacylglycerols (Jones et al. 1985). The polyacetylenic fatty acid, *trans*-11-octadecen-9-ynoic acid (santalbic acid) was found to be a major component of the oil. Santalbic acid was reported to be identical with ximenynic acid (Gunstone and Russell 1955). Polyacetylenic acids were also found in the seeds and seedlings of quandong (Bu'Lock and Smith 1963). Santalbic acid is one of the most common and unusual fatty acids found in the seed oils of these plants and has been isolated from several species of the genera *Santalum*, *Exocarpus* and *Ximenia* (Hatt et al. 1960). The following acids were found in the plant parts (root, stem and leaves) of *Ximenia* (Olacaceae), *Santalum* and L*eptomeria* (Santalaceae): (i) octadeca-*trans*-13-ene-9,ll-diynoic acid, (ii) octadeca-*trans*-11,*trans*-13-dien-9-ynoic acid, (iii) octadeca-*trans*- 11-en-9-ynoic (ximenynic) acid, and (iv) an octadeca-*trans*-*trans*-dienediynoic acid Besides santalbic and oleic acid, other fatty acids found in the kernel and oil include 16:0 (palmitic), 16:1 (palmitoleic), 18:0 (stearic), 18:2 (linoleic), 18:3 (linolenic) and stearolic (Jones et al. 1999). The

edible quandong kernels contained % moisture 1.6%, protein 15.3%, fat 67.6%, free sugars 3.1%, starch traces, and ash1.3%, (Jones et al. 1995).

Caucasian taste panels had found quandong kernels to have an objectionable aromatic flavour due to the presence of methyl benzoate (Loveys et al. 1984). Jones et al. (1994) studied the metabolism of santalbic acid in rats fed a diet enriched in quandong (*Santalum acuminatum*) seed oil, which contained 40–45% of santalbic acid. Their results indicated that santalbic acid was incorporated into different body tissues, in the blood plasma, adipose tissue, skeletal muscle, kidney, heart and liver but not in the brain. Also, rats fed quandong oil had elevated levels of hepatic cytochrome P450 and cytochrome P450 reductase compared with control animals fed canola oil. In further studies Jones et al. (1999) found feeding rats with a purified methyl santalbate preparation isolated from quandong oil at 9% of dietary energy for 4 days also elevated cytochrome P450 4A in both kidney and liver microsomes in comparison with methyl esters from canola oil. This indicated the possibility that santalbic acid may not be metabolized like a normal dietary fatty acid but as a xenobiotic compound and that the consumption of oil from quandong kernels may cause perturbations in normal fatty acid (such as arachidonic acid and other eicosanoids) biochemistry.

Antioxidant Activity

Quandong fruit displayed outstanding antioxidant capacity (Konczak et al. 2009) with the following antioxidant profile: Total phenol content (TPC) 32.87 mg GAE/g DW, total anthocyanin 0.53 mg cyanidin 3-glucoside equivalent/g DW, FRAP 454.9 umol Fe2+/g DW ORAC-H (oxygen radical absorbance capacity – hydrophilic) 1987.99 umol Trolox Equivalent (TE)/g DW, ORAC-L (oxygen radical absorbance capacity – lipohilic) 39.98 umol TE/g DW ORAC-T (oxygen radical absorbance capacity – total) 2027.97 umol TE/g DW. The major phenolic compound identified in fresh quandong fruit were cyanidin-3-glucoside 5.76 mg/g, pelargonidin-3-glucoside quercetin 1.18 mg/g, rutinoside 2.29 mg/g and kaempferol 2.6 mg/g.

Antimicrobial Activity

Santalbic acid (*trans*- 11-octa-decen-9-ynoic acid), a major constituent of *S. acuminatum* oil, was found to be an inhibitor of Gram-positive bacteria and a number of pathogenic fungi in standardised bioassays but the un-saponified oil and other kernel components were inactive (Jones et al. 1995).

Traditional Medicinal Uses

Quandong is valued by Australian aborigines for its medicinal properties. Quandong tea has been drunk as a purgative. The pulverised seed kernels have been used as a liniment. A root infusion has been drunk to treat rheumatism. Crushed quandong leaves mixed with saliva has been employed as a poultice for sores, boils and wounds. Quandong kernel oil has been similar used for skin disorders and scalp. The Anangu aboriginal people used the oily kernels to condition and strengthen their hair.

Other Uses

The seed is rich in oil and is burnt as an illuminant by spearing on a stick to make a candle. The wood is oily and makes a god friction stick for starting a fire. The hard, heavy, close-grained timber is used for furniture and cabinet but lacks the aromatic qualities of other sandalwoods. The hard and wrinkled nuts have been used ornamentally, for necklaces and shirt buttons, and were used as marbles on Chinese checkers' boards.

Comments

Quandong is usually propagated by seed but pretreatment is needed to enable moisture to reach the embryo. Loveys and Justias (1994) found that intact seeds of quandong which are normally

difficult to germinate responded to vacuum infiltration with gibberellins. In most cases GA4 was far more effective than GA3. Propagation by grafting onto seedling stock is becoming more common as particular forms are selected for their desirable fruiting characteristics.

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Dianella caerulea

Scientific Name

***Dianella caerulea* Sims.**

Synonyms

None. The species has been divided into several accepted varieties.

Family

Xanthorrhoeaceae, also placed in Phormiaceae

Common/English Names

Blue Berry Lily, Blue Flax Lily, Blueberry Lily, Blueberry Plant, Cerulean Flax Lily, Flax Lily, Paroo Lily

Vernacular Names

Australia: Snake Whistle (Abor.)

Origin/Distribution

The species is found in South New Guinea to East and southeast Australia – Victoria, New South Wales, Queensland and Tasmania.

Agroecology

In its native range, *D. caerulea* is found in a variety of habitats from coastal heath-land and sand dunes and inland to open forests and woodlands. It is a robust, snow-hardy and frost-hardy plant and long-lived plant once established. It is also tolerant to drought, strong winds and salt winds. It can tolerate damp conditions but prefers moist well-drained, weakly acid to mildly alkaline soils. It adapts readily to cultivation. It thrives in warm low sun to partial light shade situations.

Edible Plant Parts and Uses

The fruit has been reported to be eaten raw or cooked, with a sweet nutty flavour once the seed is chewed. The roots of some of these lilies have been reported to be eaten after pounding and roasting.

Botany

A tufted, strappy perennial herbaceous plant, about 1 m high with a thick, spreading underground rhizome and fibrous roots. Leaves green, alternate, (Plate 1) 10–75 cm long by 0.5–2.5 cm wide, leaf sheath condulpicate, a third to almost occluded, margin entire or minutely serrated. Inflorescence a 3–25 flowered panicle, exceeding

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Plate 1 Mature indigo fruits and leaves

the foliage. Flowers with six tepals, 5–6 mm long, spreading stellate, whitish-blue to dark blue; filaments with yellow stamens and dark yellow anthers, ovary globose and dark green with white style and stigma. Fruit globose, 8–14 mm diameter, glossy dark blue to indigo (Plate 1). Seeds ovoid, 3–4 × 2 mm.

Nutritive/Medicinal Properties

No nutritive value of the edible fruit has been published.

Compared to other *Dianella* species very little studies have been published on the phytochemicals in *Dianella careula*. Batterham et al. (1961) reported that only dianellin, a crystallineglycoside had been found in *D. caerulea*. The roots of *Dianella laevis* were found to contain a crystalline glycoside, dianellin, and the corresponding aglycone, dianellidin. Dianellidin was identified as 1,8-dihydroxy-3-methyl-2-acetonaphthone and the glycoside possessed the sugars, glucose and rhamnose, attached at the 8-position. Other coloured pigments isolated from the roots of *Dianella revoluta* included dianellinone (Cooke and Sparrow 1965); methyl 2,4-dihydroxy-3,6-dimethylbenzoate, (−)-4′-hydroxy-7-methoxy-8-methylflavan, 5,7-dihydroxy-6-methyl-2-nonacosylchromone (with homologues), and a triquinone, trianellinone (Cooke and Down 1971). Colegate et al. (1986) isolated dianellidin, stypandrol and dianellinone from *D. revoluta*. They also isolated a toxic naphthalene-14-quinone, stypandrone from *D. revoluta* which was found toxic to mice (Colegate et al. 1987). Byrne et al. (1987) isolated a novel naphthol-naphthoquinone dimer called inbricatonol, from *D. revoluta* plant. Lojanapiwatna et al. (1982) isolated musizin (dianellidin) (1); methyl 2,4-dihydroxy-3,5,6-trimethylbenzoate (8); methyl 2,4-dihydrox y-3,6-dimethylbenzoate (7);methyl2,4-dihydroxy-6-methylbenzoate (methyl orsellinate) (9); 2,4-dihydroxy-6-methoxy-3-methylacetophenone (14); 5,7-dihydroxy-2,6,8-trimethylchromone (11) and 5,7-dihydroxy-2,8-dimethylchromone (isoeugenitol) (13) from the roots of *Dianella ensifolia.* The roots of *Dianella longifolia* var. *grandis* was found to actively inhibit poliovirus type 1 at a concentration of 250 μg/mL (Semple et al. 1998).

Safety analysis carried out by Hegarty et al. (2001) reported *D. caerulea* fruit to contain virtually no cyanogens the results was below the limit of detection of 0.1 mg/100 g HCN for cyanogens.

Ripe fruit has been reported to be used as medicine for ulcers and the flower petals used as ingredient for medicine.

Other Uses

D. caerulea is commonly cultivated in gardens, as a low-hedging plant in public spaces and amenities plantings. It is also suitable for rockeries.

The leaves are used in making of decoration baskets, mats, strings, and yield very strong silky fibre. The leaf is also made into a whistle for attracting snakes which are then caught and eaten.

Comments

The plant is propagated from seed or by division of its rhizome.

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Amomum aromaticum

Scientific Name

***Amomum aromaticum* Roxb.**

Synonyms

Alpinia fasciculata (Roscoe) Steud., *Amomum fasciculatum* (Roscoe) Benth. & Hook. f. ex B.D. Jacks., *Cardamomum aromaticum* (Roxb.) Kuntze, *Geocallis fasciculata* (Steud.) Horan., *Renealmia fasciculata* Roscoe

Family

Zingiberaceae

Common/English Names

Bengal Cardamon, Jalpaiguri Cardamom, Nepal Cardamon

Vernacular Names

Chinese: Xiang Dou Kou;
Hungarian: Bengáli Álgyömbér;
India: Morang-Ilachi, Morang-Ilayechi, Morangilachi, Murang-Ilayechi (Hindu), Kaage Aelakki (Kannada), Namra (Manipuri), Veldoda (Marathi), Brhadela, Ela, Ghrtachi (Sanskrit);
Indonesia: Kapulaga Besar;
Laotian: Mak Neng Nhai;
Nepal: Alainchi, Elaa;
Vietnam: Đò Ho, Sa Nhân Cóc, Thảo Quả.

Origin/Distribution

The cardamom is native to North West Bengal, Arunachal Pradesh, Nagaland, Meghalaya and Bihar, Sikkim, Assam, Bhutan, Nepal and Bangladesh where it occurs wild and cultivated. It is widely cultivated in Lao Cai province and also in Lai Chau and Ha Giang provinces in Vietnam. In Sa Pa, Lao Cai, thao qua is cultivated under canopy of Tong qua su (*Alnus nepalensis*) plantation.

Agroecology

The plant is shade and moisture loving and occurs naturally in cool, montane forest, near stream in 1,500–2,200 m elevation on soil rich in organic matter. It thrives well under the shade of *Alnus nepalensis* an actinorhizal nitrogen fixing tree in Assam, Nepal and North Vietnam.

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Edible Plant Parts and Uses

The (fruit) seed is used as a spice and medicine by the locals and is sold as cardamoms. It is better known for its mature fruits with aromatic seeds lavishly used in confectionary for flavouring cakes.

Botany

A tall herbaceous perennial herb, 2–3 m high with underground, prostrate horizontal pinkish rootstock with many nodes and shoots growing in cluster from it. Leaves oblong-lanceolate, 40–70 cm long by 10–15 cm wide, green, sessile, lower part clasping the stem (Plates 1 and 2). Inflorescence in radical, short peduncled globose 4 cm spike found the towards the base of the plant (Plate 3). Inner floral bracts elongate, ribbed and thorn-tipped. Flowers numerous closely arranged in inflorescence, yellow with a tubular, 3-toothed calyx and tubular corolla (Plate 4). Petals 2.5 cm long, lanceolate, blunt, and somewhat cap-shaped. The yellow labellum round with a cuneiform base, twice as long as corolla segments. Anthers with large petaloid, 3-lobed connectivum. Fruit orange-crimson, 3-chambered, ovoid, capsule,

Plate 1 Basal part of leaf clasping the slender stem

Plate 2 Large oblong-lanceolate leaves

Plate 3 Inflorescences at the base of the stem

Plate 4 Yellow flowers

Plate 5 Bengal cardamom fruits (preserved)

2.5–3 cm diameter (Plate 5). Seeds numerous, 3-per chamber, 3 mm long, angular, black, arillate, with a pronounced aroma because of cineol.

Nutritive/Medicinal Properties

The seeds contain starch, alkaloids and 1–1.5% essential oil. The essential oil was reported to contain 1.8-cineole 29.44%, 7-methyl-6-octen-2-yl propionate 15.30%, 2-decenal 7.75%, geraniol 5.60%, α-citronellol 6.00, 2-*p*-tolypropanal, 7 methyl-5, 7-octadienal 5.25%, 2-dodecenal 2.60%, α-terpineole 2.60%, α-farnesene + zingiberene 2.35%, nerol 2.20%, geranial 2.20%, *p*-isopropyl benzaldehyde acetate 2.00%, α-methylcanelene acid methyl ester 1.60%, 2-methyl-3-phenylpropanal 1.25%, 8-methy-2,8-nonadienol 1.10%, 3,7-dimethyl-7-octen-2-ol 1.10% and <1.00% of others such as β-pinene, α-pinene, sabinene, α-phellandrene, myrcene, limonene, β-ocimene, *p*-cymene, 11-dodecenic acid, perylcetone, etc. (NIMM 1999).

The petroleum ether extracts of *Amomum aromaticum* seed extract exhibited a significant increase in the hypersensitivity reaction to the rabbit red blood cells (RRBC) antigen at concentration of 100 mg/kg in animal studies (Parihar et al. 2012). The petroleum ether extract also stimulated cell-mediated and antibody-mediated immune response in rats. It also enhanced the macrophage and lymphocyte count in rats. Short-term feeding of *A. aromaticum* resulted in a decrease in Klebsiella pneumoniae infection and colonization in the lungs when compare with control.

The seeds have antibacterial and stomachic properties. In Vietnam, they are used to treat dyspepsia, flatulence, colic, vomiting, diarrhoea and cough, chronic malaria, phlegm retention and halitosis in traditional medicine. They are also

prescribed as a gargle or mouth-wash or for perlingual administration to treat toothache, gingivitis and halitosis. In Laos, it is used for asthma, cough, dizziness, nausea, urination disorders, urticaria, hyperpyrexia, haemorrhoid, nausea, flatulence and emmenagogue.

Other Uses

Bengal cardamom seeds are also used for perfumery and for cosmetics.

Comments

Local ethnic growers of the spice, Tao qua in Vietnam can obtain up to 300 kg/ha of fruits; 1 kg of dried fruit can fetch US$ 1.00–2.50 across the border in China, where the seeds are used as a spice and in medicine.

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Amomum compactum

Scientific Name

***Amomum compactum* Soland. ex Maton.**

Synonyms

Alpinia striata Link, *Amomum cardamomum* Willd. nom. illeg., *Amomum kepulaga* Sprague & Burkill, *Zingiber compactum* (Sol. ex Maton) Stokes

Family

Zingiberaceae

Common/English Names

Chester Cardamom, Cluster Cardamom, False Cardamom, Java Cardamom, Round Cardamom, Siam Cardamom

Vernacular Names

Arabic: Amûmun;
Chinese: Zhao Wa Bai Dou Kou;
Czech: Kardamomovník Siamský;
Danish: Javakardemomme, Kardemomme Art;
Dutch: Ronde Kardemom;
French: Cardamome Ronde, Cardamome Grappe, Amome A Grappe;
German: Javakardamom;
Indonesia: Kapulaga, Karkolaka (Balinese), Kapulaga, Kapilogo (Javanese), Kapulaga, Kardamunggu (Batulicin, Kalimantan), Kapolagha, Palagha (Madurese), Palaga, Puwa Palago (Minangkabau), Kapol (Sudanese), Kapulaga, Garidimong (Sulawesi) Pelaga, Puwar Pelaga (Sumatra);
Malaysia: Kepulaga, Pelaga, Puar;
Vietnamese: Bach Dâu Khâu.

Origin/Distribution

The species is native to Indonesia, endemic to the mountainous areas in western Java It is commonly cultivated in Western Java southern Sumatra, Moluccas, Peninsular Malaysia and southern China – Hainan, S Yunnan. Java and Sumatra are the major growing areas.

Agroecology

A tropical species, grows well in full or partial shade in the warm tropical primary and teak forests. It thrives in areas with mean annual temperatures of 23–28°C, high relative humidity and annual rainfall of 2,500–4,000 mm at elevations of 200–1,000 m. It grows best in moist, organic rich, well-drained, loamy or sandy loam soils with pH 5–6.5 such as latosols, andosols, alluvials and red-yellow podsols.

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Edible Plant Parts and Uses

Fruit and seed are used as spice, condiment and medicine. The young shoots are eaten raw, steamed or cooked and eaten with rice. The seeds possess a peppery, ginger-like flavour and serve as a warm aromatic spice to sweeten the breath and to appetize food. The seeds are also used as a condiment in cakes.

Botany

Robust, perennial aromatic herb grows to 1–1.5 m high with much branched underground, hard subterete rhizome which give rise to leafy stems and separate inflorescence stalk. Rhizome yellow-white covered with red brown scales. Leaves (Plate 1) distichous, alternate, green, sessile with a bi-cleft orbicular, ligule; leaf blade lanceolate, 25–50 cm by 4–9 cm, glabrous but ciliate at margin, leaf apex acuminate. Inflorescence is a cylindric spike 5 × 2.5 cm, arising laterally from rhizome. Peduncle to 8 cm; bracts 2–2.5 cm × 7–10 mm, longitudinally striate, yellow, ovate-oblong, persistent, margin ciliate; bracteoles tubular. Calyx 1–1.2 cm, pubescent, apex 3-toothed. Corolla white or yellowish; tube 1–1.2 cm; lobes oblong, ca. 8 mm. Labellum yellowish with orange mid-rib and purple margin, elliptic, 1.5–1.8 × 1–1.5 cm, pubescent. Filament hairy at base; anther elliptic, about 2 mm; connective appendage 3-lobed, 4 mm. Ovary pilose. Capsule whitish brown, oblate, (depressed globose) 1.5 cm across, slightly 9-grooved when dry, pilose (Plates 2 and 3). Seeds irregularly polygonal, 4 mm in diameter with white aril.

Plate 1 Young kapulaga plant

Plate 2 Java round cardamom

Nutritive/Medicinal Properties

Java cardamom seed was reported to contain 2–5% essential oil comprising mainly 1,8 cineol (up to 70%) and β-pinene (16%) (Wolff and Hartutiningsih 1999). α-Pinene, α-terpineol and humulene were also found. Setyawan (2002) found that volatile oils in various parts of *A. compactum* varied from 1–3.5%: rhizome (1.5%), root (1.25%), stem (1%), leaf (3%), fruit (3.5%), fruit peel (1.75%), seed (1%). Sixty-one unidentified compounds were detected in the rhizomes and forty-five in other parts. Volatile oil constitutens of *Amomum* species consisted of comprise cineole, β-pinene, α-pinene, borneol, camphor,

Plate 3 Close-view of Java cardamom

terpinene, terpinyl acetate, terpineol, bisabolene, sabinene, linalool and other (Guenther 1952).

Lee et al. (2010) found that administration of *A. compactum* may have potential therapeutic value when used as an adjuvant for the immunomodulatory treatment of allergic asthma. Their results showed that *A. compactum* treatment markedly decreased the number of infiltrating eosinophils and the hypersecretion of mucus when compared with the effects on mice treated with ovalbumin alone. The treatment dose-dependently lowered the levels of reactive oxygen species (ROS) and T helper (Th)2 cytokines, including interleukin (IL)-4 and IL-5, in the bronchoalveolar lavage fluid (BALF). Further, a high dose of *A. compactum* effectively reduced the level of total immunoglobulin (Ig)E in the serum.

Amomum compactum ethanolic extract was found to have antiinflammatory effects in a lipopolysaccharide-induced RAW 264.7 cell model of inflammation (Lee et al. 2012). The extract prominently inhibited the production of nitric oxide (NO), prostaglandin E(2) (PGE(2)), interleukin (IL)-6 and tumour necrosis factor (TNF)-α, and inhibited the protein expression of inducible nitric oxide synthase and cyclooxygenase-2. Further, the extract inhibited the translocation of nuclear factor-kappaB (NF-κB) and the degradation of inhibitory factor-kappaB alpha, but enhanced the expression of heme oxygenase (HO)-1 and the nuclear translocation of nuclear factor-erythroid 2 (Nrf2). Treatment with stannous protoporphyrin IX dichloride (SnPP), a selective HO-1 inhibitor, reversed the extract-induced suppression of NO production, suggesting that the induction of HO-1 was involved in the suppression of NO, TNF-α, and IL-6 production by the extract.

In traditional medicine Java cardamom seeds have been used to alleviate damp, to remove stagnancy of food, and to promote digestion (stomachic), treat colds, cough and tonic after child birth. A decoction of the plant has been used to alleviate rheumatic pains. The dried crushed rhizomes were employed to reduce fever and combat intestinal pains.

Other Uses

Java cardamom seed yields an essential oil that is used in the perfume and flavour industry.

Comments

Java cardamom is commonly cultivated using rhizome cuttings or offsets (tillers) of the plant clump, but seeds are also used.

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Amomum longiligulare

Scientific Name

***Amomum longiligulare* T. L. Wu.**

Synonyms

None

Family

Zingiberaceae

Common/English Names

Hainan Amomum, Malabar Cardamom, Tavoy Cardamom.

Vernacular Names

Chinese: Hai Nan Sha Ren;
French: Amome A Ligule Longu;
Vietnam: Sa Nhan Tin, Me Tre Ba, Co Nenh (Thai), Mac Neng (Tay), Sa Ngan (Dao), Pa Doc (K'dong), La Ve (Ba Na).

Origin/Distribution

In Vietnam, it is found in the mountainous Central provinces and Tay Nguyen and in Phu Thao, Hoa Binh and Hai Duong in the North. It also occurs in central and southern Lao PDR, the central highlands and southern Viet Nam, Thailand and in China (Hainan). The plant occurs wild and is also cultivated in Vietnam often intercropped with forest, rubber or orchard trees.

Agroecology

A hygrophilous and shade loving species, it occurs in dense clusters in forest edges or along the banks of streams. It is usually found in the cool, humid forest of the mountainous areas under the shade of big trees.

Edible Plant Parts and Uses

The fruit is used as a spice ingredient in Vietnam, China and Taiwan. The dried fruit is used as an ingredient in health tonic wine such as "Zhuyeqing jui", and "Yuanlinqing jui" in China.

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Botany

Perennial herb, 1–2.5 m high with a slender horizontal rootstock. Leaves are alternate, distichous, lanceolate, 23–30 cm long by 5–6 cm broad, base cuneiform, apex acute, margin entire, glossy green and glabrous on 5–10 mm long petiole with thin bifid ochrea (Plate 1). Inflorescence in radical spike on 1–3 cm long peduncle, bracts brown, lanceolate, 2–2.5 cm; bracteoles tubular, ca. 2 cm. Calyx white, 2–2.2 cm, apex 3-toothed. Corolla slightly longer than calyx; lobes oblong, ca. 1.5 cm. Labellum white with purple midvein and yellow apex, orbicular-spatulate, ca. 2 × 2 cm, midvein convex, apex with 2-lobed point. Stamen 1 cm across; connective appendage 3-lobed, central lobe orbicular, lateral ones suborbicular. Capsule globular, 1.5–2.5 cm across, 3-valved with soft flaky, branched spines, 1 mm, dark red – violet-brown when ripe (Plates 2 and 3). Seeds purple-brown, 1.5–2 mm diameter, aromatic enclosed in a brown, membranous aril.

Plate 1 Young plant

Plate 2 Clusters of spiky capsules on a long peduncle arising from the horizontal rootstock

Plate 3 Closer view of the spiky fruit clusters

Nutritive/Medicinal Properties

Forty-five compounds were isolated from the essential oil of *A. longiliculare* seeds including four saponins (Nguyen et al. 1994). The essential oil and ethanol extracts exhibited marked antibacterial activity (Do et al. 1994). The essential oil (1.7–3%) from the seeds was reported to consist of borneol 19%, D-camphor 33%, bornyl acetate 26.5%; D-limonene 7%, phellandrene 2.3%, paramethoxy cinnamate 1%, α-pinene 1.8%, linalool and nerolidol (NIMM 1999).

Three compounds isolated from the essential oil of *A. longiliculare* seeds were identified as amomumoside ((+)-angelicoidenol-2-*O*-β-D-glucopyranoside), quercitrin (quercetin-3-*O*-α-L-rhamnopyranoside) and epicatechin (Do et al. 2000).

In Vietnam, Sa Nhan Tin is used in treating indigestion, abdominal burn due to cold, diarrhoea, vomiting, threatened abortion, dysentery, tooth ache and oedema. In Chinese herbal medicine, it is regarded as a stomachic and counteracts cold.

Other Uses

The dried fruits from Vietnam are exported to China, Japan and Hong Kong as a traditional medicine, spice and source of aromatic material.

Comments

The plant is propagated from young and medium tillers.

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Amomum subulatum

Scientific Name

***Amomum subulatum* Roxburgh.**

Synonyms

Cardamomum subulatum (Roxb.) Kuntze.

Family

Zingiberaceae

Common/English Names

Black Cardamom, Bengal Cardamom, Fragrant Cardamom, Greater Cardamom, Hill Cardamom, Large Cardamom, Nepal Cardamom, Winged Cardamom, Winged Bengal Cardamom.

Vernacular Names

Arabic: Hal Aswad;
Breton: Kardomom-Du;
Chinese: Ga Ge La, Hsiang Tou K'ou, Ka Ko La, Xiang Dou Kou;
Czech: Kardamomovník Šípový;
Danish: Sort Kardemomme;
Dutch: Zwarte Kardemom;
Eastonian: Must Kardemom;
Finnish: Mustakardemumma;
French: Cardamome Brune, Cardamome Noir, Cardamome Noire, Cardamome Du Népal;
German: Nepal-Cardamom, Schwarzer Cardamom;
Greek: Amomon;
Hungarian: Fekete Kardomom;
India: Bara Alachi, Boro Elach, Morung Elachi (Bengali), Gosom Ilaisi (Bodo), Badi Ilaichi (Dogri), Badi ilaichi, Big ilaichi, Doda, Heel Kalan, Kali Elaichi, (Hindu), Dodda Ailakki (Kannada), Badi Aleh (Kashmiri), Bari Ilaychi (Maithili),Harenuka, Kattelam, Karutta elakka, Karuppu elakka (Malayalam), Masalyachi velchi, Veldode (Marathi), Aleich (Oriya), Kali Ilaichi (Punjabi), Brihatupakunchika, Upakunchika (Sanskrit), Katu elam, Karupu elakkai (Tamil), Nalla Elakulu (Telugu), Bari Elaichi, Purbi Elaichi (Urdu),
Italian: Cardamomo Nero;
Lithuanian: Juodasis Kardamonas.
Nepali: Alaichi, Thulo sukumel (Nepali), Yala, Elam (Newari);
Pakistan: Iliachi Kalan;
Romanian: Cardamom Negru;
Russian: Kardamon Chyornyj;
Spanish: Cardamomo Negro;
Tibetan: Kakola.

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Origin/Distribution

Amomum subulatum is native to the Eastern Himalayas; the main production regions are Nepal, Sikkim, Bhutan and Darjeeling District of West Bengal to Central China.

Agroecology

It is found in the mid-hills of the Eastern Himalayas at altitude of 800–2,000 m, from subtropical to the cool temperate zones with rainfall of 3,000–3,500 mm distributed in about 200 days a year and temperatures ranging from 6 to 30°C. This species inhabits cool forest areas near mountain streams and damp forest floors. It is found on slopes of hills where there is plenty of well-drained water available, preferably in the north slopes of under the shade of trees e.g. Himalayan alder, *Alnus nepalensis*. This cardamom species does best in deep, well-drained soils with loamy texture and rich in organic matter and pH of 4.5–6. Even though the crop can be grown in undulating and steep terrains, land with moderate slope is preferred. It grows fast and vigorously during the summer monsoon months.

Edible Plant Parts and Uses

Dried large black cardamom capsules when dried and smoked, shrink from globose to oval, 2.5 cm across with a rough, ribbed and furry surface. It has a woody, smoky and camphorous flavor, similar but not as intense as green cardamom. It is used in India in spicy and rustic dishes; in western Asia in savoury dishes and to season pickles. It is used as a flavorant in dishes like Pulavu, Biriyani, and meat preparations. They are used as a spice in curries, soups, sweets, sausage, and other meat dishes. It imparts a delicious smoky taste to marinades for tandoori-style cooking. It is an ingredient in curry powder and spice masala mixtures. The seeds are rich in penetrating aromatics and serve as a substitute for cardamom. It also has applications in flavouring cola, biscuits, liquors. The oil, obtained from the seeds by distillation, is used as spice and for medicinal purposes. The fruit is also popular in Afghan cuisine.

Plate 1 Dried Nepal cardamom fruits

Botany

Perennial herb 1–2 m tall. The rhizomes are a dull red colour. Ligule membranous, apex rounded, emarginate; petiole absent or nearly so on proximal leaves. Leaves are found on the upper portion of the stem. Leaf blade oblong-lanceolate, 25–60 × 3.5–11 cm, glabrous, base rounded or cuneate, apex long cuspidate. Spikes appear in spring from the base of the rhizome, subturbinate, ca. 5 cm in diam.; peduncle 0.5–4.5 cm, scalelike sheaths brown; bracts pale red, ovate, ca. 3 cm, apex obtuse with horny cusp; bracteoles tubular, ca. 3 cm, apex acute, emarginate. Calyx glabrous, 3-cleft to middle; lobes subulate. Corolla tube lobes white-yellow, central one subulate at apex. Lateral staminodes red, subulate, ca. 2 mm. Labellum with yellow midvein, oblong, ca. 3 cm, white pubescent, veins conspicuous, apex involute. Filament ca. 5 mm; anther ca. 1 cm; connective appendage elliptic, entire, ca. 4 mm. Capsule purple, dark brown or red-brown, globose, 2–2.5 cm in diameter, with ten undulate wings, apex with persistent calyx (Plate 1). Seed numerous held by viscous sugary pulp.

Nutritive/Medicinal Properties

The large cardamom pericarp (husk) yielded 0.18% volatile oil (Pura Naik et al. 2004). The oil had specific gravity (0.9148), refractive index (1.4733) and optical rotation (−7.700). Thirty-seven compounds, constituting >98% of the total oil were identified in the volatile oil. The major compounds characterized were 1,8-cineole (38.7%), β-pinene (13.6%), α-terpineol (12.6%), spathulenol (8.3%), 4-terpineol (4.5%), germacrene-D (3.0%), α-pinene (2.8%) and β-selinene (2.7%). The 1,8-cineol content was less than 50% when compared with the seed oil. *A. subulatum* pod husk was found to contain a mixture of two (deep pinkish red) pigments identified as cyanidin 3-glucoside and cyanidin 3.5-diglucoside (Pura Naik et al. 1999).

The minimum, maximum and mean values of quality attributes for 12 Sikkim *A. subulatum* cultivars were moisture (7.2, 14.9 and 10.5%), bulk density (302.0, 374.8 and 344.8 g/L), husk to seed ratio (1:1.7, 1:1.25 and 1:2.2), anthocyanins (46.2, 222.3 and 98.4 mg/100 g), volatile oil (2.6, 4.2 and 3.4% v/w) and total ash (3.6, 4.3 and 3.9%) (Pura Naik et al. 2006). GC analysis of the volatile oils showed that there was considerable variation among the cultivars with respect to α-pinene (3:2–4.5%), β-pinene (6.7–8.5%), 1,8-cineol (80.4–84.6%), 4-terpineol (0.60–1.30%) and α-terpineol (3.3–4.3%). The oils were similar with respect to specific gravity and refractive index; but optical rotation values varied. Analysis for metals showed that the seeds contained cadmium (0.06, 0.07 and 0.07 ppm), lead (0.12, 0.37 and 0.24 ppm), copper (5.14, 9.68 and 6.33 ppm) and iron (28.51, 111.19 and 55.28 ppm). In the capsules the content of metals were cadmium (0.11, 0.20 and 0.15 ppm), lead (0.18, 0.39 and 0.31 ppm), copper (4.4, 7.3 and 5.8 ppm) and iron (44.5, 207.5 and 111.6 ppm). A total of 33 components were identified in the essential oil of the seeds of green, freshly dried *A. subulatum* fruits (Rout et al. 2003). The major component of the oil was 1,8-cineole (81.5–86%).

The essential oil of *A. subulatum* fruit was characterised by a high proportion of monoterpenes (ca 90%) (Kaskoos et al. 2008). The main monoterpenes were 1,9-cineole (77.4%), β-myrcene (5%), α-terpineol (4.9%), terpinen-4-ol (2.3%). Sesquiterpenic components amounted to 2.7% and comprised t-carophyllene (2.3%) and its oxide (0.4%).

Major components in the essential oil of *A. subulatum* were found to be 1,8-cineole (43.7%), α-terpineol (9.5%), terpinen-4-ol (3.2%), spathulenol (2.7%) and α-pinene (1.6%) (Kapoor et al. 2008). The oleoresins (in methanol, acetone, isooctane and carbon tetrachloride) contained 5-(hydroxymethyl)-2-furaldehyde (16.2%) in methanol; 1,8-cineole (19.7%) in acetone; 1,8-cineole (9.2%), β-sitosterol (7%) and α-terpineol (5.1%) in carbon tetrachloride; 1,8-cineole (16.2%) and α-terpineol (4.1%) in isooctane.

Seeds *of A. subulatum* were found to contain 8.6% moisture, 5% total ash value, 1.5% ash insoluble in acid, 3.5% water soluble ash value, 4.88% alcohol extract, 4% non-volatile ether extract and 91.4% of total solids (Shukla et al. 2010). Total phenolic content expressed as gallic acid equivalent was 0.00366%w/w. Total flavonoid content in the seed was 0.0361% quercetin equivalent. The seeds were found to contain the glycosides, petunidin-3,5-diglucoside and leucocynidin-3-*O*-β-D-glucopyranoside, and a new aurone glycoside, subulin (Lakshmi and Chauhan 1976, 1977). Acid hydrolysis of subulin gave the aglycone, subulaurone. A chalcone, cardamonin (2′, 4′-dihydroxy-6′-methoxy chalcone) and a flavanone, alpinetin (7-hydroxy-5-methoocy flavanone) were isolated from the seeds of *Amomum subulatum* (Bheemasankara Rao et al. 1976). *Amomum subulatum* seeds were found to contain 2–3% of essential oil. The volatile essential oil of *Amomum subulaum* consisted of monoterpenic hydrocarbons (16.3%), oxygenated monoterpenes (75.2%) and sesquiterpenes (6.3%). Among the 25 compounds, the major constituents were 1,8-cineole (61.3%), α-terpineol, α-pinene and β-pinene and alloaromadendrene (Gurudutt et al. 1996). The acetone and methanol extracts of *A. subulatum* fruits were found to contain 1.04846 and 0.8634% w/w protocatechuic acid by HPLC (Manek et al. 2009).

A total of 87 components were identified among the two essential oils from seed and rind of *Amomum subulatum*, accounting for 99.1%, and 99.0% of the oils, respectively (Satyal et al. 2012). The two essential oils were dominated by the monoterpenoids 1,8-cineole (60.8% and 39.0%), α-pinene (6.4% and 4.8%), β-pinene (8.3% and 17.7%), and α-terpineol (9.8% and 12.3%).

Amomum subulatum plant was reported to have the following proximate composition moisture 9.246%, ash 6.96%, carbohydrate 76.2%, protein 5.44%, fat 2.079%, energy value 345.47%, fibre 9.517%, Cu 7.4 ppm, Ni <0.006 ppm, Zn 57.6 ppm, Pb <0.015 ppm, Co 5.4 ppm, Cd 0.2 ppm, Fe 11.2 ppm, Cr <0.003 ppm (Hussain et al. 2009).

The pharmacological properties of *Amomum subulatum* are elaborated below.

Antioxidant Activity

The ethyl acetate soluble fraction of greater cardamom fruits (*Amomum subulatum*) exhibited high radical scavenging activity against 1,1-diphenyl-2-picrylhydrazyl (DPPH) (Kikuzaki et al. 2001). The fraction was found to contain bioactive compounds such as protocatechualdehyde (1), protocatechuic acid (2), 1,7-bis(3,4-dihydroxyphenyl) hepta-4E,6E-dien-3-one (3) and 2,3,7-trihydroxy-5-(3,4-dihydroxy-E-styryl)-6,7,8,9-tetrahydro-5H-benzocycloheptene (4) which also showed DPPH radical-scavenging activity. Compounds 1 and 3 showed stronger activity than such natural antioxidants as α-tocopherol and L-ascorbic acid. Compounds 2 and 4 were comparable to α-tocopherol and L-ascorbic acid.

Studies showed that the spices namely cloves (*Syzygium aromaticum*), licorice (*Glycyrrhiza glabra*), mace (aril of *Myristica fragrans*) and greater cardamom (*Amomum subulatum*), have antioxidant activities at various concentrations (Yadav and Bhatnagar 2007a). None of the spices showed prooxidant properties. The effect of spices on the inhibition of LPO (lipid peroxidation) was concentration dependent. Cloves, mace and cardamom inhibited the initiation as well as propagation phases of $FeCl_3$ induced lipid peroxidation LPO, while licorice inhibited the initiation phase only. The reducing power of various spices increased with concentration. The percentage inhibition of superoxide radical generation by the spices was also observed to be concentration dependent. The results show that spices used in the present study have significant ability to inhibit LPO due to their polyphenol content, strong reducing power and superoxide radical scavenging activity. Cloves showed the highest antioxidant activity probably due to the higher polyphenol content as compared to other spices. Metal chelating activity was significantly high with all the spice extracts except mace (Yadav and Bhatnagar 2007b). The spices due to higher reducing potential (in presence of bleomycin-$FeCl_3$) showed increased DNA oxidation. Cloves showed the highest DPPH radical scavenging activity, followed by licorice, mace and cardamom. FRAP (ferric reducing antioxidant power) values for cloves were also the highest, while other spices showed comparatively lesser FRAP values. The results showed that the spices tested are strong antioxidants and may have beneficial effects on human health. *Amomum subulatum* fruit exhibited strong antioxidant activity with 90% inhibition of DPPH (Ghimire et al. 2011). It was found to contain 66 mg QE/g extract of total flavonoids and 94.52 mg GAE/g extract of total phenols. The essential oil of *A. subulatum* showed significant antioxidant activities as evaluated against mustard oil by peroxide, *p*-anisidine, thiobarbituric acid, total carbonyl, ferric thiocyanate and the DPPH radical scavenging assays (Kapoor et al. 2008). Further, the oleoresins were observed as better antioxidants than butylated hydroxytoluene. The essential oil contained a high level of total phenolic content.

In a study on the antioxidant activities of cinnamon and greater cardamom, the antioxidant enzyme activities were found to be significantly enhanced whereas GSH (glutathione) content was markedly restored in rats fed a fat diet with spices like cinnamon and greater cardamom (Dhuley 1999). In addition, these spices partially counteracted increase in lipid conjugated dienes and hydroperoxides, the primary products of lipid

peroxidation. The results indicated that these spices exerted antioxidant protection through their ability to activate the antioxidant enzymes.

The ethanolic leaf extract of *A. subulatum* showed significant antioxidant activity as evaluated using DPPH free radical scavenging assay and carotene bleaching assay (Prakash et al. 2012). The IC_{50} of ethanolic extract 8.25, μg/mL, total phenolic content, 11.04% and mean antioxidant activity 41.2%

Anti inflammatory Activity

Both aqueous and ethanol extracts of black cardamom showed anti inflammatory activity against carrageenan induced paw edema in rats in a dose-dependent manner (Alam et al. 2011). Glycosides, carbohydrates, flavonoids, steroids and resins were detected in both ethanol and aqueous extracts and were postulated to suppress the formation of prostaglandins and bradykinins or antagonize their action.

Analgesic Activity

Both methanol and ethyl acetate extracts of *A. subulatum* seeds possessed significant activity as evaluated by the hot plate and writing method (Shukla et al. 2010)

Anticancer Activity

Studies demonstrated that cardamonin isolated from *A. subulatum* potentiated TRAIL (Tumour Necrosis Factor-Related Apoptosis-Inducing Ligand)-induced apoptosis of human colon cancer cells through ROS-CHOP (reactive oxygen-CCAAT/enhancer binding protein homologous protein)-mediated upregulation of death receptors and decreased expression of decoy receptor, and cell survival proteins (Yadav et al. 2012). *A. subulatum* seed and rind oils exhibited moderate brine shrimp lethality (LC_{50} = 28.1 and 15.0 μg/mL, respectively) (Satyal et al. 2012). The seed and rind oils were only marginally cytotoxic (20% and 30% kill on MCF-7 cells at 100 μg/mL, respectively).

Gastroprotective Effect

The essential oils and petroleum ether soluble fractions of small cardamom known as 'Heel Khurd' (fruits of *Elettaria cardamomum* Maton.) and large cardamom 'Heel Kalan' (fruits of *Amomum subulatum* Roxb.) inhibited gastric lesions significantly (Jamal et al. 2005). Fractions of small cardamom were found to be better than large cardamom. They were found to have inhibitory effect in over production of some products of 5-lopoxygenase pathway. Studies validated their use in Unani System of Medicine to treat gastrointestinal disorders. These seeds are used as stomachic (*Muqavvi-e-Meda*), desiccant (*Mujaffif*), resolvent (*Muhallil*), digestive (*Hazim*) carminative (*Kasir-e-Riyah*), etc. in Unani system of medicine.

Studies reported that the crude methanolic extract of *A. subulatum* and its fractions, viz. essential oil, petroleum ether and ethyl acetate, inhibited gastric lesions induced by ethanol significantly, but not those which were induced by pylorus ligation and aspirin (Jafri et al. 2001). However, ethyl acetate fraction increased the wall mucus in pylorus ligated rats. The results suggest a direct protective effect of ethyl acetate fraction on gastric mucosal barrier. While the observation of decrease in gastric motility by essential oil and petroleum ether fractions suggests the gastroprotective action of the test drug. These investigations validated the use of 'Heel kalan' in gastrointestinal disorders by Unani physicians.

Antimicrobial Activity

The essential oil from the seed was found to have significant inhibitory effect against some keratinophilic and dermophytic fungi (Jain and Agrawal 1978). The oil of *Amomum subulatum* was found effective against two strains of *Aspergillus flavus*, completely inhibiting their mycelial growth at 750 μg/mL (Singh et al. 2008). This level of activity was superior to that of the synthetic fungicides tested. In addition, the oil exhibited a broad fungitoxic spectrum against all the tested fungi (*A. niger*, *A. fumigatus*, *A. terreus*, *Alternaria alternata*, *Cladosporium herbarum*, *Curvularia lunata*, *Fusarium oxysporum*, *Helminthosporium*

oryzae, and *Trichoderma viride*), significantly inhibiting their growth at 750 µg/mL. The essential oil displayed excellent anti-aflatoxigenic efficacy, completely inhibiting aflatoxin B_1 production at 500 µg/mL. *A. subulatum* oil provides a novel, botanical antimicrobial and aflatoxin suppressor as an alternative to synthetic preservatives. The acetone, ethanol and methanol extracts of *Amomum subulatum* fruit exhibited in-vitro antimicrobial activity against the following dental caries microorganism *Streptococcus mutans*, *Staphylococcus aureus*, *Candida albicans* and *Saccharomyces cerevisiae* except *Lactobacillus acidophilus* (Aneja and Joshi 2009). The most susceptible microorganism were *S. aureus* followed by *S. mutans*, *S. cerevisiae* and *C. albicans*. The methanol extract of fruits of *A. subulatum* showed notable antimicrobial activity against *Escherichia coli* but in case of other microorganisms it was found inferior to ciprofloxacin the standard drug used (Agnihotri and Wakode 2010). Methanol extract of rind showed good antimicrobial activity against *Staphylococcus aureus*. The essential oil was found effective against majority of microorganisms used viz. *Bacillus pumilus*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and *Saccharomyces cerevisiae*. The methanol seed extract of large cardamom was found to inhibit growth of *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Bacillus subtilis*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Candida albican senegalensis* (Tijjani et al. 2012) Both the MICs and MBCs of the extract ranges from 50 to 200 mg/mL. Preliminary screening analysis of the powdered methanolic seed extracts showed the presence of carbohydrate, tannins, cardioactive glycosides, tepenes, flavonoids, alkaloids and saponins.

The essential oil and oleoresins (methanol, acetone, isooctane and carbon tetrachloride) of large cardamom were found to be a better and safer natural food preservatives for juice of sweet orange (*Citrus sinensis*) than synthetic preservatives (Kapoor et al. 2011). Essential oil and oleoresins had a significant effect on shelf life of juice. They possessed antioxidant and antimicrobial efficiency. The essential oil of *A. subulatum* showed 100% inhibition against *Aspergillus flavus* at a 6 µL dose (Kapoor et al. 2008). For other tested fungi, the essential oil and all oleoresins showed good to moderate inhibitory effects. Hence, they could be used as natural food preservatives, though the essential oil was more active than the oleoresins. *A. subulatum* seed and rind oils exhibited antibacterial activity (MIC > or = 313 µg/mL), but the rind oil was appreciably active against the fungus *Aspergillus niger* (MIC = 19.5 µg/mL) (Satyal et al. 2012).

Hepatoprotective Activity

Treatment of rats with methanolic extract of *A. subulatum* (100 and 300 mg/kg/day, p.o. for 18 days) and silymarin significantly prevented the functional, physical, biochemical and histological changes induced by ethanol, indicating the recovery of hepatic cells (Parmar et al. 2009). Ethanol produced significant changes in various liver parameters such as functional (thiopentone-induced sleeping time) and physical (increased liver weight and volume). It also increased the biochemical parameters such as serum glutamate oxaloacetic transaminase and glutamate pyruvic transaminase, alkaline phosphatase, total and direct bilirubin, total cholesterol, triglyceride and decreased total protein along with changes in histological parameters (damage to hepatocytes). These results demonstrated that the methanolic extract of *A. subulatum* seeds possessed hepatoprotective activity. Pretreatment of mice with methanol extract of *A. subulatum* seeds (100 and 300 mg/kg) significantly blocked the CCl_4 -induced increase in aspartate aminotransferase and alanine aminotransferase activities (Parmar et al. 2011). Pretreatment with the extract showed significant preservation of mitochondrial membrane potential as compared to CCl_4 control demonstrating the mitochondrial protection. Further, pretreatment with the extract exerted a dose-dependent effect against sensitivity to mitochondrial swelling induced by calcium and significantly increased the transcription and translation of voltage dependent anion channel (VDAC). The data suggested that the extract significantly prevented damage to liver mitochondria through regulation of VDAC expression.

Antihyperlipidemic Activity

A chloroform: methanol (50:50) fraction of *A. subulatum* seed was found to possess lipid-lowering and antioxidant activity and could be beneficial in the treatment of hyperlipidemia (Bairwa et al. 2011). Hyperlipidemia induced by feeding rabbits an atherogenic diet for 120 days resulted in a significant increase in serum total cholesterol, phospholipid and triglyceride levels when compared with control group. The levels of LDL and VLDL-cholesterol were increased significantly, but the HDL-cholesterol ratio was decreased. The changes in the antioxidant parameters were accompanied by an increase in lipid peroxidation and reduction in glutathione (GSH) and catalase activity. The level of lipid peroxidation was reduced whereas GSH content and catalase activity were elevated after the treatment with *A. subulatum* fraction at the dose level of 100 mg/kg body weight/day. A significant reduction was observed in total cholesterol, triglyceride, phospholipid, LDL and VLDL cholesterol where as HDL-cholesterol ratio was increased after administration of *A. subulatum*.

Studies showed *A. subulatum* to be a potent antihyperlipidaemic agent and provided antioxidant protection against oxidative stress induced by free radicals in cholesterol fed rabbits (Joshi et al. 2012). Administration of *A. subulatum* reduced the elevated levels of serum cholesterol, triglyceride, phospholipids, low density lipoprotein and very low density lipoprotein cholesterol and raised the decreased high density lipoprotein-cholesterol ratio. *A. subulatum* feeding also restored the level of lipid peroxidation, glutathione and catalase in the liver were found near to normal levels. *A. subulatum* extract feeding increased the faecal excretion of cholesterol and phospholipids.

Adaptogenic Activity

Studies in guinea pigs showed that treatment of *A. subulatum* had protective effect against the effect of acute or severe stress (swimming endurance until exhaustion) induced myocardial damages (Verma et al. 2010). Greater cardamom exhibited 62.75% protection against the effect of stress compared to 58.38% by Ashwagandha (*Withania somnifera* root extract) – a well known adaptogenic agent.

Traditional Medicinal Uses

Amomum subulatum has been used in Ayurvedic and Unani systems of traditional medicine for many ailments a long time (CSIR 1948; Chopra et al. 1986; Sharma et al. 2002; Alam et al. 2011; Bisht et al. 2011). Fruit is used as stimulant, aromatic, stomachic, aphrodisiac and infections of the teeth and gum The seeds have medicinal properties – stimulant, carminative, stomachic, stimulant, antiemetic, alexipharmic, expectorant, diuretic and astringent properties and are prescribed in the treatment of common cold and cough, leucorrhoea, indigestion, vomiting, biliousness abdominal pains and rectal diseases. They are also used in anorexia, dyspepsia, hyperacidity, dysentery, skin diseases, wounds, ulcers, cardiac debility, liver congestion, cough, fever, gonorrhoea gastrointestinal disorders and genito-urinary complaints. Seeds have been reported to be very effective in female white disease. A decoction of seeds is used as a gargle in affections of the teeth and gum. In combination with melon seeds, it is used as a diuretic in cases of kidney gravel. Seeds are also used in gonorrhoea and as aphrodisiac. The oil is applied to eyelids to allay inflammation.

Other Uses

Nepal cardamom fruits and seeds have many applications in Ayurvedic and Unani medicines. Large cardamom is planted in agroforestry systems in the fragile mountain ecosystems in Bhutan, Nepal, Sikkim and northern India as the plant efficiently conserves the soil, water and nutrients growth inhibition of *L. perenne* than of *L. sativa* (Avasthe et al. 2011).

A. subulatum seed and rind oils exhibited moderate brine shrimp lethality (LC_{50} = 28.1 and

15.0 µg/mL, respectively) (Satyal et al. 2012). The seed and rind oils were only marginally cytotoxic (20% and 30% kill on MCF-7 cells at 100 µg/mL, respectively). *A. subulatum* seed and rind oils exhibited antibacterial activity (MIC > or = 313 µg/mL), but the rind oil was appreciably active against the fungus *Aspergillus niger* (MIC = 19.5 µg/mL) (Satyal et al. 2012). The essential oils of A. subulatum were also screened for nematocidal activity against and insecticidal activity against the fruit fly and the red imported fire ant.

Insecticidal and Nematocidal Activities

A. subulatum seed and rind oils were marginally toxic to the fire ant (*Solenopsis invicta x richteri*) (LC_{50} = 1500 µg/mL), but moderately toxic to the nematode, *Caenorhabditis elegans*, and the fruit fly (*Drosophila melanogaster*) (LC_{50} = 341 and 441 µg/mL, respectively) (Satyal et al. 2012).

Comments

A number of horticultural variants of the species are grown commercially. Presently, Nepal is the largest producer of large cardamom with 68% share, followed by India (22%) and Bhutan (9%). Sikkim contributes 88% of the annual production of India (4,385 MT) (Avasthe et al. 2011).

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Amomum tsao-ko

Scientific Name

Amomum tsao-ko Crevost & Lemarié.

Synonyms

Amomum hongtsaoko C. F. Liang & D. Fang.

Family

Zingiberaceae

Common/English Names

Black Cardamom, Tsaoko Amomum

Vernacular Names

Chinese: Cao Guo, Hong Cao Guo, Xiang Dou Kou (Mandarin), Heung Dau Kau; Chou Gwo (Cantonese);
Japanese: Sōka;
Korean: Chogwa;
Vietnamese: Dòho, Sanhân Cóc, Thảo Quả

Origin/Distribution

The species is indigenous to China (Guangxi, Guizhou, Yunnan) and North Vietnam.

Agroecology

The species occurs wild in sparse forest from 1,000 to 1,800 m and is also cultivated in its native range. It thrives in well-drained, moist, organic matter rich soil in shade or partial shade.

Edible Plant Parts and Uses

Fruit and seed are used as spice and condiment in Chinese and Vietnamese cuisine. Dried fruit is used in beef herbal soup and Sichuan beef dishes and other Chinese medicinal soup dish and eaten with rice. Typical ingredients of the spice mixture called *xiang liao* (fragrant grains) consists of Cassia, Sichuan pepper, black cardamom,

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star anise and lesser galangal. In Vietnam, the pods are used as an ingredient in *phở noodle soup*.

Botany

A tall, perennial herb to 3 m tall, aromatic. Rhizomes prostrate ginger-like. Ligule entire, 0.8–1.2 cm, apex obtuse. leaf blade narrowly elliptic or oblong, 40–70 × 10–20 cm, glabrous, base attenuate, margin drying membranous, apex acuminate. Spikes 13–18 × ca. 5 cm, 5-30-flowered; peduncle at least 10 cm, scalelike sheaths dense, brown when dry, oblong or narrowly elliptic, 5.5–7 × 2.3–3.5 cm, leathery, apex rounded; bracts lanceolate, ca. 4 cm × 6 mm, apex acuminate; bracteoles tubular, apex 2- or 3-toothed. Calyx equalling bracteoles, apex obtusely 3-toothed. Corolla orange-red; tube ca. 2.5 cm; lobes oblong, ca. 2 cm × 4 mm. Labellum elliptic, ca. 2.7 × 1.4 cm, apex slightly toothed. Anther ca. 1.3 cm; connective appendage 3-lobed. Capsule red, drying brown-black and longitudinally striate, oblong or elliptic, 2.5–.5 × ca. 2 cm, glabrous (Plate 1). Seeds 4–6 mm in diam., many angled, strongly aromatic.

Nutritive/Medicinal Properties

Amomum tsao-ko peel and seeds were found to contain saccharides, protein, amino acids, phenolic compounds, tannins, organic acids, saponins, flavonoids, anthraquinone, coumarin, lactones, cardiac glycosides, steroids, terpenoids, volatile oils, grease and anthocyanins (Liu et al. 2011). Twenty-one components were identified in the seeds, of which the major ones found were 1,8-cineole (30.6%), 2-decenal (17.3%), geranial (10.6%) and neral (7.0%) (Nguyen et al. 1992). The following diarylheptanoid compounds were isolated from the methanol extract of *A. taso-ko* fruits: tsaokoarylone [7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-hepta-4*E*,6*E*-dien-3-one]; purification 6-(4-hydroxyphenyl)-4-hydroxyhexan-2-one; diarylheptanoids 1,7-bis(4-hydroxyphenyl)hepta-4*E*,6*E*-dien-3-one; (+)-hannokinol, and meso-hannokinol (Moon et al. 2005).

Plate 1 Black cardamom fruits

Twelve constituents were isolated from *Amomum tsao-ko* essential oil (Wu et al. 1997). 1, 8-cineole, *trans*-geraniol eicosatrienoic acid methylester and d-nerolidol were found to be the major constituents. Yang et al. (2010) identified 73 compound in the essential oil of *A. tsao-ko* dried fruit representing 97.56%. The components were grouped into monoterpene hydrocarbons (11compounds) 9.58%, oxygenated monoterpenes (22) 66.14%, sesquitepene hydrocarbons (5) 0.21%, oxygenated sesquiterpenes (7) 1.76% and others (28) 19.87%. The essential oil consisted mainly of 1,8-cineole (45.24%), *p*-propylbenzaldehyde (6.04%), geraniol (5.11%), geranial (4.52%), α-terpineol (3.59%), α-phellandrene (3.07%), neral (2.95%), β-pinene (2.67%), indane-4-carboxaldehye (2.41%), 2-isosproplybenzaldehyde (2.30%), (2E)-decenal (1.97%), terpinene-4-ol (1.77%), α-pinene (1.65%), 2-propenal,3-methyl-3-phenyl (1.64%), para-cymene 1.46% and geranyl acetate (1%). Thirty-eight constituents were detected in essential oil of *Amomum tsao-ko*, of which 1,8-cineole (40.891%), α-phellandrene (9.769%), 4-propylbenzaldehyde (6.988%), and (E)-citral (4.949%) were the major compounds (Li et al. 2011).

Black cardamom, (*Amomum tsao-ko*), used as a spice in Asia, produces a nice refreshing effect in the mouth. The active constituent was found to be (+/−)-*trans*-2,3,3a,7a-tetrahydro-1H-indene-4-carbaldehyde which produced a trigeminal effect in the mouth (Starkenmann et al. 2007).

Antioxidant Activity

Studies showed that the dichloromethane extract and the ethyl acetate soluble and water-soluble fractions of the 70% aqueous acetone extract *Amomum tsao-ko* fruit had higher antioxidant activity than α-tocopherol and butylated hydroxytoluene (BHT) (Martin et al. 2006). Eleven compounds were isolated from the ethyl acetate-soluble fraction: (+)-hannokinol, meso-hannokinol, (+)-epicatechin, (−)-catechin, β-sitosterol, β-sitosterol 3-*O*-glucoside, 2,6-dimethoxyphenol, protocatechualdehyde, protocatechuic acid, vanillic acid and *p*-hydroxybenzoic acid. The catechins and catechol derivatives showed strong activities in both the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity and antioxidant activity assays. The essential oil of *Amomum tsao-ko* dried fruit was found to have weak antioxidant activity as measured by DPPH radical assay, thiobarbituric acid (TBA) test and ferric reducing antioxidant power (FRAP) assay (Yang et al. 2010).

Hypoglycemic cum Antioxidant Activity

In a study, lipids extracted from tsao-ko were separated into three fractions : control – no tsao-ko, 0.05% total lipid of tsao-ko (TL), 0.0109% chloroform fraction (CF), 0.0245% acetone fraction (AF), or 0.00365% methanol fraction (MeF) and fed to mice (3 months old) for 90 days (Yu et al. 2008). Although rats fed with CF and AC diets slightly inhibited the activities of α-glucosidase, α-amylase, and lipase, intakes of these fractions had little influence on plasma and liver lipid concentrations when compared with the control diet of no tsao-ko. The MeF did not inhibit α-glucosidase but had DPPH radical scavenging activity and the mice fed this fraction had the most marked reduction in plasma glucose and thiobarbituric acid reactive substances (TBARS) concentrations compared with the other diet groups. These results suggested that the fat-soluble polar components of tsao-ko contained an active component that might be associated with decreased plasma glucose and TBARS concentrations in mice. Further studies in mice by Yu et al. (2010) found ingestion of methanol extract of *A. tsao-ko* and its A fraction significantly reduced body lipids and plasma thiobarbituric acid reactive substances (TBARS) concentrations compared with the control and inhibited lipase and α-glucosidase activities. These reductions were not observed in mice fed the B fraction and these inhibitions of B fraction were mild compared with the methanol extract and A fraction. They found that the most effective component of tsao-ko for body lipid reduction and hypoglycemic and antioxidant activity was contained in the polar fraction and the evidence suggested that this component could be epicatechin. However, the strongest triglyceride lowering components of tsao-ko may be methanol insoluble

Anticancer Activity

A diarylheptanoid compound isolated from the fruit, tsaokoarylone, exhibited cytotoxicity at 4.9 and 11.4 μg/mL (IC_{50}) against human nonsmall cell lung cancer A549 and human melanoma SK-Mel-2, respectively (Moon et al. 2005). The fruit was found to contain bicyclononane aldehydes many of which showed antiproliferative activity of when assessed in the murine neuroblastoma cell line N2a (Yang et al. 2009). The essential oil of *Amomum tsao-ko* dried fruit was cytotoxic to human liver carcinoma cell lines (HepG2 and Bel-7402), human cervix carcinoma cell line (Hela), human gastric adenocarcinome cell line (SGC-7901) and human prostate cancer cell line (PC-3) (Yang et al. 2010). The lowest IC_{50} of 31.80 μg/mL was measured for HepG2 carcinoma cell lines. The IC_{50} for normal human cell lines (HUVEC and HL-7702) was 163.91 – 272.41 μg/mL. Analyses by flow cytometry, Hoechst 33258 staining and agarose gel electrophoresis indicated that the essential oil induced apoptosis.

Antiinflammatory Activity

Two new bicyclic nonanes characterized as 6,7-dihydroxy-indan-4-carbaldehyde and 6-hydroxy-indan-4-carbaldehyde were isolated with 11 known compounds: 6,7-dihydroxy-3,

7-dimethyloct-2-enoic acid; tsaokoin; isotsaokoin; 8-oxogeraniol; *p*-menth-1-ene-5,6-diol; 3α-hydroxycarvotagenone; tsaokoarylone; 1,7-bis(4-hydroxy-3-methoxyphenyl)-4,6-heptadien-3one; (+)-hannokinol; MESO-hannokinol and hannokinin from the fruits of *A. tsao-ko* (Lee et al. 2008). All 13 compounds significantly inhibited lipopolysaccharide-induced nitric oxide production in BV2 microglial cells at concentrations ranging from 1 to 100 μM.

Antimicrobial Activity

The methanol extract from *Amomum tsao-ko* yielded bicyclic nonane, isotsaokoin as the major active principle, an isomer of tsaokoin (Moon et al. 2004). This compound exhibited antifungal activity against *Trichophyton mentagrophytes*. The essential oil of *A. tsao-ko* fruit showed a broad spectrum of antimicrobial activity against all 16 tested micro-organisms, including Gram-positive and Gram-negative bacteria, and fungi (Yang et al. 2008). The oil exerted the strongest bactericidal activity against *Staphylococcus aureus* with minimum inhibitory and bactericidal concentrations of 0.20 g/L. The order of antimicrobial activity of *Amomum tsao-ko* essential oil against the bacteria was as follows: *Bacillus subtilis* > *Staphylococcus albus* > *Escherichia coli* (Li et al. 2011). The order of antifungal activity was: *Aspergillus oryzae* > *Rhizopus* sp. > *Penicillium* sp. Its constituent 1,8-cineole showed weak inhibiting effect on the bacteria and was ineffective against fungi.

Antiviral Activity

The water extract of *A. tsao-ko* was found to have strong anti-Hepatitis B Virus effect (Li et al. 1999).

Gastroprotective Activity

The volatile oil and water extract of *Amomum tsao-ko* was shown to increase gastric mucosal blood flow and secretion of gastric juice and enhanced the activity of anti-free radical damage to the gastric mucosa (Qiu et al. 1999).

Miscellaneous Activity

In-vitro studies using Franz diffusion cells showed that *A. tsao-ko* essential oil enhanced the percutaneous permeation of rutondine (L-tetrahydropalmatine) which possesses sedative, analgesic and hypnotic effects.

Traditional Medicinal Uses

The primary used of the fruit is in oriental herbal medicine. It is used for treatment of throat infections, stomach pain, flatulence, belching, indigestion due to stomach qi stagnation, vomiting, dyspepsia, malarial disorders and drunkenness from alcohol consumption.

Other Uses

It is being harvested as a cash crop by rural communities in its native area of distribution. Besides being used as a spice, *A. tsao-ko* is also traded as a medicinal herb.

Comments

The Tsao-ko cardamom (*Amomum tsao-ko*) is listed as 'Near Threatened' because its edible fruits have been over-harvested for trading (Leong-Skornickova et al. 2012).

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Elettaria cardamomum

Scientific Name

Elettaria cardamomum (L.) Maton.

Synonyms

Alpinia cardamomum (L.) Roxb., *Amomum cardamomum* L., *Amomum ensal* Raeusch., *Amomum racemosum* Lam. nom superfl., *Amomum repens* Sonn. nom. superfl., *Amomum uncinatum* Stokes, *Cardamomum elletari* Garsault, *Cardamomum malabaricum* Pritz., *Cardamomum minus* (Gaertn.) Kuntze nom. illeg., *Cardamomum officinale* Salisb., *Cardamomum verum* Oken nom. superfl., *Elettaria cardamomum* White & Maton, *Elettaria cardamomum* var. *minuscula* Burkill, *Amomum repens* Sonner nom superfl., *Elettaria cardamomum* var. *minor* Watt nom. inval., *Elettaria repens* (Sonn.) Baillon, *Elettaria repens* Baill. nom. superfl., *Matonia cardamomum* (L.) Stephenson & J.M. Churchill, *Zingiber minus* Gaertn.

Family

Zingiberaceae

Common/English Names

Cardamon, Cluster Cardamom, Lesser Cardamom, Malabar Cardamom, Round Cardamom, Siam Cardamom, Ceylon Cardamom, Cardamon Seeds

Vernacular Names

Arabic: Hhabb El Hâl, Habbu Al Hal, Hhamâmâ, Hhabbahân, Habbu Al Han, Hel Bava, Qâqullah Saghîrah, Qaqilah;
Armenian: Shooshmir, Shushmir;
Bosnian: Grbat, Kardamomi, Srdiš;
Brazil: Cardamão, Cardamomo (Portuguese);
Burmese: Bala, Pala, Panlat, Hpa-La;
Croatian: Grbat, Kardamomi, Srdiš, Vrtni Prpr;
Czech: Kardamom Pravý;
Danish:Ceylon-Kardemomme,HvidKardemomme, Kardemomme, Malabarkardemomme;
Dutch: Echte Kardamom, Kardemom, Paradijszaadsoort of Var;
Eastonian: Harilik Kardemon;
Finnish: Kardemumma;
French: cardamomier, cardamone, elaiti, Cardamome, Cardamome Blanche, Cardamome De Ceylan, Cardamome Du Malabar, Cardamome Verte, Cardamomier, Petite Cardamome;

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German: Cardamomen, Cardamompflanze, Grüner Kardamom, Kardamom, Kleine Kardamomen, Malabarkardamom;
Greek: Kardamo;
Hebrew: Hel;
Hungarian: Kardamom, Kardamomum, Kis Kardamom, Malabári Kardamom;
India: Chhoti Elachi, Elachi (Bengali), Elaychi, Lila Alchi (Gujerati), Elachi, Elaichi, Chhoti Elaichi, Ilaayacii (Hindu), Yelakki (Kannada), Elathari, Ellaykka, Yelakkai (Malayalam), Hirvi Velchi, Velchi, Velchil, Veldoda, Veldola (Marathi), Alaichi (Oriya), Elaychi, Hari Ilaichi (Punjabi), Ela, Ellka, Suksmaila (Sanskrit), Aila Cheddi, Elakkai, Yelakkai (Tamil), Elakkayi, Yealak Kayulu, Yelakulu (Telugu), Elaichi, Ilaychi (Urdu); ***Indonesia***: Kapol, Kapolaga (Sudanese), Kapulaga Sabrang;
Italian: Cardamone, Cardamomo, Cardamomo Medio, Cardamomo Minore;
Japanese: Karadamomo, Karudamon, Shouzuku;
Khmer: Krâkô Sabt;
Korean: Sodugu;
Laotian: Hmak Hnengx;
Malaysia: Buah Pelaga, Kapulaga;
Norwegian: Kardemomme;
Persian: Hel, Kakilahe-Khurd;
Polish: Kardamon Malabarski;
Portuguese: Cardamomo;
Russian: Elettariia Kardamon;
Serbian: Grbat, Kakule, Kardamona, Kardamomi, Mirisavci, Srdiš, Srđiš;
Slovakia: Kardamom;
Sri Lanka: Enasal (Sinhalese);
Spanish: Cardamomo;
Swedish: Kardemumma;
Thai: Luk Krawan, Luk Kravan, Luk Grawan, Krawan Thet;
Turkish: Hemame, Kakule, Hiyl, Küçük Kakule;
Vietnamese: Tiểu Đậu Khấu.

Origin/Distribution

Cardamom is one of the world's very ancient spices. It is native to the India and Sri Lanka originating in the forests of the western Ghats in southern India, where it grows wild (Plate 1).

Plate 1 Cardamon Label with local names and origin

Today it cultivated in India, Nepal, Sri Lanka, Guatemala, Mexico, Tanzania, Vietnam and Thailand. The major producing areas for cardamom in India are Sikkim and Kerala.

Agroecology

Cardamom grows wild in the shade in the forests of southern India as it does not tolerate direct sun. It thrives best in areas with uniform warm temperature 24–30°C and mean annual rainfall of 1,500 mm well distributed through out the year, on well-drained, soil rich in organic matter. Shade is important during the hot summer season and during the rainy season shade is thinned. Cardamoms are traditionally cultivated under shade trees. Tall trees having well spaced branching habit and small leaves are ideal shade trees for cardamom.

Edible Plant Parts and Uses

Cardamom is used in the form of whole fruit, the decorticated seeds or ground seeds. Cardamon plays a vital role in both sweet and savoury cuisine worldwide. Ground cardamom is an essential ingredient in many Indian curries, pilaus (rice dishes), garam masala and is a primary contributor to the flavour of masala chai and it imparts character to many pulse dishes. It is widely used in many Indian sweetmeats, drinks and desserts such as the popular ice cream kulfi and milk

puddings. Cardamom has a pleasant flavour and aroma that makes it the popular condiment for tea, coffee and cool drinks.

In Scandinavian countries, cardamom is commonly added to bread, in pickles with herrings, cakes, Danish pastries, apple pies, Dutch 'windmill' biscuits and in akvavit (a flavoured spirit). It is also used in sausages, in punches and mulled wines; occasionally with meat, poultry and shellfish. It flavours custards, and some Russian liqueurs.

In Arabic countries, it is widely and popularly used to flavour coffee and tea and cardamom powder is used as spice for sweet dishes. Cardamom is added a little to ground coffee before brewing, then sweeten and top with cream. In Turkey, it is used to flavour the black Turkish tea called Kakakule.

Cardamom oil is an important ingredient in food preparations and health foods.

Cardamon seeds are chewed to sweeten the breath and to nullify caffeine in people consuming excessive amounts of coffee. In Egypt, cardamom is ground and added to coffee. In Indonesia, cardamom has been used in betel quid and has also been used to flavour tobacco.

Botany

A robust, perennial herb growing to 4 m high with branched subterranean rhizomes from which arises 10–12 erect leafy shoots (consist of leafy sheaths) and flowering shoots. Leaves distichous, petioles up to 2.5 cm long; lamina up to c. 1 m × 15 cm, lanceolate, acuminate, lightly pubescent or glabrous below; ligule to 1 cm long, entire (Plate 2). Inflorescence usually borne separately on a prostrate (occasionally semi-erect to erect) stalk up to 40 cm. Bracts 2–3 × 0.8–1 cm, lanceolate, acute, glabrous, rather persistent but becoming fimbriate with age. Each bract bears a 2–3 flowered axillary cincinnus; Bracteoles up to 2.5 cm long, tubular, mucronate, glabrous. Calyx tubular up to 2 cm long, 2- or obscurely 3-lobed, lobes mucronate. Corolla-tube with lobes 1–1.5 cm long, rounded at the apex, the dorsal lobe widest, pale green. Labellum white, streaked violet, 1.5–2 × 1 cm at widest part, obovate, obscurely 3-lobed, narrowed at the base. Lateral staminodes inconspicuous, subulate. Anther sessile; thecae c. 1 cm long, parallel, connective prolonged into a short, entire crest. Ovary 2–3 mm long, glabrous. Capsule oblong, oval or oblate, 2–5 cm long, with faint longitudinal striations, roughly triangular in cross section, pale green to yellow (Plate 3) , trilocular with 15–20 seeds per fruit. Seed small, 3 mm long, rugose, dark brown (Plate 4), aromatic, with thin mucilaginous aril.

Nutritive/Medicinal Properties

Analyses carried out in the United States reported cardamom to have the following nutrient composition (per 100 g edible portion): water 8.28 g,

Plate 2 Young cardamon plant

Plate 3 Close-up cardamom pods

Plate 4 Cardamon seeds

energy 311 kcal (1,303 kJ), protein 10.76 g, total lipid 6.70 g, ash 5.78 g, carbohydrates 68.47 g, total dietary fibre 28.0 g, Ca 383 mg, Fe 13.97 mg, Mg 229 mg, P 178 mg, K 1,119 mg, Na 18 mg, Zn 7.47 mg, Cu 0.383 mg, Mn 28 mg, Se 8.2 µg, vitamin C 21 mg, thiamine 0.198 mg, riboflavin 0.182 mg, niacin 1.102 mg, vitamin B-6 0.230 mg, total saturated fatty acids 0.680 g, 14:0 (myristic acid) 0.030 g, 16:0 (palmitic acid) 0.570 g, 18:0 (stearic acid) 0.060 g; total monounsaturated fatty acids 0.870 g, 16:1 undifferentiated (palmitoleic acid) 0.020 g, 18:1 undifferentiated (oleic acid) 0.850 g; total polyunsaturated fatty acids 0.430 g, 18:2 undifferentiated (linoleic acid) 0.310 g, 18:3 undifferentiated (linolenic acid) 0.120 g and phytosterols 46 mg (USDA 2012).

The major compounds in the glycosidically bound volatile fraction of fresh green cardamon were found to be 3-methylpentan-2-ol, linalool and the *cis*- and *trans*-isomers of nerolidol and farnesol (Menon et al. 1999).

Elettaria cardamomum essential oil was found to contain: limonene, sabinene, cineole, α-terpineol, terpinyl acetate, borneol, α-pinene, myrcene, *p*-cymene, methyl heptenone, linalool, linalyl acetate, β-terpineol, geraniol, nerol, neryl acetate, nerolidol, and heptacosane (Nigam et al. 1965). Two ketones tentatively identified as 2-undecanone and 2-tridecanone were also detected in trace amounts. Cold-pressed essential oils derived from three varieties of cardamom seeds and Oil of cardamom, N.F were found to have the following components: α-pinene, sabinene, β-pinene, myrcene, α-terpinene, D-limonene, 1,8-cineole, methyl heptenone, γ-terpinene, *trans*-sabinene hydrate, linalool, β-terpineol, borneol, 4-terpinenol, α-terpineol, nerol, linalyl acetate, geraniol, 4-terpinenyl acetate, α-terpinyl acetate, neryl acetate, nerolidol, camphene, α-phellandrene, camphor, citronellal, citral, citronellol, ascaridole, geranyl acetate, bisabolene and farnesol (Richard et al. 1971).

Cardamom volatile oil had been reported to comprise the following as major constituents:

α-pinene, β-pinene, sabinene, myrcene, α-phellandrene, limonene, 1,8-cineole, γ-terpinene, β-selinene, *p*-cymene, terpinolene, linalool, linalyl acetate, terpinen-4-ol, α-terpineol, α-terpinyl acetate, citronellol, nerol, geraniol, methyl eugenol and *trans*-nerolidol (Lawrence 1978; Govindarajan et al. 1982; Noleau et al. 1987). The minor constituents comprised:- hydrocarbons: α-thujene, camphene, α-terpinene, *cis*-β-ocimene, *trans*-β-ocimene, toluene, *p*-dimethylstyrene, cyclosativene, α-copaene, α-ylangene, γ-cadinene, δ-cadinene, 4,8-dimethyl-1-1,3,7-nonatriene, *trans*-4-*trans*-8,12-trimethyl-1, 3,7,11-tridecatetraene α-farnesene, 1,3,8-menthatriene, 1,4,8-menthatriene, β-elemene, germacrene-d, humulene, α-pinene, α-fenchene, δ-3-carene, γ-murolene, α-selinene, guaiene, valencene, β-caryophyllene, β-gurjunene, tricyclene, α,p-dimethylstyrene; acids: acetic, propionic, butyric, 2-methyl butyric, 3-methyl butyric, hexadecanoic acid, octadecanoic acid, eicosanoic acid; ketones: 6-methyl-5-hepten-2-one, geranyl acetone, farnesyl acetone, undecan-2-one, camphor, piperiterone, α-ionone, 8-acetoxy carvotanacetone; alcohols: 3-methyl butanol, *p*-methyl-3-en-1-ol, perillyl alcohol, cuminyl alcohol, 2-methylpropan-1-ol, 2-methylbutan-1-ol, 2-methyl-3-buten-2-ol, 1-hexanol,1-heptanol, 1-octanol, 1-noanol, 1-decanol, dec-9-cen-1-ol, farnesol, δ-terpineol, isopiperitenol, *cis*-carveol, *trans*-carveol, 4-thujanol, 1,8-methadien-4-ol, *p*-mentha-1(7),8-dien-2-ol, *trans*-*p*-mentha-2,8-dien-l-ol, globulol; phenols: *p*-cresol, thymol, carvacrol; aldehydes: 3-methyl butanal, 2-methyl butanal, *trans*-2-butenal, pentanal,

hexanal, octanal, *trans*-oct-2-enal, nonanal, decanal, *trans*-dec-2-enal, *cis*-dec-4-enal, *trans*-dodec-5-enal, *trans*-2-*cis*-6-dodecadienal, citronellal, geranial, neral, farnesal isomer,furfural, cuminaldehye; esters: octyl acetate, decyl acetate, decadienyl acetate, dodecyl acetate, dode-5-cenyl acetate, geranyl acetate, neryl acetate, linalyl acetate, hydroxy-methyl acetate,4-terpinyl acetate, terpinene-4-yl-acetate, α-terpinyl-propionate, dihydro-α-terpinyl acetate, bornyl acetate, 4-thujyl acetate, 6-hydroxyterpinayl acetate, 6-oxoterpinyl acetate, geranyl propionate, neryl propionate, ethyl 2-hydroxyhexanoate, menthyl geraniate, menthyl 9,12-octadienoate, menthyl cinnamate; oxides: 2,3-dehydro-1,8-cineole, *trans*-epoxyocimene, 1,2-limonene epoxide, *cis*-linalol oxide, *trans*-linalol oxide, perillene; terpenoid: carvone; and miscellaneous: pinole (Lawrence 1978; Govindarajan et al. 1982; Noleau et al. 1987). The main components of the bifunctional ultrasound assisted extraction extracted cardamom essential oil were α-terpenyl acetate (46.0%), 1,8-cineole (27.7%), linalool (5.3%), α-terpineol (4.0%), linalyl acetate (3.5%) (Sereshti et al. 2012).

Menon et al. (1999) identified 100 compounds in cardamom oil in two eluted fractions namely free volatile fraction and glycosidically bound (aglycone) fraction. The most abundant constituents of the free volatile fraction were δ-terpinyl acetate and 1,8-cineole. Other important components were α-terpineol, geraniol, *p*-menth-8-en-2-ol, β-pinene, carvone oxide, γ-terpinene, nonan-5-one and β-nerolidol. Other compounds occurring in trace amounts included *trans,trans*-farnesol; *trans,cis*-farnesol; *cis,trans*-farnesol and cubenol. The most important components in the aglycone fraction were 3-methylpentan-2-ol, α-terpineol, isosafrole, β-nerolidol, *trans,trans*-farnesol, *trans,cis*-farnesol, *cis,trans*-farnesol, T-murrolol, cubenol, 10-epi-cubenol, *cis*-linalool oxide, tetrahydrolinalol, cedrol, geraniol, linalol, oct-1-en-3-ol, 1,8-cineole and *p*-menth-8-en-2-ol.

The main components of cardamom essential oil were reported by Marongiu et al. (2004) as follows: α-terpinyl acetate, 42.3%; 1,8-cineole, 21.4%; linalyl acetate, 8.2%; limonene, 5.6%; and linalool, 5.4%, the volatile fraction of the extract was made up mainly of the following: limonene, 36.4%; 1,8-cineole, 23.5%; terpinolene, 8.6%; and myrcene, 6.6%. The oil also contained borneol, camphor, carvone, eucalyptol, terpinine, sabinene and caprylic acid. Cardamom oil was also reported to contain two unusual C11 and C16 hydrocarbons: (E)-4,8-dimethyl-1,3,7-nonatriene and (E,E)-4,8,12-trimethyl-1,3,7,11-tridecatetraene (Maurer et al. 1986).

Thirty-two compounds constituting 93–95% of oil were identified in cardamom oil (Leela et al. 2008). Eleven were identified as major compounds namely, 1,8-cineole, α-terpinyl acetate, α-pinene, sabinene, α-myrcene, linalool, 4-terpineol, α-terpineol, nerol, geranyl acetate and nerolidol. 1,8-cineole and α-terpinyl acetate were the major components in the cardamom volatile oil and the basic cardamom aroma was produced by combination of these two components. The major chemical constituents that imparted sweet flavour to the oil were α-terpinyl acetate, geranyl acetate, nerol and α-terpineol; while 1,8-cineole imparted harsh camphory note. Seven *Cardamomum* genotypes had higher level of α-terpinyl acetate compared to 1,8-cineole, indicating their superior quality. Olivero-Verbel et al. (2010) found the main components in cardamom volatile oil were 1,8-cineol (29.7%) and α-terpineol acetate (26.1%). Korikontimath et al. (1999) reported the two major components were 1,8-cineol (36.3%) and α-terpineol acetate (31.3%), and other constituents as 1.5% α-pinene, 0.2% β-pinene, 2.8% sabinene, 1.6% myrcene, 0.2% α-phellandrene, 11.6% limonene, 36.3% 1,8-cineole, 0.7% γ-terpinene, 0.5% terpinolene, 3% linalool, 2.5% linalyl acetate, 0.9% terpinen 4–01, 2.6% α-terpineol, 31.3%, α-terpinyl acetate, 0.3% citronellol, 0.5% nerd, 0.5% geraniol, 0.2% methyl eugenol and 2.7% *trans*-nerolidol. Abbasipour et al. (2011) reported the main two components as 1,8-cineol 55.65% and α-terpinyl acetate 35.27%. Other components identified included *cis*-ocimene 0.38%, terpinene 2.72%, fenchyl alcohol 2.59%, terpineol 0.04%, α-selinene 0.42%, β-selinene 0.31%, farnesol 0.18%, pinene 1.3% and linalool 0.55%.

Gopalakrishnan et al. (1990) found the non-saponifiable lipid fraction of cardamom to

consist mainly of n-alkane (C21, C23, C25, C27, C31 and C33) and n-alkene (C21, C23, C25, C27, C31 and C33) waxes and sterols like β-sitostenone and γ-sitosterol. Phtyol and methyl eugenyl acetate were also found.

Sixteen compounds constituting 93.62% of total oil were identified in the essential oil of cardamom leaves; 63% were oxygenated monoterpenes, 27.3% monoterpenes, 1.43% sesquiterpenes, 1.17% fatty acid esters and 0.63% acetates (Mahmud 2008). The major components were 4-terpineol (30.26%) and 1:8 cineole (25.75%). Other components include α-terpinolene (9.81%), *p*-cymene (5.3%), α-terpinene (4.68%), α-terpineol (3.45%), γ-terpinene (2.68%), linalool (2.68%), sabinene (2.07%), α-tujene (1.63%), *trans*-caryophyllene (1.43%), α-pinene (1.17%), hexadecanoic acid (1.167%), menth-2-en-1-ol (0.75%), apiole (0.62%) and endbornyl acetate (0.59%).

Pharmacological activities of cardamom have also been reported and are elaborated below.

Gastroprotective Activity

Studies showed cardamom to have gastroprotective activity. In the aspirin-induced gastric ulcer model, the best gastroprotective effect was found in the petroleum ether soluble fraction (PS) of the crude methanol extract of cardamom fruit, which inhibited lesions by nearly 100% at 12.5 mg/kg (Jamal et al. 2006). The PS extract at doses ≥12.5 mg/kg proved to be more active than ranitidine at 50 mg/kg. The crude methanolic extract of cardamom fruit proved to be active reducing gastric lesions by about 70% in the ethanol-induced ulcer model at 500 mg/kg. The PS fraction reduced the lesions by 50% at 50 and 100 mg/kg (no dose response was observed) with similar effect than the petroleum ether insoluble fraction at 450 mg/kg. In another study, the petroleum ether soluble fractions of the essential oils of *E. cardamomum* and *A. subulatum* inhibited significantly gastric lesions induced by asprin and ethanol (Jamal et al. 2005). Fractions of small cardamom were found to be better than large cardamom. The results supported the use of cardamom for gastric problems. Small cardamom known as 'Heel Khurd' (fruits of *Elettaria cardamomum*) and large cardamom 'Heel Kalan' (fruits of *Amomum subulatum*) are used in Unani System of Medicine to treat gastrointestinal disorders. These seeds are used as stomachic (Muqavvi-e-Meda), desiccant (Mujaffif), resolvent (Muhallil), digestive (Hazim) and carminative (Kasir-e-Riyah) (Jamal et al. 2005).

Antihypertensive Activity

Separate studies indicated that cardamom crude extract exhibited gut excitatory and inhibitory effects mediated through cholinergic and Ca++ antagonist mechanisms respectively and lowers arterial blood pressure via combination of both pathways in rats (Gilani et al. 2008). In guinea-pig atria, the extract exhibited a cardio-depressant effect. The extract (1–10 mg/kg) produced diuresis in rats, accompanied by a saluretic effect. It enhanced pentobarbital-induced sleeping time in mice. The diuretic and sedative effects may offer added value in its use in hypertension and epilepsy.

Anticancer Activity

Studies suggested aqueous suspensions of cardamom to have protective effects on experimentally induced colon carcinogenesis (Sengupta et al. 2005) Following oral treatment of 0.5% cardamom, in aqueous suspension, daily for 8 weeks, significant reduction in the incidences of aberrant crypt foci was observed in Male Swiss albino mice injected with azoxymethane. This reduction in aberrant crypt foci was accompanied by suppression of cell and induction of apoptosis. Moreover, reduction of both cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) expression were also observed. The scientists showed that the inhibitory effect of cinnamon and cardamom on azoxymethane induced colon carcinogenesis was attributed to their antiinflammatory, antiproliferative and pro-apoptotic activity (Bhattacharjee et al. 2007). Aqueous suspensions of cinnamon and cardamom were shown to enhance the level of detoxifying enzyme (GST activity) with simultaneous decrease in lipid peroxidation levels in the

treatment groups when compared to that of the carcinogen control group.

A significant reduction in the values of tumour incidence, tumour burden, and tumour yield and the cumulative number of skin papillomas was observed in mice treated orally with 0.5 mg of cardamom powder in suspension continuously at pre-, peri-, and post-initiational stages of 7,12-dimethylbenz[a]anthracene-initiated and croton oil-promoted skin papillomagenesis compared with the control group (Qiblawi et al. 2012). The average weight and diameter of tumours recorded were also comparatively lower in the cardamom-treated mouse group. Treatment of mice with cardamom suspension by oral gavage for 15 days resulted in a significant decrease in the lipid peroxidation level of the liver . Further, the reduced glutathione level was significantly elevated in comparison with the control group following cardamom suspension treatment. Taken together, the findings indicated the potential of cardamom as a chemopreventive agent against two-stage skin cancer.

Antiinflammatroy Activity

Cardamom seeds, in doses of 175 and 280 μL/kg and indomethacin in a dose of 30 mg/kg were antiinflammatory against acute carrageenan-induced planter oedema in male albino rats (Al-Zuhair et al. 1996). Additionally, a dose of 233 μL/kg of cardamom oil exhibited 50% protection against the writhing (stretching syndrome) induced by intraperitoneal administration of a 0.02% solution of *p*-benzoquinone in mice. The antispasmodic activity was determined on a rabbit intestine preparation using acetylcholine as agonist, the results proving that cardamom oil exerted its antispasmodic action through muscarinic receptor blockage.

Antiplatelet Aggregation Activity

Another study showed that aqueous extract of cardamom may have component(s), which protected platelets from aggregation and lipid peroxidation (Suneetha and Krishnakantha 2005). The study showed that an increase in concentration of cardamom decreased the malondialdehyde (MDA) formation significantly in platelet rich plasma (PRP) and platelet membranes, respectively, obtained from blood of healthy volunteers.

Drug Potentiation Activity

Studies demonstrated that cardamom oil, in ethanol/water vehicle could enhance transdermal delivery of indomethacin (Huang et al. 1999). The permeation of indomethacin was significantly enhanced after pretreatment of cardamom oil both in the in vitro and in vivo studies. The result of various pre-treatment periods showed that the indomethacin flux decreased as the length of the pretreatment increased. Both natural cardamom oil and a cyclic monoterpene mixture composed of the components of the oil showed similar enhancement on indomethacin permeation, indicating cyclic monoterpenes are the predominant components altering the barrier property of stratum corneum. The results also showed that three minor components in cardamom oil (α-pinene, 6.5%; β-pinene, 4.8%; α-terpineol, 0.4%) had a synergistic effect with 1,8-cineole (59.3%) and δ-limonene (29.0%) to enhance the permeation of indomethacin.

Antimicrobial Activity

Elettaria cardamomum exhibited antimicrobial activity against both Gram-positive and Gram-negative bacterial species (Malti et al. 2007). The acetone, ethanol and methanol extracts of cardomum fruit exhibited antimicrobial activity against all tested dental caries microorganism, *Staphylococcus aureus, Candida albicans* and *Saccharomyces cerevisiae* except *Lactobacillus acidophilus* (Aneja and Joshi 2009). The most susceptible microorganism was *S. aureus* followed by *C. albicans, S. cerevisiae* and *S. mutans*. Highest inhibitory activity was obtained with the acetone extract against *S. aureus*. Ethanol extract of dry cardamom fruit was found to have

comparatively higher antibacterial activity than other organic and aqueous extracts against *Escherichia coli, Salmonella typhi, Streptococcus pyogenes, Staphylcoccus aureus, Bacillus subtilis* and *Bacillus cereus* (Kaushik et al. 2010). Gram-positive bacteria showed variable susceptibilities to all the tested extracts.

Antilithiatic Activity

Studies showed that alcoholic and aqueous extracts of cardamom seeds exhibited antilithiatic activity in-vitro (Patel et al. 2011). Both extracts exhibited higher capacity in inhibition of calcium oxalate crystal formation and aggregation compared to ethyl acetate and petroleum ether extracts.

Toxicity Effects

Toxicity studies showed that *E. cardamomum* induced toxicity at 0.3 mg/g mouse and affected energy metabolism and oxidative stress (Malti et al. 2007). A significant increase in creatine phosphokinase level was observed. The microscopic evaluation showed that *E. cardamomum* induce morphological perturbation in mice's heart. The results showed also an inhibitory effect of glyceraldehyde 3-phosphate dehydrogenase and an important increase in the level of thiobarbituric acid reactive substances, succinate dehydrogenase and catalase activities.

Traditional Medicinal Uses

Cardamom is listed in the medical pharmacopoeias of several Asian countries. It has been used in traditional Ayurvedic and Unani medicine for a diverse range of ailments. Cardamom is regarded as carminative, stimulant (aromatic); antimicrobial, anti-aflatoxin, analgesic, anti inflammatory, diuretic, abortificient, analgesic, dessicant, resolvent and has been used asthma, constipation, colic, diarrhea, dyspepsia, hypertension, epilepsy, bronchitis, piles, consumption, strangury, scabies, pruritus, bladder and kidney diseases, lung congestion, pulmonary tuberculosis, eyelid inflammation, gastro-intestinal disorders, vomiting, colic, flatulence, cardiovascular disorders and disorders of the head (Grieve 1971; Kapoor 1989; Wardini and Thomas 1999; Duke et al. 2002; Jamal et al. 2005). Cardamom is mainly used as an adjuvant or corrective (Grieve 1971).

Cardamom water has been reported to be an excellent mouthwash to freshen breath and for gum problems (combines well with peppermint or Greek sage for this). It is often employed in mouthwash, as breath-freshener and for prevention of gingivitis.

Other Uses

The seeds and pods contain a volatile oil which is used in perfumery and medicine. Cardamom was also a favoured ingredient in ancient love potions and was believed to have aphrodisiac properties. Topically, cardamom has been used as an insect repellent. Studies showed that cardamom oil was toxic to the Coleopteran bruchid beetle, *Callosobruchus maculatus*, the red flour Coleopteran beetle, *Tribolium castaneum* and the flour moth, *Ephestia kuehniella* (Abbasipour et al. 2011). Adults of the moth were more sensitive than the Coleopteran beetles. The oil also exerted good efficacy on oviposition deterrence of *C. maculatus* females. Results suggested cardamom oil to have potential for control of stored product pests.

Comments

Cardamom is propagated from seedlings, suckers or by division of the underground rhizomes. Cardamom is the third most expensive spice in the world as each fruit must be hand-picked.

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Author's Blurb

TK Lim (Tong Kwee Lim) obtained his Bachelor and Masters in Agricultural Science from the University of Malaya and his PHD (Botanical Sciences) from the University of Hawaii. He worked in the University of Agriculture Malaysia for 20 years as a lecturer and Associate Professor; as Principal Horticulturist for 9 years for the Department of Primary Industries and Fisheries, Darwin, Northern Territory; 6 years as Manager of the Asia and Middle East Team in Plant Biosecurity Australia, Department of Agriculture, Fisheries and Forestry, Australia; and 4 years as Research Program Manager with the Australian Centre for International Agriculture Research (ACIAR), Department of Foreign Affairs and Trade, Australia before he retired from public service. He has published over a hundred scientific papers including several books: "Guava in Malaysia: Production, Pest and Diseases", "Durian Diseases and Disorders", "Diseases of Mango in Malaysia", chapters in books, international refereed journals, conference proceedings (as editor) and technical bulletins in the areas of plant pathology, crop protection, horticulture, agronomy and quarantine science. He was also a reviewer of scientific papers for several international scientific journals. As Principal Horticulturist in Darwin, he and his team were instrumental in establishing the horticultural industry in the Northern Territory, Australia, especially on tropical fruits, vegetables, culinary herbs, spices / medicinal herbs and tropical flowers. During his tenure with Plant Biosecurity, he led a team responsible for conducting pest risk analyses and quarantine policy issues dealing with the import and export of plants and plant products into and out of Australia for the Middle East and Asian region. During his time with ACIAR, he oversaw and managed international research and development programs in plant protection and horticulture covering a wide array of crops that included fruits, plantation crops, vegetables, culinary and medicinal herbs and spices mainly in southeast Asia and the Pacific. In the course of his four decades of working career he has travelled extensively worldwide to many countries in South Asia, East Asia, southeast Asia, Middle East, Europe, the Pacific Islands, USA and England, and also throughout Malaysia and Australia. Since his tertiary education days he always had a strong passion for crops and took an avid interest in edible and medicinal plants. Over the four decades, he has taken several thousands of photographs of common, known and lesser known edible, medicinal and non-medicinal plants, amassed local literature, local indigenous knowledge, books, and has developed and established close rapport with many local researchers, scientists, growers and farmers during the course of his work and travels. All relevant available and up-to-date information collated on more than a thousand species of edible, medicinal and non-medicinal plants will be provided in a comprehensive reference series fully illustrated with coloured images to help in plant identification. This work will cover scientific names, synonyms, common and vernacular names, origin and distribution, agroecology, edible plant parts and uses, plant habit /description, nutritive and medicinal value, other uses and selected current references. Additional information is provided on the medicinal uses and pharmacological properties of the plants. This work will be of significant interest to

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scientists, researchers, practitioners (medical practitioners, pharmacologists, ethnobotanists, horticulturists, food nutritionists, agriculturists, botanists, herbalogists, herbologists, naturalists, conservationists, extension scientists, teachers, lecturers), students and the general public.

Medical Glossary

AAD **A**llergic airway disease, an inflammatory disorder of the airways caused by allergens.

AAPH 2,2′-azobis(2-amidinopropane) dihydrochloride, a water-soluble azo compound used extensively as a free radical generator, often in the study of lipid peroxidation and the characterization of antioxidants.

Abeta aggregation Amyloid beta protein (Abeta) aggregation is associated with Alzheimer's disease (AD); it is a major component of the extracellular plaque found in AD brains.

Abdominal distension referring to generalised distension of most or all of the abdomen. Also referred to as stomach bloating often caused by a sudden increase in fibre from consumption of vegetables, fruits and beans.

Ablation therapy the destruction of small areas of myocardial tissue, usually by application of electrical or chemical energy, in the treatment of some tachyarrhythmias.

Abortifacient a substance that causes or induces abortion.

Abortivum a substance inducing abortion.

Abscess a swollen infected, inflamed area filled with pus in body tissues.

ABTS 2.2 azinobis-3-ethylhenthiazoline-6-sulfonic acid, a type of mediator in chemical reaction kinetics of specific enzymes.

ACAT acyl CoA: cholesterol acyltransferase.

ACE see angiotensin-converting enzyme.

ACTH (Adrenocorticotropic hormone) also known as 'corticotropin', is a polypeptide tropic hormone produced and secreted by the anterior pituitary gland.

Acetogenins natural products from the plants of the family Annonaceae, are very potent inhibitors of the NADH-ubiquinone reductase (Complex I) activity of mammalian mitochondria.

Acetyl-CoA carboxylase (ACC) enzyme that catalyzes the biotin-dependent carboxylation of acetyl-CoA to produce malonyl-CoA.

Acetylcholinesterase (AChE) is an enzyme that degrades (through its hydrolytic activity) the neurotransmitter acetylcholine, producing choline.

Acne vulgáris also known as chronic acne, usually occurring in adolescence, with comedones (blackheads), papules (red pimples), nodules (inflamed acne spots), and pustules (small inflamed pus-filled lesions) on the face, neck, and upper part of the trunk.

Acidosis increased acidity, an excessively acid condition of the body fluids.

Acquired immunodeficiency syndrome (AIDS) an epidemic disease caused by an infection by human immunodeficiency virus (HIV-1, HIV-2), retrovirus that causes immune system failure and debilitation and is often accompanied by infections such as tuberculosis.

Acridone an organic compound based on the acridine skeleton, with a carbonyl group at the 9 position.

ACTH adrenocorticotropic hormone (or corticotropin), a polypeptide tropic hormone produced and secreted by the anterior pituitary gland. It plays a role in the synthesis and secretion of gluco- and mineralo-corticosteroids and androgenic steroids.

Activating transcription factor (ATF) a protein (gene) that binds to specific DNA sequences regulating the transfer or transcription of information from DNA to mRNA.

Activator protein-1 (AP-1) a heterodimeric protein transcription factor that regulates gene expression in response to a variety of stimuli,

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including cytokines, growth factors, stress, and bacterial and viral infections. AP-1 in turn regulates a number of cellular processes including differentiation, proliferation, and apoptosis.

Acyl-CoA dehydrogenases group of enzymes that catalyzes the initial step in each cycle of fatty acid β -oxidation in the mitochondria of cells.

Adaptogen a term used by herbalists to refer to a natural herb product that increases the body's resistance to stresses such as trauma, stress and fatigue.

Adaptogenic increasing the resistance of the body to stress.

Addison's disease is a rare endocrine disorder. It occurs when the adrenal glands cannot produce sufficient hormones (corticosteroids). It is also known as chronic adrenal insufficiency, hypocortisolism or hypocorticism.

Adenocarcinoma a cancer originating in glandular tissue.

Adenoma a benign tumour from a glandular origin.

Adenopathy abnormal enlargement or swelling of the lymph node.

Adenosine receptors a class of purinergic, G-protein coupled receptors with adenosine as endogenous ligand. In humans, there are four adenosine receptors. A1 receptors and A2A play roles in the heart, regulating myocardial oxygen consumption and coronary blood flow, while the A2A receptor also has broader antiinflammatory effects throughout the body. These two receptors also have important roles in the brain, regulating the release of other neurotransmitters such as dopamine and glutamate, while the A2B and A3 receptors are located mainly peripherally and are involved in inflammation and immune responses.

ADH see alcohol dehydrogenase.

Adipocyte a fat cell involved in the synthesis and storage of fats.

Adipocytokine bioactive cytokines produced by adipose tissues

Adiponectin a protein in humans that modulates several physiological processes, such as metabolism of glucose and fatty acids, and immune responses.

Adipose tissues body fat, loose connective tissue composed of adipocytes (fat cells).

Adoptogen containing smooth pro-stressors which reduce reactivity of host defense systems and decrease damaging effects of various stressors due to increased basal level of mediators involved in the stress response.

Adrenal glands star-shaped endocrine glands that sit on top of the kidneys.

Adrenalectomized having had the adrenal glands surgically removed.

Adrenergic having to de with adrenaline (epinephrine) and/or noradrenaline (norepinephrine).

Adrenergic receptors a class of G protein-coupled receptors that are targets of the noradrenaline (norepinephrine) and adrenaline (epinephrine).

Adulterant an impure ingredient added into a preparation.

Advanced Glycation End products (AGEs) resultant products of a chain of chemical reactions after an initial glycation reaction. AGEs may play an important adverse role in process of atherosclerosis, diabetes, aging and chronic renal failure.

Aegilops an ulcer or fistula in the inner corner of the eye.

Afferent something that so conducts or carries towards, such as a blood vessel, fibre, or nerve.

Agammaglobulinaemia an inherited disorder in which there are very low levels of protective immune proteins called immunoglobulins. Cf. x-linked agammaglobulinaemia.

Agalactia lack of milk after parturition (birth).

Age-related macular degeneration (AMD) a medical condition of elderly adults that results in a loss of vision in the center of the visual field (the macula) because of damage to the retina.

Agglutinin a protein substance, such as an antibody, that is capable of causing agglutination (clumping) of a particular antigen.

Agglutination clumping of particles.

Agonist a drug that binds to a receptor of a cell and triggers a response by the cell.

Ague a fever (such as from malaria) that is marked by paroxysms of chills, fever, and sweating that recurs with regular intervals.

AHR AhR, aryl hydrocarbon receptor, a cytosolic protein transcription factor.

AIDS see Acquired Immunodeficiency Syndrome.

Akathisia a movement disorder in which there is an urge or need to move the legs to stop unpleasant sensations. Also called restless leg syndrome, the disorder is often caused by long-term use of antipsychotic medications.

AKT serine/threonine kinase (also known as protein kinase B or PKB) plays a critical regulatory role in diverse cellular processes, including cancer progression and insulin metabolism.

Akt signaling pathway Akt are protein kinases involved in mammalian cellular signaling, inhibits apoptotic processes.

Akt/FoxO pathway Cellular processes involving Akt and FoxO transcription factors that play a role in angiogenesis and vasculogenesis.

Alanine transaminase (ALT) also called Serum Glutamic Pyruvate Transaminase (SGPT) or Alanine aminotransferase (ALAT), an enzyme present in hepatocytes (liver cells). When a cell is damaged, it leaks this enzyme into the blood.

ALAT, (Alanine aminotransferase) see Alanine transaminase.

Albumin water soluble proteins found in egg white, blood serum, milk, various animal tissues and plant juices and tissues.

Albuminaria excessive amount of albumin in the urine, a symptom of severe kidney disease.

Aldose reductase, aldehyde reductase an enzyme in carbohydrate metabolism that converts glucose to sorbitol.

Alexipharmic an antidote, remedy for poison.

Alexiteric a preservative against contagious and infectious diseases, and the effects of poisons.

Alcohol dehydrogenase (ADH) an enzyme involved in the break-down of alcohol.

Algesic endogenous substances involved in the production of pain that is associated with inflammation, e.g. serotonin, bradykinin and prostaglandins.

Alkaline phosphatase (ALP) an enzyme in the cells lining the biliary ducts of the liver. ALP levels in plasma will rise with large bile duct obstruction, intrahepatic cholestasis or infiltrative diseases of the liver. ALP is also present in bone and placental tissues.

Allergenic having the properties of an antigen (allergen), immunogenic.

Allergic pertaining to, caused, affected with, or the nature of the allergy.

Allergic conjunctivitis inflammation of the tissue lining the eyelids (conjunctiva) due to allergy.

Allergy a hypersensitivity state induced by exposure to a particular antigen (allergen) resulting in harmful immunologic reactions on subsequent exposures. The term is usually used to refer to hypersensitivity to an environmental antigen (atopic allergy or contact dermatitis) or to drug allergy.

Allogeneic cells or tissues which are genetically different because they are derived from separate individuals of the same species. Also refers to a type of immunological reaction that occurs when cells are transplanted into a genetically different recipient.

Allografts or homografts, a graft between individuals of the same species, but of different genotypes.

Alloknesis itch produced by innocuous mechanical stimulation.

Allostasis the process of achieving stability, or homeostasis, through physiological or behavioral change.

Alopecia is the loss of hair on the body.

Alopecia areata is a particular disorder affecting hair growth (loss of hair) in the scalp and elsewhere.

ALP see Alkaline phosphatase.

Alpha-adrenoceptor receptors postulated to exist on nerve cell membranes of the sympathetic nervous system in order to explain the specificity of certain agents that affect only some sympathetic activities (such as vasoconstriction and relaxation of intestinal muscles and contraction of smooth muscles).

Alpha amylase α-amylase a major form of amylase found in humans and other mammals that cleaves alpha-bonds of large sugar molecules.

ALT see Alanine transaminase.

Alterative a medication or treatment which gradually induces a change, and restores healthy functions without sensible evacuations.

Alveolar macrophage a vigorously phagocytic macrophage on the epithelial surface of lung alveoli that ingests carbon and other inhaled particulate matter. Also called coniophage or dust cell.

Alzheimer's disease a degenerative, organic, mental disease characterized by progressive brain deterioration and dementia, usually occurring after the age of 50.

Amastigote refers to a cell that does not have any flagella, used mainly to describe a certain phase in the life-cycle of trypanosome protozoans.

Amenorrhea the condition when a woman fails to have menstrual periods.

Amidolytic cleavage of the amide structure.

Amoebiasis state of being infected by amoeba such as *Entamoeba histolytica*.

Amoebicidal lethal to amoeba.

AMPK (5′ AMP-activated protein kinase) or 5′ adenosine monophosphate-activated protein kinase, enzyme that plays a role in cellular energy homeostasis.

Amyloid beta (Aβ or Abeta) a peptide of 39–43 amino acids that appear to be the main constituent of amyloid plaques in the brains of Alzheimer's disease patients.

Amyloidosis a disorder that results from abnormal deposition of the protein, amyloid, in various tissues of the body.

Amyotrophic lateral sclerosis or ALS, is a disease of the motor neurons in the brain and spinal cord that control voluntary muscle movement.

Amyotrophy progressive wasting of muscle tissues. *adj*. amyotrophic.

Anaemia a blood disorder in which the blood is deficient in red blood cells and in haemoglobin.

Anaesthesia condition of having sensation temporarily suppressed.

Anaesthetic a substance that decreases partially or totally nerve the sense of pain.

Analeptic a central nervous system (CNS) stimulant medication.

Analgesia term describing relief, reduction or suppression of pain. *adj*. analgetic.

Analgesic a substance that relieves or reduces pain.

Anaphoretic an antiperspirant.

Anaphodisiac or antiaphrodisiac is something that reduces or blunts the libido.

Anaphylaxis a severe, life-threatening allergic response that may be characterized by symptoms such as reduced blood pressure, wheezing, vomiting or diarrhea.

Anaphylactic *adj*. see anaphylaxis.

Anaphylotoxins are fragments (C3a, C4a or C5a) that are produced during the pathways of the complement system. They can trigger release of substances of endothelial cells, mast cells or phagocytes, which produce a local inflammatory response.

Anaplasia a reversion of differentiation in cells and is characteristic of malignant neoplasms (tumours).

Anaplastic *adj*. see anaplasia.

Anasarca accumulation of great quantity of fluid in body tissues.

Anencephaly a cephalic disorder that results from a neural tube defect that occurs when the cephalic (head) end of the neural tube fails to close, resulting in the absence of a major portion of the brain, skull, and scalp.

Androgen male sex hormone in vertebrates. Androgens may be used in patients with breast cancer to treat recurrence of the disease.

Android adiposity centric fat distribution patterns with increased disposition towards the abdominal area, visceral fat – apple shaped cf gynoid adiposity.

Andrology branch of medicine concerned with the reproductive diseases in men.

Aneugen an agent that affects cell division and the mitotic spindle apparatus, causing the loss or gain of whole chromosomes, thereby inducing aneuploidy. *adj*. aneugenic.

Angina pectoris, Angina chest pain or chest discomfort that occurs when the heart muscle does not get enough blood.

Angiogenic *adj*. see angiogenesis.

Angiogenesis a physiological process involving the growth of new blood vessels from pre-existing vessels.

Angiotensin an oligopeptide hormone in the blood that causes blood vessels to constrict,

and drives blood pressure up. It is part of the renin-angiotensin system.

Angiotensin-converting enzyme (ACE) an exopeptidase, a circulating enzyme that participates in the body's renin-angiotensin system (RAS) which mediates extracellular volume (i.e. that of the blood plasma, lymph and interstitial fluid), and arterial vasoconstriction.

Anglioplasty medical procedure used to open obstructed or narrowed blood vessel resulting usually from atherosclerosis.

Anisonucleosis a morphological manifestation of nuclear injury characterized by variation in the size of the cell nuclei.

Ankylosing spondylitis (AS) is a type of inflammatory arthritis that targets the joints of the spine.

Annexin V or Annexin A5 is a member of the annexin family of intracellular proteins that binds to phosphatidylserine (PS) in a calcium-dependent manner.

Annexitis also called adnexitis, a pelvic inflammatory disease involving the inflammation of the ovaries or fallopian tubes.

Anodyne a substance that relieves or soothes pain by lessening the sensitivity of the brain or nervous system. Also called an analgesic.

Anoikis apoptosis that is induced by inadequate or inappropriate cell-matrix interactions.

Anorectal relating to the rectum and anus.

Anorectics appetite suppressants, substances which reduce the desire to eat. Used on a short term basis clinically to treat obesity. Also called anorexigenics.

Anorexia lack or loss of desire to eat.

Anorexic having no appetite to eat.

Anorexigenics see anorectics.

Anoxia absence of oxygen supply.

Antagonist a substance that acts against and blocks an action.

Antalgic a substance used to relive a painful condition.

Antecubital vein This vein is located in the antecubital fossa -the area of the arm in front of the elbow.

Anterior uveitis is the most common form of ocular inflammation that often causes a painful red eye.

Anthelmintic an agent or substance that is destructive to worms and used for expulsion of internal parasitic worms in animals and humans.

Anthocyanins a subgroup of antioxidant flavonoids, are glucosides of anthocyanidins. Which are beneficial to health. They occur as water-soluble vacuolar pigments that may appear red, purple, or blue according to pH in plants.

Anthrax a bacterial disease of cattle and ship that can be transmitted to man though unprocessed wool.

Anthropometric pertaining to the study of human body measurements.

Antiamoebic a substance that destroys or suppresses parasitic amoebae.

Antiamyloidogenic compounds that inhibit the formation of Alzheimer's β-amyloid fibrils (fAβ) from amyloid β-peptide (Aβ) and destabilize fAβ.

Antianaphylactic agent that can prevent the occurrence of anaphylaxis (life threatening allergic response).

Antiangiogenic a drug or substance used to stop the growth of tumours and progression of cancers by limiting the pathologic formation of new blood vessels (angiogenesis).

Antiarrhythmic a substance to correct irregular heartbeats and restore the normal rhythm.

Antiasmathic drug that treats or ameliorates asthma.

Antiatherogenic that protects against atherogenesis, the formation of atheromas (plaques) in arteries.

Antibacterial substance that kills or inhibits bacteria.

Antibilious an agent or substance which helps remove excess bile from the body.

Antibiotic a chemical substance produced by a microorganism which has the capacity to inhibit the growth of or to kill other microorganisms.

Antiblennorrhagic a substance that treats blennorrhagia a conjunctival inflammation resulting in mucus discharge.

Antibody a gamma globulin protein produced by a kind of white blood cell called the plasma cell in the blood used by the immune system to identify and neutralize foreign objects (antigen).

Anticarcinomic a substance that kills or inhibits carcinomas (any cancer that arises in epithelium/tissue cells).

Anticephalalgic headache-relieving or preventing.

Anticestodal a chemical destructive to tapeworms.

Anticholesterolemic a substance that can prevent the build up of cholesterol.

Anticlastogenic having a suppressing effect of chromosomal aberrations.

Anticoagulant a substance that thins the blood and acts to inhibit blood platelets from sticking together.

Antidepressant a substance that suppresses depression or sadness.

Antidiabetic a substance that prevents or alleviates diabetes. Also called antidiabetogenic.

Antidiarrhoeal having the property of stopping or correcting diarrhoea, an agent having such action.

Antidote a remedy for counteracting a poison.

Antidopaminergic a term for a chemical that prevents or counteracts the effects of dopamine.

Antidrepanocytary anti-sickle cell anaemia.

Antidysenteric an agent used to reduce or treat dysentery and diarrhea.

Antidyslipidemic agent that will reduce the abnormal amount of lipids and lipoproteins in the blood.

Anti-edematous reduces or suppresses edema.

Antiemetic an agent that stops vomiting and nausea.

Anti-epileptic a drug used to treat or prevent convulsions, anticonvulsant.

Antifebrile a substance that reduces fever, also called antipyretic.

Antifeedant preventing something from being eaten.

Antifertility agent that inhibits formation of ova and sperm and disrupts the process of fertilization (antizygotic).

Anti-fibrosis preventing/retarding the development of fibrosis i.e. excessive growth and activity of fibroblasts. t

Antifilarial effective against human filarial worms.

Antifungal an agent that kills or inhibits the growth of fungi.

Antigen a substance that prompts the production of antibodies and can cause an immune response. *adj*. antigenic.

Antigenotoxic an agent that inhibits DNA adduct formation, stimulates DNA repair mechanisms, and possesses antioxidant functions.

Antiganacratia anti- menstruation.

Antigastralgic preventing or alleviating gastric colic.

Antihematic agent that stops vomiting.

Antihemorrhagic an agent which stops or prevents bleeding.

Antihepatotoxic counteracting injuries to the liver.

Antiherpetic having activity against Herpes Simplex Virus (HSV).

Antihistamine an agent used to counteract the effects of histamine production in allergic reactions.

Antihyperalgesia the ability to block enhanced sensitivity to pain, usually produced by nerve injury or inflammation, to nociceptive stimuli. *adj*. antihyperalgesic.

Antihypercholesterolemia term to describe lowering of cholesterol level in the blood or blood serum.

Antihypercholesterolemic agent that lowers chlolesterol level in the blood or blood serum.

Antihyperlidemic promoting a reduction of lipid levels in the blood, or an agent that has this action.

Antihypersensitive a substance used to treat excessive reactivity to any stimuli.

Antihypertensive a drug used in medicine and pharmacology to treat hypertension (high blood pressure).

Antiinflammatory a substance used to reduce or prevent inflammation.

Antileishmanial inhibiting the growth and proliferation of *Leishmania* a genus of flagellate protozoans that are parasitic in the tissues of vertebrates.

Antileprotic therapeutically effective against leprosy.

Antilithiatic an agent that reduces or suppresses urinary calculi (stones) and acts to dissolve those already present.

Antileukaemic anticancer drugs that are used to treat leukemia.

Antilithogenic inhibiting the formation of calculi (stones).

Antimalarial an agent used to treat malaria and/or kill the malaria-causing organism, *Plasmodium* spp.

Antimelanogenesis obstruct production of melanin.

Antimicrobial a substance that destroys or inhibits growth of disease-causing bacteria, viruses, fungi and other microorganisms.

Antimitotic inhibiting or preventing mitosis.

Antimutagenic an agent that inhibits mutations.

Antimycotic antifungal.

Antineoplastic said of a drug intended to inhibit or prevent the maturation and proliferation of neoplasms that may become malignant, by targeting the DNA.

Antineuralgic a substance that stops intense intermittent pain, usually of the head or face, caused by neuralgia.

Antinociception reduction in pain: a reduction in pain sensitivity produced within neurons when an endorphin or similar opium-containing substance opioid combines with a receptor.

Antinociceptive having an analgesic effect.

Antioxytocic inhibiting premature labour. cf. tocolytic.

Antinutrient are natural or synthetic compounds that interfere with the absorption of nutrients and are commonly found in food sources and beverages.

Antioestrogen a substance that inhibits the biological effects of female sex hormones.

Antiophidian anti venoms of snake.

Antiosteoporotic substance that can prevent osteoporosis.

Antiovulatory substance suppressing ovulation.

Antioxidant a chemical compound or substance that inhibits oxidation and protects against free radical activity and lipid oxidation such as vitamin E, vitamin C, or beta-carotene (coverted to vitamin B), carotenoids and flavonoids which are thought to protect body cells from the damaging effects of oxidation. Many foods including fruit and vegetables contain compounds with antioxidant properties. Antioxidants may also reduce the risks of cancer and age-related macular degeneration(AMD).

Antipaludic antimalarial.

Antiperiodic substance that prevents the recurrence of symptoms of a disease e.g. malaria.

Antiperspirant a substance that inhibits sweating. Also called antisudorific, anaphoretic.

Antiphlogistic a traditional term for a substance used against inflammation, an anti-inflammatory.

Antiplatelet agent drug that decreases platelet aggregation and inhibits thrombus formation.

Antiplasmodial suppressing or destroying plasmodia.

Antiproliferative preventing or inhibiting the reproduction of similar cells.

Antiprostatic drug to treat the prostate.

Antiprotozoal suppressing the growth or reproduction of protozoa.

Antipruritic alleviating or preventing itching.

Antipyretic a substance that reduces fever or quells it. Also known as antithermic.

Antirheumatic relieving or preventing rheumatism.

Antiscorbutic a substance or plant rich in vitamin C that is used to counteract scurvy.

Antisecretory inhibiting or diminishing secretion.

Antisense refers to antisense RNA strand because its sequence of nucleotides is the complement of message sense. When mRNA forms a duplex with a complementary antisense RNA sequence, translation of the mRNA into the protein is blocked. This may slow or halt the growth of cancer cells.

Antiseptic preventing decay or putrefaction, a substance inhibiting the growth and development of microorganisms.

Anti-sickling agent an agent used to prevent or reverse the pathological events leading to sickling of erythrocytes in sickle cell conditions.

Antispasmodic a substance that relieves spasms or inhibits the contraction of smooth muscles; smooth muscle relaxant, muscle-relaxer.

Antispermatogenic preventing or suppressing the production of semen or spermatozoa.

Antisudorific see antiperspirant.

Antisyphilitic a drug (or other chemical agent) that is effective against syphilis.

Antithermic a substance that reduces fever and temperature. Also known as antipyretic.

Antithrombotic preventing or interfering with the formation of thrombi.

Antitoxin an antibody with the ability to neutralize a specific toxin.

Antitumoral substance that acts against the growth, development or spread of a tumour.

Antitussive a substance that depresses coughing.

Antiulcerogenic an agent used to protect against the formation of ulcers, or is used for the treatment of ulcers.

Antivenin an agent used against the venom of a snake, spider, or other venomous animal or insect.

Antivinous an agent or substance that treats addiction to alcohol.

Antiviral substance that destroys or inhibits the growth and viability of infectious viruses.

Antivomitive a substance that reduces or suppresses vomiting.

Antizygotic see antifertility.

Anuria absence of urine production and excretion. *adj*. anuric.

Anxiogenic substance that causes anxiety.

Anxiolytic a drug prescribed for the treatment of symptoms of anxiety.

APAF-1 apoptotic protease activating factor 1.

Apelin also known as APLN, a peptide which in humans is encoded by the APLN gene.

Aperient a substance that acts as a mild laxative by increasing fluids in the bowel.

Aperitif an appetite stimulant.

Aphonia loss of the voice resulting from disease, injury to the vocal cords, or various psychological causes, such as hysteria.

Aphrodisiac an agent that increases sexual activity and libido and/or improves sexual performance.

Aphthae white, painful oral ulcer of unknown cause.

Aphthous ulcer also known as a canker sore, is a type of oral ulcer, which presents as a painful open sore inside the mouth or upper throat.

Aphthous stomatitis a canker sore, a type of painful oral ulcer or sore inside the mouth or upper throat, caused by a break in the mucous membrane. Also called aphthous ulcer.

Apnoea suspension of external breathing.

Apoliprotein B (APOB) primary apolipoprotein of low-density lipoproteins which is responsible for carrying cholesterol to tissues.

Apoplexy a condition in which the brain's function stops with loss of voluntary motion and sense.

Apoprotein the protein moiety of a molecule or complex, as of a lipoprotein.

Appendicitis is a condition characterized by inflammation of the appendix. Also called epityphlitis.

Appetite stimulant a substance to increase or stimulate the appetite. Also called aperitif.

aPPT (Activated Partial Thromboplastin Time) a blood test, a measure of the part of the blood clotting pathway.

Apolipoprotein A-I (APOA1) a major protein component of high density lipoprotein (HDL) in plasma. The protein promotes cholesterol efflux from tissues to the liver for excretion.

Apolipoprotein B (APOB) is the primary apolipoprotein of low-density lipoproteins (LDL or "bad cholesterol"), which is responsible for carrying cholesterol to tissues.

Apolipoprotein E (APOE) the apolipoprotein found on intermediate density lipoprotein and chylomicron that binds to a specific receptor on liver and peripheral cells.

Apoptogenic ability to cause death of cells.

Apoptosis death of cells.

Apurinic lyase a DNA enzyme that catalyses a chemical reaction.

Arachidonate cascade includes the cyclooxygenase (COX) pathway to form prostanoids and the lipoxygenase (LOX) pathway to generate several oxygenated fatty acids, collectively called eicosanoids.

ARE antioxidant response element, is a transcriptional control element that mediates expression of a set of antioxidant proteins.

Ariboflavinosis a condition caused by the dietary deficiency of riboflavin that is characterized by mouth lesions, seborrhea, and vascularization.

Aromatase an enzyme involved in the production of estrogen that acts by catalyzing the conversion of testosterone (an androgen) to estradiol (an estrogen). Aromatase is located in estrogen-producing cells in the adrenal

glands, ovaries, placenta, testicles, adipose (fat) tissue, and brain.

Aromatic having a pleasant, fragrant odour.

Aromatherapy a form of alternative medicine that uses volatile liquid plant materials, such as essential oils and other scented compounds from plants for the purpose of affecting a person's mood or health.

ARPE-19 cells a human retinal pigment epithelial cell line with differentiated properties.

Arrhythmias abnormal heart rhythms that can cause the heart to pump less effectively. Also called dysrhythmias.

Arsenicosis see arsenism.

Arsenism an incommunicable disease resulting from the ingestion of ground water containing unsafe levels of arsenic, also known as arsenicosis.

Arteriogenic erectile dysfunction a penis dysfunction caused by the narrowing of the arteries in the penis, decreasing blood inflow to it, thus making erection impossible.

Arteriosclerosis imprecise term for various disorders of arteries, particularly hardening due to fibrosis or calcium deposition, often used as a synonym for atherosclerosis.

Arthralgia is pain in the joints from many possible causes.

Arthritis inflammation of the joints of the body.

Aryl hydrocarbon receptor (AhR) a ligand-activated transcription factor best known for mediating the toxicity of dioxin and other exogenous contaminants and is responsible for their toxic effects, including immunosuppression.

ASATor AST aspartate aminotransferase, see aspartate transaminase.

ASBT apical sodium dependent bile acid transporter, belongs to the solute carrier family (SLC) of transporters and is an important carrier protein expressed in the small intestine.

Ascaris a genus of parasitic intestinal round worms.

Ascites abnormal accumulation of fluid within the abdominal or peritoneal cavity.

Ascorbic acid See vitamin C.

Aspartate transaminase (AST) also called Serum Glutamic Oxaloacetic Transaminase (SGOT) or aspartate aminotransferase (ASAT) is similar to ALT in that it is another enzyme associated with liver parenchymal cells. It is increased in acute liver damage, but is also present in red blood cells, and cardiac and skeletal muscle and is therefore not specific to the liver.

Asphyxia failure or suppression of the respiratory process due to obstruction of air flow to the lungs or to the lack of oxygen in inspired air.

Asphyxiation the process of undergoing asphyxia.

Asthenia a nonspecific symptom characterized by loss of energy, strength and feeling of weakness.

Asthenopia weakness or fatigue of the eyes, usually accompanied by headache and dimming of vision. *adj*. asthenopic.

Asthma a chronic illness involving the respiratory system in which the airway occasionally constricts, becomes inflamed, and is lined with excessive amounts of mucus, often in response to one or more triggers.

Astringent a substance that contracts blood vessels and certain body tissues (such as mucous membranes) with the effect of reducing secretion and excretion of fluids and/or has a drying effect.

Astrocytes collectively called astroglia, are characteristic star-shaped glial cells in the brain and spinal cord.

Ataxia (loss of co-ordination) results from the degeneration of nerve tissue in the spinal cord and of nerves that control muscle movement in the arms and legs.

Ataxia telangiectasia and Rad3-related protein (ATR) also known as Serine/threonine-protein kinase ATR, FRAP-related protein 1 (FRP1), is an enzyme encoded by the ATR gene. It is involved in sensing DNA damage and activating the DNA damage checkpoint, leading to cell cycle arrest

ATF-2 activating transcription factor 2.

Athlete's foot a contagious skin disease caused by parasitic fungi affecting the foot, hands, causing itching, blisters and cracking. Also called dermatophytosis.

Atherogenic having the capacity to start or accelerate the process of atherogenesis.

Atherogenesis the formation of lipid deposits in the arteries.

Atheroma a deposit or degenerative accumulation of lipid-containing plaques on the innermost layer of the wall of an artery.

Atherosclerosis the condition in which an artery wall thickens as the result of a build-up of fatty materials such as cholesterol.

Atherothrombosis medical condition characterized by an unpredictable, sudden disruption (rupture or erosion/fissure) of an atherosclerotic plaque, which leads to platelet activation and thrombus formation.

Athymic mice laboratory mice lacking a thymus gland.

Atonic lacking normal tone or strength.

Atony insufficient muscular tone.

Atopic dermatitis an inflammatory, non-contagious, pruritic skin disorder of unknown etiology; often called eczema.

Atresia a congenital medical condition in which a body orifice or passage in the body is abnormally closed or absent.

Atretic ovarian follicles an involuted or closed ovarian follicle.

Atrial fibrillation is the most common cardiac arrhythmia (abnormal heart rhythm) and involves the two upper chambers (atria) of the heart.

Attention-deficit hyperactivity disorder (ADHD, ADD or AD/HD) is a neurobehavioral developmental disorder, primarily characterized by the co-existence of attentional problems and hyperactivity.

Auditory brainstem response (ABR) also called brainstem evoked response (BSER) is an electrical signal evoked from the brainstem of a human by the presentation of a sound such as a click.

Augmerosen a drug that may kill cancer cells by blocking the production of a protein that makes cancer cells live longer. Also called bcl-2 antisense oligonucleotide.

Auricular of or relating to the auricle or the ear in general.

Aurones [2-benzylidenebenzofuran-3(2H)-ones] are the secondary plant metabolites and is a subgroup of flavonoids. See flavonoids.

Autoantibodies antibodies manufactured by the immune system that mistakenly target and damage specific tissues and organs of the body.

Autolysin an enzyme that hydrolyzes and destroys the components of a biological cell or a tissue in which it is produced.

Autonomic disorder a neurological disease in which the autonomic nervous system ceases to function properly.

Autophagy digestion of the cell contents by enzymes in the same cell.

Autopsy examination of a cadaver to determine or confirm the cause of death.

Avenanthramides low molecular weight, soluble phenolic compounds found in oats.

Avidity Index describes the collective interactions between antibodies and a multivalent antigen.

Avulsed teeth is tooth that has been knocked out.

Ayurvedic traditional Hindu system of medicine based largely on homeopathy and naturopathy.

Azoospermia is the medical condition of a male not having any measurable level of sperm in his semen.

Azotaemia a higher than normal blood level of urea or other nitrogen containing compounds in the blood.

B-cell activating factor (BAFF) also called tumor necrosis factor ligand superfamily member 13B. It plays an important role in the proliferation and differentiation of B cells.

Babesia a protozoan parasite (malaria–like) of the blood that causes a hemolytic disease known as Babesiosis.

Babesiosis malaria-like parasitic disease caused by Babesia, a genus of protozoal piroplasms.

Bactericidal lethal to bacteria.

Balanitis is an inflammation of the glans (head) of the penis.

BALB/c mice Balb/c mouse was developed in 1923 by McDowell. It is a popular strain and is used in many different research disciplines, but most often in the production of monoclonal antibodies.

Balm aromatic oily resin from certain trees and shrubs used in medicine.

Baroreceptor a type of interoceptor that is stimulated by pressure changes, as those in blood vessel wall.

Barrett's esophagus (Barrett esophagitis) a disorder in which the lining of the esophagus is damaged by stomach acid.

Basophil a type of white blood cell with coarse granules within the cytoplasm and a bilobate (two-lobed) nucleus.

Bax/Bad proapoptotic proteins.

BCL-2 a family of apoptosis regulator proteins in humans encoded by the B-cell lymphoma 2 (BCL-2) gene.

BCL-2 antisense oligonucleotide see augmereson.

BCR/ABL a chimeric oncogene, from fusion of BCR and ABL cancer genes associated with chronic myelogenous leukemia.

Bechic a remedy or treatment of cough.

Bed nucleus of the stria terminalis (BNST) act as a relay site within the hypothalamic-pituitary-adrenal axis and regulate its activity in response to acute stress.

Belching, or burping refers to the noisy release of air or gas from the stomach through the mouth.

Beri-beri is a disease caused by a deficiency of thiamine (vitamin B1) that affects many systems of the body, including the muscles, heart, nerves, and digestive system.

Beta-carotene naturally-occurring retinol (vitamin A) precursor obtained from certain fruits and vegetables with potential antineoplastic and chemopreventive activities. As an antioxidant, beta carotene inhibits free-radical damage to DNA. This agent also induces cell differentiation and apoptosis of some tumour cell types, particularly in early stages of tumorigenesis, and enhances immune system activity by stimulating the release of natural killer cells, lymphocytes, and monocytes.

Beta-catenin is a multifunctional oncogenic protein that contributes fundamentally to cell development and biology, it has been implicated as an integral component in the Wnt signaling pathway.

Beta cells a type of cell in the pancreas in areas called the islets of Langerhans.

Beta glucans polysaccharides of D-glucose monomers linked by β-glycosidic bonds, (1→3), (1→4)-β-D-glucan, soluble, viscous component of fibres found in cereals like oats.

Beta-thalassemia an inherited blood disorder that reduces the production of hemoglobin.

Beta-lactamase enzymes produced by some bacteria that are responsible for their resistance to beta-lactam antibiotics like penicillins.

BHT butylated hydroxytoluene (phenolic compound), an antioxidant used in foods, cosmetics, pharmaceuticals, and petroleum products.

Bifidobacterium is a genus of Gram-positive, non-motile, often branched anaerobic bacteria. Bifidobacteria are one of the major genera of bacteria that make up the gut flora. Bifidobacteria aid in digestion, are associated with a lower incidence of allergies and also prevent some forms of tumour growth. Some bifidobacteria are being used as probiotics.

Bifidogenic promoting the growth of (beneficial) bifidobacteria in the intestinal tract.

Bile fluid secreted by the liver and discharged into the duodenum where it is integral in the digestion and absorption of fats.

Bilharzia, bilharziosis see Schistosomiasis.

Biliary relating to the bile or the organs in which the bile is contained or transported.

Biliary infections infection of organ(s) associated with bile, comprise: (a) acute cholecystitis: an acute inflammation of the gallbladder wall; (b) cholangitis: inflammation of the bile ducts.

Biliousness old term used in the 18th and 19th centuries pertaining to bad digestion, stomach pains, constipation, and excessive flatulence.

Bilirubin a breakdown product of heme (a part of haemoglobin in red blood cells) produced by the liver that is excreted in bile which causes a yellow discoloration of the skin and eyes when it accumulates in those organs.

Biotin also known as vitamin B7. See vitamin B7.

Bitter a medicinal agent with a bitter taste and used as a tonic, alterative or appetizer.

Blackhead see comedone.

Blackwater fever dangerous complication of malarial whereby the red blood cells burst in the blood stream (haemolysis) releasing haemoglobin directly into the blood.

Blain see chilblain.

Blastocyst blastocyst is an embryonic structure formed in the early embryogenesis of

mammals, after the formation of the morula, but before implantation.

Blastocystotoxic agent that suppresses further development of the blastocyst through to the ovum stage.

Blebbing Bulging e.g. membrane blebbing also called membrane bulging or ballooning.

Bleeding diathesis is an unusual susceptibility to bleeding (hemorrhage) due to a defect in the system of coagulation.

Blennorrhagia gonorrhea.

Blennorrhea inordinate discharge of mucus, especially a gonorrheal discharge from the urethra or vagina.

Blepharitis inflammation of the eyelids.

Blister thin vesicle on the skin containing serum and caused by rubbing, friction or burn.

Blood brain barrier (BBB) is a separation of circulating blood and cerebrospinal fluid (CSF) in the central nervous system (CNS). It allows essential metabolites, such as oxygen and glucose, to pass from the blood to the brain and central nervous system (CNS) but blocks most molecules that are more massive than about 500 Da.

Boil localized pyrogenic, painful infection, originating in a hair follicle.

Borborygmus rumbling noise caused by the muscular contractions of peristalsis, the process that moves the contents of the stomach and intestines downward.

Bowman Birk inhibitors type of serine proteinase inhibitor.

Bouillon a broth in French cuisine.

Bradicardia as applied to adult medicine, is defined as a resting heart rate of under 60 beats per minute.

Bradyphrenia referring to the slowness of thought common to many disorders of the brain.

Brain derived neutrophic factor (BDNF) a protein member of the neutrophin family that plays an important role in the growth, maintenance, function and survival of neurons. The protein molecule is involved in the modulation of cognitive and emotional functions and in the treatment of a variety of mental disorders.

Bright's disease chronic nephritis.

Bronchial inflammation see bronchitis.

Bronchiectasis a condition in which the airways within the lungs (bronchial tubes) become damaged and widened.

Bronchitis is an inflammation of the main air passages (bronchi) to your lungs.

Bronchoalveolar lavage (BAL) a medical procedure in which a bronchoscope is passed through the mouth or nose into the lungs and fluid is squirted into a small part of the lung and then recollected for examination.

Bronchopneumonia or bronchial pneumonia; inflammation of the lungs beginning in the terminal bronchioles.

Broncho-pulmonary relating to the bronchi and lungs.

Bronchospasm is a difficulty in breathing caused by a sudden constriction of the muscles in the walls of the bronchioles as occurs in asthma.

Brown fat brown adipose tissue (BAT) in mammals, its primary function is to generate body heat in animals or newborns that do not shiver.

Bubo inflamed, swollen lymph node in the neck or groin.

Buccal of or relating to the cheeks or the mouth cavity.

Bullae blisters; circumscribed, fluid-containing, elevated lesions of the skin, usually more than 5 mm in diameter.

Bursitis condition characterized by inflammation of one or more bursae (small sacs) of synovial fluid in the body.

C fibres afferent fibres found in the nerve of the somatic sensory system.

c-FOS a cellular proto-oncogene belonging to the immediate early gene family of transcription factors.

C-jun NH(2)-terminal kinase enzymes that belong to the family of the MAPK superfamily of protein kinases. These kinases mediate a plethora of cellular responses to such stressful stimuli, including apoptosis and production of inflammatory and immunoregulatory cytokines in diverse cell systems. *cf*: MAPK.

c-Jun-I (Ser 73) substrate of JNK-1 activated by phosphorylation at Ser73.

c-Jun II (Ser 63) substrate of JNK-1 activated by phosphorylation at Ser63.

C-reactive protein a protein found in the blood the levels of which rise in response to inflammation.

c-Src a cellular non-receptor tyrosine kinase.

CAAT element-binding proteins-alpha (c/EBP-alpha) regulates gene expression in adipocytes in the liver.

Cachexia physical wasting with loss of weight, muscle atrophy, fatigue, weakness caused by disease.

Caco-2 cell line a continuous line of heterogeneous human epithelial colorectal adenocarcinoma cells.

Cadaver a dead body, corpse.

Ca2+ ATPase (PMCA) is a transport protein in the plasma membrane of cells that serves to remove calcium (Ca2+) from the cell.

Calcitonin gene related peptide (CGRP) is a 37-amino acid neuropeptide that is abundant in the sensory neurons which innervate bone.

Calcium (Ca) is the most abundant mineral in the body found mainly in bones and teeth. It is required for muscle contraction, blood vessel expansion and contraction, secretion of hormones and enzymes, and transmitting impulses throughout the nervous system. Dietary sources include milk, yoghurt, cheese, Chinese cabbage, kale, broccoli, some green leafy vegetables, fortified cereals, beverages and soybean products.

Calcium ATPase is a form of P-ATPase which transfers calcium after a muscle has contracted.

Calcium channel blockers (CCBs) a class of drugs and natural substances that disrupt the calcium (Ca2+) conduction of calcium channels.

Calciuria abnormal presence of calcium in the urine.

Calculosis the tendency or deposition to form calculi or stones.

Calculus (calculi) hardened, mineral deposits that can form a blockage in the urinary system.

Calculi infection most calculi arise in the kidney when urine becomes supersaturated with a salt that is capable of forming solid crystals. Symptoms arise as these calculi become impacted within the ureter as they pass toward the urinary bladder.

Caligo dimness or obscurity of sight, dependent upon a speck on the cornea.

Calmodulin is a Calcium Modulated protein that can bind to and regulate a multitude of different protein targets, thereby affecting many different cellular functions.

cAMP dependent pathway cyclic adenosine monophosphate is a G protein-coupled receptor triggered signaling cascade used in cell communication in living organisms.

CAMP factor diffusible, heat-stable, extracellular protein produced by Group B *Streptococcus t*hat enhances the hemolysis of sheep erythrocytes by *Staphylococcus aureus*. It is named after Christie, Atkins, and Munch-Peterson, who described it in 1944.

Cancer a malignant neoplasm or tumour in nay part of the body.

Candidiasis infections caused by members of the fungus genus *Candida* that range from superficial, such as oral thrush and vaginitis, to systemic and potentially life-threatening diseases.

Canker see chancre.

Carboxypeptidase an enzyme that hydrolyzes the carboxy-terminal (C-terminal) end of a peptide bond. It is synthesized in the pancreas and secreted into the small intestine.

Carbuncle is an abscess larger than a boil, usually with one or more openings draining pus onto the skin.

Carcinogenesis production of carcinomas. *adj*. carcinogenic.

Carcinoma any malignant cancer that arises from epithelial cells.

Carcinosarcoma a rare tumour containing carcinomatous and sarcomatous components.

Cardiac relating to, situated near or affecting the heart.

Cardiac asthma acute attack of dyspnoea with wheezing resulting from a cardiac disorder.

Cardiac hypertrophy is a thickening of the heart muscle (myocardium) resulting in a decrease chamber size, including the left and right ventricles. common causes of cardiac hypertrophy include high blood pressure (hypertension) and heart valve stenosis.

Cardialgia heartburn.

Cardinolides cardiac glycosides with a 5-membered lactone ring in the side chain of the steroid aglycone.

Cardinolide glycoside cardenolides that contain structural groups derived from sugars.

Cardioactive having an effect on the heart.

Cardiogenic shock is characterized by a decreased pumping ability of the heart that causes a shock like state associated with an inadequate circulation of blood due to primary failure of the ventricles of the heart to function effectively.

Cardiomyocytes cardiac muscle cells.

Cardiomyopathy heart muscle disease.

Cardiopathy disease or disorder of the heart.

Cardioplegia stopping the heart so that surgical procedures can proceed in a still and bloodless field.

Cardiotonic something which strengthens, tones, or regulates heart functions without overt stimulation or depression.

Cardiovascular pertaining to the heart and blood vessels.

Caries tooth decay, commonly called cavities.

Cariogenic leading to the production of caries.

Carminative substance that stops the formation of intestinal gas and helps expel gas that has already formed, relieving flatulence: relieving flatulence or colic by expelling gas.

Carnitine palmitoyltransferase I (CPT1) also known as carnitine acyltransferase I or CAT1 is a mitochondrial enzyme, involved in converting long chain fatty acid into energy.

Carotenes are a large group of intense red and yellow pigments found in all plants ; these are hydrocarbon carotenoids (subclass of tetraterpenes) and the principal carotene is beta-carotene which is a precursor of vitamin A.

Carotenoids a class of natural fat-soluble pigments found principally in plants, belonging to a subgroup of terpenoids containing 8 isoprene units forming a C40 polyene chain. Carotenoids play an important potential role in human health by acting as biological antioxidants. See also carotenes.

Carotenodermia yellow skin discoloration caused by excess blood carotene.

Carpopedal spasm spasm of the hand or foot, or of the thumbs and great toes.

Caspases cysteine-aspartic acid proteases, are a family of cysteine proteases, which play essential roles in apoptosis (programmed cell death), necrosis and inflammation.

Catalase (CAT) enzyme in living organism that catalyses the decomposition of hydrogen peroxide to water and oxygen.

Catalepsy indefinitely prolonged maintenance of a fixed body posture; seen in severe cases of catatonic schizophrenia.

Catamenia menstruation.

Cataplasia Degenerative reversion of cells or tissue to a less differentiated form.

Cataplasm a medicated poultice or plaster. A soft moist mass, often warm and medicated, that is spread over the skin to treat an inflamed, aching or painful area, to improve the circulation.

Cataractogenesis formation of cataracts.

Catarrh, Catarrhal inflammation of the mucous membranes especially of the nose and throat.

Catechins are polyphenolic antioxidant plant metabolites. They belong to the family of flavonoids; tea is a rich source of catechins. See flavonoids.

Catecholamines hormones that are released by the adrenal glands in response to stress.

Cathartic is a substance which accelerates defecation.

Caustic having a corrosive or burning effect.

Cauterization a medical term describing the burning of the body to remove or close a part of it.

Caveolae tiny (50–100 nm) invaginations of the plasma membrane of the cell.

cdc2 Kinase a member of the cyclin-dependent protein kinases (CDKs).

CDKs cyclin-dependent protein kinases, a family of serine/threonine kinases that mediate many stages in mitosis.

CD 28 is one of the molecules expressed on T cells that provide co-stimulatory signals, which are required for T cell (lymphocytes) activation.

CD31 also known as PECAM-1 (Platelet Endothelial Cell Adhesion Molecule-1), a member of the immunoglobulin superfamily, that mediates cell-to-cell adhesion.

CD36 an integral membrane protein found on the surface of many cell types in vertebrate animals.

CD40 an integral membrane protein found on the surface of B lymphocytes, dendritic cells, follicular dendritic cells, hematopoietic progenitor cells, epithelial cells, and carcinomas.

CD68 a glycoprotein expressed on monocytes/macrophages which binds to low density lipoprotein.

Cecal ligation tying up the cecam.

Celiac disease an autoimmune disorder of the small intestine, triggered in genetically susceptible individuals by ingested gluten from wheat, rye, barley, and other closely related cereal grains.

Peptides resulting from partially digested gluten of wheat, barley or rye cause inflammation of the small intestinal mucosa.

Cell adhesion molecules (CAM) glycoproteins located on the surface of cell membranes involved with binding of other cells or with the extra-cellular matrix.

Cellular respiration is the set of the metabolic reactions and processes that take place in organisms' cells to convert biochemical energy from nutrients into adenosine triphosphate (ATP), and then release waste products. The reactions involved in respiration are catabolic reactions that involve the oxidation of one molecule and the reduction of another.

Cellulitis a bacterial infection of the skin that tends to occur in areas that have been damaged or inflamed.

Central nervous system part of the vertebrate nervous system comprising the brain and spinal cord.

Central venous catheter a catheter placed into the large vein in the neck, chest or groin.

Cephalagia pain in the head, a headache.

Cephalic relating to the head.

Ceramide oligosides oligosides with an N-acetyl-sphingosine moiety.

Cercariae a free-swimming larva of the parasitic schistosome worm that has a tail, and suckers on its head for penetration into a host.

Cerebral embolism a blockage of blood flow through a vessel in the brain by a blood clot that formed elsewhere in the body and traveled to the brain.

Cerebral ischemia is the localized reduction of blood flow to the brain or parts of the brain due to arterial obstruction or systematic hyperfusion.

Cerebral infarction is the ischemic kind of stroke due to a disturbance in the blood vessels supplying blood to the brain.

Cerebral tonic substance that can alleviate poor concentration and memory, restlessness, uneasiness, and insomnia.

Cerebrosides are glycosphingolipids which are important components in animal muscle and nerve cell membranes.

Cerebrovascular disease is a group of brain dysfunctions related to disease of the blood vessels supplying the brain.

Cerumen ear wax, a yellowish waxy substance secreted in the ear canal of humans and other mammals.

cFLIP cellular FLICE-inhibitory protein, an inhibitor of death ligand-induced apoptosis.

cGMP cyclic guanosine monophosphate is a cyclic nucleotide derived from guanosine triphosphate (GTP). cGMP is a common regulator of ion channel conductance, glycogenolysis, and cellular apoptosis. It also relaxes smooth muscle tissues.

Chalcones a subgroup of flavonoids.

Chancre a painless lesion formed during the primary stage of syphilis.

Chemoembolization a procedure in which the blood supply to the tumour is blocked surgically or mechanically and anticancer drugs are administered directly into the tumour.

Chemokines are chemotactic cytokines, which stimulate migration of inflammatory cells towards tissue sites of inflammation.

Chemonociceptors nociceptors or sensory pheripheral neurons that are sensitive to chemical stimuli.

Chemosensitizer a drug that makes tumour cells more sensitive to the effects of chemotherapy.

Chemosis edema of the conjunctiva of the eye.

Chickenpox is also known as varicella, is a highly contagious illness caused by primary infection with varicella zoster virus (VZV). The virus causes red, itchy bumps on the body.

Chilblains small, itchy, painful lumps that develop on the skin. They develop as an abnormal response to cold. Also called perniosis or blain.

Chlorosis iron deficiency anemia characterized by greenish yellow colour.

Cholagogue is a medicinal agent which promotes the discharge of bile from the system.

Cholecalciferol a form of vitamin D, also called vitamin D3. See vitamin D.

Cholecyst gall bladder.

Cholecystitis inflammation of the gall bladder.

Cholecystokinin a peptide hormone that plays a key role in facilitating digestion in the small intestine.

Cholera an infectious gastroenteritis caused by enterotoxin-producing strains of the bacterium *Vibrio cholera* and characterized by severe, watery diarrhea.

Choleretic stimulation of the production of bile by the liver.

Cholestasis a condition caused by rapidly developing (acute) or long-term (chronic) interruption in the excretion of bile.

Cholesterol a soft, waxy, steroid substance found among the lipids (fats) in the bloodstream and in all our body's cells.

Cholethiasis presence of gall stones (calculi) in the gall bladder.

Choline a water soluble, organic compound, usually grouped within the Vitamin B complex. It is an essential nutrient and is needed for physiological functions such as structural integrity and signaling roles for cell membranes, cholinergic neuro-transmission (acetylcholine synthesis).

Cholinergic activated by or capable of liberating acetylcholine, especially in the parasympathetic nervous system.

Cholinergic system a system of nerve cells that uses acetylcholine in transmitting nerve impulses.

Cholinomimetic having an action similar to that of acetylcholine; called also parasympathomimetic.

Chonotropic affecting the time or rate, as the rate of contraction of the heart.

Choriocarcinoma a quick-growing malignant, trophoblastic, aggressive cancer that occurs in a woman's uterus (womb).

Chromium (Cr) is required in trace amounts in humans for sugar and lipid metabolism. Its deficiency may cause a disease called chromium deficiency. It is found in cereals, legumes, nuts and animal sources.

Chromosome long pieces of DNA found in the center (nucleus) of cells.

Chronic persisting over extended periods.

Chronic Obstructive Pulmonary Disease (COPD) a progressive disease that makes it hard to breathe.

Chronic venous insufficiency (CVI) a medical condition where the veins cannot pump enough oxygen-poor blood back to the heart.

Chyle a milky bodily fluid consisting of lymph and emulsified fats, or free fatty acids.

Chylomicrons are large lipoprotein particles that transport dietary lipids from the intestines to other locations in the body. Chylomicrons are one of the five major groups of lipoproteins (chylomicrons, VLDL, IDL, LDL, HDL) that enable fats and cholesterol to move within the water-based solution of the bloodstream.

Chylorus milky (having fat emulsion).

Chyluria also called chylous urine, is a medical condition involving the presence of chyle (emulsified fat) in the urine stream, which results in urine appearing milky.

Chymase member of the family of serine proteases found primarily in mast cell.

Chymopapain an enzyme derived from papaya, used in medicine and to tenderize meat.

Cicatrizant the term used to describe a product that promotes healing through the formation of scar tissue.

C-Kit Receptor a protein-tyrosine kinase receptor that is specific for stem cell factor. this interaction is crucial for the development of hematopoietic, gonadal, and pigment stem cells.

Cirrhosis chronic liver disease characterized by replacement of liver tissue by fibrous scar tissue and regenerative nodules/lumps leading progressively to loss of liver function.

Clastogen is an agent that can cause one of two types of structural changes, breaks in chromosomes that result in the gain, loss, or rearrangements of chromosomal segments. *adj*. clastogenic.

Claudication limping, impairment in walking.

Climacterium refers to menopause and the bodily and mental changes associated with it.

Clonic seizures consist of rhythmic jerking movements of the arms and legs, sometimes on both sides of the body.

Clonus a series of involuntary muscular contractions and relaxations.

Clyster enema.

C-myc codes for a protein that binds to the DNA of other genes and is therefore a transcription factor.

CNS Depressant anything that depresses, or slows, the sympathetic impulses of the central nervous system (i.e., respiratory rate, heart rate).

Coagulopathy a defect in the body's mechanism for blood clotting, causing susceptibility to bleeding.

Cobalamin vitamin B12. See vitamin B12.

Co-carcinogen a chemical that promotes the effects of a carcinogen in the production of cancer.

Cold an acute inflammation of the mucous membrane of the respiratory tract especially of the nose and throat caused by a virus and accompanied by sneezing and coughing.

Collagen protein that is the major constituent of cartilage and other connective tissue; comprises the amino acids hydroxyproline, proline, glycine, and hydroxylysine.

Collagenases enzymes that break the peptide bonds in collagen.

Colic a broad term which refers to episodes of uncontrollable, extended crying in a baby who is otherwise healthy and well fed.

Colitis inflammatory bowel disease affecting the tissue that lines the gastrointestinal system.

Collyrium a lotion or liquid wash used as a cleanser for the eyes, particularly in diseases of the eye.

Colorectal relating to the colon or rectum.

Coma a state of unconsciousness from which a patient cannot be aroused.

Comedone a blocked, open sebaceous gland where the secretions oxidize, turning black. Also called blackhead.

Comitogen agent that is considered not to induce cell growth alone but to promote the effect of the mitogen.

Concoction a combination of crude ingredients that is prepared or cooked together.

Condyloma, Condylomata acuminata genital warts, venereal warts, anal wart or anogenital wart, a highly contagious sexually transmitted infection caused by epidermotropic human papillomavirus (HPV).

Conglutination becoming stuck together.

Conjunctival hyperemia enlarged blood vessels in the eyes.

Conjunctivitis sore, red and sticky eyes caused by eye infection.

Constipation a very common gastrointestinal disorder characterised by the passing of hard, dry bowel motions (stools) and difficulty of bowel motion.

Constitutive androstane receptor (CAR, NR113) is a nuclear receptor transcription factor that regulates drug metabolism and homoeostasis.

Consumption term used to describe wasting of tissues including but not limited to tuberculosis.

Consumptive afflicted with or associated with pulmonary tuberculosis.

Contraceptive an agent that reduces the likelihood of or prevents conception.

Contraindication a condition which makes a particular treatment or procedure inadvisable.

Contralateral muscle muscle of opposite limb (leg or arm).

Contralateral rotation rotation occurring or originating in a corresponding part on an opposite side.

Contusion another term for a bruise. A bruise, or contusion, is caused when blood vessels are damaged or broken as the result of a blow to the skin.

Convulsant a drug or physical disturbance that induces convulsion.

Convulsion rapid and uncontrollable shaking of the body.

Coolant that which reduces body temperature.

Copper (Cu) is essential in all plants and animals. It is found in a variety of enzymes, including the copper centers of cytochrome C oxidase and the enzyme superoxide dismutase (containing copper and zinc). In addition to its enzymatic roles, copper is used for biological electron transport. Because of its role in facilitating iron uptake, copper deficiency can often produce anemia-like symptoms. Dietary sources include curry powder, mushroom, nuts, seeds, wheat germ, whole grains and animal meat.

Copulation to engage in coitus or sexual intercourse. *adj*. copulatory.

Cordial a preparation that is stimulating to the heart.

Corn or callus is a patch of hard, thickened skin on the foot that is formed in response to pressure or friction.

Corticosteroids a class of steroid hormones that are produced in the adrenal cortex, used clinically for hormone replacement therapy, for suppressing ACTH secretion, for suppression of immune response and as antineoplastic, anti-allergic and anti-inflammatory agents.

Corticosterone a 21-carbon steroid hormone of the corticosteroid type produced in the cortex of the adrenal glands.

Cortisol is a corticosteroid hormone made by the adrenal glands.

Cornification is the process of forming an epidermal barrier in stratified squamous epithelial tissue.

Coryza a word describing the symptoms of a head cold. It describes the inflammation of the mucus membranes lining the nasal cavity which usually gives rise to the symptoms of nasal congestion and loss of smell, among other symptoms.

COX-1 see cyclooxygenase -1.

COX-2 see cyclooxygenase-**2**.

CpG islands genomic regions that contain a high frequency of CpG sites.

CpG sites the cytosine-phosphate-guanine nucleotide that links two nucleosides together in DNA.

cPLA(2) cytosolic phospholipases A2, these phospholipases are involved in cell signaling processes, such as inflammatory response.

CPY1B1, CPY1A1 a member of the cytochrome P450 superfamily of heme-thiolate monooxygenase enzymes.

Corticosterone a 21-carbon corticosteroid hormone produced in the cortex of the adrenal glands that functions in the metabolism of carbohydrates and proteins.

Creatin a nitrogenous organic acid that occurs naturally in vertebrates and helps to supply energy to muscle.

Creatine phosphokinase (CPK, CK) enzyme that catalyses the conversion of creatine and consumes adenosine triphosphate (ATP) to create phosphocreatine and adenosine diphosphate (ADP).

CREB cAMP response element-binding, a protein that is a transcription factor that binds to certain DNA sequences called cAMP response elements.

Crohn Disease an inflammatory disease of the intestines that affect any part of the gastrointestinal tract.

Crossover study a longitudinal, balance study in which participants receive a sequence of different treatments or exposures.

Croup is an infection of the throat (larynx) and windpipe (trachea) that is caused by a virus (Also called laryngotracheobronchitis).

Crytochidism (cryptochism) a developmental defect characterized by the failure of one or both testes to move into the scrotum as the male fetus develops.

Curettage surgical procedure in which a body cavity or tissue is scraped with a sharp instrument or aspirated with a cannula.

Cutaneous pertaining to the skin.

CXC8 also known as interleukin 8, IL-8.

Cyanogenesis generation of cyanide. *adj*. cyanogenetic.

Cyclooxygenase (COX) an enzyme that is responsible for the formation of prostanoids – prostaglandins, prostacyclins, and thromboxanes that are each involved in the inflammatory response. Two different COX enzymes existed, now known as COX-1 and COX-2.

Cyclooxygenase-1 (COX-1) is known to be present in most tissues. In the gastrointestinal tract, COX-1 maintains the normal lining of the stomach. The enzyme is also involved in kidney and platelet function.

Cyclooxygenase-2 (COX-2) is primarily present at sites of inflammation.

Cysteine proteases are enzymes that degrade polypeptides possessing a common catalytic mechanism that involves a nucleophilic cysteine thiol in a catalytic triad. They are found in fruits like papaya, pineapple, and kiwifruit.

Cystitis a common urinary tract infection that occurs when bacteria travel up the urethra, infect the urine and inflame the bladder lining.

Cystorrhea discharge of mucus from the bladder.

Cytochrome bc-1 complex ubihydroquinone: cytochrome c oxidoreductase.

Cytochrome P450 3A CYP3A a very large and diverse superfamily of heme-thiolate proteins found in all domains of life. This group of

enzymes catalyzes many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids.

Cytokine non-antibody proteins secreted by certain cells of the immune system which carry signals locally between cells. They are a category of signaling molecules that are used extensively in cellular communication.

Cytopathic any detectable, degenerative changes in the host cell due to infection.

Cytoprotective protecting cells from noxious chemicals or other stimuli.

Cytosolic relates to the fluid of the cytoplasm in cells.

Cytostatic preventing the growth and proliferation of cells.

Cytotoxic of or relating to substances that are toxic to cells; cell-killing.

D- galactosamine an amino sugar with unique hepatotoxic properties in animals.

Dandruff scurf, dead, scaly skin among the hair.

Dartre condition of dry, scaly skin

Debility weakness, relaxation of muscular fibre.

Debridement is the process of removing non-living tissue from pressure ulcers, burns, and other wounds.

Debriding agent substance that cleans and treats certain types of wounds, burns, ulcers.

Deciduogenic relating to the uterus lining that is shed off at childbirth.

Decidual stromal cells like endometrial glands and endothelium, express integrins that bind basement components.

Decoction a medical preparation made by boiling the ingredients.

Decongestant a substance that relieves or reduces nasal or bronchial congestion.

Deep venous thrombosis is a blood clot that forms in a vein deep inside a part of the body.

Defibrinated plasma blood whose plasma component has had fibrinogen and fibrin removed.

Degranulation cellular process that releases antimicrobial cytotoxic molecules from secretory vesicles called granules found inside some cells.

Delayed afterdepolarizations (DADs) abnormal depolarization that begins during phase 4 – after repolarization is completed, but before another action potential would normally occur.

Delirium is common, sudden severe confusion and rapid changes in brain function that occur with physical or mental illness; it is reversible and temporary.

Demulcent an agent that soothes internal membranes. Also called emollient.

Dendritic cells are immune cells and form part of the mammalian immune system, functioning as antigen presenting cells.

Dentition a term that describes all of the upper and lower teeth collectively.

Deobstruent a medicine which removes obstructions; also called an aperient.

Deoxypyridinoline (Dpd) a crosslink product of collagen molecules found in bone and excreted in urine during bone degradation.

Depilatory an agent for removing or destroying hair.

Depressant a substance that diminish functional activity, usually by depressing the nervous system.

Depurative an agent used to cleanse or purify the blood, it eliminates toxins and purifies the system.

Dermatitis inflammation of the skin causing discomfort such as eczema.

Dermatitis herpetiformis an autoimmune chronic blistering skin disorder characterised by blisters filled with a watery fluid.

Dermatophyte a fungus parasitic on the skin.

Dermatosis is a broad term that refers to any disease of the skin, especially one that is not accompanied by inflammation.

Dermonecrotic pertaining to or causing necrosis of the skin.

Desquamation the shedding of the outer layers of the skin.

Detoxifier a substance that promotes the removal of toxins from a system or organ.

Diabetes a metabolic disorder associated with inadequate secretion or utilization of insulin and characterized by frequent urination and persistent thirst. See diabetes mellitus.

Diabetes mellitus (DM) (sometimes called "sugar diabetes") is a set of chronic, metabolic disease conditions characterized by high blood sugar (glucose) levels that result from

defects in insulin secretion, or action, or both. Diabetes mellitus appears in two forms.

Diabetes mellitus type I (formerly known as juvenile onset diabetes), caused by deficiency of the pancreatic hormone insulin as a result of destruction of insulin-producing beta cells of the pancreas. Lack of insulin causes an increase of fasting blood glucose that begins to appear in the urine above the renal threshold.

Diabetes mellitus type II (formerly called non-insulin-dependent diabetes mellitus or adult-onset diabetes), the disorder is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency in which insulin is available but cannot be properly utilized.

Diabetic neuropathy a neuropathic disorder that is associated with diabetes mellitus. It affects all peripheral nerves including pain fibers, motor neurons and the autonomic nervous system.

Diabetic retinopathy damage to the retina caused by complications of diabetes mellitus, which can eventually lead to blindness.

Diads two adjacent structural units in a polymer molecule.

Dialysis is a method of removing toxic substances (impurities or wastes) from the blood when the kidneys are unable to do so.

Diaphoresis is profuse sweating commonly associated with shock and other medical emergency conditions.

Diaphoretic a substance that induces perspiration. Also called sudorific.

Diaphyseal pertaining to or affecting the shaft of a long bone (diaphysis).

Diaphysis the main or mid section (shaft) of a long bone.

Diarrhoea a profuse, frequent and loose discharge from the bowels.

Diastolic referring to the time when the heart is in a period of relaxation and dilatation (expansion). *cf.* systolic.

Dieresis surgical separation of parts.

Dietary fibre is a term that refers to a group of food components that pass through the stomach and small intestine undigested and reach the large intestine virtually unchanged. Scientific evidence suggest that a diet high in dietary fibre can be of value for treating or preventing such disorders as constipation, irritable bowel syndrome, diverticular disease, hiatus hernia and haemorrhoids. Some components of dietary fibre may also be of value in reducing the level of cholesterol in blood and thereby decreasing a risk factor for coronary heart disease and the development of gallstones. Dietary fibre is beneficial in the treatment of some diabetics.

Digalactosyl diglycerides are the major lipid components of chloroplasts.

Diosgenin a steroid-like substance that is involved in the production of the hormone progesterone, extracted from roots of *Dioscorea* yam.

Dipsia sensation of dryness in the mouth and throat related to a desire to drink.

Dipsomania pathological use of alcohol.

Discutient an agent (as a medicinal application) which serves to disperse morbid matter.

Disinfectant an agent that prevents the spread of infection, bacteria or communicable disease.

Distal sensory polyneuropathy (DSPN) or peripheral neuropathy, is the most common neurological problem in HIV disease. DSPN also represents a complex symptom that occurs because of peripheral nerve damage related to advanced HIV disease.

Diuresis increased urination.

Diuretic a substance that increases urination (diuresis).

Diverticular disease is a condition affecting the large bowel or colon and is thought to be caused by eating too little fibre.

DMBA 7,12-Dimethylbenzanthracene. A polycyclic aromatic hydrocarbon found in tobacco smoke that is a potent carcinogen.

DNA deoxyribonucleic acid, a nucleic acid that contains the genetic instructions used in the development and functioning of all known living organisms.

DOCA desoxycorticosterone acetate – a steroid chemical used as replacement therapy in Addison's disease.

Dopamine a catecholamine neurotransmitter that occurs in a wide variety of animals, including both vertebrates and invertebrates.

Dopaminergic relating to, or activated by the neurotransmitter, dopamine.

Double blind refer to a clinical trial or experiment in which neither the subject nor the researcher knows which treatment any particular subject is receiving.

Douche a localised spray of liquid directed into a body cavity or onto a part.

DPPH 2,2 diphenyl -1- picryl-hydrazyl – a crystalline, stable free radical used as an inhibitor of free radical reactions.

Dracunculiasis also called guinea worm disease (GWD), is a parasitic infection caused by the nematode, *Dracunculus medinensis*.

Dropsy an old term for the swelling of soft tissues due to the accumulation of excess water. *adj*. dropsical.

Drusen tiny yellow or white deposits of extracellular materials in the retina of the eye or on the optic nerve head.

DT diaphorase also called DTD or NAD(P)H:quinone oxidoreductase, is an obligate two-electron reductase which bioactivates chemotherapeutic quinones.

Dysentery (formerly known as flux or the bloody flux) is a disorder of the digestive system that results in severe diarrhea containing mucus and blood in the feces. It is caused usually by a bacterium called *Shigella*.

Dysesthesia an unpleasant abnormal sensation produced by normal stimuli.

Dysgeusia distortion of the sense of taste.

Dyskinesia the impairment of the power of voluntary movement, resulting in fragmentary or incomplete movements. *adj*. dyskinetic.

Dyslipidemia abnormality in or abnormal amount of lipids and lipoproteins in the blood.

Dysmenorrhea is a menstrual condition characterized by severe and frequent menstrual cramps and pain associated with menstruation.

Dysmotility syndrome a vague, descriptive term used to describe diseases of the muscles of the gastrointestinal tract (esophagus, stomach, small and large intestines).

Dyspedia indigestion followed by nausea.

Dyspepsia refers to a symptom complex of epigastric pain or discomfort. It is often defined as chronic or recurrent discomfort centered in the upper abdomen and can be caused by a variety of conditions. *cf*. functional dyspepsia.

Dysphagia swallowing disorder.

Dysphonia a voice disorder, an impairment in the ability to produce voice sounds using the vocal organs.

Dysplasia refers to abnormality in development.

Dyspnoea shortness of breath, difficulty in breathing.

Dysrhythmias see arrhythmias.

Dystocia abnormal or difficult child birth or labour.

Dystonia a neurological movement disorder characterized by prolonged, repetitive muscle contractions that may cause twisting or jerking movements of muscles.

Dysuria refers to difficult and painful urination.

E- Selectin also known as endothelial leukocyte adhesion molecule-1 (ELAM-1), CD62E, a member of the selectin family. It is transiently expressed on vascular endothelial cells in response to IL-1 beta and TNF-alpha.

EC 50 median effective concentration that produces desired effects in 50% of the test population.

Ecbolic a drug (as an ergot alkaloid) that tends to increase uterine contractions and that is used especially to facilitate delivery.

Ecchymosis skin discoloration caused by the escape of blood into the tissues from ruptured blood vessels.

ECG see electrocardiography.

EC–SOD extracellular superoxide dismutase, a tissue enzyme mainly found in the extracellular matrix of tissues. It participates in the detoxification of reactive oxygen species by catalyzing the dismutation of superoxide radicals.

Ectrodactyly involves the absence of one or more central digits of the hand or foot.

Eczema is broadly applied to a range of persistent skin conditions. These include dryness and recurring skin rashes which are characterized by one or more of these symptoms: redness, skin edema, itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding.

Eczematous rash dry, scaly, itchy rash.

ED 50 is defined as the dose producing a response that is 50% of the maximum obtainable.

Edema formerly known as dropsy or hydropsy, is characterized swelling caused by abnormal

accumulation of fluid beneath the skin, or in one or more cavities of the body. It usually occurs in the feet, ankles and legs, but it can involve the entire body.

Edematogenic producing or causing edema.

EGFR proteins epidermal growth factor receptor (EGFR) proteins – Protein kinases are enzymes that transfer a phosphate group from a phosphate donor onto an acceptor amino acid in a substrate protein.

EGR-1 early growth response 1, a human gene.

Eicosanoids are signaling molecules made by oxygenation of arachidonic acid, a 20-carbon essential fatty acid, includes prostaglandins and related compounds.

Elastase a serine protease that also hydrolyses amides and esters.

Electrocardiography or ECG, is a transthoracic interpretation of the electrical activity of the heart over time captured and externally recorded by skin electrodes.

Electromyogram (EMG) a test used to record the electrical activity of muscles. An electromyogram (EMG) is also called a myogram.

Electuary a medicinal paste composed of powders, or other medical ingredients, incorporated with sweeteners to hide the taste, suitable for oral administration.

Elephantiasis a disorder characterized by chronic thickened and edematous tissue on the genitals and legs due to various causes.

Embrocation lotion or liniment that relieves muscle or joint pains.

Embryotoxic term that describes any chemical which is harmful to an embryo.

Emesis vomiting, throwing up.

Emetic an agent that induces vomiting, *cf*: antiemetic.

Emetocathartic causing vomiting and purging.

Emmenagogue a substance that stimulates, initiates, and/or promotes menstrual flow. Emmenagogues are used in herbal medicine to balance and restore the normal function of the female reproductive system.

Emollient an agent that has a protective and soothing action on the surfaces of the skin and membranes.

Emphysema a long-term, progressive disease of the lungs that primarily causes shortness of breath.

Emulsion a preparation formed by the suspension of very finely divided oily or resinous liquid in another liquid.

Encephalitis inflammation of the brain.

Encephalomalacia cerebral softening, a localized softening of the brain substance, due to hemorrhage or inflammation.

Encephalopathy a disorder or disease of the brain.

Endocrine *adj*. of or relating to endocrine glands or the hormones secreted by them.

Endocytosis is the process by which cells absorb material (molecules such as proteins) from outside the cell by engulfing it with their cell membrane.

Endometrial cancer cancer that arises in the endometrium, the lining of the uterus (womb).

Endometriosis is a common and often painful disorder of the female reproductive system in which the endometrium, the tissue that normally lines the womb (uterus), grows outside the uterus. The two most common symptoms of endometriosis are pain and infertility.

Endometritis refers to inflammation of the endometrium, the inner lining of the uterus.

Endometrium the inner lining of the uterus.

Endoplasmic reticulum is a network of tubules, vesicles and sacs around the nucleus that are interconnected.

Endostatin a naturally-occurring 20-kDa C-terminal protein fragment derived from type XVIII collagen. It is reported to serve as an anti-angiogenic agent that inhibits the formation of the blood vessels that feed cancer tumours.

Endosteum the thin layer of cells lining the medullary cavity of a bone.

Endosteul pertaining to the endosteum.

Endothelial progenitor cells population of rare cells that circulate in the blood with the ability to differentiate into endothelial cells, the cells that make up the lining of blood vessels.

Endothelin any of a group of vasoconstrictive peptides produced by endothelial cells that constrict blood vessels and raise blood pressure.

Endotoxemia the presence of endotoxins in the blood, which may result in shock. *adj*. endotoxemic.

Endotoxin toxins associated with certain bacteria, unlike an 'exotoxin' that is not secreted in soluble form by live bacteria, but is a structural component in the bacteria which is released mainly when bacteria are lysed.

Encephalocele protrusion of brain tissue through a congenital fissure in the skull.

Enema liquid injected into the rectum either as a purgative or medicine, Also called clyster.

Enophthalmos a condition in which the eye falls back into the socket and inhibits proper eyelid function.

Enteral term used to describe the intestines or other parts of the digestive tract.

Enteral administration involves the esophagus, stomach, and small and large intestines (i.e., the gastrointestinal tract).

Enteritis refers to inflammation of the small intestine.

Enterocolic disorder inflamed bowel disease.

Enterocytes tall columnar cells in the small intestinal mucosa that are responsible for the final digestion and absorption of nutrients.

Enterohemorrhagic causing bloody diarrhea and colitis, said of pathogenic microorganisms.

Enterohepatonephropathy hepatorenal lesions accompanied by renal failure.

Enterolactone a lignin formed by the action of intestinal bacteria on lignan precursors found in plants; acts as a phytoestrogen.

Enteropooling increased fluids and electrolytes within the lumen of the intestines due to increased levels of prostaglandins.

Enterotoxigenic of or being an organism containing or producing an enterotoxin.

Enterotoxin is a protein toxin released by a microorganism in the intestine.

Entheogen a substance taken to induce a spiritual experience.

Enuresis bed-wetting, a disorder of elimination that involves the voluntary or involuntary release of urine into bedding, clothing, or other inappropriate places.

Envenomation is the entry of venom into a person's body, and it may cause localised or systemic poisoning.

Eosinophilia the state of having a high concentration of eosinophils (eosinophil granulocytes) in the blood.

Eosinophils (or, less commonly, acidophils), are white blood cells that are one of the immune system components.

Epididymis a structure within the scrotum attached to the backside of the testis and whose coiled duct provides storage, transit and maturation of spermatozoa.

Epididymitis a medical condition in which there is inflammation of the epididymis.

Epigastralgia pain in the epigastric region.

Epigastric discomfort bloated abdomen, swelling of abdomen, abdominal distension.

Epilepsy a common chronic neurological disorder that is characterized by recurrent unprovoked seizures.

Epileptiform resembling epilepsy or its manifestations. *adj*. epileptiformic.

Epileptogenesis a process by which a normal brain develops epilepsy, a chronic condition in which seizures occur. *adj*. epileptogenic.

Episiotomy a surgical incision through the perineum made to enlarge the vagina and assist childbirth.

Epithelioma a usually benign skin disease most commonly occurring on the face, around the eyelids and on the scalp.

Epitope a single antigenic site on a protein against which an antibody reacts.

Epitrochlearis the superficial-most muscle of the arm anterior surface.

Epistaxis acute hemorrhage from the nostril, nasal cavity, or nasopharynx (nose-bleed).

Epstein Barr Virus herpes virus that is the causative agent of infectious mononucleosis. It is also associated with various types of human cancers.

ERbeta estrogen receptor beta, a nuclear receptor which is activated by the sex hormone, estrogen.

Ergocalciferol a form of vitamin D, also called vitamin D2. See vitamin D.

Ergonic increasing capacity for bodily or mental labor especially by eliminating fatigue symptoms.

ERK (extracellular signal regulated kinases) widely expressed protein kinase intracellular signaling molecules which are involved in functions including the regulation of meiosis, mitosis, and post mitotic functions in differentiated cells.

Eructation the act of belching or of casting up wind from the stomach through the mouth.

Eruption a visible rash or cutaneous disruption.

Erysipelas is an intensely red *Streptococcus* bacterial infection that occurs on the face and lower extremities.

Erythema abnormal redness and inflammation of the skin, due to vasodilation.

Erythema multiforme is a skin disorder due to an allergic reaction or infection; characterised by fever, general ill feeling, skin itching, joint aches, and multiple skin lesions.

Erythematous characterized by erythema.

Erythroleukoplakia an abnormal patch of red and white tissue that forms on mucous membranes in the mouth and may become cancer. Tobacco (smoking and chewing) and alcohol may increase the risk of erythroleukoplakia.

Erythropoietin (EPO) a hormone produced by the kidney that promotes the formation of red blood cells (erythrocytes) in the bone marrow.

Eschar a slough or piece of dead tissue that is cast off from the surface of the skin.

Escharotic capable of producing an eschar; a caustic or corrosive agent.

Estradiol is the predominant sex hormone present in females, also called oestradiol.

Estrogen female hormone produced by the ovaries that play an important role in the estrous cycle in women.

Estrogen receptor (ER) is a protein found in high concentrations in the cytoplasm of breast, uterus, hypothalamus, and anterior hypophysis cells; ER levels are measured to determine a breast CA's potential for response to hormonal manipulation.

Estrogen receptor positive (ER+) means that estrogen is causing the tumour to grow, and that the breast cancer should respond well to hormone suppression treatments.

Estrogen receptor negative (ER-) tumour is not driven by estrogen and need another test to determine the most effective treatment.

Estrogenic relating to estrogen or producing estrus.

Estrus sexual excitement or heat of female; or period of this characterized by changes in the sex organs.

Euglycaemia normal blood glucose concentration.

Eupeptic conducive to digestion.

Exanthematous characterized by or of the nature of an eruption or rash.

Excitotoxicity is the pathological process by which neurons are damaged and killed by glutamate and similar substances.

Excipient a pharmacologically inert substance used as a diluent or vehicle for the active ingredients of a medication.

Exocytosis the cellular process by which cells excrete waste products or chemical transmitters.

Exophthalmos or exophthalmia or proptosis is a bulging of the eye anteriorly out of the orbit. *adj*. exophthalmic.

Exotoxin a toxin secreted by a microorganism and released into the medium in which it grows.

Expectorant an agent that increases bronchial mucous secretion by promoting liquefaction of the sticky mucous and expelling it from the body.

Exteroceptive responsiveness to stimuli that are external to an organism.

Extrapyramidal side effects are a group of symptoms (tremor, slurred speech, akathisia, dystonia, anxiety, paranoia and bradyphrenia) that can occur in persons taking antipsychotic medications.

Extravasation discharge or escape, as of blood from the vein into the surrounding tissues; discharge or escape from a vessel or channel.

Fabry disease is a rare X-linked (inherited) lysosomal storage disease caused by alpha-galactosidase A deficiency, which can cause a wide range of systemic symptoms such as pain in the extremities, papules on the lower body parts, cornea clouding, fatigue, neuropathy, renal and cardiac complications.

FAC chemotherapy fluorouracil, doxorubicin (adriamycin), and cyclophosphamide chemotherapy.

FADD Fas-associated protein with death domain, the protein encoded by this gene is an adaptor molecule which interacts with other death cell surface receptors and mediates apoptotic signals.

Familial amyloid polyneuropathy (FAP) also called Corino de Andrade's disease, a neurodegenerative autosomal dominant genetically transmitted, fatal, incurable disease.

Familial adenomatous polyposis (FAP) is an inherited condition in which numerous polyps form mainly in the epithelium of the large intestine.

Familial dysautonomia a genetic disorder that affects the development and survival of autonomic and sensory nerve cells.

Fanconi syndrome is a disease of the proximal renal tubes which certain substances normally absorbed into the bloodstream by the kidneys are released into the urine instead.

FasL or CD95L Fas ligand is a type-II transmembrane protein that belongs to the tumour necrosis factor (TNF) family.

FAS: fatty acid synthase (FAS) a multi-enzyme that plays a key role in fatty acid synthesis.

Fas molecule a member of the Tumour Necrosis Factor Receptors, that mediates apoptotic signal in many cell types.

Fauces the passage leading from the back of the mouth into the pharynx.

Favus a chronic skin infection, usually of the scalp, caused by the fungus, *Trichophyton schoenleinii* and characterized by the development of thick, yellow crusts over the hair follicles. Also termed tinea favosa.

Febrifuge an agent that reduces fever. Also called an antipyretic.

Febrile pertaining to or characterized by fever.

Febrile neutropenia the development of fever, often with other signs of infection, in an individual with neutropenia, an abnormally low number of neutrophil granulocytes in the blood.

Fetotoxic toxic to the fetus.

Fibrates hypolipidemic agents primarily used for decreasing serum triglycerides, while increasing High density lipoprotein (HDL).

Fibril a small slender fibre or filament.

Fibrin insoluble protein that forms the essential portion of the blood clot.

Fibrinolysis a normal ongoing process that dissolves fibrin and results in the removal of small blood clots.

Fribinolytic causing the dissolution of fibrin by enzymatic action.

Fibroblast type of cell that synthesizes the extracellular matrix and collagen, the structural framework (stroma) for animal tissues, and play a critical role in wound healing.

Fibrogenic promoting the development of fibres.

Fibromyalgia a common and complex chronic, body-wide pain disorder that affects people physically, mentally and socially. Symptoms include debilitating fatigue, sleep disturbance, and joint stiffness. Also referred to as FM or FMS.

Fibronectin a high-molecular weight (~440 kDa) glycoprotein of the extracellular matrix (ECM) that adheres to membrane-spanning receptor proteins called integrins.

Fibrosarcoma a malignant tumour derived from fibrous connective tissue and characterized by immature proliferating fibroblasts or undifferentiated anaplastic spindle cells.

Fibrosis the formation of fibrous tissue as a reparative or reactive process.

Filarial pertaining to a thread-like nematode worm.

Filariasis a parasitic and infectious tropical disease that is caused by thread-like filarial nematode worms in the superfamily Filarioidea.

Fistula an abnormal connection between two parts inside of the body.

Fistula-in-ano a track connecting the internal anal canal to the skin surrounding the anal orifice.

5′-Nucleotidase (5′-ribonucleotide phosphohydrolase), an intrinsic membrane glycoprotein present as an ectoenzyme in a wide variety of mammalian cells, hydrolyzes 5′-nucleotides to their corresponding nucleosides.

Flatulence is the presence of a mixture of gases known as flatus in the digestive tract of mammals expelled from the rectum. Excessive flatulence can be caused by lactose intolerance, certain foods or a sudden switch to a high fibre.

Flavans a subgroup of flavonoids. See flavonoids.

Flavanols a subgroup of flavonoids, are a class of flavonoids that use the 2-phenyl-3,4-dihydro-2H-chromen-3-ol skeleton. These compounds include the catechins and the catechin

gallates. They are found in chocolate, fruits and vegetables. See flavonoids.

Flavanones a subgroup of flavonoids, constitute >90% of total flavonoids in citrus. The major dietary flavanones are hesperetin, naringenin and eriodictyol.

Flavivirus A family of viruses transmitted by mosquitoes and ticks that cause some important diseases, including dengue, yellow fever, tick-borne encephalitis and West Nile fever.

Flavones a subgroup of flavonoids based on the backbone of 2-phenylchromen-4-one (2-phenyl-1-benzopyran-4-one). Flavones are mainly found in cereals and herbs.

Flavonoids (or bioflavonoids) are a group of polyphenolic antioxidant compounds in that are occur in plant as secondary metabolites. They are responsible for the colour of fruit and vegetables. Twelve basic classes (chemical types) of flavonoids have been recognized: flavones, isoflavones, flavans, flavanones, flavanols, flavanolols, anthocyanidins, catechins (including proanthocyanidins), leukoanthocyanidins, chalcones, dihydrochalcones, and aurones. Apart from their antioxidant activity, flavonoids are known for their ability to strengthen capillary walls, thus assisting circulation and helping to prevent and treat bruising, varicose veins, bleeding gums and nosebleeds, heavy menstrual bleeding and are also anti-inflammatory.

Flourine F is an essential chemical element that is required for maintenance of healthy bones and teeth and to reduce tooth decay. It is found in sea weeds, tea, water, seafood and dairy products.

Fluorosis a dental health condition caused by a child receiving too much fluoride during tooth development.

Flux an excessive discharge of fluid.

FMD (Flow Mediated Dilation) a measure of endothelial dysfunction which is used to evaluate cardiovascular risk.

Focal adhesion kinase (FAK) is a protein tyrosine kinase which is recruited at an early stage to focal adhesions and which mediates many of the downstream regulatory responses.

Follicle stimulating hormone (FSH) a hormone produced by the pituitary gland. In women, it helps control the menstrual cycle and the production of eggs by the ovaries.

Follicular atresia the break-down of the ovarian follicles.

Fomentation treatment by the application of war, moist substance.

Fontanelle soft spot on an infant's skull.

Forkhead box-O transcription factors (FOXOs) are a family of transcription factors that play important roles in regulating the expression of genes involved in cell growth, proliferation, differentiation, and longevity. It also play an important role in tumour suppression by regulating the expression of genes involved in stress resistance, DNA damage repair, cell cycle arrest and apoptosis.

Framboesia see yaws.

FRAP ferric reducing ability of plasma, an assay used to assess antioxidant property.

Friedreich's ataxia is a genetic inherited disorder that causes progressive damage to the nervous system resulting in symptoms ranging from muscle weakness and speech problems to heart disease. *cf.* ataxia.

Fulminant hepatitis acute liver failure.

Functional Dyspepsia a non-ulcer condition that causes an upset stomach or pain or discomfort in the upper belly, near the ribs.

Functional food is any fresh or processed food claimed to have a health-promoting or disease-preventing property beyond the basic function of supplying nutrients. Also called medicinal food.

Furuncle is a skin disease caused by the infection of hair follicles usually caused by *Staphylococcus aureus*, resulting in the localized accumulation of pus and dead tissue.

Furunculosis skin condition characterized by persistent, recurring boils.

GABA gamma aminobutyric acid, required as an inhibitory neurotransmitter to block the transmission of an impulse from one cell to another in the central nervous system, which prevents over-firing of the nerve cells. It is used to treat both epilepsy and hypertension.

GADD 152 a pro-apoptotic gene.

Galctifuge or lactifuge, casuing the arrest of milk secretion.

Galactogogue a substance that promotes the flow of milk.

Galactophoritis inflammation of the milk ducts.

Galactopoietic increasing the flow of milk; milk-producing.

Gall baldder a small, pear-shaped muscular sac, located under the right lobe of the liver, in which bile secreted by the liver is stored until needed by the body for digestion. Also called cholecyst, cholecystis.

Gallic Acid Equivalent (GAE) measures the total phenol content in terms of the standard Gallic acid by the Folin-Ciocalteau assay.

Galphai proteins or G alpha I proteins are heterotrimeric guanine nucleotide-regulatory (G) proteins associated with a variety of intracellular membranes and specific plasma membrane domains.

Gamma GT (GGT) Gamma-glutamyl transpeptidase, a liver enzyme.

Gastralgia (heart burn) – pain in the stomach or abdominal region. It is caused by excess of acid, or an accumulation of gas, in the stomach.

Gastric pertaining to or affecting the stomach.

Gastric emptying refers to the speed at which food and drink leave the stomach.

Gastritis inflammation of the stomach.

Gastrocnemius muscle the big calf muscle at the rear of the lower leg.

Gastrotonic (Gastroprotective) substance that strengthens, tones, or regulates gastric functions (or protects from injury) without overt stimulation or depression.

Gavage forced feeding.

Gene silencing suppression of the expression of a gene.

Genotoxic describes a poisonous substance which harms an organism by damaging its DNA thereby capable of causing mutations or cancer.

Genotoxin a chemical or other agent that damages cellular DNA, resulting in mutations or cancer.

Geriatrics is a sub-specialty of internal medicine that focuses on health care of elderly people.

Gestational hypertension development of arterial hypertension in a pregnant woman after 20 weeks gestation.

Ghrelin a gastrointestinal peptide hormone secreted by epithelial cells in the stomach lining, it stimulates appetite, gastric emptying, and increases cardiac output.

Gingival Index an index describing the clinical severity of gingival inflammation as well as its location.

Gingivitis refers to gingival inflammation induced by bacterial biofilms (also called plaque) adherent to tooth surfaces.

Gin-nan sitotoxism toxicity caused by ingestion of ginkgotoxin and characterised mainly by epileptic convulsions, paralysis of the legs and loss of consciousness.

GIP gastric inhibitory polypeptide also known as the glucose-dependent insulinotropic peptide, a member of the secretin family of hormones.

Glaucoma a group of eye diseases in which the optic nerve at the back of the eye is slowly destroyed, leading to impaired vision and blindness.

Gleet a chronic inflammation (as gonorrhea) of a bodily orifice usually accompanied by an abnormal discharge.

Glial cells support, non-neuronal cells in the central nervous system that maintain homeostasis, form myelin and provide protection for the brain's neurons.

Glioma is a type of tumour that starts in the brain or spine. It is called a glioma because it arises from glial cells.

Glioblastoma common and most lethal form of brain tumor.

Glioblastoma multiforme most common and most aggressive type of primary brain tumour in humans, involving glial cells.

Glomerulonephritis (GN) a renal disease characterized by inflammation of the glomeruli, or small blood vessels in the kidneys. Also known as glomerular nephritis. *adj*. glomerulonephritic.

Glomerulosclerosis a hardening (fibrosis) of the glomerulus in the kidney.

Glossal pertaining to the tongue.

GLP-1 glucagon-like peptide-1.

Glucagon-like peptide-1 (GLP-1) is derived from the transcription product of the proglucagon gene, reduces insulin requirement in diabetes mellitus and promotes satiety.

Gluconeogenesis a metabolic pathway that results in the generation of glucose from non-carbohydrate carbon substrates such as lactate. *adj*. gluconeogenic.

Glucose transporter type 4 (GLUT 4) insulin-regulated glucose transporter found in adipose tissues and striated muscles that modulates insulin-related translocation into the cell.

Glucose transporters (GLUT or SLC2A family) are a family of membrane proteins found in most mammalian cells.

Glucosuria or glycosuria is the excretion of glucose into the urine.

Glucosyltranferase an enzyme that enable the transfer of glucose.

Glucuronidation a phase II detoxification pathway occurring in the liver in which glucuronic acid is conjugated with toxins.

Glutamic Oxaloacetate Transaminase (GOT) catalyzes the transfer of an amino group from an amino acid (Glu) to a 2-keto-acid to generate a new amino acid and the residual 2-keto-acid of the donor amino acid.

Glutamic pyruvate transaminase (GPT) see Alanine aminotransferase.

Glutathione (GSH) a tripeptide produced in the human liver and plays a key role in intermediary metabolism, immune response and health. It plays an important role in scavenging free radicals and protects cells against several toxic oxygen-derived chemical species.

Glutathione peroxidase (GPX) the general name of an enzyme family with peroxidase activity whose main biological role is to protect the organism from oxidative damage.

Glutathione S-transferase (GST) a major group of detoxification enzymes that participate in the detoxification of reactive electrophilic compounds by catalysing their conjugation to glutathione.

Glycaemic index (GI) measures carbohydrates according to how quickly they are absorbed and raise the glucose level of the blood.

Glycaemic load (GL) is a ranking system for carbohydrate content in food portions based on their glycaemic index and the amount of available carbohydrate, i.e. GI × available carbohydrate divided by 100. Glycemic load combines both the quality and quantity of carbohydrate in one 'number'. It's the best way to predict blood glucose values of different types and amounts of food.

Glycation or glycosylation a chemical reaction in which glycosyl groups are added to a protein to produce a glycoprotein.

Glycogenolysis is the catabolism of glycogen by removal of a glucose monomer through cleavage with inorganic phosphate to produce glucose-1-phosphate.

Glycometabolism metabolism (oxidation) of glucose to produce energy.

Glycosuria or glucosuria is an abnormal condition of osmotic diuresis due to excretion of glucose by the kidneys into the urine.

Glycosylases a family of enzymes involved in base excision repair.

Goitre an enlargement of the thyroid gland leading to swelling of the neck or larynx.

Goitrogen substance that suppresses the function of the thyroid gland by interfering with iodine uptake, causing enlargement of the thyroid, i.e. goiter.

Goitrogenic *adj*. causing goiter.

Gonadotroph a basophilic cell of the anterior pituitary specialized to secrete follicle-stimulating hormone or luteinizing hormone.

Gonatropins protein hormones secreted by gonadotrope cells of the pituitary gland of vertebrates.

Gonorrhoea a common sexually transmitted bacterial infection caused by the bacterium *Neisseria gonorrhoeae*.

Gout a disorder caused by a build-up of a waste product, uric acid, in the bloodstream. Excess uric acid settles in joints causing inflammation, pain and swelling.

G-protein-coupled receptors (GPCRs) constitute the largest family of cell-surface molecules involved in signal transmission. These receptors play key physiological roles and their dysfunction results in several diseases.

Granulation the condition or appearance of being granulated (becoming grain-like).

Gravel sand-like concretions of uric acid, calcium oxalate, and mineral salts formed in the passages of the biliary and urinary tracts.

Gripe water is a home remedy for babies with colic, gas, teething pain or other stomach ailments. Its ingredients vary, and may include alcohol, bicarbonate, ginger, dill, fennel and chamomile.

Grippe an epidemic catarrh; older term for influenza.

GSH see Glutathione.

GSH-Px Glutathione peroxidase, general name of an enzyme family with peroxidase activity whose main biological role is to protect the organism from oxidative damage.

GSSG glutathione disulfides are biologically important intracellular thiols, and alterations in the GSH/GSSG ratio are often used to assess exposure of cells to oxidative stress.

GSTM glutathione S transferase M1, a major group of detoxification enzymes.

GSTM 2 glutathione S transferase M2, a major group of detoxification enzymes.

G2-M cell cycle the phase where the cell prepare for mitosis and where chromatids and daughter cells separate.

Gynecopathy any or various diseases specific to women.

Gynoid adiposity fat distribution mainly to the hips and thighs, pear shaped.

Haemagogic promoting a flow of blood.

Haematemesis, Hematemesis is the vomiting of blood.

Haematinic improving the quality of the blood, its haemoglobin level and the number of erythrocytes.

Haematochezia passage of stools containing blood.

Haematochyluria, hematochyluria the discharge of blood and chyle (emulsified fat) in the urine, see also chyluria.

Haematoma, hematoma a localized accumulation of blood in a tissue or space composed of clotted blood.

Haematometra, hematometra a medical condition involving bleeding of or near the uterus.

Haematopoiesis, hematopoiesis formation of blood cellular components from the haematopoietic stem cells.

Haematopoietic *adj*. relating to the formation and development of blood cells.

Haematuria, Hematuria is the presence of blood in the urine. Hematuria is a sign that something is causing abnormal bleeding in a person's genitourinary tract.

Haeme oxygenase (HO-1, encoded by Hmox1) is an inducible protein activated in systemic inflammatory conditions by oxidant stress, an enzyme that catalyzes degradation of heme.

Haemochromatosis iron overload in the body with a hereditary or primary cause.

Haemodialysis, Hemodialysis a method for removing waste products such as potassium and urea, as well as free water from the blood when the kidneys are in renal failure.

Haemolyis lysis of red blood cells and the release of haemoglobin into the surrounding fluid (plasma). *adj*. haemolytic.

Haemoptysis, hemoptysis is the coughing up of blood from the respiratory tract. The blood can come from the nose, mouth, throat, and the airway passages leading to the lungs.

Haemorrhage, hemaorrhage bleeding, discharge of blood from blood vessels.

Haemorrhoids, Hemorrhoids a painful condition in which the veins around the anus or lower rectum are enlarged, swollen and inflamed. Also called piles.

Haemostasis, hemostasis a complex process which causes the bleeding process to stop.

Haemostatic, hemostatic something that stops bleeding.

Halitosis (bad breath) a common condition caused by sulfur-producing bacteria that live within the surface of the tongue and in the throat.

Hallucinogen drug that produces hallucinogen.

Hallucinogenic inducing hallucinations.

Haplotype a set of alleles of closely linked loci on a chromosome that tend to be inherited together.

Hapten a small molecule that can elicit an immune response only when attached to a large carrier such as a protein.

HATs histone acetyl transferases, enzymes that regulate the acetylation of histones and transcription factors, playing a major role in the growth and differentiation of cells.

HbA1c glycosylated haemoglobin.

HBeAg hepatitis B e antigen.

HBsAg hepatitis B s antigen.

Heartburn burning sensation in the stomach and esophagus caused by excessive acidity of the stomach fluids.

Heat rash any condition aggravated by heat or hot weather such as intertrigo.

Heat Shock Chaperones (HSC) ubiquitous molecules involved in the modulation of protein conformational and complexation states, associated with heat stress or other cellular stress response.

Heat Shock Proteins (HSP) a group of functionally related proteins the expression of which is increased when the cells are exposed to elevated temperatures or other cellular stresses.

Helminthiasis a disease in which a part of the body is infested with worms such as pinworm, roundworm or tapeworm.

Hemagglutination a specific form of agglutination that involves red blood cells.

Hemagglutination–inhibition test measures of the ability of soluble antigen to inhibit the agglutination of antigen-coated red blood cells by antibodies.

Hemagglutinin refers to a substance that causes red blood cells to agglutinate.

Hemangioma blood vessel.

Hematocrit is a blood test that measures the percentage of the volume of whole blood that is made up of red blood cells.

Hematopoietic pertaining to the formation of blood or blood cells.

Hematopoietic stem cell is a cell isolated from the blood or bone marrow that can renew itself, and can differentiate to a variety of specialized cells.

Heme oxygenase-1 (HO-1) an enzyme that catalyses the degradation of heme; an inducible stress protein, confers cytoprotection against oxidative stress in-vitro and in-vivo.

Hemoglobinopathies genetic defects that produce abnormal hemoglobins and anemia.

Hemolytic anemia anemia due to hemolysis, the breakdown of red blood cells in the blood vessels or elsewhere in the body.

Hemorheology study of blood flow and its elements in the circulatory system. *adj*. hemorheological.

Hemorrhagic colitis an acute gasteroenteritis characterized by overtly bloody diarrhea that is caused by *Escherichia coli* infection.

Hemolytic-uremic syndrome is a disease characterized by hemolytic anemia, acute renal failure (uremia) and a low platelet count.

Hepa-1c1c7 a type of hepatoma cells.

Hepatalgia pain or discomfort in the liver area.

Hepatomegaly condition of enlarged liver.

Hepatectomy the surgical removal of part or all of the liver.

Hepatic relating to the liver.

Hepatic cirrhosis affecting the liver, characterize by hepatic fibrosis and regenerative nodules.

Hepatic fibrosis is overly profuse wound healing in which excessive connective tissue builds up in the liver.

Hepatitis inflammation of the liver.

Hepatitis A (formerly known as infectious hepatitis) is an acute infectious disease of the liver caused by the hepatovirus hepatitis A virus.

Hepatocarcinogenesis represents a linear and progressive cancerous process in the liver in which successively more aberrant monoclonal populations of hepatocytes evolve.

Hepatocellular carcinoma (HCC) also called malignant hepatoma, is a primary malignancy (cancer) of the liver.

Hepatocytolysis cytotoxicity (dissolution) of liver cells.

Hepatoma cancer of the liver.

Hepatopathy a disease or disorder of the liver.

Hepatoprotective (liver protector) a substance that helps protect the liver from damage by toxins, chemicals or other disease processes.

Hepatoregenerative a compound that promotes hepatocellular regeneration, repairs and restores liver function to optimum performance.

Hepatotonic (liver tonic) a substance that is tonic to the liver – usually employed to normalize liver enzymes and function.

Hernia occurs when part of an internal organ bulges through a weak area of muscle.

HER- 2 human epidermal growth factor receptor 2, a protein giving higher aggressiveness in breast cancer, also known as ErbB-2, ERBB2.

Herpes a chronic inflammation of the skin or mucous membrane characterized by the development of vesicles on an inflammatory base.

Herpes simplex virus 1 and 2 – (HSV-1 and HSV-2) are two species of the herpes virus family which cause a variety of illnesses/infections in humans such cold sores, chickenpox or varicella, shingles or herpes zoster (VZV), cytomegalovirus (CMV), and various

cancers, and can cause brain inflammation (encephalitis). HSV-1 is commonly associated with herpes outbreaks of the face known as cold sores or fever blisters, whereas HSV-2 is more often associated with genital herpes. They are also called Human Herpes Virus 1 and 2 (HHV-1 and HHV-2) and are neurotropic and neuroinvasive viruses; they enter and hide in the human nervous system, accounting for their durability in the human body.

Herpes zoster or simply zoster, commonly known as shingles and also known as zona, is a viral disease characterized by a painful skin rash with blisters.

Herpes Zoster Ophthalmicus (HZO) is a viral ocular disease characterized by a painful skin rash in one or more dermatome distributions of the fifth cranial nerve, shared by the eye and orbit.

Heterophobia term used to describe irrational fear of, aversion to, or discrimination against heterosexuals.

HDL-C (HDL Cholesterol) high density lipoprotein-cholesterol, also called "good cholesterol". See also high-density lipoprotein.

Hiatus hernia occurs when the upper part of the stomach pushes its way through a tear in the diaphragm.

High-density lipoprotein (HDL) is one of the five major groups of lipoproteins which enable cholesterol and triglycerides to be transported within the water based blood stream. HDL can remove cholesterol from atheroma within arteries and transport it back to the liver for excretion or re-utilization—which is the main reason why HDL-bound cholesterol is sometimes called "good cholesterol", or HDL-C. A high level of HDL-C seems to protect against cardiovascular diseases. cf. LDL.

HGPRT, HPRT (hypoxanthine-guanine phosphoribosyl transferase) an enzyme that catalyzes the conversion of 5-phosphoribosyl-1-pyrophosphate and hypoxanthine, guanine, or 6-mercaptopurine to the corresponding 5′-mononucleotides and pyrophosphate. The enzyme is important in purine biosynthesis as well as central nervous system functions.

Hippocampus a ridge in the floor of each lateral ventricle of the brain that consists mainly of gray matter.

Hippocampal pertaining to the hippocampus.

Hirsutism a condition where women have excess facial and body hair that is dark and coarse.

Histaminergic liberated or activated by histamine, relating to the effects of histamine at histamine receptors of target tissues.

Histaminergic receptors are types of G-protein coupled receptors with histamine as their endogenous ligand.

HIV see Human immunodeficiency virus.

Hives (urticaria) is a skin rash characterised by circular wheals of reddened and itching skin.

HLA human leukocyte antigen system, name of the major histocompatibility complex (MHC) in humans.

HLA-DQB1 human leucocyte antigen beta chain.

HLA-DR a major histocompatibility complex (MHC) class II cell surface receptor encoded by the human leukocyte antigen complex on chromosome 6 region 6p21.31.

HMG-CoAr 3-hydroxy-3-methyl-glutaryl-CoA reductase or (HMGCR) is the rate-controlling enzyme (EC 1.1.1.88) of the mevalonate pathway.

HMG-CoA 3-hydroxy-3-methylglutaryl-coenzyme A, an intermediate in the mevalonate pathway .

Hodgkin's disease disease characterized by enlargement of the lymph glands, spleen and anemia.

Homeodomain transcription factor a protein domain encoded by a homeobox. Homeobox genes encode transcription factors which typically switch on cascades of other genes.

Homeostasis the maintenance of a constant internal environment of a cell or an organism, despite fluctuations in the external.

Homeotherapy treatment or prevention of disease with a substance similar but not identical to the causative agent of the disease.

Homocysteine an amino acid in the blood.

Homograft see allograft.

Hormonal (female) substance that has a hormone-like effect similar to that of estrogen and/or a substance used to normalize female hormone levels.

Hormonal (male) substance that has a hormone-like effect similar to that of testosterone and/or

a substance used to normalize male hormone levels.

HRT hormone replacement therapy, the administration of the female hormones, oestrogen and progesterone, and sometimes testosterone.

HSP27 is an ATP-independent, 27 kDa heat shock protein chaperone that confers protection against apoptosis.

HSP90 a 90 kDa heat shock protein chaperone that has the ability to regulate a specific subset of cellular signaling proteins that have been implicated in disease processes.

hTERT – (TERT) telomerase reverse transcriptase is a catalytic subunit of the enzyme telomerase in humans. It exerts a novel protective function by binding to mitochondrial DNA, increasing respiratory chain activity and protecting against oxidative stress–induced damage.

HT29 cells are human intestinal epithelial cells which produce the secretory component of Immunoglobulin A (IgA), and carcinoembryonic antigen (CEA).

Human cytomegalovirus (HCMV) a DNA herpes virus which is the leading cause of congenital viral infection and mental retardation.

Human factor X a coagulation factor also known by the eponym Stuart-Prower factor or as thrombokinase, is an enzyme involved in blood coagulation. It synthesized in the liver and requires vitamin K for its synthesis.

Human immunodeficiency virus (HIV) a retrovirus that can lead to acquired immunodeficiency syndrome (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections.

Humoral immune response (HIR) is the aspect of immunity that is mediated by secreted antibodies (as opposed to cell-mediated immunity, which involves T lymphocytes) produced in the cells of the B lymphocyte lineage (B cell).

HUVEC human umbilical vein endothelial cells.

Hyaluronidase enzymes that catalyse the hydrolysis of certain complex carbohydrates like hyaluronic acid and chondroitin sulfates.

Hydatidiform a rare mass or growth that forms inside the uterus at the beginning of a pregnancy.

Hydrocholeretic an agent that stimulates an increased output of bile of low specific gravity.

Hydrogogue a purgative that causes an abundant watery discharge from the bowel.

Hydronephrosis is distension and dilation of the renal pelvis and calyces, usually caused by obstruction of the free flow of urine from the kidney.

Hydrophobia a viral neuroinvasive disease that causes acute encephalitis (inflammation of the brain) in warm-blooded animals. Also called rabies.

Hydropsy see dropsy.

Hydrothorax accumulation of serous fluid in the pleural cavity.

Hyperaemia the increase of blood flow to different tissues in the body.

Hyperalgesia an increased sensitivity to pain (enhanced pricking pain), which may be caused by damage to nociceptors or peripheral nerves.

Hyperammonemia, hyperammonaemia a metabolic disturbance characterised by an excess of ammonia in the blood.

Hypercalciuria (*Idiopathic***)** presence of excess calcium in the urine without obvious cause.

Hypercholesterolemia high levels of cholesterol in the blood that increase a person's risk for cardiovascular disease leading to stroke or heart attack.

Hyperemia is the increased blood flow that occurs when tissue is active.

Hyperemesis severe and persistent nausea and vomiting (morning sickness) during pregnancy.

Hyperfibrinogenemia excessive fibrinogen in the blood.

Hyperglycaemia hyperglycemic high blood sugar; is a condition in which an excessive amount of glucose circulates in the blood plasma.

Hyperglycemic a substance that raises blood sugar levels.

Hyperhomocysteinemia is a medical condition characterized by an abnormally large level of homocysteine in the blood.

Hyperinsulinemia a condition in which there are excess levels of circulating insulin in the blood; also known as pre-diabetes.

Hyperkalemia is an elevated blood level of the electrolyte potassium.

Hyperknesis enhanced itch to pricking.

Hyperleptinemia increased serum leptin level.

Hyperlipoproteinemia a metabolic disorder characterized by abnormally elevated concentrations of lipid/lipoprotein in the plasma; also known as hyperlipidemia and hyperlipemia

Hypermethylation an increase in the inherited methylation of cytosine and adenosine residues in DNA.

Hyperphagia or polyphagia abnormally large ingestion of food beyond that needed for basic energy requirements.

Hyperpiesia persistent and pathological high blood pressure for which no specific cause can be found.

Hyperplasia increased cell production in a normal tissue or organ.

Hyperprebeta-lipoproteinaemia increased concentrations of pre-beta-lipoproteins in the blood

Hyperpropulsion using water pressure as a force to move objects; used to dislodge calculi in the urethra.

Hyperpyrexia is an abnormally high fever.

Hypertension commonly referred to as "high blood pressure" or HTN, is a medical condition in which the arterial blood pressure is chronically elevated.

Hypertensive characterized or caused by increased tension or pressure as abnormally high blood pressure.

Hypertonia abnormal increase inmuscle tension and a reduced ability of the nuscel to stretch.

Hypertriglyceridaemia or hypertriglycemia a disorder that causes high triglycerides in the blood.

Hypertrophy enlargement or overgrowth of an organ.

Hyperuricemia is a condition characterized by abnormally high level of uric acid in the blood.

Hypoadiponectinemia the state of having too low level of adiponectin, a major metabolic endocrine, responsible for regulating things like glucose uptake and lipolysis (the breakdown of fat deposits); low adiponectin, is a risk factor for both Type II Diabetes and metabolic syndrome.

Hypoalbuminemia a medical condition where levels of albumin in blood serum are abnormally low.

Hypocalcemic tetany a disease caused by an abnormally low level of calcium in the blood and characterized by hyperexcitability of the neuromuscular system and results in carpopedal spasms.

Hypochlorhydria refer to states where the production of gastric acid in the stomach is absent or low.

Hypocholesterolemic (cholesterol-reducer), a substance that lowers blood cholesterol levels.

Hypocitraturia low amount of citrate in the urine, an important risk factor for kidney stone formation.

Hypocorticism see Addison's disease.

Hypocortisolism see Addison's disease.

Hypoesthesia (or hypesthesia) refers to a reduced sense of touch or sensation, or a partial loss of sensitivity to sensory stimuli.

Hypoglycemic an agent that lowers the concentration of glucose (sugar) in the blood.

Hypoperfusion decreased blood flow through an organ, characterized by an imbalance of oxygen demand and oxygen delivery to tissues.

Hypophagic under-eating.

Hypospadias an abnormal birth defect in males in which the urethra opens on the under surface of the penis.

Hypotensive characterised by or causing diminished tension or pressure, as abnormally low blood pressure.

Hypothermia a condition in which an organism's temperature drops below that required for normal metabolism and body functions.

Hypothermic relating to hypothermia, with subnormal body temperature.

Hypoxaemia is the reduction of oxygen specifically in the blood.

Hypoxia a shortage of oxygen in the body. *adj*. hypoxic.

ICAM-1 (Inter-Cellular Adhesion Molecule 1) also known as CD54 (Cluster of Differentiation 54), is a protein that in humans is encoded by the ICAM1 gene.

IC_{50} the median maximal inhibitory concentration; a measure of the effectiveness of a compound in inhibiting biological or biochemical function.

I.C.V. (intra-cerebroventricular) injection of chemical into the right lateral ventricle of the brain.

Iceterus jaundice, yellowish pigmentation of the skin.

Ichthyotoxic a substance which is poisonous to fish.

Icteric hepatitis an infectious syndrome of hepatitis characterized by jaundice, nausea, fever, right-upper quadrant pain, enlarged liver and transaminitis (increase in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST)).

Icterus neonatorum jaundice in newborn infants.

Idiopathic of no apparent physical cause.

Idiopathic sudden sensorineural hearing loss (ISSHL) is sudden hearing loss where clinical assessment fails to reveal a cause.

I.g. gastric intubation, insertion of Levin tube through the nasal passage to the stomach.

IgE Immunoglobin E - a class of antibody that plays a role in allergy.

IGFs insulin-like growth factors, polypeptides with high sequence similarity to insulin.

IgG Immunoglobin G – the most abundant immunoglobin (antibody) and is one of the major activators of the complement pathway.

IgM Immunoglobin M - primary antibody against A and B antigens on red blood cells.

IKAP is a scaffold protein of the IvarKappaBeta kinase complex and a regulator for kinases involved in pro-inflammatory cytokine signaling.

IKappa B or IkB-beta, a protein of the NF-Kappa-B inhibitor family.

Ileus a temporary disruption of intestinal peristalsis due to non-mechanical causes.

Immune modulator a substance that affects or modulates the functioning of the immune system.

Immunodeficiency a state in which the immune system's ability to fight infectious disease is compromised or entirely absent.

Immunogenicity the property enabling a substance to provoke an immune response, *adj*. immunogenic.

Immunoglobulin class switching Ig class switching a biological mechanism that changes a B cell's production of antibody from one class to another.

Immunomodulatory capable of modifying or regulating one or more immune functions.

Immunoreactive reacting to particular antigens or haptens.

Immunostimulant agent that stimulates an immune response.

Immunosuppression involves a process that reduces the activation or efficacy of the immune system.

Immunotoxin a man-made protein that consists of a targeting portion linked to a toxin.

Impaired glucose tolerance (IGT) a pre-diabetic state of dysglycemia associated with insulin resistance, increased risk of cardiovascular pathology and also a risk factor for mortality.

Impetigo a contagious, bacterial skin infection characterized by blisters that may itch, caused by a *Streptococcus* bacterium or *Staphylococcus aureus* and mostly seen in children.

Impotence a sexual dysfunction characterized by the inability to develop or maintain an erection of the penis.

Incontinence (fecal) the inability to control bowel's movement.

Incontinence (Urine) the inability to control urine excretion.

Incretin a group of gastrointestinal hormones that cause an increase in the amount of insulin released from the beta cells of the islets of Langerhans after a meal; members include GIP and GLP-1.

Index of structural atypia (ISA) index of structural abnormality.

Induration hardened, as a soft tissue that becomes extremely firm, sclerosis.

Infarct an area of living tissue that undergoes necrosis as a result of obstruction of local blood supply.

Infarction is the process of tissue death (necrosis) caused by blockage of the tissue's blood supply.

Inflammation a protective response of the body to infection, irritation or other injury, aimed at destroying or isolating the injuries and characterized by redness, pain, warmth and swelling.

Influenza a viral infection that affects mainly the nose, throat, bronchi and occasionally, lungs.

Infusion a liquid extract obtained by steeping something (e.g. herbs) that are more volatile or dissolve readily in water, to release their active ingredients without boiling.

Inguinal hernia a hernia into the inguinal canal of the groin.

Inhalant a medicinal substance that is administered as a vapor into the upper respiratory passages.

iNOS, inducible nitric oxide synthases through its product, nitric oxide (NO), may contribute to the induction of germ cell apoptosis. It plays a crucial role in early sepsis-related microcirculatory dysfunction.

Inotropic affecting the force of muscle contraction.

Insecticide an agent that destroys insects. *adj*. insecticidal.

Insomnia a sleeping disorder characterized by the inability to fall asleep and/or the inability to remain asleep for a reasonable amount of time.

Insulin a peptide hormone composed of 51 amino acids produced in the islets of Langerhans in the pancreas causes cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle. Insulin deficiency is often the cause of diabetes and exogenous insulin is used to control diabetes.

Insulin homeostasis blood sugar regulation.

Insulin-like growth factors (IGFs) polypeptides with high sequence similarity to insulin. They are part of a complex system that cells employ to communicate with their physiologic environment.

Insulin-mimetic to act like insulin.

Insulin resistance a condition where the natural hormone insulin becomes less effective at reducing blood sugars.

Insulinogenic associated with or stimulating the production of insulin.

Insulinotropic stimulating or affecting the production and activity of insulin.

Integrase an enzyme produced by a retrovirus (such as HIV) that enables its genetic material to be integrated into the DNA of the infected cell.

Interferons (IFNs) are natural cell-signaling glycoproteins known as cytokines produced by the cells of the immune system of most vertebrates in response to challenges such as viruses, parasites and tumour cells.

Interleukins a group of naturally occurring proteins and is a subset of a larger group of cellular messenger molecules called cytokines, which are modulators of cellular behavior.

Interleukin-1 (IL-1) a cytokine that could induce fever, control lymphocytes, increase the number of bone marrow cells and cause degeneration of bone joints. Also called endogenous pyrogen, lymphocyte activating factor, haemopoetin-1 and mononuclear cell factor, amongst others that IL-1 is composed of two distinct proteins, now called IL-1α and IL-1β.

Interleukin 1 Beta (IL-1β) a cytokine protein produced by activated macrophages. cytokine is an important mediator of the inflammatory response, and is involved in a variety of cellular activities, including cell proliferation, differentiation, and apoptosis.

Interleukin 2 (IL-2) a type of cytokine immune system signaling molecule that is instrumental in the body's natural response to microbial infection.

Interleukin-2 receptor (IL-2R) a heterotrimeric protein expressed on the surface of certain immune cells, such as lymphocytes, that binds and responds to a cytokine called IL-2.

Interleukin-6 (IL-6) an interleukin that acts as both a pro-inflammatory and anti-inflammatory cytokine.

Interleukin 8 (I- 8) a cytokine produced by macrophages and other cell types such as epithelial cells and is one of the major mediators of the inflammatory response.

Intermediate-density lipoproteins (IDL) is one of the five major groups of lipoproteins (chylomicrons, VLDL, IDL, LDL, and HDL) that enable fats and cholesterol to move within the water-based solution of the bloodstream. IDL is further degraded to form LDL particles and, like LDL, can also promote the growth of atheroma and increase cardiovascular diseases.

Intermittent claudication an aching, crampy, tired, and sometimes burning pain in the legs that comes and goes, caused by peripheral vascular disease. I t usually occurs with walking and disappears after rest.

Interoceptive relating to stimuli arising from within the body.

Interstitium the space between cells in a tissue.

Interstitial pertaining to the interstitium.

Intertrigo an inflammation (rash) caused by microbial infection in skin folds.

Intima innermost layer of an artery or vein.

Intoxicant substance that produce drunkenness or intoxication.

Intracavernosal within the copus cavernsoum, columns of erectile tissues forming the body of the penis.

Intraperitoneal (i.p.) the term used when a chemical is contained within or administered through the peritoneum (the thin, transparent membrane that lines the walls of the abdomen).

Intrathecal (i.t.) through the theca of the spinal cord into the subarachnoid space.

Intromission the act of putting one thing into another.

Intubation refers to the placement of a tube into an external or internal orifice of the body.

Iodine (I) is an essential chemical element that is important for hormone development in the human body. Lack of iodine can lead to an enlarged thyroid gland (goitre) or other iodine deficiency disorders including mental retardation and stunted growth in babies and children. Iodine is found in dairy products, seafood, kelp, seaweeds, eggs, some vegetables and iodized salt.

IP see Intraperitoneal.

IP3R3 (inositol 1,4,5-triphosphate receptor type 3) is an intracellular calcium release channel that mediates calcium release from the endoplasmic reticulum.

Iron (Fe) is essential to most life forms and to normal human physiology. In humans, iron is an essential component of proteins involved in oxygen transport and for haemoglobin. It is also essential for the regulation of cell growth and differentiation. A deficiency of iron limits oxygen delivery to cells, resulting in fatigue, poor work performance, and decreased immunity. Conversely, excess amounts of iron can result in toxicity and even death. Dietary sources include, certain cereals, dark green leafy vegetables, dried fruit, legumes, seafood, poultry and meat.

Ischemia an insufficient supply of blood to an organ, usually due to a blocked artery.

Ischuria retention or suppression of urine.

Isoflavones a subgroup of flavonoids in which the basic structure is a 3-phenyl chromane skeleton. They act as phytoestrogens in mammals. See flavonoids.

Isomers substances that are composed of the same elements in the same proportions and hence have the same molecular formula but differ in properties because of differences in the arrangement of atoms.

Isoprostanes unique prostaglandin-like compounds generated in vivo from the free radical-catalysed peroxidation of essential fatty acids.

Jamu traditional Indonesian herbal medicine.

Jaundice refers to the yellow color of the skin and whites of the eyes caused by excess bilirubin in the blood.

JNK (Jun N-terminal Kinase), also known as Stress Activated Protein Kinase (SAPK), belongs to the family of MAP kinases.

Jurkat cells a line of T lymphocyte cells that are used to study acute T cell leukemia.

KB cell a cell line derived from a human carcinoma of the nasopharynx, used as an assay for antineoplastic (anti-tumour) agents.

Kaliuresis the presence of excess potassium in the urine.

Kallikreins peptidases (enzymes that cleave peptide bonds in proteins), a subgroup of the serine protease family; they liberate kinins from kininogens. Kallikreins are targets of active investigation by drug researchers as possible biomarkers for cancer.

Kaposi sarcoma a cancerous tumour of the connective tissues caused by the huma herpesvirus 8 and is often associated with AIDS.

Kaposi sarcoma herpes virus (KSHV) also known as human herpesvirus-8, is a gamma 2 herpesvirus or rhadinovirus. It plays an important role in the pathogenesis of Kaposi sarcoma (KS), multicentric Castleman disease (MCD) of the plasma cell type, and primary effusion lymphoma and occurs in HIV patients.

Karyolysis dissolution and disintegration of the nucleus when a cell dies.

Karyorrhexis destructive fragmentation of the nucleus of a dying cell whereby its chromatin disintegrates into formless granules.

Keratin a sulphur-containing protein which is a major component in skin, hair, nails, hooves, horns, and teeth.

Keratinocyte is the major constituent of the epidermis, constituting 95% of the cells found there.

Keratinophilic having an affinity for keratin.

Keratitis inflammation of the cornea.

Keratomalacia an eye disorder that leads to a dry cornea.

Kidney stones (calculi) are hardened mineral deposits that form in the kidney.

Kinin is any of various structurally related polypeptides, such as bradykinin, that act locally to induce vasodilation and contraction of smooth muscle.

Kininogen either of two plasma α2-globulins that are kinin precursors.

Ki-67 human protein associated with cell proliferation.

Knockout gene knockout is a genetic technique in which an organism is engineered to carry genes that have been made inoperative.

Kunitz protease inhibitors a type of protein contained in legume seeds which functions as a protease inhibitor.

Kupffer cells are resident macrophages of the liver and play an important role in its normal physiology and homeostasis as well as participating in the acute and chronic responses of the liver to toxic compounds.

L-Dopa (L-3,4-dihydroxyphenylalanine) is an amino acid that is formed in the liver and converted into dopamine in the brain.

Labour process of childbirth involving muscular contractions.

Lacrimation secretion and discharge of tears.

Lactagogue an agent that increases or stimulates milk flow or production. Also called a galactagogue.

Lactate dehydrogenase (LDH) enzyme that catalyzes the conversion of lactate to pyruvate.

Lactation secretion and production of milk.

Lactic acidosis is a condition caused by the buildup of lactic acid in the body. It leads to acidification of the blood (acidosis), and is considered a distinct form of metabolic acidosis.

LAK cell a lymphokine-activated killer cell i.e. a white blood cell that has been stimulated to kill tumour cells.

Laminin a glycoprotein component of connective tissue basement membrane that promotes cell adhesion.

Laparotomy a surgical procedure involving an incision through the abdominal wall to gain access into the abdominal cavity. *adj*. laparotomized .

Larvacidal an agent which kills insect or parasite larva.

Laryngitis is an inflammation of the larynx.

Laxation bowel movement.

Laxatives substances that are used to promote bowel movement.

LC_{50} median lethal concentration, see LC_{50}.

LD_{50} median lethal dose – the dose required to kill half the members of a tested population. Also called LC_{50} (median lethal concentration).

LDL see low-density lipoprotein.

LDL Cholesterol see low-density lipoprotein.

LDL receptor (LDLr) a low-density lipoprotein receptor gene.

Lectins are sugar-binding proteins that are highly specific for their sugar moieties, that agglutinate cells and/or precipitate glycoconjugates. They play a role in biological recognition phenomena involving cells and proteins.

Leishmaniasis a disease caused by protozoan parasites that belong to the genus *Leishmania* and is transmitted by the bite of certain species of sand fly.

Lenitive palliative.

Lenticular opacity also known as or related to cataract.

Leprosy a chronic bacterial disease of the skin and nerves in the hands and feet and, in some cases, the lining of the nose. It is caused by the *Mycobacterium leprae*. Also called Hansen's disease.

Leptin is a 16 kDa protein hormone with important effects in regulating body weight, metabolism and reproductive function.

Lequesne Algofunctional Index is a widespread international instrument (10 questions survey) and recommended by the World Health Organization (WHO) for outcome measurement in hip and knee diseases such as osteoarthritis.

Leucocyte white blood corpuscles, colourless, without haemoglobin that help to combat infection.

Leucoderma a skin abnormality characterized by white spots, bands and patches on the skin; they can also be caused by fungus and tinea. Also see vitiligo.

Leucorrhoea commonly known as whites, refers to a whitish discharge from the female genitals

Leukemia, leukaemia a cancer of the blood or bone marrow and is characterized by an abnormal proliferation (production by multiplication) of blood cells, usually white blood cells (leukocytes).

Leukemogenic relating to leukemia, causing leukemia.

Leukocytopenia abnormal decrease in the number of leukocytes (white blood cells) in the blood.

Leukomyelopathy any diseases involving the white matter of the spinal cord.

Leukopenia a decrease in the number of circulating white blood cells.

Leukoplakia condition characterized by white spots or patches on mucous membranes, especially of the mouth and vulva.

Leukotriene a group of hormones that cause the inflammatory symptoms of hay-fever and asthma.

Luteolysis degeneration of the corpus luteum and ovarian luteinized tissues. adj. luteolytic.

Levarterenol see Norepinephrine.

LexA repressor or Repressor LexA is repressor enzyme that represses SOS response genes coding for DNA polymerases required for repairing DNA damage

Libido sexual urge.

Lichen planus a chronic mucocutaneous disease that affects the skin, tongue, and oral mucosa.

Ligroin a volatile,, inflammable fraction of petroleum, obtained by distillation and used as a solvent.

Limbic system complex set of brain structures, including the hypothalamus, amygdala, hippocampus, anterior thalamic nuclei, septum, limbic cortex and fornix that control various functions such as emotion, behaviour, motivation, memory and olfaction.

Liniment liquid preparation rubbed on skin, used to relieve muscular aches and pains.

Linterized starch starch that has undergone prolonged acid treatment.

Lipodiatic having lipid and lipoprotein lowering property.

Lipodystrophy a medical condition characterized by abnormal or degenerative conditions of the body's adipose tissue.

Lipogenesis is the process by which acetyl-CoA is converted to fats.

Lipolysis is the breakdown of fat stored in fat cells in the body.

Lipooxygenase enzyme that catalyzes the oxidation of polyunsaturated fatty acids to form a peroxide of the acid.

Liposomes artificially prepared vesicles made of lipid bilayer.

Lipotoxicity refers to tissues diseases that may occur when fatty acids spillover in excess of the oxidative needs of those tissues and enhances metabolic flux into harmful pathways of nonoxidative metabolism.

Lipotropic refers to compounds that help catalyse the breakdown of fat during metabolism in the body. e.g. chlorine and lecithin.

Lipoxygenase a family of iron-containing enzymes that catalyse the dioxygenation of polyunsaturated fatty acids in lipids containing a *cis,cis*-1,4-pentadiene structure.

Lithiasis formation of urinary calculi (stones) in the renal system (kidneys, ureters, urinary bladder, urethra) can be of any one of several compositions.

Lithogenic promoting the formation of calculi (stones).

Lithontripic removes stones from kidney, gall bladder.

Liver X receptors nuclear hormones that function as central transcriptional regulators for lipid homeostasis.

Lotion a liquids suspension or dispersion of chemicals for external application to the body.

Lovo cells colon cancer cells.

Low-density lipoprotein (LDL) is a type of lipoprotein that transports cholesterol and triglycerides from the liver to peripheral tissues. High levels of LDL cholesterol can signal medical problems like cardiovascular disease, and it is sometimes called "bad cholesterol".

LRP1 low-density lipoprotein receptor-related protein-1, plays a role in intracellular signaling functions as well as in lipid metabolism.

LTB4 a type of leukotriene, a major metabolite in neutrophil polymorphonuclear leukocytes. It stimulates polymorphonuclear cell function (degranulation, formation of oxygen-centered free radicals, arachidonic acid release, and metabolism). It induces skin inflammation.

Luciferase is a generic name for enzymes commonly used in nature for bioluminescence.

Lumbago is the term used to describe general lower back pain.

Lung abscess necrosis of the pulmonary tissue and formation of cavities containing necrotic debris or fluid caused by microbial infections.

Lusitropic an agent that affects diastolic relaxation.

Lutein a carotenoid, occurs naturally as yellow or orange pigment in some fruits and leafy vegetables. It is one of the two carotenoids contained within the retina of the eye. Within the central macula, zeaxanthin predominates, whereas in the peripheral retina, lutein predominates.Lutein is necessary for good vision and may also help prevent or slow down atherosclerosis, the thickening of arteries, which is a major risk for cardiovascular disease.

Luteinising hormone (LH) a hormone produced by the anterior pituitary gland. In females, it triggers ovulation. In males, it stimulates the production of testosterone to aid sperm maturation.

Luteolysis is the structural and functional degradation of the corpus luteum (CL) that occurs at the end of the luteal phase of both the estrous and menstrual cycles in the absence of pregnancy.

Lymphadenitis-cervical inflammation of the lymph nodes in the neck, usually caused by an infection.

Lymphatitis inflammation of lymph vessels and nodes.

Lymphadenopathy a term meaning "disease of the lymph nodes – lymph node enlargement.

Lymphadenomegaly is the enlargement of the lymph node/nodes.

Lymphoblastic pertaining to the production of lymphocytes.

Lymphocyte a small white blood cell (leucocyte) that plays a large role in defending the body against disease. Lymphocytes are responsible for immune responses. There are two main types of lymphocytes: B cells and T cells. Lymphocytes secrete products (lymphokines) that modulate the functional activities of many other types of cells and are often present at sites of chronic inflammation.

Lymphocyte B cells the B cells make antibodies that attack bacteria and toxins.

Lymphocyte T cells T cells attack body cells themselves when they have been taken over by viruses or have become cancerous.

Lymphoma a type of cancer involving cells of the immune system, called lymphocytes.

Lymphopenia abnormally low number of lymphocytes in the blood.

Lysosomes are small, spherical organelles containing digestive enzymes (acid hydrolases) and other proteases (cathepsins).

Maceration softening or separating of parts by soaking in a liquid.

Macrophage a type of large leukocyte that travels in the blood but can leave the bloodstream and enter tissue; like other leukocytes it protects the body by digesting debris and foreign cells.

Macular degeneration a disease that gradually destroys the macula, the central portion of the retina, reducing central vision.

Macules small circumscribed changes in the color of skin that are neither raised (elevated) nor depressed.

Maculopapular describes a rash characterized by raised, spotted lesions.

Magnesium (Mg) is the fourth most abundant mineral in the body and is essential to good health. It is important for normal muscle and nerve function, steady heart rhythm, immune system, and strong bones. Magnesium also helps regulate blood sugar levels, promotes normal blood pressure, and is known to be involved in energy metabolism and protein synthesis and plays a role in preventing and managing disorders such as hypertension, cardiovascular disease, and diabetes. Dietary sources include legumes (e.g. soya bean and by-products), nuts, whole unrefined grains, fruit (e.g. banana, apricots), okra and green leafy vegetables.

MAK cell macrophage-activated killer cell, activated macrophage that is much more phagocytic than monocytes.

Malaise a feeling of weakness, lethargy or discomfort as of impending illness.

Malaria is an infection of the blood by *Plasmodium* parasite that is carried from person to person by mosquitoes. There are four species of malaria parasites that infect man: *Plasmodium falciparum*, so called 'malignant tertian fever', is the most serious disease, *Plasmodium vivax*, causing a relapsing form of the disease, *Plasmodium malariae*, and *Plasmodium ovale*.

Malassezia a fungal genus (previously known as *Pityrosporum*) classified as yeasts, naturally found on the skin surfaces of many animals including humans. It can cause hypopigmentation on the chest or back if it becomes an opportunistic infection.

Mammaliantargetofrapamycin(mTOR) pathway that regulates mitochondrial oxygen consumption and oxidative capacity.

Mammogram an x-ray of the breast to detect tumours.

Mandibular relating to the mandible, the human jaw bone.

Manganese is an essential element for heath. It is an important constituent of some enzymes and an activator of other enzymes in physiologic processes. Manganese superoxide dismutase (MnSOD) is the principal antioxidant enzyme in the mitochondria. Manganese-activated enzymes play important roles in the metabolism of carbohydrates, amino acids, and cholesterol. Manganese is the preferred cofactor of enzymes called glycosyltransferases which are required for the synthesis of proteoglycans that are needed for the formation of healthy cartilage and bone. Dietary source include whole grains, fruit, legumes (soybean and by-products), green leafy vegetables, beetroot and tea.

MAO activity monoamine oxidase activity.

MAPK (Mitogen-activated protein kinase) these kinases are strongly activated in cells subjected to osmotic stress, UV radiation, disregulated K+ currents, RNA-damaging agents, and a multitude of other stresses, as well as inflammatory cytokines, endotoxin , and withdrawal of a trophic factor . The stress-responsive MAPKs mediate a plethora of cellular responses to such stressful stimuli, including apoptosis and production of inflammatory and immunoregulatory cytokines in diverse cell systems.

Marasmus is one of the 3 forms of serious protein-energy malnutrition.

Mastectomy surgery to remove a breast.

Masticatory a substance chewed to increase salivation. Also called sialogue.

Mastitis a bacterial infection of the breast which usually occurs in breastfeeding mothers.

Matrix metalloproteinases (MMP) a member of a group of enzymes that can break down proteins, such as collagen, that are normally found in the spaces between cells in tissues (i.e., extracellular matrix proteins). Matrix metalloproteinases are involved in wound healing, angiogenesis, and tumour cell metastasis. See also metalloproteinase.

MBC minimum bacterial concentration – the lowest concentration of antibiotic required to kill an organism.

MCP-1 monocyte chemotactic protein-1, plays a role in the recruitment of monocytes to sites of infection and injury. It is a member of small inducible gene (SIG) family.

MDA malondialdehyde is one of the most frequently used indicators of lipid peroxidation.

Measles an acute, highly communicable rash illness due to a virus transmitted by direct contact with infectious droplets or, less commonly, by airborne spread.

Mechanonociceptors sensory neurons that are mechanically sensitive found in all of the paraspinal connective tissues including ligament, joint capsule, annulus fibrosus of the intervertebral disk, muscle, tendon, and skin. They respond to a noxius (damaging) mechanical load.

Medial Preoptic Area is located at the rostral end of the hypothalamus, it is important for the regulation of male sexual behavior.

Megaloblastic anemia an anemia that results from inhibition of DNA synthesis in red blood cell production, often due to a deficiency of vitamin B12 or folate and is characterized by many large immature and dysfunctional red blood cells (megaloblasts) in the bone marrow.

Melaene (melena) refers to the black, "tarry" feces that are associated with gastrointestinal hemorrhage.

Melanogenesis production of melanin by living cells.

Melanoma malignant tumour of melanocytes which are found predominantly in skin but also in the bowel and the eye and appear as pigmented lesions.

Melatonin a hormone produced in the brain by the pineal gland, it is important in the regulation of the circadian rhythms of several biological functions.

Menarche the first menstrual cycle, or first menstrual bleeding, in female human beings.

Menorrhagia heavy or prolonged menstruation, too-frequent menstrual periods.

Menopausal refer to permanent cessation of menstruation.

Menses see menstruation.

Menstruation the approximately monthly discharge of blood from the womb in women of childbearing age who are not pregnant. Also called menses. *adj*. menstrual.

Mesangial cells are specialized cells around blood vessels in the kidneys, at the mesangium.

Mesothelioma is an aggressive cancer affecting the membrane lining of the lungs and abdomen.

Metabolic syndrome (MetS) represents a combination of cardiometabolic risk factors, including visceral obesity, glucose intolerance or type 2 diabetes, elevated triglycerides, reduced HDL cholesterol, and hypertension.

Metabonome complete set of metabolically regulated elements in cells.

Metalloproteinase enzymes that breakdown proteins and requiring zinc or calcium atoms for proper function.

Metallothionein (MT) a family of cysteine-rich, low molecular weight (500–14,000 Da) proteins.

Meta-analysis a statistical procedure that combines the results of several studies that address a set of related research hypotheses.

Metaphysis is the portion of a long bone between the epiphyses and the diaphysis of the femur.

Metaphyseal pertaining to the metaphysis.

Metaplasia transformation of one type of one mature differentiated cell type into another mature differentiated cell type.

Metastasis is the movement or spreading of cancer cells from one organ or tissue to another.

Metetrus the quiescent period of sexual inactivity between oestrus cycles.

Metroptosis the slipping or falling out of place of an organ (as the uterus)

Metrorrhagia uterine bleeding at irregular intervals, particularly between the expected menstrual periods.

Mevinolin a potent inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase).

MHC acronym for major histocompatibility complex, a large cluster of genes found on the short arm of chromosome 6 in most vertebrates that encodes MHC molecules. MHC molecules play an important role in the immune system and autoimmunity.

MHC 11 molecules Class II MHC molecules belong to a group of molecules known as the Immunoglobulin Supergene Family, which includes immunoglobulins, T-cell receptors, CD4, CD8, and others.

MIC minimum inhibitory concentration – lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism.

Micelle a submicroscopic aggregation of molecules.

Micellization formation process of micelles.

Microangiopathy (or microvascular disease) is an angiopathy affecting small blood vessels in the body

Microfilaria a pre-larval parasitic worm of the family Onchocercidae, found in the vector and in the blood or tissue fluid of human host.

Micronuclei small particles consisting of acentric fragments of chromosomes or entire chromosomes, which lag behind at anaphase of cell division.

Microsomal PGE2 synthase is the enzyme that catalyses the final step in prostaglandin E2 (PGE2) biosynthesis.

Microvasculature the finer vessels of the body, as the arterioles, capillaries, and venules.

Micturition urination, act of urinating.

Migraine a neurological syndrome characterized by altered bodily perceptions, severe, painful headaches, and nausea.

Mimosine is an alkaloid, β-3-hydroxy-4 pyridone amino acid, it is a toxic non-protein free amino acid and is an antinutrient.

Mineral apposition rate MAR, rate of addition of new layers of mineral on the trabecular surfaces of bones.

Miscarriage spontaneous abortion.

Mitochondrial complex I the largest enzyme in the mitochondrial respiratory oxidative phosphorylation system.

Mitochondrial permeability transition (MPT) is an increase in the permeability of the mitochondrial membranes to molecules of less than 1,500 Da in molecular weight. MPT is one of the major causes of cell death in a variety of conditions.

Mitogen an agent that triggers mitosis, elicit all the signals necessary to induce cell proliferation.

Mitogenic able to induce mitosis or transformation.

Mitogenicity process of induction of mitosis.

Mitomycin a chemotherapy drug that is given as a treatment for several different types of cancer, including breast, stomach, oesophagus and bladder cancers.

Mitosis cell division in which the nucleus divides into nuclei containing the same number of chromosomes.

MMP matrix metalloproteinases, a group of peptidases involved in degradation of the extracellular matrix (ECM).

Mnestic pertaining to memory.

Molecular docking is a key tool in structural molecular biology and computer-assisted drug design.

Molluscidal destroying molluscs like snails.

Molt 4 cells MOLT4 cells are lymphoblast-like in morphology and are used for studies of apoptosis, tumour cytotoxicity, tumorigenicity, as well as for antitumour testing.

Molybdenum (Mo) is an essential element that forms part of several enzymes such as xanthine oxidase involved in the oxidation of xanthine to uric acid and use of iron. Molybdenum concentrations also affect protein synthesis, metabolism, and growth. Dietary sources include meat, green beans, eggs, sunflower seeds, wheat flour, lentils, and cereal grain.

Monoamine oxidase A (MAOA) is an isozyme of monoamine oxidase. It preferentially deaminates norepinephrine (noradrenaline), epinephrine (adrenaline), serotonin, and dopamine.

Monoaminergic of or pertaining to neurons that secrete monoamine neurotransmitters (e.g., dopamine, serotonin).

Monoclonal antibodies are produced by fusing single antibody-forming cells to tumour cells grown in culture.

Monocyte large white blood cell that ingest microbes, other cells and foreign matter.

Monogalactosyl diglyceride are the major lipid components of chloroplasts.

Monorrhagia is heavy bleeding and that's usually defined as periods lasting longer than 7 days or excessive bleeding.

Morbidity a diseased state or symptom or can refer either to the incidence rate or to the prevalence rate of a disease.

Morelloflavone a biflavonoid extracted from *Garcinia dulcis*, has shown antioxidative, antiviral, and anti-inflammatory properties.

Morphine the major alkaloid of opium and a potent narcotic analgesic.

MTTP microsomal triglyceride transfer protein that is required for the assembly and secretion of triglyceride -rich lipoproteins from both enterocytes and hepatocytes.

MUC 5 AC mucin 5 AC, a secreted gel-forming protein mucin with a high molecular weight of about 641 kDa.

Mucositis painful inflammation and ulceration of the mucous membranes lining the digestive tract.

Mucous relating to mucus.

Mucolytic capable of reducing the viscosity of mucus, or an agent that so acts.

Mucus viscid secretion of the mucous membrane.

Multidrug resistance (MDR) ability of a living cell to show resistance to a wide variety of structurally and functionally unrelated compounds.

Muscarinic receptors are G protein-coupled acetylcholine receptors found in the plasma membranes of certain neurons and other cells.

Mutagen an agent that induces genetic mutation by causing changes in the DNA.

Mutagenic capable of inducing mutation (used mainly for extracellular factors such as X-rays or chemical pollution).

Myalgia muscle pain.

Myc codes for a protein that binds to the DNA of other genes and is therefore a transcription factor, found on chromosome 8 in human.

Mycosis an infection or disease caused by a fungus.

Myelocyte is a young cell of the granulocytic series, occurring normally in bone marrow, but not in circulating blood.

Myeloid leukaemia (Chronic) a type of cancer that affects the blood and bone marrow, characterized by excessive number of white blood cells.

Myeloma cancer that arise in the plasma cells a type of white blood cells.

Myeloperoxidase (MPO) is a peroxidase enzyme most abundantly present in neutrophil granulocytes (a subtype of white blood cells). It is an inflammatory enzyme produced by activated leukocytes that predicts risk of coronary heart disease.

Myeloproliferative disorder disease of the bone marrow in which excess cells are produced.

Myelosuppressive causing bone marrow suppression.

Myelotoxicity state of being toxic to myeloid tissues, the bone marrow.

Myocardial relating to heart muscles tissues.

Myocardial infarction (MI) is the rapid development of myocardial necrosis caused by a critical imbalance between oxygen supply and demand of the myocardium.

Myocardial ischemia an intermediate condition in coronary artery disease during which the heart tissue is slowly or suddenly starved of oxygen and other nutrients.

Myocardial lipidosis is the accumulation of fat droplets in myocardial fibers.

Myoclonus brief, involuntary twitching of a muscle or a group of muscles.

Myogenesis the formation of muscular tissue, especially during embryonic development.

Myopathy a muscular disease wherein the muscle fibres do not function for any one of many reasons, resulting in muscular weakness.

Myopia near – or short-sightedness.

Myosarcoma a malignant muscle tumour.

Myotonia dystrophica an inherited disorder of the muscles and other body systems characterized by progressive muscle weakness, prolonged muscle contractions (myotonia), clouding of the lens of the eye (cataracts), cardiac abnormalities, balding, and infertility.

Myotube a developing skeletal muscle fiber or cell with a tubular appearance and a centrally located nucleus.

Myringosclerosis also known as tympanosclerosis or intratympanic tympanosclerosis, is a condition caused by calcification of collagen tissues in the tympanic membrane of the middle ear.

Mytonia a symptom of certain neuromuscular disorders characterized by the slow relaxation of the muscles after voluntary contraction or electrical stimulation.

Myotube a developing skeletal muscle fibre with a tubular appearance.

N-nitrosmorpholine a human carcinogen.

N-nitrosoproline an indicator for N-nitrosation of amines.

NADPH The reduced form of nicotinamide adenine dinucleotide phosphate that serves as an electron carrier.

NAFLD Non-alcoholic fatty liver disease.

Narcotic an agent that produces narcosis, in moderate doses it dulls the senses, relieves pain and induces sleep; in excessive dose it cause stupor, coma, convulsions and death.

Nasopharynx upper part of the alimentary continuous with the nasal passages.

Natriorexia excessive intake of sodium evoked by sodium depletion. *adj*. natriorexic, natriorexigenic.

Natriuresis the discharge of excessive large amount of sodium through urine. *adj*. natriuretic.

Natural killer cells (NK cells) a type of cytotoxic lymphocyte that constitute a major component of the innate immune system.

Natural killer T (NKT) cells a heterogeneous group of T cells that share properties of both T cells and natural killer (NK) cells.

Nausea sensation of unease and discomfort in the stomach with an urge to vomit.

Necropsy see autopsy.

Necrosis morphological changes that follow cell death, usually involving nuclear and cytoplasmic changes.

Neointima a new or thickened layer of arterial intima formed especially on a prosthesis or in atherosclerosis by migration and proliferation of cells from the media.

Neonatal *adj*. of or relating to newborn infants or an infant.

Neoplasia abnormal growth of cells, which may lead to a neoplasm, or tumour.

Neoplasm tumour; any new and abnormal growth, specifically one in which cell multiplication is uncontrolled and progressive. Neoplasms may be benign or malignant.

Neoplastic transformation conversion of a tissue with a normal growth pattern into a malignant tumour.

Neovasculature formation of new blood vessels.

Nephrectomised kidneys surgically removed.

Nephrectomy surgical removal of the kidney.

Nephric relating to or connected with a kidney.

Nephrin is a protein necessary for the proper functioning of the renal filtration barrier.

Nephritic syndrome is a collection of signs (known as a syndrome) associated with disorders affecting the kidneys, more specifically glomerular disorders.

Nephritis is inflammation of the kidney.

Nephrolithiasis process of forming a kidney stone in the kidney or lower urinary tract.

Nephropathy a disorder of the kidney.

Nephrotic syndrome nonspecific disorder in which the kidneys are damaged, causing them to leak large amounts of protein from the blood into the urine.

Nephrotoxicity poisonous effect of some substances, both toxic chemicals and medication, on the kidney.

Nerve growth factor (NGF) a small protein that induces the differentiation and survival of particular target neurons (nerve cells).

Nervine a nerve tonic that acts therapeutically upon the nerves, particularly in the sense of a sedative that serves to calm ruffled nerves.

Neural tube defects (NTDs) are common birth defects of the brain and spinal cord.

NEU 4 sialidase this protein belongs to a family of glycohydrolytic enzymes, which remove terminal sialic acid residues from various sialo derivatives, such as glycoproteins, glycolipids, oligosaccharides, and gangliosides.

Neuralgia is a sudden, severe painful disorder of the nerves.

Neuraminidase glycoside hydrolase enzymes that cleaves the glycosidic linkages of neuraminic acids.

Neuraminidase inhibitors a class of antiviral drugs targeted at the influenza viruses whose mode of action consists of blocking the function of the viral neuraminidase protein, thus preventing the virus from reproducing.

Neurasthenia a condition with symptoms of fatigue, anxiety, headache, impotence, neuralgia and impotence.

Neurasthenic a substance used to treat nerve pain and/or weakness (i.e. neuralgia, sciatica, etc.).

Neurite refers to any projection from the cell body of a neuron.

Neuritis an inflammation of the nerve characterized by pain, sensory disturbances and impairment of reflexes. *adj*. neuritic.

Neuritogenesis the first step of neuronal differentiation, takes place as nascent neurites bud from the immediate postmitotic neuronal soma.

Neuroblastoma a common extracranial cancer that forms in nerve tissues, common in infancy.

Neuroendocrine *adj*. of, relating to, or involving the interaction between the nervous system and the hormones of the endocrine glands.

Neurogenesis process by which neurons are generated from neural stem and progenitor cells.

Neurogenic originating from the nerves of the nervous system.

Neuroleptic refers to the effects on cognition and behavior of antipsychotic drugs that reduce confusion, delusions, hallucinations, and psychomotor agitation in patients with psychoses.

Neuroma is a growth or tumour of nerve tissue.

Neuropharmacological relating the effects of drugs on the neurosystem.

Neuroradiology is a subspecialty of radiology focusing on the diagnosis and characterization of abnormalities of the central and peripheral nervous system. *adj*. neuroradiologic.

Neurotrophic relating to neutrophy i.e. the nutrition and maintenance of nervous tissue.

Neutropenia a disorder of the blood, characterized by abnormally low levels of neutrophils.

Neutrophil type of white blood cell, specifically a form of granulocyte.

Neutrophin protein that induce the survival, development and function of neurons.

NF-kappa B (NF-kB) nuclear factor kappa B, is an ubiquitous rapid response transcription factor in cells involved in immune and inflammatory reactions.

Niacin vitamin B3. See vitamin B3.

Niacinamide an amide of niacin, also known as nicotinamide. See vitamin B3.

NIH3T3 cells a mouse embryonic fibroblast cell line used in the cultivation of keratinocytes.

Niosomes are novel, vesicular, drug delivery systems composed of nonionic surfactants instead of phospholipids; they are capable of entrapping hydrophilic and hydrophobic drugs.

Nitrogen (N) is an essential building block of amino and nucleic acids and proteins and is essential to all living organisms. Protein rich vegetables like legumes are rich food sources of nitrogen.

NK cells natural killer cells, a type of cytotoxic lymphocyte that constitute a major component of the innate immune system.

NK1.1+ T (NKT) cells a type of natural killer T (NKT) cells. See natural killer T cells.

NMDA receptor N-methyl-D-aspartate receptor, the predominant molecular device for controlling synaptic plasticity and memory function. A brain receptor activated by the amino acid glutamate, which when excessively stimulated may cause cognitive defects in Alzheimer's disease.

Nociceptive causing pain, responding to a painful stimulus.

Nociceptors specialized peripheral sensory neurons that responds to potentially damaging stimuli by sending nerve signals to the spinal cord and brain.

Non-osteogenic fibromata of bone a benign tumour of bone which show no evidence of ossification.

Non-alcoholic fatty liver disease one cause of a fatty liver, occurring when fat is deposited (steatosis) in the liver not due to excessive alcohol use

Nootropics are substances which are claimed to boost human cognitive abilities (the functions and capacities of the brain). Also popularly referred to as "smart drugs", "smart nutrients", "cognitive enhancers" and "brain enhancers".

Noradrenalin see Norepinephrine.

Norepinephrine a substance, both a hormone and neurotransmitter, secreted by the adrenal medulla and the nerve endings of the sympathetic nervous system to cause vasoconstriction and increases in heart rate, blood pressure, and the sugar level of the blood. Also called levarterenol, noradrenalin.

Normoglycaemic having the normal amount of glucose in the blood.

Normotensive having normal blood pressure.

Nosebo a harmless substance that when taken by a patient is associated with unpleasant or harmful effects due to negative expectations or the psychological state of the person.

Nosocomial infections infections which are a result of treatment in a hospital or a healthcare service unit, but secondary to the patient's original condition.

NPC1L1 Niemann-Pick C1-Like 1 gene that plays a major role in cholesterol homeostasis. It is critical for the uptake of cholesterol across the plasma membrane of the intestinal enterocyte.

Nrf2 NF-E2-related factor 2, a transcription factor that activates ARE-containing genes.

Nrf2/ARE pathway plays an important role in inducing phase II detoxifying enzymes and antioxidant proteins and has been considered a potential target for cancer chemoprevention because it eliminates harmful reactive oxygen species or reactive intermediates generated from carcinogens.

Nuclear factor erythroid 2-related factor 2 (Nrf2) a transcription factor that plays a major role in response to oxidative stress by binding to antioxidant-responsive elements that regulate many hepatic phase I and II enzymes as well as hepatic efflux transporters.

Nucleosomes fundamental repeating subunits of all eukaryotic chromatin, consisting of a DNA chain coiled around a core of histones.

Nulliparous term used to describe a woman who has never given birth.

Nyctalopia night blindness, impaired vision in dim light and in the dark, due to impaired function of certain specialized vision cells.

Nystagmus fast, involuntary movements of the eyes.

Nycturia excessive urination at night; especially common in older men.

Occludin a novel integral membrane protein localizing at tight junctions *cf* tight junction.

Occlusion closure or blockage (as of a blood vessel).

Occlusive peripheral arterial disease (PAOD) also known as peripheral vascular disease (PVD), or peripheral arterial disease (PAD) refers to the obstruction of large arteries not within the coronary, aortic arch vasculature, or brain. PVD can result from atherosclerosis, inflammatory processes leading to stenosis, an embolism, or thrombus formation.

Oculomotor nerve the third of twelve paired cranial nerves.

Odds ratio a statistical measure of effect size, describing the strength of association or non-independence between two binary data values.

Odontalgia toothache. *adj*. odontalgic.

Odontopathy any disease of the teeth.

Oedema see edema.

Oligoarthritis an inflammation of two, three or four joints.

Oligonucleosome a series of nucleosomes.

Oligospermia or oligozoospermia refers to semen with a low concentration of sperm, commonly associated with male infertility.

Oliguria decreased production of urine.

Oligoanuria insufficient urine volume to allow for administration of necessary fluids, etc.

Omega 3 fatty acids are essential polyunsaturated fatty acids that have in common a final carbon–carbon double bond in the n − 3 position. Dietary sources of omega-3 fatty acids include fish oil and certain plant/nut oils. The three most nutritionally important omega 3 fatty acids are alpha-linolenic acid, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Research indicates that omega 3 fatty acids are important in health promotion and disease and can help prevent a wide range of medical problems, including cardiovascular disease, depression, asthma, and rheumatoid arthritis.

Omega 6 fatty acids are essential polyunsaturated fatty acids that have in common a final carbon–carbon double bond in the n − 6 position. Omega-6 fatty acids are considered essential fatty acids (EFAs) found in vegetable oils, nuts and seeds. They are essential to human health but cannot be made in the body. Omega-6 fatty acids – found in vegetable oils, nuts and seeds – are a beneficial part of a heart-healthy eating. Omega-6 and omega-3 PUFA play a crucial role in heart and brain function and in normal growth and development. Linoleic acid (LA) is the main omega-6 fatty acid in foods, accounting for 85–90% of the dietary omega-6 PUFA. Other omega 6 acids include gamma-linolenic acid or GLA, sometimes called gamoleic acid, eicosadienoic acid, arachidonic acid and docosadienoic acid.

Omega 9 fatty acids are not essential polyunsaturated fatty acids that have in common a final carbon–carbon double bond in the n − 9 position. Some n − 9 s are common components of animal fat and vegetable oil. Two n − 9 fatty acids important in industry are: oleic acid (18:1, n − 9), which is a main component of olive oil and erucic acid (22:1, n − 9), which is found in rapeseed, wallflower seed, and mustard seed.

Oncogenes - genes carried by tumour viruses that are directly and solely responsible for the neoplastic (tumorous) transformation of host cells.

Oncosis accidental cell death, also referred to swelling necrosis.

Ophthalmia severe inflammation of eye, or the conjunctiva or deeper structures of the eye . Also called ophthalmitis.

Ophthalmia (Sympathetic) inflammation of both eyes following trauma to one eye.

Ophthalmopathy an autoimmune disease where the thyroid gland is overactive leading to ocular manifestations.

Opiate drug derived from the opium plant.

Opioid receptors a group of G-protein coupled receptors located in the brain and various organs that bind opiates or opioid substances.

Optic placode an ectodermal placode from which the lens of the embryonic eye develops; also called lens placode.

ORAC (Oxygen radical absorbance capacity) a method of measuring antioxidant capacities in biological samples.

Oral submucous fibrosis a chronic debilitating disease of the oral cavity characterized by inflammation and progressive fibrosis of the submucosa tissues.

Oral thrush an infection of yeast fungus, *Candida albicans*, in the mucous membranes of the mouth.

Orchidectomy surgery to remove one or both testicles.

Orchidectomised with testis removed.

Orchitis an acute painful inflammatory reaction of the testis secondary to infection by different bacteria and viruses.

Orexigenic increasing or stimulating the appetite.

Orofacial dyskinesia abnormal involuntary movements involving muscles of the face, mouth, tongue, eyes, and occasionally, the neck—may be unilateral or bilateral, and constant or intermittent.

Oropharyngeal relating to the oropharynx.

Oropharynx part of the pharynx between the soft palate and the epiglottis.

Ostalgia, Ostealgia pain in the bones. Also called osteodynia.

Osteoarthritis is the deterioration of the joints that becomes more common with age.

Osteoarthrosis chronic noninflammatory bone disease.

Osteoblast a mononucleate cell that is responsible for bone formation.

Osteoblastic relating to osteoblasts.

Osteocalcin a noncollagenous protein found in bone and dentin, also refer to as bone gamma-carboxyglutamic acid-containing protein.

Osteoclasts a kind of bone cell that removes bone tissue by removing its mineralized matrix.

Osteoclastogenesis the production of osteoclasts.

Osteodynia pain in the bone.

Osteogenic derived from or composed of any tissue concerned in bone growth or repair.

Osteomalacia refers to the softening of the bones due to defective bone mineralization.

Osteomyelofibrosis a myeloproliferative disorder in which fibrosis and sclerosis finally lead to bone marrow obliteration.

Osteopenia reduction in bone mass, usually caused by a lowered rate of formation of new bone that is insufficient to keep up with the rate of bone destruction.

Osteoporosis a disease of bone that leads to an increased risk of fracture.

Osteoprotegerin also called osteoclastogenesis inhibitory factor (OCIF), a cytokine, which can inhibit the production of osteoclasts.

Osteosacrcoma a malignant bone tumour. Also called osteogenic sarcoma.

Otalgia earache, pain in the ear.

Otic placode a thickening of the ectoderm on the outer surface of a developing embryo from which the ear develops.

Otitis inflammation of the inner or outer parts of the ear.

Otorrhea running drainage (discharge) exiting the ear.

Otopathy disease of the ear.

Ovariectomised with one or two ovaries removed.

Ovariectomy surgical removal of one or both ovaries.

Oxidation the process of adding oxygen to a compound, dehydrogenation or increasing the electro-negative charge.

Oxidoreductase activity catalysis of an oxidation-reduction (redox) reaction, a reversible chemical reaction. One substrate acts as a hydrogen or electron donor and becomes oxidized, while the other acts as hydrogen or electron acceptor and becomes reduced.

Oxygen radical absorbance capacity (ORAC) a method of measuring antioxidant capacities in biological samples.

Oxytocic *adj*. hastening or facilitating childbirth, especially by stimulating contractions of the uterus.

Oxytocin is a mammalian hormone that also acts as a neurotransmitter in the brain. It is best known for its roles in female reproduction: it is released in large amounts after distension of the cervix and vagina during labor, and after stimulation of the nipples, facilitating birth and breastfeeding, respectively.

Oxyuriasis infestation by pinworms.

Ozoena discharge of the nostrils caused by chronic inflammation of the nostrils.

p.o. per os, oral administration.

P-glycoprotein (P-gp, ABCB1, MDR1) a cell membrane-associated drug-exporting protein that transports a variety of drug substrates from cancer cells.

P- Selectin also known as CD62P, GMP-140, LLECAM-3, PADGEM, a member of the selectin family. It is expressed by activated platelets and endothelial cells.

p21waf1/cip1 encodes a cyclin-dependent kinase inhibitor that is transcriptionally activated by the p53 tumor suppressor gene, transforming growth factor beta 1 (TGF-beta 1), AP2, and other pathways, all regulating apoptosis and the cell cycle.

Palliative relieving pain without alleviating the underlying problem.

Palpebral ptosis the abnormal drooping of the upper lid, caused by partial or total reduction in levator muscle function.

Palpitation rapid pulsation or throbbing of the heart.

Paludism state of having symptoms of malaria characterized by high fever and chills.

Pancreatectomized having undergone a pancreatectomy.

Pancreatectomy surgical removal of all or part of the pancreas.

Pancreatitis inflammation of the pancreas.

Pancytopenia a hematological condition in which there is a reduction in the number of red and white blood cells, as well as platelets.

Pantothenic acid vitamin B5. See vitamin B5.

Papain a protein degrading enzyme used medicinally and to tenderize meat.

Papilloma a benign epithelial tumour growing outwardly like in finger-like fronds.

Papule a small, solid, usually inflammatory elevation of the skin that does not contain pus.

Paradontosis is the inflammation of gums and other deeper structures, including the bone.

Paralytic person affected with paralysis, pertaining to paralysis.

Paraoxonase an enzyme that protects against oxidation of low density lipoprotein and affects the risk of coronary artery disease.

Parasitemia presence of parasites in blood. *adj*. parasitemic.

Parasympathetic nervous system subsystem of the nervous systems that slows the heart rate and increases intestinal and gland activity and relaxes the sphincter muscles.

Parasympathomimetic having an action resembling that caused by stimulation of the parasympathetic nervous system.

Paresthesia a sensation of tingling, burning, pricking, or numbness of a person's skin with no apparent long-term physical effect. Also known as "pains and needles".

Parenteral administration administration by intravenous, subcutaneous or intramuscular routes.

Paresis a condition characterised by partial loss of movement, or impaired movement.

Paresthesia is an abnormal sensation of the skin, such as burning, numbness, itching, hyperesthesia (increased sensitivity) or tingling, with no apparent physical cause.

Parotitis inflammation of salivary glands.

Paroxysm a sudden outburst of emotion or action, a sudden attack, recurrence or intensification of a disease.

Paroxystic relating to an abnormal event of the body with an abrupt onset and an equally sudden return to normal.

PARP see poly (ADP-ribose) polymerase.

Pars compacta is a portion of the substantia nigra (a brain structure located in the midbrain).

Parturition act of child birth.

PCAF (P300/CBP-associated factor) – a histone acetyl transferase (HAT) that plays a role in regulation of transciton, cell cycly progression and differentiation.

PCE/PCN ratio polychromatic erythrocyte/normochromatic erythrocyte ratio use as a measure of cytotoxic effects.

PCNA proliferating cell nuclear antigen, an auxiliary protein of DNA polymerase delata involve in modulating eukaryotic DNA replication.

pCREB phosphorylated cAMP (adenosine 3′5′ cyclic monophosphate)-response element binding protein.

PDEF acronym for prostate-derived ETS factor, an ETS (epithelial-specific E26 transforming sequence) family member that has been identified as a potential tumour suppressor.

PDGR receptor (platelet-derived growth factor receptor) are cell surface tyrosine kinase receptors for members of the platelet-derived growth factor (PDGF) family.

PDGFs platelet-derived growth factors constitute a group of growth factors that play a significant role in blood vessel formation, and the growth of blood vessels.

Pectoral pertaining to or used for the chest and respiratory tract.

pERK phosphorylated extracellular signal-regulated kinase, protein kinases involved in many cell functions.

P53 also known as protein 53 or tumour protein 53, is a tumour suppressor protein that in humans is encoded by the TP53 gene.

Peliosis see purpura.

Pellagra is a systemic nutritional wasting disease caused by a deficiency of vitamin B3 (niacin).

Pemphigus neonatorum Staphylococcal scalded skin syndrome, a bacterial disease of infants, characterized by elevated vesicles or blebs on a normal or reddened skin .

Peptic ulcer a sore in the lining of the stomach or duodenum, the first part of the small intestine.

Peptide YY a short (36 amino acid) pancreatic protein released by cells in the ileum and colon in response to feeding.

Percutanous pertains to a medical procedure where access to inner organs or tissues is done via needle puncture of the skin.

Perfusion to force fluid through the lymphatic system or blood vessels to an organ or tissue.

Periapical periodontitis is the inflammation of the tissue adjacent to the tip of the tooth's root.

Perifuse to flush a fresh supply of bathing fluid around all of the outside surfaces of a small piece of tissue immersed in it.

Perilipins highly phosphorylated adipocyte proteins that are localized at the surface of the lipid droplet.

Perimenopause is the phase before menopause actually takes place, when ovarian hormone production is declining and fluctuating. *adj*. perimenopausal.

Periodontal ligament (PDL) is a group of specialized connective tissue fibres that essentially attach a tooth to the bony socket.

Periodontitis is a severe form of gingivitis in which the inflammation of the gums extends to the supporting structures of the tooth. Also called pyorrhea.

Peripheral arterial disease (PAD) is a disease in which plaque builds up in the arteries that carry blood to your head, organs, and limbs.

Peripheral neuropathy refers to damage to nerves of the peripheral nervous system.

Peripheral neuropathic pain (PNP) refers to situations where nerve roots or peripheral nerve trunks have been damaged by mechanical and/or chemical stimuli that exceeded the physical capabilities of the nervous system. Symptoms may include pain, parestesia, dysesthesia, spasm, weakness, hypoesthesia or anesthesia.

Peripheral vascular disease (PVD) see peripheral artery occlusive disease .

Peristalsis a series of organized, wave-like muscle contractions that occur throughout the digestive tract.

PERK a transmembrane protein kinase of the PEK family resident in the endoplasmic reticulum (ER) membrane and is linked to insulin processing.

Perlingual through or by way of the tongue.

Perniosis an abnormal reaction to cold that occurs most frequently in women, children, and the elderly. Also called chilblains.

Per os (P.O.) oral administration.

Peroxisome proliferator-activated receptors (PPARs) a family of nuclear receptors that are involved in lipid metabolism, differentiation, proliferation, cell death, and inflammation.

Peroxisome proliferator-activated receptor alpha (PPAR-alpha) a nuclear receptor protein, transcription factor and a major regulator of lipid metabolism in the liver.

Peroxisome proliferator-activated receptor gamma (PPAR-γ) a type II nuclear receptor protein that regulates fatty acid storage and glucose metabolism.

Pertussis whooping cough, sever cough.

Peyers Patches patches of lymphoid tissue or lymphoid nodules on the walls of the ileal-small intestine.

PGE-2 Prostaglandin E2, a hormone-like substance that is released by blood vessel walls in response to infection or inflammation that acts on the brain to induce fever.

Phagocytes are the white blood cells that protect the body by ingesting (phagocytosing) harmful foreign particles, bacteria and dead or dying cells. *adj*. phagocytic.

Phagocytosis is process the human body uses to destroy dead or foreign cells.

Pharmacognosis the branch of pharmacology that studies the composition, use, and history of drugs.

Pharmacodynamics branch of pharmacology dealing with the effects of drugs and the mechanism of their action.

Pharmacokinetics branch of pharmacology concerned with the movement of drugs within the body including processes of absorption, distribution, metabolism and excretion in the body.

Pharmacopoeia authoritative treatise containing directions for the identification of drug samples and the preparation of compound medicines, and published by the authority of a government or a medical or pharmaceutical society and in a broader sense is a general reference work for pharmaceutical drug specifications.

Pharyngitis, Pharyngolaryngitis inflammation of the pharynx and the larynx.

Pharyngolaryngeal pertaining to the pharynx and larynx.

Phenolics class of chemical compounds consisting of a hydroxyl group (-OH) bonded directly to an aromatic hydrocarbon group.

Pheochromocytoma is a rare neuroendocrine tumour that usually originates from the adrenal glands' chromaffin cells, causing overproduction of catecholamines, powerful hormones that induce high blood pressure and other symptoms.

Phlebitis is an inflammation of a vein, usually in the legs.

Phlegm abnormally viscid mucus secreted by the mucosa of the respiratory passages during certain infectious processes.

Phlegmon a spreading, diffuse inflammation of the soft or connective tissue due to infection by Streptococci bacteria.

Phoroglucinol a white, crystalline compound used as an antispasmodic, analytical reagent, and decalcifier of bone specimens for microscopic examination.

Phosphatidylglycerol is a glycerophospholipid found in pulmonary active surface lipoprotein and consists of a L-glycerol 3-phosphate backbone ester-bonded to either saturated or unsaturated fatty acids on carbons 1 and 2.

Phosphatidylinositol 3-kinases (PI 3-kinases or PI3Ks) a group of enzymes involved in cellular functions such as cell growth, proliferation, differentiation, motility, survival and intracellular trafficking, which in turn are involved in cancer.

Phosphatidylserine a phosphoglyceride phospholipid that is one of the key building blocks of cellular membranes, particularly in the nervous system. It is derived from soy lecithin

Phosphaturia a urinary tract condition of excessive urine phosphorus, causing urine to appear cloudy or murky color; also called hypophosphatemia.

Phosphodiesterases a diverse family of enzymes that hydrolyse cyclic nucleotides and thus play a key role in regulating intracellular levels of the second messengers cAMP and cGMP, and hence cell function.

Phosphoenolpyruvate C kinase (PEPCK) an enzyme in the lyase family used in the metabolic pathway of gluconeogenesis.

Phospholipase an enzyme that hydrolyzes phospholipids into fatty acids and other lipophilic substances.

Phospholipase A2 (PLA2) a small lipolytic enzyme that releases fatty acids from the second carbon group of glycerol. Plays an essential role in the synthesis of prostaglandins and leukotrienes.

Phospholipase C enzymes that cleaves phospholipase.

Phospholipase C gamma (PLC gamma) enzymes that cleaves phospholipase in cellular proliferation and differentiation, and its enzymatic activity is upregulated by a variety of growth factors and hormones.

Phosphorus (P) is an essential mineral that makes up 1% of a person's total body weight and is found in the bones and teeth. It plays an important role in the body's utilization of carbohydrates and fats; in the synthesis of protein for the growth, maintenance, and repair of cells and tissues. It is also crucial for the production of ATP, a molecule the body uses to

store energy. Main sources are meat and milk; fruits and vegetables provides small amounts.

Photoaging is the term that describes damage to the skin caused by intense and chronic exposure to sunlight resulting in premature aging of the skin.

Photocarcinogenesis represents the sum of a complex of simultaneous and sequential biochemical events that ultimately lead to the occurrence of skin cancer caused by exposure to the sun.

Photodermatoses skin disorders caused by exposure to sunlight.

Photophobia abnormal visual intolerance to light.

Photopsia an affection of the eye, in which the patient perceives luminous rays, flashes, coruscations, etc.

Photosensitivity sensitivity toward light.

Phthisis an archaic name for tuberculosis.

Phytohemagglutinin a lectin found in plant that is involved in the stimulation of lymphocyte proliferation.

Phytonutrients certain organic components of plants, that are thought to promote human health. Fruits, vegetables, grains, legumes, nuts and teas are rich sources of phytonutrients. Phytonutrients are not 'essential' for life. Also called phytochemicals.

Phytosterols a group of steroid alcohols, cholesterol-like phytochemicals naturally occurring in plants like vegetable oils, nuts and legumes.

Piebaldism rare autosomal dominant disorder of melanocyte development characterized by distinct patches of skin and hair that contain no pigment.

Piles see haemorrhoids.

PI3K phosphoinositide 3-kinase.

PI13K/AKT signaling pathways are involved in the modulation of cell survival, cell cycle progression and cellular growth in cancer.

Pityriasis lichenoides is a rare skin disorder of unknown aetiology characterised by multiple papules and plaques.

PKC protein kinase C, a membrane bound enzyme that phosphorylates different intracellular proteins and raised intracellular Ca levels.

PKC Delta inhibitors Protein Kinase C delta inhibitors that induce apoptosis of haematopoietic cell lines.

Placebo a sham or simulated medical intervention.

Placode a platelike epithelial thickening in the embryo where some organ or structure later develops.

Plasma the yellow-colored liquid component of blood, in which blood cells are suspended.

Plasma kallikrien a serine protease, synthesized in the liver and circulates in the plasma.

Plasmalemma plasma membrane.

Plasmin a proteinase enzyme that is responsible for digesting fibrin in blood clots.

Plasminogen the proenzyme of plasmin, whose primary role is the degradation of fibrin in the vasculature.

Plasminogen activator inhibitor-1 (PAI-1) also known as endothelial plasminogen activator inhibitor or serpin E1 is a serine protease inhibitor (serpin) that functions as the principal inhibitor of tissue plasminogen activator (tPA) and urokinase (uPA), the activators of plasminogen and hence fibrinolysis (the physiological breakdown of blood clots).

Plaster poultice.

Platelet activating factor (PAF) is an acetylated derivative of glycerophosphorylcholine, released by basophils and mast cells in immediate hypersensitive reactions and macrophages and neutrophils in other inflammatory reactions. One of its main effects is to induce platelet aggregation.

PLC gamma phospholipase C gamma plays a central role in signal transduction.

Pleurisy is an inflammation of the pleura, the lining of the pleural cavity surrounding the lungs, which can cause painful respiration and other symptoms. Also known as pleuritis.

Pneumonia an inflammatory illness of the lung caused by bacteria or viruses.

Pneumotoxicity damage to lung tissues.

Poliomyelitis is a highly infectious viral disease that may attack the central nervous system and is characterized by symptoms that range from a mild non-paralytic infection to total paralysis in a matter of hours; also called polio or infantile paralysis.

Poly (ADP-ribose) polymerase (PARP) a protein involved in a number of cellular processes especially DNA repair and programmed cell death.

Polyarthritis is any type of arthritis which involves five or more joints.

Polychromatic erythrocyte (PCE) an immature red blood cell containing RNA, that can be differentiated by appropriate staining techniques from a normochromatic erythrocyte (NCE), which lacks RNA.

Polycystic kidney disease is a kidney disorder passed down through families in which multiple cysts form on the kidneys, causing them to become enlarged.

Polycystic ovary syndrome imbalance of woman's sex hormone, this imbalance may cause changes in menstrual cycle, skin changes, small cysts in the ovary and problem in getting pregnant.

Polycythaemia a type of blood disorder characterised by the production of too many red blood cells.

Polymorphnuclear having a lobed nucleus. Used especially of neutrophilic white blood cells.

Polyneuritis widespread inflammation of the nerves.

Polyneuritis gallinarum a nervous disorder in birds and poultry.

Polyp a growth that protrudes from a mucous membrane.

Polyphagia medical term for excessive hunger or eating.

Polyuria a condition characterized by the passage of large volumes of urine with an increase in urinary frequency.

Pomade a thick oily dressing.

Porphyrin any of a class of water-soluble, nitrogenous biological pigments.

Postherpetic neuralgia (PHN) is neuralgia (pain in the nerves) caused by the varicella Herpes Zoster virus. The pain may last for more than a month or more after a shingles infection occurred.

Postpartum Depression depression after pregnancy; also called postnatal depression.

Postprandial after mealtime.

Potassium (K) is an element that's essential for the body's growth and maintenance. It's necessary to keep a normal water balance between the cells and body fluids, for cellular enzyme activities and plays an essential role in the response of nerves to stimulation and in the contraction of muscles. Potassium is found in many plant foods and fish (tuna, halibut): chard, mushrooms, spinach, fennel, kale, mustard greens, Brussels sprouts, broccoli, cauliflower, cabbage winter squash, eggplant, cantaloupe, tomatoes, parsley, cucumber, bell pepper, turmeric, ginger root, apricots, strawberries, avocado and banana.

Poultice is a soft moist mass, often heated and medicated, that is spread on cloth over the skin to treat an aching, inflamed, or painful part of the body. Also called cataplasm.

PPARs peroxisome proliferator-activated receptors – a group of nuclear receptor proteins that function as transcription factors regulating the expression of genes.

Prebiotics a category of functional food, defined as non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improve host health. *cf*. probiotics.

Pre-ecamplasia toxic condition of pregnancy characterized by high blood pressure, abnormal weight gain, proteinuria and edema.

Prepubertal before puberty; pertaining to the period of accelerated growth preceding gonadal maturity.

Pregnane X receptor (PXR; NR1I2) is a ligand-activated transcription factor that plays a role not only in drug metabolism and transport but also in various other biological processes.

Pregnenolone a steroid hormone produced by the adrenal glands, involved in the steroidogenesis of other steroid hormones like progesterone, mineralocorticoids, glucocorticoids, androgens, and estrogens.

Prenidatory referring to the time period between fertilization and implantation.

Prenylated flavones flavones with an isoprenyl group in the 8-position, has been reported to have good anti-inflammatory properties.

Proangiogenic promote angiogensis (formation and development of new blood vessels)..

Probiotication enhancement with beneficial probitoic bacteria such as *Lactobacillus* species that can prevent the growth of intestinal pathogenic microflora.

Probiotics are dietary supplements and live microorganisms containing potentially beneficial

bacteria or yeasts that are taken into the alimentary system for healthy intestinal functions. *cf.* prebiotics.

Proctitis an inflammation of the rectum that causes discomfort, bleeding, and occasionally, a discharge of mucus or pus.

Procyanidin also known as proathocyanidin, oligomeric proathocyanidin, leukocyanidin, leucoanthocyanin, is a class of flavanols found in many plants. It has antioxidant activity and plays a role in the stabilization of collagen and maintenance of elastin.

Progestational of or relating to the phase of the menstrual cycle immediately following ovulation, characterized by secretion of progesterone.

Proglottid one of the segments of a tapeworm.

Prognosis medical term to describe the likely outcome of an illness.

Prolactin a hormone produced by the pituitary gland, it stimulates the breasts to produce milk in pregnant women. It is also present in males but its role is not well understood.

Prolapse a common condition where the bladder, uterus and or bowel protrudes into the vagina.

Prolapsus to fall or slip out of place.

Prolapus ani eversion of the lower portion of the rectum, and protruding through the anus, common in infancy and old age.

Proliferating cell nuclear antigen (PCNA) a new marker to study human colonic cell proliferation.

Proliferative vitreoretinopathy (PVR) a most common cause of failure in retinal reattachment surgery, characterised by the formation of cellular membrane on both surfaces of the retina and in the vitreous.

Promastigote the flagellate stage in the development of trypanosomatid protozoa, characterized by a free anterior flagellum.

Promyelocytic leukemia a subtype of acute myelogenous leukemia (AML), a cancer of the blood and bone marrow.

Pro-oxidants chemicals that induce oxidative stress, either through creating reactive oxygen species or inhibiting antioxidant systems.

Prophylaxis prevention or protection against disease.

Proptosis see exophthalmos.

Prostacyclin a prostaglandin that is a metabolite of arachidonic acid, inhibits platelet aggregation, and dilates blood vessels.

Prostaglandins a family of C 20 lipid compounds found in various tissues, associated with muscular contraction and the inflammation response such as swelling, pain, stiffness, redness and warmth.

Prostaglandin E2 (PEG -2) one of the prostaglandins, a group of hormone-like substances that participate in a wide range of body functions such as the contraction and relaxation of smooth muscle, the dilation and constriction of blood vessels, control of blood pressure, and modulation of inflammation.

Prostaglandin E synthase an enzyme that in humans is encoded by the glutathione-dependent PTGES gene.

Prostanoids term used to describe a subclass of eicosanoids (products of COX pathway) consisting of: the prostaglandins (mediators of inflammatory and anaphylactic reactions), the thromboxanes (mediators of vasoconstriction) and the prostacyclins (active in the resolution phase of inflammation.)

Prostate a gland that surround the urethra at the bladder in the male.

Prostate cancer a disease in which cancer develops in the prostate, a gland in the male reproductive system. Symptoms include pain, difficulty in urinating, erectile dysfunction and other symptoms.

Prostate –specific antigen (PSA) a protein produced by the cells of the prostate gland.

Protein kinase C (PKC) a family of enzymes involved in controlling the function of other proteins through the phosphorylation of hydroxyl groups of serine and threonine amino acid residues on these proteins. PKC enzymes play important roles in several signal transduction cascades.

Protein tyrosine phosphatase (PTP) a group of enzymes that remove phosphate groups from phosphorylated tyrosine residues on proteins.

Proteinase a protease (enzyme) involved in the hydrolytic breakdown of proteins, usually by splitting them into polypeptide chains.

Proteinuria means the presence of an excess of serum proteins in the urine.

Proteolysis cleavage of the peptide bonds in protein forming smaller polypeptides. *adj*. proteolytic.

Proteomics the large-scale study of proteins, particularly their structures and functions.

Prothrombin blood-clotting protein that is converted to the active form, factor IIa, or thrombin, by cleavage.

Prothyroid good for thyroid function.

Protheolithic proteolytic see proteolysis.

Proto-oncogene A normal gene which, when altered by mutation, becomes an oncogene that can contribute to cancer.

Prurigo a general term used to describe itchy eruptions of the skin.

Pruritis defined as an unpleasant sensation on the skin that provokes the desire to rub or scratch the area to obtain relief; itch, itching. *adj*. pruritic.

PSA Prostate Specific Antigen, a protein which is secreted into ejaculate fluid by the healthy prostate. One of its functions is to aid sperm movement.

Psoriasis a common chronic, non-contagious autoimmune dermatosis that affects the skin and joints.

Psychoactive having effects on the mind or behavior.

Psychonautics exploration of the psyche by means of approaches such as meditation, prayer, lucid dreaming, brain wave entrainment etc.

Psychotomimetic hallucinogenic.

Psychotropic capable of affecting the mind, emotions, and behavior.

PTEN phosphatase and tensin homolog, a tumour suppressor gene.

Ptosis also known as drooping eyelid; caused by weakness of the eyelid muscle and damage to the nerves that control the muscles or looseness of the skin of the upper eyelid..

P13-K is a lipid kinase enzyme involved in the regulation of a number of cellular functions such as cell growth, proliferation, differentiation, motility, survival and intracellular trafficking, which in turn are involved in cancer.

P13-K/AKT signaling pathway shown to be important for an extremely diverse array of cellular activities – most notably cellular proliferation and survival.

Pthysis silicosis with tuberculosis.

Ptosis drooping of the upper eye lid.

PTP protein tyrosine phosphatase.

PTPIB protein tyrosine phosphatase 1B.

P21 also known as cyclin-dependent kinase inhibitor 1 or CDK-interacting protein 1, is a potent cyclin-dependent kinase inhibitor.

Puerperal pertaining to child birth.

Puerperium post-partum period.

Pulmonary embolism a blockage (blood clot) of the main artery of the lung.

Purgative a substance used to cleanse or purge, especially causing the immediate evacuation of the bowel.

Purpura is the appearance of red or purple discolorations on the skin that do not blanch on applying pressure. Also called peliosis.

Purulent containing pus discharge.

Purulent sputum sputum containing, or consisting of, pus.

Pustule small, inflamed, pus-filled lesions.

Pyelonephritis an ascending urinary tract infection that has reached the pyelum (pelvis) of the kidney.

Pyodermatitis refers to inflammation of the skin.

Pyorrhea see periodontitis.

Pyretic referring to fever.

Pyrexia fever of unknown origin.

Pyridoxal a chemical form of vitamin B6. See vitamin B6.

Pyridoxamine a chemical form of vitamin B6. See vitamin B6.

Pyridoxine a chemical form of vitamin B6. See vitamin B6.

Pyrolysis decomposition or transformation of a compound caused by heat. *adj*. pyrolytic.

PYY Peptide a 36 amino acid peptide secreted by L cells of the distal small intestine and colon that inhibits gastric and pancreatic secretion.

QT interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. A prolonged QT interval is a biomarker for ventricular tachyarrhythmias and a risk factor for sudden death.

Quorum sensing (QS) the control of gene expression in response to cell density, is used by both gram-negative and gram-positive bacteria to regulate a variety of physiological functions.

Radiolysis the dissociation of molecules by radiation.

Radioprotective serving to protect or aiding in protecting against the injurious effect of radiations.

RAGE is the receptor for advanced glycation end products, a multiligand receptor that propagates cellular dysfunction in several inflammatory disorders, in tumours and in diabetes.

RAS see renin-angiotensin system or recurrent aphthous stomatitis.

Rash a temporary eruption on the skin, see uticaria.

Reactive oxygen species species such as superoxide, hydrogen peroxide, and hydroxyl radical. At low levels, these species may function in cell signaling processes. At higher levels, these species may damage cellular macromolecules (such as DNA and RNA) and participate in apoptosis (programmed cell death).

Rec A is a 38 kDa *Escherichia coli* protein essential for the repair and maintenance of DNA.

Receptor for advanced glycation end products (RAGE) is a member of the immunoglobulin superfamily of cell surface molecules; mediates neurite outgrowth and cell migration upon stimulation with its ligand, amphoterin.

Recticulocyte non-nucleated stage in the development of the red blood cell.

Recticulocyte lysate cell lysate produced from reticulocytes, used as an in-vitro translation system.

Recticuloendothelial system part of the immune system, consists of the phagocytic cells located in reticular connective tissue, primarily monocytes and macrophages.

Recurrent aphthous stomatitis, or RAS is a common, painful condition in which recurring ovoid or round ulcers affect the oral mucosa.

Redox homeostasis is considered as the cumulative action of all free radical reactions and antioxidant defenses in different tissues.

Refrigerant a medicine or an application for allaying heat, fever or its symptoms.

Renal calculi kidney stones.

Renal interstitial fibrosis damage sustained by the kidneys' renal tubules and interstitial capillaries due to accumulation of extracellular waste in the wall of the small arteries and arterioles.

Renal resistive index (RRI) measures the resistance of renal arterial flow to the kidney.

Renin also known as an angiotensinogenase, is an enzyme that participates in the body's renin-angiotensin system (RAS).

Renin-angiotensin system (RAS) also called the renin-angiotensin-aldosterone system (RAAS) is a hormone system that regulates blood pressure and water (fluid) balance.

Reperfusion the restoration of blood flow to an organ or tissue that has had its blood supply cut off, as after a heart attack.

Reporter gene a transfected gene that produces a signal, such as green fluorescence, when it is expressed.

Resistin a cysteine-rich protein secreted by adipose tissue of mice and rats.

Resolutive a substance that induces subsidence of inflammation.

Resolvent reduce inflammation or swelling.

Resorb to absorb or assimilate a product of the body such as an exudates or cellular growth.

Restenosis is the reoccurrence of stenosis, a narrowing of a blood vessel, leading to restricted blood flow.

Resveratrol is a phytoalexin produced naturally by several plants when under attack by pathogens such as bacteria or fungi. It is a potent antioxidant found in red grapes and other plants.

Retinol a form of vitamin A, see vitamin A.

Retinopathy a general term that refers to some form of non-inflammatory damage to the retina of the eye.

Revulsive counterirritant, used for swellings.

Rhabdomyolysis breakdown of muscle fibres leading to the release of muscle fibre content (myoglobin) into the bloodstream.

Rheumatic pertaining to rheumatism or to abnormalities of the musculoskeletal system.

Rheumatism, Rheumatic disorder, Rheumatic diseases refers to various painful medical conditions which affect bones, joints, muscles, tendons. Rheumatic diseases are characterized by the signs of inflammation – redness, heat, swelling, and pain.

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder that most

commonly causes inflammation and tissue damage in joints (arthritis) and tendon sheaths, together with anemia.

Rhinitis irritation and inflammation of some internal areas of the nose and the primary symptom of rhinitis is a runny nose.

Rhinopathy disease or malformation of the nose.

Rhinoplasty is surgery to repair or reshape the nose.

Rhinorrhea commonly known as a runny nose, characterized by an unusually significant amount of nasal discharge.

Rhinosinusitis inflammation of the nasal cavity and sinuses.

Rho GTPases Rho-guanosine triphosphate hydrolase enzymes are molecular switches that regulate many essential cellular processes, including actin dynamics, gene transcription, cell-cycle progression and cell adhesion.

Ribosome inactivating proteins protein that are capable of inactivating ribosomes.

Rickets is a softening of the bones in children potentially leading to fractures and deformity.

Ringworm dermatophytosis, a skin infection caused by fungus.

Roborant restoring strength or vigour, a tonic.

Rotavirus the most common cause of infectious diarrhea (gastroenteritis) in young children and infants, one of several viruses that causes infections called stomach flu.

Rubefacient a substance for external application that produces redness of the skin e.g. by causing dilation of the capillaries and an increase in blood.

Ryanodine receptor intracellular Ca ++ channels in animal tissues like muscles and neurons.

S.C. abbreviation for sub-cutaneous, beneath the layer of skin.

S-T segment the portion of an electrocardiogram between the end of the QRS complex and the beginning of the T wave. Elevation or depression of the S-T segment is the characteristics of myocardial ischemia or injury and coronary artery disease.

Sapraemia see septicaemia.

Sarcoma cancer of the connective or supportive tissue (bone, cartilage, fat, muscle, blood vessels) and soft tissues.

Sarcopenia degenerative loss of skeletal muscle mass and strength associated with aging.

Sarcoplasmic reticulum a special type of smooth endoplasmic reticulum found in smooth and striated muscle.

SARS Severe acute respiratory syndrome, the name of a potentially fatal new respiratory disease in humans which is caused by the SARS coronavirus (SARS-CoV)

Satiety state of feeling satiated, fully satisfied (appetite or desire).

Scabies a transmissible ectoparasite skin infection characterized by superficial burrows, intense pruritus (itching) and secondary infection.

Scarlatina scarlet fever, an acute, contagious disease caused by infection with group A streptococcal bacteria.

Schwann cells or neurolemmocytes, are the principal supporting cells of the peripheral nervous system, they form the myelin sheath of a nerve fibre.

Schistosomiasis is a parasitic disease caused by several species of fluke of the genus *Schistosoma*. Also known as bilharzia, bilharziosis or snail fever.

Schizophrenia a psychotic disorder (or a group of disorders) marked by severely impaired thinking, emotions, and behaviors.

Sciatica a condition characterised by pain deep in the buttock often radiating down the back of the leg along the sciatic nerve.

Scleroderma a disease of the body's connective tissue. The most common symptom is a thickening and hardening of the skin, particularly of the hands and face.

Scrofula a tuberculous infection of the skin on the neck caused by the bacterium *Mycobacterium tuberculosis*.

Scrophulosis see scrofula.

Scurf abnormal skin condition in which small flakes or sales become detached.

Scurvy a state of dietary deficiency of vitamin C (ascorbic acid) which is required for the synthesis of collagen in humans.

Secretagogue a substance that causes another substance to be secreted.

Sedative having a soothing, calming, or tranquilizing effect; reducing or relieving stress, irritability, or excitement.

Seizure the physical findings or changes in behavior that occur after an episode of abnormal electrical activity in the brain.

Selectins are a family of cell adhesion molecules; e.g. selectin-E, selectin –L, selectin P.

Selenium (Se) a trace mineral that is essential to good health but required only in tiny amounts; it is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes. It is found in avocado, brazil nut, lentils, sunflower seeds, tomato, whole grain cereals, seaweed, seafood and meat.

Sensorineural bradyacuasia hearing impairment of the inner ear resulting from damage to the sensory hair cells or to the nerves that supply the inner ear.

Sepsis a condition in which the body is fighting a severe infection that has spread via the bloodstream.

Sequela an abnormal pathological condition resulting from a disease, injury or trauma.

Serine proteinase peptide hydrolases which have an active centre histidine and serine involved in the catalytic process.

Serotonergic liberating, activated by, or involving serotonin in the transmission of nerve impulses.

Serotonin a monoamine neurotransmitter synthesized in serotonergic neurons in the central nervous system.

Sepsis is a potentially fatal medical condition characterized by a whole-body inflammatory response (called a systemic inflammatory response syndrome or SIRS) that is triggered by an infection.

Septicaemia a **s**ystemic disease associated with the presence and persistence of pathogenic microorganisms or their toxins in the blood.

Sequelae a pathological condition resulting from a prior disease, injury, or attack.

Sexual potentiator increases sexual activity and potency, enhances sexual performance due to increased blood flow and efficient metabolism.

Sexually transmitted diseases (STD) infections that are transmitted through sexual activity.

SGOT, Serum glutamic oxaloacetic transaminase an enzyme that is normally present in liver and heart cells. SGOT is released into blood when the liver or heart is damaged. Also called aspartate transaminase (AST).

SGPT, Serum glutamic pyruvic transaminase an enzyme normally present in serum and body tissues, especially in the liver; it is released into the serum as a result of tissue injury, also called Alanine transaminase (ALT),

Shiga–like toxin a toxin produced by the bacterium *Escherichia coli* which disrupts the function of ribosomes, also known as verotoxin.

Shiga toxigenic *Escherichia coli* **(STEC)** comprises a diverse group of organisms capable of causing severe gastrointestinal disease in humans.

Shiga toxin a toxin produced by the bacterium *Shigella dysenteriae*, which disrupts the function of ribosomes.

Shingles skin rash caused by the Zoster virus (same virus that causes chicken pox) and is medically termed Herpes zoster.

Sialogogue salivation-promoter, a substance used to increase or promote the excretion of saliva.

Sialoproteins glycoproteins that contain sialic acid as one of their carbohydrates.

Sialyation reaction with sialic acid or its derivatives; used especially with oligosaccharides.

Sialyltransferases enzymes that transfer sialic acid to nascent oligosaccharide.

Sickle cell disease is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that contain mostly hemoglobin S, an abnormal type of hemoglobin. Sometimes these red blood cells become sickle-shaped (crescent shaped) and have difficulty passing through small blood vessels.

Side stitch is an intense stabbing pain under the lower edge of the ribcage that occurs while exercising.

Signal transduction cascade refers to a series of sequential events that transfer a signal through a series of intermediate molecules until final regulatory molecules, such as transcription factors, are modified in response to the signal.

Silicon (Si) is required in minute amounts by the body and is important for the development of healthy hair and the prevention of nervous disorders. Lettuce is the best natural source of Silicon.

Sinapism signifies an external application, in the form of a soft plaster, or poultice.

Sinusitis inflammation of the nasal sinuses.

SIRC cells Statens Seruminstitut Rabbit Cornea (SIRC) cell line.

SIRT 1 stands for sirtuin (silent mating type information regulation 2 homolog) 1. It is an enzyme that deacetylates proteins that contribute to cellular regulation.

6-Keto-PGF1 alpha a physiologically active and stable hydrolysis product of Epoprostenol, found in nearly all mammalian tissues.

Skp1 (S-phase kinase-associated protein 1) is a core component of SCF ubiquitin ligases and mediates protein degradation.

Smads a family of intracellular proteins that mediate signaling by members of the TGF-beta (transforming growth factor beta) superfamily.

Smad2/3 a key signaling molecule for TGF-beta.

Smad7 a TGFβ type 1 receptor antagonist.

Smallpox is an acute, contagious and devastating disease in humans caused by *Variola* virus and have resulted in high mortality over the centuries.

Snuff powder inhaled through the nose.

SOD superoxide dismutase, is an enzyme that repairs cells and reduces the damage done to them by superoxide, the most common free radical in the body.

Sodium (Na) is an essential nutrient required for health. Sodium cations are important in neuron (brain and nerve) function, and in influencing osmotic balance between cells and the interstitial fluid and in maintenance of total body fluid homeostasis. Extra intake may cause a harmful effect on health. Sodium is naturally supplied by salt intake with food.

Soleus muscle smaller calf muscle lower down the leg and under the gastrocnemius muscle.

Somites mesodermal structures formed during embryonic development that give rise to segmented body parts such as the muscles of the body wall.

Soporific a sleep inducing drug.

SOS response a global response to DNA damage in which the cell cycle is arrested and DNA repair and mutagenesis are induced.

Soyasapogenins triterpenoid products obtained from the acid hydrolysis of soyasaponins, designated soyasapogenols A,B, C, D and E.

Soyasaponins bioactive saponin compounds found in many legumes.

Spasmogenic inducing spasm.

Spasmolytic checking spasms, see antispasmodic.

Spermatorrhoea medically an involuntary ejaculation/drooling of semen usually nocturnal emissions.

Spermidine an important polyamine in DNA synthesis and gene expression.

Spina bifida a congenital birth defect caused by the incomplete closing of the embryonic neural tube.

Sphingolipid a member of a class of lipids derived from the aliphatic amino alcohol, sphingosine.

Spleen organ that filters blood and prevents infection.

Spleen tyrosine kinase (SYK) is an enigmatic protein tyrosine kinase functional in a number of diverse cellular processes such as the regulation of immune and inflammatory responses.

Splenitis inflammation of the spleen.

Splenocyte is a monocyte, one of the five major types of white blood cell, and is characteristically found in the splenic tissue.

Splenomegaly is an enlargement of the spleen.

Sprain to twist a ligament or muscle of a joint without dislocating the bone.

Sprue is a chronic disorder of the small intestine caused by sensitivity to gluten, a protein found in wheat and rye and to a lesser extent oats and barley . It causes poor absorption by the intestine of fat, protein, carbohydrates, iron, water, and vitamins A, D, E, and K.

Sputum matter coughed up and usually ejected from the mouth, including saliva, foreign material, and substances such as mucus or phlegm, from the respiratory tract.

SREBP-1 see sterol regulatory element-binding protein-1.

Stanch to stop or check the flow of a bodily fluid like blood from a wound.

Statin a type of lipid-lowering drug.

STAT3 signal transducer and activator of transcription 3, plays a key role in many cellular processes such as cell growth and apoptosis.

Status epilepticus refers to a life-threatening condition in which the brain is in a state of persistent seizure.

STD sexually transmitted disease.

Steatorrhea is the presence of excess fat in feces which appear frothy, foul smelling and floats because of the high fat content.

Steatohepatitis liver disease, characterized by inflammation of the liver with fat accumulation in the liver.

Steatosis refer to the deposition of fat in the interstitial spaces of an organ like the liver, fatty liver disease.

Sterility inability to produce offspring, also called asepsis.

Steroidogenic relating to steroidogenisis.

Steroidogenisis the production of steroids.

Sterol regulatory element-binding protein-1 (SREBP1) is a key regulator of the transcription of numerous genes that function in the metabolism of cholesterol and fatty acids.

Stimulant a substance that promotes the activity of a body system or function.

Stomachic (digestive stimulant), an agent that stimulates or strengthens the activity of the stomach; used as a tonic to improve the appetite and digestive processes.

Stomatitis oral inflammation and ulcers, may be mild and localized or severe, widespread, and painful.

Stomatology medical study of the mouth and its diseases.

Stool faeces.

Strangury is the painful passage of small quantities of urine which are expelled slowly by straining with severe urgency; it is usually accompanied with the unsatisfying feeling of a remaining volume inside and a desire to pass something that will not pass.

Straub tail condition in which an animal carries its tail in an erect (vertical or nearly vertical) position.

STREPs sterol regulatory element binding proteins, a family of transcription factors that regulate lipid homeostasis by controlling the expression of a range of enzymes required for endogenous cholesterol, fatty acid, triacylglycerol and phospholipid synthesis.

Stria terminalis a structure in the brain consisting of a band of fibres running along the lateral margin of the ventricular surface of the thalamus.

Striae gravidarum a cutaneous condition characterized by stretch marks on the abdomen during and following pregnancy.

Stricture an abnormal constriction of the internal passageway within a tubular structure such as a vessel or duct

Strongyloidiasis an intestinal parasitic infection in humans caused by two species of the parasitic nematode *Strongyloides*. The nematode or round worms are also called thread worms.

Styptic a short stick of medication, usually anhydrous aluminum sulfate (a type of alum) or titanium dioxide, which is used for stanching blood by causing blood vessels to contract at the site of the wound. Also called hemostatic pencil. see antihaemorrhagic.

Subarachnoid hemorrhage is bleeding in the area between the brain and the thin tissues that cover the brain.

Substance P a neuropetide that functions as a neurotransmitter, neuromodulator and is associated with the sensation of pain.

Substantia nigra is a dark coloured brain structure located in the midbrain that play an important role in reward, addiction and movement.

Sudatory medicine that causes or increases sweating. Also see sudorific.

Sudorific a substance that causes sweating.

Sulfur Sulfur is an essential component of all living cells. Sulfur is important for the synthesis of sulfur-containing amino acids, all polypeptides, proteins, and enzymes such as glutathione an important sulfur-containing tripeptide which plays a role in cells as a source of chemical reduction potential. Sulfur is also important for hair formation. Good plant sources are garlic, onion, leeks and other Alliaceous vegetables, Brassicaceous vegetables like cauliflower, cabbages, Brussels sprout, Kale; legumes – beans, green and red gram, soybeans; horse radish, water cress, wheat germ.

Superior mesenteric artery (SMA) arises from the anterior surface of the abdominal aorta, just inferior to the origin of the celiac trunk, and supplies the intestine from the lower part of the duodenum to the left colic flexure and the pancreas.

Superoxidae mutase (SOD) antioxidant enzyme.

Suppuration the formation of pus, the act of becoming converted into and discharging pus.

Supraorbital located above the orbit of the eye.

Sural nerve sensory nerve comprising collateral branches off of the common tibial, and common fibular nerve.

SYK, Spleen tyrosine kinase is a human protein and gene. Syk plays a similar role in transmitting signals from a variety of cell surface receptors including CD74, Fc Receptor, and integrins.

Sympathetic nervous system the part of the autonomic nervous system originating in the thoracic and lumbar regions of the spinal cord that in general inhibits or opposes the physiological effects of the parasympathetic nervous system, as in tending to reduce digestive secretions or speed up the heart.

Synaptic plasticity the ability of neurons to change the number and strength of their synapses.

Synaptogenesis the formation of synapses.

Synaptoneurosomes purified synapses containing the pre- and postsynaptic termini.

Synaptosomes isolated terminal of a neuron.

Syncope fainting, sudden loss of consciousness followed by the return of wakefulness.

Syndactyly webbed toes, a condition where two or more digits are fused together.

Syneresis expulsion of liquid from a gel, as contraction of a blood clot and expulsion of liquid.

Syngeneic genetically identical or closely related, so as to allow tissue transplant; immunologically compatible.

Synovial lubricating fluid secreted by synovial membranes, as those of the joints.

Synoviocyte located in the synovial membrane, there are two types. Type A cells are more numerous, have phagocytic characteristics and produce degradative enzymes. Type B cells produce synovial fluid, which lubricates the joint and nurtures nourishes the articular cartilage.

Syphilis is perhaps the best known of all the STD's. Syphilis is transmitted by direct contact with infection sores, called chancres, syphitic skin rashes, or mucous patches on the tongue and mouth during kissing, necking, petting, or sexual intercourse. It can also be transmitted from a pregnant woman to a fetus after the fourth month of pregnancy.

System lupus erythematosus a long-term autoimmune disorder that may affect the skin, joints, kidneys, brain, and other organs. Symptoms may include chest pain, fatigue, fever, hair loss, malaise, mouth sores, sensitivity to sunlight, skin rash (butterfly-rash).

Systolic the blood pressure when the heart is contracting. It is specifically the maximum arterial pressure during contraction of the left ventricle of the heart.

T cells or T lymphocytes, a type of white blood cell that play a key role in the immune system.

Tachyarrhythmia any disturbance of the heart rhythm in which the heart rate is abnormally increased.

Tachycardia a false heart rate applied to adults to rates over 100 beats per minute.

Tachyphylaxia a decreased response to a medicine given over a period of time so that larger doses are required to produce the same response.

Tachypnea abnormally fast breathing.

Taenia a parasitic apeworm or flatworm of the genus, *Taenia*.

Taeniacide an agent that kills tapeworms.

Tau is a class of microtubule-associated protein (MAP) in neuronal and glial cells.

Tau-1 (Ser198/199/202), pS396 (Ser396), and pS214 (Ser214) epitopes serine phosphorylation sites of tau-1.

Tau phosphorylation plays an important role in neurodegenerative diseases and regulated by protein kinases and phosphatases.

TBARS see thiobarbituric acid reactive substances.

T-cell a type of white blood cell that attacks virus-infected cells, foreign cells and cancer cells.

TCA cycle see Tricarboxylic acid cycle.

TCID50 median tissue culture infective dose; that amount of a pathogenic agent that will produce pathological change in 50% of cell cultures.

Telencephalon the cerebral hemispheres, the largest divisions of the human brain.

Telomerase enzyme that acts on parts of chromosomes known as telomeres.

Temporomandibular joint disorder (TMJD or TMD syndrome) a disorder characterized by acute or chronic inflammation of the temporomandibular joint, that connects the mandible to the skull.

Tendonitis is inflammation of a tendon.

Tenesmus a strong desire to defaecate.

Teratogen is an agent that can cause malformations of an embryo or fetus. *adj*. teratogenic.

Testicular torsion twisting of the spermatic cord, which cuts off the blood supply to the testicle and surrounding structures within the scrotum.

Tetanus an acute, potentially fatal disease caused by tetanus bacilli multiplying at the site of an injury and producing an exotoxin that reaches the central nervous system producing prolonged contraction of skeletal muscle fibres. Also called lockjaw.

Tete acute dermatitis caused by both bacterial and fungal infection

Tetter any of a number of skin diseases.

TGF-beta transforming growth factor beta is a protein that controls proliferation, cellular differentiation, and other functions in most cells.

Th cells or T helper cells a subgroup of lymphocytes that helps other white blood cells in immunologic processes.

Thalassemia major is a genetic blood disorder that causes the body to manufacture an abnormal form of haemoglobin.

Thelarche the beginning of secondary (postnatal) breast development, usually occurring at the beginning of puberty in girls.

Thermogenic tending to produce heat, applied to drugs or food (fat burning food).

Thermogenesis is the process of heat production in organisms.

Thermonociceptors or thermal nociceptors, sensory receptors that are stimulated by noxius heat or cold at various temperature.

Thiobarbituric acid reactive substances (TBARS) a well-established method for screening and monitoring lipid peroxidation.

Thixotropy the property exhibited by certain gels of becoming fluid when stirred or shaken and returning to the semisolid state upon standing.

Thrombocythaemia a blood condition characterize by a high number of platelets in the blood.

Thrombocytopenia a condition when the bone marrow does not produce enough platelets (thrombocytes) like in leukaemia.

Thromboembolism formation in a blood vessel of a clot (thrombus) that breaks loose and is carried by the blood stream to plug another vessel. cf. deep vein thrombosis.

Thrombogenesis formation of a thrombus or blood clot.

Thrombophlebitis occurs when there is inflammation and clot in a surface vein.

Thromboplastin an enzyme liberated from blood platelets that converts prothrombin into thrombin as blood starts to clot, also called thrombokinase.

Thrombosis the formation or presence of a thrombus (clot).

Thromboxanes any of several compounds, originally derived from prostaglandin precursors in platelets that stimulate aggregation of platelets and constriction of blood vessels.

Thromboxane B2 the inactive product of thromboxane.

Thrombus a fibrinous clot formed in a blood vessel or in a chamber of the heart.

Thrush a common mycotic infection caused by yeast, *Candida albicans*, in the digestive tract or vagina. In children it is characterized by white spots on the tongue.

Thymocytes are T cell precursors which develop in the thymus.

Thyrotoxicosis or hyperthyroidism – an overactive thyroid gland, producing excessive circulating free thyroxine and free triiodothyronine, or both.

Tight junction associated areas of two cells whose membranes join together forming a virtually impermeable barrier to fluid.

TIMP-3 a human gene belongs to the tissue inhibitor of matrix metalloproteinases (MMP) gene family. see MMP.

Tincture solution of a drug in alcohol.

Tinea ringworm, fungal infection on the skin.

Tinea favosa See favus.

Tinea cruris ringworm of the groin.

Tinea pedis fungal infection of the foot, also called atheletes' foot.

Tinnitus a noise in the ears, as ringing, buzzing, roaring, clicking, etc.

Tisane a herbal infusion used as tea or for medicinal purposes.

Tissue plasminogen activator (t-PA) a serine protease involved in the breakdown of blood clots.

TNF alpha cachexin or cachectin and formally known as tumour necrosis factor-alpha, a cytokine involved in systemic inflammation. primary role of TNF is in the regulation of immune cells. TNF is also able to induce apoptotic cell death, to induce inflammation, and to inhibit tumorigenesis and viral replication.

Tocolytics medications used to suppress premature labor.

Tocopherol fat soluble organic compounds belonging to vitamin E group. See vitamin E.

Tocotrienol fat soluble organic compounds belonging to vitamin E group. See vitamin E.

Tolerogenic producing immunological tolerance.

Toll-like receptors (TLRs) a class of proteins that play a key role in the innate immune system.

Tonic substance that acts to restore, balance, tone, strengthen, or invigorate a body system without overt stimulation or depression

Tonic clonic seizure a type of generalized seizure that affects the entire brain.

Tonsillitis an inflammatory condition of the tonsils due to bacteria, allergies or respiratory problems.

TOP2A topoisomerase II alpha enzyme.

Topoisomerases a class of enzymes involved in the regulation of DNA supercoiling.

Topoiosmerase inhibitors a new class of anticancer agents with a mechanism of action aimed at interrupting DNA replication in cancer cells.

Total parenteral nutrition (TPN) is a method of feeding that bypasses the gastrointestinal tract.

Toxemia is the presence of abnormal substances in the blood, but the term is also used for a serious condition in pregnancy that involves hypertension and proteinuria. Also called preeclampsia.

Tracheitis is a bacterial infection of the trachea; also known as bacterial tracheitis or acute bacterial tracheitis.

Trachoma a contagious disease of the conjunctiva and cornea of the eye, producing painful sensitivity to strong light and excessive tearing.

TRAIL acronym for tumour necrosis factor-related apoptosis-inducing ligand, is a cytokine that preferentially induces apoptosis in tumour cells.

Tranquilizer a substance drug used in calming person suffering from nervous tension or anxiety.

Transaminase also called aminotransferase is an enzyme that catalyzes a type of reaction between an amino acid and an α-keto acid.

Transaminitis increase in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) to >5 times the upper limit of normal.

Transcatheter arterial chemoembolization (TACE) is an interventional radiology procedure involving percutaneous access of to the hepatic artery and passing a catheter through the abdominal artery aorta followed by radiology. It is used extensively in the palliative treatment of unresectable hepatocellular carcinoma (HCC)

Transcriptional activators are proteins that bind to DNA and stimulate transcription of nearby genes.

Transcriptional coactivator PGC-1 a potent transcriptional coactivator that regulates oxidative metabolism in a variety of tissues.

Transcriptome profiling to identify genes involved in peroxisome assembly and function.

Transforming growth factor beta (TGF-β) a protein that controls proliferation , cellular differentiation, and other functions in most cells.

Transient receptor potential vanilloid 1 (TRPV1) receptor also known as capsaicin receptor and vanilloid receptor, is a Ca 2+ permeable nonselective cation channel localized on a subset of primary sensory neurons and can be activated by physical and chemical stimuli.

TRAP 6 thrombin receptor activating peptide with 6 amino acids.

Tremorine a chemical that produces a tremor resembling Parkinsonian tremor.

Tremulous marked by trembling, quivering or shaking.

Triacylglycerols or triacylglyceride, is a glyceride in which the glycerol is esterified with three fatty acids.

Tricarboxylic acid cycle (TCA cycle) a series of enzymatic reactions in aerobic organisms involving oxidative metabolism of acetyl units and producing high-energy phosphate compounds, which serve as the main source of cellular energy. Also called citric acid cycle, Krebs cycle.

Trichophytosis infection by fungi of the genus *Trichophyto*n.

Trigeminal neuralgia (TN) is a neuropathic disorder of one or both of the facial trigeminal nerves, also known as prosopalgia.

Triglycerides a type of fat (lipids) found in the blood stream.

Trismus continuous contraction of the muscles of the jaw, specifically as a symptom of tetanus, or lockjaw; inability to open mouth fully.

TrKB receptor also known as TrKB tyrosine kinase , a protein in humans that acts as a catalytic receptor for several neutrophins.

Trolox Equivalent measures the antioxidant capacity of a given substance, as compared to the standard, Trolox also referred to as TEAC (Trolox equivalent antioxidant capacity).

Trypanocidal destructive to trypanosomes.

Trypanosomes protozoan of the genus *Trypanosoma*.

Trypanosomiasis human disease or an infection caused by a trypanosome.

Trypsin an enzyme of pancreatic juice that hydrolyzes proteins into smaller polypeptide units.

Trypsin inhibitor small protein synthesized in the exocrine pancreas which prevents conversion of trypsinogen to trypsin, so protecting itself against trypsin digestion.

TRPV1 see transient receptor potential vanilloid 1.

Tuberculosis (TB) is a bacterial infection of the lungs caused by a bacterium called *Mycobacterium tuberculosis*, characterized by the formation of lesions (tubercles) and necrosis in the lung tissues and other organs.

Tumorigenesis formation or production of tumours.

Tumour an abnormal swelling of the body other than those caused by direct injury.

Tussis a cough.

Tympanic membrane ear drum.

Tympanitis infection or inflammation of the inner ear.

Tympanophonia increased resonance of one's own voice, breath sounds, arterial murmurs, etc., noted especially in disease of the middle ear.

Tympanosclerosis see myringoslcerosis.

Tyrosinase a copper containing enzyme found in animals and plants that catalyses the oxidation of phenols (such as tyrosine) and the production of melanin and other pigments from tyrosine by oxidation.

Ubiquitin ligase also called an E3 ubiquitin ligase, is a protein that targets other proteins to be broken down (degraded) within cells.

UCP1 an uncoupling protein found in the mitochondria of brown adipose tissue used to generate heat by non-shivering thermogenesis.

UCP – 2 enzyme uncoupling protein 2 enzyme, a mitochondrial protein expressed in adipocytes.

Ulcer an open sore on an external or internal body surface usually accompanied by disintegration of tissue and pus.

Ulcerative colitis is one of 2 types of inflammatory bowel disease – a condition that causes the bowel to become inflamed and red.

Ulemorrhagia bleeding of the gums.

Ulitis inflammation of the gums.

Unguent ointment.

Unilateral ureteral obstruction unilateral blockage of urine flow through the ureter of 1 kidney, resulting in a backup of urine, distension of the renal pelvis and calyces, and hydronephrosis.

Uraemia an excess in the blood of urea, creatinine and other nitrogenous end products of protein and amino acids metabolism, more correctly referred to as azotaemia.

Urethra tube conveying urine from the bladder to the external urethral orifice.

Urethritis is an inflammation of the urethra caused by infection.

Uricemia an excess of uric acid or urates in the blood.

Uricosuric promoting the excretion of uric acid in the urine.

Urinary pertaining to the passage of urine.

Urinogenital relating to the genital and urinary organs or functions.

Urodynia pain on urination.

Urokinase also called urokinase-type plasminogen (u-PA), is a serine protease enzyme in human urine that catalyzes the conversion of plasminogen to plasmin. It is used clinically as a thrombolytic agent.

Urokinase-type palsminogen (u-PA) plays a key role in tumour invasion and metastasis, also see Urokinase.

Urolithiasis formation of stone in the urinary tract (kidney bladder or urethra).

Urticant a substance that causes wheals to form.

Urticaria (or hives) is a skin condition, commonly caused by an allergic reaction, that is characterized by raised red skin welts.

Uterine relating to the uterus.

Uterine relaxant an agent that relaxes the muscles in the uterus.

Uterine stimulant an agent that stimulates the uterus (and often employed during active childbirth).

Uterotonic giving muscular tone to the uterus.

Uterotrophic causing an effect on the uterus.

Uterus womb.

Vagotomy the surgical cutting of the vagus nerve to reduce acid secretion in the stomach.

Vagus nerve a cranial nerve, that is, a nerve connected to the brain. The vagus nerve has branches to most of the major organs in the body, including the larynx, throat, windpipe, lungs, heart, and most of the digestive system

Variola or smallpox, a contagious disease unique to humans, caused by either of two virus variants, *Variola major* and *Variola minor*. The disease is characterised by fever, weakness and skin eruption with pustules that form scabs that leave scars.

Varicose veins are veins that have become enlarged and twisted.

Vasa vasorum is a network of small blood vessels that supply large blood vessels. *plur*. vasa vasori.

Vascular endothelial growth factor (VEGF) a polypeptide chemical produced by cells that stimulates the growth of new blood vessels.

Vasculogenesis the process of blood vessel formation occurring by a de novo production of endothelial cells.

Vasoconstrictor drug that causes constriction of blood vessels.

Vasodilator drug that causes dilation or relaxation of blood vessels.

Vasodilatory causing the widening of the lumen of blood vessels.

Vasomotor symptoms menopausal symptoms characterised by hot flushes and night sweats.

Vasospasm refers to a condition in which blood vessels spasm, leading to vasoconstriction and subsequently to tissue ischemia and death (necrosis).

VCAM-1 (vascular cell adhesion molecule-1) also known as CD106, contains six or seven immunoglobulin domains and is expressed on both large and small vessels only after the endothelial cells are stimulated by cytokines.

VEGF Vascular endothelial growth factor.

Venereal disease (VD) term given to the diseases syphilis and gonorrhoea.

Venule a small vein, especially one joining capillaries to larger veins.

Vermifuge a substance used to expel worms from the intestines.

Verotoxin a Shiga-like toxin produced by *Escherichia coli*, which disrupts the function of ribosomes, causing acute renal failure.

Verruca plana is a reddish-brown or flesh-colored, slightly raised, flat-surfaced, well-demarcated papule on the hand and face, also called flat wart.

Verruca vulgaris small painless warts on the skin caused by the human papillomavirus.

Vertigo an illusory, sensory perception that the surroundings or one's own body are revolving; dizziness.

Very-low-density lipoprotein (VLDL) a type of lipoprotein made by the liver. VLDL is one of the five major groups of lipoproteins (chylomicrons, VLDL, intermediate-density lipoprotein, low-density lipoprotein, high-density lipoprotein (HDL)) that enable fats and cholesterol to move within the water-based solution of the bloodstream. VLDL is converted in the bloodstream to low-density lipoprotein (LDL).

Vesical calculus calculi (stones) in the urinary bladder

Vesicant a substance that causes tissue blistering.

Vestibular relating to the sense of balance.

Vestibular disorders includes symptoms of dizziness, vertigo, and imbalance; it can be result from or worsened by genetic or environmental conditions.

Vestibular system includes parts of the inner ear and brain that process sensory information involved with controlling balance and eye movement.

Vibrissa stiff hairs that are located especially about the nostrils.

Viremia a medical condition where viruses enter the bloodstream and hence have access to the rest of the body.

Visceral fat intra-abdominal fat, is located inside the peritoneal cavity, packed in between internal organs and torso.

Vitamin any complex, organic compound, found in various food or sometimes synthesized in the body, required in tiny amounts and are essential for the regulation of metabolism, normal growth and function of the body.

Vitamin A retinol, fat-soluble vitamins that play an important role in vision, bone growth, reproduction, cell division, and cell differentiation, helps regulate the immune system in preventing or fighting off infections. Vitamin A that is found in colorful fruits and vegetables is called provitamin A carotenoid. They can be made into retinol in the body. Deficiency of vitamin A results in night blindness and keratomalacia.

Vitamin B1 also called thiamine, water-soluble vitamins, dissolve easily in water, and in general, are readily excreted from the body they are not readily stored, consistent daily intake is important. It functions as coenzyme in the metabolism of carbohydrates and branched chain amino acids, and other cellular processes. Deficiency results in beri-beri disease.

Vitamin B2 also called riboflavin, an essential water-soluble vitamin that functions as coenzyme in redox reactions. Deficiency causes ariboflavinosis.

Vitamin B3 comprises niacin and niacinamide, water-soluble vitamin that function as coenzyme or co-substrate for many redox reactions and is required for energy metabolism. Deficiency causes pellagra.

Vitamin B5 also called pantothenic acid, a water-soluble vitamin that function as coenzyme in fatty acid metabolism. Deficiency causes paresthesia.

Vitamin B6 water-soluble vitamin, exists in three major chemical forms: pyridoxine, pyridoxal, and pyridoxamine. Vitamin B6 is needed in enzymes involved in protein metabolism, red blood cell metabolism, efficient functioning of nervous and immune systems and hemoglobin formation. Deficiency causes anaemia and peripheral neuropathy.

Vitamin B7 also called biotin or vitamin H, an essential water-soluble vitamin, is involved in the synthesis of fatty acids amino acids and glucose, in energy metabolism. Biotin promotes normal health of sweat glands, bone marrow, male gonads, blood cells, nerve tissue, skin and hair, Deficiency causes dermatitis and enteritis.

Vitamin B9 also called folic acid, an essential water-soluble vitamin. Folate is especially important during periods of rapid cell division and growth such as infancy and pregnancy. Deficiency during pregnancy is associated with birth defects such as neural tube defects. Folate is also important for production of red blood cells and prevent anemia. Folate is needed to make DNA and RNA, the building blocks of cells. It also helps prevent changes to DNA that may lead to cancer.

Vitamin B12 a water-soluble vitamin, also called cobalamin as it contains the metal cobalt. It helps maintain healthy nerve cells and red blood cells, and DNA production. Vitamin B12 is bound to the protein in food. Deficiency causes megaloblastic anaemia.

Vitamin C also known as ascorbic acid is an essential water-soluble vitamin. It functions as cofactor for reactions requiring reduced copper or iron metallonzyme and as a protective antioxidant. Deficiency of vitamin C causes scurvy.

Vitamin D a group of fat-soluble, prohormone vitamin, the two major forms of which are vitamin D2 (or ergocalciferol) and vitamin D3 (or cholecalciferol). Vitamin D obtained from

sun exposure, food, and supplements is biologically inert and must undergo two hydroxylations in the body for activation. Vitamin D is essential for promoting calcium absorption in the gut and maintaining adequate serum calcium and phosphate concentrations to enable normal growth and mineralization of bone and prevent hypocalcemic tetany. Deficiency causes rickets and osteomalacia. Vitamin D has other roles in human health, including modulation of neuromuscular and immune function, reduction of inflammation and modulation of many genes encoding proteins that regulate cell proliferation, differentiation, and apoptosis.

Vitamin E is the collective name for a group of fat-soluble compounds and exists in eight chemical forms (alpha-, beta-, gamma-, and delta-tocopherol and alpha-, beta-, gamma-, and delta-tocotrienol). It has pronounced antioxidant activities stopping the formation of Reactive Oxygen Species when fat undergoes oxidation and help prevent or delay the chronic diseases associated with free radicals. Besides its antioxidant activities, vitamin E is involved in immune function, cell signaling, regulation of gene expression, and other metabolic processes. Deficiency is very rare but can cause mild hemolytic anemia in newborn infants.

Vitamin K a group of fat soluble vitamin and consist of vitamin K1 which is also known as phylloquinone or phytomenadione (also called phytonadione) and vitamin K2 (menaquinone, menatetrenone). Vitamin K plays an important role in blood clotting. Deficiency is very rare but can cause bleeding diathesis.

Vitamin P a substance or mixture of substances obtained from various plant sources, identified as citrin or a mixture of bioflavonoids, thought to but not proven to be useful in reducing the extent of hemorrhage.

Vitiligo a chronic skin disease that causes loss of pigment, resulting in irregular pale patches of skin. It occurs when the melanocytes, cells responsible for skin pigmentation, die or are unable to function. Also called leucoderma.

Vitreoretinopathy see proliferative vitreoretinopathy.

VLA-4 very late antigen-4, expressed by most leucocytes but it is observed on neutrophils under special conditions.

VLDL see very low density lipoproteins.

Vomitive substance that causes vomiting.

Vulnerary (wound healer), a substance used to heal wounds and promote tissue formation.

Wart an infectious skin tumour caused by a viral infection.

Welt see wheal.

Wheal a firm, elevated swelling of the skin. Also called a weal or welt.

White fat white adipose tissue (WAT) in mammals, store of energy . cf. brown fat.

Whitlow painful infection of the hand involving 1 or more fingers that typically affects the terminal phalanx.

Whooping cough acute infectious disease usually in children caused by a *Bacillus* bacterium and accompanied by catarrh of the respiratory passages and repeated bouts of coughing.

Wnt signaling pathway is a network of proteins involved in embryogenesis and cancer, and also in normal physiological processes.

X-linked agammaglobulinemia also known as X-linked hypogammaglobulinemia, XLA, Bruton type agammaglobulinemia, Bruton syndrome, or sex-linked agammaglobulinemia; a rare x-linked genetic disorder that affects the body's ability to fight infection.

Xanthine oxidase a flavoprotein enzyme containing a molybdenum cofactor (Moco) and (Fe2S2) clusters, involved in purine metabolism. In humans, inhibition of xanthine oxidase reduces the production of uric acid, and prevent hyperuricemia and gout.

Xanthones unique class of biologically active phenol compounds with the molecular formula C13H8O2 possessing antioxidant properties, discovered in the mangosteen fruit.

Xenobiotics a chemical (as a drug, pesticide, or carcinogen) that is foreign to a living organism.

Xenograft a surgical graft of tissue from one species to an unlike species.

Xerophthalmia a medical condition in which the eye fails to produce tears.

Yaws an infectious tropical infection of the skin, bones and joints caused by the spirochete bacterium *Treponema pertenue*, characterized by papules and papilloma with subsequent deformation of the skins, bone and joints; also called framboesia.

yGCN5 a histone acetyl transferase (HAT) that plays a role in regulation of transciton, cell cycly progression and differentiation.

Yellow fever is a viral disease that is transmitted to humans through the bite of infected mosquitoes. Illness ranges in severity from an influenza-like syndrome to severe hepatitis and hemorrhagic fever. Yellow fever virus (YFV) is maintained in nature by mosquito-borne transmission between nonhuman primates.

Zeaxanthin a common carotenoid, found naturally as coloured pigments in many fruit vegetables and leafy vegetables. It is important for good vision and is one of the two carotenoids contained within the retina of the eye. Within the central macula, zeaxanthin predominates, whereas in the peripheral retina, lutein predominates.

Zinc (Zn) is an essential mineral for health. It is involved in numerous aspects of cellular metabolism: catalytic activity of enzymes, immune function, protein synthesis, wound healing, DNA synthesis, and cell division. It also supports normal growth and development during pregnancy, childhood, and adolescence and is required for proper sense of taste and smell. Dietary sources include beans, nuts, pumpkin seeds, sunflower seeds, whole wheat bread and animal sources.

ZO1 protein A high molecular weight tight junction-associated protein.

Scientific Glossary

Abaxial facing away from the axis, as of the surface of an organ.

Abscission shedding of leaves, flowers, or fruits following the formation of the abscission zone.

Acaulescent lacking a stem, or stem very much reduced.

Accrescent increasing in size after flowering or with age.

Achene a dry, small, one-seeded, indehiscent one-seeded fruit formed from a superior ovary of one carpel as in sunflower.

Acid soil soil that maintains a pH of less than 7.0.

Acidulous acid or sour in taste.

Actinomorphic having radial symmetry, capable of being divided into symmetrical halves by any plane, refers to a flower, calyx or corolla.

Aculeate having sharp prickles.

Acuminate tapering gradually to a sharp point.

Acute (Botany) tapering at an angle of less than 90 degrees before terminating in a point as of leaf apex and base.

Adaxial side closest to the stem axis.

Aldephous having stamens united together by their filaments.

Adherent touching without organic fusion as of floral parts of different whorls.

Adnate united with another unlike part as of stamens attached to petals.

Adpressed lying close to another organ but not fused to it.

Adventitious arising in abnormal positions, e.g. roots arising from the stem, branches or leaves, buds arising elsewhere than in the axils of leaves.

Adventive Not native to and not fully established in a new habitat or environment; locally or temporarily naturalized. e.g. an adventive weed.

Aestivation refers to positional arrangement of the floral parts in the bud before it opens.

Akinete a thick-walled dormant cell derived from the enlargement of a vegetative cell. It serves as a survival structure.

Alfisols soil with a clay-enriched subsoil and relatively high native fertility, having undergone only moderate leaching, containing aluminium, iron and with at least 35% base saturation, meaning that calcium, magnesium, and potassium are relatively abundant.

Alkaline soil soil that maintains a pH above 7.0, usually containing large amounts of calcium, sodium, and magnesium, and is less soluble than acidic soils.

Alkaloids naturally occurring bitter, complex organic-chemical compounds containing basic nitrogen and oxygen atoms and having various pharmacological effects on humans and other animals.

Alternate leaves or buds that are spaced along opposite sides of stem at different levels.

Allomorphic with a shape or form different from the typical.

Alluvial soil a fine-grained fertile soil deposited by water flowing over flood plains or in river beds.

Alluvium soil or sediments deposited by a river or other running water.

Amplexicaul clasping the stem as base of certain leaves.

Anatomizing interconnecting network as applied to leaf veins.

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Andisols are soils formed in volcanic ash and containing high proportions of glass and amorphous colloidal materials.

Androdioecious with male flowers and bisexual flowers on separate plants.

Androecium male parts of a flower; comprising the stamens of one flower.

Androgynophore a stalk bearing both the androecium and gynoecium above the perianth of the flower.

Androgynous with male and female flowers in distinct parts of the same inflorescence.

Andromonoecious having male flowers and bisexual flowers on the same plant.

Angiosperm a division of seed plants with the ovules borne in an ovary.

Annual a plant which completes its life cycle within a year.

Annular shaped like or forming a ring.

Annulus circle or ring-like structure or marking; the portion of the corolla which forms a fleshy, raised ring.

Anthelate an open, paniculate cyme.

Anther the part of the stamen containing pollen sac which produces the pollen.

Antheriferous containing anthers.

Anthesis the period between the opening of the bud and the onset of flower withering.

Anthocarp a false fruit consisting of the true fruit and the base of the perianth.

Anthocyanidins are common plant pigments. They are the sugar-free counterparts of anthocyanins.

Anthocyanins a subgroup of antioxidant flavonoids, are glucosides of anthocyanidins. They occur as water-soluble vacuolar pigments that may appear red, purple, or blue according to pH in plants.

Antipetala situated opposite petals.

Antisepala situated opposite sepals.

Antrorse directed forward upwards.

Apetalous lacking petals as of flowers with no corolla.

Apical meristem active growing point. A zone of cell division at the tip of the stem or the root.

Apically towards the apex or tip of a structure.

Apiculate ending abruptly in a short, sharp, small point.

Apiculum a short, pointed, flexible tip.

Apocarpous carpels separate in single individual pistils.

Apopetalous with separate petals, not united to other petals.

Aposepalous with separate sepals, not united to other sepals.

Appressed pressed closely to another structure but not fused or united.

Aquatic a plant living in or on water for all or a considerable part of its life span.

Arachnoid (Botany) formed of or covered with long, delicate hairs or fibers.

Arborescent resembling a tree; applied to non-woody plants attaining tree height and to shrubs tending to become tree-like in size.

Arbuscular mycorrhiza (AM) a type of mycorrhiza in which the fungus (of the phylum Glomeromycota) penetrates the cortical cells of the roots of a vascular plant and form unique structures such as arbuscules and vesicles. These fungi help plants to capture nutrients such as phosphorus and micronutrients from the soil.

Archegonium a flask-shaped female reproductive organ in mosses, ferns, and other related plants.

Areolate with areolea.

Areole (Botany) a small, specialized, cushion-like area on a cactus from which hairs, glochids, spines, branches, or flowers may arise; an irregular angular spces marked out on a surface e.g. fruit surface. *pl*. areolea.

Aril specialized outgrowth from the funiculus (attachment point of the seed) (or hilum) that encloses or is attached to the seed. *adj*. arillate.

Arillode a false aril; an aril originating from the micropyle instead of from the funicle or chalaza of the ovule, e.g. mace of nutmeg.

Aristate bristle-like part or appendage, e.g. awns of grains and grasses.

Aristulate having a small, stiff, bristle-like part or appendage; a diminutive of aristate

Articulate jointed; usually breaking easily at the nodes or point of articulation into segments.

Ascending arched upwards in the lower part and becoming erect in the upper part.

Ascospore spore produced in the ascus in Ascomycete fungi.

Ascus is the sexual spore-bearing cell produced in Ascomycete fungi. *pl*. asci.

Asperulous refers to a rough surface with short, hard projections.

Attenuate tapered or tapering gradually to a point.

Auricle an ear-like appendage that occurs at the base of some leaves or corolla.

Auriculate having auricles.

Awn a hair-like or bristle-like appendage on a larger structure.

Axil upper angle between a lateral organ, such as a leaf petiole and the stem that bears it.

Axile situated along the central axis of an ovary having two or more locules, as in axile placentation.

Axillary arising or growing in an axil.

Baccate beery-like, pulpy or fleshy.

Barbate bearded, having tufts of hairs.

Barbellae short, stiff, hair-like bristles. *adj*. barbellate.

Bark is the outermost layers of stems and roots of woody plants.

Basal relating to, situated at, arising from or forming the base.

Basaltic soil soil derived from basalt, a common extrusive volcanic rock.

Basidiospore a reproductive spore produced by Basidiomycete fungi.

Basidium a microscopic, spore-producing structure found on the hymenophore of fruiting bodies of Basidiomycete fungi.

Basifixed attached by the base, as certain anthers are to their filaments.

Basionym the synonym of a scientific name that supplies the epithet for the correct name.

Beak a prominent apical projection, especially of a carpel or fruit. *adj*. beaked.

Bearded having a tuft of hairs.

Berry a fleshy or pulpy indehiscent fruit from a single ovary with the seed(s) embedded in the fleshy tissue of the pericarp.

Biconvex convex on both sides.

Biennial completing the full cycle from germination to fruiting in more than one, but not more than 2 years.

Bifid forked, divided into two parts.

Bifoliolate having two leaflets.

Bilabiate having two lips as of a corolla or calyx with segments fused into an upper and lower lip.

Bipinnate twice pinnate; the primary leaflets being again divided into secondary leaflets.

Bipinnatisect refers to a pinnately compound leaf, in which each leaflet is again divided into pinnae.

Biserrate doubly serrate; with smaller regular, asymmetric teeth on the margins of larger teeth.

Bisexual having both sexes, as in a flower bearing both stamens and pistil, hermaphrodite or perfect.

Biternate Twice ternate; with three pinnae each divided into three pinnules.

Blade lamina; part of the leaf above the sheath or petiole.

Blotched see variegated.

Bole main trunk of tree from the base to the first branch.

Brachyblast a short, axillary, densely crowded branchlet or shoot of limited growth, in which the internodes elongate little or not at all.

Bracket fungus shelf fungus.

Bract a leaf-like structure, different in form from the foliage leaves, associated with an inflorescence or flower. *adj*. bracteate.

Bracteate possessing bracts.

Bracteolate having bracteoles.

Bracteole a small, secondary, bract-like structure borne singly or in a pair on the pedicel or calyx of a flower. *adj*. bracteolate.

Bran hard outer layer of grain and comprises the aleurone and pericarp. It contains important antioxidant, vitamins and fibre.

Bristle a stiff hair.

Bulb a modified underground axis that is short and crowned by a mass of usually fleshy, imbricate scales. *adj*. bulbous.

Bulbil A small bulb or bulb-shaped body, especially one borne in the leaf axil or an inflorescence, and usually produced for asexual reproduction.

Bullate puckered, blistered.

Burr type of seed or fruit with short, stiff bristles or hooks or may refer to a deformed type of wood in which the grain has been misformed.

Bush low, dense shrub without a pronounced trunk.

Buttress supporting, projecting outgrowth from base of a tree trunk as in some Rhizophoraceae and Moraceae.

Caducous shedding or falling early before maturity refers to sepals and petals.

Caespitose growing densely in tufts or clumps; having short, closely packed stems.

Calcareous composed of or containing lime or limestone.

Calcrete a hardpan consisting gravel and sand cemented by calcium.

Callus a condition of thickened raised mass of hardened tissue on leaves or other plant parts often formed after an injury but sometimes a normal feature. A callus also can refer to an undifferentiated plant cell mass grown on a culture medium. *n*. callosity. *pl*. calli, callosities. *adj*. callose.

Calyptra the protective cap or hood covering the spore case of a moss or related plant.

Calyptrate operculate, having a calyptra.

Calyx outer floral whorl usually consisting of free sepals or fused sepals (calyx tube) and calyx lobes. It encloses the flower while it is still a bud. *adj*. calycine.

Calyx lobe one of the free upper parts of the calyx which may be present when the lower part is united into a tube.

Calyx tube the tubular fused part of the calyx, often cup shaped or bell shaped, when it is free from the corolla.

Campanulate shaped like a bell refers to calyx or corolla.

Canaliculate having groove or grooves.

Candelabriform having the shape of a tall branched candle-stick.

Canescent covered with short, fine whitish or grayish hairs or down.

Canopy uppermost leafy stratum of a tree.

Cap see pileus.

Capitate growing together in a head. Also means enlarged and globular at the tip.

Capitulum a flower head or inflorescence having a dense cluster of sessile, or almost sessile, flowers or florets.

Capsule a dry, dehiscent fruit formed from two or more united carpels and dehiscing at maturity by sections called valves to release the seeds. *adj*. capsular.

Carinate keeled.

Carpel a simple pistil consisting of ovary, ovules, style and stigma. *adj*. carpellary.

Carpogonium female reproductive organ in red algae. *pl*. carpogonia.

Carpophore part of the receptacle which is lengthened between the carpels as a central axis; any fruiting body or fruiting structure of a fungus.

Cartilaginous sinewy, having a firm, tough, flexible texture (in respect of leaf margins).

Caryopsis a simple dry, indehiscent fruit formed from a single ovary with the seed coat united with the ovary wall as in grasses and cereals.

Cataphyll a reduced or scarcely developed leaf at the start of a plant's life (i.e., cotyledons) or in the early stages of leaf development.

Catkin a slim, cylindrical, pendulous flower spike usually with unisexual flowers.

Caudate having a narrow, tail-like appendage.

Caudex thickened, usually underground base of the stem.

Caulescent having a well developed aerial stem.

Cauliflory botanical term referring to plants which flower and fruit from their main stems or woody trunks. *adj*. cauliflorus.

Cauline borne on the aerial part of a stem.

Chaffy having thin, membranous scales in the inflorescence as in the flower heads of the sunflower family.

Chalaza the basal region of the ovule where the stalk is attached.

Chartaceous papery, of paper-like texture.

Chasmogamous describing flowers in which pollination takes place while the flower is open.

Chloroplast a chlorophyll-containing organelle (plastid) that gives the green colour to leaves and stems. Plastids harness light energy that is used to fix carbon dioxide in the process called photosynthesis.

Chromoplast plastid containing colored pigments apart from chlorophyll.

Chromosomes thread-shaped structures that occur in pairs in the nucleus of a cell, containing the genetic information of living organisms.

Cilia hairs along the margin of a leaf or corolla lobe.

Ciliate with a fringe of hairs on the margin as of the corolla lobes or leaf.

Ciliolate minutely ciliate.

Cilium a straight, usually erect hair on a margin or ridge. *pl*. cilia.

Cincinnus a monochasial cyme in which the lateral branches arise alternately on opposite sides of the false axis.

Circinnate spirally coiled, with the tip innermost.

Circumscissile opening by a transverse line around the circumference as of a fruit.

Cladode the modified photosynthetic stem of a plant whose foliage leaves are much reduced or absent. *cf*. cladophyll, phyllode.

Cladophyll A photosynthetic branch or portion of a stem that resembles and functions as a leaf, like in asparagus. *cf*. cladode, phyllode.

Clamp connection In the Basidiomycetes fungi, a lateral connection or outgrowth formed between two adjoining cells of a hypha and arching over the septum between them.

Clavate club shaped thickened at one end refer to fruit or other organs.

Claw the conspicuously narrowed basal part of a flat structure.

Clay a naturally occurring material composed primarily of fine-grained minerals like kaolinite, montmorrillonite-smectite or illite which exhibit plasticity through a variable range of water content, and which can be hardened when dried and/or fired.

Clayey resembling or containing a large proportion of clay.

Cleft incised halfway down.

Cleistogamous refers to a flower in which fertilization occurs within the bud i.e. without the flower opening. *cf*. chasmogamous.

Climber growing more or less upwards by leaning or twining around another structure.

Clone all the plants reproduced, vegetatively, from a single parent thus having the same gentic make-up as the parent.

Coccus one of the sections of a distinctly lobed fruit which becomes separate at maturity; sometimes called a mericarp. *pl*. cocci.

Coenocarpium a fleshy, multiple pseudocarp formed from an inflorescence rather than a single flower.

Coherent touching without organic fusion, referring to parts normally together, e.g. floral parts of the same whorl. *cf*. adherent, adnate, connate.

Collar boundary between the above- and below ground parts of the plant axis.

Colliculate having small elevations.

Column a structure formed by the united style, stigma and stamen(s) as in Asclepiadaceae and Orchidaceae.

Comose tufted with hairs at the ends as of seeds.

Composite having two types of florets as of the flowers in the sunflower family, Asteraceae.

Compost organic matter (like leaves, mulch, manure, etc.) that breaks down in soil releasing its nutrients.

Compound describe a leaf that is further divided into leaflets or pinnae or flower with more than a single floret.

Compressed flattened in one plane.

Conceptacles specialised cavities of marine algae that contain the reproductive organs.

Concolorous uniformly coloured, as in upper and lower surfaces. *cf*. discolorous

Conduplicate folded together lengthwise.

Cone a reproductive structure composed of an axis (branch) bearing sterile bract-like organs and seed or pollen bearing structures. Applied to Gymnospermae, Lycopodiaceae, Casuarinaceae and also in some members of Proteaceae.

Conic cone shaped, attached at the broader end.

Conic-capitate a cone-shaped head of flowers.

Connate fused to another structure of the same kind. *cf*. adherent, adnate, coherent.

Connective the tissue separating two lobes of an anther.

Connivent converging.

Conspecific within or belonging to the same species.

Contorted twisted.

Convolute refers to an arrangement of petals in a bud where each has one side overlapping the adjacent petal.

Cordate heart-shaped as of leaves.

Core central part.

Coriaceous leathery texture as of leaves.

Corm a short, swollen, fleshy, underground plant stem that serves as a food storage organ used by some plants to survive winter or other adverse conditions

Cormel a miniature, new corm produced on a mature corm.

Corn silk the long, filamentous styles that grow as a silky tuft or tassel at the tip of an ear of corn.

Corolla the inner floral whorl of a flower, usually consisting of free petals or a petals fused forming a corolla tube and corolla lobes. *adj*. corolline.

Corona a crown-like section of the staminal column, usually with the inner and outer lobes as in the **Stapelieae**.

Coroniform crown shaped, as in the pappus of Asteraceae.

Cortex the outer of the stem or root of a plant, bounded on the outside by the epidermis and on the inside by the endodermis containing undifferentiated cells.

Corymb a flat-topped, short, broad inflorescence, in which the flowers, through unequal pedicels, are in one horizontal plane and the youngest in the centre. *adj*. corymbose

Costa a thickened, linear ridge or the midrib of the pinna in ferns. *adj*. costate.

Costapalmate having definite costa (midrib) unlike the typical palmate leaf, but the leaflets are arranged radially like in a palmate leaf.

Cotyledon the primary seed leaf within the embryo of a seed.

Cover crop crop grown in between trees or in fields primarily to protect the soil from erosion, to improve soil fertility and to keep off weeds.

Crenate round-toothed or scalloped as of leaf margins.

Crenulate minutely crenate, very strongly scalloped.

Crisped with a curled or twisted edge.

Cristate having or forming a crest or crista.

Crozier shaped like a shepherd's crook.

Crustaceous like a crust; having a hard crust or shell.

Cucullate having the shape of a cowl or hood, hooded.

Culm the main aerial stem of the Graminae (grasses, sedges, rushes and other monocots).

Culm sheath the plant casing (similar to a leaf) that protects the young bamboo shoot during growth, attached at each node of culm.

Cultigen plant species or race known only in cultivation.

Cultivar cultivated variety; an assemblage of cultivated individuals distinguished by any characters significant for the purposes of agriculture, forestry or horticulture, and which, when reproduced, retains its distinguishing features.

Cuneate wedge-shaped, obtriangular.

Cupular cup-shaped, having a cupule.

Cupule a small cup-shaped structure or organ, like the cup at the base of an acorn.

Cusp an elongated, usually rigid, acute point. *cf*. mucro.

Cuspidate terminating in or tipped with a sharp firm point or cusp. *cf*. mucronate.

Cuspidulate constricted into a minute cusp. *cf*. cuspidate.

Cyathiform in the form of a cup, a little widened at the top.

Cyathium a specialised type of inflorescence of plants in the genus Euphorbia and Chamaesyce in which the unisexual flowers are clustered together within a bract-like envelope. *pl*. cyathia.

Cylindric tubular or rod shaped.

Cylindric-acuminate elongated and tapering to a point.

Cymbiform boat shaped, elongated and having the upper surface decidedly concave.

Cyme an inflorescence in which the lateral axis grows more strongly than the main axis with the oldest flower in the centre or at the ends. *adj*. cymose

Cymule a small cyme or one or a few flowers.

Cystidium a relatively large cell found on the hymenium of a Basidiomycete, for example, on the surface of a mushroom.

Cystocarp fruitlike structure (sporocarp) developed after fertilization in the red algae.

Deciduous falling off or shedding at maturity or a specific season or stage of growth.

Decorticate to remove the bark, rind or husk from an organ; to strip of its bark; to come off as a skin.

Decompound as of a compound leaf; consisting of divisions that are themselves compound.

Decumbent prostrate, laying or growing on the ground but with ascending tips. *cf*. ascending, procumbent.

Decurrent having the leaf base tapering down to a narrow wing that extends to the stem.

Decussate having paired organs with successive pairs at right angles to give four rows as of leaves.

Deflexed bent downwards.

Degumming removal of gum deposits (phosphatides, entrained oil and meal particles) from crude edible oils traditionally done with water. Water degumming process also remove hydrophilic substances such as sugars from the oil.

Dehisce to split open at maturity, as in a capsule.

Dehiscent splitting open at maturity to release the contents. *cf*. indehiscent.

Deltate triangular shape.

Deltoid shaped like an equilateral triangle.

Dendritic branching from a main stem or axis like the branches of a tree.

Dentate with sharp, rather coarse teeth perpendicular to the margin.

Denticulate finely toothed.

Diageotropic the tendency of growing parts, such as roots, to grow at right angle to the line of gravity.

Diadelphous having stamens in two bundles as in Papilionaceae flowers.

Dichasium a cymose inflorescence in which the branches are opposite and approximately equal. *pl*. dichasia. *adj*. dichasial.

Dichotomous divided into two parts.

Dicotyledon angiosperm with two cotyledons.

Didymous arranged or occurring in pairs as of anthers, having two lobes.

Digitate having digits or fingerlike projections.

Dikaryophyses or dendrophydia, irregularly, strongly branched terminal hyphae in the Hymenomycetes (class of Basidiomycetes) fungi.

Dimorphic having or occurring in two forms, as of stamens of two different lengths or a plant having two kinds of leaves.

Dioecious with male and female unisexual flowers on separate plants. *cf*. monoecious.

Diploid a condition in which the chromosomes in the nucleus of a cell exist as pairs, one set being derived from the female parent and the other from the male.

Diplobiontic life cycle life cycle that exhibits alternation of generations, which features of spore-producing multicellular sporophytes and gamete-producing multicellular gametophytes. mitoses occur in both the diploid and haploid phases.

Diplontic life cycle or gametic meiosis, wherein instead of immediately dividing meiotically to produce haploid cells, the zygote divides mitotically to produce a multicellular diploid individual or a group of more diploid cells.

Dipterocarpous trees of the family Dipterocarpaceae, with two-winged fruit found mainly in tropical lowland rainforest.

Disc (Botany) refers to the usually disc shaped receptacle of the flower head in Asteraceae; also the fleshy nectariferous organ usually between the stamens and ovary; also used for the enlarged style-end in Proteaceae.

Disc floret the central, tubular 4 or 5-toothed or lobed floret on the disc of an inflorescence, as of flower head of Asteraceae.

Disciform flat and rounded in shaped. *cf*. discoid, radiate.

Discoid resembling a disc; having a flat, circular form; disk-shaped *cf*. disciform, radiate.

Discolorous having two colours, as of a leaf which has different colors on the two surfaces. *cf*. concolorous.

Disomic having one or more chromosomes present twice but without the entire genome doubled.

Dispersal dissemination of seeds.

Distal site of any structure farthest from the point of attachment. *cf*. proximal.

Distichous referring to two rows of upright leaves in the same plane.

Dithecous having two thecae.

Divaricate diverging at a wide angle.

Domatium a part of a plant (e.g., a leaf) that has been modified to provide protection for other organisms. *pl*. domatia.

Dormancy a resting period in the life of a plant during which growth slows or appears to stop.

Dorsal referring to the back surface.

Dorsifixed attached to the back as of anthers.

Drupaceous resembling a drupe.

Drupe a fleshy fruit with a single seed enclosed in a hard shell (endocarp) which is tissue embedded in succulent tissue (mesocarp) surrounded by a thin outer skin (epicarp). *adj*. drupaceous.

Drupelet a small drupe.

Ebracteate without bracts.

Echinate bearing stiff, stout, bristly, prickly hairs.

Edaphic refers to plant communities that are distinguished by soil conditions rather than by the climate.

Eglandular without glands. *cf*. glandular.

Ellipsoid a 3-dimensional shape; elliptic in outline.

Elliptic having a 2-dimensional shape of an ellipse or flattened circle.

Eongate extended, stretched out.

Emarginate refers to leaf with a broad, shallow notch at the apex. *cf*. retuse.

Embryo (Botany) a minute rudimentary plant contained within a seed or an archegonium, composed of the embryonic axis (shoot end and root end).

Endemic prevalent in or peculiar to a particular geographical locality or region.

Endocarp The hard innermost layer of the pericarp of many fruits.

Endosperm tissue that surrounds and nourishes the embryo in the angiosperm seed. It contains starchy carbohydrates, proteins and small amounts of vitamins and minerals.

Endospermous refers to seeds having an endosperm.

Endotrophic as of mycorrhiza obtaining nutrients from inside.

Ensilage the process of preserving green food for livestock in an undried condition in airtight conditions. Also called silaging.

Entire having a smooth, continuous margin without any incisions or teeth as of a leaf.

Entisols soils that do not show any profile development other than an A horizon.

Ephemeral transitory, short-lived.

Epicalyx a whorl of bracts, subtending and resembling a calyx.

Epicarp outermost layer of the pericarp of a fruit.

Epicormic attached to the corm.

Epicotyl the upper portion of the embryonic axis, above the cotyledons and below the first true leaves.

Epigeal above grounds with cotyledons raised above ground.

Epiparasite an organism parasitic on another that parasitizes a third.

Epipetalous borne on the petals, as of stamens.

Epiphyte a plant growing on, but not parasitic on, another plant, deriving its moisture and nutrients from the air and rain e.g. some Orchidaceae. *adj*. epiphytic.

Erect upright, vertical.

Essential oils volatile products obtained from a natural source; refers to volatile products obtained by steam or water distillation in a strict sense.

Etiolation to cause (a plant) to develop without chlorophyll by preventing exposure to sunlight.

Eutrophic having waters rich in mineral and organic nutrients that promote a proliferation of plant life, especially algae, which reduces the dissolved oxygen content and often causes the extinction of other organisms.

Excentric off the true centre.

Excrescence abnormal outgrowth.

Excurrent projecting beyond the tip, as the midrib of a leaf or bract.

Exserted sticking out, protruding beyond some enclosing organ, as of stamens which project beyond the corolla or perianth.

Exstipulate without stipules. *cf*. stipulate.

Extra-floral outside the flower.

Extrose turned outwards or away from the axis as of anthers. *cf*. introrse, latrorse.

Falcate sickle shaped, crescent-shaped.

Fascicle a cluster or bundle of stems, flowers, stamens. *adj*. fasciculate.

Fasciclode staminode bundles.

Fastigiate a tree in which the branches grow almost vertically.

Ferrosols soils with an iron oxide content of greater than 5%.

Ferruginous rust coloured, reddish-brown.

Fertile having functional sexual parts which are capable of fertilisation and seed production. *cf*. sterile.

Filament the stalk of a stamen supporting and subtending the anther.

Filiform Having the form of or resembling a thread or filament.

Fimbriate fringed.

Fixed oils non volatile oils, triglycerides of fatty acids.

Flaccid limp and weak.

Flag leaf the uppermost leaf on the stem.

Flaky in the shape of flakes or scales.

Flexuous zig-zagging, sinuous, bending, as of a stem.

Floccose covered with tufts of soft woolly hairs.
Floral tube a flower tube usually formed by the basal fusion of the perianth and stamens.
Floret one of the small individual flowers of sunflower family or the reduced flower of the grasses, including the lemma and palea.
Flower the sexual reproductive organ of flowering plants, typically consisting of gynoecium, androecium and perianth or calyx and/or corolla and the axis bearing these parts.
Fluted as of a trunk with grooves and folds.
Fodder plant material, fresh or dried fed to animals.
Foliaceous leaf-like.
Foliar pertaining to a leaf.
Foliolate pertaining to leaflets, used with a number prefix to denote the number of leaflets.
Foliose leaf-like.
Follicle (Botany) a dry fruit, derived from a single carpel and dehiscing along one suture.
Forb any herb that is not grass or grass-like.
Free central placentation The arrangement of ovules on a central column that is not connected to the ovary wall by partitions, as in the ovaries of the carnation and primrose.
Frond the leaf of a fern or cycad.
Fruit ripened ovary with adnate parts.
Fugacious shedding off early.
Fulvous yellow, tawny.
Funiculus (Botany) short stalk which attaches the ovule to the ovary wall.
Fusiform a 3-dimensional shape; spindle shaped, i.e. broad in the centre and tapering at both ends thick, but tapering at both ends.
Gall-flower short styled flower that do not develop into a fruit but are adapted for the development of a specific wasp within the fruit e.g. in the fig.
Gamete a reproductive cell that fuses with another gamete to form a zygote. Gametes are haploid, (they contain half the normal (diploid) number of chromosomes); thus when two fuse, the diploid number is restored.
Gametophyte The gamete-producing phase in a plant characterized by alternation of generations.
Gamosepalous with sepals united or partially united.
Genome complete set of genetic material of an organism.
Geniculate bent like a knee, refer to awns and filaments.
Geocarpic where the fruit are pushed into the soil by the gynophore and mature.
Geophyte a plant that stores food in an underground storage organ e.g. a tuber, bulb or rhizome and has subterranean buds which form aerial growth.
Geotextile are permeable fabrics which, when used in association with soil, have the ability to separate, filter, reinforce, protect, or drain.
Germ of cereal is the embryo of the seed or kernel. It contains vitamins B, E, folic acid, some protein, minerals and polyunsaturated fats.
Glabrescent becoming glabrous.
Glabrous smooth, hairless without pubescence.
Gland a secretory organ, e.g. a nectary, extra-floral nectary or a gland tipped, hair-like or wart-like organ. *adj*. glandular. *cf*. eglandular.
Glaucous pale blue-green in colour, covered with a whitish bloom that rubs off readily.
Gley soils a hydric soil which exhibits a greenish-blue-grey soil color due to wetland conditions.
Globose spherical in shape.
Globular a three-dimensional shape; spherical or orbicular; circular in outline.
Glochids tiny, finely barbed hair-like spines found on the areoles of some cacti and other plants.
Glochidiate having glochids.
Glochidote plant having glochids.
Glume one of the two small, sterile bracts at the base of the grass spikelet, called the lower and upper glumes, due to their position on the rachilla. Also used in Apiaceae, Cyperaceae for the very small bracts on the spikelet in which each flower is subtended by one floral glume. *adj*. glumaceous.
Grits consist of coarsely ground corn, or sometimes alkali-treated corn.
Groats hulled, whole grains of various cereals, such as oats, wheat, barley or buckwheat, it includes the cereal germ, fiber-rich bran portion and endosperm of the grain.
Guttation the appearance of drops of xylem sap on the tips or edges of leaves of some vascular plants, such as grasses and bamboos.
Guttule small droplet.

Gymnosperm a group of spermatophyte seed-bearing plants with ovules on scales, which are usually arranged in cone-like structures and not borne in an ovary. *cf*. angiosperm.

Gynoecium the female organ of a flower; a collective term for the pistil, carpel or carpels.

Gynomonoecious having female flowers and bisexual flowers on the same plant. *cf*. andromonoecious.

Gynophore stalk that bears the pistil/carpel.

Habit the general growth form of a plant, comprising its size, shape, texture and stem orientation, the locality in which the plant grows..

Halophyte a plant adapted to living in highly saline habitats. Also a plant that accumulates high concentrations of salt in its tissues. *adj*. halophytic.

Hapaxanthic refer to palms which flowers only once and then dies. c.f. pleonanthic.

Haploid condition where nucleus or cell has a single set of unpaired chromosomes, the haploid number is designated as n.

Haplontic life cycle or zygotic meiosis wherein meiosis of a zygote immediately after karyogamy, produces haploid cells which produces more or larger haploid cells ending its diploid phase.

Hastate having the shape of an arrowhead but with the basal lobes pointing outward at right angles as of a leaf.

Hastula a piece of plant material at the junction of the petiole and the leaf blade; the hastula can be found on the top of the leaf, adaxial or the bottom, abaxial or both sides.

Heartwood wood from the inner portion of a tree.

Heliophilous sun-loving, tolerates high level of sunlight..

Heliotropic growing towards sunlight.

Herb a plant which is non-woody or woody at the base only, the above ground stems usually being ephemeral. *adj*. herbaceous.

Herbaceous resembling a herb, having a habit of a herb.

Hermaphrodite bisexual, bearing flowers with both androecium and gynoecium in the same flower. *adj*. hermaphroditic.

Heterocyst a differentiated cyanobacterial cell that carries out nitrogen fixation.

Heterogamous bearing separate male and female flowers, or bisexual and female flowers, or florets in an inflorescence or flower head, e.g. some Asteraceae in which the ray florets may be neuter or unisexual and the disk florets may be bisexual. *cf*. homogamous.

Heteromorphous having two or more distinct forms. *cf*. homomorphous.

Heterophyllous having leaves of different form.

Heterosporous producing spores of 2 sizes, the larger giving rise to megagametophytes (female), the smaller giving rise to microgametophytes (male). Refer to the ferns and fern allies. *cf*. homosporous.

Heterostylous having styles of two different lengths or forms.

Heterostyly the condition in which flowers on polymorphous plants have styles of different lengths, therby facilting cross-pollination.

Hilar of or relating to a hilum.

Hilum The scar on a seed, indicating the point of attachment to the funiculus.

Hirsute bearing long coarse hairs.

Hispid bearing stiff, short, rough hairs or bristles.

Hispidulous minutely hispid.

Histosol soil comprising primarily of organic materials, having 40 cm or more of organic soil material in the upper 80 cm.

Hoary covered with a greyish layer of very short, closely interwoven hairs.

Holdfast an organ or structure of attachment, especially the basal, root-like formation by which certain seaweeds or other algae are attached to a substrate.

Holocarpic having the entire thallus developed into a fruiting body or sporangium.

Homochromous having all the florets of the same colour in the same flower head *cf*. heterochromous.

Homogamous bearing flowers or florets that do not differ sexually *cf*. heterogamous.

Homogenous endosperm endosperm with even surface that lacks invaginations or infoldings of the surrounding tissue.

Homogonium a part of a filament of a cyanobacterium that detaches and grows by cell division into a new filament. *pl*. homogonia.

Homomorphous uniform, with only one form. *cf*. heteromorphous.

Homosporous producing one kind of spores. Refer to the ferns and fern allies. *cf*. heterosporous.

Hurd fibre long pith fibre of the stem.
Hyaline colourless, almost transparent.
Hybrid the first generation progeny of the sexual union of plants belonging to different taxa.
Hybridisation the crossing of individuals from different species or taxa.
Hydathode a type of secretory tissue in leaves, usually of Angiosperms, that secretes water through pores in the epidermis or margin of the leaf.
Hydrophilous water loving; requiring water in order to be fertilized, referring to many aquatic plants.
Hygrochastic applied to plants in which the opening of the fruits is caused by the absorption of water.
Hygrophilous living in water or moist places.
Hymenial cystidia the cells of the hymenium develop into basidia or asci, while in others some cells develop into sterile cells called cystidia.
Hymenium spore-bearing layer of cells in certain fungi containing asci (Ascomycetes) or basidia (Basidiomycetes).
Hypanthium cup-like receptacles of some dicotyledonous flowers formed by the fusion of the calyx, corolla, and androecium that surrounds the ovary which bears the sepals, petals and stamens.
Hypha is a long, branching filamentous cell of a fungus, and also of unrelated Actinobacteria. *pl*. hyphae.
Hypocotyl the portion of the stem below the cotyledons.
Hypodermis the cell layer beneath the epidermis of the pericarp.
Hypogeal below ground as of germination of seed.
Hysteresis refers to systems that may exhibit path dependence.
Imbricate closely packed and overlapping. *cf*. valvate.
Imparipinnate pinnately compound with a single terminal leaflet and hence with an odd number of leaflets. *cf*. paripinnate.
Inceptisols old soils that have no accumulation of clays, iron, aluminium or organic matter.
Incised cut jaggedly with very deep teeth.
Included referring to stamens which do not project beyond the corolla or to valves which do not extend beyond the rim of a capsular fruit. *cf*. exserted.
Incurved curved inwards; curved towards the base or apex.
Indefinite numerous and variable in number.
Indehiscent not opening or splitting to release the contents at maturity as of fruit. *cf*. dehiscent.
Indumentum covering of fine hairs or bristles commonly found on external parts of plants.
Indurate to become hard, often the hardening developed only at maturity.
Indusium an enclosing membrane, covering the sorus of a fern. Also used for the modified style end or pollen-cup of some Goodeniaceae (including Brunoniaceae). *adj*. indusiate.
Inferior said of an ovary or fruit that has sepals, petals and stamens above the ovary. *cf*. superior.
Inflated enlarged and hollow except in the case of a fruit which may contain a seed. *cf*. swollen.
Inflexed Bent or curved inward or downward, as petals or sepals.
Inflorescence a flower cluster or the arrangement of flowers in relation to the axis and to each other on a plant.
Infrafoliar located below the leaves.
Infraspecific referring to any taxon below the species rank.
Infructescence the fruiting stage of an inflorescence.
Inrolled curved inwards.
Integuments two distinct tissue layers that surround the nucellus of the ovule, forming the testa or seed coat when mature.
Intercalary of growth, between the apex and the base; of cells, spores, etc., between two cells.
Interfoliar inter leaf.
Internode portion of the stem, culm, branch, or rhizome between two nodes or points of attachment of the leaves.
Interpetiolar as of stipules positioned between petioles of opposite leaves.
Intrastaminal within the stamens.
Intricate entangled, complex.
Introduced not indigenous; not native to the area in which it now occurs.
Introrse turned inwards or towards the axis or pistil as of anthers. *cf*. extrorse, latrorse.

Involucre a whorl of bracts or leaves that surround one to many flowers or an entire inflorescence.

Involute having the margins rolled inwards, referring to a leaf or other flat organ.

Jugate of a pinnate leaf; having leaflets in pairs.

Juvenile young or immature, used here for leaves formed on a young plant which are different in morphology from those formed on an older plant.

Keel a longitudinal ridge, at the back of the leaf. Also the two lower fused petals of a 'pea' flower in the Papilionaceae, which form a boat-like structure around the stamens and styles, also called carina. *adj*. keeled. *cf*. standard, wing.

Labellum the modified lowest of the three petals forming the corolla of an orchid, usually larger than the other two petals, and often spurred.

Laciniate fringed; having a fringe of slender, narrow, pointed lobes cut into narrow lobes.

Lamella a gill-shaped structure: fine sheets of material held adjacent to one another.

Lamina the blade of the leaf or frond.

Lanate wooly, covered with long hairs which are loosely curled together like wool.

Lanceolate lance-shaped in outline, tapering from a broad base to the apex.

Landrace: Landrace plants adapted to the natural environment in which they grow, developing naturally with minimal assistance or guidance from humans and usually possess more diverse phenotypes and genotypes. They have not been improved by formal breeding programs.

Laterite reddish–coloured soils rich in iron oxide, formed by weathering of rocks under oxidizing and leaching conditions, commonly found in tropical and subtropical regions. *adj*. lateritic.

Latex a milky, clear or sometimes coloured sap of diverse composition exuded by some plants.

Latrorse turned sideways, i.e. not towards or away from the axis as of anthers dehiscing longitudinally on the side. *cf*. extrorse, introse.

Lax loose or limp, not densely arranged or crowded.

Leaflet one of the ultimate segments of a compound leaf.

Lectotype a specimen chosen after the original description to be the type.

Lemma the lower of two bracts (scales) of a grass floret, usually enclosing the palea, lodicules, stamens and ovary.

Lenticel is a lens shaped opening that allows gases to be exchanged between air and the inner tissues of a plant, commonly found on young bark, or the surface of the fruit.

Lenticellate dotted with lenticels.

Lenticular shaped like a biconvex lens. *cf*. lentiform.

Lentiform shaped like a biconvex lens, *cf*. lenticular.

Leptomorphic temperate, running bamboo rhizome; usually thinner then the culms they support and the internodes are long and hollow.

Liane a woody climbing or twining plant.

Lignotuber a woody, usually underground, tuberous rootstock often giving rise to numerous aerial stems.

Ligulate small and tongue shaped or with a little tongue shaped appendage or ligule, star shaped as of florets of Asteraceae.

Ligule a strap-shaped corolla in the flowers of Asteraceae; also a thin membranous outgrowth from the inner junction of the grass leaf sheath and blade. *cf*. ligulate.

Limb the expanded portion of the calyx tube or the corolla tube, or the large branch of a tree.

Linear a 2-dimensional shape, narrow with nearly parallel sides.

Linguiform tongue shaped *cf*. ligulate.

Lithosol a kind of shallow soils lacking well-defined horizons and composed of imperfectly weathered fragments of rock.

Littoral of or on a shore, especially seashore.

Loam a type of soil mad up of sand, silt, and clay in relative concentration of 40–40–20% respectively.

Lobed divided but not to the base.

Loculicidal opening into the cells, when a ripe capsule splits along the back.

Loculus cavity or chamber of an ovary. *pl*. loculi.

Lodicules two small structures below the ovary which, at flowering, swell up and force open the enclosing bracts, exposing the stamens and carpel.

Lyrate pinnately lobed, with a large terminal lobe and smaller laterals ones which become progressively smaller towards the base.

Macronutrients chemical elements which are needed in large quantities for growth and development by plants and include nitrogen, phosphorus, potassium, and magnesium.

Maculate spotted.

Mallee a growth habit in which several to many woody stems arise separately from a lignotuber; usually applied to certain low-growing species of *Eucalyptus*.

Mangrove a distinctive vegetation type of trees and shrubs with modified roots, often viviparous, occupying the saline coastal habitats that are subject to periodic tidal inundation.

Marcescent withering or to decay without falling off.

Margin the edge of the leaf blade.

Medulla the pith in the stems or roots of certain plants; or the central portion of a thallus in certain lichens.

Megasporangium the sporangium containing megaspores in fern and fern allies. *cf*. microsporangium.

Megaspore the large spore which may develop into the female gametophyte in heterosporous ferns and fern allies. *cf*. microspore.

Megasporophyll a leaflike structure that bears megasporangia.

Megastrobilus female cone, seed cone, or ovulate cone, contains ovules within which, when fertilized by pollen, become seeds. The female cone structure varies more markedly between the different conifer families.

Meiosis the process of cell division that results in the formation of haploid cells from diploid cells to produce gametes.

Mericarp a 1-seeded portion of an initially syncarpous fruit (schizocarp) which splits apart at maturity. *Cf*. coccus.

Meristem the region of active cell division in plants, from which permanent tissue is derived. *adj*. meristematic

-merous used with a number prefix to denote the basic number of the 3 outer floral whorls, e.g. a 5-merous flower may have 5 sepals, 10 petals and 15 stamens.

Mesic moderately wet.

Mesocarp the middle layer of the fruit wall derived from the middle layer of the carpel wall. *cf*. endocarp, exocarp, pericarp.

Mesophytes terrestrial plants which are adapted to neither a particularly dry nor particularly wet environment.

Micropyle the small opening in a plant ovule through which the pollen tube passes in order to effect fertilisation.

Microsporangium the sporangium containing microspores in pteridophyes. *cf*. megasporangium.

Microspore a small spore which gives rise to the male gametophyte in heterosporous pteridophytes. Also for a pollen grain. *cf*. megaspore.

Midvein the main vascular supply of a simple leaf blade or lamina. Also called mid-rib.

Mitosis is a process of cell division which results in the production of two daughter cells from a single parent cell.

Mollisols soils with deep, high organic matter, nutrient-enriched surface soil (A horizon), typically between 60 and 80 cm thick.

Monadelphous applied to stamens united by their filaments into a single bundle.

Monocarpic refer to plants that flower, set seeds and then die.

Monochasial a cyme having a single flower on each axis.

Monocotyledon angiosperm having one cotyledon.

Monoecious having both male and female unisexual flowers on the same individual plant. *cf*. dioecious.

Monoembryonic seed the seed contains only one embryo, a true sexual (zygotic) embryo. polyembryonic seed.

Monolete a spore that has a simple linear scar.

Monopodial with a main terminal growing point producing many lateral branches progressively. *cf*. sympodial.

Monotypic of a genus with one species or a family with one genus; in general, applied to any taxon with only one immediately subordinate taxon.

Montane refers to highland areas located below the subalpine zone.

Mucilage a soft, moist, viscous, sticky secretion. *adj*. mucilaginous.

Mucous (Botany) slimy.

Mucro a sharp, pointed part or organ, especially a sharp terminal point, as of a leaf.

Mucronate ending with a short, sharp tip or mucro, resembling a spine. cf. cuspidate, muticous.

Mucronulate with a very small mucro; a diminutive of mucronate.

Mulch protective cover of plant (organic) or non-plant material placed over the soil, primarily to modify and improve the effects of the local microclimate and to control weeds.

Multiple fruit a fruit that is formed from a cluster of flowers.

Muricate covered with numerous short hard outgrowths. *cf*. papillose.

Muriculate with numerous minute hard outgrowths; a diminutive of muricate.

Muticous blunt, lacking a sharp point. *cf*. mucronate.

MYB proteins are a superfamily of transcription factors that play regulatory roles in developmental processes and defense responses in plants.

Mycorrhiza the mutualistic symbiosis (non-pathogenic association) between soil-borne fungi with the roots of higher plants.

Mycorrhiza (vesicular arbuscular) endomycorrhiza living in the roots of higher plants producing inter-and intracellular fungal growth in root cortex and forming specific fungal structures, referred to as vesicles and arbuscles. *abbrev*. VAM.

Native a plant indigenous to the locality or region.

Naviculate boat-shaped.

Necrotic applied to dead tissue.

Nectariferous having one or more nectaries.

Nectary a nectar secretory gland; commonly in a flower, sometimes on leaves, fronds or stems.

Nervation venation, a pattern of veins or nerves as of leaf.

Nixtamalization refers to a process for the preparation of maize (corn), or other grain, in which the grains are soaked and cooked in an alkaline solution, usually limewater, and hulled.

Node the joint between segments of a culm, stem, branch, or rhizome; the point of the stem that gives rise to the leaf and bud.

Nodule a small knoblike outgrowth, as those found on the roots of many leguminous, that containing *Rhizobium* bacteria which fixes nitrogen in the soil.

Nom. ambig. nomen ambiguum (Latin) ambiguous name used in different senses which has become a long-persistent source of error.

Nom. cons. nomen nonservandum (Latin) name conserved in International Code of Botanical Nomenclature.

Nom. dub. nomen dubium (Latin) an invalid proposed taxonomic name because it is not accompanied by a definition or description of the taxon to which it applies.

Nom. illeg. nomen illegitimum (Latin) illegitimate taxon deemed as superfluous at its time of publication either because the taxon to which it was applied already has a name, or because the name has already been applied to another plant.

Nom. invalid. nomen invalidum (Latin) invalid name according to International Code of Botanical Nomenclature.

Nom. nud. nomen nudum (Latin) the name of a taxon which has never been validated by a description.

Nom. rej. nomen rejiciendum (Latin) name rejected in International Code of Botanical Nomenclature.

Notho (subsp. or var.) prefix to the rank of a hybrid taxon below the rank of species.

Nucellus central portion of an ovule in which the embryo sac develops.

Nucellar embryony a form of seed reproduction in which the nucellar tissue which surrounds the embryo sac can produce additional embryos (polyembryony) which are genetically identical to the parent plant. This is found in many citrus species and in mango.

Nut a dry indehiscent 1-celled fruit with a hard pericarp.

Nutlet a small. 1-seeded, indehiscent lobe of a divided fruit.

Ob- prefix meaning inversely or opposite to.

Obconic a 3-dimensional shape; inversely conic; cone shaped, conic with the vertex pointing downward.

Obcordate inversely cordate, broad and notched at the tip; heart shaped but attached at the pointed end.

Obdeltate inversely deltate; deltate with the broadest part at the apex.

Oblanceolate inversely lanceolate, lance-shaped but broadest above the middle and tapering toward the base as of leaf.

Oblate having the shape of a spheroid with the equatorial diameter greater than the polar diameter; being flattened at the poles.

Oblong longer than broad with sides nearly parallel to each other.

Obovate inversely ovate, broadest above the middle.

Obpyramidal resembling a 4-sided pyramid attached at the apex with the square base facing away from the attachment.

Obpyriform inversely pyriform, resembling a pear which is attached at the narrower end. *cf*. pyriform.

Obspathulate inversely spathulate; resembling a spoon but attached at the broadest end. *cf*. spathulate.

Obtriangular inversely triangular; triangular but attached at the apex. *cf*. triangular.

Obtrullate inversely trullate; resembling a trowel blade with the broadest axis above the middle. *cf*. trullate.

Obtuse with a blunt or rounded tip, the converging edges separated by an angle greater than 90 degrees.

-oid suffix denoting a 3-dimensional shape, e.g. spheroid.

Ochraceous a dull yellow color.

Ocreate having a tube-like covering around some stems, formed of the united stipules; sheathed.

Oleaginous oily.

Oligotrophic lacking in plant nutrients and having a large amount of dissolved oxygen throughout.

Operculum a lid or cover that becomes detached at maturity by abscission, e.g. in *Eucalyptus*, also a cap or lid covering the bud and formed by fusion or cohesion of sepals and/or petals. *adj*. operculate.

Opposite describing leaves or other organs which are borne at the same level but on opposite sides of the stem. *cf*. alternate.

Orbicular of circular outline, disc-like.

Order a taxonomic rank between class and family used in the classification of organisms, i.e. a group of families believed to be closely related.

Orifice an opening or aperture.

Organosols soils not regularly inundated by marine waters and containing a specific thickness of organic materials within the upper part of the profile.

Orth. Var. orthographic variant, i.e., an incorrect alternate spelling of a name.

Ovary the female part of the pistil of a flower which contains the ovules (immature seeds).

Ovate egg-shaped, usually with reference to two dimensions.

Ovoid egg-shaped, usually with reference to three dimensions.

Ovule the young, immature seed in the ovary which becomes a seed after fertilisation. *adj*. ovular..

Ovulode a sterile reduced ovule borne on the placenta, commonly occurring in Myrtaceae.

Oxisols refer to ferralsols.

Pachymorphic describes the short, thick, rhizomes of clumping bamboos with short, thick and solid internode (except the bud-bearing internodes, which are more elongated). *cf*. sympodial.

Palate (Botany) a raised appendage on the lower lip of a corolla which partially or completely closes the throat.

Palea the upper of the two membranous bracts of a grass floret, usually enclosing the lodicules, stamens and ovary. *pl*. paleae. *adj*. paleal. *cf*. lemma.

Paleate having glumes.

Palm heart refers to soft, tender inner core and growing bud of certain palm trees which are eaten as vegetables. Also called heart of palm, palmito, burglar's thigh, chonta or swamp cabbage.

Palmate describing a leaf which is divided into several lobes or leaflets which arise from the same point. *adj*. palmately.

Palmito see palm heart.

Palustrial paludal, swampy, marshy.

Palustrine marshy, swampy.

Palustrine herb vegetation that is rooted below water but grows above the surface in wetland system.

Panduriform fiddle shaped, usually with reference to two dimensions.

Panicle a compound, indeterminate, racemose inflorescence in which the main axis bears lateral racemes or spikes. *adj*. paniculate.

Pantropical distributed through-out the tropics.

Papilionaceous butterfly-like, said of the pea flower or flowers of Papilionaceae, flowers which are zygomorphic with imbricate petals, one broad upper one, two narrower lateral ones and two narrower lower ones.

Papilla a small, superficial protuberance on the surface of an organ being an outgrowth of one epidermal cell. *pl*. papillae. *adj*. papillose.

Papillate having papillae.

Papillose covered with papillae.

Pappus a tuft (or ring) of hairs, bristles or scales borne above the ovary and outside the corolla as in Asteraceae often persisting as a tuft of hairs on a fruit. *adj*. pappose.

Papyraceous resembling parchment of paper.

Parenchyma undifferentiated plant tissue composed of more or less uniform cells.

Parietal describes the attachment of ovules to the outer walls of the ovaries.

Paripinnate pinnate with an even number of leaflets and without a terminal leaflet. *cf*. imparipinnate.

-partite divided almost to the base into segments, the number of segments written as a prefix.

Patelliform shaped like a limpet shell; cap-shaped and without whorls.

Patent diverging from the axis almost at right angles.

Peat is an accumulation of partially decayed vegetation matter.

Pectin a group of water-soluble colloidal carbohydrates of high molecular weight found in certain ripe fruits.

Pectinate pinnatifid with narrow segments resembling the teeth of a comb.

Pedicel the stalk of the flower or stalk of a spikelet in Poaceae. *adj*. pedicellate.

Pedicellate having pedicel.

Peduncle a stalk supporting an inflorescence. *adj*. pedunculate

Pellucid allowing the passage of light; transparent or translucent.

Pellucid-dotted copiously dotted with immersed, pellucid, resinous glands.

Peltate with the petiole attached to the lower surface of the leaf blade.

Pendant hanging down.

Pendulous drooping, as of ovules.

Penniveined or penni-nerved pinnately veined.

Pentamerous in five parts.

Perennial a plant that completes it life cycle or lives for more than two years. *cf*. annual, biennial.

Perfoliate a leaf with the basal lobes united around – and apparently pierced by – the stem.

Pergamentaceous parchment-like.

Perianth the two outer floral whorls of the Angiosperm flower; commonly used when the calyx and the corolla are not readily distinguishable (as in monocotyledons).

Pericarp (Botany). The wall of a ripened ovary; fruit wall composed of the exocarp, mesocarp and endocarp.

Persistent remaining attached; not falling off. *cf*. caduceus.

Petal free segment of the corolla. *adj*. petaline. *cf*. lobe.

Petiolar relating to the petiole.

Petiolate having petiole.

Petiole leaf stalk. *adj*. petiolate.

Petiolulate supported by its own petiolule.

Petiolule the stalk of a leaflet in a compound leaf. adj. petiolulate.

pH is a measure of the acidity or basicity of a solution. It is defined as the cologarithm of the activity of dissolved hydrogen ions (H+).

Phenology the study of periodic plant life cycle events as influenced by seasonal and interannual variations in climate.

Phyllary a bract of the involucre of a composite plant, term for one of the scale-like bracts beneath the flower-head in Asteraceae.

Phylloclade a flattened, photosynthetic branch or stem that resembles or performs the function of a leaf, with the true leaves represented by scales.

Phyllode a petiole that function as a leaf. *adj*. phyllodineous. *cf*. cladode.

Phyllopodia refer to the reduced, scale-like leaves found on the outermost portion of the corm where they seem to persist longer than typical sporophylls as in the fern Isoetes.

Phytoremediation describes the treatment of environmental problems (bioremediation) through the use of plants which mitigate the environmental problem without the need to excavate the contaminant material and dispose of it elsewhere.

Pileus (Botany) cap of mushroom.
Piliferous (Botany) bearing or producing hairs, as of an organ with the apex having long, hair-like extensions.
Pilose covered with fine soft hairs.
Pinna a primary division of the blade of a compound leaf or frond. *pl*. pinnae.
Pinnate bearing leaflets on each side of a central axis of a compound leaf; divided into pinnae.
Pinnatifid, pinnatilobed a pinnate leaf parted approximately halfway to midrib; when divided to almost to the mid rib described as deeply pinnatifid or pinnatisect.
Pinnatisect lobed or divided almost to the midrib.
Pinnule a leaflet of a bipinnate compound leaf.
Pistil female part of the flower comprising the ovary, style, and stigma.
Pistillate having one or more pistils; having pistils but no stamens.
Placenta the region within the ovary to which ovules are attached. *pl*. placentae.
Placentation the arrangement of the placentae and ovules in the ovary.
Plano- a prefix meaning level or flat.
Pleonanthic refer to palms in which the stem does not die after flowering.
Plicate folded like a fan.
Plumose feather-like, with fine hairs arising laterally from a central axis; feathery.
Pneumatophore modified root which allows gaseous exchange in mud-dwelling shrubs, e.g. mangroves.
Pod a dry 1 to many-seeded dehiscent fruit, as applied to the fruit of Fabaceae i.e. Caesalpiniaceae, Mimosaceae and Papilionaceae.
Podzol, Podsolic soil any of a group of acidic, zonal soils having a leached, light-coloured, gray and ashy appearance. Also called spodosol.
Pollen cone male cone or microstrobilus or pollen cone is structurally similar across all conifers, extending out from a central axis are microsporophylls (modified leaves). Under each microsporophyll is one or several microsporangia (pollen sacs).
Pollinia the paired, waxy pollen masses of flowers of orchids and milkweeds.
Polyandrous (Botany) having an indefinite number of stamens.
Polyembryonic seed seeds contain many embryos, most of which are asexual (nucellar) in origin and genetically identical to the maternal parent.
Polygamous with unisexual and bisexual flowers on the same or on different individuals of the same species.
Polymorphic with different morphological variants.
Polypetalous (Botany) having a corolla composed of distinct, separable petals.
Pome a fleshy fruit where the succulent tissues are developed from the receptacle.
Pore a tiny opening.
Premorse Abruptly truncated, as though bitten or broken off as of a leaf.
Procumbent trailing or spreading along the ground but not rooting at the nodes, referring to stems. *cf*. ascending, decumbent, erect.
Pro hyb. (Latin) as a hybrid.
Pro parte (Latin) in part
Pro Parte majore (Latin) for the greater part.
Pro parte minore (Latin) for a small part.
Pro sp. (Latin) as a species.
Pro subsp. (Latin) as a subspecies.
Pro syn. (Latin) as a synonym.
Prophyll a plant structure that resembles a leaf.
Prostrate lying flat on the ground.
Protandous relating to a flower in which the anthers release their pollen before the stigma of the same flower becomes receptive.
Proximal end of any structure closest to the point of attachment. *cf*. distal.
Pruinose having a thick, waxy, powdery coating or bloom.
Pseudocarp a false fruit, largely made up of tissue that is not derived from the ovary but from floral parts such as the receptacle and calyx.
Pseudostem The false, herbaceous stem of a banana plant composed of overlapping leaf bases.
Pteridophyte a vascular plant which reproduces by spores; the ferns and fern allies.
Puberulent covered with minute hairs or very fine down; finely pubescent.
Puberulous covered with a minute down.
Pubescent covered with short, soft hairs.
Pulvinate having a swelling, pulvinus at the base as a leaf stalk.

Pulvinus swelling at the base of leaf stalk.
Pulviniform swelling or bulging.
Punctate marked with translucent dots or glands.
Punctiform marked by or composed of points or dots.
Punctulate marked with minute dots; a diminutive of punctate.
Pusticulate characterized by small pustules.
Pyrene the stone or pit of a drupe, consisting of the hardened endocarp and seed.
Pyriform pear-shaped, a 3-dimensional shape; attached at the broader end. *cf*. obpyriform.
Pyxidium seed capsule having a circular lid (operculum) which falls off to release the seed.
Raceme an indeterminate inflorescence with a simple, elongated axis and pedicellate flowers, youngest at the top. *adj*. racemose.
Rachilla the main axis of a grass spikelet.
Rachis the main axis of the spike or other inflorescence of grasses or a compound leaf.
Radiate arranged around a common centre; as of an inflorescence of Asteraceae with marginal, female or neuter, ligulate ray-florets and central, perfect or functionally male, tubular, disc florets. *cf*. disciform, discoid.
Radical arising from the root or its crown, or the part of a plant embryo that develops into a root.
Ray the marginal portion of the inflorescence of Asteraceae and Apiaceae when distinct from the disc. Also, the spreading branches of a compound umbel.
Receptacle the region at the end of a pedicel or on an axis which bears one or more flowers. *adj*. receptacular.
Recurved curved downwards or backwards.
Reflexed bent or turned downward.
Regosol soil that is young and undeveloped, characterized by medium to fine-textured unconsolidated parent material that maybe alluvial in origin and lacks a significant horizon layer formation.
Reniform kidney shaped in outline.
Repand with slightly undulate margin.
Replicate folded back, as in some corolla lobes.
Resinous producing sticky resin.
Resupinate twisted through 180 degrees.
Reticulate having the appearance of a network.
Retrorse bent or directed downwards or backwards. *cf*. antrorse.
Retuse with a very blunt and slightly notched apex. *cf*. emarginated.
Revolute with the margins inrolled on the lower (abaxial) surface.
Rhizine a root-like filament or hair growing from the stems of mosses or on lichens.
Rhizoid root-like filaments in a moss, fern, fungus, etc. that attach the plant to the substratum.
Rhizome a prostrate or underground stem consisting of a series of nodes and internodes with adventitious roots and which generally grows horizontally.
Rhizophore a stilt-like outgrowth of the stem which branches into roots on contact with the substrate.
Rhombic shaped like a rhombus.
Rhomboid shaped like a rhombus.
Rib a distinct vein or linear marking, often raised as a linear ridge.
Riparian along the river margins, interface between land and a stream.
Rosette a tuft of leaves or other organs arranged spirally like petals in a rose, ranging in form from a hemispherical tuft to a flat whorl. *adj*. rosetted, rosulate.
Rostrate beaked; the apex tapered into a slender, usually obtuse point.
Rostrum a beak-like extension.
Rosulate having a rosette.
Rotate wheel shaped; refers to a corolla with a very short tube and a broad upper part which is flared at right angles to the tube. *cf*. salverform.
Rotundate rounded; especially at the end or ends.
Rugae refers to a series of ridges produced by folding of the wall of an organ.
Rugose deeply wrinkled.
Rugulose finely wrinkled.
Ruminate (Animal) chew repeatedly over an extended period.
Ruminate endosperm uneven endosperm surface that is often highly enlarged by ingrowths or infoldings of the surrounding tissue. cf. homogenous endosperm.
Rz value is a numerical reference to the mesh/emulsion equalization on the screen.

Saccate pouched.
Sagittate shaped like an arrow head.
Saline soils soils that contain excessive levels of salts that reduce plant growth and vigor by altering water uptake and causing ion-specific toxicities or imbalances.
Salinity is characterised by high electrical conductivities and low sodium ion concentrations compared to calcium and magnesium
Salverform applies to a gamopetalous corolla having a slender tube and an abruptly expanded limb.
Samara an indehiscent, winged, dry fruit.
Sand a naturally occurring granular material composed of finely divided rock and mineral particles range in diameter from 0.0625 μm to 2 mm. *adj*. sandy
Saponins are plant glycosides with a distinctive foaming characteristic. They are found in many plants, but get their name from the soapwort plant (*Saponaria*).
Saprophytic living on and deriving nourishment from dead organic matter.
Sapwood outer woody layer of the tree just adjacent to and below the bark.
Sarcotesta outermost fleshy covering of Cycad seeds below which is the sclerotesta.
Scabrid scurfy, covered with surface abrasions, irregular projections or delicate scales.
Scabrous rough to the touch.
Scale dry bract or leaf.
Scandent refer to plants, climbing.
Scape erect flowering stem, usually leafless, rising from the crown or roots of a plant. *adj*. scapose.
Scapigerous with a scape.
Scarious dry, thin and membranous.
Schizocarp a dry fruit which splits into longitudinally multiple parts called mericarps or cocci. *adj*. schizocarpous.
Sclerotesta the innermost fleshy coating of cycad seeds, usually located directly below the sarcotesta.
Scorpoid refers to a cymose inflorescence in which the main axis appears to coil.
Scutellum (Botany) any of various parts shaped like a shield.
Secondary venation arrangement of the lateral veins arising from the midrib in the leaf lamina.
Secund with the flowers all turned in the same direction.
Sedge a plant of the family Apiaceae, Cyperaceae.
Segmented constricted into divisions.
Seminal root or seed root originate from the scutellar node located within the seed embryo and are composed of the radicle and lateral seminal roots.
Senescence refers to the biological changes which take place in plants as they age.
Sepal free segment of the calyx. *adj*. sepaline.
Septum a partition or cross wall. *pl*. septa. *adj*. septate.
Seriate arranged in rows.
Sericeous silky; covered with close-pressed, fine, straight silky hairs.
Serrate toothed like a saw; with regular, asymmetric teeth pointing forward.
Serrated toothed margin.
Serratures serrated margin.
Serrulate with minute teeth on the margin.
Sessile without a stalk.
Seta a bristle or stiff hair. *pl*. setae. *adj*. setose, setaceous.
Setaceous bristle-like.
Setate with bristles.
Setiform bristle shaped.
Setulose with minute bristles.
Sheathing clasping or enveloping the stem.
Shrub a woody plant usually less than 5 m high and many-branched without a distinct main stem except at ground level.
Silicula a broad, dry, usually dehiscent fruit derived from two or more carpels which usually dehisce along two sutures. *cf*. siliqua.
Siliqua a silicula which is at least twice as long as broad.
Silt is soil or rock derived granular material of a grain size between sand and clay, grain particles ranging from 0.004 to 0.06 mm in diameter. *adj*. silty.
Simple refer to a leaf or other structure that is not divided into parts. *cf*. compound.
Sinuate with deep wavy margin.
Sinuous wavy.
Sinus an opening or groove, as occurs between the bases of two petals.
Sodicity is characterised by low electrical conductivities and high sodium ion concentrations compared to calcium and magnesium.

Sodic soils contains high levels of sodium salts that affects soil structure, inhibits water movement and causes poor germination and crop establishment and plant toxicity.

Soil pH is a measure of the acidity or basicity of the soil. See pH.

Solitary usually refer to flowers which are borne singly, and not grouped into an inflorescence or clustered.

Sorocarp fruiting body formed by some cellular slime moulds, has both stalk and spore mass.

Sorophore stalk bearing the sorocarp.

Sorosis fleshy multiple fruit formed from flowers that are crowded together on a fleshy stem e.g. pineapple and mulberry.

Sorus a discrete aggregate of sporangia in ferns. *pl*. sori

Spadix fleshy spike-like inflorescence with an unbranched, usually thickened axis and small embedded flowers often surrounded by a spathe. *pl*. spadices.

Spathe a large bract ensheathing an inflorescence or its peduncle. *adj*. spathaceous.

Spatheate like or with a spathe.

Spathulate spatula or spoon shaped; broad at the tip and narrowed towards the base.

Spicate borne in or forming a spike.

Spiculate spikelet-bearing.

Spike an unbranched, indeterminate inflorescence with sessile flowers or spiklets. *adj*. spicate, spiciform.

Spikelet a small or secondary spike characteristics of the grasses and sedges and, generally composed of 2 glumes and one or more florets. Also applied to the small spike-like inflorescence or inflorescence units commonly found in Apiaceae.

Spine a stiff, sharp, pointed structure, formed by modification of a plant organ. *adj*. spinose.

Spinescent ending in a spine; modified to form a spine

Spinulate covered with small spines.

Spinulose with small spines over the surface.

Spodosol see podsol.

Sporidia asexual spores of smut fungi.

Sporangium a spore bearing structure found in ferns, fern allies and gymnosperms. *pl*. sporangia. *adj*. sporangial.

Sporocarp a stalked specialized fruiting structure formed from modified sporophylls, containing sporangia or spores as found in ferns and fern allies.

Sporophore a spore-bearing structure, especially in fungi.

Sporophyll a leaf or bract which bears or subtends sporangia in the fern allies, ferns and gymnosperms.

Sporophyte the spore-producing phase in the life cycle of a plant that exhibits alternation of generations.

Spreading bending or spreading outwards and horizontally.

Spur a tubular or saclike extension of the corolla or calyx of a flower.

Squama structure shaped like a fish scale. *pl*. squamae.

Squamous covered in scales.

Squarrose having rough or spreading scale-like processes.

Stamen the male part of a flower, consisting typically of a stalk (filament) and a pollen-bearing portion (anther). *adj*. staminal, staminate .

Staminate unisexual flower bearing stamens but no functional pistils.

Staminode a sterile or abortive stamen, often reduced in size and lacking anther. *adj*. staminodial.

Standard refers to the adaxial petal in the flower of Papilionaceae. cf. keel, wing.

Starch a polysaccharide carbohydrate consisting of a large number of glucose units joined together by glycosidic bonds α-1-4 linkages.

Stellate star shaped, applies to hairs.

Stem the main axis of a plant, developed from the plumule of the embryo and typically bearing leaves.

Sterile lacking any functional sexual parts which are capable of fertilisation and seed production.

Stigma the sticky receptive tip of an ovary with or without a style which is receptive to pollen.

Stilt root a supporting root arising from the stem some distance above the ground as in some mangroves, sometimes also known as a prop root.

Stipe a stalk that support some other structure like the frond, ovary or fruit.

Stipel secondary stipule at the base of a leaflet. *pl*. stipellae. *adj*. stipellate.

Stipitate having a stalk or stipe, usually of an ovary or fruit.
Stipulated having stipules.
Stipule small leaf-like, scale-like or bristle-like appendages at the base of the leaf or on the petiole. *adj*. stipulate.
Stolon a horizontal, creeping stem rooting at the nodes and giving rise to another plant at its tip.
Stoloniferous bearing stolon or stolons.
Stoma a pore in the epidermis of the leaf or stem for gaseous exchange. *pl*. stomata.
Stone the hard endocarp of a drupe, containing the seed or seeds.
Stramineous chaffy; straw-liked.
Striae parallel longitudinal lines or ridges. *adj*. striate.
Striate marked with fine longitudinal parallel lines or ridges.
Strigose bearing stiff, straight, closely appressed hair; often the hairs have swollen bases.
Strobilus a cone-like structure formed from sporophylls or sporangiophores. *pl*. strobili
Style the part of the pistil between the stigma and ovary.
Sub- a prefix meaning nearly or almost, as in subglobose or subequal.
Subcarnose nearly fleshy.
Sub-family taxonomic rank between the family and tribe.
Subglobose nearly spherical in shape.
Subretuse faintly notched at the apex.
Subsessile nearly stalkless or sessile.
Subshrub intermediate between a herb and shrub.
Subspecies a taxonomic rank subordinate to species.
Substrate surface on which a plant or organism grows or attached to.
Subtend attached below something.
Subulate narrow and tapering gradually to a fine point, awl-shaped.
Succulent fleshy, juicy, soft in texture and usually thickened.
Suckers young plants sprouting from the underground roots of a parent plant and appearing around the base of the parent plant.
Sulcate grooved longitudinally with deep furrows.
Sulcus a groove or depression running along the internodes of culms or branches.
Superior refers to the ovary is free and mostly above the level of insertion of the sepals, and petals. *cf*. inferior.
Suture line of dehiscence.
Swidden slash-and-burn or shifting cultivation.
Syconium a type of pseudocarp formed from a hollow receptacle with small flowers attached to the inner wall. After fertilization the ovaries of the female flowers develop into one-seeded achenes, e.g. fig.
Symbiosis describes close and often long-term mutualistic and beneficial interactions between different organisms.
Sympetalous having petals united.
Sympodial refers to a specialized lateral growth pattern in which the apical meristem. *cf* monopodial.
Synangium an organ composed of united sporangia, divided internally into cells, each containing spores. *pl*. synangia.
Syncarp an aggregate or multiple fruit formed from two or more united carpels with a single style. *adj*. syncarpous.
Syncarpous carpels fused forming a compound pistil.
Synteny presence of two or more genetic loci on the same chromosome.
Tannins group of plant-derived phenolic compounds.
Taxon the taxonomic group of plants of any rank. e.g. a family, genus, species or any infraspecific category. *pl*. taxa.
Tendril a slender, threadlike organ formed from a modified stem, leaf or leaflet which, by coiling around objects, supports a climbing plant.
Tepal a segment of the perianth in a flower in which all the perianth segments are similar in appearance, and are not differentiated into calyx and corolla; a sepal or petal.
Tetrasporangium a sporangium containing four haploid spores as found in some algae.
Terete having a circular shape when cross-sectioned or a cylindrical shape that tapers at each end.
Terminal at the apex or distal end.
Ternate in threes as of leaf with 3 leaflets.
Testa a seed coat, outer integument of a seed.
Thallus plant body of algae, fungi, and other lower organisms.

Thyrse a dense, panicle-like inflorescence, as of the lilac, in which the lateral branches terminate in cymes.

Tomentose refers to plant hairs that are bent and matted forming a wooly coating.

Tomentellose mildly tomentose.

Torus receptacle of a flower.

Transpiration evaporation of water from the plant through leaf and stem pores.

Tree that has many secondary branches supported clear of the ground on a single main stem or trunk.

Triangular shaped like a triangle, 3-angled and 3-sided.

Tribe a category intermediate in rank between subfamily and genus.

Trichome a hair-like outgrowth of the epidermis.

Trichotomous divided almost equally into three parts or elements.

Tridentate three toothed or three pronged.

Trifid divided or cleft into three parts or lobes.

Trifoliate having three leaves.

Trifoliolate a leaf having three leaflets.

Trifurcate having three forks or branches.

Trigonous obtusely three-angled; triangular in cross-section with plane faces.

Tripartite consisting of three parts.

Tripinnate relating to leaves, pinnately divided three times with pinnate pinnules.

Tripliveined main laterals arising above base of lamina.

Triploid describing a nucleus or cell that has three times (3n) the haploid number (n) of chromosomes.

Triveined main laterals arising at the base of lamina.

Triquetrous three-edged; acutely 3-angled.

Trullate with the widest axis below the middle and with straight margins; ovate but margins straight and angled below middle, trowel-shaped.

Truncate with an abruptly transverse end as if cut off.

Tuber a stem, usually underground, enlarged as a storage organ and with minute scale-like leaves and buds. *adj*. tuberous.

Tubercle a wart-like protuberance. *adj*. tuberculate.

Tuberculate bearing tubercles; covered with warty lumps.

Tuberization formation of tubers in the soil.

Tuft a densely packed cluster arising from an axis. *adj*. tufted.

Turbinate having the shape of a top; cone-shaped, with the apex downward, inversely conic.

Turgid distended by water or other liquid.

Turion the tender young, scaly shoot such as asparagus, developed from an underground bud without branches or leaves.

Turnery articles made by the process of turning.

Twining winding spirally.

Ultisols mineral soils with no calcareous material, have less than 10% weatherable minerals in the extreme top layer of soil, and with less the 35% base saturation throughout the soil.

Umbel an inflorescence of pedicellate flowers of almost equal length arising from one point on top of the peduncle. *adj*. umbellate.

Umbellet a secondary umbel of a compound umbel. *cf*. umbellule.

Umbellule an, a secondary umbel of a compound umbel.*cf*. umbellet.

Uncinate bent at the end like a hook; unciform.

Undershrub subshrub; a small, usually sparsely branched woody shrub less than 1 m high. *cf*. shrub.

Undulate with an edge/margin or edges wavy in a vertical plane; may vary from weakly to strongly undulate or crisped. *cf*. crisped.

Unifoliolate a compound leaf which has been reduced to a single, usually terminal leaflet.

Uniform with one form, e.g. having stamens of a similar length or having one kind of leaf. *cf*. dimorphic.

Uniseriate arranged in one row or at one level.

Unisexual with one sex only, either bearing the anthers with pollen, or an ovary with ovules, referring to a flower, inflorescence or individual plant. *cf*. bisexual.

Urceolate shaped like a jug, urn or pitcher.

Utricle a small bladdery pericarp.

Valvate meeting without overlapping, as of sepals or petals in bud. *cf*. imbricate.

Valve one of the sections or portions into which a capsule separates when ripe.

Variant any definable individual or group of individuals which may or may not be regarded as representing a formal taxon after examination.

Variegate, variegated diverse in colour or marked with irregular patches of different colours, blotched.

Variety a taxonomic rank below that of subspecies.

Vein (Botany) a strand of vascular bundle tissue.

Velum a flap of tissue covering the sporangium in the fern, Isoetes.

Velutinous having the surface covered with a fine and dense silky pubescence of short fine hairs; velvety. *cf*. sericeous

Venation distribution or arrangement of veins in a leaf.

Veneer thin sheet of wood.

Ventral (Botany) facing the central axis, opposed to dorsal.

Vernation the arrangement of young leaves or fronds in a bud or at a stem apex. *cf*. circinnate

Verrucose warty

Verticil a circular arrangement, as of flowers, leaves, or hairs, growing about a central point; a whorl.

Verticillaster false whorl composed of a pair of opposite cymes as in Lamiaceae.

Verticillate whorled, arranged in one or more whorls.

Vertisol a soil with a high content of expansive montmorillonite clay that forms deep cracks in drier seasons or years.

Vertosols soils that both contain more than 35% clay and possess deep cracks wider than 5 mm during most years.

Vesicle a small bladdery sac or cavity filled with air or fluid. *adj*. vesicular.

Vestigial the remaining trace or remnant of an organ which seemingly lost all or most of its original function in a species through evolution.

Vestiture covering; the type of hairiness, scaliness or other covering commonly found on the external parts of plants. *cf*. indumentums.

Vibratile capable of to and for motion.

Villose covered with long, fine, soft hairs, finer than in pilose.

Villous covered with soft, shaggy unmatted hairs.

Vine a climbing or trailing plant.

Violaxanthin is a natural xanthophyll pigment with an orange color found in a variety of plants like pansies.

Viscid sticky, being of a consistency that resists flow.

Viviparous describes seeds or fruit which sprout before they fall from the parent plant.

Whorl a ring-like arrangement of leaves, sepals, stamens or other organs around an axis.

Winged having a flat, often membranous expansion or flange, e.g. on a seed, stem or one of the two lateral petals of a Papilionaceous flower or one of the petal-like sepals of Polygalaceae. *cf*. keel, standard.

Xanthophylls are yellow, carotenoid pigments found in plants. They are oxidized derivatives of carotenes.

Xeromorphic plant with special modified structure to help the plant to adapt to dry conditions.

Xerophyte a plant which naturally grows in dry regions and is often structurally modified to withstand dry conditions.

Zygomorphic having only one plane of symmetry, usually the vertical plane, referring to a flower, calyx or corolla. *cf*. actinomorphic.

Zygote the fist cell formed by the union of two gametes in sexual reproduction. *adj*. zygotic.

Common Name Index

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Scientific Name Index

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