T.K. Lim

Edible Medicinal and Non Medicinal Plants

Volume 8, Flowers

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Introduction

This book continues as volume 8 of a multi-compendium on *Edible Medicinal and Non-Medicinal Plants*. It covers plants with edible flowers whose floral parts including the stalk and flower nectar are eaten as conventional or functional food and as spices and may provide a source of food colorant, additive or nutraceuticals. *Functional food* has been described as being similar in appearance to, or may be, a conventional food that is consumed as part of a usual diet and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions, i.e. they contain bioactive compounds (Health Canada 2002). A *nutraceutical* can be defined as a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with foods and is demonstrated to have a physiological benefit or provide protection against chronic disease. Biologically active components in functional foods that may impart health benefits or desirable physiological effects include carotenoids (β-carotene, lutein, lycopene), dietary fibres (β-glucans, soluble fibre), fatty acids (omega fatty acids, conjugated linoleic acid), flavonoids (anthocyanins, flavanols, flavanones, flavonols, proanthocyanidins), isothiocyanates, phenolic acids, plant sterols, polyols and prebiotics/probiotics (fructo-oligosaccharides – inulin), vitamins and phytoestrogens (isoflavones – daidzein, genistein). Many plants with edible flowers contain many of these bioactive components and essential mineral elements (Mlcek and Rop 2011; Rop et al. 2012), carbohydrates and amino acids in the flowers and other plant parts, imparting a wide array of health benefits and pharmacological properties. According to the Global Industry Analyst Inc., global nutraceuticals market is anticipated to exceed US 243 billion by 2015 (GIA 2012). The United States, Europe and Japan dominate the global market, accounting for a combined market share of more than 85 %. Spurred by the growing affluence, rising disposable income and increasing awareness, particularly in China and India, the Asia Pacific region is projected to see significant growth in the long term. Functional foods that constitute the faster-growing segment in the nutraceuticals market are rising in popularity, as the segment offers a cheaper alternative to dietary supplements. Value-added food products that feature edible flowers offer additional marketing opportunities.

This volume covers such plants with edible flowers from families Geraniaceae to Zingiberaceae in a tabular form (Table 1) and eighty such species from 32 families such as Geraniaceae, Iridaceae, Lamiaceae, Liliaceae, Limnocharitaceae, Magnoliaceae, Malvaceae, Meliaceae, Myrtaceae, Nyctaginaceae, Nymphaeaceae, Oleaceae, Onagraceae, Orchidaceae, Paeoniaceae, Papaveraceae, Plantaginaceae, Poaceae, Polygonaceae, Primulaceae, Proteaceae, Ranunculaceae, Rosaceae, Rubiaceae, Rutaceae, Solanaceae, Theaceae, Tropaeolaceae, Typhaceae, Violaceae, Xanthorrhoeaceae and Zingiberaceae in detail. Some plants with edible flowers but are better known for their edible fruits have been covered in

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Table 1 Plants with edible flowers in the families Geraniaceae to Zingiberaceae

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Geraniaceae			
Geranium bicknellii Britton	Bicknell's Cranesbill, Northern Cranesbill	Flowers eaten raw as garnish for salads	Schofield (2003)
Geranium erianthum DC.	Wooly Geranium, Cranesbill	Flowers eaten raw as garnish for salads	Schofield (2003)
Geranium × *fragrans* Dum. Cours.	Scented Pelargonium	The leaves have a powerful citrus fragrance and will add flavour to cakes and meringue roulades. The flowers have a faint citrus flavour similar to the leaves and are ideal when crystallized and scattered on desserts	Anonymous (2012a)
Geranium graveolens Stokes = *Geranium robertianum* L.	Scented Pelargonium, Rose-Scented Geranium, Herb Robert, Storkbill	The flowers have a faint citrus flavour similar to the leaves and are ideal when crystallized and scattered on desserts	Anonymous (2012a) and Roberts (2000)
Geranium incanum Burm.f.	Carpet Geranium, Creeping Geranium, Wild Geranium; Horlosies, Vrouetee, Bergtee (Afrikaans)	Flowers used, as for other geranium flowers, in salads and desserts	Roberts (2000)
Geranium quercifolium L.f. =*Pelargonium quercifolium* (L.f.) L'Her.	Scented Pelargonium	Flowers used as above	Anonymous (2012a)
Geranium robertianum L.	Herb Robert, Storkbill	Flowers eaten raw as garnish in salads	Schofield (2003)
Geranium tomentosum Andrews = *Pelargonium ovale* (Burm.f.) L'Her.	Scented Pelargonium	The flowers have a faint citrus flavour similar to the leaves and are ideal when crystallized and scattered on desserts	Roberts (2000) and Anonymous (2012a)
Geranium viscosissimum Fisch. & C.A. Mey.	Sticky Geranium, Sticky Purple Geranium	Flowers edible raw, used as garnish for salads or used to decorate hors d'oeuvres	Facciola (1990) and Schofield (2003)
Pelargonium crispum (L.) L'Her.	Crisped Leaf Pelargonium, Curled Leaved Cranesbill, Finger Bowl Geranium, Lemon Geranium, Lemon-Scented Geranium	Flowers used in salads, dessert, drinks and jellies	Barash (1997), Roberts (2000), and Deane (2007–2012j)
Pelargonium graveolens L'Her.	Rose Geranium, Old Fashion Rose Geranium, Rose-Scented Geranium	Flowers edible raw, added to salads and to lend flavour and fragrance to juice, wine, desserts, cakes, ice cream, soups, sugar, vinegar, sauces, custards and canned and baked fruits	Bryan and Castle (1975), Larkcom (1980), Facciola (1990), Barash (1997), and Roberts (2000)
Pelargonium spp.	Scented Geraniums	Scented flowers used in salads, desserts, jellies and drinks	Barash (1997), Newman and O'Connor (2009), and Deane (2007–2012j)

Pelargonium tomentosum Jacq.	Pennyroyal Pelargonium, Peppermint-Scented Pelargonium	Flowers used to flavour cakes, jellies, puddings, pies, cookies, tarts, teas and other desserts	Gessert (1983) and Facciola (1990)
Pelargonium × *nervosum* Sweet	Lime Geranium, Scented Geranium	Flowers used to flavour cakes, jellies, puddings, drinks, vinegar, wine and soups	Gessert (1983) and Facciola (1990)
Gnetaceae			
Gnetum gnemon L.	Gnetum, Joint Fir, Kampong Tree, Spanish Joint Fir; Blinjau, Meninjau (Malaysia); Melinjo, Belinjo (Indonesia)	Inflorescences/flowers cooked in *sayur*, soups and in curries in Indonesia	Ochse and Bakhuizen van den Brink (1980), Facciola (1990), and Lim (2012a)
Grossulariaceae			
Ribes aureum Pursh.	Golden Currant	Flowers eaten raw and have a very sweet flavour	Harrington (1974) and Deane (2007–2012j)
Ribes cereum Douglas	Wax Currant	As above	Harrington (1974), Clarke (1977), Facciola (1990), and Deane (2007–2012j)
Ribes nigrum L.	Black Currant	Flower buds used in ice cream and liqueurs	Deane (2007–2012j)
Ribes odoratum H.L. Wendl. = *Ribes aureum* var. *villosum* DC.	Golden Currant, Buffalo Currant	Flowers eaten raw, has a sweet taste	Harrington (1974) and Facciola (1990)
Hamamelidaceae			
Corylopsis himalayana Griff.	Dieng-Piu	Flowers eaten in Meghalaya, India	Sawian et al. (2007)
Helwingiaceae			
Helwingia chinensis Batalin	Zhong Hua Qing Jia Ye (Chinese)	Flowers and leaves are edible	Kunkel (1984)
Helwingia japonica (Thunb.) F. Dietr.	Hana-Ikada (Japanese)	Young flowers and young shoots are eaten	Read (1946), Uphof (1968), Tanaka (1976), and Facciola (1990)
Hyacinthaceae			
Muscari atlanticum Boiss. & Reut. = *Muscari neglectum* Guss. ex Ten.	Musk Hyacinth, Nutmeg Hyacinth	Flowers and flower buds can be pickled in vinegar	Newman and O'Connor (2009)
Muscari botryoides (L.) Mill.	Italian Grape Hyacinth	As above	Crowhurst (1972), Facciola (1990), and Newman and O'Connor (2009)
Muscari neglectum Guss. ex Ten.	Musk Hyacinth, Nutmeg Hyacinth	The flowers, sprinkled over rhubarb, add a wonderful scented flavour	Hedrick (1972) and Facciola (1990)
Hydrocharitaceae			
Hydrocharis dubia (Blume) Backer	Frogbit; Tochi-Kagami (Japanese)	Young inflorescence is eaten	Van den Bergh (1994b)
Ottelia alismoides (L.) Pers.	Mizu Obako (Japanese); Santawa (Thai)	Young leaves and flowers are eaten raw with chilli sauce and used as side dish	Jircas (2010)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Hypericaceae			
Cratoxylum formosum Benth. & Hook. f. ex Dyer	Pink Mempat; Tiew (Thai)	Flowers are edible	Tangkanakul et al. (2005)
Hypericum perforatum L.	St. John's Wort, Amber, Goat Weed, John's Wort, Chase Devil, Klamath Weed, Rosin Rose, Tipton Weed	Flowers used for making mead and can be tossed into salads	Crowhurst (1972), Facciola (1990), and Roberts (2000)
Iridaceae			
Crocosmia aurea (Pappe ex Hook.) Planch.	Falling Stars, Valentine Flower, Montbretia	Flowers source of yellow dye, used as substitute for saffron	Uphof (1968) and Facciola (1990)
Crocus sativus L	Saffron, Autumn Crocus, Spanish Saffron, Dyer's Saffron	Dried filaments and styles used for colouring and flavouring food and saffron tea	Hedrick (1972), Morton (1976), Kunkel (1984), Garland (1993), Facciola (1990), and Wessel-Riemens (1992)
Crocus serotinus Salisb.	Late Crocus, Ornamental Crocus	Flowers used as saffron substitute in colouring food	Tanaka (1976)
Freesia alba (G.L. Mey.) Gumbl.	Fressia, Kammetjie; Ruikpypie (Afrikaans)	Flowers used raw in salads	Deane (2007–2012h)
Freesia leichtlinii subsp. *alba* (G.L. Mey.) J.C. Manning & Goldblatt	Fressia, Kammetjie, Ruikpypie	Edible flowers used raw in salads. They are reported to be excellent, infused with a sugar syrup and are used in sorbets for flavouring	Wickes (2004) and Deane (2007–2012h)
Freesia spp.	Freesia	Highly scented flowers are used in salads raw or as a garnish. They are reported to be excellent, infused with sugar syrup and added in sorbets for flavouring	Deane (2007–2012h)
Gladiolus cruentus T. Moore	Blood Lily, Blood-Red Gladiolus, Blood Flag, Gladiolus	Flowers eaten raw or cooked, added to salads or used as a boiled vegetable	Fox et al. (1982) and Facciola (1990)
Gladiolus dalenii Van Geel	African Gladiolus, Parrot-Beaked Gladiolus; Papegaai-Gladiolus (Afrikans)	Flowers eaten raw or cooked. The anthers are removed and the flowers are added to salads or used as a boiled vegetable. Children suck the flowers for their copious quantities of nectar	Fox et al. (1982) and Facciola (1990)
Gladiolus ecklonii Lehm.	Sheathed Gladiolus	Flower eaten raw or used in potherb	Fox et al. (1982) and Facciola (1990)
Gladiolus hortulanus L.H. Bailey	Garden Gladiolus, Gladiolus, Glads	Petals eaten raw or cooked, rather bland	Deane (2007–2012b)
Gladiolus spp.	Gladiolus	As above	Newman and O'Connor (2009)
Tritonia crocata (L.) Ker-Gawl.	Orange Tritonia, Kalkoentjie	Flowers used to adulterate saffron	Kunkel (1984) and Facciola (1990)

Lamiaceae			
Acinos arvensis (Schur) Dandy = *Clinopodium acinos* (L.) Kuntze	Basil Thyme	Flowering tops used to season jugged hare and used in salads	Grieve (1971), Kunkel (1984), Facciola (1990), and Bown (1995)
Aeollanthus pubescens Benth.		Leaves, flowers used as spice (analogue of basil)	Seidemann (2005)
Agastache anethiodora Nutt. & Britton	Anise Hyssop	Aromatic leaves and flowers are used in salads for flavouring and in tea and punch	Roberts (2000) and Deane (2007–2012m)
Agastache cana (Hook.) Wooton & Standl.	Texas Hummingbird Mint, Mosquito Plant, Wild Hyssop	Aromatic leaves and flowers are used in salads for flavouring and tea	Deane (2007–2012m)
Agastache foeniculum (Pursh) Kuntze	Anise Hyssop, Blue Giant Hyssop, Blue Giant Hyssop, Lavender Hyssop, Licorice Mint, Wonder Honey Plant	Flowers used in desserts—cakes, custard, cookies; Flowers have an anise or liquorice flavour used for salad or drinks and tea	Morton (1976), Facciola (1990), Barash (1997), Lauderdale and Evans (1999), and Newman and O'Connor (2009)
Agastache mexicana (Kunth) Lint & Epling	Mexican Hyssop	Aromatic leaves and flowers are used in salads for flavouring and tea	Deane (2007–2012m)
Agastache neomexicana (Briq.) Standl. = *Agastache pallidiflora* subsp. *neomexicana* (Briq.) Lint & Epling	New Mexico Giant Hyssop	As above	Deane (2007–2012m)
Agastache rugosa (Fisch. & C.A. Mey.)	Korean Hyssop, Korean Mint	As above	Roberts (2000) and Deane (2007–2012m)
Agastache urticifolia (Benth.) Kuntze	Giant Hyssop, Nettle Leaf Giant Hyssop	Dried flowers used to make herbal tea	Yanovsky (1936) and Facciola (1990)
Calamintha ascendens Jord. = *Clinopodium menthifolium* subsp. *ascendens* (Jord.) Govaerts	Calamint, Common Calamint, Mountain Calamint, Mountain Balm	Calamint tea, calamint conserve, peach and calamint dessert	Roberts (2000)
Calamintha nepeta (L.) Savi = *Clinopodium nepeta* (L.) Kuntze	Calamint, Lesser Calamint, Cornemint, Mountain Mint		Roberts (2000)
Calamintha officinalis Moench = *Clinopodium nepeta* subsp. *glandulosum* (Req.) Govaerts	Calamint, Cornemint, Mill Mountain, Mountain Balm, Basil Thyme, Mountain Mint	Calamint tea	Roberts (2000)
Calamintha sylvatica Bromf. = *Clinopodium menthifolium* subsp. *menthifolium*	Calamint, Woodland Calamint	Flowers used for conserve	Morton (1976) and Facciola (1990)
Clerodendrum japonicum (Thunb.) Sweet	Japanese Glorybower, Kaempfer's Glorybower	Flowers are edible	Kunkel (1984)
Clerodendrum serratum Spreng. var. *wallichii* C. B. Clarke = *Rotheca serrata* (L.) Steane & Mabb.	Glorybower, Bagflower, Bleeding-Heart; Akkhi Thawan, Charak Pa (Thai); Bharangi (Indonesia); Akalbih, Akla Brikhsa (Assamese)	Inflorescences are boiled or cooked with curry in India. Young inflorescences with unexpanded flowers are eaten as lalab, side dish with rice in Indonesia	Tanaka (1976), Ochse and van den Brink (1980), Facciola (1990), Sawian et al. (2007), and JIRCAS (2010)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Clerodendrum spicatum Thunb. = *Orthosiphon aristatus* var. *aristatus*	Cat's Whiskers, Java Tea, Kidney Tea Plant; Ya Nuat Suea (Thai)	Flowers cooked as vegetable; flowers that are bitter are cooked and eaten as good vegetable	Pongpangan and Poobrasert (1985)
Clinopodium brownie (Sw.) Kuntze	Browne' Savoury, Creeping Charlie, Mint Charlie	Flowers are edible	Deane (2007–2012l)
Elsholtzia blanda (Bentham) Bentham	Llomba, Lengmaser (Manipur)	Flowers dried and stored for months, used for garnishing vegetarian and non-vegetarian dishes; used in a dish made of arbi (*Colocasia*)	Hauzel (2012) and Yumnam and Tripathi (2012)
Elsholtzia strobilifera (Benth.) Benth.	Rengma Ser, Langtu (Assamese)	Inflorescence eaten in Assam	Medhi and Borthakur (2012)
Gmelina arborea Roxb.	Yunnan Gemlina; Tian Shi Zi (Chinese); Gomari, Gameri (Assamese)	Fragrant flower gathered by Thai ethnic group of southern Yunnan for flavouring and colouring pastries. In Assam, flowers eaten cooked	Hu (2005) and Patiri and Borah (2007)
Hedeoma drummondii Benth.	Drummond's False Pennyroyal	Infusion of flowering tops used as beverage in Texas	Yanovsky (1936)
Hyssopus officinalis L.	Hyssop	Flowers, raw. Added to salads or made into syrup	Facciola (1990), Deane (2007–2012n), and Newman and O'Connor (2009)
Koellia virginiana (L.) Kuntze = *Pycnanthemum virginianum* (L.) T. Durand & B.D. Jacks. ex B.L. Rob. & Fernald.	Virginia Mountain Mint	Flowers and buds used for seasoning meat or broth by Chippewa Indians	Yanovsky (1936)
Lamium amplexicaule L	Greater Henbit, Henbit Deadnettle	Flowering tips eaten in salad, boiled as potherb, cooked in rice gruel or used in dumplings	Fernald et al. (1958), Tanaka (1976), and Facciola (1990)
Lamium galeobdolon (L.) Crantz	Yellow Archangel, Golden Deadnettle	Young flowering tips cooked	Fern (1992–2003)
Lamium purpureum L.	Archangel Red Dead Nettle	Flowering tips boiled or candied	Hedrick (1972), Kunkel (1984), and Facciola (1990)
Lavandula angustifolia Mill.	Lavender, English Lavender, True Lavender	Flowers make into conserve, crystallized and used on cakes; fresh or dried flowers used in salads or to flavour sugar and jellies; fresh or dried flowers brewed into tea; lavender flowers used in both in sweet or savoury dishes	Morton (1976), Larkcom (1980), Facciola (1990), Garland (1993), Burnie and Fenton-Smith (1996), Barash (1997), Roberts (2000), and Newman and O'Connor (2009)
Lavandula dentata L.	Fringed Lavender, French Lavender	As above	Garland (1993) and Roberts (2000)

Lavandula latifolia Medik.	Spike Lavender, Dutch Lavender	Flowers source of essential oil used for flavouring salads and jellies	Tanaka (1976), Facciola (1990), and Roberts (2000)
Lavandula multifida L.	Fernleaf Lavender, Egyptian Lavender	Use lavender flowers, both in sweet or savoury dishes. Make a delicious lavender sugar and add to biscuits, sorbets, jams or jellies	Anonymous (2012a)
Lavandula spp.	Lavender	Flowers make into conserve, crystallized and used on cakes; fresh or dried flowers used in salads; or to flavour sugar, jellies, ice cream, sorbet, cookies	Garland (1993), Burnie and Fenton-Smith (1996), Barash (1997), Lauderdale and Evans (1999), and Roberts (2000)
Lavandula stoechas L.	French Lavender, Spanish Lavender, Topped Lavender	As above	Garland (1993), Roberts (2000), and Anonymous (2012a)
Lavandula × *allardii* Hy = *Lavandula* × *heterophylla* Viv.	Blind Lavender, Allard's Lavender	As above	Roberts (2000)
Leonotis nepetifolias (L.) R.Br.	Giant Lion's Ear, Lion's Ear, Annual Lion's Ear, Christmas Candlestick, Bald Head, Bird Honey, Lion's Tail	Flowers eaten in Tanzania	Facciola (1990)
Leonurus cardiaca L.	Throw Wort, Lion's Ear, Motherwort, Common Motherwort, Lion's Tail	Flowering tops are used for flavouring beers, ales and stout. Fresh or dried flowers can also be added to soups, e.g. split pea soups, and can be brewed into tea	Crowhurst (1972) and Facciola (1990)
Leucas plukenetii (Roth) Spreng. = *Leucas aspera* (Willd.) Link	Common Leucas; Doron, Kansisa (Assamese)	Flower buds, used as vegetables in Assam	Patiri and Borah (2007)
Melissa officinalis L.	Balm, Lemon Balm, Erva Cidrera, Common Balm, Cytria	Flowers used in salads	Burnie and Fenton-Smith (1996) and Newman and O'Connor (2009)
Mentha × *piperita* L.	Peppermint	Flowers used to flavour sauces, ice cream or as garnish. These tiny flowers pack a real punch and add that something extra to green salads, fruit salads, fresh strawberries, chocolate mousse or chocolate cake. Can also be used to decorate and flavour lamb dishes	Barash (1997), Roberts (2000), and Anonymous (2012a)
Mentha aquatica L.	Water Mint	Flowers edible	Barash (1997)
Mentha aquatica var. *citrata* (Ehrh.) Benth.	Bergamot Mint, Eau de Cologne Mint, Lemon Mint, Lime Mint	Flowers of lemon bergamot mint are edible	Facciola (1990) and Roberts (2000)
Mentha arvensis L.	Field Mint, Corn Mint, Japanese Mint, Pudina	Flowers edible	Barash (1997)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Mentha arvensis L. forma *piperascens* Malinv. ex Holmes = *Mentha canadensis* L.	Japanese Mint, Japanese Field Mint	Flowers used for scenting tea	Tanaka (1976) and Facciola (1990)
Mentha longifolia (L.) Huds.	Biblical Mint, Horse Mint, Wild Mint	Leaves and flowering tops source of peppermint-like essential oil used for flavouring candy	Altschul (1973), Tanaka (1976), and Facciola (1990)
Mentha pulegium L.	English Pennyroyal, European Pennyroyal, Pennyroyal	Tiny flowers pack a real punch and add that something extra to green salads, fruit salads, fresh strawberries, chocolate mousse or chocolate cake; can also be used to decorate and flavour lamb dishes	Barash (1997) and Anonymous (2012a)
Mentha spicata L.	Spearmint, Lamb Mint, Garden Mint	Flowers used to flavour sauces, ice cream, salads, soups, fruit drinks, desserts, dressings and vegetable dish or as garnish	Grieve (1971), Facciola (1990), Barash (1997), Roberts (2000), and Anonymous (2012a)
Mentha spp.	Mint	Flowers used to flavour ice cream or as garnish	Barash (1997), Lauderdale and Evans (1999), and Newman and O'Connor (2009)
Mentha suaveolens Ehrh.	Apple Mint	As for spearmint	Roberts (2000) and Anonymous (2012a)
Mentha × *gentilis* L.	Ginger Mint, Scotch Mint	Flowers used to flavour sauces and ice cream or as a garnish	Barash (1997)
Mentha × *gracilis* Sole = *Mentha* × *gentilis* L.		As for apple mint	Anonymous (2012a)
Mentha × *citrata* Erh. = *Mentha* × *piperita* L.	Orange Bergamot Mint, Orange Mint, Eau de Cologne Mint, Pineapple Mint, Lemon Mint, Water Mint, Lime Mint	As for ginger mint	Barash (1997) and Roberts (2000)
Micromeria sp.	Emperor's Mint	Flowers edible	Roberts (2000)
Monarda citriodora Cerv. ex Lag. subsp. *austromontana* (Epling) Scora = *Monarda citriodora* Cerv.ex Lag. var. *austromontana* (Epling) B.L. Turner	Lemon Bee Balm, Lemon Mint	As well as being colourful, the petals have a sweet, spicy flavour and will enhance salads, jellies and stuffings, rice and pasta dishes. Fresh or dried leaves can be used to make delicious bergamot tea	Anonymous (2012a)

Monarda didyma L.	Bergamot, Bee Balm, Crimson Bee Balm, Scarlet Bee Balm, Scarlet Monarda, Oswego Tea	Flowers eaten raw; added as an attractive garnish to salads. An excellent aromatic tea or lemonade is made from the fresh or dried leaves and flower heads; also used in cakes, ice cream, teas, tartlets, jellies and stuffings, rice and pasta dishes. Fresh or dried leaves can be used to make delicious bergamot tea	Uphof (1968), Tanaka (1976), Facciola (1990), Phillips and Foy (1992), Bown (1995), Burnie and Fenton-Smith (1996), Barash (1997), Lauderdale and Evans (1999), Roberts (2000), Lust (2001), Newman and O'Connor (2009), and Anonymous (2012a)
Monarda fistulosa L.	Wild Bergamot, Bee Balm	The flowers make an attractive edible garnish in salads	Facciola (1990)
Monardella odoratissima Benth.	Mountain Pennyroyal, Mountain Monarda	Flower heads make a clear refreshing mint-like tea	Clarke (1977) and Facciola (1990)
Monardella villosa Benth.	Coyote Mint	As above	Clarke (1977) and Facciola (1990)
Nepeta cataria L.	Catnip, Catswort, Catmint	Flowers edible, have an aromatic, strong mint/spice flavour so should be used sparingly when cooking; ideal for adding a bit of bite to pasta or rice dishes and all types of vegetables; also makes a tasty complement to meat dishes like lamb	McVicar (2003), Anonymous (2012a), and Deane (2007–2012l)
Ocimum basilicum L.	Basil, Sweet Basil	Nice salad sprinkle; young leaves and flowering heads both fresh and dried are used for seasoning tomato sauce, vinegar, soups, salads and omelettes; flowers also used as garnish; delicious when added to salads, soups or pasta	Morton (1976), Facciola (1990), Lauderdale and Evans (1999), Aguilar et al. (1999), Newman and O'Connor (2009), and Anonymous (2012a)
Ocimum canum Sims = *Ocimum americanum* L.	Hoary Basil, Lime Basil; Mayanba (Manipur)	Young shoots and inflorescence	Yumnam and Tripathi (2012)
Ocimum minimum L.	Greek Basil, Bush Basil	The flowers are delicious when added to salads, soups or pasta	Anonymous (2012a)
Ocimum × *citriodorum* Vis. = *Ocimum* × *africanum* Lour.	Basil Lime, Basil Lemon, Variegated Basil	As above	Anonymous (2012a)
Origanum dictamnus L.	Dittany of Crete, Cretan Dittany, Hop Majoram	Flowering tops dried brewed into tea	Morton (1976) and Facciola (1990)
Origanum majorana L.	Sweet Majoram, Knotted Majoram	Flowering tops used for flavouring and preservative for ales, flowers used in salads, stuffing for meat, poultry or marinades, dried flower used for herbal tea; combines well with all chicken dishes and many fish recipes; can also be made into a flavoursome hot tea	Morton (1976), Facciola (1990), Garland (1993), Burnie and Fenton-Smith (1996), de Guzman and Jansen (1999), Newman and O'Connor (2009), and Brown (2011)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Origanum onites L.	Turkish Oregano, Pot Marjoram	Flowering tops used for flavouring and preservative for ales	Garland (1993)
Origanum spp.	Oregano	Flowering tops used for seasoning	Newman and O'Connor (2009)
Origanum syriacum L.	Syrian Oregano, Lebanese Oregano, Biblical Hyssop	Flowering tops used for seasoning	Bailey (1949) and Facciola (1990)
Origanum vulgare L.	Marjoram, Oregano, Wild Majoram, Spanish Thyme, Greek Oregano	Flowering tops used for flavouring and preservative for beer and ales	Grieve (1971), Hedrick (1972), Facciola (1990), Garland (1993), Burnie and Fenton-Smith (1996), and de Guzman and Jansen (1999)
Perilla frutescens (L.) Britton	Perilla, Beefsteak Plant, Chinese Basil, Purple Mint, Wild Sesame; Shiso, Egoma, Shisonoha (Japanese); Kkaennip Namul (Korean); Lá Tía Tô, Rau Tía Tô, Tía Tô (Vietnamese)	Flowers popularly used for flavouring or as garnish in Vietnamese, Japanese and Korean cooking; flower clusters serve as garnish for soups and tofu, while older ones fried	Yashidora (1968), Tanaka (1976), Facciola (1990), de Guzman and Siemonsma (1999), and Medhi and Borthakur (2012)
Perovskia atriplicifolia Benth.	Russian Sage	The small lavender flowers have a sweet flavour and can be eaten in salads or used as a garnish	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Poliomintha incana (Torr.) A. Gray	Frosted Mint	Flowers used for flavouring in Arizona	Yanovsky (1936) and Facciola (1990)
Prunella vulgaris L.	Selfheal, Lance Selfheal, Aleutian Selfheal, Heal-All; Xia-Ku-Kao (Chinese)	Dried inflorescence used in herbal tea	Hu (2005)
Pycnanthemum virginianum (L.) T. Durand & B.D. Jacks. ex B.L. Rob. & Fernald	Virginia Mountain Mint	Chippewa Indians used the flowers and buds for seasoning meat and broth	Yanovsky (1936) and Facciola (1990)
Rosmarinus officinalis L	Rosemary	Rosemary oil distilled from flowering tops and leaves, fresh flower good in salads or as decorations for puddings and desserts; flowers candied, preserved or added to jellies, honey, vinegar and wine; flowers and leaves can be used with poultry or pork	Grieve (1971), Morton (1976), Burnie and Fenton-Smith (1996), De Guzman (1999), Facciola (1990), Newman and O'Connor (2009), and Brown (2011)
Salvia ballotaeflora Benth. = *Salvia ballotiflora* Benth.	Shrubby Blue Sage	Infusion of flowering tops used as beverage in Texas	Yanovsky (1936)
Salvia dorisiana Standl.	Fruit Sage, Peach Sage, Fruit-Scented Sage	Flowers edible	Roberts (2000)

Salvia elegans Vahl	Pineapple Sage	Flowers used in salad, cookies or garnish	Burnie and Fenton-Smith (1996), Barash (1997), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Deane (2007–2012f)
Salvia japonica Thunb.	Japanese Woodland Sage; Shu Wei Cao (Chinese); Aki-No-Tamura-Sou (Japanese)	Children suck the flowers for the sweet nectar	Kunkel (1984) and Facciola (1990)
Salvia officinalis L.	Sage, Common Sage, Garden Sage, Golden Sage, Kitchen Sage, True Sage, Culinary Sage, Dalmatian Sage, Broadleaf Sage	Flowers used in salad or garnish; flowers eaten raw, boiled, pickled or eaten in bread and butter sandwiches	Grieve (1971), Hedrick (1972), Morton (1976), Facciola (1990), Burnie and Fenton-Smith (1996), Roberts (2000), and Newman and O'Connor (2009)
Salvia plebeia R.Br.	Australian Sage, Small-Flowered Sage	Flowers edible	Tanaka (1976)
Salvia sclarea L.	Amaro, Clarry, Clary, Clary Sage, Clear Eye	Flowers used in salad or garnish; flowers have a very aromatic flavour and, being pastel shades, make a lovely contrast when added to salads	Burnie and Fenton-Smith (1996), Grieve (1971), Morton (1976), Facciola (1990), Deane (2007–2012l), and Anonymous (2012a)
Salvia verbenaca L.	Wild Clary, Vervain Sage, Wild Sage	Flowers eaten raw for flavouring in salads	Kunkel (1984) and Facciola (1990)
Satureja hortensis L.	Summer Savoury	Flowers edible	Huyen and Brink (1999) and Newman and O'Connor (2009)
Satureja montana L.	Winter Savoury	Flowering tops used for seasoning soups, salads, sauces, fish, stuffings, egg dishes, poultry, meat, vegetables	Grieve (1971), Morton (1976), Facciola (1990), and Newman and O'Connor (2009)
Sideritis perfoliata L.	Ironwort, Mountain Tea, Shepherd Tea	Inflorescences and leaves used in herbal tea and beverages	Petreska et al. (2011)
Sideritis raeseri Boiss. & Heldr.	Ironwort, Mountain Tea, Shepherd Tea	As above	Petreska et al. (2011)
Sideritis scardica Griseb.	Bulgarian Sideritis, Ironwort, Mountain Tea, Sheperd Tea	Inflorescences and leaves used in herbal tea and beverages	Qazimi et al. (2010)
Sideritis syriaca L.	Ironwort, Mountain Tea, Sheperd Tea	As above	Petreska et al. (2011)
Sideritis taurica Steph ex Willd.	Ironwort, Mountain Tea, Sherpherd Tea	As above	Petreska et al. (2011)
Stachys officinalis (L.) Trevis.	Betony, Purple Betonybishops Wort	Infusion of flowering tops makes a refreshing, aromatic beverage	Macnicol (1967), Morton (1976), and Facciola (1990)
Teucrium scorodonia L.	Wood Germander, Sage-Leaved Germander	Infusion of leaves and flowers called ambroise used in France and Channel Islands as a substitute for hops in flavouring	Grieve (1971), Hedrick (1972), Morton (1976), and Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Thymus caespititius Brot.	Cretan Thyme, Azores Thyme, Mountain Thyme, Tiny Thyme	Aromatic leaves and flowers used locally as condiment	Lauderdale and Evans (1999), Widodo (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus capitatus (L.) Hoffmanns. & Link = *Thymbra capitata* (L.) Cav.	Headed Savoury, Conehead Thyme	Aromatic leaves and flowers used locally as condiment	Lauderdale and Evans (1999), Widodo (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus citriodorus Schreb. = *Thymus serphyllum* subsp. *serphyllum*	Lemon Thymes, Orange Thymes, Lime Thyme	Fresh flowers in salads or garnish or as flavouring for honey	Burnie and Fenton-Smith (1996), Lauderdale and Evans (1999), Widodo (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus herba-barona Loisel.	Caraway Thyme	Fresh flowers in salads or garnish or as flavouring for honey	Widodo (1999), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010), burnie
Thymus mastichina (L.) L.	Mastic Thyme, Mejorana, Pine Scented Thyme, Spanish Marjoram, Spanish Wood	Aromatic leaves and flowers used locally as condiment	Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus praecox Opiz	Creeping Thyme, Mother of Thyme, Wild Thyme	As above	Widodo (1999), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus praecox subsp. *arcticus* (Durand) Jalas = *Thymus praecox* Opiz subsp. *britannicus* (Ronninger) Holub	Mother of Thyme, Wild Thyme, Creeping Thyme	Dried flowers steeped for tea	Morton (1976), Facciola (1990), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus pulegioides L.	Broad-Leaved Thyme, Lemon Thyme	Aromatic leaves and flowers used locally as condiment	Widodo (1999), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus quinquecostatus Celak.	Japanese Thyme, Five-Ripped Thyme	Flowers edible	Widodo (1999), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus serphyllum L.	Breckland Thyme, Wild Thyme, Creeping Thyme	Flowers edible	Widodo (1999), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus spp.	Thyme	Flowers edible	Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)

Thymus vulgaris L.	Common Thyme, Garden Thyme, Rubbed Thyme, Thyme	Fresh flowers in salads or garnish or as flavouring for honey. Flowering tops used for flavouring stuffings, soups, cheese, vinegar, gravies, sausages, etc.	Morton (1976), Facciola (1990), Burnie and Fenton-Smith (1996), Lauderdale and Evans (1999), Widodo (1999), Roberts (2000), Newman and O'Connor (2009), and Stradley (2010)
Thymus × *citriodorus* (Pers.) Schreb. ex Schweigg. & Koe.	Lemon-Scented Thyme, Lemon Thyme	Aromatic leaves and flowers used locally as condiment	Widodo (1999), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)
Thymus zygis L.	Moroccan Wild Thyme, Sauce Thyme	As above	Widodo (1999), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Stradley (2010)
Lauraceae			
Lindera obtusiloba Blume	Japanese Spicebush, Blume	Young buds used as tea substitute called *jaku-zetsu cha*	Tanaka (1976) and Facciola (1990)
Lecythidaceae			
Barringtonia edaphocarpa Gagnep. = *Barringtonia acutangula* (L.) Gaertn. subsp. *acutangula*	Barringtonia, Stream Barringtonia, Indian Oak; Chiknma Chik Nom Yam (Thai)	Young leaves and flowers eaten as fresh vegetables	Pongpangan and Poobrasert (1985)
Careya sphaerica Roxb. = *Careya arborea* Roxb.	Tummy Wood; Kra Don, Phak Kadron, Kradonbok, Kradonkhon, Khui, Phuk Kui, Puikradon, Pui-Khao (Thai)	The shoots are eaten raw with chilli sauce (*nam phrik*). The flowers are also served raw with *nam phrik* or with vermicelli and fish curry. The fruit is eaten fresh	JIRCAS (2010) and Maisuthisakul (2012)
Liliaceae			
Calochortus aureus S. Watson	Mariposa Lily, Golden Mariposa Lily	Flowers edible	Moerman (1998)
Calochortus gunnisonii S. Watson	Mariposa Lily, Gunnison's Mariposa Lily	Flower buds eaten raw, added to salads	Harrington (1974) and Facciola (1990)
Calochortus macrocarpus Douglas	Sagebrush Mariposa Lily	Flower buds eaten raw, has a sweet flavour	Moerman (1998)
Calochortus nuttallii Torr.	Sego Lily	Flowers and flower buds eaten raw, a tasty addition to the salad bowl	Clarke (1977) and Facciola (1990)
Erythronium albidum Nutt.	White Trout Lily, White Fawn Lily, White Dogtooth Violet	Flowers, flower buds and flower stems eaten raw or cooked	Facciola (1990)
Erythronium americanum Ker. Gawl	Dogtooth Violet, Trout Lily, Yellow Adder's Tongue	Flower buds and flower stems eaten raw or cooked	Facciola (1990)
Fritillaria verticillata Willd.	Fritillaria, Fritillary, Baimo	Petals and flower buds cooked, used in soups	Facciola (1990); Tanaka (1976)
Hosta plantaginea (Lam.) Asch.	Plantain Lily	Flowers cooked as a delicacy but requiring parboiling to detoxify	Hu (2005)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Lilium amabile Palibin	Koma-Yuri, Korean Lily	Flower buds eaten cooked	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Lilium brownii F.E. Br ex Meillez	Hong Kong Lily	The dried flower petals are used as a flavouring in soups	Herklots (1972), Altschul (1973), and Facciola (1990)
Lilium concolor Salisb.	Morning Star Lily	Flowers edible	Stuart (1979)
Lilium dauricum Ker.-Gawl. = *Lilium pensylvanicum* Ker Gawl.	Dauricum Lily, Candlestick Lily	Flowers edible	Komarov (2006)
Lilium formosum Lem. = *Lilium pensylvanicum* Ker Gawl.	Candlestick Lily	Flowers, also bulbs, leaves and stems are edible	King (2007)
Lilium lancifolium Thunb.	Tiger Lily	Flowers eaten raw or cooked, used fresh or dried in salads, soups, rice dishes, etc.	Herklots (1972), Bryan and Castle (1975), Tanaka (1976), and Facciola (1990)
Lilium longiflorum Thunb.	White Trumpet Lily, Trumpet Lily, Easter Lily	Flower buds eaten	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Lilium maculatum Thunb.	Maculatum Lily; Sukashiyuri (Japanese)	Flower buds cooked	Tanaka (1976)
Lilium sargentiae E.H. Wilson	Sargent's Lily	Flowers consumed in parts of China	Uphof (1968), Tanaka (1976), and Facciola (1990)
Tulipa gesneriana L.	Tulip	Flowers consumed as below	Roberts (2000) and Deane (2007–2012b)
Tulipa spp.	Tulip	Flowers used in salads, crystallized, garnish stuff whole flowers with a shrimp or chicken salad; add strips of petals to salads or sandwiches for that added touch of colour	Lauderdale and Evans (1999), Roberts (2000), Mlcek and Rop (2011), and Deane (2007–2012b)
Loranthaceae			
Nuytsia floribunda R.Br.ex G. Don	Christmas Tree	Flowers soaked in water to make a sweet drink	SERCUL (2011)
Tupeia antarctica (G.Forst.) Cham. & Schltdl.	Taapia, Tupia, White Mistletoe	Flowers edible	Brooker et al. (1989), Crowe (1990), and Fern (1992–2003)
Lythraceae			
Punica granatum L.	Pomegranate, Granada, Anar	Flowers eaten in Thailand	Wongwattanasathien et al. (2010)
Sonneratia caseolaris Gaerth	Mangrove Apple, Crabapple Mangrove, Red-Flowered Apple Mangrove	As above	Wessapan et al. (2007)
Woodfordia fruticosa (L.) Kurz.	Fire-Flame Bush, Shinajitea, Woodfordia	In India (Garhwal Himalayas) flowers sucked for nectar	Gupta (1962)

Magnoliaceae			
Liriodendron tulipifera L.	Tulip Tree, American Tulip Tree, Tulip Poplar, Whitewood, Fiddle Tree, Yellow Poplar	Flowers abound in honey which can be drunk directly from the blossoms	Deane (2007–2012o)
Magnolia coco (Lour.) DC.	Chinese Magnolia; Yeh-Ye-Hua (Chinese)	Flowers used to scent tea	Tanaka (1976) and Facciola (1990)
Magnolia denudata Desr.	Yulan Magnolia White Magnolia; Bai-Yu-Lan (Chinese)	Fresh petals of partially opened flowers dipped in batter and deep-fried, calyx removed from flower bud, pickled and used for flavouring	Hedrick (1972), Facciola (1990), and Hu (2005)
Magnolia grandiflora L.	Southern Magnolia, Evergreen Magnolia, Loblolly Magnolia	Flowers are pickled in some parts of England and are also said to be used as a spice and a condiment	Hedrick (1972), Tanaka (1976), and Facciola (1990)
Magnolia kobus DC.	Kobushi Magnolia, Northern Japanese Magnolia, Kobus Magnolia, Mountain Magnolia; Kobushi, Hsin-I (Japanese)	Flowers and flower buds eaten cooked	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Michelia alba DC.	Joy Perfume Tree, White Champak, White Jade Orchid Tree, Pak-Lan, Banana Shrub; Ginko-Boku (Japanese)	Flowers used for scenting tea	Tanaka (1976) and Facciola (1990)
Malvaceae			
Abelmoschus manihot (L.) Medik.	Sunset Hibiscus, Sunset Muskmallow, Sweet Hibiscus; Qiu Kui (Chinese)	Flowers used in soups, flower buds eaten	Tanaka (1976), Ochse and van den Brink (1980), Facciola (1990), and Hu (2005)
Abelmoschus esculentus (L.) Moench	Okra, Gumbo, Lady's Finger	Blossoms are shy on taste but add colour and texture to salads as well as an attractive garnish; flower buds, flowers and calyces cooked as greens	Hedrick (1972), Halpin (1978), Facciola (1990), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Deane (2007–2012g)
Abelmoschus moschatus Medik.	Musk Okra, Musk Mallow	Edible flower pigment and used in flower tea	Puckhaber et al. (2002)
Abutilon esculentum A. St. Hil. = *Bakeridesia esculenta* (A.St.-Hil.) Monteiro	Purple-Flowered Indian, Mallow Night Flowering Maple	Brazilians eat the petals as vegetables	Hedrick (1972)
Abutilon guineense (Schumach.) Baker f. & Exell = *Abutilon indicum* var. *guineense* (Schumach.) K.M.Feng	Country Mallow, Monkey Bush	Flowers eaten raw	Uphof (1968), Hedrick (1972), Tanaka (1976), and Facciola (1990)
Abutilon indicum (Link) Sweet	Indian Abutilon, Indian Mallow	Flowers eaten in Andhra Pradesh, India, raw flowers eaten in Arabia	Hedrick (1972) and Reddy et al. (2007)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Abutilon megapotamicum (A. Spreng.) St. Hil. & Naudin	Trailing Abutilon	Flowers eaten cooked as a vegetable	Lovelock (1973), Facciola (1990), and Fern (1992–2003)
Abutilon ochsenii (Phil.) Phil. = *Corynabutilon ochsenii* (Phil.) Kearney.	Abutilon; Chile-Samtpappel (German)	Flowers edible	Hedrick (1972) and Fern (1992–2003)
Abutilon purpurascens (Link.) Schum. = = *Bakeridesia esculenta* (A.St.-Hil.) Monteiro	Purple-Flowered Indian, Mallow Night Flowering Maple	Flowers cooked as vegetable	Hedrick (1972), Tanaka (1976), and Kunkel (1984)
Abutilon vitifolium (Cav.) C. Presl = *Corynabutilon vitifolium* (Cav.) Kearney	Abutilon, Chinese Bell Flower, Flowering Maple	Flowers edible raw	Fern (1992–2003)
Abutilon × *hybridum* hort. ex Voss	Chinese Lantern, Flowering Maple, Parlour Maple	Flowers eaten raw or cooked on their own or as part of a mixed salad	Fern (1992–2003)
Abutilon × *milleri* auct.	Trailing Abutilon	Flowers eaten raw or cooked on their own or as part of a mixed salad	Fern (1992–2003)
Abutilon × *suntense* C.D. Bricknell = *Corynabutilon* × *suntense* (C. Bricknell) Fryxell	Indian Mallow, Flowering Maple	Flowers edible raw	Fern (1992–2003)
Adansonia digitata L.	African Baobab, Baobab, Bottle Tree, Cream of Tartar Tree, Dead-Rat Tree, Ethiopian Sour Tree, Judas Fruit, Monkey Bread Tree, Senegal Calabash, Sour Gourd, Upside Tree	Flowers eaten raw or used to flavour drinks	Lim (2012a)
Alcea rosea L.	Hollyhock	Flower petals and flower buds eaten raw; added to salads; a refreshing tea is made from the petals	Hedrick (1972), Lust (2001), Tanaka (1976), Kunkel (1984), Kasumov (1984), Facciola (1990), Roberts (2000), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Deane (2007–2012h)
Althaea officinalis L.	Marsh Mallow, Common Marshmallow	Flowers eaten raw or cooked; a tea is made from the flowers, flowers were the base of a famous confection *pâté de gimauve*	Macnicol (1967), Hedrick (1972), Facciola (1990), and Deane (2007–2012h)
Althaea rosea (L.) Cav. = *Alcea rosea* (L.) Cav.	Hollyhock	As for *Alcea rosea*	As for *Alcea rosea*
Bombax buonopozense P.Beauv	Red-Flowered Silk Cotton Tree	Fleshy mucilaginous calyces eaten in soups or used in sauces as substitute for roselle	Dalziel (1937), Uphof (1968), and Facciola (1990)

Bombax ceiba L.	Kapok Tree, Bombax, Red Silk Cotton Tree, Kapok, Tree Cotton; Mu Mian (Chinese); Sémul (Indian); Ngieo-Daeng (Thai)	Buds and flowers cooked and pickled. The dried stamens are collected during dried season and are added in curry dishes as spice, in typically northern Thai style of cooking. In China, fleshy flowers popular for curries, herbal tea; dried flowers used as ingredient of five flower tea *wu hua chai*. In western Rajasthan, India, flowers are dried, pounded and used in the preparation of bread—with or without the addition of corn flour	Gupta and Kanodia (1968), Saxena (1979), Hu (2005), JIRCAS (2010), Kapitany (2012), and Freedman (2013)
Bombax ceiba var. *leiocarpum* Robyns = *Bombax ceiba* L.		As above	As above
Bombax malabaricum DC. = *Bombax ceiba* L.	Kapok Tree, Bombax, Red Silk Cotton Tree, Kapok, Tree Cotton; Mu Mian (Chinese); Sémul (Indian); Ngieo-Daeng (Thai)	As above	Gammie (1902) and Gupta (1962)
Ceiba pentandra (L.) Gaertn.	Cotton Tree Kapok Tree, Silk Cotton Tree	The flowers are used in curries for flavour and to add some colour. In West Cameroons, the whole flower or more usually the calyx is eaten	Lim (2012a) and Deane (2007–2012f)
Dombeya rotundifolia Planch.	Wild Pear	Flowers cooked and eaten as side dish	Kunkel (1984) and Facciola (1990)
Durio zibethinus Murray	Durian	Flowers eaten in curries, soups	Burkill (1966) and Lim (2012a)
Hibiscus acetosella Welw. ex hiern	False Roselle, African Rosemallow, Cranberry Shield, Red Leaf Hibiscus, Red Leaf Maple	Flowers edible	Deane (2007–2012a)
Hibiscus aculeatus Walter	Comfort Root, Pinelands Mallow	Fresh flowers used in salads and garnishes, or dried and used in processed food products, nutraceuticals, dietary supplements, flower tea and natural food colorants as it yields an edible flower pigment. Flowers have commercialization potential of flower teas, vinaigrettes, bulk dried petals and concentrated edible petal pigment extracts	Puckhaber et al. (2002) and Bost (2004)
Hibiscus calyphyllus Cav.	Hibiscus, Sun Hibiscus, Lemon-Yellow Rosemallow	As above	Puckhaber et al. (2002) and Bost (2004)
Hibiscus coccineus Walter	Great Red Hibiscus, Scarlet Hibiscus, Scarlet Rose Mallow	As above	Puckhaber et al. (2002) and Bost (2004)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Hibiscus divaricatus Graham	Hibiscus	Buds of young plants eaten raw	Irvine (1957) and Freedman (2013)
Hibiscus diversifolius Jacq.	Swamp Hibiscus, Cape Hibiscus	Flowers eaten raw or cooked with other foods, e.g. groundnuts	Kunkel (1984), Fox et al. (1982), and Facciola (1990)
Hibiscus grandiflorus Michx.	Giant Rose Mallow, Swamp Hibiscus, Velvet Mallow, Giant Hibiscus	As for *Hibiscus aculeatus*	Puckhaber et al. (2002) and Bost (2004)
Hibiscus hamabo Siebold & Zucc.	Hamabo (Japanese)	As for *Hibiscus aculeatus*	Puckhaber et al. (2002) and Bost (2004)
Hibiscus heterophyllus Vent	Coral Hibiscus, Native Rosella, Wild Rosella, Native Cottonwood, Toilet Paper Bush	Young shoots, roots, leaves and flowers eaten (leaves need to be cooked); flowers and flower buds eaten raw in salads or cooked; flower buds made into jams	Wrigley and Fagg (1979), Cribb and Cribb (1987), and Low (1989)
Hibiscus laevis All.	Smooth Rose Mallow, Halberd-Leaved Rose Mallow	As for *Hibiscus aculeatus*	Puckhaber et al. (2002) and Bost (2004)
Hibiscus martianus Zucc.	Heartleaf Hibiscus, Heartleaf Rose Mallow, Tulipan del Monte	As for *Hibiscus aculeatus*	Puckhaber et al. (2002) and Bost (2004)
Hibiscus moscheutos L.	Common Rose Mallow, Swamp Rose Mallow	As for *Hibiscus aculeatus*	Puckhaber et al. (2002) and Bost (2004)
Hibiscus mutabilis L.	Confederate Rose, Cotton Rose, Common Rose Mallow, Changeable Rose	As for *Hibiscus aculeatus*	Puckhaber et al. (2002) and Bost (2004)
Hibiscus paramutabilis L.H. Bailey	Shanghai Pink Mallow	As for *Hibiscus aculeatus*	Puckhaber et al. (2002) and Bost (2004)
Hibiscus pentaphyllus F. von Mueller	Hibiscus, Five-Fingered Mallow	Young buds eaten raw	Irvine (1957) and Freedman (2013)
Hibiscus rosa-sinensis L.	Chinese Hibiscus, China Rose, China Shoe Flower, Lipstick Flower, China Rose, Shoeback Plant; Bunga Raya (Malaysia)	The slightly acidic petals are used sparingly in salads or as garnish. Flowers are reported eaten as pickles and the young leaves are eaten cooked in Papua New Guinea. The flowers are eaten in salads in the Pacific Islands. In Andhra Pradesh, India, the flowers are pounded into a paste and used as chutney. The flowers also used in herbal teas and as food colouring	Hedrick (1972), Tanaka (1976), French (1986), Johansson (1989), Reddy et al. (2007), Wongwattanasathien et al. (2010), Facciola (1990), and Duke (2012)

Hibiscus sabdariffa L.	Roselle, Red Roselle, Jamaica Sorrel, Sorrel, Roselle, Florida Cranberry, Rosella, Indian Sorrel	Fleshy red calyx used fresh in salad and for making roselle wine, jelly, syrup, gelatin, refreshing beverages, puddings, chutneys, pickles, cakes, herbal teas, jellies, marmalades, ices, ice cream, sherbets, butter, pies, sauces, tarts and other desserts	Burkill (1966), Tanaka (1976), Duke (1983), Chopra et al. (1986), Morton (1987), Facciola (1990), Boonkerd et al. (1994), Rao (1996), Roberts (2000), Woodward (2000), Duke et al. (2002), Mohamad et al. (2002), Hu (2005), Tanaka and Nguyen (2007), Mohamed et al. (2007), and Wikipedia (2013)
Hibiscus schizopetalus (Dyer) Hook.f.	Lantern Flower, Coral Hibiscus, Japanese Lantern, Fringed Rosemallow, Chinese Lantern, Skeleton Hibiscus	Flowers used in food in Taiwan	Hu (2005)
Hibiscus sinosyriacus L.H. Bailey	Rose of Sharon	Flowers eaten raw or cooked or made into tea	Grieve (1971), Kunkel (1984), Tanaka (1976), and Facciola (1990)
Hibiscus striatus Cav.	Striped Hibiscus	As for *Hibiscus aculeatus*	Puckhaber et al. (2002) and Bost (2004)
Hibiscus syriacus L.	Rose of Sharon, Shrub Althea; Mgunghwa (Korean)	Flowers eaten raw or cooked, used in soups and also to make tea, flower pigment edible	Grieve (1971), Kunkel (1984), Tanaka (1976), Chopra et al. (1986), Facciola (1990), Hu (2005), Bost (2004), Puckhaber et al. (2002), Newman and O'Connor (2009), and Deane (2007–2012d)
Hibiscus tiliaceus L.	Sea Hibiscus, Cotton Tree, Beach Hibiscus, Coastal Cottonwood, Cottonwood	Buds, flower and young shoots are eaten	Burkill (1966), Cribb and Cribb (1987), Facciola (1990), Puckhaber et al. (2002), Bost (2004), and Duke (2012)
Kleinhovia hospita L.	Guest Tree, Timanga Tree, Apong-Apong	Flowers cooked and eaten	Burkill (1966), Hedrick (1972), Tanaka (1976), and Facciola (1990)
Kosteletzkya pentacarpos (L.) Ledeb.	Seashore Mallow, Virginia Saltmarsh Mallow	Flowers eaten raw, added to salads	Usher (1974)
Kosteletzkya virginica (L.) C.Presl ex A.Gray	Virginia Saltmarsh Mallow, Virginia Fen-Rose, Seashore Mallow, Salt Marsh Mallow, Pink Marsh Mallow	Leaves used as potherbs; flowers eaten uncooked; roots cooked as vegetables; teas made from flower, edible pigment from flower; plant parts boiled used as an egg white substitute for making meringues	Puckhaber et al. (2002)
Lavatera thuringiaca L. = *Malva thuringiaca* (L.) Vis.	Lavatera, Pink Tree Mallow, Garden Tree Mallow	Flowers have a pleasant mild flavour; they make a decorative addition to the salad bowl. Many named cultivars have considerably larger flowers than the type species and are thus worthwhile for the salad bowl	Fern (1992–2003)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Malva alcea L.	Vervain Mallow, European Mallow, Hollyhock Mallow	Flowers edible raw	Fern (1992–2003)
Malva excisa Rchb. = *Malva alcea* L.	Vervain Mallow, European Mallow, Hollyhock Mallow	Flowers eaten raw, provide a decorative addition to the salad bowl	Fern (1992–2003)
Malva sylvestris L.	Common Mallow, High Mallow, Tall Mallow, Blue Mallow, Cheese Cake, Cheeses, Pick-Cheese, Round Dock, Country Mallow, Wild Mallow	Flowers eaten raw; added to salads or used as a garnish; flowers can be crystallized	Hedrick (1972) and Facciola (1990)
Malvastrum lateritium G. Nicholson	Malvastrum, False Mallow, Creeping Mallow	Flowers eaten raw	Fern (1992–2003)
Malvaviscus arboreus Cav.	Sleeping Hibiscus, Firecracker Hibiscus, Wax Mallow, Turk's Cap; German Wachsmalve; Chaba (Thai)	Flowers used in salad and in light curry	Kaisoon et al. (2011)
Malvaviscus arboreus var. *drummondii* (Torr. & A.Gray) Schery	Turk's Cap, Wax Mallow, Texas Mallow, Manzanilla, Sleeping Hibiscus	Edible flower pigment and flower tea	Puckhaber et al. (2002)
Malvaviscus arboreus var. *mexicanus* Schltdl.	Turk's Cap Hibiscus, Mexican Turk's Cap, Sleepy Hibiscus, Lipstick Hibiscus	Edible flower pigment and flower tea	Puckhaber et al. (2002)
Pachira aquatica Aubl.	Malabar Chestnut, Guiana Chestnut, Provision Tree, Money Tree, Saba Nut	Flowers edible raw	Hedrick (1972), Menninger (1977), and Facciola (1990)
Pachira insignis (Sw.) Savigny	Malabar Chestnut, Wild Chestnut, Wild Breadnut	Flowers edible raw	Hedrick (1972), Tanaka (1976), Menninger (1977), and Facciola (1990)
Pavonia hastata Cav.	Pink Pavonia, Cape Mallow, Spearleaf Swamp Mallow	Edible flower pigment and flower tea	Puckhaber et al. (2002)
Pavonia lasiopetala Scheele	Texas Swamp Mallow, Wright Pavonia	Edible flower pigment and flower tea	Puckhaber et al. (2002)
Pterospermum acerifolium (L.) Willd.	Maple-Leaved Bayur Tree, Maple Twist	Flowers edible	Burkill (1966), Tanaka (1976), and Facciola (1990)
Quararibea funebris (La Llave) Visch.	Flor de Cacao, Rosita de Cacao, Madre de Cacao (Spanish)	Dried flowers afford a highly pungent spice. In Mexico, the flower spice is used to flavour 'ponzonque' or 'tejate', a frothy, thick, aromatic beverage made with chocolate, finely ground maize meal and water	Jansen (1999)
Salmalia malabarica (DC.) Schott. & Endl. = *Bombax ceiba* L.	Red Cotton Silk Tree, Silk Cotton Tree, Kapok Tree, Semal, Pan-Ya	Flowers and buds eaten as vegetables. Fleshy calyces of large, red flowers are used in curries	Watt (1908), Burkill (1966), Tanaka (1976), and Facciola (1990)

Sida spinosa L.	Arrowleaf Sida, Paddy's Lucerne, Jelly Leaf	Edible flower pigment and flower tea	Puckhaber et al. (2002)
Thespesia lampas (Cav.) Dalzell & A.Gibson	Hairy Portia Tree, Xiao Jin (Chinese)	Young shoots and flowers are eaten in China	Hu (2005)
Thespesia populnea (L.) Sol. ex Correa	Milo, Portia Tree, Pacific Rosewood, Seaside Mahoe, Indian Tulip Tree; Paras Pipal (Assamese)	Flowers, flower buds, also young leaves, are fried and eaten in Assam or boiled and put into soup	Burkill (1966), Kunkel (1984), Facciola (1990), and Patiri and Borah (2007)
Tilia cordata Mill.	Lime, Linden, Small Leaved Lime, Little Leaf Linden, Basswood Tree	Flowers and bracts dried used for lime tea	Uphof (1968), Facciola (1990), Garland (1993), Barash (1997), and Deane (2007–2012c)
Tilia japonica (Miq.) Simonk.	Japanese Lime; Shona-No-Ki (Japanese)	Flowers are parboiled to remove the bitterness and used as greens or added to soups; a tea is made from the flowers	Kunkel (1984) and Facciola (1990)
Tilia platyphyllos Scop.	Large-Leaved Lime, Broad-Leaved Lime, Linden	Flowers and bracts dried and used for lime tea	Garland (1993) and Barash (1997)
Tilia spp.	Linden	Linden flower tea	
Tilia × *europaea* L.	Common Lime, Common Linden, European Lime, European Linden	Flowers and bracts dried and used for lime tea. Flowers have a honey-like fragrance and make excellent tea sold as '*yilleul*' in France	Garland (1993), Tanaka (1976), and Facciola (1990)
Urena lobata L.	Caesar Weed Cadillo, Pink Flowered Chinese Burr, Urena Burr, Caesarweed, Candillo, Congo Jute, Burr, Urena, Pink Flowered Chinese, Aramina Plant, Aramina, Urena Weed, Pink Burr, Bur Mallow; Yakuwa (Nigeria–Hausa); Karasu (Nigeria–Kanuri)	Nigeria (Kano State, northern), leaves, calyces and flowers are eaten. Pink blossoms toss in salads and eaten raw	Mortimore (1989) and Deane (2007–2012q)
Marantaceae			
Calathea allouia (Aubl.) Lindl.	Guinea Arrowroot, Sweet Corn Root	Young flower clusters cooked	Deane (2007–2012o)
Curcuma sessilis Gage = *Calathea micans* (L. Mathieu) Korn.	Calathea	Flowers edible	Wongwattanasathien et al. (2010)
Thalia geniculata L.	Alligator Flag, Alligator Flag, Arrowroot, Bent Alligator Flag, Bent Alligator Flag, Fire Flag, Fire Flag, Giant Water Canna, Greater Thalia, Hardy Water Canna, Water Canna	Flowers edible	Wetwitayaklung et al. (2008)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Melastomataceae			
Melastoma polyanthum Blume = *Melastoma malabatrichum* L.	Native Lasiandra, Indian Rhododendron, Harendog, Malabar Melastome, Straits Rhododendron, Rhodendron, Blue Tongue, Lasiandra	Flowers edible	King (2007)
Meliaceae			
Aglaia odorata Loureiro	Mock Lime, Chinese Perfume Plant; Mi Zai Lan (Chinese)	Flowers used in Hebei for flavouring tea	Burkill (1966), Hedrick (1972), Facciola (1990), and Hu (2005)
Azadirachta indica A. Juss.	Bead Tree, Burmese Neem Tree, Chinaberry, Indian Cedar, Indian Lilac, Margosa, Margosa Tree, Neem, Neem Tree, Nimtree; Sadao (Thai); Geed Hindi (Somalia)	Young shoots and young inflorescences are eaten raw or steamed and dipped in sweet, sour and hot sauce	Pongpangan and Poobrasert (1985), Rojanapo and Tepsuwan (1992, 1993), Kusamaran et al. (1998a, b), Tanaka and Nguyen (2007), Maisuthisakul et al. (2008), Anonymous (2010), and Maisuthisakul (2012)
Melia azedarach L.	Chinaberry, Persian Lilac, White Cedar, Texas Umbrella, Bead Tree, Cape Lilac, Tulip Cedar, Karabil; Ghoraneem (Assamese)	Bitter flowers eaten as vegetables in Assam; some tribes of western Assam prepare dishes from the flowers with pounded rice	Patiri and Borah (2007) and Hauzel (2012)
Melianthaceae			
Melianthus major L.	Cape Honey Flower, Giant Honey Flower, Honey Bush	Flower nectar collected and eaten	Hedrick (1972) and Facciola (1990)
Melianthus minor L.	Dwarf Honey Flower, Honey Flower, Lesser Honey Bush	Flower nectar collected and eaten	Tanaka (1976) and Facciola (1990)
Menyanthaceae			
Nymphoides indica (L.) Kuntze	Water Snowflake, Floating Hearts, Marshwort; Thariktha Macha (Manipur)	Flower buds used as potherb	Tanaka (1976), Facciola (1990), and Yumnam and Tripathi (2012)
Nymphoides peltata (S.G. Gmelin) Kuntze	Water Snowflake Water Fringe, Fringed Water Lily, Entire Marshwort, Yellow Floating Heart	Flower buds cooked as a potherb	Tanaka (1976) and Facciola (1990)
Montiaceae			
Claytonia acutifolia Pall.ex Schult.	Bering Sea Spring Beauty	Flowers edible raw as garnishes	Schofield (2003)
Claytonia megarhiza (A. Gray) Parry ex S. Watson	Alpine Spring Beauty	Leaves and flowering tops eaten raw or cooked as a potherb; succulent, juicy and mild in flavour	Facciola (1990), Harrington (1974), and Schofield (2003)

Claytonia perfoliata Donnex Willd.	Miner's Lettuce, Winter Purslane, Indian Lettuce	Flowers and stalks eaten raw	Larkcom (1980)
Claytonia scammaniana Hulten	Scamman's Claytonia, Scamman's Springbeauty	Flowers edible raw as garnishes	Schofield (2003)
Claytonia sibirica L.	Pink Purslane, Siberian Miners Lettuce, Candy Flower, Siberian Purslane	Flowers edible raw as garnishes	Schofield (2003)
Claytonia tuberosa Pall. ex Schult.	Tuberous Spring Beauty	Flowers edible raw as garnishes	Schofield (2003)
Claytonia umbellata S. Watson	Great Basin Spring Beauty	Flowers edible raw as garnishes	Schofield (2003)
Claytonia virginica L.	Spring Beauty, Virginia Spring Beauty	Flowers and aerial parts edible raw or cooked	Deane (2007–2012p)
Montia perfoliata (Donn ex Willd.) Howell = *Claytonia perfoliata* Donn ex Willd.	Winter Purslane, Miner's Lettuce, Indian Lettuce	Flowers edible, excellent when tossed in salads	Larkcom (1980) and Facciola (1990)
Montia sibirica (L.) Howell = *Claytonia sibirica* L.	Pink Purslane, Siberian Purslane, Siberian Miners Lettuce, Candy Flower	Flowers used in salad or cooked	Schofield (2003)
Moraceae			
Artocarpus altilis (Parkinson ex F.A. Zorn) Fosberg	Breadfruit	Male inflorescences eaten as vegetable or used in the preparation of sweet meat	Facciola (1990) and Morton (1987)
Artocarpus heterophyllus Lam.	Jackfruit	Young male inflorescences mixed with chillies, fish paste, sugar, salt, etc.	Facciola (1990), Morton (1987), and Ochse and van den Brink (1980)
Artocarpus lakoocha Roxb.	Red Jackfruit, Monkey Jack; Lakuchi (India); Dewa Chali, Bohot (Assamese); Tampang (Malaysia)	Male inflorescence acid and astringent used as pickles	Morton (1987), Kunkel (1984), Facciola (1990), and Patiri and Borah (2007)
Broussonetia kazinoki Siebold	Kozo, Hime Kozo (Japanese)	Flowers edible	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Broussonetia kurzii (J.D. Hooker) Corner	Sa Lae (Thai)	Flowers edible	Tangkanakul et al. (2005)
Broussonetia luzonica (Blanco) Bureau	Birch Flower; Alokon, Alakon, Alucon, Himbabao (Philippines); Ragantulu (Indonesia)	Male inflorescences used as an ingredient in vegetable stews to add texture and aroma. Both inflorescence and young leaves commonly consumed in north-east Luzon, Philippines	Van den Bergh (1994a, b) and Rojo (1999)
Broussonetia papyrifera (L.) L'Her. ex Vent.	Paper Mulberry	Flowers edible	Read (1946)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Moringaceae			
Moringa oleifera Lam.	Moringa, Horseradish Tree, Drumstick Tree; Wasabinoki (Japanese); Maroom (Thai); Kelor (Malay); Shekta (India); Sajin (Assamese)	In Sudan, small leaflets are stripped from the leaf stalks and eaten raw in salads. Young pods are eaten like green beans and the flowers and leaves are eaten as vegetables in India (Rajasthan, western). Flowers cooked as vegetable or in soup in Thailand; young fruits and young shoots are usually put in *kang som* (sour and sweet curry); young shoots and inflorescence are boiled or blanched and served with chilli sauce	Gupta and Kanodia (1968), Morton (1976, 1991), Ochse and van den Brink (1980), Facciola (1990), Abdelmuti (1991), Polprasid (1994), Woodward (2000), Sawian et al. (2007), JIRCAS (2010), and Hauzaul (2012)
Moringa pterygosperma Gaertn. = *Moringa oleifera* Lam.	Moringa, Horseradish Tree, Drumstick Tree; Wasabinoki (Japanese); Maroom (Thai); Kelor (Malay); Shekta (India)	As above	Gammie (1902)
Musaceae			
Musa acuminata Colla	Wild Banana, Dwarf Banana; Kluai-Pa (Thai); Pisang Utan (Sabah, Malaysia)	Banana blossoms and core of stem eaten	Pongpangan and Poobrasert (1985) and Noweg et al. (2003)
Musa balbisiana Colla	Wild Banana; Athia Kol, Guti Kol (Assamese)	Inflorescences eaten as vegetables	Patiri and Borah (2007)
Musa brachycarpa Backer = *Musa balbisiana* var. *brachycarpa* (Backer) Häkkinen	Pisang Klutuk (Java)	Terminal buds of inflorescence eaten	Ochse and van den Brink (1980)
Musa campestris Becc.	Pisang Hutan, Kelalang	Banana blossoms and core of stem eaten	Noweg et al. (2003)
Musa glauca Roxb. = *Ensete glaucum* (Roxb.) Cheesman	Seeded Sweet Banana; Pisang Pidak (Java)	Terminal male buds eaten	Ochse and van den Brink (1980)
Musa hirta Becc.	Tangutui (Sabah, Malaysia)	Banana blossoms and core of stem eaten	Noweg et al. (2003)
Musa laterita Cheeseman	Bronze Banana	Terminal male buds eaten	
Musa paradisiaca L. = *Musa* (AAB group) French Plantain	Plantain Banana; Laphu Tharo (Manipur); Koldil (Assamese)	Terminal male inflorescences eaten in Indonesia. In Manipur, flowers used with chillies and dry fish in a dish called *ironba*; in Assam it is used as a vegetable and eaten pickled	Ochse and van den Brink (1980) and Hauzel (2012)

Musa salaccensis H. Zollinger	Javanese Wild Banana	Terminal male inflorescences eaten in Indonesia	Ochse and van den Brink (1980)
Musa spp.	Banana Flowers; Kluai (Thai)	Young fruits, young pseudostem and inflorescence are common ingredients of various local dishes throughout Thailand. Young inflorescences are sometimes eaten raw with local hot and spicy dishes. They are normally cooked as a main ingredient of curries. Some recipes include banana flower paella, banana flower kari-kari, banana flower and mushroom sauce	Nasution (1994), Valmayor and Wagih (1996), Roberts (2000), and JIRCAS (2010)
Musa textilis Nee	Manila Hemp, Abaca; Punti (Sabah, Malaysia)	Unopened flowers are eaten	Kulip (2003)
Musa velutina H. Wendl & Drude	Dwarf, Banana, Pink Banana, Velvet Banana, Velvel Pink Banana, Baby Pink Banana, Hairy Banana	Inflorescences or pink flowering parts and young stems are cooked as vegetables in Assam	Patiri and Borah (2007)
Musa violascens Ridley	Pisang Hutan	Banana blossoms and core of stem eaten	Noweg et al. (2003)
Musa zebrina Van Houtte ex Planchon = *Musa acuminata* ssp. *zebrina*(Van Houtte) R.E. Nasution	Blood Banana	Terminal male inflorescences eaten in Indonesia	Ochse and van den Brink (1980)
Myricaceae			
Myrica gale L.	Bog Myrtle, Sweet Gale	Compact flower buds used as spice, dried grind for seasoning stews (meat), poultry	Schofield (2003)
Myrtaceae			
Acca sellowiana (O. Berg) Burret	Pineapple Guava, Feijoa, Guavasteen	Flowers eaten raw; petals are sweet, crisp and delicious and are used in fruit salads and sorbets	Taylor (1990), Facciola (1990), Barash (1997), Roberts (2000), and Newman and O'Connor (2009)
Baeckea frutescens L	Shrubby Baeckea	Flowers used in herbal tea to refresh	Burkill (1966)
Callistemon spp.	Bottlebrush	Pour a cup of warm water over the flower spike to get the nectar.	Schaeffer and Fletcher (2012)
Cleistocalyx operculatus (Roxb.) Merr. & L.M. Perry = *Syzygium nervosum* A. Cunn. ex DC.	Water Banyan; Vối (Vietnamese)	Inflorescence; the leaves and buds are harvested, dried and brewed as an herbal tea in Vietnam known as '*nước vối*'	Hu (2005), Nguyen (1994), and Truong and Nguyen (2007)
Corymbia calophylla (R.Br. ex Lindl.) K.D. Hill & L.A.S. Johnson	Marri, Red Gum, Port Gregory Gum	Flowers rich in nectar soaked in water to make a sweet drink	SERCUL (2011)
Corymbia gummifera (Gaertn.) K.D. Hill & L.A.S. Johnson	Red Bloodwood, Pale Bloodwood	Flowers useful source of nectar	Steenbeeke (2001)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Eucalyptus gummifera (Gaertn.) Hochr. = *Corymbia gummifera* (Gaertn.) K.D. Hill & L.A.S. Johnson	Red Bloodwood, Pale Bloodwood	Flowers sucked for nectar or mixed with water to make a sweet drink called '*bool*'	Cribb and Cribb (1987) and Facciola (1990)
Eucalyptus intermedia F.Muell ex R.T. Baker = *Corymbia intermedia* (F. Muell ex R.T. Baker) K.D. Hill & L.A.S. Johnson	Pink Bloodwood	Flowers sucked for nectar or mixed with water to make a sweet drink	Cribb and Cribb (1987) and Facciola (1990)
Eucalyptus pachyphylla F. Muell.	Red Bud Malee, Thick-Leaved Mallee	Flowers sucked for nectar or mixed with water to make a sweet drink	Cribb and Cribb (1987) and Facciola (1990)
Feijoa sellowiana (O. Berg) O. Berg = *Acca sellowiana* (O. Berg) Burret	Pineapple Guava, Feijoa, Guavasteen	Spicy, sweet petals nibble or added to fruit salads	Clarke (1977), Morton (1987), Facciola (1990), Taylor (1990), and Barash (1997)
Leptospermum corsiacum Cheel.	None Recorded	In South Australia: blossoms sucked for nectar by aborigines	Irvine (1957)
Melaleuca alternifolia (Maiden & Betche) Cheel	Narrow-Leaved Paperbark, Narrow-Leaved Tea Tree, Narrow-Leaved Ti Tree, Snow in Summer	Flowers with nectar dipped in water to make a sweet drink	Harden (1991) and Steenbeeke (2001)
Melaleuca armillaris (Sol. ex Gaertn.) Sm.	Bracelet Honey Myrtle	Flowers with nectar dipped in water to make a sweet drink	Harden (1991) and Steenbeeke (2001)
Melaleuca bracteata F. Muell.	Black Tea Tree, Mock Olive, River Tea Tree	Flowers with nectar dipped in water to make a sweet drink	Harden (1991) and Steenbeeke (2001)
Melaleuca densispicata Byrnes	Miles Honey Myrtle	Flowers with nectar dipped in water to make a sweet drink	Harden (1991) and Steenbeeke (2001)
Melaleuca erubescens Nees	Blush Honey Myrtle, Rosy Paperbark, Pink Honey Myrtle	Flowers with nectar dipped in water to make a sweet drink	Harden (1991) and Steenbeeke (2001)
Melaleuca hypericifolia Sm	Hillock Bush, Red-Flowered Paperbark, Red Honey Myrtle	Flowers with nectar used to make a sweet, cool drink	Fairley and Moore (2000)
Melaleuca linariifolia Sm.	Flax-Leaved Paperbark, Snow in Summer Budjur (Gadigal)	Nectarous white blossoms can be used to make a sweet cool drink	Fairley and Moore (2000)
Melaleuca nodosa (Sol. ex Gaertn.) Sm.	Prickly Leaved Paperbark, Honey Ball Myrtle	Yellow, nectarous blossoms that can be used to Make a sweet cool drink.	Fairley and Moore (2000)
Melaleuca quinquenervia (Cav.) S.T. Blake	Paperbark Tea Tree, Broad-Leaved Paperbark, Melaleuca, Paperbark, Cajeput, Punk Tree	Blossoms steeped in water to prepare tangy brew and to make a sweet tea	Low (1989) and Deane (2007–2012q)
Melaleuca spp	Paperbarks, Tea Tree	Nectar of blossoms, Pollen from flowers can be eaten.	Cribb and Cribb (1987) and Schaeffer and Fletcher (2012)
Melaleuca styphelioides Sm.	Prickly Paperbark, Prickly Leaved Tea Tree	Nectarous white blossoms that can be used to make a sweet drink	Fairley and Moore (2000)

Melaleuca thymifolia Sm.	Thyme Honey Myrtle, Thyme-Leaved Bottlebrush	Flowers with nectar dipped in water to make a sweet drink	Steenbeeke (2001)
Melaleuca tortifolia Byrnes	Twist Leaf Paperbark	Flowers with nectar dipped in water to make a sweet drink	Steenbeeke (2001)
Myrtus communis L.	Myrtle, Common Myrtle, True Myrtle	In Italy the flower buds are eaten. The flowers have a sweet flavour and are used in salads	Tanaka (1976), Morton (1976), Facciola (1990), and Chevallier (1996)
Syzygium aromaticum (L.) Merr. & Perry	Clove, Cloves	Dried Flower buds used as spice to season ham, sausages, baked apples, mincemeat, pies, casserole, stews, preserves, pickles, etc.	Burkill (1966), Tanaka (1976), Morton (1976), Ochse and van den Brink (1980), Facciola (1990), Garland (1993), Verheij and Snijders (1999), and Hu (2005)
Syzygium formosum (Wall.) Masam	Bhukua Chepa, Labung Garai (Assamese)	Fleshy calyces are eaten cooked with fish or other vegetables	Patiri and Borah (2007)
Syzygium jambos (L.) Alston	Rose Apple, Malabar Plum, Pomarossa	Flowers candied	Uphof (1968), Hedrick (1972), Morton (1987), and Facciola (1990)
Syzygium malaccense (L.) Merr. & L.M. Perry	Malay Apple, Pomerac, Mountain Apple, Pink Satinash	Flowers eaten in Thailand; flowers preserved in syrup or eaten in salads	Hedrick (1972), Ochse and van den Brink (1980), Morton (1987), Facciola (1990), Wetwitayaklung et al. (2008), and Wongwattanasathien et al. (2010)
Nelumbonaceae			
Nelumbo nucifera Gaertn.	Sacred Lotus Sacred Water Lotus; Bua Luang (Thai); Thambul (Manipur)	Petals used in salad, soups frying, flower stalk. Stamen used for flavouring tea, petals floated in soups	Tanaka (1976), Facciola (1990), Woodward (2000), McCullough (2007), Wongwattanasathien et al. (2010), Kaisoon et al. (2011), and Yumnam and Tripathi (2012)
Nyctaginaceae			
Bougainvillea glabra Choisy	Bougainvillea, Paper Flower, Lesser Bougainvillea	Stewed bracts to colour drinks violet	Kaisoon et al. (2011, 2012)
		Floral bracts are edible, used in salad and drinks	
Bougainvillea hybrida (not an acceptable binomial name)	Bougainvillea, Paper Flower; Fuengfa (Thai)	Flowers used in salad and stir-fried	Kaisoon et al. (2011)
Bougainvillea sp.	Bougainvillea, Paper Flower	Stewed bracts to colour drinks violet	King (2007) and Kaisoon et al. (2011)
		Salad frying	
Bougainvillea spectabilis Willd.	Bougainvillea, Great Bougainvillea	Stewed bracts to colour drinks violet	Kaisoon et al. (2012)
		Salad frying	
Mirabilis jalapa L.	Marvel of Peru, Four o'clock Flower, Beauty of the Night, Jalap, Bonina, Bonita	Edible flower pigment used for colouring cakes and jellies	Uphof (1968), Usher (1974), Tanaka (1976), Kunkel (1984), and Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Nymphaeaceae			
Nuphar luteum Sibth. & Sm.	Yellow Water Lily, Yellow Pond Lily, Cow Lily, Spatterdock	Flowers make a refreshing drink	Macnicol (1967), Hedrick (1972), and Facciola (1990)
Nymphaea alba L.	White Lotus, Water Lily, European White Water Lily, Nenuphar	Edible flowers	Roberts (2000)
Nymphaea caerulea Savigny = *Nymphaea nouchali var. caerulea (Savigny)* Verdc.	Blue Water Lily, Blue Lotus of Egypt, Egyptian Blue Water Lily, Blue Lily of the Nile, Egyptian Louts	Flowers used as vegetables	Tanaka (1976), Fox et al. (1982), and Facciola (1990)
Nymphaea lotus L.	Water Lily Tiger Lotus, White Lotus, Egyptian White Water Lily; Nettai Suiren (Japanese); Bua Kin Saai (Thai)	The stalks of the flowers are edible. They are eaten raw with chilli sauce or added to *kaeng som* (sweet and sour curry) or cooked with mackerel in curry or fried with pork, prawns or shrimp	Hedrick (1972), Tanaka (1976), Pongpangan and Poobrasert (1985), Facciola (1990), and JIRCAS (2010)
Nymphaea nouchali Burm.f.	Indian Water Lily, Red and Blue Water Lily, Blue Water Lily, Blue Lotus of India; Bông Súng Lam (Vietnamese); Thariktha (Manipur)	Flower stalk and flowers are eaten	Van den Bergh (1994a, b), Tanaka and Nguyen (2007), and Yumnam and Tripathi (2012)
Nymphaea odorata Aiton	Fragrant Water Lily, Beaver Root	Flower buds cooked as a vegetable or pickled; young flowers eaten raw	Harris (1975), Tanaka (1976), Kunkel (1984), Facciola (1990), and Deane(2007–2012h)
Nymphaea pubescens Willd.	Hairy Water Lily, Pink Water Lily, Red Water Lily; Tharo (Manipur)	Flower stems and flowers edible	Tanaka and Nguyen (2007) and Yumnam and Tripathi (2012)
Nymphaea stellata Willd. = *Nymphaea nouchali* Burm.f.	Indian Water Lily, Red and Blue Water Lily, Blue Water Lily, Blue Lotus of India; Bông Súng Lam (Vietnamese)	Flowers are eaten	Uphof (1968), Hedrick (1972), Tanaka (1976), and Facciola (1990)
Olacaceae			
Ximenia americana L.	Wild Olive, Tallow Wood, Yellow Plum, Sea Lemon	Flower petals eaten in soup	Facciola (1990)
Oleaceae			
Forsythia sp.	Golden Bells	The blossoms are spicy, minty and slightly bitter. They add a cheery garnish to salads. These beautiful flowers can be steamed and dried, used in decoctions and infusions and made as a tea or forsythia syrup	Deane (2007–2012d) and Anonymous (2012b)
Forsythia x intermedia	Zabel Border Forsythia, Forsythia, Golden Bells, Showy Forsythia	As above	(Deane 2007–2012; Anonymous 2012a)

Jasminum multipartitum	Starry Wild Jasmine; Sterretjies-Jasmyn (Afrikaans)	Flowers used in herbal tea	Roberts (2000)
Jasminum odoratissimum L.	Madeira Jasmine, Yellow Jasmine	Flowers used for scenting tea	Tanaka (1976) and Facciola (1990)
Jasminum officinale L.	Jasmine, Poet's Jasmine, True Jasmine, White Jasmine	Flowers eaten or used to flavour or scent tea; dried flowers also used as tea substitute. Flowers added to dry ingredients (e.g. tea, rice) for fragrance. An essential oil from the flowers is used as a condiment in various foods, especially maraschino cherries but also baked goods, ice cream, sweets, chewing gum, etc. It imparts a bittersweet floral tone	Kunkel (1984), Facciola (1990), Bown (1995), Morton (1976), and Roberts (2000)
Jasminum paniculatum Roxb. = *Jasminum lanceolaria* subsp. *lanceolaria*	Jasmine; Sieu Hing Hwa (Chinese)	Flowers used for scenting tea in combination with *Jasminum sambac*	Grieve (1971), Hedrick (1972), and Facciola (1990)
Jasminum sambac (L.) Sol.	Jasmine, Arabian Jasmine, Tuscan Jasmine; Mo Li Hua (Chinese)	Jasmine flowers are edible, primarily used in teas and flavouring; the flowers are also source of an essential oil employed as flavouring. Flowers also added to dry food stuff (tea, rice) for fragrance	Grieve (1971), Morton (1976), Tanaka (1976), Facciola (1990), Barash (1997), Creasey (1999), Roberts (2000), Hu (2005), Wetwitayaklung et al. (2008), and Mittal et al. (2011)
Nyctanthes arbor-tristis L.	Night Flowering Jasmine, Night Jasmine, Coral Jasmine; Sewali, Sewali Phul (Assamese)	Flowers fresh and dried are eaten as vegetable. Flower is also a source of yellow dye food colorant. Flower is a popular cooking ingredient in Assamese homes. The flower is slightly bitter and can be used to make a dry *subji*	Uphof (1968), Facciola (1990), Patiri and Borah (2007), and Hauzel (2012)
Osmanthus americana (L.) Benth. ex Hook.f. =*Osmanthus americanus* (L.) A. Gray	Devilwood, American Olive, Wild Olive; Yen-Kuei (Chinese)	Flowers used to flavour tea, wine, liqueurs and confections. The blossoms can be preserved in a salty brine or made into a sugary paste	Tanaka (1976) and Deane (2007–2012m)
Osmanthus fragrans Lour.	Tea Olive, Fragrant Olive, Sweet Olive, Sweet Osmanthus; Gui-Hua, Kwei Hua (Chinese)	Flowers used for flavouring tea, mixed with honey or sugar, bottled and used for making pastries regarded as a delicacy. Flowers also added to rice gin for preparing *gui-hua* liquor. Fragrant flowers impart pleasant aroma to tea, wine sweets such as lotus seed soup, pastries and steamed pears. In the United States, flowers available in oriental food stores preserved in sweetened brine or as a sugary paste called cassia blossom jam	Hu (2005), Tanaka (1976), and Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Syringa microphylla Diels = *Syringa pubescens* subsp. *microphylla* (Diels) M.C. Chang & X.L. Chen	Little Leaf Lilac; Sung Lo Cha (Chinese)	Flowers used as substitute for tea in China	Altschul (1973) and Facciola (1990)
Syringa vulgaris L.	Lilac, Common Lilac, French Lilac	Flowers edible raw or folded into batter and fried to make fritters and used in yogurt	Macnicol (1967), Facciola (1990), Barash (1997), and Lauderdale and Evans (1999)
Onagraceae			
Epilobium angustifolium L.	Fireweed, Rosebay Willowherb, Great Willowherb, Spiked Willowherb	Flower bud stalks eaten raw or cooked, added to salads	Harrington (1974), Schofield (2003), and McCullough (2007)
Epilobium latifolium L.	River Beauty	As above	Harrington (1974), Schofield (2003), and Facciola (1990)
Fuchsia corymbiflora Ruiz & Pav.	Cluster-Flowered Fuchsia, Peruvian Berry Bush	Blossoms edible	Roberts (2000)
Fuchsia excorticata (G. Forst.) L.f.	Tree Fuchsia, Kotukutuku, New Zealand Fuchsia	Blossoms edible	Facciola (1990)
Fuchsia magellanica Lam.	Hardy Fuchsia, Fuchsia	Blossoms edible	Facciola (1990) and Roberts (2000)
Fuchsia spp.	Fuchsia	Blossoms edible	Roberts (2000) and Deane (2007–2012b)
Fuchsia × *hybrida* Voss	Fuchsia, Lady's Eardrops, Hardy Fuchsia, Hybrid Fuchsia	Flowers eaten in salad or crystallized	Deane (2007–2012e) and Rop et al. (2012)
Oenothera biennis L.	Evening Primrose, Evening Star	Flowers sweet eaten raw or cooked, in salads or as a garnish	Fernald et al. (1958), Facciola (1990), and King (2007)
Oenothera macrocarpa Nutt.	Missouri Evening Primrose, Pink Evening Primrose	The flowers have a similar taste to lettuce so will make a fine addition to any green salad while also adding some colour	Anonymous (2012a)
Oenothera missouriensis Sims = *Megapterium missouriensis* (Sims) Spach.	Sundrop Ozark	As above	Anonymous (2012a)
Oenothera odorata Jacq.	Fragrant Evening Primrose, Scented Evening Primrose	As above	Anonymous (2012a)
Oenothera speciosa Nutt.	Pink Ladies, Showy Evening Primrose, Pink Primrose	As above	Anonymous (2012a)
Oenothera versicolor Lehm.	Evening Primrose	As above	Anonymous (2012a)
Opiliaceae			
Melientha suavis Pierre	Phak Waan Paa, Pak Wan (Thai); Rau Sắng, Rau Ngót Núi, Ngót Rừng, Phắc Van (Vietnamese)	The young shoots, leaves and flowers highly esteemed as vegetables; used in soup or dried fish curry. People eat this plant as delicacy and it is one of the most expensive indigenous vegetable in Thailand and Vietnam	Pongpangan and Poobrasert (1985), Nguyen (1994), and JIRCAS (2010)

Urobotrya latisquama (Gagnep.) Hiepko	Mountain Mustard Blue; Shan-Jie-Lan (Chinese); Đuôi Vảy; Lân Vĩ Vảy Rộng (Vietnamese)	Young inflorescences and flowers eaten as delicacy	Hu (2005)
Orchidaceae			
Cymbidium elegans Lindl.	Elegant Cymbidium; Suo Cao Lan (Chinese)	Buds used by Bhutanese as ingredient in curries	Du Puy and Cribb (2007) and Sotirov (2012)
Cymbidium hookerianum Rchb.f.	Hooker's Cymbidium	As above	Rao (2004), Du Puy and Cribb (2007), Thapa (2009), and Sotirov (2012)
Dendrobium bigibbum Lindl.	Cooktown Orchid, Two-Humped Dendrobium	Flowers are sold in the United States as edible decorations for food	Sotirov (2012)
Dendrobium chrysotoxum Lindl.	Golden Bow Dendrobium	Flowers dried and consumed as tea for good health and pleasure in Tianzi, China	Pfingst and Hensel (2010) and Sotirov (2012)
Dendrobium longicornu Lindl.	Long-Horned Dendrobium; Bawar (Nepali)	Flowers used by Tamang communities in Nepal as pickles	Sotirov (2012)
Dendrobium nobile Lindl.	Noble Dendrobium	Blossoms and stems are edible	Wang et al. (2010) and Sotirov (2012)
Dendrobium phalaenopsis Fitzg. = *Dendrobium bigibbum* Lindl.	Dendrobium Orchid	Blossoms used in salads and as a garnish	Deane (2007–2012h)
Dendrobium spp.	Dendrobium Orchid	In Thailand, Dendrobium flowers are dipped in batter and deep-fried, while many European cooks garnish desserts and cakes with them. In Hawaii, locals use orchids to prepare salad dishes, sugar coated candies and main Orchid dishes cooked with scallops	Wetwitayaklung et al. (2008) and Sotirov (2012)
Orobanchaceae			
Castilleja linariifolia Benth.	Narrow-Leaved Indian Paintbrush, Desert Paintbrush, Wyoming Desert Paintbrush, Wyoming Indian Paintbrush, Linaria-Leaved Indian Paintbrush, Indian Paint Brush	Flowers eaten raw	Facciola (1990)
Pedicularis kanei Durand = *Pedicularis lanata* Willd. ex Steven	Wooly Lousewort	Sweet flowers made a delightful salad garnish. Young flowering tops fermented in water like sauerkraut. Sometimes they are eaten with oil and sugar.	Schofield (2003)
Oxalidaceae			
Averrhoa bilimbi L.	Bilimbi, Cucumber Tree, Tree Sorrel	Flowers made into conserve	Hedrick (1972), Popenoe (1974), Morton (1987), and Facciola (1990)
Averrhoa carambola L.	Star Fruit, Carambola, Five Corner	As above	Hedrick (1972), Popenoe (1974), Morton (1987), and Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Oxalis acetosella L.	Wood Sorrel, Common Wood Sorrel	Flowers edible raw, a decorative addition to salads	Fern (1992–2003)
Oxalis articulata Savigny	Pink Sorrel, Pink Wood Sorrel	Leaves and flowers edible raw or cooked, impart a pleasant lemony flavour to salads	Fern (1992–2003)
Oxalis corniculata L.	Yellow Sorrel, Creeping Wood Sorrel, Procumbent Yellow Sorrel, Sleeping Beauty	Flowers edible raw, impart nice acid flavour to the salad	Fern (1992–2003)
Oxalis corymbosa DC. = *Oxalis debilis* var. *corymbosa* (DC.) Lourteig	Pink Wood Sorrel, Pink Woodsorrel, Lilac Oxalis Pink Shamrock	As above	Fern (1992–2003)
Oxalis deppei Loddiges ex Sweet	Iron Cross Plant, Lucky Clover, Good Luck Plant, Good Luck Leaf	Flowers have a delicious lemony flavour; they make a delightful thirst-quenching munch and impart excellent flavouring to salads	Grieve (1971), Facciola (1990), and Fern (1992–2003)
Oxalis enneaphylla Cav.	Scurvy Grass, Scurvy Grass Sorrel	Flowers edible raw or cooked	Fern (1992–2003)
Oxalis exilis A. Cunn.	Least Yellow Sorrel, Shady Wood Sorrel	Flowers, raw. A nice acid flavour and a pleasant addition to the salad bowl[K]	Fern (1992–2003)
Oxalis magellanica G.Forst.	Snowdrop Wood Sorrel	Flowers edible raw, a pleasant and decorative addition to salad	Fern (1992–2003)
Oxalis oregana Nutt.	Redwood Sorrel, Oregon Wood Sorrel	As above	Fern (1992–2003)
Oxalis pes-caprae L.	Cape Sorrel, Bermuda Buttercup, Soursob, Sour Grass, Suring	Flowers edible raw with a pleasant acid flavour; they make an attractive addition to the salad bowl and pickled fish	Roberts (2000)
Oxalis spp.		Flowers edible	McCullough (2007)
Oxalis stricta L.	Yellow Wood Sorrel, Yellow Oxalis, Upright Yellow Sorrel, Lemon Clover, Pickle Plant	Flowers eaten in Nebraska	Yanovsky (1936) and Facciola (1990)
Oxalis tetraphylla Cav.	Four-Leaved Pink Sorrel, Goodluck Plant, Lucky Clover, Mexican Wood Sorrel	Flowers edible raw, a pleasant and decorative addition to salad	Fern (1992–2003)
Oxalis triangularis A. St. Hil	False Shamrock, Love Plant, Purple Shamrock, Lucky Shamrock	Flowers edible raw, a pleasant and decorative addition to salad	Fern (1992–2003)
Oxalis tuberosa Molina	Oca, Oka, New Zealand Yam	Edible young leaves and flowers eaten raw or cooked [34, 37, 103]	Masefield et al. (1969) and Heywood (1993)
Oxalis violacea L.	Violet Wood Sorrel, Shamrock	Flowers eaten by children in Nebraska; flowers make attractive garnish	Yanovsky (1936), Tanaka (1976), and Facciola (1990)

Paeoniaceae			
Paeonia delavayi Franch	Tree Peony, Victorian Tree Peony	Flowers eaten cooked	Uphof (1968), Kunkel (1984), and Facciola (1990)
Paeonia japonica (Makino) Miyabe & H.Takeda = *Paeonia obovata* Maxim.	Japanese Peony; Yama-Shakuyaku (Japanese)	Flowers edible	Kunkel (1984)
Paeonia lactiflora Pall.	Chinese Peony, Common Garden Peony	Petals are edible and used in salad or floated in punches and lemonade. Bottle of Steenbergs Dried Peony Flowers are a beautiful rose pink coloured, natural flower that look great in salads or used in home baking or added as a flourish over fruit salads	Deane (2007–2012e) and Steenbergs Organic (2012)
Paeonia lutea Delavay ex Franch = *Paeonia delavayi* Franch	Tree Peony	As for *Paeonia* × *suffruticosa*	Fern (1992–2003)
Paeonia officinalis L.	Common Peony, European Peony, Peony	Flowers cooked as a vegetable or to scent tea	Macnicol (1967), Kunkel (1984), and Facciola (1990)
Paeonia ostii T. Hong & J.X. Zhang	Tree Peony, Osti's Moutan Peony, Osti's Tree; Feng Dan Bai (Chinese)	Flowers eaten cooked	Uphof (1968), Usher (1974), and Kunkel (1984)
Paeonia potaninii Komar = *Paeonia delavayi* Franch.	Tree Peony	Flowers eaten cooked	Uphof (1968), Usher (1974), and Kunkel (1984)
Paeonia szechuanica W.P. Fang = *Paeonia decomposita* Hand.-Mazz.	Tree Peony	Flowers eaten cooked	Uphof (1968), Usher (1974), and Kunkel (1984)
Paeonia × *suffruticosa* Andrews	Moutan, Moutan Peony, Tree Peony	Since ancient times, the flowers of tree peony have been used to prepare traditional food such as casseroles, cakes, herbal tea and drinks. The petals are also reported to be parboiled and sweetened for tea-time delicacy or cooked in various dishes	Uphof (1968), Usher (1974), Kunkel (1984), Tanaka (1976), Facciola (1990), and Voon et al. (2013)
Pandanaceae			
Freycinetia marquisensis F.Br = *Freycinetia demissa* Benn.		Marquesas Islands: fleshy floral bracts eaten raw	Currey (1980)
Freycinetia monticola Rendle	'Le,'Le'ie (Hawaian)	Austral Islands: fleshy floral bracts eaten	Currey (1980)
Pandanus fascicularis Lam. = *Pandanus odorifer* (Forssk.) Kuntze	Pandan Laut (Indonesian, Malay); Keteki (Assamese); Ketaki, Keya (Bengali)	Tender floral leaves are eaten raw, or cooked with various condiments	Gammie (1902) and Facciola (1990)
Pandanus odoratus Salisb. = *Pandanus odorifer* (Forssk.) Kuntze	Frgrant Screwpine; Thalay (Tamil); Mogheli (Telugu)	Floral leaves eaten raw or cooked	Shortt (1887–1888)
Pandanus tectorius Parkinson ex Du Roi	Pandanus, Coastal Screwpine,Thatch Screwpine; Hala (Hawaiian)	Flowers and pollen edible. Infloresence bracts used for scenting coconut oil	Uphof (1968), Tanaka (1976), and Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Papaveraceae			
Eschscholzia californica Cham.	California Poppy, Golden Poppy, California Sunlight, Cup of Gold	Flowers used in teas, salads, aubergine stir-fried	Roberts (2000)
Papaver rhoeas L.	Corn Poppy, Corn Rose, Field Poppy, Flanders Poppy, Red Poppy, Red Weed	A syrup can be prepared from the scarlet flower petals; it is used in soups, gruels, etc. A red dye from the petals is used as a food flavouring, especially in wine; petals used as garnish	Grieve (1971) and Facciola (1990)
Passifloraceae			
Passiflora biflora Lam.	Twoflower Passionflower, Two-Lobed Passionflower, Boomerang Passionvine, Passion Vine	Flowers and flower buds are eaten	Van den Burgh (1994b)
Passiflora caerulea L.	Blue Crown Passionflower, Blue Passion Flower	Flowers can be made into a syrup	Crowhurst (1972), Kunkel (1984), and Facciola (1990)
Passiflora edulis Sims	Purple Granadilla, Purple Grenadilla, Purple Passionfruit, Passion Fruit, Common Passionfruit	Flowers edible	Roberts (2000)
Passiflora incarnata L.	Maypop, Purple Passionflower, Apricot Vine	Flowers cooked as a vegetable or made into syrup	Fernald et al. (1958) and Facciola (1990)
Passiflora lunata Willd. = *Passiflora biflora* Lam.	Twoflower Passionflower, Two-Lobed Passionflower, Boomerang Passionvine, Passion Vine	Flower buds and flowers much sought after for sambal goreng	Ochse and van den Brink (1980)
Passiflora spp.	Passion flower	Flowers edible	Lauderdale and Evans (1999)
Paulowniaceae			
Paulownia tomentosa Steud.	Empress Tree, Karri, Foxglove Tree, Princess Tree, Paulownia	Flowers eaten with miso	Tanaka (1976) and Kunkel (1984)
Phyllanthaceae			
Sauropus androgynus (L.) Merr.	Sweet Leaf Bush, Star Gooseberry, Chinese Malunggay	Leaves, immature fruits, flowers cooked and eaten as potherb	Ochse and van den Brink (1980) and Facciola (1990)
Pinaceae			
Picea abies (L.) H. Karst.	Norway Spruce, Common Spruce	Young male catkins eaten raw or cooked and used as flavouring. Immature female cones eaten cooked; the central portion, when roasted, is sweet and syrupy	Schofield (2003)
Picea asperata Mast.	Chinese Spruce, Dragon Spruce	As above	Schofield (2003)

Picea brachytyla (Franch.) E.Pritz	Sargent Spruce, Chinese Weeping Spruce	As above	Schofield (2003)
Picea breweriana S. Watson	Brewer's Spruce, Weeping Spruce	As above	Schofield (2003)
Picea engelmannii Parry ex Engelm.	Engelmann Spruce, Mountain Spruce	As above	Schofield (2003)
Picea glauca (Moench) Voss	White Spruce, Western White Spruce, Cat Spruce, Canadian Spruce, Black Hills Spruce	As above	Fernald et al. (1958), Kunkel (1984), Facciola (1990), Moerman (1998), and Schofield (2003)
Picea glehnii (F. Schmidt) Mast.	Sakhalin Spruce	As above	Schofield (2003)
Picea jezoensis (Siebold & Zucc.) Carrière	Yezo Spruce	As above	Schofield (2003)
Picea mariana (Mill.) Britton, Sterns & Poggenb.	Black Spruce, Bog Spruce, Swamp Spruce	As above	Schofield (2003)
Picea omorika (Pančić) Purk.	Dwarf Serbian Spruce,Serbian Spruce	As above	Schofield (2003)
Picea orientalis (L.) Peterm.	Caucasian Spruce, Oriental Spruce	As above	Schofield (2003)
Picea pungens Engelm.	Colorado Spruce, Colorado Blue Spruce, Blue Spruce	As above	Schofield (2003)
Picea purpurea Mast.	Purple-Coned Spruce	As above	Schofield (2003)
Picea rubens Sarg.	Red Spruce, Yellow Spruce, West Virginia Spruce	As above	Schofield (2003)
Picea sitchensis (Bong.) Carrière	Sitka Spruce	As above	Schofield (2003)
Picea smithiana (Wall.) Boiss	Morinda Spruce, Himalayan Spruce	As above	Schofield (2003)
Pinus banksiana Lamb.	Jack Pine, Eastern Jack Pine, Black Jack Pine, Black Pine, Jerry Pine, Prince's Pine	Young cones cooked	Kunkel (1984)
Pinus densiflora Siebold. & Zucc.	Japanese Red Pine, Dragon's-Eye Japanese Red Pine	The male catkins can be eaten	Tanaka (1976) and Facciola (1990)
Pinus edulis Engelm.	Colorado Pinon, Rocky Mountain Nut Pine	Soft centres of green immature cone when roasted afford a syrupy food	Harrington (1974) and Facciola (1990)
Pinus sabiniana Douglas	Digger Pine, Gray Pine	The green cones, roasted for about 20 min are soft and syrupy in their centre	Facciola (1990)
Pinus strobus L.	White Pine, Eastern White Pine	The firm unexpanded male cones can be boiled and used as a flavouring	Fernald et al. (1958), Kunkel (1984), and Facciola (1990)
Piperaceae			
Macropiper excelsum (G. Forst.) Miq. = *Piper excelsum* G. Forst.	New Zealand Pepper Tree, Kawakawa	In Polynesia, the flower clusters are eaten raw	Lovelock (1973) and Facciola (1990)
Piper cubeba L.f.	Cubeb, Tailed Pepper	Dried infructescense used as spice are used as a spice for curries, preserves and pickles	Uphof (1968), Morton (1976), Facciola (1990), and Lim (2012b)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Piper excelsum G. Forst.	New Zealand Pepper Tree, Kawakawa	In Polynesia, the flower clusters are eaten raw	Lovelock (1973) and Facciola (1990)
Piper guineense Schumach. & Thonn.	Ashanti Pepper, Benin Pepper, False Cubeb Pepper, Guinea Cubeb, West-African Black Pepper	Dried infructescense used as spice	Dalziel (1937), Kunkel (1984), and Facciola (1990)
Piper longum L.	Indian Long Pepper, Long Pepper, Pippali, Pipal	Dried infructescence used as spice	Hedrick (1972), Morton (1976), and Facciola (1990)
Piper retrofractum Vahl	Long Pepper, Balinese Long Pepper, Javanese Long Pepper, Javanese Pepper	Dried unripe and ripe infructescences are used as a spice for curries, preserves and pickles	Maisuthisakul et al. (2008), Maisuthisakul (2012), and Lim (2012b)
Piper sarmentosum Roxb.	Wild Betel; Kadok, Sirih Tanah, Chabei (Malay)	Dried infructescence used as spice	Jansen (1999)
Plantaginaceae			
Adenosma indianum (Lour.) Merr.	Qiu Hua Mao She Xiang (China); Prik Kra Taai (Thai)	Dried inflorescences used as spice; added to chilli paste. Dried inflorescences are found on sale in local markets in Thailand	JIRCAS (2010)
Antirrhinum majus L.	Snapdragon	Flowers have been reported to be used in a moderate way in salads or crystallized	Anonymous (2004), Lauderdale and Evans (1999), Roberts (2000), Stradley (2010), and Rop et al. (2012)
Plantago media L.	Hoary Plantain, Lanceleaf Plantain	Inflorescence is sweet and is sucked by children	Kunkel (1984) and Facciola (1990)
Veronica americana Schwein.ex Benth.	American Veronica, Speedwell, American Speedwell, American Brooklime	Flowers can be steeped for tea	Schofield (2003)
Poaceae			
Imperata cylindrica (L.) Raeusch.	Cogongrass, Blady Grass, Santintail, Alang-Alang, Lalang, Kunai, Paillotte	Young inflorescence and young shoots cooked	Read (1946) and Kunkel (1984)
Miscanthus floridulus (Labill.) Warb.ex K. Schum. & Lauterb.	Giant Chinese Silver Grass, Giant Miscanthus, Giant Eulalia Grass, Japanese Silver Grass, Amur Silver Grass, Pacific Island Silver Grass	Unopened flower spikes are edible	Tanaka (1976) and Kunkel (1984)

Saccharum edule Hassk.	Lowland Pitpit, Fiji Asparagus, Duruka, Pitpit, Coastal Pitpit, Vegetable Cane	Young contracted panicles enclosed within leaf sheaths are eaten raw, steamed, roasted, fried, added to soups or cut into pieces and added to meat and stuffed poultry and eaten cooked. In Malaysia, the young inflorescence is eaten in *ulam*, in creamy coconut dish or in mixed vegetable soup	Herklots (1972), Ochse and van den Brink (1980), Facciola (1990), and Saidin (2000)
Saccharum spontaneum L.	Wild Sugarcane, Egyptian Sugarcane	Young inflorescence enclosed in leaf sheaths eaten as lalab raw or cooked	Ochse and van den Brink (1980) and Facciola (1990)
Setaria palmifolia (J. Konig) Stapf	Highland Pitpit, Palm-Leaved Setaria, Palmgrass, Palm Grass, Broad-Leaved Bristlegrass, Hailans Pitpit, Short Pitpit	In the highlands of New Guinea, it is much cultivated in gardens where the malformed inflorescence consisting only of tender leaflets rolled in the upper part of the tillers is eaten as vegetable	French (1986), Shrivastava (1995), and King (2007)
Zea mays L.	Corn, Maize	Young tassels boiled and eaten; pollen used as ingredient in soups. Fresh succulent silks are chopped fine and mixed with massa in making tortillas	Uphof (1968), Tanaka (1976), Facciola (1990), and Duke (2012)
Zea mexicana (Schrad.) Kuntze	Mexican Teosinte, Teosinte, Annual Teosinte	Young flowering spikes are eaten before seeds have mature	Altschul (1973), Tanaka (1976), and Facciola (1990)
Zizania latifolia (Griseb.) Turcz. ex Stapf.	Water Bamboo, Manchurian Wild Rice, *Canada Rice, Indian Rice, Water Oats;* Coba, Kuw-Sun, Kwo-Bai, Jiao-Bai (China, Taiwan); Makomo Dake (Japan)	Young inflorescences cooked and used as a vegetable	Fernald et al. (1958), Herklots (1972), Tanaka (1976), and Facciola (1990)
Polemoniaceae			
Phlox paniculata L.	Garden Phlox, Summer Phlox, Fall Phlox, Perennial Phlox, Tall Phlox	Flowers added to fruit and floral salads and a colourful addition to any floral salad. Flowers are small and colourful; they are superb when crystallized and added as decoration to cakes or desserts	Anonymous (2012a) and Deane (2007–2012d)
Polygonaceae			
Antigonon leptopus Hook. & Arn.	Coral Vine, Chain of Love, Queen's Wreath; Puangchompoo (Thai)	In Thailand, the leaves and flowers are dipped in flour, fried and served with vermicelli. The flowers are also mixed into omelettes. Herbal teas are made from the leaves and blossoms	Uphof (1968), Facciola (1990), Pongpangan and Poobrasert (1985), Wessapan et al. (2007), Wetwitayaklung et al. (2008), Vanisree et al. (2008), and Wongwattanasathien et al. (2010)
Calligonum comosum L'Hér.	Abal	Flowers eaten in Spring	McCullough (2007)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Calligonum polygonoides L.	Phog (Hindi)	Western Rajastha: fruit usually eaten raw; buds and flowers eaten as vegetable; flowers made into bread or cooked with *ghee* (clarified butter) or coconut oil	Bhandari (1974), Saxena (1979), and Singhi and Joshi (2010)
Fagopyrum esculentum Moench	Buckwheat	Flowers make a pleasant tea	Roberts (2000)
Polygonum densiflorum Meisn. = *Persicaria glabra* (Willd.) M Gomez	Smartweed, Dense Knotweed	Hot spicy flavour seasoning, soups and perhaps salads	Deane (2007–2012v)
Polygonum hydropiperoides Michx. = *Persicaria hydropiperoides* (Michx.) Small	Waterpepper, Swamp Smartweed	Hot spicy flavour seasoning, soups and perhaps salads	Deane (2007–2012v)
Polygonum multiflorum Thunb. = *Fallopia multiflora* (Thunb.) Haraldson	Chinese Knotweed, Climbing Knotweed, Flowery Knotweed; He Shou Wu (Chinese)	Flowers eaten in China	Read (1946)
Polygonum persicaria L. = *Persicaria maculosa* A.Gray	Lady's Thumb, Red Leg	Leaves, flowers and shoots can be eaten raw or cooked and are mild tasting, similar to lettuce.	Brill (1994)
Polygonum punctatum Elliot = *Persicaria punctata* (Elliot) Small	Smartweed, Dotted Smartweed, Water Pepper	Flowers with hot spicy flavour used for seasoning, soups and perhaps salads	Deane (2007–2012r)
Rheum rhabarbarum L.	Rhubarb, Garden Rhubarb	Young inflorescence resembles cauliflower and may be deep-fried or boiled and served as '*au gratin*' with cream sauce	Grieve (1971) and Facciola (1990)
Rheum rhaponticum L.	Rhubarb, False Rhubarb, Rutabaga	The young flower pouch, harvested before the flowers open, is said to form a dish of great delicacy	Hedrick (1972)
Rheum tataricum L.f.	Tartarian Rhubarb	Unexpanded flower clusters are eaten cooked	Hedrick (1972), Tanaka (1976), Kunkel (1984), and Facciola (1990)
Rheum × *cultorum* Thorsrud. & Reis	Rhubarb	Immature flowers cooked and used like cauliflower	Facciola (1990)
Rumex acetosa L.	Common Sorrel, Spinach Dock, Narrow-Leaved Dock	Flowers cooked as a vegetable or used as a garnish	Grieve (1971) and Facciola (1990)
Pontederiaceae			
Eichornia crassipes (Mart.) Solms	Water Hyacinth, Floating Water Hyacinth; Luc Binh (Vietnamese)	Young leaves, petioles and inflorescence sometimes eaten after cooking in Java and Indo-China In the Mekong delta in Vietnam, the cores of young shoots and flowers are eaten as vegetable, fresh or boiled in steam-boat dishes. Javanese sometimes cook and eat the green parts and inflorescence	Ochse and van den Brink (1980) and Tanaka and Nguyen (2007)

Monochoria hastata (L.) Solms-Laub.	Arrowleaf Pondweed, Arrowleaf Monochoria, Hastate-Leaf Pondweed, Monochoria; Phak Top (Thai); Janki Phul (Assamese)	Flowers, leaves and petioles are cooked and consumed as vegetables in southeast Asia but the flowers can also be eaten raw. The leaves and inflorescences are eaten raw or cooked by steam or boiling and served cold in vinegar; for *lalab* the inflorescence is used to prepare *sayur*. Flowers and young inflorescences are eaten cooked as vegetable, or with fish by Bodos, Koch-Rajbongshis people in lower Assam, India	Burkill (1966), Ochse and van den Brink (1980), Pongpangan and Poobrasert (1985), and Patiri and Borah (2007)
Monochoria vaginalis (Burm.f.) C. Presl.	Monochoria, Oval-Leaf Monochoria, Pickerelweed; Bhat Meteka (Assamese)	As above	Burkill (1966), Ochse and van den Brink (1980), Pongpangan and Poobrasert (1985), and Patiri and Borah (2007)
Portulacaceae			
Portulaca oleracea L.	Common Purslane, Verdolaga, Pigweed, Little Hogweed, Pusley, Moss Rose; Leibak Kundo (Manipur)	Leafy vegetable eaten along with the stem and flowers in Manipur; used in *saag*, a dry-fry side dish	Hauzel (2012) and Deane (2007–2012f)
Primulaceae			
Ardisia boissieri A.DC. = *Ardisia purpurea* Reinw. ex Blume	Ardisia	Flowers used as flavouring for fish dishes	Brown (1954), Uphof (1968), and Facciola (1990)
Ardisia griffithii (C.B. Clarke) Kuntze	Dieng Pylieng	Flowers eaten in Meghalaya, India	Sawian et al. (2007)
Ardisia squamulosa C. Presl. = *Ardisia elliptica* Thunb.	Ardisia, Shoebutton Ardisia	Flower used as flavouring for fish dishes	Jansen (1999)
Lysimachia clethroides Duby	Gooseneck Loosestrife	Fruits and flowers are said to be edible	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Lysimachia nummularia L.	Moneywort, Creeping Jenny	Flowers used as tea	Uphof (1968) and Facciola (1990)
Primula denticulata Sm.	Drumstick Primula, Tooth-Leaved Primula, Purple Nepal Cowslip, Indian Primrose	Flowers edible raw, make a very attractive addition to salads	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Primula veris L.	Buckles, Cowslip, Cowslip Primrose, Crewel, Fairy Cups, Herb Peter, Herba Sancti Petri, Key Flower, Key of Heaven, Mayflower, Our Lady's Keys, Paigle, Palsywort, Password, Peggle, Petty Mulleins, Plumrocks, Primavera, Yellow Star of Bethlehem	Flowers eaten raw or cooked, used in salads, conserves, garnish, conserve. Flowers can be crystallized or use for cakes, pancakes, etc.	Grieve (1971), Hedrick (1972), Facciola (1990), Bown (1995), and Anonymous (2012a)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Primula vulgaris Huds.	English Primrose, Common Primrose	Flowers eaten raw or cooked. They make an attractive garnish to salads and can also be used as a cooked vegetable or in conserves, etc. The blossoms when fermented with water and sugar make a very pleasant and intoxicating wine. Both the flowers and the leaves can be made into a syrup or a tea. Flowers can be crystallized or use in pancakes or cakes	Grieve 1971, Facciola (1990), Bown (1995), Hedrick (1972), Deane (2007–2012a, b, c, d, e, f, g, h, i, j, k, l, m, n, o, p, q), and Anonymous (2012a)
Primula polyantha Mill.	Polyanthus Primrose	As above	Anonymous (2012a)
Proteaceae			
Banksia attenuata R. Br.	Candle Banksia, Candlestick Banksia, Slender Banksia, Biara	Flowers rich in nectar, soaked in water to produce a sweet, high energy rich drink	Cribb and Cribb (1987) and Zanthorrea Nursery (2012)
Banksia cunninghamii Sieber ex Rchb.	Shrubby Honeysuckle	As above	Cribb and Cribb (1987) and Harden (1991)
Banksia ericifolia L.f.	Heath Banksia, Heath-Leaved Banksia; Wadanggari (Australia—Cadigal)	As above	Cribb and Cribb (1987) and Harden (1991)
Banksia grandis Willd.	Bull Banksia, Giant Banksia, Mangite; Poolgarla (Australia—Aboriginal)	As above	Zanthorrea Nursery (2012) and SERCUL (2011)
Banksia intergrifolia L.f.	Coast Banksia, Coastal Banksia, Mountain Banksia	The flowers are rich in nectar and this is sometimes harvested as a food. The flowers can be sucked or soaked in water in order to obtain the nectar	Cribb and Cribb (1987), Low (1989), and Harden (1991)
Banksia marginata Cav.	Silver Banksia, Warrock	Nectar sucked from flowers or washed out with water to make a drink	Cribb and Cribb (1987), Facciola (1990), Harden (1991), and Schaeffer and Fletcher (2012)
Banksia serrata L.f.	Old Man Banksia, Saw Banksia, Sawtooth Banksia, Red Honeysuckle	Pour a cup of warm water over the flower spike to get the nectar	Cribb and Cribb (1987) and Schaeffer and Fletcher (2012)
Banksia spinulosa Sm.	Hairpin Banksia	Nectar sucked from flowers	Cribb and Cribb (1987) and Harden (1991)
Banksia spp.	Banksias	Nectar sucked	Cribb and Cribb (1987)
Grevillea australis R. Br.	Alpine Grevillea, Southern Grevillea	Nectar can be sucked, flowers used as a garnish on salads	Schaeffer and Fletcher (2012)
Grevillea eriostachya Lindl.	Honey Grevillea, Desert Grevillea, Yellow Flame Grevillea	Nectar sucked	Cribb and Cribb (1987)

Grevillea juncifolia Hook.	Honeysuckle Grevillea, Tarrakirra	Flowers and nectar eaten, flower nectar sipped directly or mixed with water to make a sweet drink	O'Connell et al. (1983), Cribb and Cribb (1987), and Facciola (1990)
Grevillea kennedyana F. Muell.	Flame Spider Flower	Nectar sucked	Cribb and Cribb (1987)
Grevillea pteridifolia Knight	Fernleaf Grevillea, Golden Tree, Ferny Leaved Silky Oak, Silky Grevillea, Fernleaf Woodland Oak, Kimberley Christmas Tree, Golden Grevillea	Nectar sucked	Cribb and Cribb (1987)
Grevillea robusta A. Cunn.ex R. Br.	Silky Oak, Australian Silver Oak, Southern Silky Oak	Nectar sucked and fermented to produce an intoxicating drink	Cribb and Cribb (1987), Facciola (1990), and Steenbeeke (2001)
Hakea eriantha R. Br.	Tree Hakea	Flowers useful source of nectar	Steenbeeke (2001)
Hakea fraseri R. Br.	Corkwood Oak, Fraser's Hakea	Flowers useful source of nectar	Steenbeeke (2001)
Hakea pulvinifera L.A.S. Johnson	Corkwood, Crokbark, Keepit Hakea	Flowers useful source of nectar	Steenbeeke (2001)
Hakea suberea S. Moore	Corkwood	Flowers rich in nectar crushed and soaked in water to make a sweet drink	Cribb and Cribb (1987) and Facciola (1990)
Hakea tephrosperma R. Br.	Hooked Needlewood	Flowers useful source of nectar	Steenbeeke (2001)
Lambertia formosa Sm. = *Lambertia proxima* Gand.	Mountain Devil, Red-Flowered Lambertia	The flowers are a useful source of nectar, the whole inflorescence is picked and the bottom is pinched off so the nectar can be sucked out of the tubular flowers	Low (1989), Facciola (1990), and Harden (1991)
Protea cynaroides (L.) L.	King Protea, Giant Protea	Flower nectar consumed directly	Schery (1972) and Facciola (1990)
Protea repens L.	Honey Flower, Common Sugarbush, Sugarbush	Flower nectar consumed directly or made into delicious syrup	Fox et al. (1982) and Facciola (1990)
Telopea aspera Crisp & P.H. Weston	Gibraltar Range Waratah	Flowers sucked for nectar	Steenbeeke (2001)
Telopea speciosissima R. Br.	Waratah, New South Wales Waratah	Flowers sucked for nectar or made into a sweet drink	Cribb and Cribb (1987), Low (1989), and Facciola (1990)
Telopea truncata (Labill.) R. Br.	Tasmanian Waratah	Flowers sucked for nectar	Schaeffer and Fletcher (2012)
Ranunculaceae			
Aquilegia brevistyla Hook.	Blue Columbine, Smallflower Columbine	Flowers eaten raw; sweet and delightful, they make a very attractive addition to mixed salads and can also be used as a thirst-quenching munch	Fern (1992–2003) and Schofield (2003)
Aquilegia buergeriana Siebold. & Zucc.	Columbine; Yama Odamaki (Japanese)	As above	Facciola (1990), Tanaka (1976), Fern (1992–2003), and Schofield (2003)
Aquilegia caerulea E. James	Rocky Mountain Columbine, Colorado Blue Columbine	The nectar-heavy flowers are eaten as a snack or tossed into salads. They also make a good jelly	Deane (2007–2012u)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Aquilegia caerulea var. flavescens (S. Watson) M.E. Jones = *Aquilegia flavescens* S. Watson	Rocky Mountain Columbine, Colorado Blue Columbine	Flowers eaten raw, sweet and delightful, added to salads	Schofield (2003)
Aquilegia canadensis L.	Wild Columbine, Canada Columbine	As above	Schofield (2003)
Aquilegia flabellata Sieb. & Zucc.	Fan Columbine	As above	Schofield (2003)
Aquilegia flavescens S. Watson	Yellow Columbine, Granny's Bonnet, Columbine	As above	Schofield (2003)
Aquilegia formosa Fisch. ex DC.	Crimson Columbine, Western Columbine	As above	Schofield (2003)
Aquilegia formosa var. *truncata* (Fisch. & C.A. Mey.) Payson = *Aquilegia formosa* Fisch. ex DC.	Western Columbine, Crimson Columbine, Columbine	As above	Schofield (2003)
Aquilegia jonesii Parry	Blue Limestone Columbine, Columbine	As above	Schofield (2003)
Aquilegia karelinii (Baker.) O. & B. Fedtsch.	Afghan Columbine	As above	Fern (1992–2003)
Aquilegia pubescens Coville.	Columbine, Sierra Columbine, Coville's Columbine, Yellow Columbine	As above	Fern (1992–2003) and Schofield (2003)
Aquilegia shockleyi Eastw.	Desert Columbine	As above	Fern (1992–2003) and Schofield (2003)
Aquilegia vulgaris L.	European Columbine, Common Columbine, Granny's Nightcap, Granny's Bonnet	As above	Kunkel (1984), Fern (1992–2003), and Schofield (2003)
Caltha biflora DC = *Caltha leptosepala* var. *howellii* Huth.	Alpine White Marsh Marigold, Two-Flowered Marsh Marigold	Buds eaten raw, cooked or pickled and used as a caper substitute and fermented for wine making	Schofield (2003)
Caltha leptosepala DC.	Western Marsh Marigold, White Marsh Marigold	As above	Harrington (1974), Tanaka (1976), Facciola (1990), and Schofield (2003)
Caltha leptosepala var. *howellii* Huth	Howell's Marsh Marigold	As above	Schofield (2003)
Caltha natans Palls	Floating Marsh Marigold	As above	Schofield (2003)
Caltha palustris L.	Yellow Marsh Marigold, Marsh Marigold, King Cup, Mayflower, May Blobs, Waster Bubbles, Gollins	As above	Fernald et al. (1958), Crowhurst (1972), Facciola (1990), and Schofield (2003)
Caltha palustris var. *barthei* Hance	Marsh Marigold, Ezo-Ryukin-Ka (Japanese)	Flowers eaten with miso in Japan	Tanaka (1976) and Facciola (1990)

Clematis maximowicziana Franch. & Sav. = *Clematis terniflora* DC.	Sweet Autumn Clematis	Young buds pickle, flowers edible	Tanaka (1976), Facciola (1990), and Deane (2007–2012p)
Clematis paniculata J.F.Gmel.	White Clematis, Puawananga, Sweet Autumn Clematis	China: leaves and flowers eaten	Read (1946)
Clematis terniflora DC.	Sweet Autumn Clematis, Autumn Clematis, Japanese Clematis, Sennin-So (Japanese)	Flowers eaten	Tanaka (1976) and Facciola (1990)
Ranunculus bulbosus L.	St. Anthony's Turnip, Bulbous Buttercup	Young flowers pickled	Fernald et al. (1958), Facciola (1990), and Deane (2007–2012p)
Ranunculus ficaria L. = *Ficaria verna* Huds.	Fig Buttercup, Lesser Celandine, Pilewort	Flower buds make good substitute for capers	Uphof (1968), Launert (1981), and Facciola (1990)
Ranunculus kochii Ledeb.	Crowfoot, Buttercup	Petals eaten	Kunkel (1984)
Resedaceae			
Reseda odorata L.	Mignonette, Common Mignonette, Garden Mignonette	Flowers occasionally floated into a bowl of wine	Burkill (1966), Macnicol (1967), and Facciola (1990)
Rhamnaceae			
Ceanothus cuneatus (Hook.) Nutt.	Buckbrush, Wedgeleaf Ceanothus, Buckbrush Ceanothus,	Flowers steeped in boiling water make an excellent tea	Facciola (1990)
Ceanothus ovatus Desf. = *Ceanothus herbaceus* Raf.	Smaller Red Root, Jersey Tea, New Jersey Tea	As above	Fernald et al. (1958), Harrington (1974), and Facciola (1990)
Ziziphus nummularia (Burm.f.) Wight & Arn.	Jujube; Bordi (Rajasthan)	The locals in Rajasthan used to distill liquor from fruit, flowers, bark and roots	Singhi and Joshi (2010)
Rosaceae			
Agrimonia eupatoria L.	Agrimony, Hurch Steeples, Churchsteeples, Cockleburr, Sticklewort, Stickwort	Harvested flowers make a refreshing tea	Macnicol (1967), Grieve (1971), and Facciola (1990)
Amygdalus persica L. = *Prunus persica* (L.) Batsch	Peach	Flowers eaten in salads, used as garnish or brewed into tea	Macnicol (1967), Grieve (1971), Tanaka (1976), and Facciola (1990)
Armeniaca mume Siebold	Mume, Ume, Mei Flower, Chinese Plum, Japanese Apricot	Flowers used for scenting tea in China	Hedrick (1972), Tanaka (1976), and Facciola (1990)
Armeniaca vulgaris Lam. = *Prunus armeniaca* L.	Apricot, Armenian Plum	Buds of cultivar 'Ansu' eaten	Tanaka (1976) and Facciola (1990)
Crataegus monogyna Jacq.	Hawthorn, May, Whitethorn, Red Haw; Mayflower Maythorn, Quickthorn, Bread & Butter Tree	The flowers are used in syrups and sweet puddings, tea and drinks. Country children love eating the flowers in their springtime abundance	Facciola (1990), Roberts (2000), and Deane (2007–2012f)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Crataegus oxyacantha L. = *Crataegus curvisepala* Lindm.	English Hawthorn, May Blossom, May Bush, May Tree, Quickset, Thornapple Tree, Weissdorn, Whitethorn, Bread & Butter Tree	As above	Roberts (2000)
Cydonia oblonga Mill.	Quince, Cydonian Apple, Elephant Apple, Pineapple Quince	Flowers eaten	Facciola (1990)
Filipendula ulmaria (L.) Maxim.	Meadowsweet, European Meadowsweet, Lady of the Meadow, Meadow Queen, Meadow Wort, Meadsweet, Queen of the Meadow, Pride of the Meadow, Bridewort	Young leaves, flowers and roots are brewed into a tea. The flowers are used as flavouring in various alcoholic beverages and in stewed fruits Flowers used to flavour liquor and wine tea, herbal tea, drinks or made into a syrup and used in cooling drinks and fruit salad or used as toppings for ice cream	Macnicol (1967), Morton (1976), Facciola (1990), and Garland (1993)
Fragaria × *ananassa* (Weston) Duchesne	Strawberry	The flowers retain their strawberry fragrance as well as a milder strawberry flavour. Petals floated in drinks, added to salads or candied and added to desserts for decoration	Anonymous (2012a, b, c) and Roberts (2000)
Fragaria vesca L.	Wild Strawberry, Alpine Strawberry, Woodland Strawberry	As above	Anonymous (2012a, b, c)
Fragaria virginiana Duchesne	Wild Strawberry, Virginia Strawberry	Flowers edible	Deane (2007–2012h)
Malus domestica Borkh.	Apple	Apple blossoms have a slightly floral taste and the petals are lovely in salads and fruit dishes. Infuse petals in whipped cream or ice cream to go over an apple tart. Blossoms look attractive when floated in a fruit punch	Barash (1997), Deane (2007–2012b), and Anonymous (2012a)
Malus floribunda Siebold ex Van Houtte	Japanese Crab Apple, Japanese Flowering Crab Apple, Purple Chokeberry, Showy Crab Apple	Flowers edible	Roberts (2000)
Malus pumila Mill.	Paradise Apple	Flowers dipped in batter, deep-fried and served sprinkled with sugar or added to batter. Also used in fruit dishes	Macnicol (1967), Uphof (1968), Tanaka (1976), Facciola (1990), Barash (1997), and Roberts (2000)
Malus × *robusta* (Carriere) Rehder	Crab Apple, Siberian Crab Apple	As for *Malus domestica*	Anonymous (2012a)
Malus spp.	Apple	Flowers use in fruit dishes, as garnish and candied	Barash (1997), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Deane (2007–2012b)

Malus zumi (Matsum.) Rehder	Zumi Crab Apple, Ō-Zumi (Japanese)	As for *Malus domestica*	Anonymous (2012a)
Poterium sanguisorba L. = *Sanguisorba minor* Scop.	Salad Burnet, Garden Burnet, Small Burnet, Burnet	Blossoms edible	Newman and O'Connor (2009) and Deane (2007–2012c)
Prunus angustifolia Marshall	Chickasaw Plum, Cherokee Plum, Florida Sand Plum, Sandhill Plum	Blossoms edible	Deane (2007–2012f)
Prunus domestica L.	European Plum, Plum, Damson	The flowers are eaten, used as a garnish for salads and ice cream or brewed into a tea	Facciola (1990), Macnicol (1967), Uphof (1968), and Roberts (2000)
Prunus grayana Maxim. = *Padus grayana* (Maxim.) C.K. Schneid.	Japanese Bird Cherry, Gray's Chokecherry	The salted flower buds and young fruits are eaten in Japan. They have a pungent taste	Uphof (1968), Tanaka (1976), and Facciola (1990)
Prunus hortulana L.H. Bailey	Hortulan Plum	Flower buds eaten	Uphof (1968)
Prunus jamasakura Siebold. ex Koidz. = *Cerasus jamasakura* (Siebold ex Koidz.) Ohba.	Japanese Mountain Cherry; Yamazakura (Japanese)	The flowers are pickled in salt and consumed in tea or with rice gruel	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Prunus lannesiana (Carrière) E.H. Wilson = *Cerasus serrulata* var. *lannesiana* (Carrière) T.T. Yu & C.L. Li	Oshima Cherry; Ukon-Zakura (Japanese)	Flowers preserved in salt and used in tea	Facciola (1990)
Prunus maximowiczii Rupr. = *Cerasus maximowiczii* (Rupr.) Kom.	Miyama Cherry, Korean Cherry	Flowers preserved in salt and used as a condiment	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Prunus mume (Siebold.) Siebold. ex Koidz. = *Armeniaca mume* var. *mume*	Mume, Ume, Mei Flower, Chinese Plum, Japanese Apricot	Flowers are used as a flavouring in tea	Hedrick (1972) and Facciola (1990)
Prunus padus L. = *Padus avium* var. *avium*	Bird Cherry, Hackberry	Flowers edible	Hedrick (1972), Tanaka (1976), Kunkel (1984), and Facciola (1990)
Prunus persica var. *nucipersica* (Suckow.) C.K. Schneid.	Nectarine	Flowers eaten raw or cooked, added to salads or used as a garnish	Facciola (1990)
Prunus persica (L.) Batsch	Peach	Flowers eaten raw or cooked, added to salads or used as a garnish. They can also be brewed into a tea. The distilled flowers yield a white liquid which can be used to impart a flavour resembling the seed	Facciola (1990) and Roberts (2000)
Prunus pseudocerasus Lindl. = *Cerasus pseudocerasus* (Lindl.) Loudon	Cambridge Cherry	Flowers salted and used as tea	Tanaka (1976) and Facciola (1990)
Prunus serrulata Lindl. = *Cerasus serrulata* var. *serrulata*	Japanese Cherry, Hill Cherry, Oriental Cherry, East Asian Cherry	The flowers are pickled in salt and consumed in tea or with rice gruel	Kunkel (1984) and Facciola (1990)
Prunus spinosa L.	Sloe, Blackthorn, Sloe Berry, Sloe Flower, Wild Plum Flower	The flowers are edible and can be crystallized or candied	Hedrick (1972), Tanaka (1976), Launert (1981), and Facciola (1990)
Prunus spp.	Plum	Flowers edible	Newman and O'Connor (2009)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Prunus subhirtella Miq. = *Cerasus subhirtella* var. *subhirtella*	Rosebud Cherry, Higan Cherry, Weeping Higan Cherry Spring Cherry, Winter Flowering Cherry	The flowers are preserved in salt and added to tea	Tanaka (1976), Kunkel (1984), and Facciola (1990)
Prunus tomentosa Thunb. = *Cerasus tomentosa* (Thunb.) Wall. ex T.T. Yu & C.L. Li.	Nanking Cherry, Korean Cherry, Manchu Cherry, Downy Cherry, Shanghai Cherry, Ando Cherry, Mountain Cherry, Chinese Bush Cherry, Chinese Dwarf Cherry, Hansen's Bush Cherry	Buds cooked and eaten	Uphof (1968), Hedrick (1972), Tanaka (1976), and Facciola (1990)
Pyrus betulifolia Bunge	Birch-Leaved Pear, Birch Leaf Pear	China: sun-dried flowers powdered and baked into 'cakes'	Read (1946), Hedrick (1972), and Facciola (1990)
Rosa arkansana Porter	Low Prairie Rose, Dwarf Prairie Rose, Prairie Rose, Prairie Wild Rose	Flower petals used for tea	Turner et al. (1980) and Facciola (1990)
Rosa blanda Aiton	Labrador Rose	Flowers eaten raw or cooked. They can be processed into rose water or used in cakes, sweets, desserts, etc.	Turner et al. (1980) and Facciola (1990)
Rosa canina L.	Dog Rose, Haggebutt, Wild Rose, Brier Rose, Brier Hip, Witches Brier, Hip Tree, Wild Brier	Petals used in salad, sandwiches, cooked in jams, jellies, used for flavouring butter, vinegar or desserts	Hedrick (1972), Launert (1981), Facciola (1990), and Garland (1993)
Rosa carolina L.	Prairie Rose, Carolina Rose, Pasture Rose	Flowers eaten raw in salads or cooked	Crowhurst (1972) and Facciola (1990)
Rosa chinensis Jacq.	China Rose, Chinese Tea Rose; Yue Ji Hua (Chinese)	Flower buds and flowers are parboiled and eaten as potherbs or added to soups or preserved	Read (1946), Kunkel (1984), and Facciola (1990)
Rosa gallica L.	Apothecary Rose; Xiao Jin Ying (Chinese)	Petals used to flavour vinegar or crystallized and eaten or preserved in syrup. Flowers also dried and used to impart flavour and fragrance to teas, beverages, cakes, honey and liqueurs	Morton (1976), Tanaka (1976), Facciola (1990), and Burnie and Fenton-Smith (1996)
Rosa gigantea Collett. ex Crép. = *Rosa* × *odorata* nothovar. *gigantea* (Collett ex Crep.) (Rehder & E. H. Wilson)	Manipur Wild, Tea Rose, Giant Tea Rose	Petals very fragrant, used as a flavouring in sorbets, confections, etc.	Facciola (1990)
Rosa gymnocarpa Nutt.	Wood Rose, Baldhip Rose, Dwarf Rose	Petals used in salads, sandwich spread and omelettes, steep in hot water for tea	Schofield (2003)

Rosa majalis Herrmann	Cinnamon Rose, Double Cinnamon Rose	Petals used in making jam	Komarov (2004)
Rosa moschata Mill.	Musk Rose	Flowers consumed fresh or cooked	Ochse and van den Brink (1980) and Facciola (1990)
Rosa nutkana C. Presl	Nootka Rose, Bristly Rose, Wild Rose	As for *Rosa gymnocarpa*	Schofield (2003)
Rosa odorata (Andrews) Sweet	Tea Rose	Flowers edible	Rop et al. (2012)
Rosa rubiginosa L.	Sweet Briar, Briar Rose, Wild Rose	Petals eaten raw or cooked. Mixture of flower petals and honey called *gulangabin* is used in confectionery	Uphof (1968), Kunkel (1984), Facciola (1990), and Schofield (2003)
Rosa spp.	Rose	Petals used in salads, sauces, sherbet, sandwich spread and omelettes, steep in hot water for tea and rose water. The 'Mon' rose petals are also used to decorate desserts, such as Woon Ga-thi (pandan jelly with coconut cream) and Ta-go (coconut pudding). Another dish that incorporates the Mon rose is Yam Kularb sai Goong (rose salad with shrimps). Rosehips and petals can both be used in jellies and jams. When crystallized, flowers make attractive cake decorations	Barash (1997), Schofield (2003), Newman and O'Connor (2009), Brown (2011), and Mlcek and Rop (2011)
Rosa virginiana Mill.	Prairie Rose, Virginia Rose, Common Wild Rose	Buds eaten by Chippewa Indians	Yanovsky (1936) and Facciola (1990)
Rosa woodsii Lindl.	Western Wild Rose, Woods Rose, Common Wild Rose, Mountain Rose	Petals eaten raw after removal of bitter white base	Schofield (2003)
Rosa × *centifolia* L.	Provence Rose, Burgundy Rose, Cabbage Rose, Holland Rose, Pale Rose, Rose De Mai	The blossoms are used for scenting tea. The petals are preserved in sugar and used as a delicacy. They can also be added to fruit pies as a flavouring	Uphof (1968), Hedrick (1972), Tanaka (1976), Morton (1976), Kunkel (1984), and Facciola (1990)
Rosa hybrida	Rose, Hybrid Rose	As for *Rosa* spp.	Barash (1997), Newman and O'Connor (2009), and Brown (2011)
Rosa × *damascena*	Damask Rose	Petals source of 'attar of rose', rose absolute and rose water and use as flavouring for beverages, candy, ice cream, bakery goods and also used to make jam	Uphof (1968), Morton (1976), Tanaka (1976), Ochse and van den Brink (1980), Facciola (1990), Komarov (2004), and Wetwitayaklung et al. (2008)
Rosa × *rugosa* Thunb.	Rugosa Rose, Japanese Rose, Ramanas Rose	Flowers edible raw nibbled or prepared as a salad, candied or used for jams, tea and syrups; an aromatic flavour, they are also used in jellies and preserves	Fernald et al. (1958), Harrington (1974), and Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Rubus arcticus L.	Arctic Bramble, Nagoon Berry	Flowers sweet and delicious eaten raw	Schofield (2003)
Rubus caesius L.	European Dewberry, Dewberry	As above	Schofield (2003)
Rubus chamaemorus L.	Cloudberry, Bakeapple	Flowers eaten raw, added to salads	Schofield (2003)
Rubus parviflorus Nutt.	Salmonberry, Thimbleberry, Flowering Raspberry, Western Thimbleberry	As above	Schofield (2003)
Rubus pedatus Sm.	Trailing Wild Raspberry, Five-Leaved Bramble, Strawberryleaf Raspberry, Creeping Raspberry	As above	Schofield (2003)
Rubus rosifolius Sm.	Australian Raspberry, West Indian Raspberry, Ola'a, Roseleaf Raspberry, Roseleaf Bramble, Thimbleberry	As above	stgmagazine
Rubus spectabilis Pursh	Salmonberry	As above	Schofield (2003)
Sanguisorba minor Scop.	Salad Burnet, Garden Burnet, Small Burnet, Burnet	Flowers used for tea	Schofield (2003)
Sanguisorba officinalis L.	Great Burnet, Garden Burnet, Common Burnet, Greater Burnet, Italian Burnet, Italian Pimperne	Flower buds eaten in salads or parboiled and eaten fried added to soups or preserved in salt	Macnicol (1967), Grieve (1971), Tanaka (1976), Morton (1976), and Facciola (1990)
Sorbus aucuparia L.	Rowan Tree, Rowan, Cardinal Royal, European Mountain Ash	Flowers used to adulterate tea	Grieve (1971), Launert (1981), and Facciola (1990)
Spiraea × *pyramidata* Greene = *Spiraea menziesii* var. *pyramidata* Piper	Pyramid Spirae	Flowers boiled to make beverage	Yanovsky (1936)
Rubiaceae			
Burchellia bubalina (L.f.) Sims	Wild Pomegranate	Flowers sucked for the rich nectar	Facciola (1990)
Galium aparine L.	Cleavers, Clivers, Goosegrass, Kisses, Stickyweed, Stickybud, Sticky Willy	Flowers edible	Deane (2007–2012g)
Galium odoratum (L.) Scop.	Sweet Woodruff, Sweet White Woodruff, Wild Baby's Breath	The sweet-scented flowers are eaten or used as a garnish, in wine, ice cream, yogurt, custard	Morton (1976), Facciola (1990), Barash (1997), Lauderdale and Evans (1999), and Newman and O'Connor (2009)
Galium verum L.	Curdwort, Yellow Bedstraw, Cheese Rennet, Lady's Bedstraw, Maid's Hair, Yellow Cleavers, Bedstraw	Flowering tops used in preparation of a refreshing acid drink	Fernald et al. (1958), Grieve (1971), Hedrick (1972), Morton (1976), and Facciola (1990)
Gardenia augusta Merr. = *Gardenia jasminoides* J. Ellis	Togor (Assamese)	Flower petals fried and eaten with rice or gram in Assam	Patiri and Borah (2007)

Gardenia coronaria Buch.-Ham.	Golden Gardenia, Malaysian Tree Gardenia; Hageir, Ring-Hkat-Ping, Hkhinkang, Mai-Yan-Kat, Thit-Gan, Yin-Gat-Gyi (Burmese)	Flowers edible, used for aroma (volatile oil)	Wetwitayaklung et al. (2008)
Gardenia jasminoides J. Ellis	Common Gardenia, Cape Jasmine Cape Jasmine; Phut Nam But (Thai)	The mild sweet gardenia blossoms are edible and used dried or fresh to impart fragrance to jasmine tea in the far east. Blossoms tucked into rice, oats and sago will impart the same mild sweet fragrance. Gardenia flowers can be added to sugar, drinks, fruit salads, cakes, desserts and syrups. Gardenia flowers are also eaten raw as delicacy, pickled or preserved in honey when they are called *mi-ts'ai*	Altschul (1973), Tanaka (1976), Facciola (1990), Sangat-Roemantyo and Wirdateti (1992), Roberts (2000), Anonymous (2012a), and Deane (2007–2012h)
Ixora chinensis Lam.	Chinese Ixora West Indian Jasmine, Jungle Flame, Needle Flower; Long Chuan Hua (Chinese)	Fresh flowers boiled with pork chops for soup in Guangdong. Flowers used in salad and fried dishes in Thailand	Hu (2005) and Kaisoon et al. (2011)
Ixora coccinea L.	Jungle Flame, Needle Flower, Flame of the Woods, Jungle Geranium	Flowers edible, used as condiment	Wongwattanasathien et al. (2010), Altss-chul (1973), Burkill (1966), and Facciola (1990)
Ixora congesta Roxb.	Malayan Ixora	Appetite stimulant, constipation, red-eye symptom, anthelmintic (leaf)	Wetwitayaklung et al. (2008)
Ixora javanica (Blume) DC.	Jungle Flame, Jungle Geranium, Javanese Ixora	Young flowers popularly used in Thai vegetable soup	King (2007)
Ixora subsessilis Wall. Ex G. Don	Dieng Jowat	Flowers, shoots, roots eaten in Meghalaya, India	Sawian et al. (2007)
Mussaenda frondosa L.	Flag Bush, Dhoby Bush, Dobi Tree, White Mussaenda; Balik Adap (Indonesia)	Young tops, flowers and flower buds eaten in Indonesia. In India (Deccan), flowers are also eaten	Watt (1908) and Ochse and van den Brink (1980)
Mussaenda roxburghii Hook.f.		Flowers eaten in Meghalaya, India	Wessapan et al. (2007)
Nauclea latifolia Sm. = *Sarcocephalus latifolius* (Sm.) E.A. Bruce	Negro Peach, African Peach, Bishop's Head, Pin-Cushion Fruit	Flower heads eaten as vegetable in tropical Africa	Uphof (1968), Hedrick (1972), and Facciola (1990)
Paederia foetida L.	Skunkvine, Stinkvine, Chinese Fever Vine; Ya Tod Ma (Thai)	Young leaves and flowers cooked as vegetables	Pongpangan and Poobrasert (1985)
Pavetta indica L.	Indian Pavetta, Indian Pellet Shrub; Kankara, Paapidi (India)	Flowers used in curries in Andhra Pradesh, India	Reddy et al. (2007)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Rutaceae			
Aegle marmelos (L.) Correa	Bengal Quince, Stone Apple, Bael, Bael Fruit Tree, Baeltree, Belfruit Tree, Bengal Quince, Elephant Apple, Golden Apple, Indian Bael Fruit, Indian Quince, Japanese Bitter Orange, Quince-Apple of India, Wood Apple; Matoom (Thai)	Young leaves and young inflorescences are sometimes eaten with chilli sauce by the locals in the north-east Thailand. Flower infusion afford a refreshing beverage	Morton (1987), Facciola (1990), and JIRCAS (2010)
Boronia megastigma Nees ex Bartlett	Brown Boronia	Fragrant flowers—as source of essential oil with an aroma of cinnamon and tobacco, sold as boronia absolute used in food manufacture to create black currant flavour and to enrich other fruit flavours in beverages, ice creams, candy and baked products	Morton (1976), Facciola (1990), and Plummer et al. (1996)
Citrus × *bergamia* Risso & Poit. = *Citrus* × *limon* (L.) Osbeck	Bergamot Orange	In Morocco, the flowers are preferred for making orange flower water	Uphof (1968), Morton (1976), Tanaka (1976), and Facciola (1990)
Citrus aurantiifolia (Christm.) Swingle	Key Lime, Mexican Lime, West Indian Lime, Acid Lime	Citrus flowers are overwhelming in scent and flavour and go really well with many different foods from stir-fries to puddings. They are also ideal for crystallizing and decorating cakes or desserts	Anonymous (2012a)
Citrus aurantium L.	Sour Orange, Bitter Orange, Seville Orange, Bigarade Orange, Marmalade Orange	Flowers used for scenting tea, citrus flowers are overwhelming in scent and flavour and go really well with many different foods from stir-fries to puddings. They are also ideal for crystallizing and decorating cakes or desserts	Tanaka (1976) and Facciola (1990)
Citrus aurantium var. amara L. = *Citrus aurantium* L.	Bitter Orange, Neroli; Dai Dai Hua (Chinese)	Fresh and dried flowers used for tea or flavouring in cooking	Hu (2005) and Deane (2007–2012b)
Citrus japonica Thunb.	Kumquats	Blossoms edible	Deane (2007–2012b)
(Tanaka ex Yu.) Tanaka	Tahitian Lime	As for *Citrus aurantium*	Deane (2007–2012b) and Anonymous (2012a)
Citrus × *limon* (L.) Burm.f.	Lemon	*As for Citrus aurantium*	Tanaka (1976), Uphof (1968), Morton (1987), Facciola (1990), Barash (1997), Newman and O'Connor (2009), Deane (2007–2012b), and Anonymous (2012a)

Citrus maxima (Burm.) Osbeck	Pummelo, Pomelo, Pommel, Shaddock	Petals edible	Deane (2007–2012b)
Citrus × *microcarpa* Bunge	Calamondin	Petals edible	Deane (2007–2012b)
Citrus reticulata Blanco	Mandarin, Satsuma, Tangerine	Petals edible	Deane (2007–2012b)
Citrus sinensis (L.) Osbeck	Sweet Orange, Navel Orange, Valencia Orange	Flowers cooked as a vegetable or made into a tea	Morton (1987), Facciola (1990), Newman and O'Connor (2009), and Deane (2007–2012b)
Clausena excavata Brum. f.	Pink Wampee; Samui, Mui (Thai)	Young leaves and flowers are aromatic and used to flavour curries and other food	Burkill (1966), Tanaka (1976), Pongpangan and Poobrasert (1985), and Facciola (1990)
Feroniella lucida (Scheff.) Swingle	Wood Apple, Java Feroniella; Ma Sung (Thai)	Flowers eaten	Tangkanakul et al. (2005)
Micromelum pubescens Blume	Thnk pui	Young shoots with inflorescence eaten as vegetables	Medhi and Borthakur (2012)
Murraya koenigii (L.) Sprengel = *Bergera koenigii* L.	Curry Tree, Curry Leaf	India (Madras Presidency): the deciduous, fleshy corolla is eaten raw or roasted.	Shortt (1887–1888)
Murraya paniculata (L.) Jack	Mock Orange, Jasmine Orange, Orange Jessamine	Fragrant flowers used for scenting tea	Hedrick (1972), Tanaka (1976), and Facciola (1990)
Zanthoxylum piperitum (L.) DC.	Japanese Pepper, Japanese Pepper Tree, Japanese Pricklyash; Sansho (Japanese)	Flowers pickled or preserved in soy sauce	Yashidora (1968), Morton (1976), and Facciola (1990)
Salicaceae			
Populus balsamifera L.	Balsam Poplar, East Asian Balsam Poplar, Korean Poplar, Canadian Poplar, Western Balsam, Black Cottonwood	Catkins have a bitter flavour, eaten raw or cooked, added to soups and stews	Schofield (2003)
Populus deltoides subsp. *wislizenii* (S. Watson) Eckenw. = *Populus deltoides* var. *wislizeni* (S. Watson) Dorn	Rio Grande Cottonwood	Catkins eaten raw. The cotton from the pistillate catkins has been used by children as a chewing gum	Uphof (1698), Usher (1974), Tanaka (1976), and Moerman (1998)
Populus fremontii S. Watson	Fremont Cottonwood, Alamo Cottonwood	Catkins eaten raw or cooked, eaten as a snack	Coon (1958), Moerman (1998), and Elias and Dykeman (2009)
Populus tremuloides Michx.	American Aspen, Quaking Aspen	Catkins have a bitter taste, eaten raw or cooked, added to soups and stews	Schofield (2003)
Populus trichocarpa Torr. & Gray	Black Cottonwood, Western Balsam Poplar, California Poplar	As above	Schofield (2003)
Salix aegyptiaca L.	Willow, Musk Willow	Male catkins candied. A perfumed drink is made from the catkins	Bean (1970), Kunkel (1984), and Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Salix babylonica L.	Babylon Willow, Weeping Willow	Flower buds parboiled and eaten	Tanaka (1976) and Facciola (1990)
Salix daphnoides Vill.	Violet Willow	Young catkin-bearing shoots eaten raw or cooked in seal oil by Eskimos of Alaska	Facciola (1990)
Salix gooddingii C.R. Ball	Goodding's Willow	The catkins can be eaten raw	Moerman (1998)
Salix gracilistyla Miq.	Rosegold Pussy Willow, Japanese Pussy Willow	Flowers parboiled and eaten as vegetables	Tanaka (1976)
Salix pulchra Cham. = *Salix planifolia* subsp. *pulchra* (Cham.) Argus	Diamondleaf Willow, Tealeaf Willow, Thin Red Willow	Catkins eaten	Kunkel (1984)
Sapindaceae			
Acer macrophyllum Pursh	Oregon Maple, Big Leaf Maple	Yellow flower clusters are sweet with nectar and are eaten raw	Facciola (1990)
Blighia sapida K.D. Koenig	Akee, Akee Apple	Flowers used in preparation of an aromatic water	Morton (1987) and Facciola (1990)
Paullinia pinnata L.	Barbasco, Timbo	Flowers edible	Facciola (1990)
Xanthoceras sorbifolium Bunge	Yellowhorn, Shiny Leaf Yellowhorn, Goldenhorn, Chinese Flowering Chestnut	Flowers cooked China: leaves and flowers boiled and eaten	Read (1946), Hedrick (1972), Tanaka (1976), and Facciola (1990)
Sapotaceae			
Bassia latifolia Roxb. = *Madhuca longifolia* var. *latifolia* (Roxb.) A. Chev.	Indian Butter Tree, Honey Tree; Mahwa, Mahua (Hindi)	India: sun-dried fruits and flowers eaten	Shortt (1887–1888), Gammie (1902), and Watt (1908)
Bassia longifolia J. Konig. ex L. = *Madhuca longifolia* (J. Konig ex L,) J.F. Macbr.	Indian Butter Tree, Honey Tree, Mahwa, Mahua (Hindi)	As above	Shortt (1887–1888), Gammie (1902), and Watt (1908)
Butyrospermum paradoxum ssp. *parkii* (G. Don) Hepper = *Vitellaria* subsp. *paradoxa*	Shea Butter Tree	Nigeria: flowers eaten	Mortimore (1989)
Madhuca indica J.F. Gmel. = *Madhuca longifolia* var. *latifolia* (Roxb.) A. Chev.	Indian Butter Tree, Honey Tree, Mahwa, Mahua (Hindi)	India (Rajasthan, western): ripe fruit eaten, also fleshy corolla of flower eaten raw or roasted; juice of the corolla used for making a beverage	Gupta and Kanodia (1968) and Patiri and Borah (2007)
Madhuca longifolia (J. König ex L.) J.F. Macbr.	Indian Butter Tree, Honey Tree, Mahwa, Mahua (Hindi)	Fleshy edible flowers are eaten dried, roasted or made into jelly, sugar or wine	Macmillan (1956), Hedrick (1972), Tanaka (1976), and Facciola (1990)
Saxifragaceae			
Saxifraga stolonifera Curtis	Creeping Saxifrage, Strawberry Saxifrage, Creeping Rockfoil, Strawberry Geranium; Yuki-No-Shita (Japanese)	Flower scapes said to be tasty when salted	Yashidora (1968) and Tanaka (1976)

Scrophulariaceae			
Buddleja asiatica Lour.	Dog Tail, Dog Tail, Asian Butterfly Bush; Agiachita, Posutia, Bonchini (Assamese)	Flowers eaten in Assam and Meghalaya, north-east India	Patiri and Borah (2007) and Sawian et al. (2007)
Capraria biflora L.	Goat Weed, Stow Weed, Hairy Capraria	Flowers edible	Hedrick (1972), Altschul (1973), and Tanaka (1976)
Eremophila latrobei F. Muell.	Crimson Turkey Bush, Emu Bush, Spotted Fuchsia	Flower nectar sucked	Cribb and Cribb (1987)
Eremophila oldfieldii F. Meull.	Pixie Bush, Silky Eremophila	As above	Cribb and Cribb (1987)
Mimulus guttatus Fisch.ex DC.	Yellow Monkey Flower, Seep Monkey Flower, Common Monkey Flower	Blossom added to gelatin moulds	Schofield (2003)
Mimulus lewisii Pursh	Great Purple Monkey Flower, Lewis' Monkey Flower	Blossom added to gelatin moulds	Schofield (2003)
Sutera atropurpurea Hiern	Cape Saffron	Flowers used as spice	Seidemann (2005)
Verbascum thapsus L.	Great Mullein, Common Mullein, Aaron's Rod, Blanket Weed	Flower infusion in water or milk drank for cold and cough. An aromatic tea can be brewed from fresh or dried flowers	Crowhurst (1972), Facciola (1990), and Garland (1993)
Solanaceae			
Capsicum annuum L.	Sweet Pepper, Bell Pepper	Flowers eaten raw or cooked	Allardice (1993)
Petunia grandiflora Juss.	Petunia	Flowers used in salad as garnish	Deane (2007–2012i)
Petunia × *hybrida* hort. ex Vilm.	Petunia	Flowers edible, used in salads or as garnish	Coyle (1999), Deane (2007–2012i), and Rogala and Pothour (2013)
Staphyleaceae			
Staphylea colchica Stev	Bladdernut, Colchis Bladdernut	Flower buds eaten	Komarov (2006)
Staphylea pinnata L.	Bladdernut, European Bladdernut	Flower bud used as condiment, used as substitute for capers	Seidemann (2005)
Theaceae			
Camellia japonica L.	Camellia, Japanese Camellia	Dried flowers cooked, used as a vegetable or mixed with gelatinous rice to make a Japanese food called '*mochi*'	Tanaka (1976) and Facciola (1990)
Camellia sinensis (L.) Kuntze	Tea	Flowers made into tempura	Tanaka (1976) and Facciola (1990)
Camellia thea Link = *Camellia sinensis* (L.) Kuntze	Tea	Flowers cooked	Deane (2007–2012k)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Tiliaceae			
Tilia americana L.	American Linden, American Basswood, Whitewood, Bee Tree Linden, White Basswood	Flowers, sweet and fragrant, can be added to salads or used as a tea substitute. A very good chocolate substitute is made from a paste of the ground fruits and flowers	Fernald et al. (1958), Tanaka (1976), Hedrick (1972), Kunkel (1984), Facciola (1990), and Barash (1997)
Tilia spp.	Linden	Flowers used as above	Lauderdale and Evans (1999)
Tropaeolaceae			
Tropaeolum majus L.	Nasturtium, Garden Nasturtium, Indian Cress	Nasturtium flower is one of the most popular and best-known edible flowers with attractive blossoms that have a sweet, peppery spicy flavour similar to watercress. Buds and flowers can be added to salads, sandwich spread, vegetable dishes, butter; to flavour vinegar, stuffed or crystallized. Flowers combine well with cream cheese or butter in canapés, or in a cheese and tomato sandwich. The buds can be used as caper substitute. The blossoms can make a nutritious addition to salads and an attractive, decorative garnish to steak and casseroles	Tanaka (1976), Larkcom (1980), Facciola (1990), Mackin (1993), Garland (1993), Burnie and Fenton-Smith (1996), Lauderdale and Evans (1999), Roberts (2000), Friedman et al. (2005), Anonymous (2012a), Rop et al. (2012), and Newman and O'Connor (2009)
Tropaeolum minus L.	Dwarf Nasturtium, Bush Nasturtium	As above	Hedrick (1972), Facciola (1990), and Anonymous (2012a)
Tropaeolum tuberosum Ruiz. & Pav.	Anu, Mashua	Flowers eaten raw in salads	Herklots (1972), Popenoe (1974), Facciola (1990), and Groen et al. (1996)
Typhaceae			
Typha angustata Bory & Chaub. = *Typha domingensis* Pers.	Bulrush, Southern Cattail, Long-Bracted Cattail, Narrow-Leaved Cumbungi	Inflorescences are eaten	Patiri and Borah (2007)
Typha angustifolia L.	Small Reedmace, Cattail, Lesser Bulrush, Lesser Reedmace, Narrow-Leaf Cattail, Narrow-Leaved Cattail, Reedmace, Small Bulrush, Cumbungi (Australia—Aboriginal)	As for *Typha orientalis*	Tanaka (1976), Morton (1977), Launert (1981), Facciola (1990), and Schofield (2003)
Typha australis K. Schum. & Thonn. = *Typha domingensis* Pers.	Southern Cattail, Bulrush, Narrow-Leaved Cumbungi, Cumbungi (Australia—Aboriginal)	Nigeria (Bornu): the immature spikes, called *Laka*, are eaten with a local variety of salt called *Manda*	Irvine (1957) and Uphof (1968)

Typha bungeana Presl	Cattail	As for *Typha orientalis*	Launert (1981) and Facciola (1990)
Typha capensis (Rohr.) N.E. Br.	Cape Bulrush, Common Bulrush, Cossack Asparagus	Male inflorescence used as food	Fox et al. (1982), Kunkel (1984), and Facciola (1990)
Typha davidiana (Kronf.) Hand.-Mazz		As for *Typha orientalis*	Launert (1981) and Facciola (1990)
Typha domingensis Pers.	Southern Cattail, Bulrush, Narrow-Leaved Cumbungi, Cumbungi (Australia—Aboriginal)	As for *Typha orientalis*	Launert. E. Edible and Medicinal Plants. Tanaka (1976), Facciola (1990), and Schofield (2003)
Typha elephantina Roxb.	Elephant Grass	In Sindh, India, a bread called *booree* or *booratoo* is made from the pollens	Uphof (1968), Hedrick (1972), and Facciola (1990)
Typha latifolia L.	Bulrush, Broadleaf Cattail, Broad-Leaved Cattail, Cattail, Cat's Tail, Common Cattail, Great Reedmace, Marsh Pestle	As for *Typha orientalis*	Yanovsky (1936), Facciola (1990), and Schofield (2003)
Typha laxmannii Lepech.	Graceful Cattail	As for *Typha orientalis*	Facciola (1990)
Typha orientalis C. Presl	Broad-Leaved Cumbungi, Cumbungi (Australia—Aboriginal); Dong Fang Xiang Pu (Chinese); Ko Gama (Japanese)	Young flowering spikes before the pollen is shed, can be eaten either raw or cooked; they are best served with butter like corn on the cob, the hard central core being discarded. The young flowering, green stalk is eaten raw or cooked. Pollens released from the stamens can be collected, eaten raw or cooked or baked into cakes; the protein-rich pollens can be mixed with milk or flour and fried into crumbly pancakes or made into bread and porridge	Launert (1981), Cribb and Cribb (1987), Brooker et al. (1989), Crowe (1990), Facciola (1990), and Low (1991)
Typha spp.	Bulrush, Cattails	As above	Cribb and Cribb (1987)
Typha × *glauca* Godr.	Hybrid Cattail, Glaucus Cattail, White Cattail	As above	Tanaka (1976), Launert (1981), Facciola (1990), and Schofield (2003)
Urticaceae			
Cecropia palmata Willd.	Trumpet Tree, Indian Snake Tree, Snakewood	Young buds eaten as potherb	Kunkel (1984) and Facciola (1990)
Cecropia peltata L.	Trumpet Tree, Pumpwood, Trumpet Tree, Snakewood, Congo Pump, Wild Pawpaw, Pop-a-Gun	Young buds eaten as potherb	Hedrick (1972) and Kunkel (1984)
Dendrocnide sinuata (Blume) Chew.	Fever Nettle, Elephant Nettle; Torash, Sorot Gosh (Assamese)	Flowers are picked and used as vegetable with fish, considered as medicinal by Bodo people in Assam, India	Patiri and Borah (2007)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Verbenaceae			
Aloysia triphylla (L'Her.) Britton	Lemon Verbena, Lemon Beebrush	Tiny cream-coloured citrus-scented blossoms and leaves can be steeped as an herbal tea and used to flavour custards and flans	McVicar (2003)
Lippia graveolens Kunth		Fresh or dried leaves as well as flower used for seasoning, suitable for fish, sausages, tomato sauce	Ong and Brink (1999)
Stachytarpheta jamaicensis (L.) Vahl	Blue Porterweed, Blue Snakeweed, Brazilian Tea, Jamaica Vervain, Bastard Vervain	Flowers used as flavouring, for tea, beer, etc.	Deane (2007–2012b)
Stachytarpheta urticifolia (Salisb.) Sims	Blue Porter Weed, Blue Rat's Tail, Nettleleaf Velvetberry	As above	Deane (2007–2012b)
Verbena officinalis L.	Vervain, Simpler's Joy, Holy Herb	The flowers used as a garnish or fermented into wine. In Turkey salt flavoured with vervain flowers is popular. Flowering top infuse in water is drank as herbal medicine	MacNicol (1967), Tanaka (1976), Kunkel (1984), Facciola (1990), and Garland (1993)
Violaceae			
Viola acuminata Ledeb.	Acuminate Violet; Ezo-No-Tachitsubo-Sumire (Japanese)	Young leaves and flower buds eaten raw or cooked	Tanaka (1976)
Viola adunca Sm.	Western Dog Violet, Hookedspur Violet, Sand Violet	As above	Kunkel (1984) and Facciola (1990)
Viola banksii K.R. Thiele & Prober	Native Violet, Wild Violet, Tasmanian Violet	Flowers used in salads, butter or crystallized	King (2007)
Viola biflora L.	Twoflower Violet	Flowers eaten raw added to salads	Schofield (2003)
Viola brevistipulata (Franch. & Sav.) W. Becker	Miyama-Ki-Sumire (Japanese)	Young leaves and flower buds eaten raw or cooked	Tanaka (1976) and Kunkel (1984)
Viola canadensis L.	Canada Violet	As above	Harrington (1974), Kunkel (1984), and Facciola (1990)
Viola canina L.	Dog Violet	As above	Tanaka (1976) and Kunkel (1984)
Viola collina Besser	Maruba-Ke-Sumire (Japanese)	As above	Tanaka (1976) and Kunkel (1984)
Viola cornuta L.	Horned Violet, Horned Pansy	Flowers have a lettuce-like flavour and make a decorative addition to a green salad or to garnish a pâté or dessert. They can be crystallized and used on cakes, cookies or creamy desserts or used in syrup, butter, vinegar	Tanaka (1976), Kunkel (1984), and Anonymous (2012a, b, c)

Viola cucullata Aiton	Hooded Violet, Marsh Blue Violet	Flower buds eaten raw or cooked	Usher (1974) and Tanaka (1976)
Viola diffusa Ging. = *Viola cerasifolia* Saint-Hilarie	Tsukushi Violet, Tsukushi-Sumire (Japanese)	As above	Tanaka (1976)
Viola epipsila Ledeb. = *Viola palustris* L.	Dwarf Marsh Violet, Northern Marsh Violet	Raw added to salads	Schofield (2003)
Viola glabella Nutt.	Stream Violet, Yellow Wood Violet, Pioneer Violet	Raw added to salads	Schofield (2003)
Viola grypoceras A. Gray	Ko-Tachi-Tsubo-Sumire (Japanese)	Flower buds eaten raw or cooked	Tanaka (1976) and Kunkel (1984)
Viola hederacea Labill.	Curtis' Violet, Ivy-Leaf Violet, Native Violet	Flowers can be used in a salad or as a garnish. Flowers coated with beaten egg white and dust with icing sugar. Great for cakes or ice cream or deserts	King (2007), Haslam (2011), and Schaeffer and Fletcher (2012)
Viola hybrida Schur	Viola	Flowers have a lettuce-like flavour and make a decorative addition to a green salad or to garnish a pâté or dessert. They can be crystallized and used on cakes, cookies or creamy desserts	Anonymous (2012a, b, c)
Viola japonica Langsd. ex DC.	Ko-Sumire (Japanese)	Flower buds eaten raw or cooked	Tanaka (1976)
Viola keiskei Miq.	Maruba Sumire (Japanese)	As above	Tanaka (1976) and Kunkel (1984)
Viola labradorica Shrank	Labrador Violet	As above	Tanaka (1976)
Viola langsdorffii Fisch. ex Ging.	Alaska Violet	Flowers edible raw added to salads	Schofield (2003)
Viola mandschurica W. Becker	Manchurian Violet; Jebikkot (Korean)	Jebikkot hwajeon cake	Anonymous (2012c)
Viola mirabilis L.	Wonder Violet	Flower buds eaten raw or cooked	Tanaka (1976)
Viola obtusa (Makino) Makino	Blunt Violet; Nioi-Tachi-Tsubo-Sumire (Japanese)	As above	Tanaka (1976) and Kunkel (1984)
Viola odorata L.	Sweet Violet, Ordinary Violet, Garden Violet	Young leaves, flower buds and flowers are edible raw or cooked. The flowers have a sweet mild, lettuce-like flavour with a delicate fragrance and can be used in salads, desserts, butter and vinegar; added to drinks or as a decorative addition to a green salad or to garnish a pâté or dessert. Flowers are also used fresh to flavour and colour confectionery. They can be crystallized and used on cakes, cookies or creamy desserts or eaten as sweet treats. Flower infusion or syrup with added sugar is used to flavour cream puddings, sorbets, syrup, cakes or ices	Macnicol (1967), Morton (1976), Facciola (1990), Garland (1993), Mackin (1993), Burnie and Fenton-Smith (1996), Barash (1997), Lauderdale and Evans (1999), Newman and O'Connor (2009), Mlcek and Rop (2011), and Anonymous (2012a, b, c)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Viola palmata L.	Palmate Violet	Flowers used as tea	Fern (1992–2003)
Viola papilionacea Pursh. = *Viola sororia* var. *sororia*	Blue Violet, Common Blue Violet, Common Meadow Violet	Flowers made into jams, jellies, sweetmeats, syrup and used in salads	Crowhurst (1972) and Facciola (1990)
Viola patrinii Ging.	China Violet	Flower buds eaten raw or cooked	Read (1946) and Tanaka (1976)
Viola pedata L.	Bird's Foot Violet, Crowfoot Violet, Pansy Violet	Flower buds eaten raw or cooked or candied	Tanaka (1976) and Facciola (1990)
Viola pedunculata Torr. & A. Gray	Grass Pansy, Yellow Pansy, Johnny-Jump-Up, California Golden Violet, Yellow Violet	Flower buds eaten raw or cooked	Tanaka (1976), Kunkel (1984), and Yanovsky (1936)
Viola pinnata L.	Finger Leaved Violet	As above	Tanaka (1976) and Stuart (1979)
Viola prionantha Bunge		As above	Tanaka (1976)
Viola renifolia A. Gray = *Viola blanda* var. *renifolia* (A.Gray) A. Gray	Hite Violet, Kidneyleaf Violet	Flower buds and flowers eaten raw or cooked, in salad and casserole and also for tea	Schofield (2003)
Viola riviniana Rchb.	Wood Violet	Flower buds eaten raw or cooked	Harrington (1974) and Tanaka (1976)
Viola selkirkii Pursh ex Goldie	Great-Spurred Violet, Northern Violet, Selkirk's Violet	Flower buds and flowers eaten raw or cooked, in salad and casserole and also for tea	Schofield (2003)
Viola sempervirens Greene	Redwood Violet	As above	Schofield (2003)
Viola sororia Willd.	Wooly Blue Violet, Marsh Blue Violet	Flower buds eaten raw or cooked	Fernand et al. (1958), Crowhurst (1972), and Facciola (1990)
Viola tokubuchiana Makino	Arage-Sumire (Japanese)	As above	Fernand et al. (1958), Crowhurst (1972), Tanaka (1976), Kunkel (1984), and Facciola (1990)
Viola tricolor L.	Johnny-Jump-Up, Heartsease, Heart's Ease, Heart's Delight, Tickle-My-Fancy, Jack-Jump-Up-and-Kiss-Me, Come-and-Cuddle-Me, Three Faces in a Hood, Love-in-Idleness	Young tender leaves; flower buds and flowers are eaten raw or cooked. The attractive small flowers are added to salads or used as a garnish and to embellish desserts—frosted cakes, sorbets, etc. and iced drinks. They also can be crystallized, eaten as a sweet treat and used on cakes, cookies or creamy desserts. Some common recipe names include crystallized violets, triple violet salads, violet–lavender sorbet, wild spring flower salad	Tanaka (1976), Launert (1981), Facciola (1990), Barash (1997), Mackin (1993), Lauderdale and Evans (1999), and Anonymous (2012a, b, c)
Viola vaginata Maxim.	Sheathed Violet; Sumire Saishin (Japanese)	Flower buds eaten raw or cooked	Tanaka (1976)
Viola variegata Fisch. ex Link	Genji-Sumire (Japanese)	As above	Tanaka (1976) and Kunkel (1984)

Viola verecunda A. Gray	Tsubo-Sumire (Japanese)	As above	Tanaka (1976) and Kunkel (1984)
Viola violacea Makino	Makino-Sumire, Shihai-Sumire (Japanese)	As above	Tanaka (1976) and Kunkel (1984)
Viola × *wittrockiana* Gams	Pansy, Ladies Delight	The attractive flowers are added to salads or used as a garnish and to embellish desserts—frosted cakes, sorbets, etc. and iced drinks. They also can be crystallized and eaten as a sweet treat	MacNicol (1967), Larkcom (1980), Facciola (1990), Mackin (1993), Lauderdale and Evans (1999), Newman and O'Connor (2009), and Rop et al. (2012)
Viola yezoensis Maxim.	Chinese Violet	Young leaves and flower buds eaten raw or cooked	Tanaka (1976)
Vitaceae			
Vitis vinifera L.	Grapes, Table Grapes, Wine Grapes	Flower clusters are used as a vegetable	Macnicol (1967), Bryan and Castle (1975), and Facciola (1990)
Xanthorrhoeaceae			
Asphodeline lutea (L.) Rchb.	Yellow Asphodel, King's Spear	Flowers eaten on its own or in salad or steamed with butter	Toensmeier (2007) and Deane (2007–2012o)
Hemerocallis altissima Stout = *Hemerocallis citrina* Baroni	Tall Daylily	Flower buds eaten	Erhardt (1992)
Hemerocallis aurantiaca Baker = *Hemerocallis fulva* var. *aurantiaca* (Baker) M. Hotta	Orange-Fulvous *Daylily;* Tou-Kanzo (Japanese)	Flowers and flower buds eaten raw or cooked	Erhardt (1992)
Hemerocallis bulbiferum L.	Daylily	Flowers and flower buds eaten raw or cooked	Erhardt (1992)
Hemerocallis citrina Baroni	Daylily; Jin-Zhen-Cai (Chinese)	Mature flower bud eaten, steamed sund-ried	Hu (2005)
Hemerocallis coreana Nakai = *Hemerocallis thunbergii* Baker	Long Yellow Daylily	Flowers and flower buds eaten raw or cooked	Kunkel (1984) and Erhardt (1992)
Hemerocallis darrowiana S.Y. Hu	Daylily	As above	Erhardt (1992)
Hemerocallis dumortieri C. Morren	Daylily	As above	Tanaka (1976), Kunkel (1984), and Erhardt (1992)
Hemerocallis exaltata Stout	Tobishima-Kanzō (Japanese)	As above	Kunkel (1984) and Erhardt (1992)
Hemerocallis forrestii Diels	Forrest's Daylily	Flowers and flower buds—raw or cooked	Fern (1992–2003)
Hemerocallis fulva (L.) L.	Orange Daylily, Tawny Daylily, Tiger Daylily, Ditch Lily	Young buds, fresh, dried flowers eaten raw or cooked. The petals are thick and crunchy, making very pleasant eating raw, with a nice sweetness at the base because of the nectar. The flowers can also be dried and used as a thickener in soups	Read (1946), Harrington (1974), Tanaka (1976), Facciola (1990), Erhardt (1992), Roberts (2000), Woodward (2000), Hu (2005), McCullough (2007), Tanaka and Nguyen (2007), and Newman and O'Connor (2009)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Hemerocallis fulva var. longituba (Miq.) Maxim. = *Hemerocallis fulva* var. *angustifolia* Baker	Yellow Daylily; Chang Guan Xuan Cao (Chinese)	As above	Kunkel (1984) and Erhardt (1992)
Hemerocallis graminea Andrews = *Hemerocallis minor* Mill.	Grassleaf Daylily	Flowers and flower buds eaten raw or cooked	Kunkel (1984) and Erhardt (1992)
Hemerocallis hakuunensis Nakai	Hakuun-Kisuge (Japanese)	As above	Erhardt (1992)
Hemerocallis lilioasphodelus L.	Yellow Daylily, Lemon Lily, Lemon Daylily	Flower buds and flowers are eaten raw or cooked. They are mildly sweet and are use for crowning a frosted cake or used as a dramatic garnish, or the succulent petals can be added to spring salads. Flowers and buds dipped in batter of milk, flour and eggs, seasoned and browned like fritter in oil or butter. In China and southeast Asia, the flowers are harvested just before they open and are boiled or steamed and then dried as a traditional food (spice or condiment) called *Kum Cham* in Cantonese or *Jīnzhēn*, in pinyin, meaning 'golden needles'. Dried flowers give flavour to soups, stir-fries and noodle dishes	Tanaka (1976), Gessert (1983), Facciola (1990), Erhardt (1992), Roberts (2000), Hu (2005), and Tanaka and Nguyen (2007)
Hemerocallis littorea Makino = *Hemerocallis fulva* var. *littorea* (Makino) M. Matsuoka & M. Hotta	Coastal Daylily	Flowers and flower buds eaten raw or cooked. They can be dried and used as a thickener in soups	Erhardt (1992) and Kunkel (1984)
Hemerocallis micrantha Nakai = *Hemerocallis hakuunensis* Nakai	Hakuun-Kisuge (Japanese)	As above	Erhardt (1992) and Kunkel (1984)
Hemerocallis middendorffii Trautv. & C.A. Mey.	Amur Daylily	As above	Tanaka (1976), Kunkel (1984), Erhardt (1992), and Facciola (1990)
Hemerocallis middendorffii var. *esculenta* (Koidz,) Ohwi = *Hemerocallis esculenta* Koidz.	Daylily	As above	Tanaka (1976), Kunkel (1984), Erhardt (1992), and Facciola (1990)
Hemerocallis minor Mill.	Grassleaf Daylily	Mature flower bud steamed and sun-dried. Flowers eaten as a relish with meat, or dried and used in soups and stir-fries	Hedrick (1972), Tanaka (1976), Gessert (1983), Facciola (1990), and Hu (2005)

Hemerocallis multiflora Stout	Daylily	Flowers and flower buds eaten raw or cooked. Flowers are crisp with a pleasant sweetness and no aftertaste; they make a delicious addition to salads. The flowers can also be dried and used as a thickener in soups	Erhardt (1992) and Fern (1992–2003)
Hemerocallis pedicellata Nakai = *Hemerocallis esculenta* Koidz.	Daylily	Flowers and flower buds eaten raw or cooked	Erhardt (1992)
Hemerocallis plicata Stapf.	Daylily	As above	Erhardt (1992)
Hemerocallis spp.	Daylily, Lily of a Day	Petals edible	Low (1989), Lauderdale and Evans (1999), and Mlcek and Rop (2011)
Hemerocallis thunbergii Baker	Late Yellow Daylily, Thunberg's Daylily; Asama-Kisuge, Yusuge (Japanese)	Mature flower buds steamed, sun-dried and used for cooking	Hu (2005)
Hemerocallis yezoensis H. Hara	Ezo-Kisuge (Japanese)	Flowers and flower buds eaten raw or cooked. They can be dried and used as a thickener in soups	Erhardt (1992)
Lomandra longifolia	Mat Rush, Long-Leaved Mat Rush	Flowers edible raw or cooked	Low (1989, 1991)
Phormium tenax J.R. Forst. & G. Forst.	New Zealand Flax, New Zealand Hemp	Nectar sucked from flowers makes wholesome eating	Natusch (1979) and Facciola (1990)
Xanthorrhoea acaulis (A.T. Lee) D.J. Bedford	Ground Blackboy, Tussock Grass Tree	The flowers produce nectar that may be licked from the opened flowers, or the spike may be soaked in water and then drunk fresh or after a short period of fermentation	Harden (1993) and Steenbeeke (2001)
Xanthorrhoea glauca subsp. *angustifolia* D.J. Bedford	Grass Tree, Blackboy	As above	Harden (1993) and Steenbeeke (2001)
Xanthorrhoea glauca subsp. *glauca* D.J. Bedford	Grass Tree, Blackboy	As above	Harden (1993) and Steenbeeke (2001)
Xanthorrhoea johnsonii A.T. Lee	Johnson's Grass Tree	As above	Harden (1993) and Steenbeeke (2001)
Xanthorrhoea spp.	Grass Tree, Blackboy	As above	Cribb and Cribb (1987) and Schaeffer and Fletcher (2012)
Zamiaceae			
Encephalartos caffer (Thumb.) Lehm.	Kaffir Bread	Female cone source of starch to make bread	Uphof (1968), Hedrick (1972), and Facciola (1990)

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Zingiberaceae			
Achasma sphaerocephalum (Baker) Holttum = *Etlingera metriocheilos* (Griff.) R.M. Sm	Kha-Daeng (Thai)	Flowers aromatic and sour, used to flavour food	Pongpangan and Poobrasert (1985)
Alpinia galanga (L.) Willd.	Galanga, Galanga Major, Galangal, Greater Galanga, Languas, Laos Root, Siamese Ginger, Spice Ginger; Khaa, Kha Taa Daeng (Thai); Lengkuas (Malay)	Young rhizomes, young shoots, flower buds, opened flowers and young inflorescences are eaten as vegetable either fresh or cook, steamed, pickled, added to soups or mixed with chilli paste	Morton (1976), Ochse and van den Brink (1980), Facciola (1990), and Scheffer and Jansen (1999)
Alpinia nigra (Gaertn.) Burtt	Derangong, Aihre don	Inflorescence eaten in Assam	Medhi and Borthakur (2012)
Alpinia regia K. Heyne ex R.M. Smith		Flowers edible	Van den Bergh (1994b)
Alpinia speciosa (Blume) D. Dietr = *Etlingera elatior* (Jack) R.M. Sm.	See *Etlingera elatior*	As for *Etlingera elatior*	Burkill (1966), Tanaka (1976), and Facciola (1990)
Amomum maximum Roxb.	Java Cardamom, Winged Java Cardamom; Resak (Indonesia)	Young inflorescences eaten cooked with rice	Ochse and van den Brink (1980) and Woodward (2000)
Amomum xanthophlebium Baker	Luchol, Halia Jacus, Halia Landak (Malaysia)	Flower used for flavouring curries	Jansen (1999)
Achasma megalocheilos Griff. = *Etlingera megalocheilos* (Griff.) A.D. Poulsen	Tepu	Heart of young shoots, flower buds and fruits eaten	Noweg et al. (2003)
Curcuma aurantiaca Zijp	Temu blobo, Temu Purut (Javanese)	Young inflorescences are eaten in Java	Burkill (1966)
Curcuma alismatifolia Gagnep.	Thai Tulip	Flower bracts are widely eaten as vegetable	King (2007)
Curcuma longa L.	Turmeric, Turmeric Root, Indian Saffron, Kunyit	Flowers eaten as vegetable	Woodward (2000)
Curcuma mangga Valeton & Zijp	Mango Ginger; Temu Mangga, Kunyit Putih (Malay); Khamin-Khao (Thai)	Young inflorescences are eaten raw with many kinds of hot and spicy	Morton (1976), Ochse and van den Brink (1980), Facciola (1990), Van den Bergh (1994a, b), and JIRCAS (2010)
Cucurma parvifolia Wall.		Inflorescence is eaten as vegetable	Sirirugsa (1997)
Curcuma spp.	Hidden Ginger Lilies	Flower bracts are widely eaten as a vegetables	King (2007)
Curcuma zanthorrhiza Roxb.	False Turmeric, Giant Curcuma, Javanese Turmeric; Temu Lawak, Temu Putih (Malay, Javanese); Koneng Gede (Sundanese); Temu Labak (Madurese)	Inflorescences eaten cooked with rice	Ochse and van den Brink (1980)

Etlingera elatior (Jack) R.M. Sm.	Torch Ginger, Ginger Flower, Red Ginger Lily, Torch Lily, Philippine Wax Flower, Indonesian Tall Ginger, Boca De Dragón, Rose De Porcelaine, Porcelain Rose; Xiang Bao Jiaing (Chinese); Bunga Combrang, Honje (Indonesia); Bunga Kantan (Malay); Daalaa (Thai)	Flower petal, and receptacle, hearts of young leafy shoots, flower buds, fruit seed and rhizome are used as condiments eaten raw as salad, or cooked in various ways, or pickled. Flower petals and half-ripe fruiting shoots are widely used in curries, particularly in penang laksa, nasi ulam, nasi kerabu, rojak or cooked in mixed vegetables. They are also eaten fresh as ulam. In North Sumatra, the flower buds are used for a dish called *arsik ikan mas* (Andaliman/Szechuan pepper Spiced Carp). In North Sumatra, another common Karo dish with the flower bud is *asam cekala*	Burkill (1966), Tanaka (1976), Facciola (1990), Ochse and van den Brink (1980), Noweg et al. (2003), Wetwitayaklung et al. (2008), and Chan et al. (2011)
Etlingera hemisphaerica (Blume) R.M. Sm.	Kantan Liar (Malay); Honje Hutan, Honje, Ondje (Indonesia)	Inflorescences used for sayur lodeh	Ochse and van den Brink (1980)
Etlingera littoralis (J. König) Giseke	Earth Ginger	In Sabah, Malaysia, the hearts of young shoots, flower buds and fruits are eaten	Noweg et al. (2003)
Etlingera maingayi (Baker) R.M. Smith	Malay Rose	Flowers are eaten as vegetables	Sirirugsa (1999)
Etlingera punicea (Roxb.) R.M. Sm.	Tuhau, Tepu, Tutubuh	Heart of young shoots, flower buds and fruits eaten	Noweg et al. (2003)
Etlingera rubrolutea (Baker) C.K. Lim = *Etlingera megalocheilos* (Griff.) A.D. Poulsen	Wild Ginger	In Sabah, Malaysia, the hearts of young shoots, flower buds and fruits are eaten	Noweg et al. (2003)
Hedychium coronarium J. König	Butterfly Ginger, Butterfly Ginger Lily, White Garland Lily, Garland Flower, White Ginger; Li-Ji (Chinese)	Young flowers and buds steamed Used as vegetable and flavouring	Tanaka (1976), Kunkel (1984), Facciola (1990), Sirirugsa (1997), and Hu (2005)
Hornstedtia sp.	Talirusan	Heart of young shoots, flower buds and fruit seeds are eaten	Noweg et al. (2003)
Kaempferia galanga L.	Cekur (Malay)	Inflorescence bracts used in ulam or as flavouring in mixed vegetables	Saidin (2000)
Nicolaia elatior (Jack) Horan = *Etlingera elatior* (Jack) R.M. Sm.	See *Etlingera elatior*	As for *Etlingera elatior*	See *Etlingera elatior*

(continued)

Table 1 (continued)

Scientific name	English/Common vernacular name	Flower edible uses	Reference
Phaeomeria atropurpurea (Teijsm. & Binn.) K. Schum = *Etlingera hemisphaerica* (Blume) R.M. Sm.	See *Etlingera hemisphaerica*	Inflorescence used for sayur lodeh	See *Etlingera hemisphaerica*
Phaeomeria speciosa (Blume) Koord. = *Etlingera elatior* (Jack) R.M. Sm.	See *Etlingera elatior*	See *Etlingera elatior*	See *Etlingera elatior*
Scaphochlamys sp.	Kua-Kabig (Thai)	Young shoots and flowers cooked as vegetables	Pongpangan and Poobrasert (1985)
Zingiber amaricans Blume = *Zingiber zerumbet* subsp. *zerumbet*	Shampoo Ginger, Bitter Ginger, Pinecone Ginger	Young flower spikes eaten raw or cooked as lalab. Young flowers used as spice, eaten raw or cooked	Ochse and van den Brink (1980), Facciola (1990), and Wolff et al. (1999)
Zingiber cassumunar Roxb. = *Zingiber montanum* (J. Konig) Link exA. Dietr.	Cassumunar Ginger, Phlai, Bpulai, Wan-Fai (Thai)	Flowers eaten	Wetwitayaklung et al. (2008)
Zingiber mioga (Thunb.) Roscoe	Japanese Ginger, Mioga Ginger; Myoga (Japanese)	Flowers and buds used for flavouring	Wolff et al. (1999) and Hu (2005)
Zingiber odoriferum Blume	Balakatoa, Tolol, Tongkak (Indonesia)	Flower buds eaten raw or cooked	Ochse and van den Brink (1980)
Zingiber officinale Roscoe	Ginger, Common Ginger, Cooking Ginger, Canton Ginger; Hajing, Aithing, Theing, Kaphul Kebeb (Assam)	Ginger blossoms are gingery and fragrant. They can be eaten raw	Deane (2007–2012m) and Medhi and Borthakur (2012)
Zingiber sp.	Kham Noi (Thai)	Young inflorescence and shoot eaten cooked	Pongpangan and Poobrasert (1985)
Zingiber zerumbet (L.) Smith	Pinecone Ginger, Shampoo Ginger	The flower buds are eaten boiled as vegetable	Sirirugsa (1997)
Zygophyllaceae			
Larrea tridentata (Sessé & Moc. ex DC.) Coville	Creosote Bush, Chaparral	Flower buds pickled in vinegar and used like capers	Uphof (1968), Clarke (1977), Kunkel (1984), and Facciola (1990)
Zygophyllum fabago L.	Syrian Bean Caper	Flower buds pickled and used as caper substitute	Hedrick (1972), Tanaka (1976), and Facciola (1990)

earlier volumes and plants better known for other non-floral parts will be covered in subsequent volumes. The edible flower species dealt with in this volume include both lesser-known, wild and underutilized plants and also common and widely grown ornamentals.

As in the preceding seven 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.

Use of Edible Flowers

Since antiquity right through the Middle Ages and the seventeenth century, flowers have been featured as an integral part of human nutrition in Europe—ancient Rome, medieval France, Victorian England, Middle East and in Asia particularly in China, India, Thailand and Japan. Flowers have long been used as decorations in food prepared for the nobility. Today, consumption of edible flowers is increasing worldwide (Mlcek and Rop 2011; Rop et al. 2012). Edible flowers are becoming more popular as evidenced by the profusion of cookbooks and scientific papers on edible flowers and plenitude of edible flower recipes presented in culinary magazines, newspaper and on-line articles, radio and television shows. Flowers are consumed in various forms, colours and flavours to enhance the nutritional and sensory qualities of foods. Its qualities, freshness and safety depend on the care taken in its harvesting and storage. Many of the lesser-known edible flowers are harvested in the wild from plants in the forests, wastelands, disturbed sites, near waterways and roadsides often occurring as weeds (e.g. *Limnocharis*, milkweeds, beggarticks, dandelion, *Acacia* spp). In contrast, many of the commonly known edible flowers (e.g. roses, chrysanthemums, carnations, marigolds, daylilies, cornflower) are harvested from cultivated garden ornamentals or culinary herb garden (e.g. chives, *Mentha* spp. borage, rosemary, chamomile).

Edible flowers can be used raw or fresh as a garnish or as an integral part of a dish, such as a vegetable or fruit salad. Today, many restaurant chefs and innovative home cooks garnish their entrees with flower blossoms for a touch of elegance. Many flowers can be fried in light batter or cornmeal, e.g. squash, zucchini flowers or in fritters (e.g. Acacia blossoms). Some flowers can be steamed, boiled, grilled or used in soups and curries. Some flowers can be stuffed or used in stir-fry dishes. Edible flowers can be crystallized, candied; frozen in ice cubes and added to beverages; made into jellies and jams; used to make teas or wines; to flavour liquors, vinegar, oil, honey, scented sugars; added to punch, cocktail, ice cream, sorbet and other beverages; and minced and added to cheese spreads, herbal butters, pancakes, crepes and waffles. Many flowers can be used to make vinegars for cooking, marinades or dressings for salads.

Some important rules on the use of edible flowers are:

- Flowers have to be accurately identified before eating.
- Do not eat flowers from florists, nurseries, garden centres, fruit orchards or flowers from plants found on the side of the road and in murky waterways because of possible contamination from pesticide sprays, vehicle carbon emissions and industrial and effluent runoff.
- Harvest/pick flowers that are free from diseases, insects, insect damage and soil particles.
- Pick young fresh flowers and buds on dry mornings, before the sun becomes too strong, to retain the bright colours and intense flavours.
- Use flowers immediately for best results or refrigerate in a plastic bag for a few days. Dried, frozen or freeze-dried flowers are best used in infusions or cooked.
- For medium and large flowers like hollyhocks, roses, lilies, calendula, chrysanthemum, lavender, rose, tulip, yucca, hibiscus, lavender, tulip and marigolds, use only the petals and discard stamens, pistil and calyx. The bitter 'heel' at the base of the petal should be removed.

– Eat edible flowers in moderation.
– People with hay fever, asthma or allergies should best avoid eating flowers since many allergies are due to sensitivity to pollen of specific plants.

Selected References

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Pelargonium crispum

Scientific Name

***Pelargonium crispum* (L.) L'Hér.**

Synonyms

Anisopetala crispa (P.J. Bergius) Walp., *Geraniospermum crispum* (P.J. Bergius), *Geranium crispum* P.J. Bergius

Family

Geraniaceae

Common/English Names

Crisped Leaf Pelargonium, Curled Leaved Cranesbill, Finger Bowl Geranium, Lemon Geranium, Lemon-Scented Geranium, Lemon-Scented Leaved Geranium, Variegated Lemon-Scented Pelargonium

Vernacular Names

Afrikaans: Dassiepoeier
Czech: *Muskát Stojaty*
Danish: Citrongeranie, Geranie
Estonian: Kähar Pelargoon
German: Orangenpelargonie, Zitronengeranie, Zitronenpelargonie
Italian: Geranio Crispum

Origin/Distribution

Lemon Geranium is a native of South Africa. It occurs from Worcester to Bredasdorp in south Western Cape.

Agroecology

In its native habitat, it occurs on rocky lower mountain or hill slopes, growing in the shelter of boulders in fairly dry sandy soils. Lemon Geranium prefers well-drained, light-textured neutral to alkaline soil in a sunny position, although it is tolerant of partial shade. It tolerates low temperatures down to about −3 °C.

Edible Plant Parts and Uses

The leaves have a pleasant lemon aroma and are used to flavour soups, fruit dishes, jellies, sorbets, ice cream, cakes, etc. (Facciola 1990; Bown 1995). Cake pans can be lined with the leaves and the pastry will be infused with their essence. An infusion of the leaves is used as a tea (Bown 1995). The scented geranium flowers

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are also edible. They are used in salads, desserts, drinks and jellies (Barash 1997; Roberts 2000; Deane 2007–2012).

Botany

An erect, small, much-branched shrub growing 100 cm high with an extensive spreading superficial root system. Stems soft, green, pubescent becoming darker and woody with age. Leaves opposite, lemon scented, fan shaped in outline with palmatifid lamina, hirsute with glandular and non-glandular hairs, soft, green with cordate base, lobes obtuse to acute apexes with crisped, serrated to irregularly dentate margins (Plates 1 and 2). Flowers borne in terminal, 2–4 flowered pseudo-umbel inflorescences. Flowers are zygomorphic, pentamerous and rose-violet; receptacle forming a hypanthium which houses a nectariferous gland in a nectariferous spur opening at base of the posterior sepal; sepals lanceolate, imbricate, unequal, connate at base, green-brown; petals free, spatulate, 2 posterior larger than the 3 anterior ones; stamens 10, connate at base, staminodial; ovary superior, 5-lobed, style filiform, stigma with 5 recurved, red or pink thin branches (Plates 1 and 2).

Nutritive/Medicinal Properties

Pelargonium species including *P. crispum* had been reported to accumulate tartaric acid (Stafford 1961). Studies by Wagner and Loewus (1973) found that in *P. crispum* cv. Prince Albert (Lemon Geranium), L-galactono-1,4-lactone was readily converted to L-ascorbic acid which was found to be a precursor of tartaric acid and oxalic acid. D-glucose-6-^{14}C was found to be a better source of label to tartaric acid than D-glucose-l-^{16}C in *Pelargonium crispum*. In Lemon Geranium apices, L-[4-(14)C]ascorbic acid yielded internal labelled (+)-tartaric acid, while L-[6-(14)C]ascorbic acid gave an equivalent conversion to carboxyl labelled (+)-tartaric acid (Williams and Loewus 1978). Conversion of d-[5-(3)H,6-(14)C]glucose to L-ascorbic acid in detached apices of *Pelargonium crispum* (L.) L'Hér cv. Prince Rupert (Lemon Geranium) was accompanied by complete loss of tritium in the product (Grün et al. 1982). Chemical degradation of D-glucose which was recovered from the labelled apices yielded D-glyceric acid. Sucrose and fructose were also identified in the apices. Metabolic product derived from cleavage

Plate 1 Pink flowers and palmatifid leaves of red-styled cultivar

Plate 2 Pink flowers and palmatifid leaves of pink-style cultivar

of ascorbic acid from carbons 2 and 3 yielded the 2-carbon compound, oxalic acid. L-threonic acid and L-tartaric acid were the C_4 products of ascorbic acid cleavage at the carbon 2/carbon 3 bond. L-threonic acid is a natural constituent in the leaves of *Pelargonium crispum* (Helsper and Loewus 1982). They demonstrated that detached leaves of *P. crispum* oxidized l-[U-(14)C]threonate to l-[(14)C]tartrate. A small quantity of [(14)C] glycerate was also produced which suggested a process involving decarboxylation of l-[U-(14)C] threonate. Tannins, namely, proanthocyanidins and ellagitannins (in 53 % of taxa) and free ellagic acid (in 50 %), were major components of the leaves of *Pelargonium* species including *P. crispum*. Myricetin (in 38 %), flavone *C*-glycosides (in 36 %) and luteolin (in 49 % of taxa) were other regular constituents. Myricetin was also found in *P. crispum*.

Chrysin (5,7-dihydroxyflavone) and a related C-methylflavanone were identified as major leaf surface constituents of *P. crispum* (Williams et al. 1997). Many in vitro studies reported that chrysin possessed potent anti-inflammatory, anticancer and antioxidative properties (Woo et al. 2005).

Antioxidant Activity

In-vitro studies showed that significant cell protection was observed upon preincubation of pancreatic beta cells with chrysin, quercetin, catechin or caffeic acid (50 μM, each) prior to application of oxidative stress (Lapidot et al. 2002).

Anticancer Activity

Of the flavones tested, chrysin and apigenin markedly augmented the cytotoxicity of tumour necrosis factor-α (TNF) in L-929 tumour cells, while luteolin showed a weak protective effect (Habtemariam 1997). Studies showed that chrysin induced apoptosis U937 human leukemic promonocytic cells in association with the activation of caspase-3 and Akt signal pathway (Woo et al. 2004). The results suggested that Akt pathway played a major role in regulating the apoptotic response of human leukaemia cells to chrysin and raise the possibility that combined interruption of chrysin and PI3K/Akt-related pathways may represent a novel therapeutic strategy in haematological malignancies. Pretreatment with chrysin greatly sensitized various human cancer cells to tumour necrosis factor-alpha (TNF-α)-induced apoptosis (Li et al. 2010). Pretreatment with chrysin inhibited TNF-α-induced degradation of inhibitor of kappaB (IκB) protein and subsequent nuclear translocation of p65. As a result, chrysin suppressed the expression of NF-κB-targeted anti-apoptotic gene; c-FLIP-L pretreatment with chrysin greatly sensitized various human cancer cells to tumour necrosis factor-alpha (TNF-α)-induced apoptosis (Li et al. 2010).

Antiviral Activity

Chrysin inhibited HIV expression in TNF-α-treated OM-10.1 cultures (Critchfield et al. 1996). Chrysin also inhibited HIV expression in response to PMA in OM-10.1 cells, in ACH-2 cells stimulated with either TNF-α or PMA and in 8E5 cultures.

Anti-inflammatory Activity

Chrysin demonstrated concentration-dependent inhibitory or modulatory effects in a fibroblast cell culture model but was less potent than apigenin (Koganov et al. 1999). Of the compounds tested, apigenin, chrysin and kaempferol significantly stimulated peroxisome proliferator-activated receptor (PPAR)gamma transcriptional activity in a transient reporter assay (Liang et al. 2001). PPARgamma transcription factor had been implicated in anti-inflammatory response. Moreover, these three flavonoids strongly enhanced the inhibition of inducible cyclooxygenase and inducible nitric oxide synthase promoter activities in lipopolysaccharide-activated macrophages which contain the PPAR-gamma expression plasmids. Studies by Cho et al. (2004) found that nitrate production triggered by lipopolysaccharide (LPS) was suppressed by treatment of cultured Raw264.7

cells (mice macrophage/monocyte) with chrysin and its derivatives, 5-hydroxy-7-methoxyflavone (Ch-2) and 5,7-diacetylflavone (Ch-4). Further, COX-2 enzyme was strongly inhibited by Ch-4 (IC_{50} = 2.7 μM) but not by other derivatives. Woo et al. (2005) found that chrysin significantly suppressed the LPS-induced COX-2 protein and mRNA expression in a dose-dependent manner in Raw 264.7 These effects were mediated, at least in part, by inhibition of NF-IL6 activation.

Antimicrobial Activity

Steam-distilled essential oil and petroleum spirit and methanol extracts of scented *Pelargonium* leaves including *P. crispum* (cvs. Crispum variegatum and Lemon fancy) exhibited antibacterial activity in vitro against *Staphylococcus aureus*, *Proteus vulgaris*, *Bacillus cereus* and *Staphylococcus epidermidis* (Lis-Balchin et al. 1998). The most potent antibacterial activity for all components was shown by citral, citronellal, citronellic acid, geraniol, linalool and α-pinene. Major components for the two *P. crispum* cultivars were neral, geranial and sesquiterpenes.

Traditional Medicinal Uses

All parts of the plant are astringent (Grieve 1971).

Other Uses

An essential oil is obtained from the leaves and young shoots are used in perfumery and soap making (Usher 1974). The leaves are dried for potpourri and for making herb pillows (Bown 1995).

Comments

Pelargonium crispum can be readily grown from cuttings.

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Crocus sativus

Scientific Name

***Crocus sativus* L.**

Synonyms

Crocus autumnalis Sm. (Illeg.), *Crocus officinalis* (L.) Honck., *Crocus orsinii* Parl., *Crocus pendulus* Stokes, *Crocus sativus* var. *cashmerianus* Royle, *Crocus sativus* var. *officinalis* L., *Crocus sativus* var. *orsinii* (Parl.) Maw, *Crocus sativus* subsp. *orsinii* (Parl.) K. Richt., *Crocus setifolius* Stokes, *Geanthus autumnalis* Raf., *Safran officinarum* Medik.

Family

Iridaceae

Common/English Names

Asian Saffron, Bulgarian Saffron, Greek Saffron, Indian Saffron, Italian Saffron, Persian Saffron, Saffron, Saffron Cress, Saffron Crocus, True Saffron

Vernacular Names

Afrikaans: Saffraan
Albanian: Kaçe, Shafran
Amharic: Safron
Arabic: Jafrana, Krûkû, Kurkum, Quste Talkh, Za'farân, Zaafaran, Zahafaran
Aramaic: Kurkam, Zapran
Armenian: Kerkoom, Kerkum
Azeri: Zəfəran
Basque: Azafraia, Azaparán, Hupa
Belarusian: Shafran
Brazil: Açafrão Verdadeiro
Breton: Safron
Bulgarian: Shafran
Burmese: Koan°-ku-man°
Catalan: Safrà
Chinese: Faan Hunhg Faa, Fān Hóng Huā, Xi Hong Hua, Zàng Hóng Huā
Croatian: Vrtni Šafran
Czech: Šafrán, Šafrán Setý
Danish: Høstkrokus, Safran-Krokus, Saffran
Dutch: Krokus Sort, Saffraan, Saffraankrokus, Saffraankrokus Soort
Estonian: Krookus, Safran, Safrankrookus
Esperanto: Safrano
Finnish: Maustesahrami, Sahrami
French: Crocus Cultivé, Safran, Safran Cultivé
Gaelic: Crò, Cròch, Còdh
Galician: Azafrán
German: Echter Krokus, Echter Safran, Echter Saffran, Krokus, Safran, Saffran
Georgian: Zaprana, Zaphrana
Greek: Ktokos, Safrani, Zaforá
Hebrew: Karkom, Safran, Za'afran, Zafran
Hungarian: Füszersáfrány, Jóféle Sáfrány, Sáfrány, Valódi Sáfrány
Icelandic: Saffran

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India: Jafaran, Kunkum, Kungkum (Assamese), Jafran, Japhran, Keshar (Bengali), Kukum (Dhivehi), Keshar (Gujarati), Kesar, Saphran, Zaffran, Zafraan (Hindi), Agnishikhe, Kaesari, Kesari, Kunkuma-Kesara, Kunkuma kesari (Kannada), Kashmeeran, Kashmiran, Kungumampoovu, Kunkumapu (Malayalam), Kesar, Keshar, Kung-Kum (Manipuri), Kaesar, Kesar, Kesara (Marathi), Kesara, Kumkuma Phul (Oriya), Keshar (Punjabi), Agneeshekhar, Agnishekhara, Agnishikha, Aruna, Asra, Asrika, Asrugvar, Bahlikabc, Balhika, Bhavarakta, Chandana, Charu, Dhira, Dipaka, Gaura, Ghasra, Ghusriam, Ghusrna, Ghusruna, Harichandana, Jaguda, Kaisara, Kaleyaka, Kanta, Kashmara, Kashmiraja, Kashmirajanma, Kasmira, Kashmiria, Kasmiraja, Kasmirajanma, Kesara, Kesaram, Kesaravara, Keshara, Khala, Ksataja, Kumkuma, Kumkumam, Kunkuma, Kunkumam, Kusrunam, Kusumatmaka, Lohita, Mangal, Mangalya, Pishuna, Pitaka, Pitana, Raja, Rakta, Raktachandana, Raktasanjna, Ruchira, Rudhira, Sankoca, Sankocha, Sankochapishuna, Saubhara, Saurab, Shatha, Shonit, Shonita, Shonitavhaya, Valhika, Vara, Varabalhika, Varenya, Vira (Sanskrit), Akkinicekaram, Avakam, Avam, Cankocapicunam, Catikecam, Catimaracam, Centurukkam, Cukkilapputta, Irattam, Irattancapittam, Kacimiram, Kasmiram, Kecaram, Kecaravaram, Kecari, Kecarippu, Khoongoomapoo, Kirucan, Klungumapu, Kucumpam, Kungu Mappoo, Kungumappoo, Kungumapu, Kunkumam, Kunkumappu, Malam, Marali, Maralukam, Maravam, Maravatam, Mavacciram, Mavananki, Nalal, Nalalpu, Nalarpu, Naravam, Naravucaram, Palapaliriti, Piriyakam, Pumalekinam, Putpika, Turukkam, Turumam, Ulokitacantanam, Ulukalam, Vallapetam, Vanita, Vanmikam, Vareniyam, Vatankura (Tamil), Kunkuma-Puvva, Kunkumamu, Kunkumapave, Kunkumapuvve, Kunkumma-Purru (Telugu), Kesari (Tulu), Jafranekar, Kisar, Safran, Zafran, Zafran Sayida (Urdu)

Indonesia: Kuma-Kuma, Kunti Kering, Sapran

Iran: Larkimasa, Za'farân, Zaafaran (Farsi), Kurkum (Pahlavi)

Italian: Croco, Croco Fiorito, Croco Senza Fiori, Fior Cuculo, Giallone, Grogo Domestic, Zafferano, Zafferano Domestic, Zafferano Vero

Japanese: Bankōka, Bankoka, Safuran

Kashmiri: Kung, Zafran

Kazakh: Jawqazın, Zağıparan, Zapırangül

Khmer: Romiet

Korean: Saphran, Sapuran, Syapuran

Laos: Ya faran, Yafan

Latvian: Safrāns, Safrāna Krokuss, Safrānaugs

Lithuanian: Šafranas, Šafronas

Macedonian: Safran

Malaysia: Kuma-Kuma, Kunyit Kering, Sapran

Maltese: Żagħfran, Żafran

Nepal: Kaashmirii Keshara, Kashmiri Keshar, Kesari, Keshara, Keshar, Kung Kum

Norwegian: Safran, Safrankrokusen, Safrankrokus

Pashto: Zaffaron

Philippines: Kashubha (Tagalog)

Polish: Krokus Uprawny, Szafran, Szafran Uprawny

Portuguese: Açaflor, Açafrão

Provencal: Safran

Romanian: Safran, Şofran;

Russian: Shafran, Schafran

Serbian: Šafran

Slovašcina: Pravi Žafran, Žafran

Slovencina: Šafrán, Šafran Siaty

Spanish: Azafrán, Azafrí, Croco, Hupa, Rosa Del Azafrá

Sri Lanka: Kaha Mal (Sinhala)

Swahili: Zafarani

Swedish: Saffran, Saffranskrokus

Thai: Ya Faran, Yafan

Tibetan: Gur-Gum, Gur-kum, Kha Che, Kha-che kye

Turkish: Safran, Zafran, Zağferan

Ukrainian: Krokus, Shafran

Uzbek: Zafaron

Vietnamese: Mau Vang Nghe, Nghe Tay, Qui Nghe

Welsh: Saffrwm

Yiddish: Zafren, Zafron

Origin/Distribution

There are two different views on the geographical origin of *Crocus sativus*, a Mediterranean origin (Greece) versus the Western–Central Asia origin, and mixed views on its parental ancestry. Botanical research by Mathew (1977) appeared to suggest Crete, Eastern Greece, as the centre of origin, disproving the view of a Western or Central Asia origin. However, more recent studies suggested that saffron may have originated in Mesopotamia (Alavi-Kia et al. 2008). *Crocus sativus* is a triploid species (Karasawa 1933; Pathak 1940) with a karyotype similar to diploid *C. cartwrightianus* and *C. thomasii*, both native to the Mediterranean region (Grilli Caiola and Canini 2010). Comparative morphological, cytological, cytogenetical and phenological studies (Karasawa 1933; Pathak 1940; Feinbrun 1958; Brighton 1977; Mathew 1977, 1982; Ghaffari 1986; Brandizzi and Grilli Caiola 1996, 1998; Grilli Caiola et al. 2004) lend support to the hypothesis that the most probable ancestors of *C. sativus* were *C. cartwrightianus* (Mathew 1982) or *C. thomasii* (Chichiriccò 1989) from which saffron may be derived by polyploidy. Quantitative and qualitative DNA analysis studies (Brandizzi and Grilli Caiola 1996, 1998; Grilli Caiola et al. 2004) indicated that the DNA composition of *C. sativus* was more similar to that of *C. cartwrightianus*, from which it could have been originated by polyploidy or mutation and polyploidy. Further data from several studies supported the alloploidy of *C. sativus*, the parents being *C. cartwrightianus* and *C. hadriaticus*, both with $2n = 16$ and found in Greece but not in overlapping areas (Frello and Heslop-Harrison 2000). However, other possible parents, e.g. *C. thomasii* from Italy and Croatia, *C. mathewii* from Turkey and *C. pallasii* ssp. *haussknechtii* from Iran, cannot be excluded (Frello and Heslop-Harrison 2000; Grilli Caiola et al. 2001, 2004). More recent DNA studies using inter-retrotransposon amplified polymorphism suggested that Iranian *C. almehensis* and *C. michelosnii* are the closest relatives of saffron and probably the possible wild ancestors of this cultivated species (Alavi-Kia et al. 2008). Thus, the Mediterranean region was deduced to be one of the probable sites of saffron origin; another site could be in the East, in Turkey, Iran and India, where saffron had been cultivated for thousands of years (Grilli Caiola and Canini 2010).

Today almost all saffron grows in a belt bounded by the Mediterranean in the West and the rugged region encompassing Iran, Turkey and Kashmir and Kishtwar in Jammu, India, in the East. Elsewhere in other continents, except Antarctica, comparatively insignificant amounts are being produced.

Agroecology

In its native range, *Crocus sativus* thrives in a Mediterranean environment characterized by cool to cold winters and warm, dry summers with sparse autumn–winter–spring rainfall (400–500 mm per annum) (Deo 2003). It can withstand considerable frosts (−10 °C) and can tolerate occasional snow in the winter. Saffron is also grown successfully under nonirrigated conditions (1,000–1,500 mm per annum) in Kashmir, India. Rain immediately preceding flowering boosts saffron yields, whereas rainy or cold weather during flowering promotes disease and reduces yields.

C. sativus thrives in full sun and prefers friable, deep, low-density, well-watered and well-drained clay-calcareous soils with high organic content and loose textures that allow easy root penetration.

Edible Plant Parts and Uses

Saffron is the dried, brilliant, orange-red style and stigmata of *Crocus sativus* flowers, widely used in food as spice and colouring agent (Plates 5 and 6). Saffron's aroma is described by food aficionado as evocative of honey, with grassy, hay-like and metallic notes, while its taste has also been described as hay-like and sweet. Saffron imparts a luminous yellow-orange colouring to foods and is used globally in everything from cheeses, confectioneries, liquors

to baked food, curries, rice, meat dishes and soups. Saffron is widely featured in Persian, European, Arabic, Turkish, North African and Asian cuisines, for example, from the Milanese *risotto* of Italy or the *bouillabaisse* of France to Indian *biryani* with various meat accompaniments in South and Southeast Asia.

Botany

Small, stemless, erect, perennial, herbaceous geophyte 20–30 cm tall, with a depressed-globose subterranean corm 3–5 cm in diameter, surrounded by a finely reticulate-fibrous tunic and rooting at the flattened base. Cataphylls up to 5, membranous, white, enclosing the aerial shoot. Leaves about 8, usually appearing with flowers (synanthous), erect, green, linear, 1.5–2(–3) mm broad (Plates 1 and 2), with a white median stripe above, keeled below, glabrous or ciliate. Flowers 1–3, bisexual, regular, each on a short subterranean pedicel, subtended by membranous bracts; perianth with a long cylindrical tube 4 cm long and six oblanceolate segments in two whorls, 2.5–4 cm × 1–2 cm, deep lilac-purple or mauve coloured with darker veins, white or lilac in the throat and pubescent, apex obtuse; stamens with 3 short (1mm) filaments, anthers linear, erect, 2 cm long and bright yellow; ovary inferior, style 2.5–3.5 cm long, brilliant orange-red dividing into three branches with expanded tips bearing the stigmas (Plates 2, 3, 4, 5 and 6). Capsules and seeds have been only rarely reported, saffron being considered a sterile species.

Plate 1 Flowering saffron plants with unopened flowers

Plate 3 Close-up of opened saffron flower

Plate 2 Saffron flowers at different opening stages

Plate 4 Harvested saffron flowers

Plate 5 Mass of saffron styles and stigmata removed from the flowers

Plate 6 Close-up of saffron style and stigmata

Nutritive/Medicinal Properties

Saffron Flower Phytochemicals

Saffron had been found to contain more than 150 volatile and several non-volatile compounds; approximately 40–50 constituents had already been identified (Abdullaev 2002). Studies showed that saffron contained three main pharmacologically active metabolites (Rödel and Petrzika 1991; Abdullaev 2002): (1) saffron-coloured compounds called crocins, unusual water-soluble carotenoids (mono- and diglycosyl esters of a polyene dicarboxylic acid, named crocetin); the digentiobiosyl ester of crocetin—α-crocin—had been reported as the major component of saffron; (2) picrocrocin, the main substance responsible of the bitter taste in saffron; and (3) safranal, the volatile oil constituent responsible of the characteristic saffron odour and aroma. Furthermore, saffron had also been reported to contain proteins, sugars, vitamins, flavonoids, amino acids, mineral matter, gums and other chemical compounds.

Proximate nutrient composition (per 100 g edible portion) of saffron had been reported as follows: water 11.90 g, energy 310 kcal (1,298 kJ), protein 11.43 g, fat 5.85 g, ash 5.45 g, carbohydrate 65.37 %, total dietary fibre 3.9 g, Ca 111 mg, Fe 11.10 mg, Mg 264 mg, P 252 mg, K 17.24 mg, Zn 1.09 mg, Cu 0.328 mg, Mn 28.408 mg, Se 5.6 µg, vitamin C 80.8 mg, thiamin 0.115 mg, riboflavin 0.267 mg, niacin 1.460 mg, vitamin B6 1.010 mg, total folate 93 µg, vitamin A 27 µg RAE, vitamin A 530 IU, total saturated fatty acids 1.586 g, 14:0 (myristic acid) 0.006 g, 16:0 (palmitic acid) 1.157 g, 18:0 (stearic acid) 0.247 g, total monounsaturated fatty acids 0.429 g, 16:1 undifferentiated (palmitoleic acid) 0.003 g, 18:1 undifferentiated (oleic acid) 0.390 g, 20:1 (gadoleic acid) 0.006 g, total polyunsaturated fatty acids 2.067 g, 18:2 undifferentiated 0.754 g (linoleic acid), 18:3 undifferentiated (linolenic acid)1.242 g, 20:4 undifferentiated (arachidonic acid) 0.013 g and 22:5 *n*-3 (DPA) (docosapentaenoic acid) 0.006 g (USDA 2013). Earlier, saffron was found to be the richest known source of riboflavin and also contained thiamin (Bhat and Broker 1953). A chitinase named SafchiA was isolated from *C. sativus* (Castillo et al. 2007). SafchiA protein shared close similarities with chitinases belonging to family 19 of glycosyl hydrolases, although, some changes in the enzyme catalytic domain were present.

Saffron contained a complex mixture of volatile and non-volatile compounds responsible for its overall aroma and flavour (Tarantilis and Polissiou 1997). The major components of saffron reported were the apocarotenoids *cis*-crocins, *trans*-crocins, picrocrocin (β-D-glucopyranoside of hydroxyl-β-cyclocitral) and its degradation product, the odour-active safranal (Kanakis et al. 2004). However, studies revealed a different volatile composition in unprocessed,

natural stigma tissues (Rubio et al. 2009; Moraga et al. 2009b), suggesting the presence of a degradation process responsible for the organoleptic properties of saffron from preformed apocarotenoid compounds (D'Auria et al. 2006). The concentration of volatiles changed with saffron stigma development from orange, red and scarlet pre-anthesis (−2days), anthesis (day) and post-anthesis (+3days), with the highest levels in the latest stages (up to 13 % by fresh weight) (Rubio et al. 2009). Nine individual volatiles were studied:9-apo-β-caroten-9-one(β-ionone),7,8-dihydro-β-ionone, 6,10-dimethyl-3,5,9-undecatrien-2-one (pseudoionone), 9-apo-α-caroten-9-one (α-ionone), 6,10-dimethyl-5,9-undecadien-2-one (geranylacetone),megastigma-4,6,8-triene,4-(2,6,6-trimethylcyclohexa-1,3-dienyl)but-2-en-4-one (damascenone), 6-methyl-5-hepten-2-one (6-methyl-5-hepten-2-one) and 2,6,6-trimethyl-1,3-cyclo hexadiene-1-carboxaldehyde (safranal). With the exception of safranal, the other eight compounds were selected because they were the known 9,10(9′,10′)- and 5,6(5′,6′)-carotenoid dioxygenase products that may potentially be generated depending on the availability of specific carotenoids in the stigma. In the yellow, orange and red stigma stages, apocarotenoid C_{13} volatiles were practically undetectable. Similarly, geranylacetone and 6-methyl-5-hepten-2-one were detected at low levels even in the more advanced developmental stigma stages. β-Ionone, 7,8-dihydro-β-ionone and megastigma-4,6,8-triene were detected prior to anthesis, and their levels increased up to the time of anthesis, rapidly decreasing thereafter. The presence of these volatiles indicated β-carotene to be the principal precursor of the monoterpene volatiles in the developed stigma. Additionally, four carotenoid cleavage dioxygenase (CCD) genes, CsCCD1a, CsCCD1b, CsCCD4a and CsCCD4b, were isolated. CsCCD1a was constitutively expressed, CsCCD1b was unique to the stigma tissue, but only CsCCD4a and CsCCD4b had expression patterns consistent with the highest levels of β-carotene and emission of β-ionone derived during the stigma development. The CsCCD4 enzymes were localized in plastids and more specifically were present in the plastoglobules. Moraga et al. (2009b) found that the main compounds that accumulated throughout *C. sativus* stigma development were crocetin, its glucoside derivatives and picrocrocin, all of which increased as stigmas reached a fully developed stage. The volatile composition of *C. sativus* stigmas changed markedly as stigmas developed with each developmental stage being characterized by a different volatile combination. In red stigmas, β-cyclocitral, the 7,8 cleavage product of β-carotene, was abundantly produced, suggesting the implication of both β-carotene and zeaxanthin in crocetin formation. As stigmas matured, hydroxy-β-ionone and β-ionone were produced, while safranal, the most typical aroma compound of the processed spice, was only detected at low levels. However, a safranal-related compound 2,2,2-trimethyl-2-cyclohexene-1,4-dione (4-oxoisophorone) increased rapidly at the anthesis stage and also in senescent stigmas. Monoterpenes were mainly emitted at the time of anthesis, and the emission patterns followed the expression patterns of two putative terpene synthases CsTS1 and CsTS2. Fatty acid derivatives, which predominated at the earlier developmental stages, were observed at low levels in later stages. From *Crocus sativus* stigmas, eight glycosides were isolated including a new safranal glycoside, (4R)-4-hydroxy-2,6,6-trimethylcyclohex-1-enecarbaldehyde 4-*O*-[β-D-glucopyranosyl(1→3)-β-D-glucopyranoside], and a new carotenoid pigment, *trans*-crocetin-1-al 1-*O*-β-gentiobiosyl ester, along with picrocrocin, crocetin mono(β-gentiobiosyl) ester (crocin-3), crocin, crocetin-(-β-D-glucosyl)-(β-gentiobiosyl) ester (crocin-2), kaempferol-7-sophoroside and sophoraflavonoloside (Tung and Shoyama 2013).

Numerous studies had reported on the separation and characterization of the volatile and non-volatile components of the dried stigmas of *Crocus sativus* (saffron) (Liakopoulou-Kyriakides and Kyriakidis 2002). The volatiles with a very strong odour comprised more than 34 components, mainly terpenes, terpene alcohols and their esters. Non-volatiles included crocin-1, crocin-2, crocin-3 and crocin-4 responsible for the red or reddish brown colour of stigmas together

with carotenes; crocetin; picrocrocin (a glycosidic precursor of safranal), the bitter substance; and safranal, the major organoleptic principle of the stigmas.

The following carotenoid glycosides were detected in saffron: crocin = crocetin-di-(β-D-gentiobiosyl)-ester(I),crocetin-(β-D-gentiobiosyl)-(β-D-glucosyl)-ester(II),crocetin-di-(β-D-glucosyl)-ester (III), crocetin-di-(2,3,4,8,9,10,12-hepta-*O*-acetyl-β-D-gentiobiosyl)-ester (IV) and crocetin-di-(2,3,4,6-tetra-*O*-acetyl-β-D-glucosyl)-ester (VI) (Pfander and Wittwer 1975). The following carotenoids were isolated from *C. sativus*: phytoene, phytofluene, tetrahydrolycopene, β-carotene, zeaxanthin and crocetin (Pfander and Schurtenberger 1982). Rios et al. (1996) reported the following crocins in *C. sativus* flowers: crocetin tri(β-D-glucosyl)-(β-D-gentiobiosyl) ester; crocetin di(β-D-gentiobiosyl) ester; crocetin (β-D-glucosyl)-(β-D-gentiobiosyl) ester; crocetin (β-D-gentiobiosyl) ester; crocetin di(β-D-glucosyl) ester; crocetin (β-D-glucosyl) ester; crocetin; picrocrocin; sinapic acid derivative; sinapic acid, crocusatin B; crocusatin C and safranal. Montoro et al. (2012) identified crocetin di(β-D-gentiobiosyl) ester; crocetin (β-D-glucosyl)-(β-D-gentiobiosyl) ester; crocetin (β-D-gentiobiosyl) ester; crocetin di(β-D-glucosyl) ester; crocetin (β-D-glucosyl) ester; crocetin; picrocrocin and sinapic acid derivative in *C. sativus* petals and found only sinapic acid derivative in the stamen and flower.

Five major biologically active ingredients of saffron, namely, crocin-1, crocin-2, crocin-3, crocin-4 and crocetin were simultaneously quantified using high-performance liquid chromatography–UV (HPLC–UV) (Li et al. 1999). Seven carotenoid metabolites (aroma precursors) were identified from saffron methanolic extract: (4*R*)-4-hydroxy-2,6,6-trimethylcyclohex-1-enecarbaldehyde *O*-β-D-gentiobioside; (4*R*)-4-hydroxy-2,6,6-trimethylcyclohex-1-enecarboxylic acid *O*-β-D-glucopyranoside; 6-hydroxy-3-(hydroxymethyl)-2,4,4-trimethylcyclohexa-2,5-dienone 6-*O*-β-D-glucopyranoside; (2*Z*)-3-methylpent-2-enedioic acid 1-[1-(2,4,4-trimethyl-3,6-dioxocyclohexenyloxy)-*O*-β-D-glucopyranosid-6-yl] ester (4),(5*S*)-5-hydroxy-7,7-dimethyl-4,5,6,7-tetrahydro-3*H*-isobenzofuran-1-one *O*-β-D-glucopyranoside; (1*R*,5*S*,6*R*)-5-(hydroxymethyl)-4,4,6-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one *O*-β-D-glucopyranoside and (1*R*)- 3,5,5-trimethylcyclohex-3-enol *O*-β-D-glucopyranoside (Straubinger et al. 1998). The following crocetin derivative compounds were found in saffron stigma: *all-trans*-crocetin di(β-D-gentiobiosyl) ester; *all-trans*-crocetin β-D-gentiobiosyl-β-D-glucosyl ester; *all-trans*-crocetin di(β-D-glucosyl) ester and *all-trans*-crocetin mono(β-D-gentiobiosyl) ester, as well as 13-*cis*-crocetin di(β-D-gentiobiosyl) ester and 13-*cis*-crocetin β-D-gentiobiosyl-β-D-glucosyl ester (Van Calsteren et al. 1997). The following glycoconjugates were isolated and identified from fractions of saffron methanolic extract: the β-D-glucosides of (4*R*)-4-hydroxy-3,5,5-trimethylcyclohex-2-enone, (4*S*)-4-hydroxy-3,5,5-trimethylcyclohex-2-enone and (4*S*)-4-(hydroxymethyl)-3,5,5-trimethylcyclohex-2-enone, as well as the β-D-gentiobiosyl ester of 2-methyl-6-oxohepta-2,4-dienoic acid and known saffron constituents, di-β-D-gentiobiosyl and β-D-gentiobiosyl-β-D-glucopyranosyl esters of crocetin (Straubinger et al. 1997a). Ten saffron metabolites responsible for the taste, flavour and colour were identified in commercial saffron: picrocrocin, 4-hydroxy-2,6,6-trimethyl-1-cyclohexene-1-carboxaldehyde (HTCC), 3-gentiobiosyl-kaempferol, α-crocin, crocin-2, crocin-3, safranal, crocin-4, crocin-5 and crocin-6 (Lozano et al. 1999). Twelve components were isolated from saffron: crocin-1, crocin-2, crocin-3, picrocrocin, acid form of picrocrocin, HTCC-diglycosyl-kaempferol, *trans*-crocin-4, *trans*-crocin-2, *trans*-crocin-3, safranal, crocetin and *cis*-crocin-3 (Abdullaev et al. 2002). Volatile compositions of saffron from Tibet using diethyl ether, ethanol, ethyl acetate, dichloromethane and acetone solvents were respectively as follows (Jia et al. 2011): 3,5,5-trimethyl-2-cyclohexen-1-one 1.35, 2.82, 2.13, 2.45, 2.13 %; 2,6,6-trimethyl-2-cyclohexene-1,4-dione 1.13, 2.08, 13, 1.90, 1.48 %; 2,2,6-trimethyl-1,4-cyclohexanedione 1.08, 1.91, 1.37, 1.93, 1.42 %; 2,2,6-trimethyl-1,3-cyclohexadiene-1-carboxaldehyde 5.83, 40.7, 16.1, 16.1, 25.7 %; 4-hydroxy-3,5,5-trimethylcyclohex-2-enone 1.72,

2.52, 1.80, 2.5, 2.09 %; 3-hydroxymethylene-1,7,7-trimethylbicyclo[2.2.1]heptane-2-one 2.35, 3.77, 3.55, 4.49, 3.16 %; 2-ethenyl-1,3,3-trimethyl-cyclohexene 3.65, 6.50, 5.49, 7.50, 5.62 %; *n*-hexadecanoic acid, nd, 3.97, 5.95, 6.10, 5.34 %; (*Z,Z*)-9,12-octadecadienoic acid nd, 9.91, 16.32, 15.23, 12.41 %; oleic acid, nd, nd, nd, 5.18 %, nd; octacosane nd, nd, 2.17, 1.88 %, nd; stigmasterol 11.8 %, nd, nd, nd, nd; squalene 2.57 %, nd, nd, 2.96 %, nd; nonacosanol/1-pentacosanol nd, nd, 2.90 %, nd, nd; nonacosanol nd, nd, 2.22, 1.88 %, nd; nonacosane nd, nd, 2.17 %, nd, nd; γ-sitosterol 4.82 %, nd, nd, nd, nd; and β-amyrin 4.22 %, nd, nd, nd, nd. The number of volatile components identified in saffron from Henan using similar solvents was different and very much less than found in saffron from Tibet.

Of the fifteen crocetin esters identified in saffron stigma and *Gardenia jasminoides* fruit, five new compounds were tentatively identified: *trans* and *cis* isomers of crocetin (β-D-triglucoside)-(β-D-gentiobiosyl) ester, *trans* and *cis* isomers of crocetin (β-D-neapolitanose)-(β-D-glucosyl) ester and *cis*-crocetin (β-D-neapolitanose)-(β-D-gentiobiosyl) ester (Carmona et al. 2006c). The most relevant differences between both species were a low content of the *trans*-crocetin (β-D-glucosyl)-(β-D-gentiobiosyl) ester, the absence of *trans*-crocetin di-(β-D-glucosyl) ester in gardenia and its higher content of *trans*-crocetin (β-D-gentiobiosyl) ester and *cis*-crocetin di-(β-D-gentiobiosyl) ester. Also, ten glycosidic compounds in saffron extracts with a UV/Vis pattern similar to that of picrocrocin were identified; among them, 5-hydroxy-7,7-dimethyl-4,5,6,7-tetrahydro-3*H*-isobenzofuranone 5-*O*-β-D-gentiobioside and 4-hydroxymethyl-3,5,5-trimethyl-cyclohexen-2-one 4-*O*-β-D-gentiobioside were tentatively identified for the first time in saffron. Of these ten glycosides, only the *O*-β-D-gentiobiosyl ester of 2-methyl-6-oxo-2,4-hepta-2,4-dienoic acid was found in Gardenia samples, but it was possible to identify the iridoid glycoside, geniposide. The ethanolic extract from saffron tepals contained 16 compounds; the most abundant were 2-phenylethyl alcohol (15.0 %), tetracosane (10.5 %), ethyl hexadecanoate (10.0 %) and heptadecane (9.6 %) (Tirillini et al. 2006). The Tirillini extract from anthers contained 26 compounds, the major compounds being 2-phenylethyl alcohol (50.4 %) and 2-phenethyl acetate (15.4 %). Two new glycosides were isolated saffron pollens and elucidated as isorhamnetin-4′-*O*-α-L-rhamnopyranosyl(1→2)-β-D-glucopyranoside (crosatoside A) and β-(p-hydroxyphenyl) ethanol-α-*O*-L-rhamnopyranosyl (1→2)-β-D-glucopyranoside (crosatoside B), and the third compound was the known kaempferol-3-*O*-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside (Song and Xu 1991). Five new naturally occurring monoterpenoids, crocusatins A, B, C, D and E; a new lactate, sodium (2S)-(*O*-hydroxyphenyl)lactate; and eighteen known compounds, namely, 3,5,5-trimethyl-2-hydroxy-1,4-cyclohexadion-2-ene; 2,4,4-trimethyl-3-formyl-6-hydroxy-2,5-cyclohexadien-1-one; 3,5,5-trimethyl-4-hydroxy-1-cyclohexanon-2-ene; methylparaben; protocatechuic acid methyl ester; 4-hydroxybenzoic acid; kaempferid; 4-hydroxyphenethyl alcohol; benzoic acid; pyridine-3-yl-methanol; nicotinamide; 1-*O*- (4-hydroxybenzoyl)-β-D-glucose; adenosine; isorhamnetin-3,4′-diglucoside; isorhamnetin-3,-*O*-robinobioside; isorhamnetin-3-β-D-glucoside; 5-methyluracil and uracil were isolated and characterized from the pollen of *Crocus sativus* (Li and Wu 2002a).

Four new compounds, crocusatins F, G, H and I, together with 21 known compounds, were isolated from an aqueous extract of the stigmas of *Crocus sativus* (Li and Wu 2002b). Three new monoterpenoids, crocusatins J, K and L, and a new naturally occurring acid, (3S),4-dihydroxybutyric acid, together with 31 known compounds, were isolated and identified from the methanol extract of saffron petals (Li et al. 2004).

Two flavonoids, kaempferol 7-*O*-glucopyranoside-3-*O*-sophoroside and kaempferol 7-*O*-sophoroside, were isolated from saffron (Tarantilis et al. 1995; Straubinger et al. 1997b). The following flavonols: quercetin, kaempferol, and galangin were isolated from the fresh saffron petals (Kubo and Kinst-Hori 1999). Kaempferol

was isolated from saffron petals (Hadizadeh et al. 2010). Five kaempferol derivatives were identified in the flavonoid fraction of saffron spice from different regions: kaempferol-3-sophoroside; kaempferol-3-sophoroside-7-glucoside; kaempferol-3,7,4′-triglucoside; kaempferol tetrahexoside; and kaempferol-3-dihexoside (Carmona et al. 2007). Three significant flavonoids, kaempferol 3-*O*-sophoroside-7-*O*-glucopyranoside; kaempferol 3,7,4′-triglucoside; and kaempferol 7-*O*-sophoroside, were isolated from saffron stigma (Moraga et al. 2009a). All three flavonoids increased with stigma development. The relative levels of kaempferol 7-*O*-sophoroside, which reached the maximum levels at anthesis, were much higher than those observed for both kaempferol 3-*O*-sophoroside-7-*O*-glucopyranoside and kaempferol 3,7,4′-triglucoside, with relative high levels in the scarlet stages. They also isolated an enzyme glucosyltransferase CSGT45 from saffron stigma, involved in flavonoid glucosylation (formation of flavonoid glucosides). This enzyme catalyses the transfer of glucose from uracil-diphosphate glucose (UDP-glucose) to kaempferol and quercetin. Trapero et al. (2012) isolated UGT707B1, a new glucosyltransferase that localized in the cytoplasm and the nucleus of stigma and tepal cells of *C. sativus* and involved in the formation of kaempferol and quercetin sophorosides in *Crocus sativus*. They found in *Crocus* tepals two major flavonoid compounds: kaempferol-3-*O*-β-D-glucopyranosyl-(1-2)-β-D-glucopyranoside and quercetin-3-*O*-β-D-glucopyranosyl-(1-2)-β-D-glucopyranoside, both of which were absent from the tepals of those *Crocus* species that did not express UGT707B. Levels of flavonoids measured in extracts of the transgenic plants showed changes in the composition of flavonols when compared with wild-type plants. The major differences were observed in the extracts from stems and flowers, with an increase in 3-sophoroside flavonol glucosides. A new compound kaempferol-3-*O*-sophoroside-7-*O*-rhamnoside was also identified.

The major flavonoid constituents identified in diethyl ether, ethyl acetate and aqueous fractions of saffron petals corresponded to kaempferol, quercetin, naringenin and some flavanone and flavanol derivatives glycosylated and esterified with phenylpropanoic acids (Termentzi and Kokkalou 2008). The flavonoids identified in *C. sativus* petals included 4′-methyl ether dihydrokaempferol 3-*O*-deoxy-hexoside, taxifolin 7-*O*-hexoside, dihydrokaempferol 3-*O*-hexoside, naringenin 7-*O*-hexoside and naringenin. Additionally, the presence of some nitrogen-containing substances, as well as other phenolics and phenylpropanoic derivatives, was also detected. From the methanolic extract of *Crocus sativus* petals, nine known flavonoids were isolated and identified, including glycosidic derivatives of quercetin and kaempferol as major compounds (1–2), and their methoxylated and acetylated derivatives (Montoro et al. 2008). The high content of glycosylated flavonoids could give value to *C. sativus* petals, a waste product in the production of the spice saffron. The flavonoid pyrogallol and gallic acid were isolated from saffron stigma (Karimi et al. 2010).

Kaempferol and kaempferol-3-*O*-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside were found in the petals (Song 1990). Thirty-one flavonoids were identified in *C. sativus* petal extracts comprising mainly glycosidated and metoxilated derivatives of kaempferol, quercetin, isorhamnetin and tamarixetin (Montoro et al. 2012): kaempferol 7-*O*-bihexoside-3-*O* hexoside; kaempferol 3-*O* (*p*-coumaroyl)-bihexoside; 3,3′-4′-trimethyl ether quercetin 7-*O*-bihexoside; quercetin 3,3′-dimethyl ether 7-*O*-bihexoside; kaempferol-3-*O*-β-D-(2-*O*-β-D-6-*O*-acetylglucosyl)-glucopyranoside; kaempferol 3-*O*-hexoside,7-*O*-(acetyl)-hexoside; kaempferol 3-*O*- (acetyl-) hexoside-7-*O*-hexoside; kaempferol 3-*O*-(acetyl-) bihexoside; isorhamnetin-3,7-di-*O*-β-D-glucopyranoside; tamarixetin 3-*O*-bihexoside; quercetin-3,7-di-*O*-β-D-glucopyranoside; 4′-methyl ether dihydrokaempferol 3-*O*-deoxy-hexoside; quercetin-*O*-bihexoside; tamarixetin-caffeoyl-*p*-coumaroyl biester; isorhamnetin 3-*O*-(desoxyherosyl)-hexoside; quercetin 3-*O* (*p*-coumaroyl)-hexoside; di-glucosyl-kaempferol; kaempferol-3,7-di-*O*-β-D-glucopyranoside; kaempferol-3-*O*-β-D- (2-*O*-β-D-glucosyl) glucopyranoside; kaempferol 3,7-*O*-bihexoside; kaempferol 3-*O*-bihexoside; kaempferol caffeoyl

p-coumaroyl biester; kaempferol esterified derivative; kaempferol 3-*O*- (acetyl)-hexoside; isorhamnetin-3-*O*-β-D-glucopyranoside;quercetin-3-*O*-β-D-glucopyranoside; kaempferol-3-*O*-β-D-glucopyranoside; kaempferol-*O*-hexoside; kaempferol-7-*O*-β-D-glucopyranoside; rhamnetin; kaempferol; dihydrokaempferol 3-*O*-hexoside and naringenin. The flavonoids tamarixetin *O*-kaempferol biflavonoid hexoside, taxifolin 7-*O*-hexoside and naringenin 7-*O*-hexoside were not detected in the petals. In the stamens, all the above flavonoids as reported in the petals and taxifolin 7-*O*-hexoside were found except for kaempferol 7-*O*-bihexoside-3-*O* hexoside; kaempferol 3-*O* (*p*-coumaroyl)-bihexoside; tamarixetin *O*-kaempferol biflavonoid hexoside; kaempferol-3-*O*-β-D- (2-*O*-β-D-6-*O*-acetyl-glucosyl)-glucopyranoside; kaempferol 3-*O*-hexoside,7-*O*- (acetyl)-hexoside; kaempferol 3-*O*- (acetyl-) hexoside-7-*O*-hexoside; kaempferol 3-*O*- (acetyl-) bihexoside; kaempferol esterified derivative; kaempferol 3-*O*-(acetyl)-hexoside; dihydrokaempferol 3-*O*-hexoside; and naringenin 7-*O*-hexoside. In the flowers, all the flavonoids as listed for the petals were found except for kaempferol 7-*O*-bihexoside-3-*O* hexoside; kaempferol 3-*O* (*p*-coumaroyl)-bihexoside; tamarixetin *O*-kaempferol biflavonoid hexoside; 3,3′-4′-trimethyl ether quercetin 7-*O*-bihexoside; kaempferol-3-*O*-β-D-(2-*O*-β-D-6-*O*-acetylglucosyl)-glucopyranoside; kaempferol 3-*O*-hexoside,7-*O*-(acetyl)-hexoside; kaempferol 3-*O*- (acetyl-) hexoside-7-*O*-hexoside; kaempferol 3-*O*- (acetyl-) bihexoside; kaempferol esterified derivative; kaempferol 3-*O*-(acetyl)-hexoside; taxifolin 7-*O*-hexoside; naringenin 7-*O*-hexoside; and naringenin. The following flavanol kaempferol 3-*O*-sophoroside; kaempferol 3-*O*-glucoside; kaempferol 3-*O*-sophoroside; quercetin 3-*O*-sophoroside; kaempferol 3-*O*-sophoroside-7-*O*-glucoside; isorhamnetin 3,4′-*O*-diglucoside; kaempferol 3-*O*-rutinoside; kaempferol 3-*O*-glucoside and kaempferol; and anthocyanins delphinidin 3,5-*O*-diglucoside, delphinidin 3-*O*-glucoside, malvidin 3,5-*O*-diglucoside and petunidin 3,5-*O*-diglucoside were identified in saffron floral bio-residues (Serrano-Díaz et al. 2013).

Nineteen flavonols, kaempferol, quercetin and isorhamnetin glycosides as mono-, di- or triglycosides, and five anthocyanins reported as delphinidin, petunidin and malvidin glycosides were isolated from *C. sativus* tepals (Goupy et al. 2013). Kaempferol glycosides were the major flavonols (84.0 % of total flavonol content) with kaempferol 3-*O*-sophoroside as the main compound. Isorhamnetin 3-*O*-sophoroside, kaempferol 3-*O*-rutinoside and quercetin 3-*O*-glucoside 7-*O*-rhamnoside in *C. sativus tepals* were newly identified. Some others included kaempferol 3-*O*-glucoside; kaempferol 3-*O*-sophoroside; quercetin 3-*O*-sophoroside; kaempferol 3-*O*-sophoroside-7-*O*-glucoside; isorhamnetin 3,4′-di-*O*-glucoside; kaempferol 3-*O*-glucoside; and kaempferol. Anthocyanins were quantified for the first time in *C. sativus* tepals (4,804 μg/g DW); the main anthocyanin identified was delphinidin 3,7-*O*-diglucoside; others included delphinidin 3,5-*O*-diglucoside; delphinidin 3-*O*-glucoside; delphinidin 3,5-*O*-diglucoside; malvidin 3,5-*O*-diglucoside; and petunidin 3,5-*O*-diglucoside. For the first time, (*E*) and (*Z*) isomers of lutein diesters with lauric, myristic, palmitic and stearic acids were found in *C. sativus*: (*Z*)-lutein-*O*-laurate-*O*-palmitate; (*E*)-lutein-*O*-laurate-*O*-palmitate;(*E*)-lutein-*O*-myristate-*O*-laurate; (*9* or *9′Z*)-lutein-*O*-laurate-*O*-palmitate and(*9* or *9′Z*)-lutein-*O*-dipalmitate. Lutein diesters' content (21.46 mg 100/g DW) in tepals from *C. sativus* was comparable to food products; lutein diesters represented 69 % of the total lutein diesters' content.

The characteristic volatile compounds of saffron, the dried, dark-red stigmata of *Crocus sativus* flowers, were determined as 2,6,6-trimethyl-1,3-cyclohexadien-1-carboxaldehyde, namely, safranal; 3,5,5-trimethyl-2-cyclohexen-1-one, namely, isophorone; 3,5,5-trimethyl-3-cyclohexen-1-one, isomer of isophorone; 2,6,6-trimethyl-2-cyclohexen-1,4-dione; and 2,6,6-trimethyl-1,4-cyclohexadiene-1-carboxaldehyde, isomer of safranal (Tarantilis and Polissiou 1997). The quantity of safranal (2,6,6-trimethyl-1,3-cyclohexadiene-1-carboxaldehyde), the main component of saffron's essential oil, isolated by

microsimultaneous hydro-distillation–extraction (MSDE) ranged between 288.1 and 687.9 mg/100 g of saffron, whereas in the case of ultrasound-assisted extraction (USE), safranal ranged between 40.7 and 647.7 mg/100 g of saffron (Kanakis et al. 2004). Its precursor, 4-hydroxy-2,6,6-trimethyl-1-cyclohexene-1-carboxaldehyde (HTCC) ranged between 41.7 and 397.7 mg/100 g of saffron, respectively. Over years of storage at 4 °C, the quantity of safranal remained mostly constant, while the quantity of HTCC decreased over the same periods. Chemicals identified in the essential oil of dried stigmas included 2,6,6-trimethyl-1,3-cyclohexadiene-1-carboxaldehyde (safranal) (81.82 %); α-isophorone (5.57 %); 2-isopropylidene-3-methylhexa-3,5-dienal (4.45 %); 2-hydroxy-3,5,5-trimethyl-2-cyclohexen-1-one (1.90 %); β-isophorone (1.32 %); αβ-dihydro-β-ionone (1.19); 3,4,5,6-tetramethyl-2H-pyran-2-one (1.14 %); eucarvone (0.31 %); β-linalool (0.27 %); 6-(2-butenylidene)-1,5,5-trimethyl-(*Z*,*E*)-cyclohexene (0.26 %); 6-(2-butenylidene)-1,5,5-trimethyl-(*E*,*E*)-cyclohexene (0.21 %); and palmitic acid methyl ester (0.13 %) (Yu-Zhu et al. 2008).

Five main crocetin glycosides were found to be responsible for saffron colour, the best correlations being for *trans*-crocetin di-(β-D-gentiobiosyl) ester ($R^2=0.93$), *trans*-crocetin (β-D-glucosyl)-(β-D-gentiobiosyl) ($R^2=0.94$) and picrocrocin ($R^2=0.92$), the compound accepted as responsible for saffron bitterness (Zalacain et al. 2005). The carotenoid pigments of saffron were found to consist of crocetin di-(β-D-glucosyl)-ester [dicrocin], crocetin-(β-D-gentiobiosyl)-(β-D-glucosyl)-ester[tricrocin]andcrocetin-di-(β-D-gentiobiosyl)-ester [crocin] (Ochiai et al. 2007). The best predictions for quality control of saffron were obtained with the sum of crocetin esters model, followed by the model for *cis*-crocetin (β-D-glucosyl)-(β-D-gentiobiosyl) ester, *trans*-crocetin di-(β-D-gentiobiosyl) ester and *trans*-crocetin (β-D-glucosyl)-(β-D-gentiobiosyl) ester, whereas the worst predictions were found with the picrocrocin and *trans*-crocetin (β-D-gentiobiosyl) ester models (Sánchez et al. 2008).

Safranal was the main volatile component in all of saffron samples, namely, 1, 2 and 3 derived from cultivations of *Crocus sativus* in Salerno (Southern Italy) from 2000 to 2002 and samples 4, 5 and 6 derived from cultivations in Sardinia, Italy, from 1998, 2000 and 2001 (D'Auria et al. 2006). In all samples, 3,5,5-trimethyl-2-cyclohexen-1-one; 3,5,5-trimethyl-2-cyclohexen-1,4-dione; safranal; and 2,4,4-trimethyl-6-hydroxy-3-carboxaldehyde-2,5-cyclohexadien-1-one were found. 5,5-Dimethyl-2-methylene-1-carboxaldehyde-3-cyclohexene; 3,5,5-trimethyl-1,4-cyclohexanedione; and b-ionone were found with nonanal, dihydro-β-ionone and 2,6-di-*t*-butylphenol. Volatile composition of saffron obtained from Salerno in 2001 and 2002 had different profiles determined respectively as 2-methylpropanal (0.02 %, 0.03 %), acetic acid (0.05 %, nd), 3-methylbutanal (nd, 0.03 %), 2-methylbutanal (0.04 %, 0.04 %), 1-pentanol (nd, 0.02 %), hexanal (0.03 % < 0.24 %), 1-t-butylcyclopentadiene (0.08 %, nd), heptanal (nd, 0.21 %), 2(5*H*)-furanone (0.16 % < 0.89 %), octanal (nd, 0.08 %), β-phellandrene (nd, 0.02 %), 6-methyl-5-hepten-2-one (nd, 0.02 %), 3,5,5,-trimethylcyclohex-3-en-1-one (nd, 8.45 %), 2,5-dimethyl-2,4-hexadiene (0.06 %, nd), 1,3,5-trimethylbenzene (0.02 %, nd), benzaldehyde (nd, 0.01 %), nonanal (nd, 0.5 %), 5,5-dimethyl-2-methylene-1-cyclohexylcarbaldehyde (3.50 %, nd), 2-phenylethanol (nd, 0.06 %), 3,5,5-trimethylcyclohexenone (1.77 %, 4.18 %), 4-(1-methylethyl)-benzaldehyde (0.06 %, nd), 3,5,5-trimethylcyclohex-2-en-1,4-dione (0.63 %, 1.09 %), 3,5,5-trimethylcyclohexane-1,4-dione (0.28 %, 3.54 %), 2-hydroxy-3,5,5-trimethylcyclohexenone (0.10 %, nd), safranal (83.97, 49.63 %), 2,7,7-trimethyl-2-4-cycloheptadien-1-one (0.10 %, nd), 2-hydroxy-3,5,5-trimethylcyclohex-2-en-1,4-dione (0.14 %, nd), 4-hydroxy-3,5,5-trimethylcyclohex-2-enone (nd, 0.48 %), 2,6,6-trimethyl-4-hydroxycyclohexa-1,4-dien-3-on-1-carbaldehyde (0.85 %, 5.62 %), dihydro-β-ionone (0.09 %, 0.26 %), dihydro-β-ionol (nd, 0.18 %), 2,6-di-(1,1-dimethylethyl)4-hydroxy-4-methylcyclohexa-2,5-dien-1-one (nd, 0.06 %), 2,6,6-trimethyl-4-hydroxycyclohexen-1-

carbaldehyde (0.73 %, nd), β-ionone (0.09 %, 0.22 %), pentadecane (0.03 %, 0.02 %) and 2,6-di-(1,1-dimethylethyl)-phenol (0.03 %, nd).

Ten main compounds were identified and quantified from saffron samples of Azerbaijanian, Spanish, Indian and Iranian saffron as follows: picrocrocin (1), HTCC (2), kaempferol (3), crocin-1 (4), crocin-2 (5), crocin-3 (6), crocin-4 (7), safranal (8), crocin-5 (9) and crocin-6 (10) (Caballero-Ortega et al. 2004). It was found that the total content of carotenoids in Azerbaijanian and Iranian saffron samples was higher in comparison to other samples. Eleven certified saffron samples (*Crocus sativus*), one each from Azerbaijan, China, Greece, France, India, Iran, Italy, New Zealand, Spain, Turkey and the Sigma Chemical Company, were analysed and quantified for 10 major saffron compounds, namely, picrocrocin, HTCC, 3-gentiobiosyl-kaempferol, *trans*-crocin-4, *trans*-crocin-3, *trans*-crocin-2′, safranal, *cis*-crocin-4, *trans*-crocin-2 and *cis*-crocin-2 (Caballero-Ortega et al. 2007). Results indicated that the Greek, Indian, New Zealand and Spanish saffron extracts possessed the highest concentrations of water-soluble glycosidic carotenoids (⩾8.0 %), suggesting that they could be a good source of this type of metabolites. Forty constituents were identified in Iranian saffron representing 90 % of the total peak area (Jalali-Heravi et al. 2009). The major components were 2,6,6-trimethyl-1,3-cyclohexadiene-1-carboxaldehyde, namely, safranal (26.29 %), bicyclo[3,2,0]hept-2-ene-,4-ethoxy-,endo (5.69 %) and linoleic acid (4.77 %), and 4-hydroxy-2,6,6-trimethyl-1-cyclohexene-1-carboxaldehyde, namely, HTCC (4.44 %) and nonadecanol (3.32 %). Saffron from different regions of Iran varied in volatile components and quantity (Jalali-Heravi et al. 2010). Safranal was the main component of all samples. In addition, 4-hydroxy-2,6,6-trimethyl-1-cyclohexene-1-carboxaldehyde (HTCC), 2(5*H*)-furanone, 2,4,4-trimethyl-3-carboxaldehyde-5-hydroxy-2,5-cyclohexadien-1-one and 2(3*H*)-furanone, dihydro-4-hydroxy were common in all samples with high percentages. Twenty aroma compounds were detected in Spanish saffron, comprising safranal (modified frequency value [MF] 93 %), followed by 2,3-butanedione, hexanal, E-2-nonenal and an odorant with a characteristic aroma of burnt curry that could not be identified (Culleré et al. 2011). All of them had MF values higher than 70 %. Carbonyl compounds showed an important role in saffron aroma. Safranal and isophorone, both volatiles with aromatic descriptors of 'saffron', were quantified. It was demonstrated by means of GC-MS that 3,5,5-trimethyl-2-cyclohexenone; 2,6,6-trimethylcyclohexane-1,4-dione; and acetic acid could be used to differentiate saffron from its source of origin (Carmona et al. 2006a). The saffron volatiles identified included (1) acetic acid; (2) 3,5,5-trimethyl-3-cyclohexen-1-one; (3) 3,7-dimethyl-1,6-octadien-3-ol; (4) 2,6,6-trimethyl, 1,4-cyclohexadiene-1-carboxaldehyde; (5) 3,5,5-trimethyl-2-cyclohexen-1-one; (6) 2,6,6-trimethyl, 1,3-cyclohexadiene-1-carboxaldehyde; (7) 2,6,6-trimethyl-2-cyclohexen-1,4-dione; (8) 2-hydroxy-4,4,6-trimethyl-2,5-cyclohexadien-1-one; and (9) 2,6,6-trimethyl-1,4-cyclohexanedione. The content of acetic acid was very high in samples from Iran or Morocco, while low or undetectable content was observed in Greek and Spanish samples.

Using a two-step, low-pressure liquid chromatography, the following crocins were isolated from the hydroalcoholic extract of yellow pigments of saffron: crocin-1 [crocetin (di-β-D-gentiobiosyl) ester], crocin-2 [crocetin (mono-β-D-gentiobiosyl-mono-β-D-glycoside) ester] and crocin-3 [crocetin (β-D-gentiobiosyl)-ester] with purity as high as 99.04 %, 97.40 %, and 96.70 %, respectively (Zhang et al. 2004). This provided 40 mg crocin-1, 20 mg crocin-2 and 8 mg crocin-3 from 1 g saffron. A liquid chromatographic/tandem mass spectrometric validated method was developed for the detection of chemicals attributing colour, flavour, taste and medicinal properties to saffron (*Crocus sativus* stigma) (Verma and Middha 2010). MS–MS detection was by monitoring precursor (*m/z*) fragmentations of 149 →113 (safranal), 327 → 283 (crocetin), 329 → 167 (picrocrocin), 355 → 327 (dimethylcrocetin), 489 → 327 (crocin E), 535 → 489 (carotenes), 651 → 327 (crocin C), 813 → 652 (crocin B), 975 → 651 (crocin A) and 1,137 → 813 (crocin F). A specification for high-quality saffron of >20 % crocins, >6 % picrocrocin

and not less than 0.3 % of volatiles, calculated as sum of safranal, isophorone and ketoisophorone, was developed by Lechtenberg et al. (2008). Using a micellar electrokinetic chromatography (MEKC) method allowed the quantification of picrocrocin, safranal, crocetin-di-(β-D-gentiobiosyl) ester and crocetin (β-D-glycosyl)-(β-D-gentiobiosyl) ester within 17.5 min, with limit of detection values ranging from 0.006 to 0.04 mg/ml, from a single stigma (Gonda et al. 2012). Employing various tandem mass spectrometric techniques, it was found that saffron comprised a complex mixture of glycoconjugates varying not only in the aglycon structure but also in glycosylation pattern (Koulakiotis et al. 2012). The highest number of structurally diagnostic product ions allowing also determination of the carbohydrate linkage of the gentiobiose moiety of isomeric crocins ((0,4)A(2), (3,5)A(2) product ions indicating a 1→6 carbohydrate linkage) was only achievable by high energy (20 keV) collision-induced dissociation (CID). Fragmentation of the aglycon was not observed by any collision energy regime applied.

Harvest Time, Processing and Storage Effects on Saffron Phytochemicals

Morimoto et al. (1994) found that an indoor cultivation system of *Crocus sativus* was more favourable with regard to the quality of saffron, as compared to the usual cultivation in an open field. Carotenoid glucose esters increased from the period before blooming and reach the maximum in the full blooming period, and were sensitive for the presence of oxygen, light irradiation and beta-glucosidase. Moreover, it was evident that storage of saffron at −20 °C promoted the constant supply of saffron with a homogeneous pharmacological activity. A study on the influence of climatic condition and genotype on compositional characteristics of saffron revealed that of the main crocetin esters in saffron, namely, *trans*-crocetin di-(β-D-gentiobiosyl) ester (1), *trans*-crocetin (β-D-glucosyl)-(β-D-gentiobiosyl) ester (2), *trans*-crocetin (β-D-gentiobiosyl) ester (3), *trans*-crocetin (β-D-glucosyl) ester (4) and picrocrocin, crocetin esters 1 and 2 represented the major components of total crocetin ester amount, as indicated by the high positive correlation (0.971 and 0.833, respectively) (Siracusa et al. 2010). Contents of crocetin esters 2 and 4 and total crocetin ester amount correlated with picrocrocin content (0.794, 0.818 and 0.678, respectively).

The main compounds identified in saffron stigma collected at different harvest times were safranal, picrocrocin, crocin, *cis*-crocin and crocetin (Esmaeilian et al. 2012). Other components included 1,8-cineol, α-pinene, oleanolic acid, kaempferol, 3-gentiobiosyl-kaempferol, cineole and echinocystic acid. Their results revealed that different harvesting times significantly influenced the compounds percentage of saffron. The high content of crocin and picrocrocin resulted in harvest at last harvest time (6:00 h of after flower emergence day). Safranal content decreased due to delay of harvest and highest value was obtained from first harvest time (06:00 h). The most important saffron components, crocins, picrocrocin, and safranal which were respectively responsible for its colour, taste and odour, had respective average values of 29, 14.04 and 0.22 % dry matter across all Moroccan sites (Lage and Cantrell 2009). The statistical analysis showed that crocins were stable under each specific environment tested for 3 years of study. Meanwhile, there was a large variability in safranal content for the same period. Analysis of environmental impact on saffron quality showed that altitude affected crocins ($R^2 = 0.84$).

Crocin pigment concentration was highest (15–17 %) in the saffron samples dried between 35 and 50 °C either in a solar dryer or in an oven dryer, and this also resulted in considerable reduction of normal drying time (Raina et al. 1996). Under these conditions the main flavouring component, safranal, was at its peak value of 60 % in the oil in almost all the samples except the vacuum oven-dried samples which contained 4-β-hydroxysafranal in major amounts. Studies indicated that 4-β-hydroxysafranal may be an intermediate in the formation of safranal. It was observed that prolonged storage affected the pigments and flavour concentration to a great extent, but proper packaging and storage with 5 % moisture in the saffron reduced the deterioration,

thereby increasing the shelf life of the product. A dehydration postharvesting treatment was found to be necessary to convert *Crocus sativus* stigmas into saffron spice (Carmona et al. 2005). They found that the higher the temperature during the process, the higher the proportion of *trans*-crocetin di-(β-D-gentiobiosyl) ester, although *trans*-crocetin (β-D-glucosyl)-(β-D-gentiobiosyl) and *trans*-crocetin di-(β-D-glucosyl) ester decreased while *cis*-crocins did not change significantly. A thermal aging process revealed that *trans*-crocetin di-(β-D-gentiobiosyl) ester increased when saffron was resubmitted to a heating treatment before it was decomposed by the extreme conditions. The picrocrocin extinction during the aging process did not imply a consistent generation of safranal. During the aging process of saffron spice, while the amounts of C10 compounds such as safranal and HTCC increased, the amounts of C9 compounds such as isophorone and 2,6,6-trimethylcyclohexane-1,4-dione decreased (Carmona et al. 2006b). A new compound identified as 4,5,6,7-tetrahydro-7,7-dimethyl-5-oxo-3H-isobenzofuranone appeared to play a very important role in the aging process. It was structurally similar to dihydroactindiolide.

The time of storage and drying method were found to have significant effects of saffron on chemical properties such as colouring strength, aroma and bitterness values (Bolandi and Ghoddusi 2006). Samples dried in microwave oven (300 W) had the highest colouring strength, aroma and bitterness values. Samples dried by a modified Spanish method (55 °C) had higher colouring strength than samples dried by a traditional method (25 °C), but for aroma, traditional samples had significantly higher values. Regarding bitterness, samples dried by microwave oven and modified Spanish method were the same, but traditional samples had significantly lower values. It was also observed that in samples exposed to artificial light (20 W), the colouring strength was decreased while bitterness values were unchanged and aroma values increased at first but remained almost intact after 6 months. Gregory et al. (2005) showed that a brief (20 min) initial period at a relatively high temperature (between 80 and 92 °C) followed by continued drying at a lower temperature (43 °C) produced saffron with a safranal content up to 25 times that of saffron dried only at lower temperatures. They also found that drying with significant airflow reduced the safranal concentration. The results, moreover, indicated that high-temperature treatment had allowed greater retention of crocin pigments than in saffron dried at intermediate temperatures (46–58 °C). Crocetin esters, the compounds responsible for saffron colour, increased their content with no significant differences from other processes when high temperatures (55 °C) were used, thus producing a noticeable increment in saffron colouring capability (del Campo et al. 2010). Similar behaviour was obtained for picrocrocin, the compound responsible for saffron taste, with higher average content at the highest temperature (55 °C) but without significant differences with inferior conditions (40–50 °C). However, more volatile compounds were generated, especially safranal, at higher temperatures, e.g. 55 °C, during the dehydration procedure. Picrocrocin showed high stability with half-life periods ($T_{1/2}$) ranging from >3,400 h at 5 °C in saffron extracts degrading to 9 h in experiments with purified picrocrocin at 100 °C (Sánchez et al. 2011). In saffron extracts, the evolution of the rate constant (k) with temperature showed maximum values at 35 °C, and filtration of the extracts contributed to picrocrocin stability. Large amounts of floral bio-residues rich in phenols (flavonols and anthocyanins) are wasted in saffron (stigma) spice production and need to be stabilized because of rapid deterioration (Serrano-Díaz et al. 2013). It was found that anthocyanins and flavonols were degraded at 110 and 125 °C. The best drying temperatures were 70 and 90 °C for maintaining their physicochemical quality. Anthocyanins and flavonols were stable at 70 and 90 °C with 2, 4, 6 and 8 m/s. Dehydrations at 90 °C with 2, 4 and 6 m/s were the most appropriate, due to a better colour and greater similarity to control samples for their flavonols and anthocyanins.

Ultrasound-assisted extraction was found to enhance and speed up the recovery of the bioactive apocarotenoids, i.e. crocins and picrocrocin from dry saffron stigmas (Kyriakoudi et al. 2012).

The recoveries of crocins and picrocrocins were 50 %, 30 min, 0.2 s and 0.44 %, 30 min, 0.6 s, respectively. They found that the extraction conditions were useful for both industrial and analytical applications and should be considered in a forthcoming revision of the ISO 3632-2 technical standard.

Nineteen volatile compounds were identified in 73 saffron samples belonging to three different storage times (<1 year, 3–4 and 8–9 years) and their aromatic notes were assigned (Maggi et al. 2010): safranal; 4-hydroxy-2,6,6-trimethyl-3-oxocyclohexa-1,4-diene-1-carboxaldehyde; HTCC(4-hydroxy-2,6,6-trimethyl-1-cyclohexen-1-carboxaldehyde; isophorone (3,5,5-trimethyl)-2-cyclohexene-1-one; 2,2,6-trimethyl-1,4-cyclohexanedione; hydroxy-3,5,5-trimethyl-2-cyclohex-1-one; 2,6,6-trimethyl-2-cyclohexene-1,4-dione, known also as 4-ketoisophorone; 2-hydroxy-4,4,6-trimethyl-2,5-cyclohexadien-1-one; 4-hydroxy-2,6,6-trimethyl-3-oxocyclohex-1-en-1-carboxaldehyde; isophorone-4-methylene; 2-hydroxy-3,5,5-trimethylcyclohex-2-en-1,4-dione; 2,6,6-trimethyl-1,4-cyclohexadiene-1-carboxaldehyde; isomer of 4-hydroxy-2,6,6-trimethyl-3-oxocyclohex-1-en-1-carboxaldehyde; 2-phenylethanol; 3-[(*E*)-but-1-enyl]-2,4,4-trimethyl-cyclohex-2-enol;2,6,6-trimethyl-3-oxo-1-cyclohexen-1-carboxaldehyde; 2,2-dimethyl-cyclohexane-1-carboxaldehyde; and 4-hydroxy-3,5,5-trimethyl-2-cyclohex-1-one. In addition to safranal (30.14–43.94 % in mass of total volatiles), the main compound found, other major compounds were 4-hydroxy-2,6,6-trimethyl-1-cyclohexen-1-carboxaldehyde (HTCC) and 3,5,5-trimethyl-2-cyclohexene-1-one. These compounds were significantly different for less than 1 year of storage when compared with the 3–4 and 8–9 years of storage, although the minor constituents 2-hydroxy-3,5,5-trimethylcyclohex-2-en-1,4-dione and isomer of 4-hydroxy-3,5,5-trimethyl-2-cyclohex-1-one varied significantly for all three harvests. Saffron with less than 1 year of storage contained a higher proportion of saffron, flower and spicy descriptors, while the oldest saffrons (3–4 and 8–9 years of storage) contained volatiles with vegetal, caramel and citrus notes. The aromatic notes that contributed most to saffron storage differentiation were spicy, freshly cut grass and vegetable.

Corm/Bulb Phytochemicals

Amines, starch, fatty acids and sterols were found in *C. sativus* bulbs (Loukis et al. 1983).

As sprouting progressed, starch content decreased and total sugars increased steadily in saffron corms (Chrungoo and Farooq 1985). During dormancy, tissue concentration of soluble protein did not change appreciably but increased steadily as growth and development proceeded in the buds. Protein-related specific activity of amylase increased steadily as sprouting progresses. The specific activity of soluble starch phosphorylase did not change markedly during the period of development between May and October, but that of granule-bound enzyme decreased progressively during the same period.

Phenolic compounds detected in saffron corms included catechol, vanillin, salicylic acid, cinnamic acid, *p*-hydroxy benzoic acid, gentisic acid, syringic acid, *p*-coumaric acid, gallic acid, *t*-ferulic acid and caffeic acid (Esmaeili et al. 2011). The highest phenolic content in waking corms was observed for gentisic acid (5.693 μg/g) and the lowest for gallic acid (0.416 μg/g); also these two phenolic compounds are the highest (0.929 μg/g) and lowest (0.017 μg/g) phenolics in dormant corms, respectively. A mixture of highly glycosylated triterpenoid saponins (CS5) was isolated from *Crocus sativus* corms (Rubio-Moraga et al. 2011). The mixture (CS5-1) contained two new oleanane-type saponins, denominated Azafrine 1 and Azafrine 2. The bidesmosidic saponins were respectively characterized as 3-*O*-β-D-glucopyranosiduronic acid echinocystic acid 28-*O*-β-D-galactopyranosyl-(1→2)-α-l-arabinopyranosyl-(1→2)-[β-D-xylopyranosyl-(1→4)]-α-D-rhamnopyranosyl-(1→2)-[4-*O*-di-α-l-rhamnopyranosyl-3,16-dihydroxy-10-oxo-hexadecanoyl]-α-D-fucopyranoside and 3-*O*-β-D-galactopyranosiduronic acid echinocystic acid 28-*O*-β-D-galactopyranosyl-(1→2)-α-l-arabinopyranosyl-(1→2)-[β-D-xylopyranosyl-

(1→4)]-α-L-rhamnopyranosyl-(1→2)-[4-*O*-di-α-L-rhamnopyranosyl-3,16-dihydroxy-10-oxo-hexadecanoyl]-β-D-fucopyranoside.

Volatile compounds identified in the corm extract included hexadecanoic acid (33.23 %); octadecadienoic acid (27.55 %); palmitic acid ethyl ester (11.21 %); *n*-tetradecane (6.17 %); 1,3,5-tribenzoylbenzene (2.78 %); *n*-heptadecane (2.02 %); *n*-pentadecane (1.74 %); *n*-catane (1.39 %); diethyltoluamide (1.342 %), *n*-tridecane (1.31 %); *n*-octadecane (1.13 %); and *n*-eicosane (0.97 %) (Yu-Zhu et al. 2008). Thirty-four components were extracted from the volatile oil from *C. sativus* corms comprising monoterpenoids (1.215), sesquiterpenoids (1.59 %), total terpenoids (2.80 %), hydrocarbons (0.46 %), alcohols (0.26 %), aldehydes (8.80 %), esters (0.43 %), acids (26.75 %), sum aliphatics (36.7 %), aldehydes (0.58 %), frans (0.12 %), latones (59.80 %) and total aromatics (60.50 %) (Masuda et al. 2012). The main components were 2(*5H*)-furanone (59.8 %), hexadecanoic acid (15.65 %), (*E*)-2-methyl-2-butenal (8.44 %), (*Z,Z*)-9,12-octadecadienoic acid (4.74 %) and heptadecanoic acid (3.98 %). Other minor components were ethyl acetate (0.43 %), (*E*)-2-hexanal (0.17 %), hexanol (tr), 1-octen-3-ol (0.26 %), 2-pentylfuran (0.12 %), phenylacetaldehyde (0.58 %), nonanal(0.19%),2,6,6-trimethyl-1,3-cyclohexadiene-1-carboxaldehyde safranal (1.21 %), decanol (tr), tetradecane (tr), β-caryophyllene (0.15 %), *ar*-curcumene (0.23 %), α-zingiberene (0.72 %), pentadecane (tr), β-bisabolene (tr), β-sesquiphellandrene (0.49 %), tetradecanoic acid (0.32 %), octadecane (tr), pentadecanoic acid (0.32 %), nonadecane (tr), eicosane (tr), *(Z)*-9-octadecanoic acid (1.74 %), docosane (tr), tetracosane (tr), pentacosane (tr), hexacosane (tr), heptacosane (0.46 %), octacosane (tr) and nonacosane (tr). Seventeen mineral and trace elements (Mg, Na, Ca, K, Mn, Zn, Cu, Pb, Hg, Ni, Fe, Co, Cd, Sr, Rb, Sc and Br) were found in *Crocus sativus* corms in two different physiological (dormancy and waking) stages (Esmaeili et al. 2013).

A novel glycoconjugate isolated from saffron corm composed mainly of polysaccharide, representing 94.5 % of the molecule, and was dominated by a 36.4 % of rhamnose; its protein backbone was composed mainly of aspartic acid/asparagine, alanine, glutamic acid/glutamine, glycine and serine (Escribano et al. 1999c, 2000a). A glycoconjugate was also synthesized in callus cultures of saffron corm, made up of about 90 % carbohydrate and 10 % protein (Escribano et al. 1999b). A mannan-binding lectin was isolated from the corms (Escribano et al. 2000b). The native protein formed noncovalently linked aggregates of about 80 kDa apparent molecular mass, mainly composed of two charged heterogeneous basic subunits of approximately 12 kDa. Their *N*-terminal sequences shared 25 % similarity and were homologous to the *N*- and *C*-terminal domains of monocotyledonous mannose-binding lectins, respectively. Further, the *N*-terminal domain subunit exhibited 56 % similarity with curculin, a sweet protein with taste-modifying activity. *Crocus sativus* lectin (CSL) was isolated from the bulbs and found to be truly mannose specific (Kakehi et al. 2003). Three L-lactate dehydrogenase isoenzymes were detected in saffron corms (Keyhani and Sattarahmady 2002). All three dehydrogenases were substrate inhibited by ferricyanide, but at different concentrations. Catalytic efficiency, calculated per mg corm extract protein, was 1.9, 1.0 and 0.4 per minute, respectively at pH 5.5, 7.5 and 9.5.

Phytochemicals from Sprouts and Cell Suspension Cultures

Two new phenolic glucosides, a new γ-lactone glucoside and adenosine were isolated from the sprouts of *Crocus sativus* (Gao et al. 1999). The new compounds were characterized as 2,4- dihydroxy-6-methoxyacetophenone-2β-D-glucopyranoside, 2,3,4-trihydroxy-6-methoxyacetophenone-3-β-D-glucopyranoside and 3-(S)-3-β-D-glucopyranosyloxybutanolide, respectively.

Callus extracts of *Crocus sativus* exhibited the ability to transform all-*trans*-crocetin into its related glycosides between pH 7.0 and 7.6 in the presence of uridine diphosphoglucose (Dufresne et al. 1997). The kinetics of synthesis for each glycoside appeared to indicate that two distinct

glucosyl transferases were implicated in the synthesis of crocin, all-*trans*-crocetin di-(β-D-gentiobiosyl) ester. *Crocus sativus* cell suspension culture converted crocetin into several glycosyl esters when the culture was fed with the encapsulated substrate (Dufresne et al. 1999). A new major pigment crocetin di-neapolitanosyl ester was identified in *C. sativus* cell suspension culture. The other pigments were mixed forms of neapolitanosyl, gentiobiosyl and glucosyl esters. Glycosylated pigments were stored in vacuoles. A UDP-Glc–crocetin 8,8′-glucosyltransferase involved in the biosynthesis of crocetin monoglucosyl and diglucosyl esters was extracted from saffron cell cultures and purified 300-fold (Côté et al. 2001). The purified enzyme preparation was highly specific for crocetin and formed ester bonds between the glucose moiety of UDP-Glc and the free carboxyl functions of crocetin. Yang et al. (2005) found that *C. sativus* cells could synthesize crocin, crocetin digentiobiosyl ester, in suspension cultures. They found that GTase1 and GTase2 could catalysed the formation of crocetin glucosides in vitro. GTase1 activity was higher during the first 4 days of crocin glucosides biosynthesis, but decreased after 4 days. The formation and accumulation of crocin increased during the first 6 days and stabilized on the eighth day.

Metabolites derived from saffron stigmata had been shown to exert numerous therapeutic effects such as hypolipidaemic, antitussive, antioxidant, anticancer, antidiabetic activities and many others (Rios et al. 1996; Abdullaev 2002; Melnyk et al. 2010; Poma et al. 2012; Gutheil et al. 2012). Many of the pharmacological properties of saffron could be attributed to a number of its compounds such as crocetins, crocins and other substances having strong antioxidant and radical scavenger properties against a variety of radical oxygen species and proinflammatory cytokines. *C. sativus* had been reported to possess a number of medicinally important activities such as antihypertensive, anticonvulsant, antitussive, antigenotoxic and cytotoxic effects, cardioprotective, neuroprotective anxiolytic aphrodisiac, antioxidant, antidepressant, antinociceptive, anti-inflammatory and relaxant activity (Srivastava et al. 2010; Melnyk et al. 2010). Saffron and its bioactive constituents had been reported to improve memory and learning skills, increase blood flow in retina and choroid and alleviate or prevent such health problems as gastric disorders, cardiovascular disease, insulin resistance, depression, premenstrual syndrome, insomnia and anxiety. Saffron also shows promise in the prevention and maintenance of cancer due to its antioxidant properties (Abdullaev 2002; Abdullaev and Espinosa-Aguirre 2004; Melnyk et al. 2010).

Antioxidant Activity

Saffron flower and its floral parts (tepals, stamens, styles and stigmas) and floral bio-residues studied were found to be potential antioxidants (Serrano-Díaz et al. 2012). The highest phenolic, flavonoid and anthocyanin contents were observed in tepals. Stamens showed lower phenolic, flavonoid and anthocyanin contents than those of whole flowers, tepals and floral bio-residues. Crocetin esters were not found in tepals or stamens. Stamens exhibited the most potent LOO(•) and OH(•) radical scavenging activity, being higher than those of food antioxidant propyl gallate. Flowers of saffron, tepals, stamens, styles and floral bio-residues showed LOO(•), OH(•) and ABTS(•-) radical scavenging activity, while stigmas showed LOO(•) and ABTS(•-) radical scavenging activity. All samples studied improved the oxidative stability of sunflower oil in Rancimat test. These antioxidant properties could suggest the application of this floral material as functional ingredients with the subsequent added value. Montoro et al. (2012) reported the following antioxidant activity of *C. sativus* flower waste products to scavenge the cation 2,2′-azinobis(3-ethylbenzothiozoline-6-sulphonate) ($ABTS^+$) and expressed in Trolox equivalent antioxidant capacity (TEAC): petals 0.233 μg/ml, flowers 0.097 μg/ml, stamens 0.222 μg/ml and flower juice 0.263 μg/ml.

A methanol extract of *Crocus sativus* exhibited high antioxidant activity (Assimopoulou et al. 2005), although it contains several active and inactive constituents. In trying to approximate

a structure–activity relationship, of two bioactive constituents of saffron, crocin showed high DPPH radical scavenging activity (50 and 65 % for 500 and 1,000 ppm solution in methanol, respectively), followed by safranal (34 % for 500 ppm solution). Protocatechuic acid, kaempferol and kaempferol 7-*O*-β-D-glucopyranoside isolated from saffron petals were more effective in scavenging DPPH radicals than alpha-tocopherol (Li et al. 2004). In the DPPH radical scavenging activity and the Co(II)-induced luminol chemiluminescence assay, the diethyl ether, ethyl acetate and aqueous fractions of saffron petals demonstrated the strongest antioxidant capacity (Termentzi and Kokkalou 2008). The good antioxidant capacity detected in the various fractions of *Crocus sativus* petals could be attributed to the presence of flavonoids.

Studies by Ordoudi et al. (2009) found that saffron extracts exhibited a remarkable intracellular antioxidant activity that could not be revealed using assays repeatedly applied to the evaluation of phenolic-type antioxidants. Saffron extract activity was found to be rather negligible in all cell-free model systems. In contrast in the human monocyte system, saffron extracts or free crocetin was found to reduce ROS (reactive oxygen species) production as effectively as the phenolic antioxidants. The crocins, water-soluble carotenoids responsible for the colour of saffron and gardenia, were found to possess antioxidant activity when tested by four in vitro antioxidant models (Chen et al. 2008). However, in anti-haemolysis, DPPH radical scavenging and lipid peroxidation assays, gardenia resin fraction exhibited significantly stronger antioxidant activity than crocins, and no correlation between total crocin contents and antioxidative function was found. In the phosphomolybdenum assay, antioxidant capacities of fractions and extracts correlated with total crocin contents ($R = 0.93$). Also, comparison of results indicated that sugars attached to the crocetin moiety appeared to be beneficial for the antioxidant activity of these water-soluble pigments.

The activity of antioxidant enzymes during in vitro organogenesis in *Crocus sativus* was investigated by Vatankhah et al. (2010). They found that protein content and superoxide dismutase activity decreased in regenerated shoots and roots and increased in sprouting shoots, while catalase (CAT), peroxidase (POX) and polyphenol oxidase (PPO) activities increased during organogenesis and decreased in sprouting shoots. High CAT and PPO activities were detected in regenerated roots, whereas high POX activity was observed in regenerated shoot. Seven POX isoforms were expressed in regenerated root and shoot, while two isoforms (POX1 and POX2) were expressed in meristem explant. The radical scavenging activities of saffron corms evaluated by 1,1-diphenyl-2-pycrylhydrazyl (DPPH) test gave EC_{50} values about 2,055 ppm and 8,274 ppm for waking and dormant corms, respectively (Esmaeili et al. 2011). Studies by Karimi et al. (2010) showed that saffron stigma possessed antioxidant activity. The free radical scavenging and ferric reducing power activities were higher for the methanolic extract of saffron stigma at a concentration of 300 µg/ml, with values of 68.2 % and 78.9 %, respectively, as compared to the corresponding boiling water and ethanolic extracts, but the activities were lower than those of antioxidant standards such as BHT and α-tocopherol. Total phenolic content for methanolic saffron extract was 6.54 mg gallic acid equivalent (GAE)/g dry weight (DW), and for total flavonoids, 5.88 mg rutin equivalent/g DW, which were also higher than values obtained from the ethanolic and boiling water extracts. Additionally the RP-HPLC analyses indicated the presence of gallic acid and pyrogallol as two bioactive compounds.

In model systems of beta-carotene–linoleate and DPPH, saffron petal extract at 500 ppm concentration showed 91.4 and 74.2 % antioxidant activity which was comparable with that of TBHQ (93.1 and 77.9 %) at 100 ppm (Goli et al. 2012). Total phenolic content in saffron petal extract was 3.42 mg gallic acid/g dry weight. The results showed that saffron petal could be considered as a bioresource of phenolic compounds with high antioxidant activity. Saffron corm, tepal and leaf extracts were assayed for antioxidant activity using β-carotene/linoleate model system, reducing power, DPPH and nitric oxide

radical scavenging, and iron and copper ion chelation (Sánchez-Vioque et al. 2012). Best antioxidant properties were observed for leaf extract, which totally inhibited the oxidation of β-carotene at 10 μg/ml and showed a DPPH scavenger activity up to 32 times higher than those reported for traditional sources of antioxidants like grapes and berries. Tepal extract showed an extensive inhibition of β-carotene oxidation, and significant scavenging NO radical and Cu^{2+}-chelating activities. In contrast, corm extract was a poor antioxidant although it showed a slight Cu^{2+}-chelating activity. They concluded that tepals and especially leaves of saffron constituted an exploitable source of antioxidant and metal chelating compounds.

The pattern of reactive oxygen species-scavenging enzyme production was different in saffron corms cultivated in normoxic and hypoxic–anoxic conditions (Keyhani et al. 2006). In normoxic conditions, only the activities of peroxidases and superoxide dismutase (SOD) were stimulated. In dormant corms placed under hypoxia–anoxia, the activities of catalase, SOD and glutathione peroxidase were stimulated, with the highest stimulation observed for catalase, followed by SOD and then glutathione peroxidase. In corms that had been rooted for 3 days before being placed in hypoxia–anoxia, the activities of all ROS-scavenging enzymes studied were stimulated with the highest stimulation still observed for catalase, followed by the peroxidases and finally SOD. Catalase was the prevailing enzyme produced under hypoxia–anoxia.

Anticancer Activity

In Vitro Studies

Abdullaev and Frenkel (1992b) examining the effect of saffron extract on macromolecular synthesis in three human cell lines, A549 cells (derived from a lung tumour), WI-38 cells (normal lung fibroblasts) and VA-13 cells (WI-38 cells transformed in vitro by SV40 tumour virus), found that the malignant cells were more sensitive than the normal cells to the inhibitory effects of saffron on both DNA and RNA synthesis. There was no effect on protein synthesis in any of the cells. Incubation of HeLa cells with saffron flower extract for 3 h resulted in significant inhibition of colony formation and cellular nucleic acid synthesis with EC_{50} of approximately 100–150 μg/ml (Abdullaev and Frenkel 1992a). In contrast, there was no inhibition of cellular protein synthesis at concentrations of saffron extract as high as 400 μg/ml. Incubation of three malignant HeLa (cervical epithelioid carcinoma), A549 (lung adenocarcinoma) and VA13 (SV-40 transformed foetal lung fibroblast) cells with crocetin for 3 h caused a dose-dependent inhibition of nucleic acid and protein synthesis (Abdullaev 1994). Crocetin also had a dose-dependent inhibitory effect on DNA and RNA synthesis in isolated nuclei and suppressed the activity of purified RNA polymerase II. Separate studies demonstrated that the doses inducing 50 % inhibition of promyelocytic leukaemia HL-60 cell growth were 0.12 μM for all-*trans* retinoic acid (ATRA) and for carotenoids of saffron 0.8 μM for dimethylcrocetin (DMCRT), 2 μM for crocetin CRT and 2 μM for crocins (CRCs) (Tarantilis et al. 1994). At 5 μM, all these compounds induced differentiation of HL-60 cells, at 85 % for ATRA, 70 % for DMCRT, 50 % for CRT and 48 % for CRCs. The seminatural (DMCRT and CRT) and natural carotenoids (CRCs) of *Crocus sativus* are not provitamin A precursors and could therefore be less toxic than retinoids, even at high doses. Nair et al. (1995) first reported the anticancer activity of saffron extract (dimethylcrocetin) against a wide spectrum of murine tumours and human leukaemia cell lines. Dose-dependent cytotoxic effect to carcinoma, sarcoma and leukaemia cells in vitro was noted. Their results indicated significant inhibition in the synthesis of nucleic acids but not protein synthesis and that saffron (dimethylcrocetin) disrupted DNA–protein interactions, e.g. topoisomerases II, important for cellular DNA synthesis.

Saffron and its main components crocin, crocetin, picrocrocin and safranal exhibited anticancer activity in vitro (Escribano et al. 1996). Doses inducing 50 % cell growth inhibition (LD_{50}) on HeLa cells were 2.3 mg/ml for an ethanolic extract of saffron dry stigmas, 3 mM for crocin,

0.8 mM for safranal and 3 mM for picrocrocin. Crocetin did not show cytotoxic effect. Cells treated with crocin exhibited wide cytoplasmic vacuole-like areas, reduced cytoplasm, cell shrinkage and pyknotic nuclei, suggesting apoptosis induction. A novel glycoconjugate isolated from saffron corm extracts shows remarkable cytotoxic activity on cultured human cancer cells (HeLa) (Escribano et al. 1999c). HeLa cells exposed to this glycoconjugate showed swelling and local plasma membrane evaginations, suggesting that cytotoxicity is mediated by extracellular fluid uptake. A glycoconjugate from saffron corm callus was cytotoxic against human cervical epithelioid carcinoma cells ($IC_{50} = 7$ mg/ml) (Escribano et al. 1999b). The glycoconjugate isolated from saffron corm exhibited potent cytotoxic activity in vitro against human tumoral cells derived from fibrosarcoma, cervical epithelioid carcinoma and breast carcinoma, with IC_{50} values of 7, 9 and 22 µg/ml, respectively (Escribano et al. 2000a). Studies of intracellular calcium fluctuations, and release of lactate dehydrogenase in human cervical epithelioid carcinoma cells, showed that this compound caused plasma membrane damage, allowing movements of both calcium and macromolecules and leading to cell lysis. Analysis of DNA fragmentation showed that cell death was not mediated by apoptosis. The proteoglycan was about eight times more cytotoxic for malignant cells than for their normal counterparts. In addition, 100 µg/ml of proteoglycan produced 50 % in vitro lysis of normal human erythrocytes, whereas 320 µg/ml induced about 60 % cell death on cultured human hair follicles. The results suggested a distinctive cytotoxic activity of this molecule on different human cell types.

In vitro studies showed that saffron was not toxic, non-mutagenic, non-antimutagenic and non-comutagenic (Abdullaev et al. 2002). However, when using the *Salmonella typhimurium* TA98 strain in the Ames/*Salmonella* test system, saffron showed non-mutagenic as well as non-antimutagenic activity against benzo[a]pyrene (BP)-induced mutagenicity and demonstrated a dose-dependent comutagenic effect on 2-aminoanthracene (2AA)-induced mutagenicity (Abdullaev et al. 2003). The saffron component responsible for this unusual comutagenic effect was safranal. Saffron extract itself and some of its ingredients displayed a dose-dependent inhibitory activity against different types of human malignant cells HeLa (human cervical epithelioid carcinoma), A-204 (human rhabdomyosarcoma) and HepG2 (human hepatocellular carcinoma) in vitro (Abdullaev et al. 2002, 2003). HeLa cells were more susceptible to saffron than other tested tumour cells. Saffron crocin derivatives possessed a stronger inhibitory effect on tumour cell colony formation. The results suggested that saffron itself, as well as its carotenoid components, might be used as potential cancer chemopreventive agents. In a recent study, MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium] assay revealed a significant and concentration-dependent cytotoxic effect of safranal on HeLa and MCF-7 cancer cell lines (Malaekeh-Nikouei et al. 2013). Liposomal safranal showed enhanced effect compared to the safranal solution, based on its IC_{50} concentrations. Flow cytometry results revealed induction of apoptosis of both cancer cells by safranal. It was concluded that liposome encapsulation improved antitumour effect of safranal. Of ten compounds, viz., picrocrocin, HTCC, kaempferol, crocin, crocin-2, crocin-3, crocin-4, safranal, crocin-5 and crocin-6 from Spain tested for cytotoxicity activities in vitro on human HeLa tumour cells, crocin-2 gave 36 % inhibition, HTCC 30 %, picrocrocin and crocin-1 gave 27 %, crocin-4 and crocin-5 25 %, crocin-6 18 %, crocin-3 10 % and safranal 3 %, the lowest (Caballero-Ortega et al. 2004).

Saffron could decrease cell viability in malignant cancerous cells in a concentration and time-dependent manner (Tavakkol-Afshari et al. 2008). The IC_{50} values against HeLa and HepG2 were 800 and 950 µg/ml after 48 h, respectively. The data indicated that saffron could cause cell death in HeLa and HepG2 cells, in which apoptosis or programmed cell death played an important role. Separate in vitro studies showed that crocin exerted antiproliferative activity of hepatocarcinoma HepG2 cells by inhibition of telomerase activity and also down-regulation of hTERT gene expression (Noureini and Wink 2012).

Studies by Samarghandian et al. (2010) showed that the ethanolic extract of saffron decreased cell viability in malignant carcinomic human alveolar basal epithelial cells in a concentration and time-dependent manner. The IC_{50} values against the lung cancer cell line were determined as 1,500 and 565 µg/ml after 24 and 48 h, respectively. However, the extract at different and higher concentrations could not significantly decrease the cell viability in non-malignant L929 cells. The results indicated saffron to be safe for L929, but the extract exerts pro-apoptotic effects in a lung cancer-derived cell line and could be considered as a potential chemotherapeutic agent in lung cancer.

In vitro studies showed that crocin from *Crocus sativus* possessed significant antiproliferation effects on human colorectal cancer cells (HCT-116, SW-480 and HT-29) (Aung et al. 2007). The purity of crocin was found to be 95.9 %, and the content of crocin in the extract was 22.9 %. Significant concentration-related inhibition effects of the extract on all three colorectal cancer cell lines were observed. The proliferation was reduced most significantly in HCT-116 cells, to 45.5 % at 1.0 mg/ml and to 6.8 % at 3.0 mg/ml. Crocin at 1.0 mM significantly reduced HCT-116, SW-480 and HT-29 cell proliferation to 2.8 %, 52 %, and 16.8 %, respectively. Significant antiproliferative effects were also observed in non-small cell lung cancer cells. However, *Crocus sativus* extract did not significantly affect the growth of noncancer young adult mouse colon cells. The study demonstrated that *Crocus sativus* extract and its major constituent, crocin, significantly inhibited the growth of colorectal cancer cells while not affecting normal cells. In vitro studies showed the varying effect of saffron in HCT-116 colorectal cancer cells with different p53 status (HCT wild type and HCT p53−/−) (Bajbouj et al. 2012). Saffron induced DNA damage and apoptosis in both cell lines with a more pronounced apoptosis induction in HCT-116 p53 wild-type cells. However, autophagy delayed the induction of apoptosis in HCT-116 p53 −/− cells.

Saffron extract (200–2,000 µg/ml) decreased cell viability in breast cancer MCF-7 cells in a concentration- and time-dependent manner with an IC_{50} of 400 µg/ml after 48 h (Mousavi et al. 2009). Analysis of DNA fragmentation showed apoptotic cell death in MCF-7 cell treated with saffron extract. Saffron-induced apoptosis could be inhibited by pan-caspase inhibitors, indicating caspase-dependent pathway was induced by saffron in MCF-7 cells. Bax protein expression was also increased in saffron-treated cells. In another study, saffron ethanolic extract decreased cell viability of the malignant carcinomic human alveolar basal epithelial cells (A549) in a concentration- and time-dependent manner (Samarghandian et al. 2011). The IC_{50} values against the A549 cell lines were determined as 1,200 and 650 µg/ml after 24 and 48 h, respectively. Saffron induced apoptotic cell death of the A549 cells in a concentration-dependent manner. Saffron aqueous extract exhibited inhibitory effects on the growth of both human transitional cell carcinoma TCC 5637 at concentration >200 µg/ml and mouse non-neoplastic fibroblast L929 cell lines at concentrations of 50–200 µg/ml (Feizzadeh et al. 2008). Significant reduction of the survived cells was seen at concentrations of 400 and 2,000 µg/mL for TCC and L929 cell lines, respectively. This effect was dose dependent.

Studies showed that crocin induced apoptosis and G1-phase cell cycle arrest of human pancreatic cancer cell line (BxPC-3) while decreasing cell viability in a dose-dependent and time-dependent manner (Bakshi et al. 2010). Cells treated with 10 µg/L crocin exhibited apoptotic morphology and reduction of volume. DNA analysis revealed typical ladders as early as 12 h after treatment indicative of apoptosis. Separate studies showed that crocin and its liposomes could cause cell death in HeLa and MCF-7 cells, in which liposomal encapsulation improved cytotoxic effects (Mousavi et al. 2011). The 3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay revealed a remarkable and concentration-dependent cytotoxic effect of crocin on HeLa and MCF-7 cells in comparison with non-malignant cell line (L929). Crocin liposomal forms (IC_{50} values after 48 h: 0.61, 0.64 and 1.2 mM) showed enhanced cytotoxic effect compared with the crocin (IC_{50} after

48 h: 1.603 mM) in HeLa cells. Crocin and its liposomal form induced a sub-G1 peak in treated cells, indicating apoptosis is involved in this toxicity. Liposomal encapsulation was found to enhance apoptogenic effects of crocin on cancerous cells. A mixture of highly glycosylated triterpenoid saponins (CS5) isolated from *Crocus sativus* corms showed cytotoxic activity against HeLa tumoral cells (Rubio-Moraga et al. 2011).

Chryssanthi et al. (2011a) found that after 24 h incubation, crocetin significantly inhibited not only proliferation of MDA-MB-231 cells but also invasion at 1 and 10 μM and also that cancer invasiveness and metastasis were associated with the expression of matrix metalloproteinases (MMPs). Incubation with 10 μM crocetin for 24 h in serum-free conditions reduced pro-MMP-9 activity and pro-MMP-2/MMP-2 protein levels. When cultured in media with sera 2 and 5 %, crocetin at 10 μM also reduced gelatinase activity. The above findings showed that crocetin, the main metabolite of crocins, inhibited MDA-MB-231 cell invasiveness via downregulation of MMP expression. Crocetin exhibited protective effect against angiogenesis induced by vascular endothelial growth factor (VEGF) (Umigai et al. 2012). Crocetin significantly suppressed VEGF-induced tube formation by human umbilical vein endothelial cells and migration of human retinal microvascular endothelial cells. It was found that crocetin suppressed VEGF-induced angiogenesis by inhibiting migration and that the inhibition of phosphorylated p38 and protection of vascular endothelial-cadherin expression may be involved in its underlying mechanism of action.

Animal Studies

Oral administration of 200 mg/kg body weight of saffron extract increased the life span of sarcoma-180 (S-180), Ehrlich ascites carcinoma (EAC) and Dalton's lymphoma ascites (DLA) tumour-bearing mice to 111.0, 83.5 and 112.5 %, respectively (Nair et al. 1991a). The same extract was found to be cytotoxic to P38B, S-180, EAC and DLA tumour cells in vitro. The mechanism of action of the extract was indicated at the site of DNA synthesis. Toxicity studies showed that the haematological and biochemical parameters were within normal range. Saffron delayed ascites tumour growth and increased the life span of the treated mice compared to untreated controls by 45–120 % (Nair et al. 1995). In addition, it delayed the onset of papilloma growth, decreased incidence of squamous cell carcinoma and soft tissue sarcoma in treated mice. Bakshi et al. (2009) found that crocin decreased cell viability in Dalton's lymphoma cells in a concentration- and time-dependent manner. Significant increase in the life span of Dalton's lymphoma-bearing mice was observed by 37 % and 44 %, respectively. Furthermore, animals given treatment before induction of cancer showed 58 % increase in life span, and there was 95.6 % reduction of solid tumour in crocin-treated animals on the 31st day after tumour inoculation. Crocin also showed significant impact on haematological parameters, like the haemoglobin count and numbers of lymphocytes. These findings supported the conclusion that crocin from *Crocus sativus* possessed significant antitumour activity.

Topical application of *Nigella sativa* and *Crocus sativus* extracts 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 these extracts delayed the onset of papilloma formation and reduced the mean number of papillomas per mouse, respectively. Also, intraperitoneal administration of *Nigella sativa* (100 mg/kg body wt.) and oral administration of *Crocus sativus* (100 mg/kg body wt.) 30 days after subcutaneous administration of 20-methylcholanthrene (MCA) (745 nmol×2 days) to albino mice restricted soft tissue sarcoma incidence to 33.3 % and 10 %, respectively, compared with 100 % in MCA-treated controls. Significant reduction in mouse skin papilloma formation, initiated by 7–12 dimethylbenz[a] anthracene (DMBA) and promoted with croton oil, was found with saffron aqueous infusion application in the pre-initiation and post-initiation periods and in particular when the agent was administered both pre- and post-initiation (Das et al. 2004). The inhibition was partly attributed

to the modulatory effects of saffron on some phase II detoxifying/antioxidant enzymes like glutathione S-transferase and glutathione peroxidase, as well as catalase and superoxide dismutase.

Animal studies by Garcia-Olmo et al. (1999) found that life span was extended and tumour growth was slower in crocin-treated adenocarcinoma-bearing female rats, but no significant antitumour effect was found in male rats. In assays in vitro, crocin had a potent cytotoxic effect on human and animal adenocarcinoma cells (HT-29 and DHD/K12-PROb cells, $LD_{50} = 0.4$ and 1.0 mM, respectively). It was concluded that long-term treatment (13 weeks) with crocin enhanced survival selectively in female rats with colon cancer without major toxic effects. The effects of crocin might be related to its strong cytotoxic effect on cultured tumour cells. Saffron ingestion inhibited the formation of 7,12 dimethylbenz[a]anthracene (DMBA)-induced skin papillomas in mice and simultaneously reduced their size (Das et al. 2010). This may be due, at least in part, to the induction of antioxidant cellular defence systems.

In a recent study, saffron aqueous extract dose-dependently inhibited 1-methyl-3-nitro-1-nitrosoguanidine (MNNG)-induced gastric cancer progression in Wistar albino rat (Bathaie et al. 2013). Twenty percent of cancerous rats treated with higher doses of saffron extract were completely normal at the end of experiment, and there was no rat with adenoma in the saffron extract-treated groups. Further the elevated lactate dehydrogenase and decreased plasma antioxidant activity due to cancer induction were ameliorated after saffron treatment of rats.

Polyethylene glycolated nanoliposomes containing crocin at doses of 50 and 100 mg/kg significantly decreased tumour size of C26 colon carcinoma in mice and increased survival rate compared with PBS and crocin in buffer (100 mg/kg) groups (Rastgoo et al. 2013). The IC_{50} of crocin itself against C26 colon carcinoma was 0.73 mM. The results indicated that liposomal encapsulation of crocin could increase its antitumorigenic activity.

Antityrosinase Activity

The flavonol kaempferol isolated from the fresh saffron petals was found to inhibit the oxidation of L-3,4-dihydroxyphenylalanine (L-DOPA) catalysed by mushroom tyrosinase with an ID_{50} of 67 μg/ml (0.23 mM) (Kubo and Kinst-Hori 1999). Interestingly, its 3-*O*-glycoside derivatives did not inhibit this oxidation. Kaempferol was found to be a competitive inhibitor, and this inhibitory activity presumably emanated from its ability to chelate copper in the enzyme. This copper chelation mechanism could be applicable for all of the flavonols as long as their 3-hydroxyl group remained free. However, quercetin, kaempferol and galangin each affected the oxidation of L-tyrosine in somewhat different ways.

Of several constituents of saffron pollens tested for antityrosinase activity, isorhamnetin-3,4′-diglucoside (IC_{50} 1.8 mM) inhibited tyrosinase, and its activity was stronger than arbutin (IC_{50} 24 mM) or hydroquinone (IC_{50} 1.8 mM) but weaker than kojic acid (IC_{50} 235.2 μM) which is usually present in whitening cosmetics (Li and Wu 2002a). The tyrosinase inhibitory activities of all 25 compounds isolated from saffron stigma were evaluated in vitro using mushroom tyrosinase. Among them, crocusatin H, crocin-1 and crocin-3 isolated from saffron stigma showed significant tyrosinase inhibitory activity (Li and Wu 2002b). Among compounds isolated from saffron petals, crocusatin K, crocusatin L and 4-hydroxy-3,5,5-trimethylcyclohex-2-enone showed significant antityrosinase activity (Li et al. 2004). Crocusatin K exhibited inhibitory activity equal to that of kojic acid.

Cardioprotective Activity

Crocetin, a carotenoid of *C. sativus*, exhibited a protective effect of crocetin on primary culture of cardiac myocyte treated with noradrenaline in vitro (Shen et al. 2004). Crocetin significantly decreased the activity of lactic dehydrogenase in culture supernatant and increased the activity of mitochondrion succinic dehydrogenase ATPase (Na^+-K+ATPase, Ca^{2+} ATPase) and mitochondrion

membrane potential. Crocetin decreased the percentage of apoptosis of cardiac myocyte treated with noradrenaline. They also found that crocetin markedly reduced the content of lipid peroxidation (LPO), increased myocardial superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activity in cardiac hypertrophy induced by norepinephrine and significantly improved the myocardial pathological histological changes induced by norepinephrine (Shen and Qian 2006). The results suggested that the cardioprotective effects of crocetin were related to modulation of endogenous antioxidant enzymatic activities.

The hydroalcohol extract effects of *Crocus sativus* exhibited a depressant effect during experimental atrial fibrillation (Khori et al. 2012). It exerted a depressant effect on atrioventricular nodal rate-dependent properties; it increased Wenckebach block cycle length, functional refractory period, facilitation, fatigue and the zone of concealment in experimental atrial fibrillation. These depressant effects of saffron were found to be mediated by endogenous NO.

Results of animal studies suggested that saffron consumption had a cardioprotective role in rats with myocardial infarction (Joukar et al. 2010). Saffron plus isoproterenol-treated rats showed remarkably decreased intensity of heart tissue destruction and significantly decreased serum levels of heart troponin I, when compared to the isoproterenol group. The level of glutathione peroxidase activity in Saffron + isoproterenol animals did not have significant decline. Results of another study suggested that saffron at all the doses exerted significant cardioprotective effect against isoproterenol-induced myocardial damage in male Wistar rats by preserving haemodynamics and left ventricular functions, maintaining structural integrity and augmenting antioxidant (superoxide dismutase and catalase) status and creatine kinase-MB and lactate dehydrogenase levels (Sachdeva et al. 2012). Among the different doses used, saffron at 400 mg/kg dose exhibited maximum protective effects which could be due to the maintenance of the redox status of the cell reinforcing its role as an antioxidant. A recent animal study found that saffron pretreatment (20, 40, 80 and 160 mg/kg IP) or safranal pretreatment (0.025, 0.050, 0.075 ml/kg IP) for 8 days to rats significantly decreased the serum lactate dehydrogenase and creatine kinase-MB and myocardial lipid peroxidation as compared to isoproterenol-induced rats (Mehdizadeh et al. 2013). Histological findings of the heart sections confirmed myocardial injury with isoproterenol administration and the preservation of nearly normal tissue architecture with saffron or safranal pretreatment. The results indicated that saffron and safranal may have cardioprotective effect in isoproterenol-induced myocardial infarction through modulation of oxidative stress in such a way that they maintain the redox status of the cell. Results of a recent study suggested that pretreatment with saffron, especially at a dosage of 100 mg/kg/day, attenuated the susceptibility and incidence of fatal ventricular arrhythmia during the reperfusion period in the rat (Joukar et al. 2013). This cardioprotective effect appeared to be mediated through reduction of electrical conductivity and prolonging the action potential duration.

Separate animal studies suggested that crocin, active constituent of *Crocus sativus*, may have cardioprotective effect in isoproterenol (ISO)-induced cardiac toxicity through modulation of oxidative stress by maintaining the redox status of the cell (Goyal et al. 2010). ISO-control rats showed cardiac dysfunction as indicated by lowering of systolic, diastolic, mean arterial blood pressures, a marked reduction in the activities of myocardial creatine kinase-MB (CK-MB) isoenzyme, lactate dehydrogenase (LDH), superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH) levels along with an increase in content of malondialdehyde (MDA). Also, myocardial necrosis, oedema and inflammation were evident from the light microscopic and ultrastructural changes. Crocin at a dose of 20 mg/kg/day significantly modulated haemodynamic and antioxidant derangements. The preventive role of crocin on ISO-induced myocardial toxicity was reconfirmed by histopathological and ultrastructural examinations. Bharti et al. (2011) showed that safranal alleviated myocardial ischaemia–reperfusion (IR) injury in rats.

Safranal-induced myocardial protection was found to be mediated by enhanced Akt/GSK-3β/eNOS phosphorylation and suppressed IKK-β/NF-κB protein expressions in IR-challenged myocardium. Also safranal exhibited strong anti-apoptotic potential, as evidenced by up-regulated Bcl-2 expression and downregulated Bax and caspase-3 expression with decreased TUNEL positivity, and safranal dose-dependently normalized myocardial antioxidant and nitrotyrosine levels, cardiac injury markers (LDH and CK-MB) and decreased TNF-α level in IR-insulted myocardium. Crocin, main component of *Crocus sativus*, exhibited protective effect against diazinon-induced cardiotoxicity in rats in subchronic exposure (Razavi et al. 2013b). Crocin (25 and 50 mg/kg) improved histopathological damages of cardiac tissues, decreased MDA and creatine phosphokinase MB, increased glutathione (GSH) content and attenuated the increase of Bax/Bcl2 ratio, activation of caspase-3 and release of cytochrome c to the cytosol and alleviate apoptosis induced by diazinon. The results showed that crocin, as an antioxidant, exerted protective effects against diazinon cardiotoxicity by reducing lipid peroxidation and alleviating apoptosis.

Hypotensive Activity

Aqueous and ethanol extracts of *C. sativus* petals reduced the blood pressure of rats in a dose-dependent manner. For example, administration of 50 mg/100 g of aqueous extract changed the blood pressure from 133.5 to 117 (mmHg) (Fatehi et al. 2003). Aqueous–ethanol saffron extract exhibited potent inhibitory effect on the calcium channel of isolated guinea pig heart (Boskabady et al. 2008). In perfused heart with ordinary Krebs solution, the extract (1.0 and 5.0 mg%) caused significant reduction in heart rate and contractility. In perfused heart with calcium-free Krebs solution, only the highest concentration (5.0 mg%) of the extract showed significant reductions in the heart rate and contractility. Studies showed that the aqueous extract of saffron stigma, safranal and crocin reduced the mean arterial blood pressure (MABP) in normotensive and hypertensive anaesthetized rats in a dose-dependent manner (Imenshahidi et al. 2010). The hypotensive activity of saffron stigma appeared to be attributable, in part, to the actions of two major constituents of this plant, crocin and safranal. In a recent animal study, crocin alone did not exhibit any effect on systolic blood pressure (SBP) and heart rate (Razavi et al. 2013a). Concurrent administration of crocin and diazinon improved the reduction of SBP and the elevation of heart rate induced by subchronic administration of diazinon in rats. Crocin and vitamin E plus diazinon decreased MDA elevation induced by diazinon in aortic tissue. A significant decrease in cholinesterase activity was observed in diazinon group. Crocin did not show any effects on cholinesterase activity.

Antigenotoxic/Genoprotective Activity

The results of studies suggested that pretreatment of Swiss albino mice with saffron (20, 40, 50, 80 and 100 mg/kg body weight) significantly inhibited the genotoxicity of genotoxins cisplatin, cyclophosphamide, mitomycin C and urethane (Premkumar et al. 2001, 2003a, b, 2006). No significant change in glutathione S-transferase (GST) activity was observed after pretreatment with saffron alone. Treatment with the genotoxins alone significantly inhibited GST activity. Saffron pretreatment attenuated the inhibitory effects of the genotoxins on GST activity. A significant reduction in the extent of lipid peroxidation with a concomitant increase in the liver enzymatic (SOD, CAT, GST, GPx) and nonenzymatic antioxidants (reduced glutathione) was observed in saffron (20, 40 and 80 mg/kg body weight)-pretreated mice compared with the genotoxins (cisplatin, cyclophosphamide, mitomycin C and urethane) alone-treated mice (Premkumar et al. 2003b). However, the modulatory effects were not always dose dependent. The data suggested that saffron may exert its chemopreventive effects by modulation of lipid peroxidation, antioxidants and detoxification systems. Premkumar

et al. (2004) reported that pretreatment of mice with saffron, garlic and curcumin together elicited maximum reduction in frequencies of micronucleated polychromatic erythrocytes (Mn PCEs) induced by cyclophosphamide in the mouse bone marrow. They also found that pretreatment of mice with saffron (20, 40 and 80 mg/kg b.w.) significantly inhibited antitumour drugs (cisplatin, cyclophosphamide and mitomycin C)-induced cellular DNA damage (strand breaks) as revealed by decreased comet tail length, tail moment and percent DNA in the tail (Premkumar et al. 2006) These findings and earlier findings (Premkumar et al. 2001, 2003b) suggested a potential role for saffron as an antigenotoxic, antioxidant and chemopreventive agent and could be used as an adjuvant in chemotherapeutic applications.

Studies found that methyl methanesulphonate (MMS)-induced DNA migration in safranal-pretreated mice (363.75 mg/kg) was reduced between 4.54-fold (kidney) and 7.31-fold (liver) as compared with those of MMS-treated animals alone (Hosseinzadeh and Sadeghnia 2007a). This suppression of DNA damage by safranal was found to be dependent on the dose, and pretreatment with safranal (72.75 mg/kg) only reduced DNA damage by 25.29, 21.58, 31.32 and 25.88 % in liver, lung, kidney and spleen, respectively, as compared with saline-treated group. The results showed that safranal clearly repressed the genotoxic potency of MMS, as measured by the comet assay, in different mouse organs. They also found that methyl methanesulphonate (MMS)-induced DNA damage in aqueous saffron extract-pretreated mice (80 mg/Kg) declined between 2.67-fold (kidney) and 4.48-fold (lung) compared to those of MMS-treated animals alone (Hosseinzadeh et al. 2008a). This suppression of DNA damage by saffron extract was found to be dose-dependent as pretreatment with the extract (5 mg/Kg) only reduced DNA damage by 6.97, 6.57, 7.27 and 9.90 % in liver, lung, kidney and spleen, respectively, as compared with MMS-treated group. Crocin also significantly decreased DNA damage by MMS (between 4.69-fold for liver and 6.55-fold for spleen, 400 mg/Kg) in a dose-dependent manner. The data suggested the presence of genoprotective property in saffron extract and crocin, as revealed by the comet tail assay, in vivo.

Antihyperlipidaemic/ Antihypercholesterolemic Activity

Crocin was found to prevent atherosclerosis in diet-induced hyperlipidaemic rats (Xu et al. 2005). Crocin significantly decreased the content of cholesterol, triglyceride and density lipoprotein in blood, but increased the content of high density lipoprotein. Crocin also inhibited the proliferation of smooth muscle cells and the activation of p38 MAPK in vitro. In another study of diet-induced hyperlipidaemic rats, a 10-day treatment with crocin significantly reduced serum triglyceride, total cholesterol, low-density lipoprotein (LDL) cholesterol and very low-density lipoprotein (VLDL) cholesterol level in the daily dose range of 25–100 mg/kg (Sheng et al. 2006). Crocin inhibited the absorption of fat and cholesterol, and this inhibition was closely related to the hydrolysis of fat. Also, crocin increased the faecal excretion of fat and cholesterol in rats, but had no influence on the elimination of bile acids. The results of the in situ loop method and enzyme assay indicated that crocin could not directly block the absorption of cholesterol from rat jejunum but could selectively inhibit the activity of pancreatic lipase as a competitive inhibitor. The findings suggested that crocin imparted its hypolipidaemic effect by inhibiting pancreatic lipase, leading to the malabsorption of fat and cholesterol.

Studies in hyperlipidaemic rats showed that oral administration of both saffron (25, 50 and 100 mg/kg) and crocin (4.84, 9.69 and 19.38 mg/kg) was effective in decreasing the elevated levels of triglyceride, total cholesterol, alkaline phosphatase, aspartate transaminase, alanine aminotransferase, malondialdehyde, glutathione peroxidase enzyme activity, total glutathione and oxidized glutathione in serum and increasing superoxide dismutase, catalase, ferric reducing/antioxidant power (FRAP) and total sulphhydryl values in liver tissue with reduction in thiobarbituric-acid reactive species (Asdaq and Inamdar 2010). Saffron was found to be superior to crocin, indicating the involvement of other potential constituents of saffron apart from crocin for its synergistic behaviour of quenching the free radicals and ameliorating the damages of hyperlipidaemia.

Studies showed that crocetin could ameliorate endothelial dysfunction in hypercholesterolemic rabbits (Tang et al. 2006). Endothelium-dependent relaxation in hypercholesterolemic rabbit was seriously impaired, and the maximal relaxation induced by acetylcholine ($10^{-5.5}$ M) was only 54 % that in control rabbit fed with regular diet. Oral supplementation with crocetin (15, 30 mg/kg) dose-dependently improved this impairment and restored the maximal relaxation to 68 % and 80 % that in control group, respectively. Crocetin simultaneously increased serum level of nitric oxide (NO) and up-regulated vessel activity and mRNA expression of endothelial NO synthase (eNOS) as well as vessel cyclic GMP (cGMP) content compared with hypercholesterolemic rabbits. The findings suggested that crocetin significantly restored the endothelium-dependent relaxation of thoracic aorta in hypercholesterolemic rabbit increasing eNOS activity.

Weight Loss Activity

In an 8-week randomized, placebo-controlled, double-blind study of 60 mildly overweight, healthy women, consumption of Satiereal (a *C. sativus* extract) as a supplement to an adequate diet elicited a reduction of snacking and created a satiating effect that could contribute to body weight loss (Gout et al. 2010).

Amyloid-Beta Aggregation Inhibitory Activity and Alzheimer's Disease

The water–methanol (50:50, v/v) extract of *C. sativus* stigmas exhibited good antioxidant properties, higher than those of tomatoes and carrots, and inhibited Abeta fibrillogenesis in a concentration- and time-dependent manner (Papandreou et al. 2006). The main carotenoid constituent, *trans*-crocin-4, the digentiobiosyl ester of crocetin, inhibited Abeta fibrillogenesis at lower concentrations than dimethylcrocetin, indicating that the action of the carotenoid was enhanced by the presence of the sugars.

In a 22-week, multicentre, randomized, double-blind controlled trial of 54 Persian-speaking adults 55 years of age or older, saffron administered as a capsule saffron 30 mg/day (15 mg twice per day) was found to be effective similar to donepezil in the treatment of mild-to-moderate Alzheimer's disease (Akhondzadeh et al. 2010a). The frequency of adverse events was similar between saffron extract and donepezil groups with the exception of vomiting, which occurred significantly more frequently in the donepezil group. In another double-blind study of parallel groups of 46 patients with mild-to-moderate Alzheimer's disease (AD), 16-week saffron treatment produced a significantly better outcome on cognitive function than placebo (Akhondzadeh et al. 2010b). There were no significant differences in the two groups in terms of observed adverse events. The results suggested saffron to be both safe and effective in mild-to-moderate AD. *Crocus sativus* may inhibit the aggregation and deposition of amyloid β in the human brain and may therefore be useful in Alzheimer's disease.

Formation of toxic amyloid structures is believed to be associated with various late-onset neurodegenerative disorders such as Alzheimer's and Parkinson's diseases (Ebrahim-Habibi et al. 2010). They found that crocin and safranal, two principal components of saffron, had inhibitory effect on fibrillation of apo-alpha-lactalbumin (a-alpha-LA), used as a model protein, under amyloidogenic conditions. In the absence of any ligand, formation of soluble oligomers became evident after 18 h of incubation, followed by subsequent appearance of mature fibrils. Upon incubation with crocin or safranal, while transition phase to monomeric beta structures was not significantly affected, the formation of soluble oligomers and following fibrillar assemblies were inhibited. While both safranal and crocin had the ability to bind to hydrophobic patches provided in the intermediate structures and thereby inhibit protein aggregation, crocin was found more effective, possibly due to its simultaneous hydrophobic and hydrophilic character. Cell viability assay indicated that crocin could diminish toxicity while safranal acted in reverse

order. Saffron extract showed moderate acetylcholinesterase (AChE) inhibitory activity (up to 30 %), but IC_{50} values of crocetin, dimethylcrocetin and safranal were 96.33, 107.1 and 21.09 μM, respectively (Geromichalos et al. 2012). Safranal interacted only with the binding site of the AChE, but crocetin and dimethylcrocetin bound simultaneously to the catalytic and peripheral anionic sites. The results reinforced previous findings about the beneficial action of saffron against Alzheimer's disease and may be of value for the development of novel therapeutic agents based on carotenoid-based dual binding inhibitors. Saffron had been used in traditional medicine against Alzheimer's disease. They reported that inhibitors of acetylcholine breakdown by acetylcholinesterase (AChE) constituted the main therapeutic modality for Alzheimer's disease.

Neuroprotective and Cognitive Enhancement Activities

A single oral administration of saffron alcohol extract had no effects on memory registration, consolidation or retrieval in normal mice (Zhang et al. 1994). In contrast, the extract reduced ethanol-induced impairment of memory registration both in step-through (ST) and step-down (SD) tests and the ethanol-induced impairment of memory retrieval in SD test. The extract decreased the motor activity and prolonged the sleeping time induced by hexobarbital. These results suggested that saffron extract ameliorated the impairment effects of ethanol on learning and memory processes and possessed a sedative effect. Saffron alcohol extract (250 mg/kg, p.o.) was found to be effective in preventing acetaldehyde-induced inhibition of long-term potentiation in the dentate gyrus of anaesthetized rats (Abe et al. 1999). The results suggested saffron extract could prevent aversive effects induced by ethanol as found in earlier study and its metabolite acetaldehyde.

Soeda et al. (2001, 2003) demonstrated that crocin suppressed the effect of tumour necrosis factor (TNF)-alpha on neuronally differentiated PC12 cells. Crocin suppressed the TNF-alpha-induced expression of Bcl-Xs and LICE mRNAs and simultaneously restored the cytokine-induced reduction of Bcl-X(L) mRNA expression. Crocin also blocked the cytochrome c-induced activation of caspase-3. They also found that crocin inhibited the effect of daunorubicin. Their findings suggested that crocin inhibited neuronal cell death induced by both internal and external apoptotic stimuli. Ochiai et al. (2004a) reported on the effects of crocin on neuronally differentiated pheochromocytoma (PC12) cells deprived of serum/glucose. Depriving the PC12 cells of serum/glucose caused peroxidation of their cell membrane lipids and decreased intercellular superoxide dismutase (SOD) activity. Treating the PC12 cells with 10 μM crocin inhibited the formation of peroxidized lipids, partly restored the SOD activity and maintained the neuron's morphology. These antioxidant effects of crocin were more effective than those of α-tocopherol at the same concentration. Crocin also suppressed the activation of caspase-8 caused by serum/glucose deprivation. The results suggested crocin to be a unique and potent antioxidant to combat oxidative stress in neurons. Further they found that crocin repelled the serum/glucose deprivation-induced ceramide formation in PC12 cells by increasing GSH levels and preventing the activation of JNK pathway, which had been reported to have a role of the signalling cascade downstream ceramide for neuronal cell death (Ochiai et al. 2004b). Measurements of PC12 cell viability, peroxidized membrane lipids and caspase-3 activity showed that the rank order of the neuroprotective potency at a concentration of 10 μM afforded by saffron carotenoids and picrocrocin was crocetin-di-(β-D-gentiobiosyl)-ester [crocin] > crocetin-(β-D-gentiobiosyl)-(β-D-glucosyl)-ester [tricrocin] > crocetin di-(β-D-glucosyl)-ester [dicrocin] and picrocrocin (the latter two crocins had a little or no potency) (Ochiai et al. 2007). In addition, they showed that among this saffron's constituents, crocin most effectively promoted mRNA expression of γ-glutamylcysteinyl synthase (γ-GCS), which contributed to glutathione (GSH) synthesis as the rate-limiting enzyme, and that the carotenoid could significantly reduce infarcted areas caused by occlusion of the middle cerebral artery (MCA) in mice.

Animal studies showed that retreatment of *C. sativus* stigma extract (100 mg/kg of body weight, p.o.) 7 days before the induction of cerebral ischaemia by middle cerebral artery occlusion (MCAO) significantly attenuated all the adverse alterations induced by ischaemia in rats (Saleem et al. 2006). MCAO caused significant depletion in the contents of reduced glutathione (GSH) and its dependent enzymes while significant elevation of malondialdehyde, glutamate and aspartate. The activities of Na(+),K(+)-ATPase, superoxide dismutase and catalase were decreased significantly by MCAO. The neurobehavioral activities (grip strength, spontaneous motor activity and motor coordination) were also decreased significantly in the MCAO group. Another study showed that pretreatment with crocin markedly inhibited oxidizing reactions and modulated the ultrastructure of cortical microvascular endothelial cells in mice with 20 min of bilateral common carotid artery occlusion (BCCAO) followed by 24 h of reperfusion in vivo (Zheng et al. 2007). Further, crocin inhibited G protein-coupled receptor kinase 2 (GRK2) translocation from the cytosol to the membrane and reduced extracellular signal-regulated kinase 1/2 (ERK1/2) phosphorylation and matrix metalloproteinase-9 (MMP-9) expression in cortical microvessels. It was proposed that crocin protected the brain against excessive oxidative stress and may constitute a potential therapeutic candidate in transient global cerebral ischaemia.

After daily oral dosage, saffron ethanol extract significantly reduced the clinical symptoms in C57BL/6 mice with experimental autoimmune encephalomyelitis (EAE) (Ghazavi et al. 2009). Also, saffron-treated mice displayed a delayed disease onset compared with control mice. Total antioxidant capacity production assessed by ferric reducing/antioxidant power (FRAP) method was significantly elevated in saffron-treated mice. Effect of saffron on serum NO production was not significant. Typical spinal cord leukocyte infiltration was observed in control mice compared with saffron-treated mice. The results suggested that saffron was effective in the prevention of symptomatic EAE by inhibition of oxidative stress and leukocyte infiltration to CNS and may be potentially useful for the treatment of multiple sclerosis (MS). Mousavi et al. (2010) reported that saffron extract (5 and 25 mg/ml), crocin (10 and 50 μM) and GSH (10 μM) could decrease the neurotoxic effect of glucose on PC12 cells. They found that glucose (13.5 and 27 mg/ml) reduced the cell viability of PC12 cells after 4 days and was consistent with increased ROS production which was reduced by saffron, crocin and GSH pretreatment. They concluded that saffron and its carotenoid crocin could be potentially useful in diabetic neuropathy treatment. Separate studies showed that administration of saffron extract (200 mg/kg b.wt.) and honey syrup (500 mg/kg b.wt.) for 45 days ameliorated aluminium chloride neurotoxicity in mice brain (Shati et al. 2011). The neuroprotective effect was attributed to the antioxidant property of saffron extract. Also there was an indication of carcinogenicity in the $AlCl_3$-treated mice evidenced by an increase in serum tumour markers such as arginase and α-L-fucosidase.

Crocetin exerted neuroprotective effect in a hemi-parkinsonian rat model (Ahmad et al. 2005). Levels of glutathione and dopamine were protected, while thiobarbituric acid-reactive substance (TBARS) content was attenuated in crocetin-treated groups. The activity of antioxidant enzymes was decreased in the lesion group, but protected in the crocetin-treated groups. Histopathologic findings in the substantia nigra showed that crocetin protected neurons from deleterious effects of a 6-hydroxydopamine.

Separate animal studies demonstrated that the neuroprotective effects of crocetin upon brain injury may be related to its ability to inhibit apoptosis at early stages of the injury and its ability to promote angiogenesis at the subacute stage as indicated by higher expression levels of vascular endothelial growth factor receptor-2 (VEGFR-2) and serum response factor (SRF) in the crocetin therapy rats in comparison to the cerebral trauma control group (without treatment) and sham operation control group (Bie et al. 2011). Studies by Vakili et al. (2013) found crocin to have protective effects against ischaemia–reperfusion injury and cerebral oedema in a rat model of stroke with crocin at doses of 30, 60 and 120 mg/kg significantly

decreased infarct volume by 64 %, 74 % and 73 %, respectively. Administration of crocin (60 mg/kg) 1 h before, at the start, or 1 h after ischaemia reduced brain oedema by 48 %, 52 % and 51 %, respectively. Moreover, crocin (60 mg/kg) significantly reduced malondialdehyde (MDA) content and increased activity of superoxide dismutase (SOD) and glutathione peroxidase (GPx) in the ischaemic cortex. The results indicated that the cerebral protective effects of crocin may have been exerted primarily by suppression of the production of free radicals and increased antioxidant enzyme activity. Studies found that although saffron extract co-administration with aluminium had no effect on cognitive performance of mice, it reversed significantly the aluminium-induced changes in monoamine oxidase (MAO-A, MAO-B) activity and the levels of lipid peroxidation (MDA) and reduced glutathione (GSH), in whole brain and cerebellum (Linardaki et al. 2013). Acetylcholinesterase activity was further significantly decreased in cerebral tissues of Al+saffron group. The biochemical changes supported the neuroprotective potential of saffron under Al-toxicity.

In in-vitro studies, hydroethanolic saffron extract and its component *trans*-crocetin inhibited glutamatergic synaptic transmission in rat cortical brain slices (Berger et al. 2011). Saffron extract decreased glutamate-induced membrane depolarization. Additionally, the extract at 100 μg/ml decreased *N*-methyl-D-aspartate (NMDA) (20 μM) and kainate (1 μM)-induced depolarization, whereas alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) (1 μM)-induced depolarization was not affected. *Trans*-crocetin (1–50 μM) showed inhibition of evoked postsynaptic potentials and glutamate-induced membrane depolarization comparable to saffron extract. *Trans*-crocetin at 10 μM decreased NMDA (20 μM)-induced membrane depolarization, but did not inhibit the isolated non-NMDA component of postsynaptic potentials. They concluded that *trans*-crocetin was involved in the antagonistic effect of saffron extract on NMDA but not on kainate receptors. Earlier, Lechtenberg et al. (2008) found that saffron extracts and crocetin had a clear binding capacity at the phencyclidine (PCP) binding side of the NMDA (*N*-methyl-D-aspartate) receptor and at the sigma(1) receptor, while the crocins and picrocrocin were not effective. Their results elucidated the biochemical clinical effects of saffron for the treatment of depression and cancer.

Hosseinzadeh and Sadeghnia (2005) found safranal to have some protective effects on different markers of oxidative damage in hippocampal tissue from ischaemic rats. The transient global cerebral ischaemia induced a significant increase in TBARS levels, decrement in both antioxidant power (FRAP value) and total sulphhydryl (SH) concentrations in comparison with sham-operated animals. Following safranal administration, total SH contents and antioxidant capacity were elevated in hippocampus in comparison with ischaemic group. The malondialdehyde level declined significantly in the hippocampus. Studies in anaesthetized rats showed that acute systemic injection of safranal, a constituent of *C. sativus*, reduced the extracellular concentrations of excitatory amino acids (glutamate and aspartate) in the rat hippocampus following kainic acid administration (Hosseinzadeh et al. 2008b). Sadeghnia et al. (2013) found that safranal exerted protective effects on different markers of oxidative damage in hippocampal tissue following quinolinic acid (QA) administration. QA-mediated excitotoxicity was characterized by a significant increase in TBARS levels and %tail DNA and remarkable decrease in antioxidant power (FRAP value) and total sulphhydryl content of hippocampus. Systemic administration of safranal (291 mg/kg, IP) effectively and dose-dependently decreased the QA-induced lipid peroxidation and oxidative DNA damage. Safranal also prevented the decrease of hippocampal thiol redox and antioxidant status produced by QA. Their findings suggested the possibility of potential therapeutic application of safranal for preventing and treating neurodegenerative disorders such as Alzheimer's disease.

Saffron extract was found to improve ethanol-induced impairments of learning behaviours in mice and prevented ethanol-induced inhibition of hippocampal long-term potentiation (LTP), a form of activity-dependent synaptic plasticity

that may underlie learning and memory (Abe and Saito 2000). This effect of saffron extract was attributed to crocin (crocetin digentiobiose ester), but not crocetin. The results indicated that saffron extract or its active constituents, crocetin and crocin, could be useful as a treatment for neurodegenerative disorders accompanying memory impairment. The LTP-blocking effect of ethanol was significantly improved by oral, intravenous and intracerebroventricular administration of *C. sativus* ethanol extract, respectively (Saito et al. 2001; Soeda et al. 2003). Crocin at 50 mg/kg ameliorated the blocking effect of ethanol on the LTP at 84 % compared to the control. Crocetin gentiobiose glucose ester also antagonized the blocking effect of ethanol on the LTP dose-dependently indicating about a half of crocin. Crocetin di-glucose ester did not remove the inhibitory effect of ethanol on the LTP. It was concluded that two gentiobiose moieties were necessary for the appearance of pharmacological activity of crocin in the central nervous system. Some plants and their extracts that had produced promising clinical data in dementia patients, with respect to cognition, include saffron (*Crocus sativus*), ginseng (*Panax species*), sage (*Salvia species*) and lemon balm (*Melissa officinalis*) (Howes and Perry 2011). *Crocus sativus*, *Ginkgo biloba* and *Salvia* spp. had been reported to show some promising effects in clinical studies with dementia patients (Howes and Houghton 2012).

In the first experiment, post-training administration of *Crocus sativus* extract (30 and 60 g/kg) successfully counteracted extinction of recognition memory in the normal rat, suggesting that saffron extract modulated storage and/or retrieval of information (Pitsikas and Sakellaridis 2006). In a subsequent experiment, pretraining treatment with saffron extract (30 and 60 mg/kg) significantly antagonized the scopolamine (0.75 mg/kg)-induced performance deficits in the step-through passive avoidance test. These results supported and extended earlier findings about the implication of *Crocus sativus* extract in learning and memory mechanisms. Similar results were obtained for crocin (Pitsikas et al. 2007). Treatment of rats with crocins (30 mg/kg and to a lesser extent also 15 mg/kg) attenuated scopolamine (0.2 mg/kg)-induced performance deficits in the radial water maze test. Pretreatment of male Wistar rats with safranal (291 mg/kg) significantly reduced locomotor hyperactivity and behavioural changes elicited by MK-801 (the psychotomimetic, noncompetitive *N*-methyl-D-aspartate (NMDA) receptor antagonist) (Asadpour and Sadeghnia 2011) in the radial maze test. Average reference errors were also significantly decreased in comparison with MK-801 treated animals. The data indicated that treatment with safranal attenuated behavioural and spatial memory deficits in a rat model of an acute psychotic episode.

Khalili and Hamzeh (2010) found that crocin (30 mg/kg)-treated streptozotocin-injected rats showed higher correct choices and lowered errors in Y-maze than vehicle-treated streptozotocin-injected rats. Additionally, crocin at the mentioned dose could significantly attenuate learning and memory impairment in treated streptozotocin-injected group in passive avoidance test. The results demonstrated the effectiveness of crocin (30 mg/kg) in antagonizing the cognitive deficits caused by streptozotocin-intracerebroventricular injection in rats and its potential in the treatment of neurodegenerative diseases such as Alzheimer's disease. Studies showed that saffron-treated mice exhibited significant improvement in learning and memory, accompanied by reduced lipid peroxidation products, higher total brain antioxidant activity and reduced caspase-3 activity in both age (4 and 20 months) groups of mice (Papandreou et al. 2011). Further, salt- and detergent-soluble acetylcholinesterase activity was significantly decreased only in adult mice. They found that both saffron and crocetin provided strong protection against hydrogen peroxide-induced toxicity in human neuroblastoma SH-SY5Y cells, in rescuing cell viability (MTT assay), repressing ROS production (DCF assay) and decreasing caspase-3 activation. In another study, treatment of rats with saffron extract or crocin blocked the ability of chronic restraint stress to impair spatial learning and memory retention (Ghadrdoost et al. 2011). Relative to controls that received vehicle, stressed animals that received saffron extract or crocin

had significantly lower levels of lipid peroxidation products and significantly higher activities of antioxidant enzymes including glutathione peroxidase, glutathione reductase and superoxide dismutase. Finally, crocin significantly decreased plasma levels of corticosterone, as measured after the end of stress. The results suggested that saffron and its active constituent crocin could prevent the impairment of learning and memory as well as the oxidative stress damage to the hippocampus induced by chronic stress. In separate studies administration of saffron extract and crocin to male adult Wistar rats improved spatial cognitive abilities following chronic cerebral hypoperfusion and that these effects may be related to the antioxidant effects of these compounds (Hosseinzadeh et al. 2012). Pretreatment of PC12 cells with 10–50 μM crocin before acrylamide (ACR) treatment significantly attenuated ACR cytotoxicity in a dose-dependent manner (Mehri et al. 2012). Crocin inhibited the downregulation of Bcl-2 and the up-regulation of Bax and decreased apoptosis in treated cells and also inhibited ROS generation in cells exposed to ACR. The results indicated that the neuroprotective effect of crocin on acrylamide-induced cytotoxicity in PC12 cells may be partly by inhibition of intracellular ROS production.

Intraperitoneal (i.p.) injections of clonidine, the aqueous and ethanolic extracts of saffron, reduced the jumping activity of morphine-administered mice; jumping during 30 min was deemed as the intensity of the withdrawal syndrome (Hosseinzadeh and Jahanian 2010). Safranal injected (s.c.) 30 min prior and 1 and 2 h after the injection of morphine potentiated some signs of withdrawal syndrome. The aqueous saffron extract decreased the movement in all of the doses (80, 160, 320 mg/kg), and the ethanolic extract decreased it in a dose of 800 mg/kg in open-field test. But crocin and a dose of 400 mg/kg ethanolic extract showed no effect on activity in this test. It was concluded that saffron extracts and crocin may have interaction with the opioid system to reduce withdrawal syndrome. Studies showed that both ethanolic saffron extract (10, 50, 100 mg/kg) and safranal (1, 5, 10 mg/kg) administered intraperitoneally could inhibit the acquisition and expression of morphine-induced place preference in male Swiss Webster mice (Ghoshooni et al. 2011). Animal studies revealed that saffron aqueous extract attenuated morphine-induced memory impairment (Naghibi et al. 2012). The time latency in morphine-treated group was lower than control. Treatment of mice with 150 and 450 mg/kg of saffron extract before the training trial increased the time latency at 24 and 48 h after the training trial. Administration of both 150 and 450 mg/kg doses of the saffron aqueous extract before retention trials also increased the time latency.

Animal studies showed that crocins, components of *C. sativus*, had an effect on obsessive–compulsive disorder (OCD), a common psychiatric disorder defined by the presence of obsessive thoughts and repetitive compulsive actions, such as excessive self-grooming (Georgiadou et al. 2012). Their study showed that crocins (30 and 50 mg/kg, i.p.) attenuated serotonin (5-HT) receptor agonist m-chlorophenyl-piperazine (mCPP)-induced excessive self-grooming in rats. The results indicated that these effects of crocins on an animal model of OCD could not be attributed to changes in locomotor activity. The findings suggested that crocins may play a role in compulsive behaviour and support a functional interaction between crocins and the serotonergic system.

Antidepressant Activity

Intraperitoneal administration of the aqueous and ethanolic extracts of stigma (0.2–0.8 g/kg) and its constituents safranal (0.15–0.5 ml kg) and crocin (50–600 mg/kg) decreased mice immobility time in the swimming test in comparison to normal saline (Hosseinzadeh et al. 2004). Swimming time was increased by fluoxetine, both extracts and safranal. Climbing time was increased by imipramine and both extracts. Safranal with a higher dose (0.5 mg/kg) and crocin at doses 50 and 600 increased climbing time. In the open-field activity test, the ethanolic extract and safranal increased stereotypic activities. On the basis of these results, the antidepressant effect of *C. sativus* stigma extracts may be mediated via

safranal and crocin. It was also suggested that crocin may act via the uptake inhibition of dopamine and norepinephrine, and safranal via serotonin.

In a 6-week pilot double-blind, single-centre, randomized trial of 30 adult outpatients who met the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM IV) for major depression, ingestion of saffron capsule 30 mg/day was found to be effective similar to imipramine, 100 mg/day, in the treatment of mild-to-moderate depression (Akhondzadeh et al. 2004). In the imipramine group anticholinergic effects such as dry mouth and also sedation were observed more often that was predictable.

In another 6-week double-blind, placebo-controlled, single-centre and randomized trial, 40 patients with mild-to-moderate depression were randomly assigned to receive a capsule of saffron 30 mg/day or a capsule of placebo (Akhondzadeh et al. 2005). *Crocus sativus* produced a significantly better outcome on the Hamilton Depression Rating Scale than the placebo. There were no significant differences in the two groups in terms of the observed side effects. Noorbala et al. (2005) found in a 6-week double-blind, randomized trial of 40 adult outpatients with mild-to-moderate depression, saffron capsule at 30 mg/day (BD) was as effective as fluoxetine capsule 20 mg/day (BD) in the treatment of mild-to-moderate depression. In another 6-week double-blind, randomized and placebo-controlled study of 40 adult outpatients who met the DSM-IV criteria for major depression, *C. sativus* petal was found to be effective in treating mild-to-moderate depression (Moshiri et al. 2006). At 6 weeks, petal of *C. sativus* produced a significantly better outcome on Hamilton Depression Rating Scale than placebo. There were no significant differences in the two groups in terms of observed side effects. Similarly in an 8-week pilot double-blind, randomized trial involving 40 adult outpatients who met the DSM-IV criteria for major depression, *C. sativus* petal was found to be effective similar to fluoxetine in the treatment of mild-to-moderate depression (Akhondzadeh et al. 2007). In addition, in both treatments, the remission rate was 25 %. There were no significant differences in the two groups in terms of observed side effects. The present study confirmed findings of other studies which showed antidepressant effect of *C. sativus*. Animal studies showed that administration of petroleum ether fraction and dichloromethane fraction of *C. sativus* corm ethanol extract produced antidepressant-like effects (Wang et al. 2010). The immobility time in the forced swimming test and tail suspending test was significantly reduced by the two fractions, without accompanying changes in ambulation when assessed in the open-field test. Aqueous stigma extract also exerted antidepressant effects in the behavioural models. Crocin-1 and crocin-2 were identified in the aqueous stigma extract. The data indicated that antidepressant-like properties of aqueous stigma extracts may be due to crocin-1.

In a review of prospective human trials assessing herbal medicines for the management of mild-to-moderate depression, saffron stigma was found to be significantly more effective than placebo and equally as efficacious as fluoxetine and imipramine (Dwyer et al. 2011). Saffron petal was also significantly more effective than placebo and was found to be equally efficacious compared to fluoxetine and saffron stigma.

Anxiolytic Activity

Preclinical evidence of anxiolytic activity (without human clinical trials) was found for *Crocus sativus* (Sarris et al. 2013). Crocins, active components of *Crocus sativus*, exhibited anxiolytic activity in a light/dark test with rats (Pitsikas et al. 2008). Either crocins, at a dose which did not influence animals' motor activity (50 mg/kg), or diazepam (1.5 mg/kg) significantly increased the latency to enter the dark compartment and prolonged the time spent in the lit chamber in the rats. Conversely, lower doses of crocins (15–30 mg/kg) did not substantially modify animals' behaviour. Studies showed that saffron aqueous extract and safranal had anxiolytic and hypnotic effects (Hosseinzadeh and Noraei 2009). The aqueous extract of saffron stigma reduced the locomotor activity of mice dose-dependently in

the open-field test. At low doses, saffron showed a significant increase in the time on the open arms of the maze. When using the Rotarod method, the aqueous extract showed considerable effect on motor coordination of the mice. In the hypnotic test, only a dose of 0.56 g/kg of saffron increased the total sleep. Crocin showed no anxiolytic, hypnotic or myorelaxation effects. Safranal, in higher doses, 0.15 and 0.35 ml/kg, showed anxiolytic effects. Safranal increased the total sleep time dose-dependently. This constituent at lower doses (0.05 and 0.15 mL/kg) decreased some locomotion activity parameters. Safranal demonstrated no effects on motor coordination.

Anticonvulsant Activity

Studies showed that the aqueous and ethanol extracts of *C. sativus* stigma may be beneficial in both absence and tonic–clonic seizures in mice (Hosseinzadeh and Khosravan 2002). In the pentylenetetrazole test, the extracts delayed the onset of tonic convulsions, but failed to produce complete protection against mortality. In the maximal electroshock seizure (MES) test, both extracts decreased the duration of tonic seizures. Studies showed that the aqueous and ethanol extracts of *C. sativus* stigma may be beneficial in both absence and tonic–clonic seizures (Hosseinzadeh and Khosravan 2002). In the pentylenetetrazole test, the extracts delayed the onset of tonic convulsions, but failed to produce complete protection against mortality. In the maximal electroshock seizure (MES) test, both extracts decreased the duration of tonic seizures. Safranal, an active constituent of *Crocus sativus* stigmas (0.15 and 0.35 ml/kg, i.p.), reduced pentylenetetrazole-induced seizure duration, delayed the onset of tonic convulsions and protected mice from death (Hosseinzadeh and Talebzadeh 2005). In contrast, crocin (200 mg/kg, i.p.) did not show anticonvulsant activity. In another study, safranal was found to exert anticonvulsant activity in pentylenetetrazole-induced seizures in the rat and that this effect may be mediated, at least partly, through GABA(A)-benzodiazepine receptor complex (Hosseinzadeh and Sadeghnia 2007b). Peripheral administration of safranal (72.75, 145.5 and 291 mg/kg body wt., i.p.) induced a dose-dependent decrease in the incidence of both minimal clonic seizures (MCS) (145.5 mg/kg body wt.) and generalized tonic–clonic seizures (GTCS) (145.5 mg/kg body wt.) following pentylenetetrazole administration. Pretreatment with flumazenil and naloxone 15 min prior to safranal administration (145.5 mg/kg body wt., i.p.) abolished the protective effect of safranal on MCS. The systemic administration of safranal resulted in a significant and dose-dependent attenuation in experimental absence seizures elicited by either gamma-butyrolactone, baclofen or low doses of GABAA receptor antagonists: pentylenetetrazole, picrotoxin and bicuculline (Sadeghnia et al. 2008). After a single intraperitoneal administration of safranal (291 mg/kg), no changes in baseline electrocorticographic recording were observed; however, a significant decrease in [3H] flunitrazepam binding was seen in the cortex (33.16 %), hippocampus (27.36 %) and thalamus (29.91 %) of mouse brain, while the [3H] CGP54626A binding did not show any modification in the same brain regions. The data suggested the presence of an antiabsence seizure property in safranal and its effect may be due to modifications on the benzodiazepine binding sites of the GABAA receptor complex.

Anticataractogenic and Ocular Protective Activities

Crocin analogues isolated from *Crocus sativus* were found to significantly increase the blood flow in the retina and choroid presumably by improved oxygenation and nutrient supply of retinal structures, thus facilitating retinal function recovery (Xuan et al. 1999). The results indicated that crocin analogues could be used to treat ischaemic retinopathy and/or age-related macular degeneration. It was noted that disaccharide analogues of crocin, such as crocin-1 and crocin-2, were less potent than monosaccharide analogues of crocin, such as crocin-3 and crocin-4,

constituting an interesting structure–activity relationship. In an in vitro model, crocin was found to protect retinal photoreceptors against light-induced cell death (Laabich et al. 2006). Twenty-four hour exposure to blue and white light induced death in 70–80 % of the photoreceptors in bovine and primate retinal cell cultures. Crocin protected the photoreceptors against blue light- or white light-mediated damage in a concentration-dependent manner with an EC_{50} of approximately 30 microM. TUNEL assays confirmed that crocin protected photoreceptors from light damage.

The results of animal studies showed that saffron may protect photoreceptors from retinal stress, maintaining both morphology and function and probably acting as a regulator of programmed cell death (Maccarone et al. 2008). The photoreceptor layer was largely preserved in saffron-treated rats because it was the flash electroretinograms (fERGs) response. Additionally, the rate of photoreceptor death induced by bright continuous light appeared drastically reduced in treated animals. In β-carotene prefeeding experiments, morphological analysis showed preservation of the outer nuclear layer similar to that obtained with saffron prefeeding, whereas the fERG response was unrecordable. In a randomized, placebo-controlled study of 25 patients with early age-related macular degeneration, short-term saffron supplementation was found to improve retinal flicker sensitivity (Falsini et al. 2010). Flash electroretinogram (fERG) thresholds were decreased after saffron supplementation but not placebo, compared with baseline.

Studies demonstrated that crocetin had protective effects against retinal damage in vitro and in vivo, suggesting that the mechanism may inhibit increase in caspase-3 and caspase-9 activities after retinal damage (Yamauchi et al. 2011). Crocetin at a concentration of 3 μM showed the inhibitory effect of 50–60 % against tunicamycin- and H_2O_2-induced cell death and inhibited increase in caspase-3 and caspase-9 activity. Moreover, crocetin inhibited the enzymatic activity of caspase-9 in a cell-free system. In vivo crocetin at 100 mg/kg, p.o., significantly inhibited photoreceptor degeneration and retinal dysfunction caused by exposure to white light at 8,000 lx for 3 h after dark adaptation, and halved the expression of terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL)-positive cells. Qi et al. (2013) demonstrated that crocin exhibited neuroprotective effect on retinal ganglion cell (RGC) apoptosis induced by retinal ischaemia/reperfusion (IR) injury by activating the PI3K/Akt signalling pathway in rats. Studies showed that oral administration of crocetin in mice prevented N-methyl-D-aspartate (NMDA)-induced retinal damage via inhibition of the caspase pathway (Ohno et al. 2012). NMDA injection decreased the cell number in the ganglion cell layer, and crocetin at a dose of 100 mg/kg inhibited this reduction. TUNEL-positive cells were observed in both ganglion cell layer and inner nuclear layer after NMDA injection, and crocetin inhibited the increase in number of TUNEL-positive cells. ERG analysis showed that both a- and b-wave amplitudes were decreased by NMDA injection. Crocetin inhibited the reduction in the b-wave amplitude, but not in the a-wave. NMDA injection activated caspase-3/7 and increased expression of cleaved caspase-3 in the GCL and INL, which were both inhibited by crocetin.

Studies on Chinchilla rabbits with experimental models of retinal dystrophy indicated that antioxidative function played a crucial role in the curative action of saffron extract and served as a pathogenetic basis for its application in visual impairments of various origins (Shukurova and Babaev 2010). Fernández-Sánchez et al. (2012) demonstrated that saffron attenuated retinal degeneration in the P23H rat model of autosomal dominant retinitis pigmentosa by impeding photoreceptor cell degeneration and ameliorating the loss of retinal function and vascular network disruption in P23H rats. Dietary supplementation of safranal to homozygous P23H line-3 rats preserved both photoreceptor morphology and number. Electroretinographic recordings showed higher a- and b-wave amplitudes under both photopic

and scotopic conditions in safranal-treated versus nontreated animals. Additionally, the capillary network in safranal-treated animals was preserved, unlike that found in untreated animals. This study suggested that safranal could be potentially useful to retard retinal degeneration in patients with retinitis pigmentosa.

Saffron extract prevented selenite-induced cataract formation in Wistar rats, possibly through the reinforcement of antioxidant status, reduction of the intensity of lipid peroxidation, protection of the sulphhydryl groups and inhibition of proteolysis of the lens water-soluble fraction (WSF) of lens proteins (Makri et al. 2013). Activities of antioxidant enzymes, namely, superoxide dismutase, glutathione peroxidase, and catalase, and glutathione levels were significantly increased in saffron-treated rats compared to the selenite-treated group.

Recent studies showed that crocetin inhibited retinal ischaemic damage through its inhibition of oxidative stress in mice (Ishizuka et al. 2013). Ischaemia/reperfusion (I/R) decreased the cell number in the ganglion cell layer (GCL) and the thickness of inner nuclear layer (INL), and that crocetin inhibited GCL and INL. Electroretinogram (ERG) measurements revealed that crocetin prevented the I/R-induced reductions in a- and b-wave amplitudes seen at 5 days after I/R. Further, crocetin decreased the numbers of TUNEL-positive cells and expression of 8-hydroxy-2-deoxyguanosine (8-OHdG; used as a marker of oxidative stress)-positive cells, and the phosphorylation levels of p38, JNK, NF-κB and c-Jun present in the retina after I/R.

Antinociceptive Activity

The aqueous and ethanolic extracts of *Crocus sativus* stigma and petals exhibited antinociceptive activity against acetic acid-induced writhing (Hosseinzadeh and Younesi 2002). Naloxone partially blocked only the antinociceptive activity of the stigma aqueous extract. In the hot plate tests, intraperitoneal injection of both extracts showed no significant antinociceptive activity in mice.

Anti-inflammatory Activity

The aqueous and ethanolic saffron stigma extracts showed weak to moderate effect against acute inflammation using xylene-induced ear oedema in mice (Hosseinzadeh and Younesi 2002). In chronic inflammation assessed by formalin-induced oedema in the rat paw, both aqueous and ethanolic stigma extracts, as well as ethanolic petal extract, exerted anti-inflammatory effects. Crocin, 500 mg/kg (ig), inhibited the swelling of mouse ear induced by xylene, the increase of capillary permeability and writhing induced by acetic acid in mice (Ma et al. 1998). Crocin at 50 mg/kg inhibited the oedema of hind paw induced by carrageenan and fresh egg white in rats. The weights of thymus and spleen and humoral immune response were not significantly influenced. At a dose of 200 mg/kg, crocin inhibited footpad reaction induced by sheep red blood cells (SRBC) and markedly inhibited contact dermatitis induced by picryl chloride. In another study, crocin exhibited anti-inflammatory effects in vitro and in vivo (Xu et al. 2009). In vitro, cyclooxygenase (COX) inhibition assays showed that crocin exhibited a dual inhibitory activity against the COX-1 and COX-2 enzymes. Pretreatment with crocin (p.o.) dose-dependently inhibited the xylene-induced ear oedema in mice and carrageenan-induced paw oedema in rats. In gastric lesion tests, crocin was gastric sparing in that it elicited markedly fewer stomach lesions as compared to the number of stomach lesions caused by indomethacin in rats. In addition, crocin was found to significantly inhibit the productions of prostaglandin E_2 (PGE_2) in lipopolysaccharide-challenged RAW 264.7.

Crocin, safranal and vitamin E administered intraperitoneally to rats prevented the toxic effect of diazinon on some biochemical indices and enzyme levels (Hariri et al. 2010). The levels of serum TNF-α, direct 8-iso-prostaglandin F2α and soluble protein-100 β (S100β) were increased significantly by diazinon. The augmentation of direct 8-iso-prostaglandin F2α and S100β levels by diazinon was significantly decreased by crocin, safranal and vitamin E. TNF-α level was significantly decreased in diazinon plus crocin

50 and 100 mg/kg-treated groups compared to the diazinon group. This study showed that vitamin E, safranal and crocin could prevent diazinon-induced enzyme elevation and augmentation of some specific biomarkers. Vitamin E was able to only reduce 8-iso-prostaglandin F2α and S100β levels. Similarly, they found that intraperitoneal injection of aqueous extract of saffron prevented diazinon-induced rise of serum tumour necrosis factor-α (inflammation marker), direct 8-iso-prostaglandin F2α (oxidative stress marker) and soluble protein-100 β (S100β, neuronal damage marker) in rats (Moallem et al. 2013). In contrast, vitamin E was able to only reduce 8-iso-prostaglandin F2α and S100β levels. Further Hariri et al. (2011) found that vitamin E and, at lower doses, safranal (0.025 and 0.05 ml/kg) and crocin (50 mg/kg) restored the reduction of red blood cell, haemoglobin and haematocrit indices induced by diazinon and also prevented the reduction in platelet count indices in diazinon-treated group. Vitamin E, safranal (0.025 or 0.05 ml/kg) and all doses of crocin decreased the elevation in reticulocyte induced by diazinon. In all doses vitamin E, crocin and safranal did not inhibit the effect of diazinon on RBC cholinesterase activity. Vitamin E, safranal and crocin could not prevent this genotoxicity (increase in micronucleus indices) induced by diazinon. The study showed that vitamin E, safranal and crocin (without effects on cholinesterase) reduced diazinon haematological toxicity, but they did not prevent the genotoxicity induced by diazinon.

In an arthritic animal model, crocin effectively neutralized the augmented serum levels of enzymatic (MMP-13, MMP-3 and MMP-9 and HAases) and nonenzymatic (TNF-α, IL-1β, NF-κB, IL-6, COX-2, PGE2 and ROS) inflammatory mediators (Hemshekhar et al. 2012). Further, crocin restored the arthritis altered antioxidant status of the system (GSH, SOD, CAT and GST). It also protected bone resorption by inhibiting the elevated levels of bone joint exoglycosidases, cathepsin-D and tartrate-resistant acid phosphatases. Together the data showed crocin revitalized the arthritis induced cartilage and bone deterioration along with inflammation and oxidative damage that could be accredited to its antioxidant nature. *C. sativus* extract and its constituent safranal exhibited a preventive effect on lung inflammation of ovalbumin-sensitized guinea pigs (Boskabady et al. 2012). Treatment of ovalbumin-sensitized guinea pigs (S group) administered drinking water only with dexamethasone, all concentrations of saffron extract and safranal significantly improved lung pathological changes, most types of WBC and serum histamine levels compared to group S. Treatment with safranal was more effective in improvement of most pathological changes, total and differential WBC count as well as serum histamine level. The results also showed that the effect of the plant was perhaps due to its constituent safranal. *C. sativus* extract exhibited a preventive effect on tracheal responses and decreased serum levels of inflammatory mediators IL-4, IFN-γ, IFN-γ/IL-4, total NO and nitrite in ovalbumin-sensitized guinea pigs but also elicited increased Th1/Th2 balance (Byrami and Boskabady 2012; Byrami et al. 2013).

Recent studies showed that IL-1β markedly up-regulated the expression of MMP-1, MMP-3 and MMP-13 in culture rabbit chondrocytes, and this activation was inhibited by co-incubation with crocin in a dose-dependent manner, in comparison to the control group (Ding et al. 2013). Additionally, crocin inhibited IL-1β-induced activation of the nuclear factor-kappa B pathway by suppressing degradation of inhibitory-kappa-B-α. In vivo investigations showed that crocin ameliorated cartilage degeneration and that expression of the MMP-1, MMP-3 and MMP-13 genes in cartilage was significantly inhibited by crocin. The findings suggested that the anti-inflammatory activity of crocin may be of potential value in the prevention and treatment of osteoarthritis.

Anti-hyperinsulinemic/ Antidiabetic Activity

Studies found that crocetin had a beneficial effect on insulin sensitivity in fructose-fed male Wistar rats (Xi et al. 2007a). The favourable impact on adiponectin, TNF-α and leptin expression in

white adipose tissue may be involved in the improvement of insulin sensitivity observed in crocetin-treated rats. Fructose feeding caused a marked increase in the weight of epididymal white adipose tissue, a significant reduction in the expression of both protein and mRNA of adiponectin (an insulin-sensitizing adipocytokine) and enhancement of tumour necrosis factor (TNF)-α and leptin in epididymal white adipose tissue in fructose-fed rats. These disorders were effectively normalized in crocetin-treated rats. Crocetin also alleviated free fatty acid (FFA)-induced insulin insensitivity and dysregulated mRNA expression of adiponectin, TNF-α and leptin in primary cultured rat adipocytes.

Studies by Kang et al. (2012) indicated the potential of saffron as a therapeutic agent in diabetic patients. Saffron was found to strongly enhance glucose uptake and the phosphorylation of AMPK (AMP-activated protein kinase)/ACC (acetyl-CoA carboxylase) and MAPKs (mitogen-activated protein kinases), but not PI 3-kinase (phosphatidylinositol 3-kinase)/Akt. Interestingly, the co-treatment of saffron and insulin further improved the insulin sensitivity via both insulin-independent (AMPK/ACC and MAPKs) and insulin-dependent (PI 3-kinase/Akt and mTOR) pathways. Cross-linkage between the two signalling pathways of glucose metabolism in skeletal muscle cells was also suggested. Their studies highlighted the major role of AMPK in effects of saffron on glucose uptake and insulin sensitivity in skeletal muscle cells.

Studies showed that crocin at a dose of 60 mg/kg for 6 weeks was found to significantly reduce the blood glucose level in streptozotocin-induced diabetic rats (Rajaei et al. 2013). Additionally, there was a significant increase in thiobarbituric acid-reactive substance (TBARS) levels and decreased total thiol concentrations in the liver and kidney of diabetic animals. Crocin, at doses of 30 and 60 mg/kg, appeared to exert an antioxidative activity demonstrated by a lowering of lipid peroxidation levels in these organs. Their findings suggest that crocin elicited hypoglycemic and antioxidative activities in streptozotocin-induced diabetes and it may be useful in the management of diabetic patients.

Antitussive Activity

Intraperitoneal administration of the ethanolic extract of *C. sativus* stigma (100–800 mg/kg) and safranal (0.25–0.75 ml/kg) to guinea pigs reduced the number of coughs (Hosseinzadeh and Ghenaati 2006). The ethanolic and aqueous extracts of petal and crocin did not exhibit antitussive activity.

Antimicrobial Activity

The ethanolic and methanolic extracts of *Crocus sativus* showed anti-Brucella activity against tetracycline-resistant *Brucella melitensis* (Motamedi et al. 2010). Pintado et al. (2011) found that safranal and crocin, and probably their chemical relatives, were involved in the antibacterial activity of saffron and that this effect could significantly reduce the risk of food contamination with *Salmonella enterica* by this spice. The antibacterial activity against five different serovars of *Salmonella* were in the order of 8–16 and 64–128 mg/mL for safranal and crocin, respectively.

Studies demonstrated that the saffron stamen and perianth possessed significant antifungal, cytotoxic and antioxidant activities as well as the stigma, though not to the same extent (Zheng et al. 2011). The ether fraction composition of the three *C. sativus* parts was different from each other, but lauric acid, hexadecanoic acid, 4-hydroxydihydro-2(3*H*)-furanone and stigmasterol were the common constituents shared by all the three fractions. The stamen ether fraction displayed the strongest antifungal and cytotoxic activities, whereas both the saffron stamen and perianth ether fractions exhibited significant antioxidant activities.

Hepatoprotective Activity

Results of studies suggested that crocin dyes possessed chemopreventive effects on the early acute hepatic damage induced by aflatoxin B1 (AFB1) and dimethylnitrosamine (DMN) in rats (Lin and

Wang 1986). Feeding experiments demonstrated that crocin dyes at 0.1 % in the diet could suppress partially the chronic hepatic damage induced by multiple dosages of AFB1 or DMN, but at a higher concentration of 1 % crocin dyes failed to do so because of their host toxicity. Studies by Amin et al. (2011) indicated that saffron exerted a significant chemopreventive effect against diethylnitrosamine (DEN)-induced liver cancer via inhibition of cell proliferation and induction of apoptosis, suppression of inflammatory response and modulation of oxidative damage. Saffron inhibited the DEN-mediated elevations in numbers of cells positive for Ki-67, cyclooxygenase-2, inducible nitric oxide synthase, nuclear factor-kappa B p65 and phosphorylated tumour necrosis factor receptor. Saffron counteracted DEN-induced oxidative stress in rats as assessed by restoration of superoxide dismutase, catalase and glutathione S-transferase levels and diminishing of myeloperoxidase activity, malondialdehyde and protein carbonyl formation in the liver. El-Beshbishy et al. (2012) found the significant decrease in haematocrit value, RBCs count and haemoglobin concentration and catalase and superoxide dismutase activities and significant increase in rat liver and brain malondialdehyde level, lactate dehydrogenase and protein carbonyl content in BeCl2-treated rats were restored near to normal levels by prior crocin treatment. Their results suggested that BeCl2 induced oxidation of cellular lipids and proteins and that administration of crocin reduced BeCl2-induced oxidative stress combined with initiation of mRNA expression of antioxidant genes.

Nephroprotective Activity

El Daly (1998) reported that concurrent administration of cysteine together with vitamin E, *Crocus sativus* and *Nigella sativa* reduced the toxicity of cisplatin in rats. Blood urea nitrogen (BUN) and serum creatinine levels as well as cisplatin-induced serum total lipid increases were significantly reduced. The protective agents given together with cisplatin led to an even greater decrease in blood glucose than that seen with cisplatin alone. The serum activities of alkaline phosphatase, lactate dehydrogenase, malate dehydrogenase, aspartate aminotransferase and alanine aminotransferase of cisplatin-treated rats were significantly decreased, whereas the activities of glutathione reductase and isocitrate dehydrogenase were significantly increased. In cisplatin-treated rats, the liver activities of isocitrate dehydrogenase and aspartate aminotransferase were significantly increased, whereas much greater changes were found in the kidneys, with increased activity of glucose-6-phosphate dehydrogenase and decreased activities of alkaline phosphatase, isocitrate dehydrogenase, malate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, sorbitol dehydrogenase and gamma-glutamyl transferase, as well as a decreased phosphorylation to oxidation ratio in the mitochondria, indicating reduced adenosine triphosphate production. Administration of the combined treatment together with cisplatin partially reversed many of the kidney enzyme changes induced by cisplatin. The combined treatment also tended to protect from cisplatin-induced falls in leucocyte counts, haemoglobin levels and mean osmotic fragility of erythrocytes and also prevented the increase in haematocrit. It was concluded that cysteine, vitamin E, *Crocus sativus* and *Nigella sativa* combination may be a promising strategy for reducing cisplatin-toxic side effects including nephrotoxicity. Earlier studies reported that in mice, an extract of *Crocus sativus* stigmas partially prevented the decreases in body weight, haemoglobin levels and leucocyte counts caused by 2 mg/kg of cisplatin i.p. for 5 days (Nair et al. 1991b). Treatment with the *C. sativus* extract also significantly prolonged the life span of cisplatin-treated mice almost threefold.

Studies suggested that the aqueous saffron extract (*Crocus sativus*) and its active constituent, crocin, may be useful agents for the prevention of renal ischaemia–reperfusion (IR)-induced oxidative injury in rats (Hosseinzadeh et al. 2005). In crocin-pretreated groups, a reduction in TBARS levels and an elevation in antioxidant power (FRAP value) and total thiol concentrations, as compared with control

group, were observed. The aqueous extract also reduced lipid peroxidation products and increased antioxidant power in ischaemia–reperfusion injured rat kidneys. Saffron at 40 mg/kg/day administered to male Wistar rats significantly reduced gentamicin-induced increases in blood urea nitrogen (BUN) and histological scores in the kidney (Ajami et al. 2010). Gentamicin-induced increases in BUN, serum creatinine, malondialdehyde and histological injury were significantly reduced by treatment with saffron 80 mg/kg/day. The results suggested that saffron treatment reduced gentamicin-induced nephrotoxicity in a dose-dependent manner. Studies showed that crocin attenuated cisplatin-induced renal oxidative stress in rats (Naghizadeh et al. 2010, 2011). Blood urea and creatinine and urinary glucose and protein concentrations in crocin-treated groups were significantly lower compared to the cisplatin-treated group. Histopathological studies showed massive damage in the S3 segment of proximal tubules in cisplatin-treated group but not in crocin-treated groups. Crocin treatment elicited a significant reduction in malondialdehyde (MDA) concentration and produced a significant elevation in total thiol and glutathione peroxidase concentrations. There was a significant increase in the mRNA expression of glutathione peroxidase in crocin-treated groups.

Adaptogenic Activity

Studies revealed that saffron water extract and safranal had an important impact on the reduction of both metabolic and behavioural signs of stress in male Wistar rats (Hooshmandi et al. 2011). Stress elevated the corticosterone plasma (115 nmol/L) concentration in the control and intra-amygdala (1, 5 and 10 μg/rat)-treated groups but not in groups that received saffron extract or safranal (55 nmol/L) intraperitoneally (1, 5 and 10 mg/kg). Further, anorexia was reduced only in groups that received the saffron extract (1, 5 and 10 mg/kg) or safranal (1, 5 and 10 mg/kg) intraperitoneally. Stress increased sniffing, rearing, locomotion and coping time, which were decreased by intraperitoneal (1, 5 and 10 mg/kg) but not by intra-amygdala (1, 5 and 10 μg/rat) administration of saffron extract and safranal. In another study, intraperitoneal (i.p.) administration of the aqueous but not the ethanol extract (10, 50 and 100 mg/kg) of saffron significantly reduced the anorexic time in mice (Halataei et al. 2011). The results were similar for crocin (1, 5 and 10 mg/kg; i.p.). In addition, a reduction in weight gain was observed in the controls as well as in the groups that received alcohol extract or safranal. However, this was not observed in animals treated with aqueous extract or crocin. It was concluded that the saffron aqueous extract and its constituent crocin reduced side effects of electroshock stress in mice. Crocetin administration to male Sprague-Dawley rats during resuscitation post-haemorrhage increased survival, at least in part by protecting the liver from activation of apoptotic cell death (Yang et al. 2011). Crocetin continued to show promise as a potential treatment strategy for haemorrhagic shock.

Relaxant Activity

Electrical field stimulation of the isolated rat vas deferens and guinea pig ileum evoked contractions were decreased by aqueous and ethanol extracts of *C. sativus* petals (Fatehi et al. 2003). The aqueous extract (560 mg/ml) significantly reduced the contractile responses of vas deferens to epinephrine (1 μM) without any change in contraction induced by KCl (300 mM). The results suggested the relaxant action of *C. sativus* petals' extract on contraction induced by electrical field stimulation in the rat isolated vas deferens to be a postsynaptic effect. Another study showed aqueous–ethanolic extracts of *C. sativus* and one of its main constituents, safranal, exerted potent relaxant effect on tracheal chains of guinea pigs that was comparable to or even higher than that of theophylline at the concentrations used (Boskabady and Aslani 2006). The results indicated that safranal was, at least in part, responsible for the relaxant effect of *C. sativus.* In a study on the mechanism(s) of the relaxant effects of *Crocus sativus*, the aqueous–ethanolic extracts of *C. sativus* and one of its constituent, safranal, exhibited potent stimulatory effect on

beta-adrenoceptors in tracheal chains of guinea pig (Nemati et al. 2008). A possible inhibitory effect of the aqueous–ethanolic extract on histamine (H_1) receptors was also suggested which was confirmed in a subsequent study on guinea pig tracheal chains (Boskabady et al. 2010). The EC_{50} (effective concentration of histamine causing 50 % of maximum response) obtained in the presence of chlorpheniramine and all concentrations of saffron extract in all three groups: trachea incubated with (1) indomethacin; (2) indomethacin, propranolol and atropine; and (3) indomethacin and propranolol were significantly greater than those of saline except low concentration of the extract in groups 1 and 3. In a more recent study, Boskabady et al. (2011a) reported that the EC_{50} (effective concentration of histamine causing 50 % of maximum response) obtained in the presence of chlorpheniramine and all concentrations of safranal in both groups of tracheal chains incubated with (1) indomethacin and (2) indomethacin, propranolol and atropine were significantly greater than those of saline. The EC_{50} obtained in the presence of all concentrations of safranal and maximum response of its two higher concentrations (1.25 and 2.5 μg/ml) in group 2 were greater than in group 1.

Spasmodic Activity

Hydroalcoholic extract of *C. sativus* (200–1,600 μg/ml) was found to increase the spontaneous rhythmic contraction of isolated rat uterus due to KCl (10 mM) in vitro in comparison with the control tissues (Sadraei et al. 2003). However, they did not increase the uterus response to acetylcholine. The spasmodic action of *C. sativus* hydroalcoholic extracts suggested that some materials in the plant could increase uterus spontaneous contraction and may have the potential to induce early uterus contraction during the pregnancy.

Analgesic Activity

A 7-day treatment with the ethanolic and aqueous saffron extracts (50,100 and 200 mg/kg, i.p.) and safranal (0.025, 0.05 and 0.1 mg/kg, i.p.) attenuated allodynia and hyperalgesia induced by chronic constriction injury model of neuropathic pain in rats in a dose-dependent manner (Amin and Hosseinzadeh 2012). Crocin even at the high dose (50 mg/kg) failed to produce any protective role. However, gabapentin (100 mg/kg) as a reference drug significantly alleviated all behavioural manifestations of neuropathic pain compared to control group. The results suggested that ethanolic and aqueous extracts of saffron as well as safranal could be useful in the treatment of different kinds of neuropathic pains and as an adjuvant to conventional medicines.

Effect on Menstrual Distress

In a double-blind, randomized and placebo-controlled trial of women 20–45 years with regular menstrual cycles and experience of premenstrual syndrome (PMS) symptoms, saffron was found to be effective in relieving symptoms of PMS (Agha-Hosseini et al. 2008). A significant difference was observed in efficacy of saffron in cycles 3 and 4 in the Total Premenstrual Daily Symptoms and Hamilton Depression Rating Scale.

Studies by Fukui et al. (2011) supported the existence of physiological and psychological effects of saffron odour in women suffering menstrual distress. Their results indicated that saffron odour exerted some effects in the treatment of premenstrual syndrome, dysmenorrhoea (menstrual pain) and irregular menstruation. Saffron odour significantly decreased cortisol levels after short-term stimulation (20 min) in both follicular and luteal phases. 17β-Estradiol level after exposure to saffron odour was increased in both the follicular- and luteal-phase groups.

Aphrodisiac Activity

Crocin, at all doses, and aqueous saffron stigma extract, especially at doses 160 and 320 mg/kg body wt., increased mounting frequency, intromission frequency and erection frequency

behaviours and reduced ejaculation latency, intromission latency and mounting latency parameters in male rats (Hosseinzadeh et al. 2008c). In contrast, safranal did not show aphrodisiac effects. The study revealed an aphrodisiac activity of saffron aqueous extract and its constituent crocin. In a 3-month clinical trial, of 52 nonsmoker men with idiopathic infertility, consumption of saffron (50 mg) mixed in milk thrice a week was found to have a positive effect on sperm morphology and motility while it did not increase sperm count (Heidary et al. 2008). In a pilot study of 20 male patients with erectile dysfunction, ingestion of a tablet containing 200 mg of saffron for 10 days was found to have a positive effect on sexual function with increased number and duration of erectile events (Shamsa et al. 2009). The International Index of Erectile Function questionnaire (IIEF-15) total scores were significantly higher in patients after saffron treatment (before treatment 22.15; after treatment 39.20). Contrariwise, the findings of an open-label, randomized, fixed-dose, crossover study comparing efficacy and safety of sildenafil citrate and saffron for treating erectile dysfunction in men (346, mean age 46.6+/−8.4 years) did not support a beneficial effect of saffron administration (Safarinejad et al. 2010). No significant improvements were observed with regard to the IIEF (International Index of Erectile Function) sexual function domains, SEP (Sexual Encounter Profile) questions and EDITS (Erectile Dysfunction Inventory of Treatment Satisfaction) scores with saffron administration. No improvement in 15 individual IIEF questions in patients was observed while taking saffron. Treatment satisfaction as assessed by partner versions of EDITS was found to be very low in saffron patients (72.4 vs. 25.4). Mean per patient 'yes' responses to GEQ (Global Efficacy Question) was 91.2 and 4.2 % for sildenafil and saffron, respectively.

In a separate 26-week, prospective, double-blind, randomized, placebo-controlled study of 260 infertile men with idiopathic oligoasthenoteratozoospermia (OAT), saffron, 60 mg/day, administration did not result in beneficial effects (Safarinejad et al. 2011). At the end of the study, no statistically significant improvements were observed in either group (saffron treated and placebo) in any of the studied semen parameters (sperm density, morphology and motility). Also, saffron administration did not improve total seminal plasma antioxidant capacity, compared with baseline and placebo subjects.

In a 4-week, randomized, double-blind, placebo-controlled trial of 30 married male patients with major depressive disorder whose depressive symptoms had been stabilized on fluoxetine and had subjective complaints of sexual impairment, ingestion of saffron (15 mg twice per day) resulted in significantly greater improvement in erectile function and intercourse satisfaction domains, and total scores by week 4 than the placebo group (Modabbernia et al. 2012). Effect of saffron did not differ significantly from that of placebo in orgasmic function, overall satisfaction and sexual desire domain scores. Nine patients (60 %) in the saffron group and one patient (7 %) in the placebo group achieved normal erectile function (score >25 on erectile function domain) at the end of the study. The results indicated saffron to be a tolerable and efficacious treatment for fluoxetine-related erectile dysfunction. In a 6-week, randomized, double-blind, placebo-controlled study involving 38 women with major depression who were stabilized on fluoxetine 40 mg/day, patients administered saffron (30 mg/daily) showed effective improvement in some of the fluoxetine-induced sexual dysfunctions including arousal, lubrication and pain but not in desire, satisfaction and orgasm domains (Kashani et al. 2013). Frequency of side effects was similar between the saffron and placebo groups.

Immunomodulatory Activity

Non-cytotoxic concentrations of a proteoglycan from saffron corms promoted significant macrophage activation, detected by the release of nitric oxide (Escribano et al. 1999a). A rapid activation of protein kinase C and NF-kappaB was obtained after proteoglycan treatment, which could explain the induction of nitric oxide synthase. Proteoglycan concentrations ranging from 10 to 1,000 ng/ml specifically promoted apoptosis of

macrophages, probably triggered by their activation. This molecule did not inhibit in vitro migration or invasion of human tumour cells. They concluded that the results supported a plausible immune-modulating activity for this saffron Crocus proteoglycan. Boskabady et al. (2011b) investigated the *Crocus sativus* extract on human lymphocytes' cytokines and T helper 2/T helper 1 balance. In peripheral blood mononuclear cells stimulated with phytohaemagglutinin, different concentrations of the extract significantly inhibited cell viability of lymphocytes. High concentrations of the extract (500 μg/ml) also inhibited secretion of IFN-γ in stimulated cells and IL-10 secretion in both stimulated and non-stimulated cells. The extract showed a stimulatory effect on IFN-γ and IL-4 secretion in non-stimulated cells. The ratios of IFN-γ to IL-4 in the presence of all concentrations of saffron on stimulated cells were significantly higher than for the control group. These results indicated that the extract of saffron led to increased ratio of IFN-γ to IL-4. In a separate study, oral administration of alcoholic extract of *Crocus sativus* at graded dose levels from 1.56 to 50 mg/kg p.o. potentiated the Th(2) response of humoral immunity causing significant increases in agglutinating antibody titre in mice at a dose of 6.25 mg/kg and an elevation of CD19(+) B cells and IL-4 cytokine, a signature cytokine of Th(2) pathway (Bani et al. 2011). Appreciable elevation in levels of IgG1 and IgM antibodies of the primary and secondary immune response was also observed. However, saffron extract showed no appreciable expression of the Th(1) cytokines IL-2 (growth factor for CD4(+) T cells) and IFN-γ (signature cytokine of Th(1) response). The results suggested the selective up-regulation of the Th(2) response of saffron indicating its use for subsequent selective Th(2) immunomodulation.

Kianbakht and Ghazavi (2011) elevated the immunomodulatory effects of saffron in a randomized, double-blind, placebo-controlled clinical trial of healthy men aged 21.4 ± 0.8 years comprising 45 men taking 100 mg saffron tablet daily for 6 weeks and 44 men taking placebo. After 3 weeks, saffron increased the IgG (immunoglobulin) level and decreased the IgM (immunoglobulin M) level compared with the baseline and placebo, decreased the percentage of basophils and the count of platelets compared with baseline but increased the percentage of monocytes compared with placebo. However, these parameters returned to the baseline levels after 6 weeks. No adverse effects were reported. The results suggested that the subchronic daily use of 100 mg saffron had temporary immunomodulatory activities without any adverse effects.

Spanish saffron was found to contain novel saponins with adjuvant properties (Castro-Díaz et al. 2012). In vivo immunization studies and tumour protection experiments unambiguously established the value of saffron saponins as candidate adjuvants. These saponins were able to increase both humoral and cellular immune responses to protein-based vaccines, ultimately providing a significant degree of protection against tumour challenge when administered in combination with a tumour antigen.

Sleep Enhancement Activity

Administration of crocin (30 and 100 mg/kg) to mice increased the total time of non-rapid eye movement (non-REM) sleep by 60 and 170 %, respectively, during a 4 h period from 20:00 to 24:00 after its intraperitoneal administration at a lights-off time of 20:00 (Masaki et al. 2012). Crocetin (100 mg/kg) also increased the total time of non-REM sleep by 50 % after administration. These compounds did not change the amount of REM sleep or show any adverse effects, such as rebound insomnia, after the induction of sleep.

Wound Healing Activity

Saffron pollen extract cream was found to have wound healing effect on thermal induced burn wounds in rats (Khorasani et al. 2008). The wound size of saffron group was significantly smaller than other groups. On day 25, average size of wound was 5.5, 4, 0.9 and 4.1 cm^2 in control, base, saffron and silver sulphadiazine

groups, respectively. Histological comparison revealed that saffron significantly increased reepithelialization in burn wounds, as compared to other cream-treated wounds.

Antiplatelet Activity

Bulbs of *Crocus sativus* var. *cartwrightianus* were found to contain both a platelet aggregation inducer and inhibitor (Liakopoulou-Kyriakides and Skubas 1990). The aggregating factor has a molecular weight of 42 kDa (Liakopoulou-Kyriakides et al. 1985; Liakopoulou-Kyriakides and Skubas 1990) and lacked enzymatic activity such as proteinase, esterase and acid or alkaline phosphatase. The inhibitory factor had a molecular weight of 27 kDa and was found to possess strong proteinase activity. Saffron extract was found to protect human platelets from aggregation and lipid peroxidation stimulated by a variety of agonists like ADP (61 μM), epinephrine (76 μM), collagen (11 μg/ml), calcium ionophore A 23,187 (6 μoM) and ristocetin (1.25 μg/ml) (Jessie and Krishnakantha 2005). The inhibitory effect was dose dependent with concentrations varying between 0.16 and 0.80 mg and time dependent at IC_{50}. A significant decrease was observed in malondialdehyde (MDA) formed, one of the end products of arachidonic acid metabolism and of serotonin released from dense granules of platelets at respective IC_{50}. Lipid peroxidation in platelet membranes induced by iron–ascorbic acid system was inhibited by saffron extract significantly with an IC_{50} of 0.33 mg.

Crocetin showed a dose-dependent inhibition of platelet aggregation induced by ADP and collagen, but not by arachidonic acid (AA) (Yang et al. 2008). Crocetin significantly attenuated dense granule release, while neither platelet adhesion to collagen nor cyclic AMP level was altered by crocetin. Pretreatment with crocetin was confirmed to partially inhibit Ca (2+) mobilization via reducing both intracellular Ca (2+) release and extracellular Ca (2+) influx. Additionally, crocetin prolonged the occlusive time in electrical stimulation-induced carotid arterial thrombosis. These findings suggested that the inhibitory effect of crocetin on platelet activity and thrombosis formation may be related to the inhibition of Ca (2+) elevation in stimulated platelets.

Crocetin administration (3 mg/kg), 30 min before the beginning of endotoxin infusion, improved disseminated intravascular coagulation (DIC)-related haemostatic indices such as platelet blood counts, blood plasma fibrinogen and protein C concentration in rabbits (Tsantarliotou et al. 2013). Further, it ameliorated DIC-associated disease and fibrin deposition in the glomeruli. These results indicated that crocetin exhibited a preventive antithrombotic role in vivo and the potential of developing crocetin-based DIC treatment modalities.

In a 1-week, double-blind, placebo-controlled study involving 60 healthy volunteers, administration of 200 and 400 mg saffron tablets did not elicit any effect on coagulant and anticoagulant system (Ayatollahi et al. 2013). Statistical analysis showed no difference between groups for plasma levels of fibrinogen, factor VII (as coagulant agent), C and S protein (as anticoagulant agent), prothrombin time and partial prothrombin time.

Antivenin Activity

Crocin (from *Crocus sativus*), a potent antioxidant, demonstrated anti-ophidian against viper, *Vipera russelli*, venom-induced oxidative stress (Santhosh et al. 2013a). Crocin ameliorated the venom-induced elevated oxidative stress; elevated proinflammatory cytokine levels including IL-1β, TNF-α and IL-6; and haematological alteration, namely, depletion of haemoglobin, haematocrit, mean corpuscular volume and platelet count, in experimental animals. They also showed that *Vipera russelli* venom-induced platelet apoptotic events including endogenous reactive oxygen species (ROS) generation, intracellular Ca(2+) mobilization, mitochondrial membrane depolarization, cyt-c translocation, caspase activation and phosphatidylserine externalization were effectively mitigated when the venom was pretreated with crocin (Santhosh et al. 2013b). Snake venom metalloproteinases (SVMPs) and phospholipase

A_2 (PLA_2) had been reported to play crucial roles in the pathophysiology of haemorrhage by targeting/altering the platelets function which may result in thrombocytopenia. The study highlighted one of the less studied features of venom-induced secondary complications, i.e. platelet apoptosis, and revealed the underlying basis for venom-induced thrombocytopenia, systemic haemorrhage and in vivo anticoagulant effect.

Protective Activity Against Extremity Ischaemia–Reperfusion Injury

Studies showed that saffron extract and its constituents exhibited a protective effect against lower limb ischaemia–reperfusion in rat (Hosseinzadeh et al. 2009). Following saffron, crocin and safranal administration, the total sulphhydryl H contents and antioxidant capacity were elevated in the skeletal muscle. The malondialdehyde level was decreased significantly in test groups.

Protein Interaction (Binding and Polymerization) Activity

Crocus sativus lectin (CSL) was found to be mannose-specific plant lectins with a unique binding specificity (Oda et al. 2000). CSL was found to bind to the branched mannotriose structure Man3GlcNAc in the N-glycan core. This unique binding specificity of CSL may offer many possibilities of its use in analytical and preparative applications. *Crocus sativus* lectin (CSL) from the bulbs was found to be truly mannose specific—its binding was inhibited only by mannooligosaccharides and not by glucose or its oligomers or polymers (Kakehi et al. 2003). Also, hen ovomucoid was a good inhibitor of CSL, but it did not inhibit other mannose-specific lectins from other plant bulbs. It was found that CSL specifically recognized the N-glycan core pentasaccharide.

Crocetin (CRT) and dimethylcrocetin (DMCRT) from saffron stigma and safranal, the main component of saffron's essential oil, were found to bind to human serum albumin in aqueous solution at physiological conditions using constant protein concentration and various ligand contents (Kanakis et al. 2007a). Structural analysis showed that crocetin, dimethylcrocetin and safranal bind nonspecifically (H-bonding) via protein polar groups with binding constants of $Kcrt = 2.05 \times 10^3/M$, $Kdmcrt = 9.60 \times 10^4/M$ and $Ksaf = 2.11 \times 10^3/M$. The protein secondary structure showed no major alterations at low ligand concentrations (1 μM), whereas at higher content (1 mM), decrease of alpha-helix from 55 % (free HSA) to 43–45 % and increase of beta-sheet from 17 % (free HSA) to 18–22 % and random coil 7 % (free HSA) to 10–14 % occurred in the ligand–HSA complexes. All three exhibited lower antioxidant than the standard antioxidants trolox and butylated hydroxytoluene (BHT) when tested using DPPH assay. The IC_{50} values were CRT (17.8 μg/ml), safranal (95 μg/ml), trolox (5.2 μg/ml) and BHT (5.3 μg/ml), and the inhibition of DMCRT reached a point of 38.8 %, which corresponded to a concentration of 40 μg/ml. Safranal, crocetin and dimethylcrocetin were also found to bind to calf-thymus DNA in aqueous solution at physiological conditions (Kanakis et al. 2007b). Both intercalative and external binding modes were observed, with overall binding constants $K(safranal) = 1.24 \times 10^3/M$, $K(CRT) = 6.2 \times 10^3/M$ and $K(DMCRT) = 1.85 \times 10^5/M$. A partial B- to A-DNA transition occurred at high carotenoids and safranal concentrations. In vitro studies showed that saffron and its carotenoids interacted with calf-thymus DNA (ctDNA) and induced some conformational changes in it (Bathaie et al. 2007). There was a decrease in the Delta $G(H_2O)$, indicating the ctDNA destabilization due to its interaction with the mentioned ligands. Of these carotenoids, the order of potential of interaction with DNA was crocetin > dimethylcrocetin >> crocin.

Results of in vitro studies showed that safranal physically bound to target proteins beta-actin, cytochrome b-c1 complex subunit 1, trifunctional enzyme subunit beta and ATP synthase subunit alpha and beta (Hosseinzadeh et al. 2013). These protein interactions may explain part of safranal's pharmacological effects. Crocin was found

to significantly affect microtubular protein polymerization and structure (Zarei Jaliani et al. 2013). Crocin dose-dependently increased tubulin polymerization and microtubule nucleation rate. After entering a cell, crocin could modulate cellular proteins and their functions.

Reproductive/Oestrogenic Activity

Studies showed that addition of appropriate amounts of saffron aqueous to the maturation medium improved mouse oocyte maturation and embryo development (Tavana et al. 2012). The maturation rate was significantly higher in all groups treated with different concentrations of saffron aqueous extract compared with the control group. However, the lower concentrations of saffron extract (10 and 5 μg/ml) in maturation medium respectively increased the fertilization rate of oocytes and in vitro developmental competence when compared with the control group.

Saffron was found to induce uterine stimulant and oestrogenic effects in guinea pigs and mice, respectively (Chang et al. 1964). In traditional medicine, saffron was reported to induce menstruation (an emmenagogue), and the aqueous extract of saffron had been used for amenorrhoea and dysmenorrhoea.

Pharmacokinetic, Safety and Toxicity Studies

Animal studies indicated that the oral LD_{50} of saffron was 20.7 g/kg administered as a decoction (Chang et al. 1964). Their studies demonstrated that oral administration of saffron extract at concentrations from 0.1 to 5 g/kg was nontoxic in mice (Abdullaev 2002). Li et al. (2007b) found that in rats, orally administered crocin was not absorbed either after a single dose or repeated doses, (1) crocin was excreted largely through the intestinal tract following oral administration, (2) plasma crocetin concentrations did not accumulate with repeated oral doses of crocin, and (3) the intestinal tract served as an important site for crocin hydrolysis.

Crocetin was shown to be quickly absorbed into the blood through the gastrointestinal tract in rats (Liu and Qian 2002). The lowest detectable concentration of crocin-1 in rabbit plasma was 0.42 mg/l (Tang et al. 2004). After administration of crocin-1 in rabbit, the concentration-time curves of crocin-1 was shown to fit two-compartment open model. Animal studies by Xi et al. (2007a, b) found that crocin was excreted largely through the intestinal tract following oral administration and that orally administered crocin was not absorbed either after a single dose or repeated doses. Also plasma crocetin concentrations did not tend to accumulate with repeated oral doses of crocin, and the intestinal tract served as an important site for crocin hydrolysis.

The ethanolic extracts of *Crocus sativus* and propolis did not cause any mortalities or signs of toxicity in mice when administered orally at doses up to 5 g/kg b.wt. In the subchronic study; the tested extracts did not produce any significant change in liver and kidney functions of rats, following oral administration for 8 successive weeks at a dose of 500 mg/kg b.wt. each (Ramadan et al. 2012). Antioxidant study showed that propolis ethanolic extract was a more potent antioxidant than *C. sativus* ethanol extract.

In an open-label study of ten healthy Filipino volunteers, single-dose oral administration of crocetin produced no serious adverse events up to 22.5 mg dose of crocetin, while crocetin was found to be absorbed more quickly than the other carotenoids such as β-carotene, lutein and lycopene (Umigai et al. 2011). Results of a study on four healthy human volunteers before and after consumption of one cup of saffron tea (200 mg of saffron in 80 °C water for 5 min) showed that the concentration of crocetin in the plasma was high after 2 h (1.24–3.67 μM) and could still be determined after 24 h (0.10–0.24) (Chryssanthi et al. 2011b). Interestingly, the percentage of the cis-isomer ranges from 25 to 50 %, suggesting in vivo isomerization.

A double-blind, placebo-controlled design consisting of a 1-week treatment of saffron tablets in healthy volunteers revealed that saffron tablets may change some haematological and biochemical parameters (Modaghegh et al. 2008). However, these alterations were in normal ranges, and they were not important clinically. Saffron at a high dose (400 mg) decreased standing systolic blood pressure and mean arterial pressures

significantly. Saffron decreased slightly some haematological parameters such as red blood cells, haemoglobin, haematocrit and platelets and increased sodium, blood urea nitrogen and creatinine. To date, very few adverse health effects of saffron had been demonstrated (Poma et al. 2012). At high doses (more than 5 g/day), saffron should be avoided in pregnancy owing to its uterine stimulation activity.

Allergy Problems

Of fifty saffron workers evaluated for occupational saffron allergy, three of them were sensitized to saffron pollen and stamen proteins, giving prick and RAST positive values; one patient presented asthma, showing a positive bronchial provocation test, and two patients, rhinoconjunctivitis, showing positive conjunctival provocation tests (Feo et al. 1997). Of a general allergic population of 237, 10 patients also presented cutaneous test and IgE positive to saffron. Saffron allergens were characterized by SDS-PAGE immunoblotting. A relevant allergen of 15.5 kDa with profilinic nature was detected from saffron pollen and stamens. A significant degree of cross-reactivity was demonstrated between saffron and *Lolium*, *Salsola* or *Olea*.

Studies indicated that two lipid transfer proteins (LTPs) rCro s 3.01 and rCro s 3.02 were minor allergens of saffron, at least in saffron-allergic patients (Gómez-Gómez et al. 2010). Full cDNA corresponding to 2 saffron LTP variants was isolated and expressed in *Pichia pastoris*. The molecular weight of rCro s 3.01 and rCro s 3.02 was 9.15 and 9.55 kDa, respectively. Both proteins were recognized by anti-Pru p 3 antibodies. Specific IgE to the purified allergens was found in 50 % of patients for rCro s 3.01 and 33 % for rCro s 3.02 and Pru p 3 in the saffron-allergic patients.

Traditional Medicinal Uses

Crocus sativus is used in folk medicine for various purposes such as an aphrodisiac, antispasmodic and expectorant (Yu-Zhu et al. 2008). As a therapeutic plant, saffron is considered excellent for stomach ailments and as an antispasmodic, to help digestion and to increase appetite. It is also used for depression in Persian traditional medicine (Akhondzadeh et al. 2005). *Crocus sativus* was one of many traditional medicinal plants documented to be used as treatment of kidney and urinary disorders in the tribal communities of Ladakh region in India (Ballabh et al. 2008) where problems in urine discharge, burning sensation and painful urination, inflammation and bleeding in the kidney, irritable condition of bladder, haemorrhage of kidney and removal of blocked urine and kidney stone were the frequently reported disorders. Saffron has been largely used in traditional medicine for its anti-apoptotic and anticarcinogenic properties (Fernández-Sánchez et al. 2012).

Some medical and pharmaceutical applications of saffron listed by Moghaddasi (2010) included: (a) helps digestion, strengthens the stomach and is anti-tympanites; (b) aphrodisiac, activates the sexual desire; (c) is analgesic, especially for colicky pains and gingivitis; (d) anticancerous, fights tumours and accumulation of free radicals; (e) is euphoriant and alleviates neuralgia, acts as a tranquilizer, cures insomnia, strengthens memory power, improves concentration, reacts against spasm, fights depression, the Alzheimer's and Parkinson's diseases; (f) controls blood pressure disorders, lowers high cholesterol levels, cures iron deficiency (anaemia) in girls, reduces chances of such heart diseases as arteriosclerosis and helps improve heart conditions (due to the presence of thiamin, riboflavin and mineral components); (g) cures respiratory disorders such as asthma, cough, influenza and cold; (h) helps blood circulation in the retina and cures macula lutea and ischaemic retinopathy caused by old age; (i) cures rheumatism and bruises when used externally; and (j) cures amoebic dysentery, measles and inflammation of the liver, splenomegaly and urogenital infections.

Other Uses

Saffron can be used promisingly in functional foods, drinks with antioxidant activity and pharmaceutical and cosmetic preparations for its antioxidant activity and probably for its anti-aging

activity (Assimopoulou et al. 2005). Saffron can also be used internally in the form of powder or other pharmacotechnical formulas as a food supplement with antioxidant properties. Saffron has a wide range of usefulness in medicine, cosmetics, and colouring industries, so it can be used for new drug designs (Bathaie and Mousavi 2010). Compounds in saffron find use as colouring agents (crocins and carotenes) in dying cotton and wool fabrics and/or other uses in industry (Liakopoulou-Kyriakides and Kyriakidis 2002).

Saffron spice, the most valuable spice worldwide, is the dried stigma that only represents 7.4 % of *Crocus sativus* flowers (Serrano-Díaz et al. 2012). It is possible to extend the uses of *C. sativus* flowers beyond the production of saffron spice as saffron flowers possessed high phenolic content and excellent antioxidant properties that could contribute to their application as functional ingredients.

Comments

Iran, Greece, Morocco, Kashmir, Spain and Italy (in descending order) are the major countries producing saffron (Ghorbani 2008). According to 2005 statistics Iran produced about 230 tons which constituted 93.7 % of the world saffron production, 82 % of it being exported. Greece with 5.7 tons and Morocco and Kashmir with 2.3 tons come respectively in second and third positions. Major importer countries of Iran's saffron are the United Arab Emirates (UAE), Spain, Turkmenistan, France and Italy.

Consumers may regard certain cultivars as 'premium' quality. The 'Aquila' saffron, or *zafferano dell'Aquila*, is defined by high safranal and crocin content, distinctive thread shape, unusually pungent aroma and intense colour; it is grown exclusively on 8 ha in the Navelli Valley of Italy's Abruzzo region, near L'Aquila. It was first introduced to Italy by a Dominican monk from Inquisition-era Spain. But the biggest saffron cultivation in Italy is in San Gavino Monreale, Sardinia, where it is grown on 40 ha, representing 60 % of Italian production; it too has unusually high crocin, picrocrocin and safranal content. Another is the 'Mongra' or 'Lacha' saffron of Kashmir (*Crocus sativus* 'Cashmirianus'), which is among the most difficult for consumers to obtain. Repeated droughts, blights and crop failures in the Indian-controlled areas of Kashmir combine with an Indian export ban to contribute to its prohibitive overseas prices. Kashmiri saffron is recognizable by its dark maroon-purple hue; it is among the world's darkest, which hints at strong flavour, aroma and colourative effect.

Approximately 150,000 flowers are needed for 1 kg of dried saffron; typically, one would need 2,000 m^2 field area per kg harvest. Less expensive qualities include also the yellow stamina (male sexual organ), which do not have any taste of their own.

Saffron, a sterile triploid, belong to subgenus *Crocus* series *Crocus sativus*—series with closely related species that are difficult to be separated taxonomically and have a complex cytology (Saxena 2010).

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Freesia leichtlinii subsp. *alba*

Scientific Name

***Freesia leichtlinii* subsp. *alba* (G.L.Mey.) J.C. Manning & Goldblatt**

Synonyms

Freesia alba (G.L. Meyer) Gumbleton, *Freesia gentilis* N.E.Br., *Freesia herbertii* N.E.Br., *Freesia picta* N.E. Br., *Freesia refracta* (Jacquin) Klatt var. *alba* G.L. Meyer

Family

Iridaceae

Common/English Names

Freesia

Vernacular Names

Afrikaans: Kammetjie, Ruikpypie
German: Freesie
Japanese: Furījia

Origin/Distribution

The species is native to South Africa. Elsewhere, it is found growing naturalized in the wild in many areas, such as several Australian states and Chile.

Agroecology

In its native range in South Africa, this spring flowering species is found growing in well-drained, sandy or gravelly soils among dune scrub, open forest or at forest edges, usually in light shade and also in damp places near water, mainly along the coast, from Hermanus to Plettenberg Bay (Goldblatt 1982). It is a geophyte, producing underground fleshy buds and arising from an underground corm. They grow in autumn to winter, flowering in spring and dying back to the ground in summer and remaining dormant in summer.

Edible Plant Parts and Uses

Freesia blossoms are edible (Wickes 2004). The highly scented blossoms are used in salads raw or as a garnish (Deane 2007–2012). They are reported to be excellent infused with a sugar syrup and are used in sorbets for flavouring.

T.K. Lim, *Edible Medicinal and Non Medicinal Plants: Volume 8, Flowers*,
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Botany

A small, herbaceous plant 10–40 cm high, arising from an underground corm. Leaves (4–)6–8, erect or inclined, lanceolate or sword shaped (ensiform), pale green, with prominent midribs, entire margins and acute tips, 8–30 cm long by 5–10 mm wide (Plate 1). Flowering stems (scape) erect, unbranched, weakly pubescent to glabrous, green in colour, bases covered by leaf sheaths but bent horizontally during flowering bearing 4-6-(8) flowers (Plates 1 and 2). Flowers strongly scented, actinomorphic, broadly funnel shaped, 20–30 mm long; tepals spreading, cream to white, often with yellow markings on lower tepals, tepals and perianth tube flushed with purple abaxially; filaments included, 15–25 mm; anthers 6–9 mm, unilateral, sometimes parallel; ovary 2–3 mm; style branching opposite anther apices (Plates 1, 2, and 3). Fruit a weakly papillose capsule, 10 mm across. Seeds 2 mm.

Plate 1 Flowering scape bent horizontally with 4–7 flowers

Nutritive/Medicinal Properties

A total of 16 volatile compounds were detected in the flowers of *F. alba*, *F. corymbosa* and *F. elimensis*: α-pinene tr (trace)- 1.7 %, sabinene tr-0.4 %, myrcene 0.2–1.6 %, limonene 0.1–0.8 %,

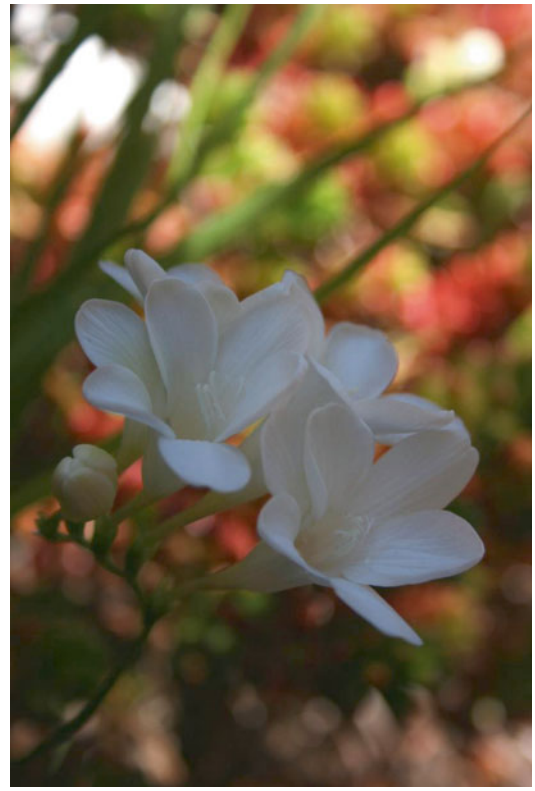

Plate 2 Freesia flowers and buds

Plate 3 Close-view of Freesia flowers

ocimene tr-0.3 %, terpinolene 0.2–1.7 %, hexyl acetate tr-1.1 %, *cis*-3-hexenyl acetate tr-0.8 %, linalool 87.8–96.4 %, α-terpineol tr-0.1 %, α-selinene 0.1–4.7 %, dehydro-α-ionone tr, 2-phenylethyl acetate tr-0.1 %, benzyl alcohol tr-0.4 %, 2-phenylethyl alcohol tr-0.8 % and α-ionone 0.0–0.9 % (Wongchaochant et al. 2005). Fu et al. (2007) found 75 compounds, comprising mainly terpenes, hydrocarbons, alcohols, fatty acid esters and aromatic class compounds in Freesia parental species and hybrids. Among these, linalool was detected from all the sweet-scented flowers except for scentless white tetraploid *F. hybrida.*

The following volatile compounds were identified in Freesia essential oil (Harada and Mihara 1984): 2-methyl-1-pentene 0. 12 %; acetone tr <0.1 %; ethyl acetate tr; ethanol tr; 3-methylheptadiene tr; toluene 0.03 %; 2, 3-dimethyl-2-butanol tr; methyl *n*-butyl ketone tr; 2,2,6-trimethyl-6-vinyltetrahydropyran tr; myrcene 0.02 %; 3-hexanol 0.03 %; 2-hexanol 0.11 %; limonene 0.79 %; 1,9-cineol 0.17 %; γ-terpinene 0.02 %; 2-methylcyclopentanone tr; *cis*-3-hexenyl acetate 0.05 %; *n*-hexanol 0.03 %; *cis*-3-hexenol 0.11 %; *trans*-2-hexenol 0.13 %; trimethyl-pyrazine tr; acetic acid tr; 3-isopropyl-3-methoxypyrazine tr; linalool oxide 0.11 %; linalool oxide (furanoid) 10.13 %; 3-methyl-bicyclo(4,1,0)heptan-2-one tr; 2-isobutyl-3-methoxypyrazine tr; linalool 67.96 %; $C_{15}H_{24}$ (sesquiterpene mw = 204) 0.02 %; *n*-octanol tr; terpinene-4-ol 0.11 %; β-caryophyllene 0.03 %; β-cyclocitral 0.04 %; isovaleric acid tr; geranial 0.02 %; carvone 0.08 %; α-selinene 0.71 %; linalool oxide (pyranoid) 0.06–0.08 %, nerol tr; γ-heptalactone tr; *n*-hexanoic acid tr; geraniol 0.02 %; α-ionone 0.10 %; guaiacol tr; benzyl alcohol tr; phenylethyl alcohol 0.07 %; dimethyl benzyl carbonyl *n*-butyrate 1.11 %; β-ionone 0.28 %; *n*-heptanoic acid tr; benzothiazole tr; *n*-octanoic acid tr; γ-nonalactone tr; 2,4-dimethylphenol tr; *p*-cresol tr; menthane-l,8-diol hydrate (terpin hydrate) 0.03 %; *trans-p*-menthane-1, 8-diol tr; *n*-nonanoic acid tr; eugenol tr; 3-(2-pentyl)-1,2,4-cyclopentatrione tr; *n*-decanoic acid tr; β-geranic acid tr; α-terpineol 19.9 %; and dihydroactinidiolide tr. Linalool (67.92 %) and α-terpineol (19.09 %) with a refreshingly floral odour and citrusy notes were the major components. *cis*-3-Hexenyl acetate 0.05 %, *n*-hexanol 0.03 %, *cis*-3-hexenol 0.11 % and *trans*-2-hexenol 0.13 % were important contributors to the green notes. Pyrazines and lactones such as γ-nonalactone and γ-heptalactone were responsible for the earthy and sweet odour.

Seventy-eight compounds were found in red *Freesia hybrida* steam-distilled essential oil; the major constituents were linalool (30.511 %), dimethyl sulphoxide (24.191 %) and α-terpineol (18.701 %) (Yang et al. 2010). However, the major constituents of the essential oil from microwave extraction were fatty acids (51.369 %) such as linoleic acid (18.691 %), hexadecanoic acid (17.387 %) and linolenic acid (15.291 %).

Other Uses

This plant and its hybrids are grown as ornamental. Due to their specific and delightful aroma, they are often used in hand creams, shampoos, candles and cosmetics.

Comments

The plant can be propagated by seeds or vegetatively by 'bulbs' (i.e. corms) and bulbils.

This species can form dense infestations that compete with native vegetation, particularly native ground orchids and grasses in Victoria, New South Wales and Tasmania and has been deemed an environmental weed in some states in Australia.

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Gladiolus dalenii

Scientific Name

***Gladiolus dalenii* Van Geel**

Synonyms

Gladiolus dracocephalus Hook. f., *Gladiolus natalensis* Reinw. ex Hook. f., *Gladiolus psittacinus* Hook., *Gladiolus psittacinus* Hook. f. var. *cooperi* (Baker) Baker

Family

Iridaceae

Common/English Names

African Gladiolus, Dragon's Head Lily, Gladiolus, Natal Lily, Parrot Lily, Parrot-Beaked Gladiolus, Parrot Gladiolus, Sword Lily

Vernacular Names

Burundi: Ikirungu (Kirundi)
Democratic Republic of Congo: Karungu (Kinyarwanda), Negenege (Kifuleru)
Madagascar: Sakavirondambo (Betsileo country)
South Africa: Papegaai-Gladiolus, Wildeswaardlelie (Afrikaans), Phende–phende (Luvenda), Kxahla-e-kholo (Shoto), Khahla-E-Kholo (South Sotho), Sidvwana (Swazi), Isidwi Esibomvu, Udwendweni, Uhlakahle (Zulu)

Origin/Distribution

Gladiolus dalenii is one of the most widely distributed species of *Gladiolus,* occurring from eastern South Africa and Madagascar throughout tropical Africa and into western Arabia. It is a primary parental species of the large flowering modern Grandiflora hybrids. The species comprised diploid, tetraploid and hexaploid races often giving rise to tetraploid hybrids.

Agroecology

In its native range of summer rainfall areas, it is found in open grasslands, savanna woodlands and scrub and in rocky areas, often among rocks along streams, at altitudes up to 2,500 m. *G. dalenii* is absent from the winter rainfall (Cape) regions and from the semiarid and arid regions including the Karoo, Kalahari and Namib. It is cold hardy and tolerant of low temperatures down 0 °C. It thrives in sunny but sheltered locations on light sandy or gritty loamy soil, with neutral to slightly acid soils of pH between 6.5 and 7.

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Edible Plant Parts and Uses

The flowers can be eaten raw or cooked after removal of the anthers. They are added to salads or used as boiled vegetable (Fox et al. 1982; Facciola 1990; Roberts 2000; Newman and O'Connor 2009; Deane 2007–2012, 183). Children suck the flowers for their copious quantities of nectar. Corms of *G. dalenii* are also used as food in southern Congo (Zaire) (Goldblatt and Manning 1998). The starchy corms are boiled and then leached in water before consumption.

Botany

Gladiolus dalenii is a deciduous evergreen perennial cormous geophyte, 70–100 cm (up to 2 m) tall. Leaves grey-green, erect, ensiform (sword shaped), about 20 mm wide, and equitant (in a loose fan). Inflorescences are produced in tall terminal, on-sided spikes with up to 7 or more large, intensely scarlet orange to red with a bright yellow throat (Plate 1) or variously coloured yellow to greenish, often speckled brown to red, hooded flowers; bracts green to red-brown and clasping. Flowers large, 60–10 mm long. Perianth zygomorphic and bilabiate with a short tube 35–50 mm, narrow at base and widening towards the throat, tepals unequal the lower three forming a recurved lip and the upper largest and somewhat hoodlike. Stamens unilateral and arcuate. Style slender branching into near the anthers into three short branches with expanded, bilobed tips. Capsules usually slightly inflated, oblong to ellipsoid or globose. Seeds many light to dark, globose or angular. Flowers are rich in nectar.

Nutritive/Medicinal Properties

Extracts of *Gladiolus dalenii* corms had been reportedly used in the treatment of fungal infections in HIV/AIDS patients in the Lake Victoria region (Odhiambo et al. 2009). They found that soluble dichloromethane (CH_2CL_2) and methanol extracts showed antifungal activity in vitro against *Aspergillus niger*. The activities of both extracts were higher than that of griseofulvin. Dichloromethane soluble extract in addition exhibited ability to delay sporulation in *A. niger*. The active group of compounds in the extracts was identified as alkaloids

Plate 1 Flowers of *G. dalenii*

Results of studies suggested that *G. dalenii* extracts possessed anticonvulsant and sedative activities and may have potential use against secondarily generalized tonic–clonic seizures and primary generalized seizures and insomnia in humans (Ngoupaye et al. 2013). The macerated plant aqueous and lyophilized plant extracts of *G. dalenii* all protected 100 and 83.3 % of mice against pentylenetetrazol (PTZ)-induced and maximal electroshock (MES)-induced seizures, respectively. Co-administration of *G. dalenii* with diazepam resulted in an additive effect, while the co-administration of *G. dalenii* with flumazenil or FG7142 resulted in

antagonistic effects. The maceration of *G. dalenii* also exerted sedative activity by reducing the latency time to sleep and increasing the total duration of sleep induced by diazepam. The sleeping time increased from 16 min in the control group to 118 min at a dose of 150 mg/kg of *G. dalenii*.

In southern Sotho traditional medicine, *Gladiolus dalenii* is a common constituent in the *lenaka* (medicine horn) of the South Sotho-speaking herbalists (Watt and Breyer-Brandwijk 1962). The Zulu and Sotho people have for many generations used the corms of wild gladiolus ground down to a meal to treat dysentery, diarrhoea and stomach upsets (Roberts 2000). A decoction of the corm is used for treating colds and dysentery; alternatively, the smoke from the burning corm is inhaled to treat colds, and the powdered corm is taken for treating dysentery (Watt and Breyer-Brandwijk 1962). In South Africa (Zulu, Xhosa and Sotho zone), the plant is employed as a treatment for headache and lumbago (Hutchings and van Staden 1994). In South Africa (Venda country), the corm is macerated and used as eye drop and ear drop; a decoction of the corm and roots of *Gyrocarpus americanus* is used to wash wounds, and the powder is used to cover the wounds (Arnold and Gulumian 1984). In Mozambique the plant is used in traditional medicine to treat diarrhoea, dysentery, cholera (Bandeira et al. 2001). In Madagascar (Betsileo country), a pomade from the corms is used for abscesses (Carrière et al. 2005). *Gladiolus dalenii* is commonly used in traditional medicine in Africa to treat epilepsy and many other diseases (Ngoupaye et al. 2013).

In the Democratic Republic of Congo, the pounded sap of the corm is used as nose drop for cattle and corm mixture used as medicine for the vagina (Byavu et al. 2000).

Other Uses

Cultivars and hybrids of *G. dalenii* developed in Europe in the early 1900s are grown globally as ornamentals and have become very successful cut flowers. The leaves are plaited into ropes.

Comments

The plant is propagated from seeds, corms or cormels.

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Gladiolus grandiflorus

Scientific Name

***Gladiolus grandiflorus* Andrews**

Synonyms

Geissorhiza grandis Hook.f., *Gladiolus fasciatus* Roem. & Schult., *Gladiolus floribundus* subsp. *fasciatus* (Roem. & Schult.) Oberm., *Gladiolus floribundus* subsp. *milleri* (Ker Gawl.) Oberm., *Gladiolus milleri* Ker Gawl., *Gladiolus scaphochlamys* Baker, *Gladiolus socium* L.Bolus, *Gladiolus vittatus* Hornem. (illeg.)

Family

Iridaceae

Common/English Names

Flag Flower, Garden Gladiolus, Gladiola, Gladiolus, Glads, Sword Lily

Vernacular Names

Afrikaans: Galdiolus
Albanian: Gladiolë, Shpatëz
Catalan: Gladiol
Chinese: Jiàn Lán
Croatian: Gladiola
Czech: Mečík
Danish: Gladiolus
Dutch: Gladiool
Eastonian: Gladiool
Finnish: Gladiolus
French: Glad'eul, Glaïeul
German: Gladiolen
Hungarian: Kardvirág
Icelandic: Galdiolus
India: Ek Fuladar Paudha, Ek Phooladaar Paudhaa, Ek Phuladar Paudha (Hindi), Urōsthīcā Madhya Bhāga (Marathi), Vāḷ Pōṉra Ilaikaḷ Koṇṭa Ceṭi (Tamil)
Indonesia: Bunga Galdiol; Galdiol
Italian: Gladiolo
Japanese: Gurajiorasu
Korean: Geulladiolleoseu
Latvian: Gladiola
Lithuanian: Kardelis
Malay: Gladiol
Norwegian: Galdiolus
Philippines: Galdiolus
Polish: Mieczyk
Portuguese: Gladiolo
Romanian: Gladiole
Russian: Gladiolus
Serbian: Gladiola
Slovencina: Mečík
Spanish: Estoque, Gladiolo
Thai: Phṳ̄ch Mî Dxk

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Turkish: Glayöl
Vietnamese: Cây Lai Ơn
Yoruba: Baka

Origin/Distribution

Most modern cultivated gladioli, *Gladiolus* × *grandiflorus* Hort. (= *G. hortulanus*), are large-flowered, attractive tetraploid ($2n=4x=60$) interspecific hybrids and have been cultivated for more than 260 years (Goldblatt 1996). Modern *G.* × *grandiflorus* hybrids are derived from $n=6$–12 South African species (Barnard 1972). Modern gladioli are primarily grown as summer-growing cut flowers and tender annuals (Anderson et al. 2012). They are derived from summer-growing species, including G. *dalenii*, *G. oppositiflorus*, *G. papilio*, and *G. saundersii. Gladiolus cardinalis*, a winter growing species (winter rainfall region), has also been used in hybridization.

Most of the commercial varieties of gladiolus (*Gladiolus* × *grandiflora* Hort.) had been raised by cross breeding during the last ten decades (Kasumi 2001). Although mutation breeding had been an effective means for obtaining novel varieties in vegetatively propagated ornamental plants, mutant isolation had been restricted by the phenomenon of diplontic selection and subsequent chimera formation that was due to the multicellular origin of the plants. They found that solid mutants of gladiolus having novel flower colour could be obtained by using gamma irradiation and/or tissue culture. Comparative studies on the capability of various explant sources for regenerating plants revealed that the cormel shoot apex was superior to the cormel pieces and leaf blades for its ability of embryogenesis, cost of preparing materials and easiness to be handled.

Agroecology

Gladiolus is frost intolerant and prefers a mild cool climate with 10–25 °C in the daytime and night temperatures of 16–18 °C. However, it can tolerate temperature up to 50 °C only if the relative humidity is high and soil moisture levels are optimum. It grows best in full sun on well-drained, rich fertile sandy-loam soils. It abhors heavy clay soil as it is sensitive to water-logging. It is sensitive to salinity and soil pH 6–7 is ideal.

The interaction of various environmental factors was found to be important on flowering of gladiolus (Shillo and Halevy 1976d). Low light intensity from sprouting to the 4-leaf stage decreased both the percentage of flowering and the number of florets per spike (Shillo and Halevy 1976a). The effect of short-day treatment was similar to that of reduction in light intensity attributable to a reduction in total solar irradiance (Shillo and Halevy 1976b). In winter, photoperiodic low light intensity extension of natural daylength (LD) delayed flowering and increased the number of florets per spike, the number of secondary inflorescences and sometimes also the flowering percentage. Quality of flower spikes and yield is better in a long-day conditions (12–16 h photoperiod) than short days. Under conditions of low light intensity in winter, low temperatures (1–4 °C) increase the occurrence of flower blasting (Shillo and Halevy 1976c). Gladioli were found to be extremely tolerant to high temperatures (up to 50 °C) as long as air humidity and soil moisture are at an optimum. Decrease in soil moisture reduced flowering at most stages of development. The stages immediately after planting and just before spike emergence were the most sensitive. Natural short day (SD) promoted flower development and advanced anthesis but reduced the final size of the flower while long day (LD), with 4 h low intensity light at midnight increased weight and size of leaves and flowers (Shillo et al. 1981). Final corm weight was also promoted by LD. Long-day treatment promoted flowering percentage (by reducing 'blindness') and enhanced flower quality features (length of stem and spike and number of florets per spike) of all cultivars of *Gladiolus grandiflorus* except the miniature cv. "Charm" (Shillo et al. 1981). Most of the promotive effects were obtained by lighting for 4 h as day extension or as night break, and this treatment was recommended for commercial use. Mckay et al. (1981a) found that degree-day summations to flowering suggested that temperature was the major factor influencing the number of days to

flowering and that many cultivars (except for 'Bali and 'Auroa') were essentially daylength-insensitive for the 12.3–15.8-h photoperiods sampled. Extending the photoperiod to 24 h delayed flowering by approximately 15 days and increased the number of inflorescences harvested from low-, medium- and high-density treatments by 20, 91 and 169 %, respectively, when compared to the inflorescence yield from these density treatments under natural daylengths (12.3–14.5 h) (Mckay et al. 1981b). The average weight of new corms and the weight of cormlets per plot and per corm were reduced by approximately 32, 71 and 63 %, respectively, when compared to the results obtained from plants grown under natural daylengths. These results suggest that flowers compete for available photosynthates with corms and cormlet development. Further they found that 97 % of maximum inflorescence yield was obtained at a daylength extension illuminance of 144 lx, while 97 % of the maximum number of florets per spike and the other flower quality characteristics were obtained at a daylength extension illumination level of approximately 100 lx (Mckay et al. 1982). Ninety-seven percent of the maximum number of days to flowering was approached at a daylength extension illuminance of 45 lx. There was no clear relationship between the illumination level of daylength extension and number and weight of new corms or the average weight of each new corm.

Edible Plant Parts and Uses

Flowers are edible raw or cooked (Roberts 2000; Deane 2007–2012; Wilson 2013). The stamens are removed and the flowers are added to salads or used as a boiled vegetable. The petals do not have a punch of flavour but do make a stunning salad garnish (Wilson 2013). The flowers can be used as containers for dips with chicken, prawn or tuna salads. Some recipes with gladioli flowers include stuffed gladiolus flowers, gladiolus and bean stew, gladiolus and avocado open sandwiches (Roberts 2000).

In Ghana, Nigeria, Cameroon and Botswana, gladiolus corms are used in food (Hutchinson and Dalziel 1968; Ameh et al. 2011). In Idomaland, Benue State, Nigeria, gladiolus corms called 'okpendu' or 'okredu' are used in the preparation of 'enyi' or 'umu'—a non-alcoholic drink made from millet, sorghum or maize (Ameh et al. 2011).

Botany

Gladiolus hybrids are perennial herbaceous, cormous geophyte 1–2 m high, with subterranean large symmetrical corms enclosed by several layers of brownish, fibrous tunics and with short simple stem. Leaves 2–9 erect, ensiform, vaginate, equitant, with thickened and grooved midribs (Plate 1). Inflorescences spicate, terminal on a tall (90–150 cm) peduncle, many flowered up to 20, monostichous or weakly distichous; each flower subtended by 2 bracts green, sometimes flushed greyish purple, unequal. Perianth zygomorphic, gamophyllous; tepals basally connate into infundibular or cylindric hypanthial tube; tepals plain, frilled, ruffled, semi-ruffled or deeply cut, variously coloured in a myriad of colours,

Plate 1 Yellow-flowered gladiolus

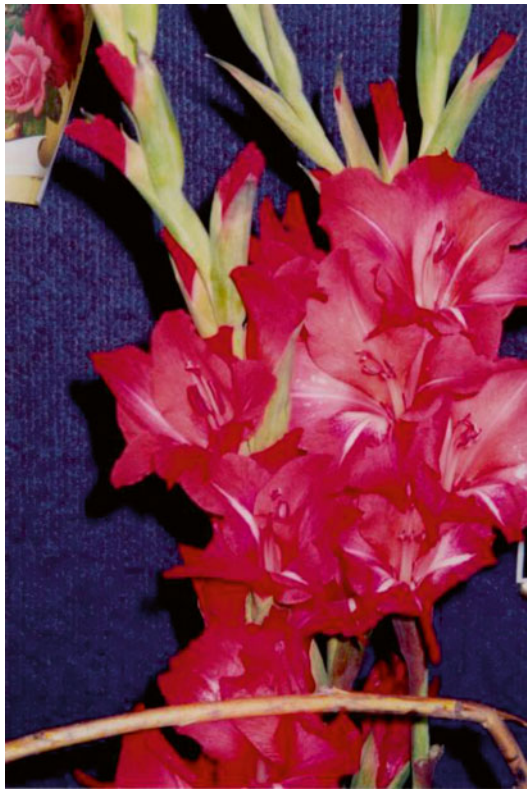

Plate 2 Red-flowered gladiolus

tints and shades, usually with contrasting markings comprising nectar guide on outer tepals, usually unequal, dorsal tepal largest, arched to hooded over stamens, outer three tepals narrower (Plates 1 and 2). Stamens usually unilateral; anthers usually parallel; style usually arching over stamens, dividing into three filiform branches, with distally expanded apices. Ovary 3-locular capsules usually slightly inflated, oblong to ellipsoid or globose, softly cartilaginous. Seeds when formed, usually many, broadly winged; globose or angular, light to dark brown.

Nutritive/Medicinal Properties

Several flower anthocyanins were isolated from ten gladiolus cultivars: pelargonidin-3-rhamnosylglucoside; peonidin 3-*O*-rhamnosylglucoside-5-*O*-glucoside; pelargonidin 3-*O*-diglucoside-5-*O*-glucoside; cyanidin 3,5-di-glucoside; delphinidin 3,5,di-glucoside and delphinidin triglucoside (Shibata and Nozaka 1963).Yatomi and Arisumi (1968) isolated 13 anthocyanins from the flowers: pelargonidin-3-rhamnosylglucoside, pelargonidin-3,5-diglucoside, pelargonidin-3-rhamnosylglucoside-5-glucoside, peonidin-3-rhamnosylglucoside, peonidin-3,5-diglucoside, peonidin-3-rhamnosylglucoside-5-glucoside, cyanidin-3,5-diglucoside, malvidin-3-rhamnosylgucoside, malvidin-3,5-diglucoside, malvidin-3-rhamnosylglucoside-5-glucoside, petunidin-3,5-diglucoside, petunidin-3-rhamnosylglucoside-5-glucoside and delphinidin-3,5-diglucoside. Arisumi and Kobayashi (1971) isolated 12 flower anthocyanins: pelargonidin-3-glucoside;pelargonidin-3-rhamnosylglu-coside; pelargonidin-3, 5-diglucoside; pelargonidin-3-rhamnosylglucoside-5-glucoside; malvidin-3-glucoside; malvidin-3-rhamanosylglucoside; malvidin-3, 5-diglucoside; malvidin-3-rhamnosylglucoside-5-glucoside; petunidin-3-glucoside; petunidin-3-rhamnosylglucoside and petunidin-3, 5-diglucoside and petunidin-3-rhamnosylglucoside-5-glucoside. Akavia et al. (1981) identified the following anthocyanins in the flower petals of *G. gandavensis*: pelargonidin, cyanidin, delphinidin, peonidin, petunidin and malvidin 3-rutinosides and 3-rutinoside-5-glucosides.

Takatsu et al. (2000) clarified that pinkish-white, pink, red and bluish-purple flowers of *Gladiolus grandiflorus* contained either anthocyanin or flavonoid. Orange flowers were found to contain both anthocyanin and carotenoid. They observed that flavonoid and carotenoid were responsible for the production of yellowish-white flowers and vivid yellow flowers, respectively. Also, anthocyanin was responsible for red purple coloured flowers while blue colour of gladiolus might be derived from co-pigmentation of anthocyanin and flavonoid. Their results would contribute to manipulation of flower colour in a breeding programme of gladiolus. The anthocyanins and other flavonoids of the bluish cultivar, *G.* × *grandiflorus* 'Ariake', were isolated and identified (Takemura et al. 2005). They found that the flower colour was changed to more purple by the presence of co-pigments. Three anthocyanins and some flavonoids were present in the crude flower extract. The major anthocyanin was

identified as malvidin 3,5-di-*O*-glucoside (malvin) and the two minor ones were characterized as malvidin glycosides. Of the flavonoids, three were identified as kaempferol 3-*O*-rutinoside, kaempferol 3-*O*-sophoroside and quercetin 3-*O*-rutinoside (rutin). The remaining pigments were characterized as flavonol 3-*O*-glycosides of kaempferol, quercetin, myricetin, laricitrin and syringetin. The purple flower cultivar contained many flavonols compared with other flower colours, e.g. pink and red, suggesting that the flavonol glycosides contributed to the more purplish colour as co-pigments. Eleven anthocyanins were isolated from the flowers of 6 selected *Gladiolus grandiflorus* cultivars and identified as 3-*O*-rutinoside-5-*O*-glucosides of cyanidin, malvidin, pelargonidin and peonidin and 3, 5-di-*O*-glucosides of petunidin, malvidin, pelargonidin, cyanidin and peonidin and pelargonidin 3-*O*-rutinoside and malvidin 3-*O*-glucoside (Takemura et al. 2008). Of these anthocyanins, the first 4 and pelargonidin 3-*O*-rutinoside had previously been characterized as 3-*O*-rhamnosyl-glucoside-5-*O*-glucoside and 3-*O*-rhamnosylglucoside. In this survey, they were clearly identified as 3-*O*-rutinoside-5-*O*-glucoside and 3-*O*-rutinoside, for the first time. They found that the major anthocyanins of purple flowers were malvidin glycosides together with petunidin 3, 5-di-*O*-glucoside as a minor component, but delphinidin glycoside was not detectable. Red flowers were due to pelargonidin glycosides. Pink flowers consisted of various anthocyanins, pelargonidin, cyanidin, peonidin, petunidin and malvidin glycosides, in trace amounts compared with those of purple and red flowers. Generally, anthocyanins were not detected from yellow and white flowers; however, a few yellow and white cultivars contained an extremely small amount of anthocyanins. Such cultivars had a coloured spot or streak on the perianth.

Gladiolus corm extracts, at concentrations of 75–400 mg of the plant material per mL of water, were active against *Pseudomonas aeruginosa* and *Aspergillus niger* but relatively inactive against *Escherichia coli, Staphylococcus aureus* and *Listeria monocytogenes* and fungi: *Candida albicans* and *Trichophyton mentagrophyte* (Ameh et al. 2011). The corm extracts contained alkaloids, tannins, saponins, cardiac glycosides, flavonoids and carbohydrates.

Traditional Medicinal Uses

Refer to notes under *Gladiolus dalenii.*

Other Uses

Gladiolus is especially valued for its cut flowers for use in floral arrangements as well as a popular garden ornamental plant. Gladiolus occupies a prime position among commercial flower crops with a high demand in both domestic and international markets. It occupies eighth position in the world cut flower trade (Anonymous 2006). A total of 19,900 stems of gladiolus were imported into European market (excluding the Netherlands) at the rate of 0.52 US$ per stem during 2006. Japan produced 82,760 stems of cut gladiolus domestically at the price of 0.45 US$ per stem while imported 28,800 stems from the Netherlands and Taiwan at the price of 0.27 US$ per stem. Singapore imported gladiolus stems from China and Malaysia at the rate of 0.44 US$ and 0.61 US$, respectively

In China, gladioli flowers are used for ceremonies and funerals, which is believed to help people find their way to heaven.

Comments

Modern-type gladioli are divided into seven groups based on plant height, flower size and arrangement on the spike:

1. Grandiflorus or large-flowered hybrids, in a wide assortment of colours.
2. Primulinus hybrids: plants less vigorous than Grandiflorus, stems 75–105 cm, florets hooded (uppermost inner petals form hood over the anthers and stigma) and dainty, 5–9 cm across, well spaced on 40–45 cm spike.
3. Butterfly hybrids: stems 75–120 cm, spikes shorter than 45 cm, florets 7.5–10 cm wide

with attractive throat markings or blotches and are arranged symmetrically and closely on the spike.

4. Minature hybrids: stem 75–105 cm, florets 2.5–5 cm across borne on about 40 cm spikes; tepals generally ruffled. These hybrids produce very small corms and multiply very slowly.

   Face ups: The stem is dwarf, usually 60–90 cm tall. Florets are nearly 5–6 cm wide and face upwards and quaint.
5. Colvillei hybrids: derived from hybridizing *G. tristis* with *G. cardinalis*. The plant grows hardly more than 60 cm tall. Flowers are 5–6 cm wide and star-shaped. These are early flowering hybrids and are more suitable for growing under greenhouses.
6. Ochideola: a recent group of gladiolus developed in Israel. Spikes are light in weight, producing smaller florets or shorter stems.
7. Nanus hybrids were introduced in 1855 from *Gladiolus cardinalis* and *Gladiolus venustus*.

   Decorative and early-flowering. They come in white, pink, salmon and some varieties are nearly red, have narrow leaves and have two to four flower stalks with many side shoots. They have graceful spikes with fewer than 12 buds. Dwarf quite hardy, plant 60 cm high.

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Agastache foeniculum

Scientific Name

***Agastache foeniculum* (Pursh) Kuntze**

Synonyms

Agastache anethiodora (Nutt.) Britton & A.Br., *Agastache foeniculum* f. *bernardii* B. Boivin, *Agastache foeniculum* f. *candicans* B. Boivin, *Hyptis marathrosma* (Spreng.) Benth., *Hyssopus anethiodorus* Nutt., *Hyssopus anisatus* Nutt., *Hyssopus discolor* Desf., *Hyssopus foeniculum* (Pursh) Spreng., *Lophanthus anisatus* (Nutt.) Benth., *Lophanthus foeniculum* (Pursh) E. Mey., *Perilla marathrosma* Spreng., *Stachys foeniculum* Pursh, *Vleckia albescens* Raf., *Vleckia anethiodora* (Nutt.) Greene, *Vleckia anisata* (Nutt.) Raf., *Vleckia bracteata* Raf., *Vleckia bracteosa* Raf., *Vleckia discolor* Raf., *Vleckia foeniculum* (Pursh) MacMill., *Vleckia incarnata* Raf.

Family

Lamiaceae

Common/English Names

Anise Hyssop, Anise-Hyssop, Anise-Mint, Blue Giant-Hyssop, Fennel Giant Hyssop, Fragrant Giant Hyssop, Giant Hyssop, Lavender Giant Hyssop, Lavender Hyssop, Licorice-Mint, Wonder Honey Plant

Vernacular Names

Chinese: Huo Xiang
Danish: Anis Isop, Indianermynte
Dutch: Anijsplant
Estonian: Aniisi-Hiidiisop
Finnish: Intianminttu, Minttuanis, Yrtti-Iiso
French: Agastache Fenouil, Anis Hysope, Hysope Anysée, Duft-Nessel
German: Anis-Ysop
Norwegian: Anisisop
Swedish: Anis-Isop, Indianmynta

Origin/Distribution

The species is indigenous from Southern Canada (Alberta, Ontario) to the northern-central states of the United States (Wisconsin, Minnesota, Illinois, Iowa, Dakota, Colorado).

Agroecology

A cool temperate species, its natural habitats include openings in dry to mesic open upland forests, upland areas of prairies, scrubby barrens, clearings and thickets. It prefers full or partial sun and mesic to dry conditions and grows on loam, clay-loam or stony soils. Cultivated forms of

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anise hyssop are often grown in flower gardens; these cultivars are often hybrids and vary in their fidelity to the wild forms of the plant.

Edible Plant Parts and Uses

In Northern America, anise hyssop is cultivated as honey plant by beekeepers and in house gardens for tea and as culinary seasoning, in the same way used already earlier by the Indian tribes (Morton 1976; Moerman 1998). It has also been experimentally grown as essential oil plant in the former Soviet Union (Moldova, Crimea) and in Southern Finland, here also in house gardens as tea and spice plant for cakes and sweets (Galambosi and Galambosi-Szebeni 1992).

Leaves, seeds and flowers have a sweet anise flavour and are eaten raw or cooked (Kunkel 1984; Moerman 1998; Facciola 1990). They are used as a flavouring in raw or cooked dishes and present a delicious addition to the salad bowl. The seeds are used in cookies, cakes and muffins. A pleasant tasting tea is made from the leaves (Yanovsky 1936; Uphof 1968; Usher 1974; Facciola 1990).

Botany

A perennial herb with creeping rhizome and erect, glabrous, sparingly branched, 4-angled stems, 50–100 (−150) cm tall. Leaves are opposite, anise-scented, ovate to cordate, pointed tips and crenate margin; upper surface conspicuously veined and dull green, lower surface is whitish with minute appressed hairs (Plate 1). Inflorescence an interrupted terminal, hairy spike; calyx tubular, violet or bluish, hairy, with 5 teeth; corolla tubular divided into a short upper lip and a longer lower lip, violet, lower lip with 2 small lateral lobes and wide central lobe (Plate 2); stamens 4 with blue-violet anthers, exserted, the upper pair curved downward and crossing lower 2; style subequally 2-cleft. Nutlets, 4, oblong, 2 mm long, brown, with hairy apex.

Plate 1 Anise hyssop foliage

Plate 2 Terminal inflorescence with purple flowers (M Landry)

Nutritive/Medicinal Properties

Floral volatiles of *A. foeniculum* obtained by headspace analysis included 1R-pulegone, estragole (methyl chavicol), neral, myrcene, methyl eugenol,

linalool, limonene, geranial, δ-cadinene, camphene, bornyl acetate, β-caryophyllene and α-pinene (Wilson et al. 1992).

Flavonoid aglycones apigenin, apigenin-4′-methyl ether, sculellarein-6,7-dimethyl ether and luteolin (trace) and flavonoid glycosides kaempferol 3-glucoside (astragalin), kaempferol 3-rhamnoside and quercetin-3-glucoside (isoquercetin) were detected in the herb (Nikolova and Dzhurmanski 2009).

Over 50 compounds were detected in oils and headspace of 14 different clones of *Agastache foeniculum* (Mazza and Kiehn 1992). Only ten constituents, however, accounted for more than 0.1 %, and methyl chavicol constituted 95–98 % of the essential oil. The main components of the secretory mixture from the secretory hairs of *Agastache foeniculum* Kuntze leaves were methyl chavicol (59.5 %) and (*E*)-anethole (19.6 %) (Tirillini et al. 1997). Fuentes-Granados et al. (2000) elucidated genetic control of volatile oil production in *Agastache foeniculum*, more specifically of the production of its three major components: myrcene, limonene and methyl chavicol. Total aromatic volatile emittance was found to be under polygenic control with additive gene effects, and each of the three major components was controlled by one to a few genes with recessive to additive effects. The essential oil of *Agastache foeniculum* cultivated in Iran afforded an oil content of 1.87 % w/w based on dry weight 46 components (Omidbaigi and Sefidkon 2003). The essential oils obtained from hydrodistillation of aerial parts of *Agastache foeniculum* grown at Bangalore (India) and harvested at two plant growth stages, at the end of the vegetative stage and at full bloom, were found to contain methyl chavicol (91.7 and 95.2 %) and limonene (3.6 and 3.9 %) as the major constituents (Mallavarapu et al. 2004). The infection of *A. anethiodora* plant by cucumber mosaic virus was found to induce significant reduction in the yield of essential oil and several changes in the relative composition of the main components: pulegone, menthone, iso-menthone, methyl chavicol and limonene (Bruni et al. 2006). Methyl chavicol content, in particular, was drastically reduced. Methyl chavicol constituted 87.5 % of the oil; other major components were limonene (2.4 %), 1,8-cineole (2.0 %) and globulol (1.4 %). *Agastache foeniculum* essential oil was found to contain 0.1–0.3 % essential oil, and the main components were methyl chavicol (74.6 %), α-limonene (8.5 %), β-caryophyllene (5.5 %) and germacrene B (3.3 %), totalling 92 % altogether (Nykänen et al. 2007). In addition 35 components, each accounting for less than 1 % of the total essential oil, were identified and bornyl acetate was not detected. Fard et al. (2012) found the essential oil of *Agastache foeniculum* to have mainly methyl chavicol (94.70 %) and limonene (4.20 %). Other components less than 1 % included octen-3-ol, linalool *E*-caryophyllene, carvacrol, cuminaldehyde, octen-3-yl-acetate and 3-octanone.

Three types of essential oil, anethole, sweet menthol and menthol, were obtained from *Agastache foeniculum* leaves and blossoms (Zhekova et al. 2010). The anethole type had the least number of components and contained about 86.9 and 90 % of methyl chavicol followed by 5.6 and 3.1 % limonene in the leaves and inflorescence, respectively, its aroma being typically anethole with some additional spicy notes. The other two types of oils had similar profiles of the main components, with emerging menthofuran, pulegone and increasing limonene. The main differences of the sweet menthol and the menthol oils were in the ratio of their components. With the menthol type, the smell was sharper and fresh, with green, grassy notes, whereas with the sweet menthol type it was warmer and flavoured with additional notes. In another study, *Agastache foeniculum* essential oil was found to have mainly estragole (methyl chavicol) 94.003 % and 1, 8 cineole 3.334 % as the major components (Ebadollahi 2011). Other minor components included 1-octen-3-ol 0.461 %, 3-octanone 0.407 %, octen-3-yl-acetate 0.386 %, α-copaene 0.029 %, β-bourbonene 0.084 %, *E*-caryophyllene 0.058 %, germacrene D 0.430 %, bicyclogermacrene 0.020 %, spathulenol 0.039 % and β-eudesmol 0.015 %, altogether totalling 99.266 %.

Twenty-six compounds were identified in the essential oils of 19 accessions of *Agastache foeniculum* (anise hyssop), *A. rugosa* (catnip

giant hyssop), *A. nepetoides* (Korean mint) and putative hybrids, with methyl chavicol being the major constituent (46.7–94.6 %) in 14 lines of *A. foeniculum, A. rugosa* and putative hybrids (Charles et al. 1991). In contrast, δ-cadinol was the major oil constituent (39.6 %) in *A. nepetoides*. Additional oil constituents found in these species in concentrations above 1 % include β-bourbonene, bornyl acetate, gamma-cadinene, α-cadinol, δ-cadinene, α-camphene, β-caryophyllene, damascenone, β-ionone, isomenthone, α-limonene, linalool, methyl eugenol, β-myrcene, *cis*-ocimene, 7-octen-4-ol, pulegone and spathulenol. Methyl chavicol was found to be the major compound in most accessions from the USDA germplasm collection of anise hyssop (*Agastache foeniculum*), catnip giant hyssop (*A. nepetoides*) and Korean mint (*A. rugosa*) and putative hybrids and accounted for >92 % of the total essential oil in six lines and one putative hybrid (Charles et al. 1992). Results indicated a wide range in the relative concentrations of other compounds (α-limonene, menthone, methyl eugenol, bornyl acetate, spathulenol, cadinol and β-caryophyllene) and in essential oil content. In a commercial *A. foeniculum* accession, 88.1 % methyl chavicol, α-limonene 2.2 %, menthone nd, bornyl acetate <0.1 %, methyl eugenol 2.7 %, spathulenol nd, cadinol nd and β-caryophyllene 0.13 % were obtained.

Under all the experimental conditions examined, *Agastache foeniculum* shoots cultured in vitro produced high percentages of methyl chavicol and trace amounts of *trans*-anethole (Menghini et al. 1992). Addition of shikimic acid to the culture media increased the concentration of chlorophyll (*a* and *b*) and some carotenoids and methyl chavicol compared to untreated media.

Antioxidant Activity

Agastache foeniculum plant extract was found to have significant DPPH free radical scavenging activity with an IC_{50} value of 57.86 μg/mL (Nikolova and Dzhurmanski 2009). *Agastache foeniculum* herb was found also to have ferric reducing antioxidant power (FRAP) of 1.15 mmol Fe/100 g FW and total phenolic content of 7.19 mg GAE/g FW (Derakhshani et al. 2012).

Insecticidal Activity

Fumigation bioassays revealed that *A. foeniculum* essential oil had strong insecticidal activity on red flour beetle, *Tribolium castaneum* and lesser grain borer *Rhyzopertha dominica* (Ebadollahi 2011). *Rhyzopertha dominica* was more susceptible than *T. castaneum* for all exposure times (24, 48 and 72 h). Probit analysis showed that increased exposure time and essential oil concentration increased mortality.

Traditional Medicinal Uses

The herb is employed for cardiac, pectoral and diaphoretic complaints, as poultice and for treating herpes simplex (Bown 1995; Foster and Duke 1998; Moerman 1998). An infusion of the leaves is used in the treatment of colds, fevers, chest pains and weak heart. A poultice of leaves and stems can be used to treat burns.

Other Uses

Anise hyssop is grown as a culinary herb and ornaments and is also an excellent honey plant. The flowers attract bees, butterflies and hummingbirds. The safety and uses of methyl chavicol (estragole), the main constituent in the essential oil of *Agastache*, in the food industry as well as the herbal, flavouring and medicinal uses of *Agastache* have been reviewed by Fuentes-Granados et al. (1998).

Comments

Anise hyssop can be propagated by division of the rhizomes or from seeds.

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Lavandula angustifolia

Scientific Name

***Lavandula angustifolia* Mill.**

Synonyms

No synonyms recorded

Family

Lamiaceae

Common/English Names

Common Lavender, English Lavender, Garden Lavender, Lavender, Narrow-Leaved Lavender, Old English Lavender, Spike Lavender, True Lavender

Vernacular Names

Albanian: Livande E Vertete
Arabic: Khuzama, Lafand
Armenian: Hoosam, Husam
Azerbaijani: Lavanda
Brazil: Alfazema, Lavanda
Bulgarian: Lavandula
Catalan: Aspic, Barballó, Barbayó, Barmaió, Berbelló, Espic, Espich, Espígol, Espigolina, Espit, Lavanda
Chinese: Xun Yi Cao
Croatian: Ljekovita Lavanda
Czech: Levandule, Levandule Lekařská, Levandule Pravá
Danish: Hunlavendel, Lavendel
Dutch: Echte Lavendel, Gewone Lavendel, Lavendel, Lavendel Sort, Spijklavendel
Estonian: Tähklavendel
Esperanto: Lavendo
Finnish: Laventeli, Tupsupäälaventeli
French: Lavand, Lavande, Lavande À Feuilles Étroites, Lavande Commune, Lavande Femelle, Lavande Vraie
Gaelic: An Lus Liath, Lus-Na-Tùise
Galician: Lavanda
German: Echter Lavendel, Gartenlavendel, Grosser Speik, Lavendel, Lavendelernte, Spik-Lavendel
Greek: Lebánta, Levanta
Hebrew: Lavender
Hungarian: Közönséges Levendula, Levendula, Szagos Levendula
Icelandic: Lofnarblóm
Italian: Fior Di Spigo, Lavanda, Lavanda Vera, Spigo
Japanese: Rabenda, Ravunda
Korean: Ra-Ban-Din, Ra-Ben-Deo, Rabandin, Rabendeo, Rabendo
Latvian: Lavandīna, Šaurlapu Lavanda
Lithuanian: Tikroji Levanda
Maltese: Lavandra
Norwegian: Ekte Lavendel, Lavendel
Persian: Asṭwḫwdws, Ostukhudus
Polish: Lawenda Lekarska, Lawenda Wąskolistna Lawenda

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Portuguese: Alfacema, Alfasema, Alfazema, Espigue, Lavanda
Romanian: Levănţică
Russian: Lavanda, Lavanda Aptečnaja
Slovencina: Levanduľa, Levanduľa Úzkolistá
Slovašcina: Lavenda, Lavendin, Prava Sivka, Sivka, Sivka Prava
Spanish: Alfazema, Alhucema, Aljucema, Espigol, Espigola, Espilgolina, Espliego, Espliego Común, Espligo, Lavanda, Lavanda Fina, Lavandula, Tuma
Swedish: Lavendel
Thai: Lawendeort
Turkish: Lavânta, Lavânta Çiçeği
Ukrainian: Lavanda

Origin/Distribution

L. angustifolia is native to western Mediterranean, around the Pyrenees and adjacent mountains in northern Spain.

Agroecology

Although a native of the Mediterranean, lavender is winter hardy and will tolerate subfreezing temperatures of −10 and −15 °C. Lavender will grow in almost any soil that is well drained, evenly moist and not too acidic. However, it thrives best in neutral to alkaline soils in full sun with good mulch. When grown in rich soils, it tends to produce more leaves but less essential oil. When growing for maximum essential oil content, the plant must be established in a warm sunny position and will do best in a light sandy soil, the fragrance being especially pronounced in a chalky soil. Established plants are drought tolerant and tolerant of salt wind exposure.

Edible Plant Parts and Uses

Flower petals, flowering tips and leaves are edible fresh or dried (Hedrick 1972; Facciola 1990; Bown 1995), used in small quantities as condiment for flavouring soups, salads, dressings, sauces, jams, stews, vinegar and jellies. Diminutive flowers add a mysterious scent to custards, flans or sorbets or ice creams. Flowers look beautiful and taste good too in a glass of champagne, with chocolate cake. Dried buds, flowers and leaves are increasingly popular in cookery. The flowers are also used as a culinary herb, most often as part of the French herb blend called *herbes de Provence*. The fresh or dried flowers are used as a tea. The fresh flowers are also crystallized. Lavender is fragrant and spicy and the flowers can be used in both sweet and savoury dishes; in the 2013 Chelsea Flower Show, Irish chef Richard Corrigan combines them with roast Elwy Valley lamb (Wilson 2013).

Lavender extract and/or essential oil are used as flavouring for various foods and beverages including alcoholic types, ice cream, candy, chewing gum, baked goods and other confectionery products (Kim and Lee 2002; Chatzopolou et al. 2003; Da Porto et al. 2009).

Botany

A small branched, strongly aromatic, semi-woody, semievergreen perennial shrub, 0.5 (in dwarf cultivars, Plate 1) to1.5 m high with grey-brown, angular branches and longitudinally flaking bark. Leaves are evergreen, grey green, widely spaced on flowering shoots, clustered on leafy shoots, linear to linear-lanceolate, 3–5 cm by 3–5 mm (Plate 2) on flowering shoots, <17 × 2 mm on leafy shoots, grey stellate tomentose, tip obtuse, base attenuated to a very short petiole, margin entire and revolute. Lavender inflorescences are spiciform thyrses, i.e. inflorescences, made of an indeterminate main axis (central flower stalk) and cymose subaxes that are organized as whorls of opposite pairs of multiflowered cymes (Plate 3). Verticillasters 6–10 flowered with a remote verticillaster at the base of its unbranched central axis, and all verticillasters are of equal size to the top of the inflorescence. Bracts dry, rhombic-ovate or acuminate-subulate; bracteoles indistinct. Pedicel short. Calyx ovoid–tubular to subtubular, 4–5 mm, densely grey stellate tomentose outside; upper

Plate 1 Profuse flowering English lavender (Hidcote)

Plate 2 Linear-lanceolate, smooth margin leaves

Plate 3 Harvested lavender inflorescences

lip entire, lower lip equally 4-toothed. Corolla blue or lilac, 8–10 mm, densely tomentose outside, base subglabrous, throat and limb glandular hairy, upper lip straight, with lobes circular and slightly overlapping; lower lip spreading (Plate 4). Nutlets 4.

Plate 4 Open flowers and buds

Nutritive/Medicinal Properties

Seven flavonoids were isolated from *Lavandula angustifolia* and identified as apigenin, ladanein, apigenin-7-*O*-β-D-(6′-*p*-hydoxy-cinnamoyloxy)-mannoside, luteolin, apigenin-7-*O*-β-D-glucoside, luteolin-7-*O*-β-D-glucoside and 5, 4′-dihydroxy flavonoid-7-*O*-β-D-pyranglycuronate butyl ester (Wu et al. 2007).

Yusufoglu et al. (2004) reported the essential oils of *Lavandula angustifolia* flowers and leaves to be colourless or light yellow liquids with slightly bitter tastes; flower concretes and leaf concretes to be dark green and dark yellow solids, respectively; and absolutes prepared from the concretes to be viscous liquids of green colour from the flowers and yellow from the leaves. The main components of the essential oil of the flowers were 45.09 % linalool, 13.32 % camphor, 8.82 % terpinen-4-ol, 5.81 % 1,8-cineole, 5.22 % borneol and 3.08 % linalyl acetate. In the essential oil of the leaves, however, 49.23 % 1,8-cineole, 34.67 % camphor, 4.60 % isoborneol, 2.13 % D-3-carene and 2.11 % sabinene were the main components. Linalool and linalyl acetate, existing in the flowers, were not detected in the leaves. The flowers afforded a concrete composition of 53.73 % linalool, 22.60 % camphor, 15.99 % 1,8-cineole, 2.98 % 4-methyl-1-(methylethyl)-3-cyclohexen-1-ol and 2.56 % isoborneol and an absolute composition of 50.00 % linalool, 24.10 % camphor, 10.27 % 4-methyl-1-(methylethyl)-3-cyclohexen-1-ol, 9.48 % 1,8-cineole and 3.95 % isoborneol as the main components. The concrete and absolute of the flowers were similar to each other. The lack of

linalyl acetate, responsible for the characteristic odour, decreased the cosmetic value of these extracts, but their medicinal and insecticidal uses could become important due to the increased percentages of camphor and 1,8-cineole.

The main components of the concrete of the leaves were 48.49 % 2,4-dimethyl-7-ethyl-6,8-dioxabicyclo-[3.2.1]-3-octene, 12.45 % triacontane, 9.44 % camphor, 9.01 % docosane and 8.15 % 1,8-cineole and of the absolute 38.43 % 1,8-cineole, 28.3 % camphor, 10.67 % γ-muurolene and 5.80 % γ-bisabolene. Common components of the essential oil, concrete and absolute of the leaves were 1,8-cineole, camphor, isoborneol, 2,4-dimethyl-7-ethyl-6,8-dioxabicyclo-[3.2.1]-3-octene and triacontane. The increase of the contents of γ-muurolene and γ-bisabolene could make the absolute useful in the pharmaceutical industry. Basch et al. (2004) reported that lavender essential oil contained both limonene and perillyl alcohol.

Thirty-four components amounting to 98.91 % of the oil were identified in the flower essential oil of *Lavandula angustifolia* in Iraq (Hamad et al. 2013), the major component being linalool (24.63 %). The other significant constituents were camphor (13.58 %), linalyl acetate (8.89 %), (Z)-β-ocimene (7.59 %), 1,8-cineole (7.14 %), borneol (6.41 %), (*E*)-β-ocimene (4.76 %), hotrienol (4.42 %), hexyl butyrate (2.96 %), α-bisabolol (1.13 %) and caryophyllene oxide (1.02 %). Other minor components were n-hexanol (0.45 %), 3-nonyne (0.11), 2,7-dimethyl oxepin (0.52 %), camphene (0.36 %), 3-octanone (0.37 %), myrcene (0.74 %), *cis*-linalool oxide (0.95 %), hexyl acetate (0.96 %), γ-valerolactone (0.72 %), 3-octyl acetate (0.28 %), nerol oxide (0.74 %), *trans*-linalool oxide (0.57 %), isobornyl formate (0.59 %), hexyl-2-methyl butyrate (0.61 %), 2-cyclohexene-1-one-2-methyl-5-(1-methyl ethane) (0.11 %), lavandulyl acetate (0.27 %), hexyl tiglate (0.69 %), 8-acetoxy linalool (0.18 %), geranyl acetate (0.32 %), *trans*-verbenol acetate (0.58 %), lavandulyl isovalerate (0.13 %) and α-bisabolol oxide B (0.13 %). Seventy-eight compounds were identified in the flower essential oil of *Lavandula angustifolia*, cultivated in Poland (Smigielski et al. 2009). The major constituents of the oil were linalool (30.6 %), linalyl acetate (14.2 %), geraniol (5.3 %), β-caryophyllene (4.7 %) and lavandulyl acetate (4.4 %). The major constituents (>1.0 %) of lavender inflorescence essential oil cultivated in the mid-hills of Uttarakhand, India, were linalyl acetate (47.56 %), linalool (28.06 %), lavandulyl acetate (4.34 %), α-terpineol (3.75 %), geranyl acetate (1.94 %), caryophyllene oxide (1.38 %) and 1,8-cineole (1.14 %) (Verma et al. 2010). Other minor components (<1.0 and > 0.10 %) identified in the oil were β-caryophyllene (0.93 %), borneol (0.85 %), epi-α-cadinol (0.70 %), nerol (0.59 %), terpinen-4-ol (0.56 %), β-myrcene (0.55 %), limonene (0.55 %), 1-octen-3-ol (0.53 %), *p*-menthyl-8-acetate (0.42 %), 1-octen-3-yl acetate (0.35 %), (*E*)-linalool oxide (furanoid) (0.24 %), camphene (0.23 %), (*Z*)-linalool oxide (furanoid) (0.22 %), geraniol (0.21 %), lavandulol (0.25 %), (*E*)-isoeugenol (0.17 %), myrtenol (0.13 %), thymol acetate (0.13 %), γ-cadinene (0.12 %), elemol (0.12 %), camphor (0.11 %) and β-cadinene (0.11 %). Components (<0.1 %) included tricyclene (0.03 %), α-pinene (0.09 %), (*E*)-β-ocimene (0.08 %) and *p*-cymenol (0.06 %).

Linalyl acetate (35.44 %) and linalool (18.70 %) were predominant components of *Lavandula angustifolia* Hidcote lavender (aerial parts) samples grown in Korea and obtained by solid-phase trapping solvent extraction (SPTE), whereas those levels were 2.63–4.04 and 36.80–43.47 % in the same samples by reduced pressure steam distillation (RPSD) and simultaneous steam distillation–solvent extraction (SDE), respectively (Kim and Lee 2002). A total of 33 fragrance compounds were identified by SPTE: ethyl benzene (0.34 %), *m*-xylene or *p*-xylene (0.85 %), *o*-xylene (0.4 %), thujene (0.36 %), α-pinene (0.97 %), camphene (1.57 %), β-pinene (0.63 %), β-myrcene (0.91 %), *p*-cymene (0.11 %), limonene (1.23 %), cineol (5.94 %), linalyl oxide (0.21 %), linalool (18.70 %), octen-1-ol, acetate (0.45 %), camphor (0.45 %), lavandulol (0.25 %), borneol (1.88 %), α-terpinen-4-ol (4.63 %), *p*-cymen-8-ol (0.53 %), linalyl acetate (35.44 %), bornyl acetate (5.88 %), geranyl acetate (0.27 %), caryophyllene (0.39 %), farnesene isomers (2.60 %), calamenene (1.21 %),

caryophyllene oxide (1.80 %) and bis(2-ethylhexyl)phthalate (3.0 %). Using headspace solvent microextraction combined with continuous hydrodistillation (HD-HSME), 36 compounds were extracted and identified in the essential oil components of *Lavandula angustifolia* (Fakhari et al. 2005). Linalool (32.8 %), linalyl acetate (17.6 %), lavandulyl acetate (15.9 %), α-terpineol (6.7 %) and geranyl acetate (5.0 %) were found to be the major constituents. Other constituents were lavandulol 4.3 %, borneol 3.8 %, cumin aldehyde 2.5 %, neryl acetate 2.4 %, camphor 1.9 %, *trans*-caryophyllene 1.5 %, nerol 1 %, α-phellandrene 0.9 %, 1,8-cineole 0.8 %, *cis*- linalool oxide 0.7 %, *trans*-β-farnesene 0.5 %, 1-octen-3-ol 0.4 %, 3-octanone 0.3 %, α-terpinene 0.3 %, β-pinene 0.2 %, hexyl acetate 0.1 %, camphene 0.1 %, tricyclene tr (trace), α-pinene tr, γ-terpine tr, *cis*-ocimene tr, α-terpinolene tr, *trans*-linalool oxide tr, *p*-cymene tr, bornyl acetate tr, verbenone tr, cryptone tr, myrcene tr, chrysanthenone tr and terpin-4-ol tr. *L. angustifolia* essential oil was found to be rich in linalool (49.2 %), linalyl acetate (12.3 %), lavandulyl acetate (6.5 %) and 4-terpineol (5.9 %) (Behnam et al. 2006).

Lavandin cultivars *(Lavandula* × *intermedia*) produced significantly higher oil yield (7.1–9.9 % dry inflorescences) compared to six lavender (*L. angustifolia*) cultivars (2.8–5.0 % dry inflorescences), with cultivars 'Grosso', 'Abriallii' and 'Super' yielding the highest (9.9, 9.0 and 8.7 %, respectively) (Renaud et al. 2001). Lavender 'Grey Lady' produced the highest oil yield (5.0 %) and 'Lady' the least (2.8 %). All lavandins produced acceptable flowers for the dried market except 'Provence' whose flower colour was pale purple. Lavender flowers from 'Hidcote', 'Munstead' and 'English' were acceptable for the dried floral market. By year 2, lavender cultivars reached full bloom and could be harvested for oil prior to the lavandins. Lavandin 'Grosso' oil possessed the highest camphor (8.1 as relative % of total oil). The essential oil yields were determined to be 4.4, 7.5 and 8.5 % in *Lavandula angustifolia* and lavandin 'super' and 'special' hybrids, respectively (Chatzopolou et al. 2003). Fifty-nine constituents were identified representing 99 % of the oils. Linalool (50.63, 23.01, 37.69 %) and linalyl acetate (15.72, 20.35, 29.14 %) were the predominant constituents for lavender and lavandin hybrids 'super' and 'special', respectively. Other notable differences in constituent percentages among lavender, lavandin 'super' and 'special' hybrid essential oils were, respectively, 1,8-cineole (0.66, 15.85, 5.39 %), camphor (0.06, 11.35, 5.03 %), terpinene-4-ol (7.84, 6.67, 0.08 %), α-terpineol (1.52, 3.81, 2.91 %), *cis*-ocimene (4.25, 2.67, 1.35 %), *trans*-ocimene (2.73 %, 1.90, 2.08 %), lavandulyl acetate (2.73, 0.37, 2.20 %) and β-caryophyllene (2.04,0.91,0.55 %). The following minor compounds (<2 %) were found in lavender essential oil: α-thujene, α-pinene, camphene, sabinene, 1-octen-3-ol, β-pinene, 3-octanone, β-myrcene, 3-octanol, α-phellandrene, Δ3-carene, *p*-cymene, limonene, γ-terpinene, octeny-3-yl-acetate, allo-ocimene, borneol, lavandulol, cryptone, nerol, cumin aldehyde, carvone, cumin alcohol, neryl acetate, geranyl acetate, α-santalene, *trans*-β-bergamotene, α-humulene, β-farnesene, germacrene D, caryophyllene oxide and τ-cadinol. Changes in biosynthesis of terpene were found to occur during inflorescence development of lavender (*Lavandula angustifolia*) and its natural hybrid lavandin (*L.* × *intermedia*) involving two terpene synthase (TPS) genes, LaLIMS and LaLINS (Guitton et al. 2010). Camphor, 1,8-cineol, borneol and linalool were characteristics *of L.* × *intermedia* and *trans*-β-ocimene, *cis*-β-ocimene, lavandulyl acetate, lavandulol, linalyl acetate and the sesquiterpenes germacrene D, *trans*-β-farnesene and β-caryophyllene being characteristics of *L. angustifolia. Cis*-β-ocimene was, in fact, only detected in *L. angustifolia*. Calyces were found to be the main sites of volatile organic compound (VOC) accumulation. Changes in calyx VOC accumulation were linked to the developmental stage of individual flowers. The 20 most abundant VOCs could be separated into three subgroups according to their patterns of concentration changes. The three groups of VOCs sequentially dominated the global scent bouquet of inflorescences, the transition between the first and second groups occurring around the opening of the first flower of the inflorescence and the one between the second and third groups at the start of seed set. Group 1

included monoterpenes: δ-3-carene, limonene, myrcene, bornyl acetate, borneol, camphor, 1,8-cineol and *trans*-ocimene. Group 2 included monoterpene acetates and sesquiterpenes: linalyl acetate, lavandulyl acetate, germacrene D, β-caryophyllene and *trans*-β-farnesene. Group 3 included monoterpenes: linalool and terpinen-4-ol. Camphene, camphor, α-pinene and β-pinene were seen in too few samples to be included in the analysis. Leaves accumulated a smaller number of VOCs which were a subset of those seen in preflowering inflorescences.

Comparative analysis of *L. angustifolia* cultivated in Friuli-Venezia Giulia (north-east Italy) using headspace solid-phase microextraction (HS-SPME) coupled to gas spectrometry and mass spectrometry highlighted that the contents of linalool and linalyl acetate were the major differences between the volatile composition of flowers and the hydrodistilled products (Da Porto and Decorti 2008). Lavender essential oil from middle Friuli-Venezia Giulia was evaluated as the highest quality for its high level of linalyl acetate (31.7 %) and linalool (45.0 %) and low percentage of camphor (0.5 %). The use of headspace SPME was shown to be a convenient and effective analytical tool for the sampling of volatile compounds and could be employed to test the quality of flowers and essential oils from *Lavandula* species. Comparison of the total essential oil yield quantified by hydrodistillation of the lavender infusion (0.7 % v/w, corresponding to plant material) with the essential oil yield of the blossoms (5.1 % v/w) revealed that only 13.9 % of the initial oil could be extracted by infusion (Tschiggerl and Bucar 2010). The main constituents of the volatile fraction of lavender infusion (hydrodistillation/solid-phase extraction (SPE)) were linalool (39.3/28.2 %), 1,8 cineole (24.8/18.9 %), *cis*-linalool oxide (furanoid) (5.8/8.0 %), *trans*-linalool oxide (furanoid) (4.1/7.1 %), camphor (5.3/4.0 %) and α-terpineol (4.0/3.0 %). The major constituents of lavender essential oil were linalool (28.8), 1,8-cineole (18.05 %), linalyl acetate (13.9 %) and α-terpineol (4.0 %).

A total of 47 compounds representing 98.4–99.7 % of lavender (aerial parts) essential oil were identified in China (Lu et al. 2010). Lavender essential oil consisted 1,5-dimethyl-1-vinyl-4-hexenyl butyrate as the most abundant component (43.73 %), followed by 1,3,7-octatriene, 3,7-dimethyl- (25.10 %), eucalyptol (7.32 %), caryophyllene (4.38 %) and camphor (3.79 %). Other constituents included α-phellandrene (0.09 %), 1S-α-pinene (0.3 %), camphene (0.27 %), 1-octen-3-ol (0.17 %), 4-methylene-1-(1-methylethyl)- bicyclo[3.1.0]hexane (0.15 %), β-pinene (0.43 %), 4-methyl- 1-(1-methylethyl)-bicyclo[3.1.0]hex-2-ene (0.39 %), acid hexyl ester (0.25 %), 3-carene (0.16 %), 1-methyl-4-(1-methylethyl)-benzene (0.04 %), 1-methyl-2-(1-methylethyl)-benzene (0.19 %), D-limonene (0.55 %), 3,7-dimethyl- 1,3,7-octatriene (0.99 %), 1-methyl-4-(1-methylethyl)- 1,4-cyclohexadiene (0.05 %), *trans*-linalool oxide (0.30 %), *cis*-β-terpineol (0.13 %), 1S-α-pinene (0.34 %), octen-1-ol acetate (0.62 %), butanoic acid, hexyl ester (0.12 %), (R)-5-methyl-2-(1-methylethenyl)-4-hexen-1-ol, (0.22 %), borneol (1.54 %), 4-methyl-1-(1-methylethyl)- 3-cyclohexen-1-ol (1.56 %), butanoic acid, octyl ester (0.48 %), *p*-menth-1-en-8-ol (0.98 %), bornyl acetate (0.17 %), 2,6-octadien-1-ol, 3,7-dimethyl-, acetate (1.42 %), 4-hexen-1-ol, 5-methyl-2-(1-methylethenyl)-, acetate (0.27 %), 5-amino-1-ethyl-1H-benzimidazole (0.07 %), 4-hexen-1-ol, 5-methyl-2-(1-methylethenyl)-, acetate (0.40 %), 1,3,6,10-dodecatetraene, 3,7,11-trimethyl-, (*Z,E*)- (0.06 %), isocaryophyllene (0.05 %), α-caryophyllene (0.11 %), di-epi-α-cedrene (0.20 %), 1,6,10-dodecatriene, 7,11-dimethyl-3-methylene-, (*Z*)- (0.58 %), 1,6-cyclodecadiene, 1-methyl-5-methylene-8-(1-methylethyl)-, [s-(*E,E*)]- (0.68 %), 1,6,10-dodecatriene, 7,11-dimethyl −3-methylene-, (*E*)- (0.07 %), spiro[5.5]undec-2-ene, 3,7,7-trime thyl-11-methylene-, (−)- (0.07 %), 2,6-octadien-1-ol, 3,7-dimethyl-, acetate (*E*)- (0.20 %), 2-isopropyl-5-methyl-9-methylene-bicyclo[4.4.0]dec-1-ene (0.20 %), 1-methylene-2-vinylcyclopentane (0.05 %), caryophyllene oxide (0.61 %) and copaene (0.17 %). Linalool (27.2 %) and linalyl acetate (27.5 %) were the most abundant components in *Lavandula angustifolia* essential oil (yield is 3 % (v/w) (Soković et al. 2010). Other components included tricyclene

0.1 %, α-thujene 0.6 %, α-pinene 0.2 %, α-terpinene 0.3 %, limonene 8.5 %, 1,8-cineole 3.3 %, *cis*-linalool oxide 2.4 %, fenchone 0.6 %, endo-fenchol 0.1 %, camphor 1.1 %, borneol 2.5 %, terpin-4-ol 2.1 %, α-terpineol 4.2 %, bornyl acetate 0.1 %, lavandulyl acetate 6.6 %, *trans*-pinocarveol 0.2 %, neryl acetate 2 % and geranyl acetate 3 % totalling 92.7 %.

The main compounds in all lavender volatile oils (*Lavandula angustifolia* ssp. *angustifolia*, *L. hybrida*, *L. angustifolia* spp. *pyrenaica*, *L. angustifolia* spp. *angustifoli*a cv. Munstead and cv. Hidcote blue) from Galati, Romania, were linalool (20.60–35.99 %), linalyl acetate (12.58–19.65 %), lavandulyl acetate (3.74–10.48 %), t-p3-ocimene (1.26–9.23 %), α-terpineol (3.67–6.73 %), nerol (0.81–3.32 %), neryl acetate (0.95–3.64 %) and β-caryophyllene (0.93–2.43 %) (Robu et al. 2011). The essential oil yield from the flowering spikes of *L. angustifolia* from India was 1.56 %, comprising 31 components which amounted to 91.7 % (Raina and Negi 2012). The major components were linalool (23.6 %), linalyl acetate (35.8 %), α-terpinolene (6.3 %), lavandulyl acetate (4.8 %), 1,8-cineole (1.5 %), terpinen-4-ol (2.0 %), β-caryophyllene (1.8 %), camphor (1.4 %) and borneol (1.4 %). The essential oil was rich in oxygenated monoterpenes (82.6 %). Lavender essential oil yield reached 6.64 % after 150 min distillation time (DT; at 180 min DT, yield was maximum 6.83 %, and its various major components cineole 6.61 %, fenchol 1.76 %, camphor 7.37 % and linalool acetate 37.5 %) (Zheljazkov et al. 2013). The primary components of the essential oils of *L. angustifolia* varieties 'Munstead', 'Munstead Strain', 'Lavender Lady', 'Ellagance Purple' and 'Blue River' were linalool (23.9–15.8 %), linalyl anthranilate (12.3–1.6 %), 1-terpinen-4-ol (9.7–5.5 %), *p*-menth-1-en-8-ol (7.9–4.0 %) and linalool oxide (4.7–1.1 %) (Adaszyńska et al. 2013).

The essential oil composition of seven Bulgarian lavender varieties comprised linalool 28.92–40.58 % and linalyl acetate 19.91–37.63% as major components; other constituents included origanene tr (trace) -0.23 %, α-pinene 0.12–071 %, camphene 0.21–0.5 %, β-pinene 0.2–0.53 %, 3-octanone 0.50–2.98 %, myrcene 0.53–0.9 %, 1-octen-3-ol 0.1–0.56 %, 6-methyl-5-hepten-2-one 0.06–0.49 %, hexyl acetate 0.44–1.21 %, α-phellandrene tr-0.08, *p*-cymene 0.10–0.27 %, 1,8-cineole 0.31–4.23 %, limonene 0.25–1.96 %, *cis*-β-ocimene 1.70–7.09 %, *trans*-β-ocimene 0.55–4.18 %, γ-terpinene tr -0.24 %, *cis*-linalool oxide tr -0.15 %, *trans*-linalool oxide 0.05–0.18 %, α-terpinolene 0.11–0.22 %, linalool 28.92–40.58 %, chrysanthenone 0.07–0.1 %, octene-3-yl-acetate 0.79–2.27 %, 5-caranol tr-0.33 %, camphor 0.09–0.38 %, borneol 0.5–2.06 %, lavandulol tr-0.12 %, 1-terpinen-4-ol 0.08–7.35 %, *p*-cymene-1-ol-8 0.21–0.79 %, α-terpineol 1.24–1.76 %, hexyl butyrate 0.24–0.36 %, geraniol 0.07–0.28 %, bornyl acetate tr-0.33 %, lavandulyl acetate 2.45–4.43 %, neryl acetate 0.26–0.42 %, geranyl acetate 0.40–0.78 %, β-caryophyllene 1.73–5.19 %, α-santalene 0.09–0.17 %, β-farnesene 1–4.69 %, germacrene D 0.08–1.05 %, γ-cadinene tr-0.15 %, caryophyllene oxide 0.17–0.45 % and α-cadinol tr-0.26 % (Milina et al. 2012). Volatile components found in headspace gas chromatography of fresh flowers from several Bulgarian lavender varieties included linalool 12.32–35.29 % and linalyl acetate 16.85–23 % as major components and *cis*-β-ocimene 5.06–18.40 %, *trans*-β-ocimene 1.94–13.03 % and 3-octanone 1.46–7.52 %. Other components were origanene, α-pinene, camphene, β-pinene, myrcene, 1-octen-3-ol, 6-methyl-5-hepten-2-one, hexyl acetate, α-phellandrene, *p*-cymene, 1,8-cineole, limonene γ-terpinene, *cis*-linalool oxide, *trans*-linalool oxide, α-terpinolene, chrysanthenone, octene-3-yl-acetate, 5-caranol, camphor, borneol, lavandulol, 1-terpinen-4-ol, *p*-cymene-1-ol-8, α-terpineol, hexyl butyrate, geraniol, bornyl acetate, neryl acetate, geranyl acetate, β-caryophyllene, α-santalene, β-farnesene, germacrene D, γ-cadinene, caryophyllene oxide and α-cadinol (Milina et al. 2012).

Of three extraction methods for lavender, hydrodistillation, supercritical CO_2 extraction (SFE) and ultrasound-assisted extraction, the best extracts, in terms of the amount of isolated compounds, flavour quality and stability were those obtained with SFE (Da Porto et al. 2009). Sonication performed at low amplitude for 5 min offered respect to high amplitude a promising

alternative to hydrodistillation as a source of lavender flavouring. Sixty compounds were identified and quantified including a true quantification of 1–8 cineol, camphor, linalool, linalyl acetate and β-caryophyllene.

For both *L. angustifolia and L.* × *intermedia* 'Budrovka', leaf extracts (5.32, 3.80 %) were the richest sources of phenolic acids, followed by flowers (5.00, 3.42 %) and inflorescence stalk (2.41, 1.62 %), respectively (Blazeković et al. 2010). There were no significant differences in flavonoid contents among the extracts of *L. angustifolia* and *L.* × *intermedia* 'Budrovka', leaf extracts (0.25, 0.26 %), flower (0.09, 0.10 %) inflorescence stalk (0.19, 0.22 %), respectively, and also in flower anthocyanin—0.03 % for *L. angustifolia* and 0.02 % for *L.* × *intermedia* 'Budrovka'. Total tannins in *L.* × *intermedia* 'Budrovka' extracts differed significantly decreasing in the order as follows: leaf (2.21 %), flower (2.02 %) and inflorescence stalk (1.01 %). *L. angustifolia extracts* contained significantly higher amount of tannins, 3.18, 2.77 and 1.38 %, respectively, following the same order of plant parts. The content of procyanidin group of tannins varied between 0.86 and 1.44 % for all *Lavandula* extracts. Total polyphenol content of *L.* × *intermedia* 'Budrovka' ethanolic extracts was highest in leaf (7.05 %), followed by flower (6.65 %) and inflorescence stalk (3.09 %) extracts. However, similar extracts obtained from *L. angustifolia* contained significantly greater quantity of total polyphenols, 9.20, 8.46 and 4.54 %, respectively.

Fatty acids, *cis*- and *trans*-*p*-coumaric acids (= *p*-hydroxy cinnamic acids) and β-sitosterol were isolated from cell suspension cultures of *Lavandula angustifolia* (Topçu et al. 2007).

Antioxidant Activity

Lavandula angustifolia extract elicited considerable concentration-dependent inhibition of lipid peroxidation (Hohmann et al. 1999). Phenolic components present in the plant extracts were evaluated for antioxidant activity and were found effective in both enzyme-dependent and enzyme-independent lipid peroxidation tests. Lavender essential oil displayed strong antioxidant activity against lipid peroxidation in a linoleic acid model system (Lu et al. 2010). The percentage of inhibition of peroxidation in linoleic acid system of test samples (essential oil) reached to 87.9 %, when 4 mg/mL of essential oil were added. Operating conditions of supercritical CO_2 extraction, namely, pressure and time, had a significant linear effect on both yield and antioxidant activity of lavender essential oil extracts tested by the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay, while temperature had a lesser impact except for the effect of its interaction with pressure on extract yield (Danh et al. 2012). Generally, the yield and antioxidant activity of the extracts increased with pressure and time. However, antioxidant activity of extracts examined by the 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) assay was not affected by any operating conditions. Studies suggested the use of lavender oil as effective natural antioxidants (Hamad et al. 2013). Values of percentage inhibition of 2,2-diphenyl-1-picrylhydrazyl-hydrate (DPPH) free radical ranged from 3.28 to 88.91 % for 7.81 μg/mL and 1,000 μg/mL, respectively, with an IC_{50} value of 216 μg/mL for lavender essential oil.

L. angustifolia and L. × *intermedia* 'Budrovka' extracts exhibited potent antiradical activity in a concentration-dependent manner (Blazeković et al. 2010). The effectiveness of *L.* × *intermedia* 'Budrovka' and *L. angustifolia* extracts decreased in the following sequence: leaf > flower > inflorescence stalk. At higher concentrations (40–160 μg/mL) most of the tested extracts were more effective in DPPH radical scavenging than the widely used synthetic antioxidant BHT, while at lower concentrations (≤10 μg/mL) BHT was considerably more potent. IC_{50} values for *L.* × *intermedia* 'Budrovka' extracts ranged from 15.06 to 45.25 μg/mL, while those obtained for extracts of *L. angustifolia* were significantly lower (IC_{50} 10.62–33.95 μg/mL), reflecting their better free radical scavenging activity. Rosmarinic acid, an important constituent of both *Lavandula* extracts, was found to be a very strong DPPH radical scavenger with IC_{50} value of 1.51 μg/mL,

being even four times more effective than positive control BHT (IC_{50} 6.45 μg/mL).

All *L. angustifolia and L.* × *intermedia* 'Budrovka' extracts exhibited significant and concentration-dependent iron chelating activity (Blazeković et al. 2010). The inflorescence stalk extracts of both *Lavandula* plants were found to be significantly more active than related flower and leaf extracts. The effectiveness of plant extracts as iron ion chelators was in the following descending order: *L. angustifolia* inflorescence stalk > *L.* × *intermedia* 'Budrovka' *inflorescence* stalk > *L. angustifolia* leaf > *L. angustifolia* flower > *L.* × *intermedia* 'Budrovka' leaf > *L.* × *intermedia* 'Budrovka' flower, with IC_{50} values ranging between 236.92 and 397.71 μg/mL. However, the chelating ability of all tested extracts was much lower compared to reference EDTA, one of the most powerful metal chelators known (IC_{50} 13.37 μg/mL). Contrary to the plant extracts, neither rosmarinic acid nor BHT exhibited any iron chelating activity at the concentrations studied. All *L. angustifolia and L.* × *intermedia* 'Budrovka' extracts possessed the ability to reduce Fe^{3+} ions. The reducing power of the *Lavandula* extracts increased in a concentration-dependent manner. For the *L.* × *intermedia* 'Budrovka', the leaf extract showed the strongest reducing ability with IC_{50} 28.73 μg/mL, followed by the flower extract (IC_{50} 33.78 μg/mL) and inflorescence stalk extract (IC_{50} 66.92 μg/mL), but all extracts were significantly less active than related *L. angustifolia* extracts: leaf IC_{50} (24.26 μg/mL), flower (IC_{50} 25.17) and inflorescence stalk IC_{50} (55.22 μg/mL). The reducing power of rosmarinic acid (IC_{50} 1.26 μg/mL) was considerably more pronounced relative to that of BHT (IC_{50} 4.64 μg/mL), suggesting its strong influence on the reductive properties of *Lavandula* extracts. All tested *Lavandula* extracts inhibited lipid peroxidation in a concentration-dependent manner. At a concentration of 100 μg/mL, the flower, inflorescence stalk and leaf extracts of *L.* × *intermedia* 'Budrovka' effected 49.30, 36.14 and 69.21 % inhibition of lipid peroxidation activity, while the extracts from *L. angustifolia* effected 56.17, 37.20 and 70.75 %, respectively. Generally, *Lavandula* extracts were less potent then fisetin and rosmarinic acid. Leaf extracts of *L. angustifolia* and *L.* × *intermedia* 'Budrovka' displayed stronger activity than extracts from other plant parts and proved to be able to prevent lipid peroxidation in significantly lower concentrations (IC_{50} 54.57 and 74.56 μg/mL, respectively). Total antioxidant capacity (mg AAE/g) of *L.* × *intermedia* 'Budrovka' plant parts (flower 294 mg, inflorescence stalk 240.75 mg, leaf 290.75 mg) was higher than *L. angustifolia* corresponding plant parts (flower 261.50 mg, inflorescence stalk 238.08 mg, leaf 274.18 mg). Total antioxidant capacity (mg AAE/g) of rosmarinic acid was 1,064.47 mg compared to BHT 414.74 mg.

Studies showed that lavender (*L. angustifolia*) total flavonoids could effectively scavenge superoxide anion with EC_{50} value of 60 μg/mL, hydroxyl radical with EC_{50} of 182 μg/mL and DPPH radical with EC_{50} of 189 μg/mL (Yang and Gao 2010). Spiridon et al. (2011) found that *Origanum vulgare* and *Melissa officinalis* extracts were more effective than *Lavandula angustifolia* in scavenging DPPH radicals. Major phenolic acids identified in the analyzed species were ferulic, rosmarinic, *p*-coumaric and caffeic, while predominant flavonoids were quercetin, apigenin and kaempferol, which were present as glucosides.

Neuroprotective Activity

In comparison with the model group, treatment with lavender oil significantly decreased neurological deficit scores, infarct size, and the levels of malondialdehyde, carbonyl and reactive oxygen species; attenuated neuronal damage; up-regulated superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) activities; and reduced glutathione (GSH)/glutathione disulphide (GSSG) ratio in mice with cerebral ischaemia/reperfusion injury (Wang et al. 2012). The results suggested that the neuroprotective effects of lavender oil against cerebral ischaemia/reperfusion injury may be attributed to its antioxidant effects.

In scopolamine-treated rats, lavender essential oils (*Lavandula angustifolia* ssp. *angustifolia* and *Lavandula* hybrid) showed potent antioxidant and anti-apoptotic activities (Hancianu et al. 2013). Subacute exposures (daily, for seven continuous days) to lavender oils significantly increased antioxidant enzyme activities (SOD, GPX and CAT) and total content of reduced GSH and reduced lipid peroxidation (MDA level) in rat temporal lobe homogenates, suggesting antioxidant potential. Also, DNA cleavage patterns were absent in the lavender groups, suggesting anti-apoptotic activity. The results suggested that antioxidant and anti-apoptotic activities of the lavender essential oils were the major mechanisms for their potent neuroprotective effects against scopolamine-induced oxidative stress in the rat brain.

Antimicrobial Activity

Essential oils from *Lavandula angustifolia* and three hybrids of *Lavandula latifolia* × *Lavandula angustifolia* (Lavandin 'Super', Lavandin 'Abrialis' and Lavandin 'Grosso') inhibited growth of selected food-borne pathogens: *Salmonella enteritidis, Salmonella typhimurium, Escherichia coli* O157:H7, *Yersinia enterocolitica, Shigella flexneri, Listeria monocytogenes* serovar 4b and *Staphylococcus aureus* in vitro (Rota et al. 2004).

In vitro study found that lavender oil inhibited growth of *Trichophyton rubrum* strains, as did its component linalool (Cassella et al. 2001). *Lavandula angustifolia* essential oil exhibited both fungistatic and fungicidal activity against *Candida albicans* strains (D'Auria et al. 2005). It inhibited *C. albicans* growth with mean minimum inhibitory concentration (MIC) of 0.69 % (vol./vol.) (vaginal strains) and 1.04 % (oropharyngeal strains) and mean minimum fungicidal concentration (MFC) of 1.1 % (vaginal strains) and 1.8 % (oropharyngeal strains). Linalool, one of its components, was more effective than the essential oil: mean MIC of 0.09 % (vaginal strains) and 0.29 % (oropharyngeal strains) and mean MFC of 0.1 % (vaginal strains) and 0.3 % (oropharyngeal strains). Linalyl acetate was almost ineffective. Lavender oil (2 % concentration) killed 100 % of *the C. albicans* cells within 15 min, while linalool (0.05 % concentration) killed 100 % of the cells within 30 s. The essential oil inhibited germ tube formation (mean MIC of 0.09 %), as did the main components (MIC of 0.11 % for linalool and 0.08 % for linalyl acetate). Both the essential oil and its main components inhibited hyphal elongation of *C. albicans. L. angustifolia* essential oil showed stronger fungistatic activity in vitro than *Mentha piperita* essential oil (Behnam et al. 2006). *Lavandula* oil exhibited complete growth inhibition of pathogenic fungi (*Rhizopus stolonifer, Botrytis cinerea* and *Aspergillus niger*) at 1,000 ppm with a minimum EC_{50} (311.24 ppm) against *B. cinerea*.

When lavender oil was assayed in 1:1 ratios with 45 other oils, synergistic (26.7 %), additive (48.9 %), noninteractive (23.7 %) and antagonistic (0.7 %) interactions in antimicrobial activity were observed (de Rapper et al. 2013). The most favourable interactions were when *L. angustifolia* was combined with *Cinnamomum zeylanicum* or with *Citrus sinensis*, against *Candida albicans* and *Staphylococcus aureus*, respectively. In 1:1 ratios, 75.6 % of the essential oils investigated showed either synergistic or additive results, lending in vitro credibility to the use of essential oil blends in aromatherapeutic practices. Methanol flower extract of *L. angustifolia* had an MIC of 100 µg/mL against the Gram-negative bacterium *Helicobacter pylori*, the primary aetiological factor associated with the development of gastritis and peptic ulcer disease and also associated with chronic gastritis, gastric carcinoma and primary gastric B cell lymphoma (Mahady et al. 2005).

Lavandula angustifolia, Carum carvi and *Trachyspermum copticum* essential oils were found to be promising for the treatment of intestinal dysbiosis (Hawrelak et al. 2009). These essential oils displayed the greatest degree of selectivity, inhibiting the in vitro growth of potential pathogens such as *Bacteroides fragilis, Clostridium difficile, Clostridium perfringens* and *Candida albicans* at concentrations that had no effect on four beneficial gastrointestinal bacteria, *Lactobacillus acidophilus, Lactobacillus plantarum, Bifidobacterium bifidum*

and *Bifidobacterium longum*. The antibacterial potential of essential oils tested in vitro was ranked in ascending order as follows: *Matricaria chamomilla* < *Salvia officinalis* < *Citrus aurantium* < *Citrus limon* < *Lavandula angustifolia* < *Ocimum basilicum* < *Mentha piperita* < *Mentha spicata* < *Thymus vulgaris* < *Origanum vulgare* (most active) (Soković et al. 2010). The antibacterial potential of essential oils' components tested in increasing order was found as follows: linalyl acetate < limonene < β-pinene < α-pinene < camphor < linalool < 1,8-cineole < menthol < thymol < carvacrol (highest). Linalool (27.2 %) and linalyl acetate (27.5 %) were the most abundant components in *Lavandula angustifolia* essential oil (yield is 3 % (v/w). *Pseudomonas aeruginosa* and *Proteus mirabilis* were found to be the most resistant species; some of the essential oils and compounds were not active against them. *Micrococcus flavus* was the most sensitive bacterial species to oils and components tested. The MIC and MBC μg/mL of *L. angustifolia* oil against the tested bacteria were, respectively, *Bacillus subtilis* (4, 4.5), *Micrococcus flavus* (4,4), *Enterobacter cloacae* (6,7), *Escherichia coli* (6,6), *Proteus mirabilis* (8,7), *Pseudomonas aeruginosa* (9,5.5), *Salmonella enteritidis* (5,6), *Salmonella epidermidis* (4,5), *Salmonella typhimurium* (5,6), *Staphylococcus aureus* (5,5.5) and *Listeria monocytogenes* (5.5,6).

Lavender (*L. angustifolia*) essential oil displayed good antibacterial activity against four rhinitis-related bacteria in vitro: *Staphylococcus aureus, Micrococcus ascoformans, Proteus vulgaris* and *Escherichia coli* (Lu et al. 2010). Thyme and lavender essential oils were active against multidrug-resistant clinical strains of *Escherichia coli* genera (Sienkiewicz et al. 2011a). Both essential oils from *Thymus vulgaris* and *L. angustifolia* were active against all 30 clinical strains of *Escherichia coli*, but thyme oil demonstrated the highest activity in vitro. Also thyme oil elicited higher activity than lavender oil against clinical strains of *Staphylococcus, Enterococcus* and *Escherichia* genus (Sienkiewicz et al. 2011b). Lavender oil exhibited higher antibacterial ability in comparison with *Calamintha nepeta* essential oil (Miladinović et al. 2012). The essential oils of *L. angustifolia* 'Blue River' and 'Munstead' varieties exhibited the greatest antibacterial activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Adaszyńska et al. 2013).

All four lavender oils, namely, *Lavandula angustifolia, L. latifolia, L. stoechas* and a necrodane-rich *L. luisieri*, inhibited growth of both methicillin-sensitive and methicillin-resistant *Staphylococcus aureus* (MSSA and MRSA) by direct contact but not in the vapour phase (Roller et al. 2009). Inhibition zones ranged from 8 to 30 mm in diameter at oil doses ranging from 1 to 20 μL, respectively, demonstrating a dose response. Several binary combinations of the oils tested showed that the necrodane-rich *L. luisieri* oil interacted synergistically with *L. stoechas* (high in 1,8-cineole, fenchone and camphor) and *L. angustifolia* (rich in linalool and linalyl acetate) to produce larger inhibition zones than those produced using each oil individually. The results suggested that combinations of lavender oils should be investigated further for possible use in antibacterial products. *Escherichia coli* and *Staphylococcus aureus* were found to be susceptible to *Lavandula angustifolia* flower essential oil (Lodhia et al. 2009). With increase in concentration of essential oil, increase in zone of inhibition was observed.

Lavender oil, in combination with other essential oils and salicylic acid, may be a potential treatment option for patients with plantar warts caused by the human papillomavirus (Forbes and Schmid 2006).

Kang et al. (2010) reported that patients with terminal cancer that received essential oil (lavender, geranium, tea tree, peppermint) treatment orally twice daily for 1 week had fewer numbers of colonizing *Candida albicans* as compared with the control (saline) group. Additionally, scores for subjective comfort and objective oral state were higher in the essential oil group as compared with the control group.

Anticancer Activity

Monoterpenes such as D-limonene and perillyl alcohol found in orange peels and lavender,

respectively, had been shown to possess chemopreventive properties against mammary, liver, lung, colon and pancreatic carcinogenesis (Elegbede et al. 1984; Haag and Gould 1994; Mills et al. 1995; Stark et al. 1995; Reddy et al. 1997; Bardon et al. 2002; Matos et al. 2008). Elegbede et al. (1984) found that rats fed with 10,000 ppm of D-limonene had a 72 % reduction in mammary tumours when compared to controls at 18 weeks post 7,12-dimethylbenz[a] anthracene (DMBA) induction. In addition to inhibiting the appearance of mammary tumours, D-limonene was also found to cause the regression of frank mammary tumours. Dietary perillyl alcohol was shown to induce the regression of 81 % of small mammary carcinomas and up to 75 % of advanced mammary carcinomas initiated by 7,12-dimethylbenz(a)anthracene (DMBA) in the Wistar-Furth rat and was 5 times more potent than limonene at inducing tumour regression (Haag and Gould 1994). It was suggested that the increased potency of perillyl alcohol over limonene in causing tumour regression may be due at least in part to differences in the pharmacokinetics of these two monoterpenes. For example, rats given with a 2 % perillyl alcohol diet for 10 weeks had plasma levels of terpene metabolites of 0.82 mM, whereas those fed with a 10 % limonene diet for the same period had blood levels of 0.27 mM. In vitro studies showed that perillyl alcohol inhibited ubiquinone synthesis and blocked the conversion of lathosterol to cholesterol in murine embryonic fibroblast NIH3T3 cells (Ren and Gould 1994). These two cellular effects of perillyl alcohol may contribute to the antitumour activity of the monoterpenes.

Dietary perillyl alcohol was shown to induce the regression of 81 % of small mammary carcinomas and up to 75 % of advanced mammary carcinomas initiated by 7,12-dimethylbenz(a) anthracene (DMBA) in the Wistar-Furth rat and was greater and 5 times more potent than limonene at inducing tumour regression (Haag and Gould 1994). It was suggested that the increased potency of perillyl alcohol over limonene in causing tumour regression may be due at least in part to differences in the pharmacokinetics of these two monoterpenes. For example, rats given with a 2 % perillyl alcohol diet for 10 weeks had plasma levels of terpene metabolites of 0.82 mM, whereas those fed with a 10 % limonene diet for the same period had blood levels of 0.27 mM. Mills et al. (1995) reported that perillyl alcohol inhibited liver tumour growth in rats induced by diethylnitrosamine exposure. It enhanced tumour cell loss through apoptosis. Perillyl alcohol reduced the growth of hamster pancreatic tumours to less than half that of controls (Stark et al. 1995). Moreover, 16 % of perillyl alcohol-treated pancreatic tumours completely regressed, whereas no control tumours regressed. Reddy et al. (1997) showed that administration of perillyl alcohol in the diet of rats with invasive colon adenocarcinomas induced by azoxymethane significantly inhibited the incidence (percentage of animals with tumours) and multiplicity (tumours/animals) of tumours of the colon and small intestine. The chemopreventive activity of perillyl alcohol was mediated through the tumour cell loss by apoptosis. Perillyl alcohol i.p. treatment of male (C3H/HeJ X A/J) F1 hybrid mice 1 week prior to initiation with the carcinogen4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and continuing for 22 weeks after initiation elicited a 22 % reduction in lung tumour incidence and a 58 % reduction in tumour multiplicity (Lantry et al. 1997). Perillyl alcohol and to a lesser extent its major metabolite perillic acid exerted a dose-dependent inhibitory effect on HCT 116 human colon cancer cell growth correlated with a G1 arrest (Bardon et al. 2002). The two monoterpenes induced growth arrest of colon cancer cells through the up-regulation of p21Waf1/Cip1 and the down-expression of cyclin D1 and its partner cdk4.

The monoterpenes limonene and perillyl alcohol had been shown to induce the complete regression of rat mammary carcinomas by a cytostatic and differentiation process (Shi and Gould 1995). Perillyl alcohol was found to be a potent inducer of differentiation in a well-characterized neuroblastoma-derived cell line Neuro-2A. Several cellular effects of monoterpenes were ruled out as contributing to Neuro-2A differentiation including its cytostatic

effect and its ability to inhibit ubiquinone (CoQ) syntheses.

Perillyl alcohol caused both cytostasis and apoptosis in rat mammary carcinomas (Shi and Gould 2002). In vitro, perillyl alcohol inhibited cellular proliferation in a variety of mammalian cell lines. In murine mammary transformed cell line TM6, perillyl alcohol caused an early G1 cell cycle block and decelerated the G2–M transition. An increase in pRB in its hypophosphorylated state was associated with the early G1 block caused by perillyl alcohol. Perillyl alcohol treatment inhibited two important targets in the cells during the G1–S transition: cyclin D1- and cyclin E-associated kinase. Additionally, perillyl alcohol treatment induced an increased association of p21WAF1 with cyclin E–Cdk2 complexes and inhibited the activating phosphorylation of Cdk2. All these effects of perillyl alcohol may contribute to the inhibition of the transition out of the G1 phase of the cell cycle.

Liston et al. (2003) found that perillyl alcohol had a weakly promoting effect early in nitrosamine-induced oesophageal tumorigenesis and suggested that perillyl alcohol may not be an effective chemopreventive agent for oesophageal cancer in humans.

In a pilot study of eight patients with resectable pancreatic cancer, tumour size and CA 19–9 level were unchanged with perillyl alcohol treatment (Matos et al. 2008). Survival time was longer in patients who received full perillyl alcohol treatment (288 ± 32 days) compared to those who did not (204 ± 96 days) although this was not significant. There was a trend towards greater apoptosis in patients receiving perillyl alcohol compared to fresh operative controls; there was also a suggestion of greater apoptosis in tumour compared to normal pancreatic tissue in the same patient.

In a phase I clinical trial, Ripple et al. (1998) treated 18 patients who had advanced malignancies with perillyl alcohol. Two heavily pretreated ovarian cancer patients experienced reversible > or = grade 3 granulocytopenia. Grade 1–2 fatigue was also noted. Disease stabilization for > or = 6 months was seen, although no objective tumour responses were noted. In a phase I dose-escalation trial of perillyl alcohol, evidence of antitumour activity was seen in a patient with metastatic colorectal cancer who had an ongoing near-complete response of >2 years duration (Ripple et al. 2000). Several other patients were on study for > or = 6 months with stable disease. The maximum tolerated dose of perillyl alcohol given continuously four times a day was 1,200 mg/m^2/dose. Gastrointestinal toxicity was dose limiting, although significant interpatient variability in drug tolerance was seen. The predominant toxicities seen were gastrointestinal (nausea, vomiting, satiety and eructation), which were dose limiting. There appeared to be a dose-dependent increase in levels of the two main metabolites, perillic acid and dihydroperillic acid. Approximately 9 % of the total dose was recovered in the urine in the first 24 h, the majority as perillic acid.

Anxiolytic Activity

Basch et al. (2004) in their review asserted that evidence indicated strongly to inhaled lavender's anxiolytic effects. This effect may be due to potentiation of the inhibitory neurotransmitter GABA as well as a dose-related binding to glutamate, one of the main excitatory neurotransmitters in the central nervous system.

Animal Studies

Exposure to lavender odour over 2 weeks or 24 h periods was found to have an anxiolytic profile in gerbils similar to that of the anxiolytic diazepam (Bradley et al. 2007). Further, prolonged, 2-week lavender odour exposure increased exploratory behaviour in females indicating a further decrease in anxiety in females.

Chronic exposures of scopolamine (0.7 mg/kg)-induced dementia male Wistar rat to lavender essential oils (daily, for seven continuous days) significantly reduced anxiety-like behaviour and inhibited depression in elevated plus-maze and forced swimming tests, suggesting anxiolytic and antidepressant activity (Hritcu et al. 2012). Also, spatial memory performance in Y-maze and radial arm-maze tasks was improved, suggesting

positive effects on memory formation. The results suggested that multiple exposures to lavender essential oils could effectively reverse spatial memory deficits induced by dysfunction of the cholinergic system in the rat brain and might provide an opportunity for the management of neurological abnormalities in dementia conditions.

Studies showed that the inhalation of essential oils could induce anxiolytic effects through the central nervous system (e.g. lung absorption and bloodstream transport) or stimulation of the olfactory system and secondary activation of brain regions (Chioca et al. 2013a). The results of their studies in mice suggested that olfactory system activation was unlikely to participate in the anxiolytic-like effect of lavender essential oil inhalation. Zinc gluconate + zinc acetate-induced anosmia in mice did not interfere with the anxiolytic-like effect of lavender essential oil inhalation in the marble-burying test at concentrations of 2.5 and 5 %. Lavender essential oil at a concentration of 0.5 % was ineffective. In further animal studies, they (Chioca et al. 2013b) reported that lavender essential oil (1–5 %) decreased the number of marbles buried compared with the control and amyl acetate groups. In the elevated plus maze, 5 % lavender essential oil inhalation increased the percentage of time spent and number of entries into the open arms compared with controls. No effect was seen in the number of closed arm entries or number of beam interruptions in the automated activity chamber. Pretreatment with the GABA receptor antagonist picrotoxin (0.5 mg/kg) did not modify the behavioural effect of 5 % lavender essential oil in the marble-burying test. Lavender essential oil also did not alter [(3)H]flunitrazepam binding to the benzodiazepine site on the GABA receptor. Pretreatment with the serotonin 5-HT1A receptor antagonist WAY100635 (3 mg/kg) blocked the anxiolytic-like effect of lavender essential oil and the 5-HT1A receptor agonist 8-OH-DPAT (3 mg/kg). A combination of ineffective doses of 8-OH-DPAT (0.5 mg/kg) and lavender essential oil (0.1 %) reduced the number of marbles buried. Finally, 5 % lavender essential oil attenuated the serotonin syndrome induced by 40 mg/kg fluoxetine plus 80 mg/kg 5-hydroxytryptophan. These results suggested the anxiolytic-like effect of lavender essential oil to be mediated by the serotonergic system rather than by the GABA/benzodiazepine neurotransmission pathway.

Aqueous extract of *L. angustifolia* at a dose of 100 and 200 mg/kg and 200 mg/kg was found to improve spatial performance of rats with Alzheimer's disease induced by intracerebroventricular injection of 10 μg Aβ1-42 twenty days prior to administration of the lavender extract in Morris water maze and probe test, respectively (Kashani et al. 2011).

Clinical Studies

Hardy et al. (1995) found the effects of lavender oil aromatherapy for insomnia and was comparable with hypnotics or tranquilizers. In a study of 16 healthy females (38 ± 8 years old) randomly assigned to three treatments applied by a robotic oil-dripping system, plain sesame oil (plain Shirodhara), medicated sesame oil with a 0.3 vol.% of lavender essential oil (lavender Shirodhara) or the control supine, lavender Shirodhara showed potent anxiolytic and altered state of consciousness (ASC)-inducing or ASC-promoting effects and induced the largest increase in foot skin temperature (Xu et al. 2008). These effects were larger in the lavender Shirodhara than in the other two conditions. It was speculated that the psychophysiological effects of lavender Shirodhara would be mediated via three mechanisms: (1) the well-known relaxing action of essential oils from *L. angustifolia* mediated by olfactory nerves, (2) the pharmacological action of substances absorbed through the skin or mucosa in the sesame oil or lavender essential oil and (3) the physiological effect of sesame oil dripped on the forehead induced by the somatoautonomic reflex through thermosensors or pressure sensors in the skin or hair follicles via the trigeminal cranial nerve. In a double-blind, randomized placebo study of 97 subjects, lavender was found to have anxiolytic effects in humans under conditions of low anxiety, but these effects may not extend to conditions of high anxiety (Bradley et al. 2009). In subjects orally administered with lavender capsule (200 μL) during the

neutral film clip, there was a trend towards reduced state anxiety, galvanic skin response (GSR) and heart rate and increased heart rate variation (HRV). In the anxiety-eliciting film, lavender was mildly beneficial in females but only on HRV measures. In males, sympathetic arousal increased during the anxiety film (GSR). HRV significantly increased at 200 μL during all three film clips in females, suggesting decreased anxiety. In a semi-comparative study of 12 breast cancer patients, a 30-min aromatherapy massage with lavender oils (and other oils) twice a week for 4 weeks resulted in a reduction in anxiety (Imanishi et al. 2009). Specifically, anxiety was reduced after one massage session, as measured by the State Trait Anxiety Inventory test, and after eight sessions, as measured by the Hospital Anxiety and Depression Scale test. In another randomized, double-blind, placebo-controlled trial of 221 adults suffering from anxiety disorder, oral administration of Silexan, a new oral lavender oil capsule preparation, was found to be effective in the treatment of 'subsyndromal' anxiety disorder (Kasper et al. 2010). Patients treated with Silexan showed a total score decrease by 16.0 points (59.3 %) for the Hamilton Anxiety Scale (HAMA) and by 5.5 points (44.7 %) for the Pittsburgh Sleep Quality Index (PSQI) compared to 9.5 (35.4 %) and 1 points (30.9 %) in the placebo group. *Lavandula* oil preparation had a significant beneficial influence on quality and duration of sleep and improved general mental and physical health without causing any unwanted sedative or other drug-specific effects. There were no adverse effects reported. In a cluster randomized controlled trial, patients' ($N = 340$) anxiety was assessed while waiting for a scheduled dental appointment; it was found that lavender scent reduced anxiety state in dental patients, and the lavender group reported significantly lower current anxiety as indicated by the State Trait Anxiety Indicator than the control group (Kritsidima et al. 2010).

In a 6-week, multicentre, double-blind, randomized study of the lavender oil preparation Silexan versus lorazepam for generalized anxiety disorder, Silexan effectively ameliorated generalized anxiety comparable to lorazepam (Woelk and Schläfke 2010). The Hamilton Anxiety Rating Scale (HAMA total score) decreased by similar extent with both treatments. During the active treatment period, the two HAMA subscores 'somatic anxiety' (HAMA subscore I) and 'psychic anxiety' (HAMA subscore II) also decreased to a similar extent in both groups. The changes in other subscores, such as the SAS (Self-Rating Anxiety Scale), PSWQ-PW (Penn State Worry Questionnaire), SF-36 Health Survey questionnaire and Clinical Global Impressions of severity of disorder (CGI item 1, CGI item 2, CGI item 3), and the results of the sleep diary demonstrated comparable positive effects of the two compounds. Since lavender oil exhibited no sedative effects in their study and had no potential for drug abuse, Silexan appeared to be an effective and well-tolerated alternative to benzodiazepines for amelioration of generalized anxiety. In an open-label exploratory phase II trial involving 50 male and female patients with neurasthenia, post-traumatic stress disorder or somatization disorder, administration of 1×80 mg/day Silexan (lavender preparation) over 6 weeks elicited comparable improvements with most outcomes (Uehleke et al. 2012). For all patients, mean depression scale score decreased by 32.7 % and Symptom Checklist-90-Revised (SCL-90-R) Global Severity Index by 36.4 % as compared to baseline, while the 36-item Short Form Health Survey questionnaire (SF-36) score increased by 48.2 %. Waking up frequency, Waking up duration and morning tiredness were reduced, while efficiency of sleep and mood improved. Adverse reactions, predominantly gastrointestinal complaints, were judged as mild or moderate.

Findings from a 4-week pilot study of 28 women indicated positive findings with minimal risk for the use of aromatherapy (essential oil blend of rose otto and *Lavandula angustifolia* at 2 % dilution) as a complementary therapy in both anxiety and depression scales with the postpartum woman (Conrad and Adams 2012). The midpoint and final scores indicated that aromatherapy had significant improvements greater than the control group on both Edinburgh Postnatal Depression Scale (EPDS) and Generalized Anxiety Disorder Scale (GAD-7) scores.

In a study of 20 healthy volunteers, lavender oil inhalation caused significant decreases of blood pressure, heart rate and skin temperature, which indicated a decrease of autonomic arousal (Sayorwan et al. 2012). In terms of mood responses, volunteers in the lavender oil group categorized themselves as more active, fresher and relaxed than subjects just inhaling base oil. Compared with base oil, lavender oil increased the power of theta (4–8 Hz) and alpha (8–13 Hz) brain activities. Findings from a 4-week pilot study indicated positive findings with minimal risk for the use of aromatherapy (essential oil blend of rose otto and *Lavandula angustifolia* at 2 % dilution) as a complementary therapy in both anxiety and depression scales with the postpartum woman (Conrad and Adams 2012).

Perry et al. (2012) conducted a systematic review of 15 randomized clinical trials on the anxiolytic efficacy of lavender and concluded that the best evidence suggested that oral lavender supplements may have some therapeutic effects. However, further independent replications were needed before firm conclusions could be drawn.

Anticonvulsant Activity

Studies in rats showed that inhalation of lavender oil vapour was associated with anticonvulsive effects on pentetrazol-, nicotine- and electroshock-induced convulsions but not strychnine-induced convulsions (Yamada et al. 1994). *Lavandula angustifolia* flower aqueous extract at doses of 100 µg/mL and 1 mg/mL significantly blocked glutamate-induced neurotoxicity in rat pup cerebellar granular cell culture, with the most effective dose being 1 mg/mL (Büyükokuroğlu et al. 2003). All groups of mice treated with essential oils from eight aromatic plants including *Lavandula angustifolia* showed reduced seizure activity and stability after the administration of the oil, except for those treated with *Origanum vulgare* (100 % mortality after the administration of the oil) (Koutroumanidou et al. 2013). After pentylenetetrazol (PTZ) administration, mice from the different essential oil groups showed increased latency and reduced severity of seizures (ranging from simple twitches to complete seizures). Mice who had received *Mentha piperita* demonstrated no seizures and 100 % survival. The different drastic component and its concentration could account for the diversity of anticonvulsant effects.

Anti-inflammatory/Analgesic Activities

Gedney et al. (2004) conducted a sex-balanced (13 men and 13 women) randomized crossover design study to evaluate the effects of olfactory absorption of two lavender and rosemary essential oils on sensory and affective responses to experimentally induced pain. While not causing a direct analgesic effect, inhalational lavender was found to be associated with less pain intensity and pain unpleasantness compared to marginal reduction by rosemary oil.

Studies showed that the hydroalcoholic leaf extract of *Lavandula angustifolia* (400–1,600 mg/kg, p.o.) inhibited the second phase of formalin pain test, while the polyphenolic fraction (800 and 1,600 mg/kg, p.o.) and essential oil (100 and 200 mg/kg, p.o.) suppressed both phases (Hajhashemi et al. 2003). In acetic acid-induced writhing test, polyphenolic fraction (400 and 800 mg/kg, p.o.) and essential oil (100 and 200 mg/kg, p.o.) reduced the number of abdominal constrictions. Essential oil at a dose of 200 mg/kg also inhibited carrageenan-induced paw oedema. The results confirmed the traditional use of *Lavandula angustifolia* for the treatment of painful and inflammatory conditions. In a randomized trial of 70 patients, the effectiveness of a combination herbal drop (Lamigex) composed of essential oils from *Syzygium aromaticum, Lavandula angustifolia* and *Geranium robertianum* was compared to ciprofloxacin in the alleviation of acute external otitis (AEO) (Panahi et al. 2013). All assessed symptoms (tenderness, itching, erythema, oedema and discharge) were equally improved in the ciprofloxacin and Lamigex groups by the end of trial. Lamigex exhibited good efficacy in reducing the burden of infection as well as AEO symptoms.

Huang et al. (2012) found treatment of 0.1 % lavender essential oil significantly increased cell viability and inhibited interleukin IL-1β and superoxide anion generation in lipopolysaccharide (LPS)-stimulated human monocytic THP-1 cells (Huang et al. 2012). Treatment with lavender essential oil downregulated both LPS-induced protein levels of phospho-NF-κB and membrane Toll-like receptor 4. Further, lavender essential oil increased heat shock protein (HSP) 70 expression in LPS-stimulated THP-1 cells, suggesting that lavender essential oil inhibition of LPS-induced inflammatory effect might be associated with the expression of HSP70.

Lavender oil is often used as a bath additive postnatally for mothers to reduce perineal discomfort after childbirth (Dale and Cornwell 1994). In a blind randomized clinical trial, they found that when compared with placebo and synthetic lavender oil, analysis of daily discomfort scores shows less discomfort between days 3 and 5 with true lavender oil use. In a prospective, randomized, placebo-controlled clinical study, the effects of lavender aromatherapy on opioid requirement was assessed in 54 patients undergoing laparoscopic adjustable gastric banding (Kim et al. 2007). Analgesics were required in 82 % of patients receiving placebo as compared with 46 % in those receiving inhalational lavender. Lavender patients required significantly less morphine postoperatively than placebo patients: 2.38 mg vs 4.26 mg, respectively. No differences in the requirements for postoperative antiemetics, use of antihypertensives or postanaesthesia care unit discharge time were noted between treatments. In a randomized clinical trial of 60 qualified Iranian primiparous women admitted for labour, the use of lavender oil essence was found to be effective in reducing perineal discomfort (redness, oedema, ecchymosis) following episiotomy (Sheikhan et al. 2012). It was suggested that lavender oil essence may be preferable to the use of Betadine for episiotomy wound care. In a randomized controlled prospective clinical trial of 48 post-tonsillectomy patients aged 6–12 years, aromatherapy with lavender essential oil decreased the number of required analgesics following tonsillectomy in paediatric patients but had no significant effects on pain intensity and frequency of nocturnal awakening (Soltani et al. 2013).

Anaesthetic Activity

L. angustifolia essential oil, linalyl acetate and linalool (0.01–10 μg/mL) drastically reduced, in a dose-dependent manner, the electrically evoked contractions of rat phrenic hemidiaphragm (Ghelardini et al. 1999). In in vivo rabbit conjunctival reflex test, treatment with lavender essential oil, linalyl acetate and linalool (30–2,500 μg/mL administered in the conjunctival sac) allowed a dose-dependent increase in the number of stimuli necessary to provoke the reflex, thus confirming in vivo the local anaesthetic activity observed in vitro.

Adaptogenic/Antistress Activity

In a randomized, double-blind, placebo-controlled trial of 16 healthy volunteers (8 males and 8 females), changes in the electrical activity of the human brain were observed after exposure to a lozenge containing 4 different herbal preparations (lavender oil, extracts from hops, lemon balm and oat) (Dimpfel et al. 2004). Increases in alpha 1, alpha 2 and beta 1 electrical activity were seen as indicator of a relaxational psychophysiological state. The data suggested that ingestion of herbal lozenge would allow better coping of psychological and emotional stress.

In a randomized, crossover study, 70 Chinese older adults with dementia were assigned to receive lavender inhalation for 3 weeks and then control for 3 weeks or vice versa (Lin et al. 2007). Agitated and aggressive behaviour, irritability and night-time behaviours were improved with lavender therapy. The mean Cohen–Mansfield Agitation Inventory (CMAI) total scores decreased from 24.68 to 17.77. The Chinese Neuropsychiatric Inventory (CNPI) scores changed from 63.17 to 58.77 after receiving lavender therapy. A small pilot study evaluating the effect of a topical application of the *Lavandula angustifolia* and *Salvia sclarea* essential oils on

work-related stress of nurses in an ICU setting found decreased perception of stress level in the intervention group during three 12-h worked shifts (Pemberton and Turpin 2008). In a clinical study of 30 young healthy men (mean age 34 years, range 24–40 years), lavender aromatherapy reduced serum cortisol and improved coronary flow velocity reserve (Shiina et al. 2008). The findings suggested that lavender aromatherapy had relaxation effects and may have beneficial acute effects on coronary circulation.

In a randomized, controlled, blinded study, the use of topical and inhalational lavender and ginger oils was associated with a lower mean distress level, as measured by the Face, Legs, Activity, Cry, Consolability (FLACC) scale, in children in a perianaesthesia setting; but the finding was not statistically significant(Nord and Belew 2009). In a randomized study of 30 healthy volunteers, lavender aromatherapy in volunteers provided a significant decrease in the stress levels and in the bispectral index values (Kim et al. 2011). Additionally, it significantly reduced the pain intensity of needle insertion. In a study of 19 healthy medical personnel, the effect of inhaled lavender oil was assessed on endothelial function following night-shift work (Shimada et al. 2011). Flow-mediated dilation (FMD) of the brachial artery was lower after night-shift work, and FMD improved with lavender inhalation. The mean value of sleep time during night-shift work was 3.3 h.

In a double-blind, randomized, controlled trial of 34 female patients with urinary incontinence undergoing urodynamic assessment, the group that inhaled lavender oil experienced increase in systolic and diastolic blood pressure compared with the control (almond oil) group (Seol et al. 2013). The clary (*Salvia sclarea*) oil group experienced a significant decrease in systolic blood pressure compared with the control and lavender oil groups, a significant decrease in diastolic blood pressure compared with the lavender oil group and a significant decrease in respiratory rate compared with the control group. Compared with the control group, inhalation of lavender oil and clary oil resulted in statistically significant reductions in respiratory rate. The results suggested that lavender oil inhalation may be inappropriate in lowering stress during urodynamic examinations, despite its antistress effects, while clary oil inhalation may be useful in inducing relaxation in female urinary incontinence patients undergoing urodynamic assessments.

In a blind, randomized, controlled crossover trial involving persons with moderate to severe dementia and associated behavioural problems living in aged care facilities, the use of lavender oil was found to be effective in reducing challenging behaviours (e.g. pacing, aggression, calling out) (van der Ploeg et al. 2010). The authors asserted that lavender oil would potentially provide a safer intervention rather than reliance on pharmacology alone.

Menopausal/Premenstrual Symptom Alleviation Activity

In an 8-week pilot-controlled clinical study, the effects of aromatherapy massage on menopausal symptoms were assessed in 52 Korean climacteric women (Hur et al. 2008). Menopausal symptoms such as hot flushes, melancholia, arthralgia and myalgia were significantly lower in the group that received a 30-min massage with essential oils (i.e. lavender, rose geranium, rose and jasmine in almond and primrose oils) compared with the control group.

In a randomized crossover study of 17 women (20.6 ± 0.2 years) with mild-to-moderate subjective premenstrual symptoms, lavender aromatherapy was found to have potential therapeutic modality in alleviating premenstrual emotional symptoms, which, at least in part, was attributable to the improvement of parasympathetic nervous system activity (Matsumoto et al. 2013). A 10-min inhalation of the lavender scent was found to significantly increase the high-frequency (HF) power reflecting parasympathetic nervous system activity in comparison with water. The rate of increase in HF power was greater at 10–15 and 20–25 min in the lavender trial than in the control trial with water. Further, Profile of Mood States (POMS) tests revealed that inhalation of the aromatic lavender oil significantly decreased two

POMS subscales depression–dejection and confusion, common premenstrual symptoms, in the late luteal phase, as long as 35 min after lavender aroma stimulation. The results further suggested that heart rate variability (HRV) could evaluate the efficacy of aromatherapy using various fragrances to relieve premenstrual symptoms and, ultimately, support the mind and body health of women.

Wound/Graft Healing Activity

Oral treatment of perillyl alcohol to rabbits with vein bypass graft surgery reduced vein graft intimal hyperplasia, a major impediment to graft patency (Fulton et al. 1997). Therapy with perillyl alcohol altered the early development of intimal hyperplasia reducing the intimal response but increasing the medial response without significant changes in the physiological responses of the smooth muscle cells. Modulating G-proteins would affect the intimal hyperplastic response in vein grafts.

Animal studies showed that wound closure progressed more rapidly in the transcutaneous electrical nerve stimulation (TENS) and lavender oil rat groups than in the control and other study groups (saline solution, povidone-iodine) (Koca Kutlu et al. 2013). In particular, platelet-derived growth factor (PDGF)-A expressions in the dermis and epidermal growth factor (EGF) expression in the epidermis were significantly intense in the TENS group. In addition, ELISA levels of growth factors such as PDGF-A and EGF were significantly higher in TENS group compared to the control group. The immunohistochemical and ELISA results suggested that TENS may improve wound healing through increasing growth factors in the dermis and epidermis more than other topical applications.

Absence of Interoceptive Activity

Silexan, an essential oil produced from the flowering tops of *Lavandula angustifolia*, elicited no diazepam-like interoceptive property in adult, male rats (Silenieks et al. 2013). Silexan tested at doses 3–30 mg/kg i.p. produced almost exclusively (>90 %) saline-like responding. Also there was no effect of Silexan on response rate, i.e. rate of lever pressing, at any dose suggesting that the test article was well tolerated and did not exert a sedating effect. The results suggested that Silexan did not share the potential of benzodiazepines to induce the development of tolerance, dependence and addiction.

Depressant/Sedative Activity

Oral administration of lavender essential oil exerted neurodepressive effect on Swiss mice (Guillemain et al. 1989). Sedative effects were observed with some tests (hole-board test, four-plate test, plus-maze test, potentiation of barbiturate sleeping time). A significant interaction exists with pentobarbital: the sleeping time was increased and the falling asleep time shortened. Lavender essential and its major constituent linalool and linalyl acetate exhibited sedative activity in animal studies (Buchbauer et al. 1991). The significant decrease in the motility of female and male laboratory animals under standardized experimental conditions was found to be closely dependent on the exposure time to the drugs. The correlation of the motility of the animals to linalool in serum was experimentally confirmed, thus furnishing evidence of the aromatherapeutic use of herbal pillows employed in folk medicine since ancient times in order to facilitate falling asleep or to minimize stressful situations of man. Jäger et al. (1992) found that the sedative and relaxing effect of lavender oil after a massage may be based on two different ways of incorporation: the inhalation of fragrant molecules and the penetration through the skin. Within 5 min of finishing, the massage traces of linalool and linalyl acetate as the main constituents of lavender oil could be detected in the blood of the male subject.

In a 4-week, double-blind, randomized, single-centre trial of 45 adult outpatients who met the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) criteria for

depression, *Lavandula* tincture (1:5 in 50 % alcohol) was found to be less effective than imipramine in the treatment of mild-to-moderate depression (Akhondzadeh et al. 2003). Headache was observed more in the *Lavandula* tincture group. A combination of imipramine and *Lavandula* tincture was more effective than imipramine alone. In a 4-week pilot study with randomized, single-blind, crossover design (baseline, two treatment (lavender and sweet almond oil) periods and a washout period, each of 1 week duration) of 10 volunteers, lavender treatment gave an improvement of −2.5 points in the Pittsburgh Sleep Quality Index (PSQI) (Lewith et al. 2005). Women and younger volunteers with a milder insomnia improved more than the others. In a pilot study, aromatherapy massage with lavender oil was not associated with positive effects on sleep patterns (i.e. sleep duration, time to fall asleep, number of awakenings) in 12 autistic patients (2 girls and 10 boys) with learning impairment (Williams 2006). Though the massage fell within 2 h of the children going to bed, closer control of the timing of the massage and larger sample size may be warranted in future clinical studies.

In a single-blind, randomized clinical trial of 64 male and female patients with ischaemic heart disease, suffering from unstable angina and myocardial infarction, the mean score of sleep quality in the experimental group after aromatherapy with lavender oil was significantly different than that in the controls (Moeini et al. 2010). The mean score of sleep quality in the experimental group after aromatherapy with lavender oil was significantly different than that in the controls. In another single-blind randomized Japanese study on the effectiveness of lavender aroma on quality of sleep comprising seven (two men, five women) in the intervention group and eight participants (three men, five women) in the control group, lavender aroma improved sleepiness at awakening after the intervention (Hirokawa et al. 2012). Sex differences and daily variation in quality of sleep during the intervention period were not observed. The findings suggested that night-time exposure to lavender aroma relieved sleepiness at awakening.

Both *Melissa officinalis* (Mo) and *Lavandula angustifolia* (La) essential oils elicited putative anti-agitation properties in humans, indicating common components with a depressant action in the central nervous system (Huang et al. 2008). La inhibited [35S] TBPS binding to the rat forebrain gamma-aminobutyric acid (GABA) receptor channel (apparent IC_{50}=0.040 mg/mL), but had no effect on *N*-methyl-D-aspartate (NMDA), alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) or nicotinic acetylcholine receptors. A 50:50 mixture of Mo and La essential oils inhibited [3H] flunitrazepam binding, whereas the individual oils had no significant effect. Electrophysiological analyses with rat cortical primary cultures demonstrated that La reversibly inhibited GABA-induced currents in a concentration-dependent manner (0.01–1 mg/mL), whereas no inhibition of NMDA- or AMPA-induced currents was noted. La elicited a significant dose-dependent reduction in both inhibitory and excitatory transmission, with a net depressant effect on neurotransmission (in contrast to the classic GABA antagonist picrotoxin which evoked profound epileptiform burst firing in these cells).

Cognitive Behaviour Effects

A study involving 144 healthy volunteers found that aromas of rosemary and lavender essential oils elicited different effects on cognition and mood in healthy adults (Moss et al. 2003). The volunteers were randomly assigned to one of three independent groups and subsequently performed the Cognitive Drug Research (CDR) computerized cognitive assessment battery in a cubicle containing either rosemary or lavender essential oils or no odour (control). It was revealed that lavender produced a significant decrement in performance of working memory and impaired reaction times for both memory- and attention-based tasks compared to controls. Contrariwise, rosemary produced a significant enhancement of performance for overall quality of memory and secondary memory factors, but also produced an impairment of speed of memory

compared to controls. With regard to mood, both the control and lavender groups were significantly less alert than the rosemary condition; however, the control group was significantly less contented than both rosemary and lavender conditions. These findings suggested that the olfactory properties of these essential oils could produce objective effects on cognitive performance, as well as subjective effects on mood. In a study of 10 healthy women, lavender aromatic stimuli induced not only relaxation but also increased arousal level in these subjects as reflected by increases in the parasympathetic tone after the lavender fragrance stimulus as seen in increases in the high-frequency (HF) component and decreases in the low- to high-frequency ratio LF/HF in electrocardiographic measurements (Duan et al. 2007). Additional measurement with positron emission tomography demonstrated the regional metabolic activation in the orbitofrontal, posterior cingulate gyrus, brainstem, thalamus and cerebellum, as well as the reductions in the pre-/post-central gyrus and frontal eye field.

A study found that the use of lavender oil by humans was useful to maintain attention spans during long-term tasks (Shimizu et al. 2008). Twenty-eight patients (77 ± 10 years) with moderate to severe dementia were randomized to receive lavender aromatherapy 3 times daily for 1 h after meals or placebo for 4 weeks (Fujii et al. 2008). Neuropsychiatric Inventory scores (31–18) and behavioural and psychological symptoms were significantly improved with lavender therapy and no significant changes were noted in the control group (32–27).

Antiulcerogenic Activity

Rabbits treated with lavender oil showed a significant aphthous ulcer size reduction, increased rate of mucosal repair and healing within 3 days of treatment compared to baseline and placebo groups (Altaei 2012). The intraperitoneal LD_{50} value in mice was 6.5 g/kg; clinical dermal irritation test showed no sign of irritation in the tested products. Lavender oil showed a broad antibacterial activity against all tested strains taken from human subjects, and it exhibited significant inhibition on tested bacteria where the value of zone of inhibition ranged from 14.5 to 24 mm versus streptomycin (25 µg/disc) 12–22 mm; MIC was >6.4–36 mg/mL. Patients with recurrent aphthous ulceration treated with lavender oil showed a significant reduction in inflammation level, ulcer size, healing time, from 2 to 4 days [2 days (40 %), 3 days (50 %), 4 days (10 %)], and pain relief mostly from the first dose, compared to baseline and placebo. No side effects were reported.

Spasmolytic Activity

Lavender essential oil exhibited in vitro spasmolytic activity in a guinea pig ileum smooth muscle preparation (Lis-Balchin and Hart 1999). The mechanism of action was suggested to be postsynaptic and not atropine-like and to be likely mediated through cAMP, and not through cGMP. The mode of action of linalool, one of lavender's major components, reflected that of the whole oil.

Anti-gout Activity

Lavandula angustifolia was one of the four plants tested that exhibited xanthine oxidase inhibitory activity (28.7 % inhibition) and may have potential to be developed as herbal drugs for treatment of gout and other xanthine oxidase-related disorders (Hudaib et al. 2011).

Antimutagenic Activity

Using the bacterial reverse mutation assay, lavender (*L. angustifolia)* essential oil exerted strong antimutagenic activity in a dose-dependent manner, reducing mutant colonies in the *Salmonella typhimurium* TA98 strain exposed to the direct mutagen 2-nitrofluorene (Evandri et al. 2005). The maximal concentration (0.80 mg/plate) reduced the number of histidine-independent

revertant colonies by 66.4 %. Lavender oil (0.80 mg/plate) also showed moderate antimutagenicity against the TA98 strain exposed to the direct mutagen 1-nitropyrene.

Choleretic/Cholagogic Activity

Gruncharov (1973) reported on choleretic and cholagogic activity of Bulgarian lavender oil. Lavender oil increased biliary secretion by 118 % compared to magnesium sulphate. However, it was also reported that lavender oil had far inferior cholecystokinetic effects compared to magnesium sulphate (2.65 % activity).

Antiprotozoal Activity

Low concentrations (<or = 1 %) of *Lavandula angustifolia* and *L.* × *intermedia* oil completely eliminated human protozoal pathogens *Giardia duodenalis* and *Trichomonas vaginalis* and the fish pathogen *Hexamita inflata* in vitro (Moon et al. 2006). At 0.1 % concentration, *L. angustifolia* oil was found to be slightly more effective than *L.* × *intermedia* oil against *G. duodenalis* and *H. inflata*.

Insecticidal Activity

The *Lavandula angustifolia* essential oil and some of its main constituents linalool and linalyl acetate exhibited potent miticidal activity against *Psoroptes cuniculi*, mite of rabbit (Perrucci et al. 1994). Subsequent study confirmed the acaricidal properties of lavender essential oil and its component linalool against *Psoroptes cuniculi* by inhalation, indicating an additional route for possible use of these substances both for prophylactic and therapeutic purposes (Perrucci et al. 1996). *L. angustifolia* oil when diluted to 1 % in 1,2-propanediol had weak repellent activities on *Ixodes ricinus* nymphs but when diluted to 30 % in 1,2-propanediol had 100 % repellency in vitro (Jaenson et al. 2006). High repellency (range 70–100 %) was shown at all concentrations of the essential oil of *L. angustifolia* against adults of *Hyalomma marginatum rufipes* in the tick climbing bioassay, although at 5 % v/v it only persisted for the first 40 min compared with 120 min at other concentrations (10 and 20 % v/v) (Mkolo and Magano 2007). The repellent strength of *L. angustifolia* compared well with that of DEET (*N*,*N*-diethyl-m-toluamide), a commercial reference repellent, for the 2-h period of the study. In vitro studies showed *Lavandula angustifolia* essential oil to have promising acaricidal against *Rhipicephalus (Boophilus) annulatus* females (Pirali-Kheirabadi and Teixeira da Silva 2010). A positive correlation between *L. angustifolia* essential oil concentration and tick control, assessed by relative mortality rate and egg laying weight, was observed by the essential oil LC/EC_{50}, which, when calculated using the probit test, was 2.76-fold higher than the control.

A randomized, assessor blind, parallel group comparative efficacy trial in 123 paediatric patients with head lice found that a tea tree/lavender oil product applied once weekly for 2 weeks on days 0, 7 and 14 was comparable in efficacy with a head lice suffocation product applied similarly (Barker and Altman 2010). Both products were associated with a higher percentage of patients (97.6 % for both groups) that were louse free 1 day after the last treatment as compared with subjects receiving pyrethrins and piperonyl butoxide applied twice on days 0 and 7 (25 % for both comparisons).

L. angustifolia essential oil at 300 ppm dosage caused 55 % larval mortality of the Culicidae mosquito *Aedes albopictus* (Conti et al. 2010). Ten percent concentrations of *Cymbopogon citratus* (lemongrass), *Mentha piperita* (peppermint) and *Lavandula angustifolia* (lavender) essential oils were the most effective, showing 100 % knockdown of housefly, *Musca domestica*, at 30 and 60 min (Sinthusiri and Soonwera 2013). These essential oils caused 100 % mortality among houseflies 24 h after exposure; the LC_{50} values for *C. citratus, M. piperita* and *L. angustifolia* were 2.22, 2.62 and 3.26 min, respectively.

Pharmacokinetic Studies

Preliminary pharmacokinetic data from a rat following i.v. administration of perillyl alcohol at 23 mg/kg and from a patient receiving perillyl alcohol at 500 mg/m^2 p.o. showed that intact perillyl alcohol, perillic acid and *cis*- and *trans*-dihydroperillic acids [DHPA, 4-(1′-methylethenyl)-cyclohexane-1-carboxylic acid] were all detected in plasma in both cases (Zhang et al. 1999). Two new major metabolites were found in human and one in the rat plasma.

Adverse Activities

Male prepubertal gynaecomastia was reported in three boys following topical application of lavender and tea tree oils in a balm, styling gel, shampoo, soap and lotion (Henley et al. 2007). The symptoms resolved within several months upon discontinuation of the two oils. It was found that lavender and tea tree oils exhibited estrogenic and antiandrogenic effects on human cell lines.

The study by Prashar et al. (2004) demonstrated that lavender (*L. angustifolia*) oil, chiefly composed of linalyl acetate (51 %) and linalool (35 %), was cytotoxic to human skin cells in vitro (endothelial cells and fibroblasts) at a concentration of 0.25 % (v/v) in all cell types tested (HMEC-1, HNDF and 153BR). The activity of linalool reflected that of the whole oil, indicating that linalool may be the active component of lavender oil. Linalyl acetate cytotoxicity was higher than that of the oil itself suggesting suppression of its activity by an unknown factor in the oil.

A case of a physiotherapist who developed several episodes of facial dermatitis was reported with use of Difflam gel containing benzydamine hydrochloride and lavender fragrance (Rademaker 1994). She would occasionally massage her patients with the gel, and on the last occasion she inadvertently rubbed her face without washing her hands; she developed erythema followed by acute vesicular dermatitis the next evening. Patch testing revealed a 2+ reaction at 2 and 4 days to Difflam gel and to lavender absolute. Contact allergy to various essential oils including lavender oil used in aromatherapy was demonstrated on patch testing in a 53-year-old patient suffering from relapsing eczema resistant to therapy on various uncovered parts of the skin, in particular the scalp, neck and hands (Schaller and Korting 1995). Sensitization was due to previous exposure to lavender, jasmine and rosewood. Earlier Brandão (1986) reported a case of occupational allergy to lavender oil. Sugiura et al. (2000) reported an increase in frequency of positive patch tests (0–13.9 %) to lavender oil in annual reports from 1990 to 1998 on patients suspected of having cosmetic contact dermatitis in Japan. The positive rate of lavender oil increased suddenly in 1997. They found that the increase in patch test-positive rates to lavender oil especially in 1997 and 1998 was due to the practice of placing dried lavender flowers in pillows, drawers, cabinets or rooms rather than due to lavender fragrances in cosmetic products.

Traditional Medicinal Uses

Lavender is used in traditional medicines in Asia, Europe, ancient Greece and Rome and was mentioned in the Bible and in ancient Jewish texts (Hancianu et al. 2013). Lavender is reported to be an effective medicinal plant in treating inflammation, depression, stress and headache. Folk and traditional therapeutic uses of the essential oil of English lavender for pain, infection, relaxation and sedation date back centuries (Denner 2009). Lavender is also a popular treatment for stress and mild anxiety in Europe and the United States (Bradley et al. 2007). *Lavandula angustifolia* (lavender) inhalation has been used in folk medicine for the treatment of anxiety (Chioca et al. 2013b). In the olden days, lavender was used as a condiment and for flavouring for food to comfort the stomach (Grieve 1971). An essential oil obtained from lavender flowers is antihalitosis, powerfully antiseptic, antispasmodic, aromatic, carminative, cholagogic, diuretic, nervine, sedative, stimulant, stomachic and tonic (Grieve 1971;

Lust 1974; Launert 1981; Chiej 1984; Bown 1995). It is not often used internally; though it is a useful carminative and nervine, it is commonly used as a restorative and tonic against faintness, giddiness, nervous palpitations, spasms and colic (Grieve 1971). Lavender oil is used in foot bath to relieve fatigue; lavender is prescribed as a powerful stimulant for hysteria, palsy and similar disorders of debility and lack of nerve power. Outwardly applied, lavender oil relieves toothache, neuralgia, sprains and rheumatism. Lavender oil is much more gentle in its action than most other essential oils and can be safely applied directly to the skin as an antiseptic to help heal wounds, burns, etc. (Chevallier 1996). Lavender oil is very useful in the treatment of burns, sunburn, scalds, bites, vaginal discharge, anal fissure, etc., where it also soothes the affected part of the body and can prevent the formation of permanent scar tissue (Grieve 1971; Bown 1995). Extracts obtained from the leaves of *Lavandula angustifolia* are used in Iranian folk medicine as remedies for the treatment of various inflammatory diseases (Hajhashemi et al. 2003).

Other Uses

Lavandula angustifolia Mill. (fine lavender) and its natural hybrid *L. x intermedia* Emeric ex Loisel. (lavandin) are cultivated for their essential oils which mostly contain a rich blend of mono- and sesquiterpenes (De Pascual-Teresa et al. 1991). Besides being grown commercially for its essential oil, lavender may be grown as bedding plant, hedge, herb specimen, tea plant, bee forage or source of fragrance in landscaping designs. Lavender essential oil has a very wide range of applications, both in the home and commercially. Commercially, it is commonly used in soap making and in making high-quality perfumes and cologne (e.g. 'Eau de Cologne'), cosmetics, detergents and cleaning agents, room fresheners and food flavouring. The aromatic leaves and flowers are used in potpourri and sachets and as an insect repellent in the linen cupboard or be tied in small bundles and burnt as incense sticks. They have been used in the past as a strewing herb in order to impart a sweet smell to rooms and to deter insects and mice. The flowers and leaves are also used as a herbal medicine, either in the form of lavender oil or as a herbal tea. The leaves are also used in herbal bath water for their fragrance and therapeutic properties.

Lavender essential oil has good insecticidal and insect-repellent activities which have been confirmed by several studies.

All 98 plant essential oils tested including lavender (*Lavandula angustifolia*, $LC_{50}=0.61–0.99$ mg/cm^3) showed low toxicity against third instars of cecidomyiid gall midge *Camptomyia corticalis* compared to the conventional insecticide dichlorvos ($LC_{50}=0.027$ mg/cm^3) (Kim et al. 2012). Eight essential oils including *Lavandula angustifolia* were highly toxic to the third instar of *Spodoptera littoralis* larvae with $LD_{50}<$ or $=0.05$ µL/larvae (Pavela 2005). Results of insect repellency tests indicated that *Myrtus communis* and *L. angustifolia* essential oils displayed high repellent activity to the stored food insect *Sitophilus zeamais* adults (Bertoli et al. 2012). Mortality rate never exceeded 76 %. All essential oils, tea tree (*Melaleuca alternifolia*), lavender (*Lavandula angustifolia*), peppermint (*Mentha piperita*), eucalyptus (*Eucalyptus globulus*) and clove bud (*Eugenia caryophyllata*) except camphor *(Cinnamomum camphora*), showed high levels of toxicity against the chewing louse, *Bovicola (Werneckiella) ocellatus*, collected from donkeys, with significant dose-dependent mortality and an LC_{50} at concentrations below 2 % (v/v) (Talbert and Wall 2012). Hundred percent mortality was achieved at concentrations of 5–10 % (v/v). Two essential oil components, eugenol and (+)-terpinen-4-ol, showed similar levels of toxicity.

The essential oils (EO) of *Hyptis suaveolens, Rosmarinus officinalis* and *Lavandula angustifolia* exhibited dose-dependent toxicity on *Bactrocera oleae*, the olive fruit fly, with mortality rates ranging from 12 % (EO concentration, 0.01 % w:v) to 100 % (EO concentration, 1.75 % w:v) (Canale et al. 2013). Semi-field results highlighted the toxicity of *L. angustifolia* and

H. suaveolens EO, which exerted more than 60 % of fly mortality at a concentration of 1.75 % (w:v).

Comments

Lavender can be propagated by vegetative stem cuttings taken in late spring or summer, clump division or seeds.

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Lavandula dentata

Scientific Name

***Lavandula dentata* L.**

Synonyms

Stoechas dentata (L.) Mill., *Lavandula dentata* var. *vulgaris* Ging., nom. inval.

Family

Lamiaceae

Common/English Names

French Lavender, Fringed Lavender, Gray French Lavender, Lavender, Toothed Lavender

Vernacular Names

Afrikaans: Franse Lavantel
Arabic: Duzan, Helhal, Lizer
Catalan: Espígol, Espígol Dentat, Espígol Retallat, Gallanda, Lavanda
Chinese: Chǐ Yè Xūnyī Cǎo
Danish: Tandet Lavendel
Dutch: Getande Lavendel, Lavendel Sort, Tandlavendel
French: Lavande Anglaise, Lavande Dentée
German: Französischer Lavendel, Gezähnter Lavendel, Zahn-Lavendel
Hungarian: Francia Levendula
India: Astukhudas
Italian: Spigo-Nardo
Portuguese: Alecrim Francés, Alfazema-Brava
Slovaščina: Nazobčana Sivka
Spanish: Alhucema Inglesa, Alhucema Rizada, Cantueso, Cantueso Dentado, Cantueso Rizado, Espliego Dentado, Galland, Garlanda, Lavanda, Tomany
Swedish: Kamlavendel
Turkish: Fransız Lavantası

Origin/Distribution

The species is indigenous to southern and eastern Spain, Gibraltar, the Balearic Islands, northwestern Africa, Ethiopia, Eritrea, Israel, Jordan and the Arabian Peninsula. It is naturalized elsewhere around the Mediterranean and in Western Australia, New Zealand and California.

Agroecology

Fringed Lavender requires full sun in a warm sheltered position, well-protected from strong winds. It thrives best in well-drained, light, rich soils and abhors heavy, water-logged soils. Its aromatic fragrance has been reported to be stronger when grown in chalky soils. It is tolerant of low temperatures down to −5 °C.

T.K. Lim, *Edible Medicinal and Non Medicinal Plants: Volume 8, Flowers*,
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Edible Plant Parts and Uses

Refer to culinary uses described for *L. angustifolia* (Burnie and Fenton-Smith 1996; Barash 1997; Lauderdale and Evans 1999; Roberts 2000). Use Fringed Lavender flowers for cooking as you would sage.

Botany

Lavandula dentata is a tender, spreading, aromatic, perennial shrub, growing up to 1 m high and wide with upright branches and woody at the base. Leaves sessile, narrow, linear, thick, with squarish-serrated to dentate margin, sticky, 3 cm long and borne in whorls up the woody quadrangular stem (Plates 1 and 2). Flowers occur in tight clusters in a spike at the top of slender, long grey leafless stems and consist of violet-blue, papery bracts and tiny, paler violet-blue flowers (Plates 2, 3 and 4).

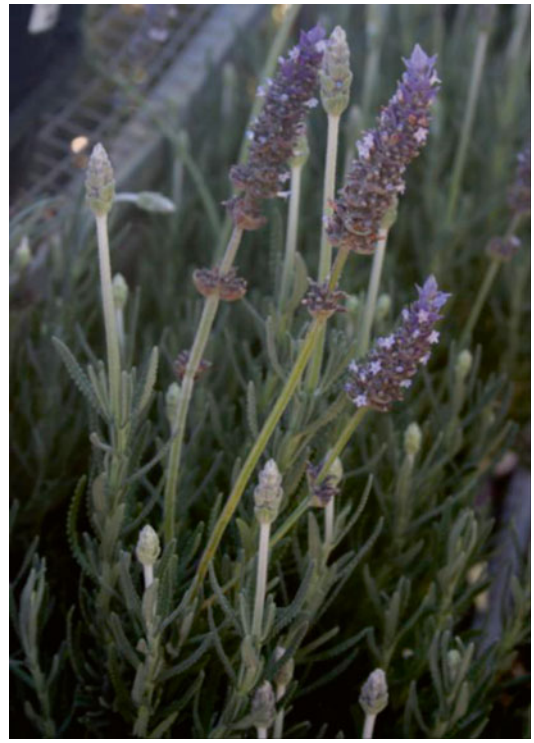

Plate 2 Terminal flowering heads on leafless stems

Plate 1 Leaves with dentate margins

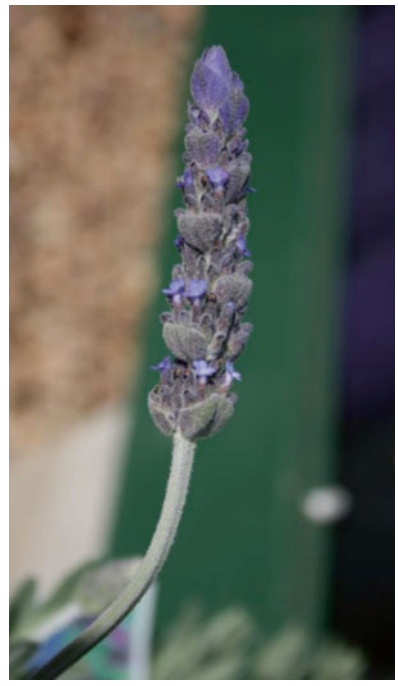

Plate 3 Close view of flower head

Plate 4 Flower head with open flowers and floral bract

The spike is topped by a tuft of large, showy, sterile bracts which are the more conspicuous part of the inflorescence.

Two varieties of *L. dentata* are currently recognized: *L. dentata* var. *dentata*, with greyish-green leaves, occasionally with white or pink flowers, and *L. dentata* var. *candicans*, with more pronounced silvery-grey leaves.

Nutritive/Medicinal Properties

The following flavonoids were reported from *L. dentata*: genkwanin (apigenin 7-methyl ether), luteolin, apigenin, luteolin 7-glucoside, apigenin 7-glucoside, luteolin 7-rutinoside, vitexin and vicenin-2 (Ferreres et al. 1986). Flavonoids found in the leaves of *L. dentata* included scutellarein 7-*O*-glycoside, vitexin, luteolin 7-*O*-glucoside, luteolin 7-*O*-glucuronide; apigenin-7-*O*-glucoside, apigenin-7-*O*-glucuronide and their derivatives, 6-OH-luteolin 7-*O*-glycoside, apigenin and genkwanin (Upson et al. 2000).

The hydro-distilled essential oil of *Lavandula dentata* growing spontaneously in Cherchell (northwest of Algiers region, Algeria) afforded 67 identified compounds, comprising 76.5 % of the total oil (Dob et al. 2005). The major components were 1,8-cineole (38.4 %), *cis*-verbenol (4.3 %), *p*-cymen-8-ol (3.8 %) and fenchone (2.3 %). Twenty nine compounds were identified in the essential oil of *L. dentata* aerial parts (Imelouane et al. 2009). The major components were the following: 1,8-cineole (41.28 %), sabinene (13.89 %), bicyclo[3.1.0]hexan-3-ol, 4-methylene-1-(1-methylethyl) (6.76 %), myrtenal (5.1 %) and α-pinene (4.05 %) as the major compounds. Other significant constituents were verbenol (2.1 %), linalool oxide (2.49 %), *cis*-linalool oxide (2.66 %), bicyclo[3.1.1]heptan-2-one, 6,6-dimethyl (2.36 %), myrtenol (2.75 %) and L-borneol (2.84 %).

A total of 27 fragrance compounds were identified in *L. dentata* (aerial parts) by solid-phase trapping solvent extraction (SPTE) in Korea (Kim and Lee 2002). The major components were cineol (47.02 %) and β-pinene (11.24 %) and other components were ethyl benzene (0.31 %), *m*-xylene or *p*-xylene (0.92 %), *o*-xylene (0.36 %), thujene (0.18 %), α-pinene (4.48 %), camphene (0.83 %), β-myrcene (0.12 %), *p*-cymene (1.11 %), limonene (4.60 %), *trans*-1-methyl-4(1-methylethyl)-2-cyclohexen-1-ol (0.32 %), linalyl oxide (1.55 %), linalool (4.42 %), *cis*-verbenol (0.27 %), *cis*-sabinol (4.5 %), camphor (5.69 %), borneol (2.69 %), *p*-cymen-8-ol (1.80 %), verbenone (0.37 %), *p*-cuminic aldehyde (0.80 %), geranyl acetate (0.08 %), farnesene isomers mixture (3.10 %), γ-cadinene (1.45 %) and calamenene (1.21 %).

Forty-two components (84.76 % of total oil) and 47 components (85.48 % of total oil) were identified in the aerial part and flower oils of *L. dentata* in eastern Morocco (Imelouane et al. 2010), respectively, of which β-pinene (27.08 %, 30.06 %), pinocarveol (14.77 %, 8.59 %), myrtenal (8.18 %, 6.81 %), α-pinene (7.78 %, 1,8-cineole (5.53 %, 5.47 %), linalool (4.7 %, 4.46 %), pinocavone (2.36 %, 2.44 %) and borneol (2.56 %, 1.66 %) were the main components in the oil of the aerial part and flowers, respectively. The other components were, respectively, tricylene

(0.3 %, 0.34 %), camphene (1.13 %, 0.79 %), γ-terpinene (tr, tr), *cis*-linalool oxide (1.81 %, 0.98 %), 4-terpineol (0.58 %, 0.41 %), verbenone (0.73 %, 0.5 %), *cis*-carveol (0.57 %, 0.39 %), D-carvone (0.26 %, 0.24 %), hexyl tiglate (0.37 %, 0.43 %), hexyl hexanoate (tr, tr), *cis*-α-bergamotene (tr, tr), *trans*-α-bergamotene (tr, 0.38 %), *trans*-β-farnese (tr, 0.27 %), β-selinene (0.59 %, 0.9 %), β-bisabolene (tr, tr), calamine (0.38 %, 0.85 %), caryophyllene oxide (0.42 %, 1.04 %), β-eudesmol (0.68 %, 1.36 %) and 1, 4-dimethyl-7-1-methylethyl)azulene (tr, 0.21 %). The following minor components were found only in the oil of the aerial parts: 1,3,8-*p*-menthatriene (tr), α-terpinene (0.35 %), *O*-cresol (tr), *trans*-linalool oxide (2.13 %), verbenol (0.31 %), cuminic aldehyde (0.27 %), 1-bornyl acetate (tr), perillol (0.66 %), piperitone (tr), cryptone (0.3 %), α-cedrene (tr), γ-elemene (tr), β-funebrene (tr), *epi*-bicyclosesquiphellandrene (tr) and γ-cadinene (tr). The following constituents were found only in the flower oil: β-myrcene (0.3 %), 1,5,8-p-menthatriene (tr), 2-(bromomethyl)-1,3,3-trimethylcyclohexene (tr), α-campholene aldehyde (0.54 %), veratrol (0.24 %), camphor (2.32 %),α-terpineol (0.5 %), perilla alcohol (tr), α-cubebene (tr), *trans*-caryophyllene (tr), β-sesquiphellandrene (0.23 %), β-cubebene (tr), 1,4-dihydro-3,5-dimethoxy-2-methylnaphthalene (tr), germacrene D (0.4 %), *cis*-α-bisabolene (0.3 %), 4.7-dimethyl-1-tetralone (0.86 %), bicyclo[4.4.0]dec-1-ene, 2-isopropyl-5-methyl-9-methylene (0.48 %), 1,4-dimethyl-7-1-methylethyl)azulene (0.21 %), α-bisabolol (0.77 %) and 14-norcadin-5-en-4-one isomer (1.1 %). Essential oil extracted from aerial parts of *L. dentata* in Tunisia was dominated by linalool (47.30 %), linalyl acetate (28.65 %), bicyclogermacrene (3.40 %), camphor (2.32 %) and δ-terpineol (1.47 %) (Msaada et al. 2012).

The average essential oil yields were higher for Tunisian *Lavandula dentata* flowers (8.60 mg/g) than for the leaves (6.56 mg/g) (Touati et al. 2011). A total of 72 compounds were identified, accounting for 98.1 and 97.7 % of the total oil composition of the leaves and flowers, respectively. The main essential oil constituents were 1,8-cineole, camphor and L-fenchone, accounting for 33.54, 18.89 and 8.36 % in the leaf oils and 19.85, 23.33 and 7.13 % in the flower oils, respectively.

Antioxidant Activity

L. dentata aerial part oil showed higher DPPH free radical scavenging activity with an IC_{50} value of 32.12 compared to the flower oil 41.29 μL/mL (Imelouane et al. 2010).

Anticancer Activity

L. dentata flower oil exhibited more potent cytotoxicity on human cancer cell lines than the aerial part oil with IC_{50} values of = 98.5 μg/mL, 101 μg/mL for MCF-7 cancer cell line; 46 μg/mL, 72 μg/mL for U-373 cancer cell line; and 52 μg/mL, >600 μg/mL for P388DI cancer cell line, respectively (Imelouane et al. 2010).

Antimicrobial Activity

L. dentata (aerial parts) essential oil had a substantial inhibitory effect on all assayed bacteria strains (Imelouane et al. 2009). Gram-positive *Listeria monocytogenes* was the most sensitive strain followed by *Streptococcus* sp. The oil also exhibited high antimicrobial activity against *Streptococcus pneumoniae* but modest activity against *Staphylococcus aureus.* Gram-negative strains also displayed variable degree of susceptibility against investigated oil. Maximum activity was observed against *Neisseria meningitidis* and *Haemophilus influenzae*, followed by *Klebsiella pneumoniae*, *Salmonella* sp., *Proteus mirabilis*, *Pantoea* sp. *and Enterobacter cloacae*. Modest activities were observed against important food pathogens such as *Escherichia coli*. MIC values shown by the essential oil were in the range of 0.041–10 mg/mL. The Gram-negative *Pseudomonas aeruginosa* appeared to be resistant to the investigated oil with an MIC of 10 mg/mL. Maximum activity was observed against *Staphylococcus aureus*, *Streptococcus*

pneumoniae and *Streptococcus* sp. with an MIC of 0.041 mg/mL. *Streptococcus* sp. was the least sensitive bacteria with an MIC of 0.338 mg/mL. *Staphylococcus epidermidis*, *Haemophilus influenzae* and *Proteus mirabilis* showed similar susceptibility to the investigated oil, ranging from 0.167 mg/mL. The oil exhibited highest inhibitory effect against Gram-negative bacteria *Escherichia coli*, *Neisseria meningitidis* and *Pantoea* sp. in a range between 0.083 and 0.041 mg/mL.

Antiprotozoal Activity

L. dentata plant extract exhibited antiplasmodial activity against *Plasmodium falciparum*, inhibited growth of amastigotes of *Trypanosoma cruzi* and free trypomastigotes of *Trypanosoma brucei* (Al-Musayeib et al. 2012).

Spasmolytic Activity

In the rat, the essential oil of *L. dentata* showed spasmolytic activity against both acetylcholine- and calcium chloride-induced contractions in rat duodenal tissue in vitro (Gamez et al. 1990). In the guinea pig, the oil (particularly linalool) exerted spasmolytic activity in smooth muscle, inhibiting the contractile responses to acetylcholine and histamine (Lis-Balchin and Hart 1997, 1999).

Hypoglycemic Activity

In hyperglycemic and normoglycemic rats, infusions of *L. dentata* and *L. latifolia* exerted hypoglycemic effects. The infusions had significant antidiabetic activity against glucose-induced hyperglycemia measured at 30 and 90 min post-administration (Gamez et al. 1988).

Traditional Medicinal Uses

As described for English Lavender. It has aromatic, carminative and nervine properties. Lavender oils have been used as restorative and tonic against giddiness, nervous palpitation, faintness, spasms and colic (Grieve 1971).

Other Uses

The plant is grown as an ornamental medicinal and erosion control plant. It is also useful as a conservatory plant in the Northern Hemisphere because of its extended winter-flowering season.

Dried flowers are used to repel clothes and wallet moths and used in potpourri. The flowering stems after removal of the flowers can be tied in small bundles and burnt as incense sticks (Genders 1994).

Comments

Lavender oil should be used sparingly as it can cause dermatitis.

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Lavandula stoechas

Scientific Name

***Lavandula stoechas* L.**

Synonyms

Stoechas officinarum Mill.

Family

Lamiaceae

Common/English Names

Arabian Lavender, Bush Lavender, Butterfly Lavender, Common French Lavender, Italian Lavender, Quasti Lavender, Rabbit Ears, Spanish Lavender, Top Lavender, Topped Lavender

Vernacular Names

Arabic: Arshameesa, Arshaneesa, Astuhudus, Halhaal, Moqif Rwah, Meharga Sunbul Al-Ahaaniya, Ustookhoodoos, Washa'i Al-Shaikh
Berber: Amezzir, Timerza, Imezzir
Chinese: Xun Yi Cao
Danish: Sommerfuglelavendel,Vælsk Lavendel
Dutch: Franse Lavendel, Kuiflavendel, Stechas Lavendel, Stechas Sort
Finnish: Tupsupäälaventeli
French: Lavande, Lavande Maritime, Lavande Papillon, Lavande Stéchade, Lavande Stéchas, Lavande À Toupet, Stoechas Arabique
German: Ährenförmiger Lavendel, Schopf-Lavendel
Hungarian: Spanyol Levendula
India: Tuntuna (Bengali), Lavendara No Phul (Gujarati), Dharu (Hindi), Kale Weouth (Kashmiri), Ustkhuddus (Urdu)
Italian: Lavanda Di Monte, Lavanda Selvatica, Lavanda Stoechas, Steca, Stecaole, Stigadosso
Norwegian: Fransk Lavendel
Persian: Jarub Dimagh, Ustkhuddus
Portuguese: Alfazema, Arçã, Rosmaninho
Spanish: Arçã, Astecados, Azaya, Cantahueso, Cantuerca, Cantueso, Cantueso Morisco, Cap D'ase, Estecados, Hierba De San Juan, Lavándula, Romero De Piedra, Romero Santo Tomillo, Tomillo Borriquero
Swedish: Skärmlavendel
Turkish: Karabaşotu
Welsh: Lafant

Origin/Distribution

The species is indigenous to northwestern Africa (i.e. Algeria, Morocco and Tunisia), the Madeira Islands, the Canary Islands, southern Europe (i.e. Greece, Italy, France, Portugal and Spain) and

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Western Asia (i.e. Cyprus, Israel, Lebanon, Syria and Turkey). It has been introduced throughout Europe and to temperate/subtemperate areas in the Americas, Asia and Australia.

Agroecology

In its native range, it thrives in full sun in dry hills, garrigue, maquis shrubland or open woodlands and on well-drained limestone or granite soils. It requires dry or moist soil and is drought resistant.

Edible Plant Parts and Uses

The lavender flowers can be used both in sweet and savoury dishes (Garland 1993; Burnie and Fenton-Smith 1996; Barash 1997; Lauderdale and Evans 1999; Roberts 2000; Anonymous 2012). A delicious lavender sugar can be made with the flowers to add to biscuits, sorbets, jams or jellies. Flowers look beautiful and taste good too in a glass of champagne, with chocolate cake, or as a garnish for sorbets or ice creams. Diminutive blooms add a mysterious scent to custards, flans or sorbets. The flowers can be added to vegetable stock and stews and to create a tasty sauce for duck, chicken or lamb dishes.

Botany

A low-growing, erect, evergreen, perennial shrub 0.3–1 m high with quadrangular, pubescent stems becoming woody and rough with age. Leaves are sessile, opposite, greyish-green, pubescent, small, linear or lanceolate 11–30 mm by 2–5 mm with obtuse or acute tips, entire margin and recurved (Plates 1 and 2). Flowers are fragrant, inconspicuous, tubularly arranged in dense cylindrical clusters (2–5 cm long) at the tips of leafless stems and are topped with up to five distinctive, purple- or violet-coloured, petal-like bracts (10–50 mm long) (Plates 2 and 3). The small tubular flowers (5–8 mm long) are deep purple in colour and are subtended by deep bluish-purple bracts, with sepals fused into a short calyx tube

Plate 1 Sessile foliage of Spanish Lavender

Plate 2 Terminal inflorescences

4–5 mm long, five petals fused into a corolla tube with five spreading lobes; stamens four, yellow and an ovary topped with a very short style. Fruit

Plate 3 Close-up of inflorescences topped by 3–4 purple floral bracts

a schizocarp, brown, woody, dehiscent containing four subglobose, brown, mottled seeds.

Nutritive/Medicinal Properties

Lavanol was isolated from *L. stoechas* (Manzoor-I-Khuda and Khan 1967; Manzoor-I-Khuda 1971). The major flavonoids in *L. stoechas* were apigenin 7-glucoside, luteolin, luteolin 7-glucoside and luteolin 7-glucuronide (Xaver and Andary 1988). The isolation of a smooth muscle relaxant principle identified as 7-methoxycoumarin from *Lavandula stoechas* was reported by Aftab et al. (1998). Also reported were lingipinen derivatives: ursolic acid, β-sitosterol, flavonoids, luteolin, acacetin, vitexin and coumarin. Flavonoids found in the leaves of *L. stoechas* subsp. *stoechas* included luteolin 7-*O*-glucoside, luteolin 7-*O*-glucuronide chrysoeriol 7-*O*-glucoside, apigenin-7-*O*-glucoside, apigenin-7-*O*-glucuronide and their derivatives, vitexin, apigenin and genkwanin (Upson et al. 2000).

A total of 28 fragrance compounds in *L. stoechas* aerial plant parts were identified by solid-phase trapping solvent extraction (SPTE) in Korea (Kim and Lee 2002). Major components were camphor (53.40 %) and fenchone (24.30 %); other components included ethyl benzene (0.05 %), *m*-xylene or *p*-xylene (0.16 %), *o*-xylene (0.09 %), thujene (0.07 %), α-pinene (0.78 %), camphene (2.30 %), β-pinene (0.15 %), β-myrcene (0.09 %), *p*-cymene (0.54 %), limonene (0.15 %), cineol (12.50 %), *trans*-1-methyl-4(1-methylethyl)-2-cyclohexen-1-ol (0.03 %), linalyl oxide (0.70 %), linalool (0.11 %), *cis*-sabinol (0.19 %), borneol (0.38 %), α-terpinen-4-ol (0.56 %), *p*-cymen-8-ol (0.56 %), verbenone (0.28 %), carvone (0.43 %), linalyl acetate (0.50 %), bornyl acetate (1.14 %), terpineol acetate (0.09 %), geranyl acetate (0.02 %), caryophyllene (0.02 %) and farnesene isomers mixture (0.41 %). The major volatile compounds (in varying amounts) of *Lavandula stoechas* flowers obtained by hydrodistillation (HD), subcritical water extraction (SbCWE) and organic solvent extraction under ultrasonic irradiation (USE) were fenchone, camphor, myrtenyl acetate, myrtenol and 1,8-cineol (Giray et al. 2008). The total monoterpene hydrocarbons were higher in HD and USE extracts than those of SbCWE extract. However, SbCWE extract had higher concentration of light-oxygenated compounds which contributed largely to the fragrance of the oil. Heavy-oxygenated compounds were also more in SbCWE extract (9.90 %) compared to HD (3.19 %) and USE extracts (4.78 %).

The 11 oils from the aerial flowering parts of wild growing *Lavandula stoechas* collected from 11 different locations in northern Algeria afforded 121 compounds accounting for 69.88–91.2 % of the total oil composition and differed greatly in their compositions, since only 66 compounds were common to all oils (Benabdelkader et al. 2011). Major components were fenchone (11.27–37.48 %), camphor (1.94–21.8 %), 1,8-cineole (0.16–8.71 %) and viridiflorol (2.89–7.38 %). The essential oil yield from the flowering spikes of *Lavandula stoechas* from India was 0.86 %, comprising 25 components which amounted to 96.7 % (Raina and Negi 2012). The major components were camphor (52.1 %), fenchone (12.0 %), 1,8-cineole (9.7 %), bornyl acetate (6.2 %), camphene (3.3 %), α-pinene (1.1 %) and terpinen-4-ol (0.6 %). The essential oil was rich in oxygenated monoterpenes (86.3 %). Earlier, Skoula et al. (1996) reported the main essential oil constituents from four wild populations of *Lavandula stoechas* ssp. *stoechas* of Crete, Greece, were α-pinene, 1,8-cineole, fenchone, camphor and myrtenyl acetate. Three of the different

populations were fenchone/camphor type and one 1,8-cineole/fenchone type. The variation in the quantitative essential oil composition between leaves and inflorescences was also significant. In all cases, inflorescences contained more fenchone, myrtenyl acetate and α-pinene, while leaves contained more 1,8-cineole and camphor. Additionally, the inflorescences produced notably larger essential oil amounts than the leaves. The major compounds in the essential oils from the stems/leaves (L) and flowers (F) of *Lavandula stoechas* ssp. *stoechas* growing wild in southern Sardinia (Italy) were fenchone (52.60 % in L and 66.20 % in F), followed by camphor (13.13 % in L, 27.08 % in F) (Angioni et al. 2006). In another study, 55 and 66 constituents were identified in the leaf and flower essential oils of *Lavandula stoechas* ssp. *stoechas* from Turkey representing more than 90 and 94 % of the total, respectively (Kirmizibekmez et al. 2009). The main components were α-fenchone (41.9 %), 1,8-cineole (15.6 %), camphor (12.1 %) and viridiflorol (4.1 %) in the leaves and α-fenchone (39.2 %), myrtenyl acetate (9.5 %), α-pinene (6.1 %), camphor (5.9 %) and 1,8-cineole (3.8 %) in the flowers. In the inflorescence and leaf essential oils of *L. stoechas* subsp. *stoechas* in Greece, the main constituents were fenchone (39.9, 21.0 %) and camphor (24.2, 26.3 %), respectively (Tzakou et al. 2009). Both enantiomers of camphor were present, whereas only (+) fenchone was detected.

The essential oil of flowers and leaves of *L. stoechas* grown in Iran contained 1,8-cineol (7.02 %), γ-cadinene (5.33 %), T-cadinol (5.07), *p*-mentha-1-en-8-ol (5.02 %), caryophyllene (5.01 %), 2-ethenylidene-6,6-dimethylbicyclo [3.1.1]heptane (4.98 %), borneol (4.87 %), 1,3,3-trimethyl-2-vinyl-1-cyclohexene (4.76 %), alcanfor (4.16 %), β-terpineol (4.11 %), geranial acetate (3.64 %), α-bisabolol (3.23 %), cedrene (2.91 %), cubenol (2.85 %), (+)-α-pinene (2.71 %), (−)-β-pinene (2.35 %), cuminyl alcohol (2.53 %), nerolidyl acetate (2.92 %), caryophyllene oxide (2.80 %), 2,6,10-trimethyltetradecane (2.31 %), isoledene (1.57 %), 2-methylene-5α-cholestan-3α-ol (1.47 %), α-cadinol (1.44 %) and 7,7-dichloro-2-heptanone (1.01 %), (Ebadollahi et al. 2010).

L. stoechas essential oil from the Greece afforded 51 components corresponding to 99.96 % of the total, which was dominated by fenchone (30.85 %) and pinocarvyl acetate (10.20 %) and other compounds like borneol, linalool, linalyl acetate, α-pinene, camphor, eucalyptol and myrtenol (Kokkalou 1988). The major compounds of the essential oils of *L. stoechas* ssp. *atlantica* and *L. stoechas* ssp. *stoechas* from Morocco were camphor (39 and 18 %, respectively) and fenchone (9 and 30 %, respectively) (Zrira and Benjilali 2003). Essential oil extracted from aerial parts of *L. stoechas* in Tunisia was dominated by linalyl acetate (64.30 %), linalool (20.25 %) and β-thujone (8.97 %) (Msaada et al. 2012). *Lavandula stoechas* (from Tunisia) oil was found to be rich in fenchone (34.3 %) and camphor (27.4 %) (Messaoud et al. 2012).

The aerial parts of *Lavandula stoechas* subsp. *stoechas* afforded two longipinene derivatives: longipin-2-ene-7β,9α-diol-1-one and longipin-2-ene-7β,9α-diol-1-one 9-monoacetate; also isolated were oleanolic acid, ursolic acid and vergatic acid (Ulubelen et al. 1988). The following were also isolated: sterols, β-sitosterol, α-amyrin, α-amyrin acetate, lupeol, erythrodiol and flavonoids luteolin, acacetin and vitexin (Ulubelen and Olcay 1989). Fractionation of ethyl acetate extract of *Lavandula stoechas* aerial parts afforded a novel acetylated glucoside, luteolin (3p,4p,5-tri-*O*-acetyl)-7-*O*-glucopyranoside(2-*O*-[3-(1-acetoxy-4-oxocyclohexa-2,5-dienyl)acryloyl]) together with apigenin 7-*O*-glucoside and luteolin 7-*O*-glucoside (Gabrieli and Kokkalou 2003).

The composition of essential oil of the leaves of *Lavandula stoechas* ssp. *stoechas* was analyzed by means of capillary GC–MS. The main components of *L. stoechas* ssp. *stoechas* leaf essential oil were pulegone (40.4 %), menthol (18.1 %) and menthone (12.6 %) (Gören et al. 2002). The minor components were: eucalyptol (3.9 %), 2,6,6,-trimethyl-1-cyclohexene-1-carboxaldehyde (3.2 %), β-pinene (3.2 %), β-terpineol (2.3 %), *p*-cymene (1.4 %), D-limonene (1.3 %), α-thujune (0.1 %), α-pinene (1.2 %), *trans*-dihydrocarvone (0.9 %), carvacrol (0.6 %), *p*-mentha-1(7),8(10)-dien-9-ol (0.6 %), borneol (0.5 %), isopulegol (0.4 %), camphene (0.4 %), α-terpineol (0.4 %), spathulenol

(0.4 %), γ-terpinene (0.4 %), sabinene (0.3 %), myrcene (0.3 %), 3-carene (0.3 %), *cis*-verbenol (0.2 %), piperitone (0.2 %), unidentified (0.2 %), thymol (0.2 %), α-terpinene (0.1 %), β-phellandrene (0.1 %), isolimonene (0.1 %), isoterpinolene (0.1 %), *trans-p*-2,8,-menthadiene-1-ol (0.1 %), *cis*-carveol (0.1 %), piperitenone (0.1 %), α-citral (0.1 %), bornyl acetate (0.1 %), β-caryophyllene (0.1 %), nerolidol (0.1 %), caryophyllene oxide (0.1 %) and β-cadiene (0.1 %). Twenty-eight components corresponding to 96.6 % of total oil were identified in the leaf essential oil of *L. stoechas* from Tunisia (Bouzouita et al. 2005). The major components were fenchone (68.2 %), camphor (11.2 %) and a mixture of 1,8-cineole/limonene (4.9 %). Other minor components included α-pinene (0.4 %), camphene (0.8 %), oct-1-en-3-ol (0.2 %), *p*-cymene (0.4 %), *cis*-linalool oxide (tr), linalool (0.3 %), α-fenchol (1.9 %), α-campholenol (tr), borneol (0.6 %), terpinen-4-ol (0.2 %), *p*-cymen-8-ol (0.4 %), α-terpineol (0.2 %), myrtenol (0.6 %), α-fenchyl acetate (0.8 %), carvone (0.3 %), bornyl acetate (1.4 %), myrtenyl acetate (1.2 %), cyclosativene (0.2 %), α-copaene (0.2 %), allo-aromadendrene (0.2 %), BHT (antioxidant from diethyl ether) (1.5 %), δ-cadinene (0.4 %), selina-3,7(11)-diene (0.2 %) and viridiflorol (1.4 %).

The roots of *L. stoechas* ssp. *stoechas* from Turkey afforded triterpenes (18-hydroxy-27-norolean-12,14-dien-30-al-28-oicacid;3β-hydroxy-1-oxo-olean-12-ene-30-al-28-oic acid; 16β-hydroxylupeol-3-*O*-palmitate; 16β-hydroxylupeol-3-*O*-myristate; 11-oxo-β-amyrin; monogynol A *cis*-coumaryl ester; monogynol A *trans*-coumaryl ester; 18-hydroxy-27-norolean-12,14-dien-30-al-28-oic acid; and 3β-hydroxy-1-oxo-olean-12-ene-30-al-28-oic acid), aromatics (*cis*-4-*O*-methyl caffeic acid octanol ester and *trans*-4-*O*-methyl caffeic acid octanol ester) and two steroids (Topçu et al. 2001).

Antioxidant Activity

The extracts of *Lavandula stoechas* exhibited strong total antioxidant activity (Gülçin et al. 2004). At the concentrations of 20, 40 and 60 μg/mL, water extract of lavender showed 95.5, 86.9 and 94.8 % inhibition on lipid peroxidation of linoleic acid emulsion, respectively. At the same concentrations, ethanol extract lavender exhibited 95.5, 92.5 and 96.5 %, respectively. Comparably, 60 μg/mL of standard antioxidants such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and α-tocopherol exhibited 96.5, 99.2 and 61.1 % inhibition on peroxidation of linoleic acid emulsion, respectively. Lavender extracts had effective reductive potential, free radical scavenging, superoxide anion radical scavenging and metal chelating activities at all tested concentrations (20, 40 and 60 μg/mL). Those various antioxidant activities were comparable to standard antioxidants such as BHA, BHT and α-tocopherol. The 11 essential oils from the aerial flowering parts of wild growing *Lavandula stoechas* collected from 11 different locations in northern Algeria differed in the DPPH-based radical-scavenging activities and the inhibition of the β-carotene/linoleic acid-based lipid oxidation by an eightfold factor between the most and the least active oils and were linked to different sets of molecules in the different essential oils (Benabdelkader et al. 2011).

Hypoglycemic Activity

In hyperglycemic and normoglycemic rats, infusions of *L. latifolia* and *L. dentata* exerted hypoglycemic effects. The infusions had significant antidiabetic activity against glucose-induced hyperglycemia measured at 30 and 90 min post-administration (Gamez et al. 1987).

Anticancer Activity

Lavandula stoechas ssp. *stoechas* leaf essential oil was found to be active against cancer cell line COL-2 (9.8 μg/mL) and weakly active against LNCaP (17.6 μg/mL), while the chloroform extract of the same plant was found to be highly active against cancer cell line P-388 (1.4 μg/mL). None of them showed any activity against the ASK cancer cell line (Gören et al. 2002).

Antimicrobial Activity

Lavandula stoechas ssp. *stoechas* leaf essential oil exhibited antimicrobial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Proteus mirabilis*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* but not against *Staphylococcus epidermidis*, *Enterococcus faecalis* and *Candida albicans* (Gören et al. 2002). The essential oils of Turkish oregano (*Origanum minutiflorum*), bay laurel (*Laurus nobilis*), Spanish Lavender (*Lavandula stoechas* subsp. *stoechas*) and fennel (*Foeniculum vulgare*) exhibited a potent antibacterial activity against the following food-borne bacteria: *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Salmonella typhimurium* and *Staphylococcus aureus* (Dadalioğlu and Everendiliek 2004).

Lavandula stoechas leaf essential oil exhibited antimicrobial activity in submerged broth culture against *Staphylococcus aureus*, *Streptococcus* A, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella enteritidis* and fungi *Candida albicans* and *Geotrichum candidum* (Bouzouita et al. 2005) The Gram-positive bacteria were more sensitive and *Staphylococcus aureus* was the most susceptible. Among the Gram-negative bacteria, *Pseudomonas aeruginosa* was the most susceptible. *L. stoechas* oil 1 % (V/V) completed inhibited growth of fungi *Candida albicans* and *Geotrichum candidum.* Essential oils in the following lavender species: *Lavandula vera*, *L. intermedia*, *L. pyrenaica* and *L. stoechas* subsp. *stoechas* exhibited antipseudomonal effect with MBC values in the range 12.5–50 µL/mL using the tube dilution method (Végh et al. 2012).

The essential oils of *Lavandula stoechas* ssp. *stoechas* were found inhibitory to *Rhizoctonia solani* and *Fusarium oxysporum* and less effective against *Aspergillus flavus* (Angioni et al. 2006). Among the oil components tested, fenchone, limonene and myrtenal appeared to be the more effective on the inhibition of *R. solani* growth. The flower essential oil was found to be relatively more active than the leaf oil towards the tested pathogenic microorganisms (Kirmizibekmez et al. 2009). Methicillin-resistant *Staphylococcus aureus* was more susceptible to the flower oil (MIC = 31.2 µg/mL). Essential oils from *Lavandula angustifolia*, *L. latifolia*, *L. stoechas* and a necrodane-rich *L. luisieri* inhibited growth of both methicillin-sensitive and methicillin-resistant *Staphylococcus aureus* (MSSA and MRSA) by direct contact at oil doses ranging from 1 to 20 µL but not in the vapour phase (Roller et al. 2009). Testing of binary combinations of the oils showed that the *L. luisieri* oil interacted synergistically with *L. stoechas* (high in 1,8-cineole, fenchone and camphor) and *L. angustifolia* (rich in linalool and linalyl acetate) to produce larger inhibition zones than those produced using each oil individually.

All the essential oils isolated from Lamiaceous plants in Turkey including *Lavandula stoechas* ssp. *stoechas* were very effective against Gram-positive and Gram-negative bacteria, which included multiple antibiotic-resistant strains, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus mutans*, *Escherichia coli*, *Pseudomonas stutzeri*, *Stenotrophomonas maltophilia*, *Micrococcus luteus*, *Chryseomonas luteola* and *Bacillus subtilis*, except *Pseudomonas aeruginosa* and *Pseudomonas fluorescens* (Sarac and Ugur 2009). The oils except from *Salvia tomentosa* and *Salvia fruticosa* were also effective against *Candida albicans*. The 11 essential oils from the aerial flowering parts of wild growing *Lavandula stoechas* collected from 11 different locations in northern Algeria exhibited good antimicrobial activities against most of the 16 tested strains of bacteria, filamentous fungi and yeasts, with minimum inhibitory concentrations (MICs) ranging from 0.16 to 11.90 mg/mL (Benabdelkader et al. 2011).

Antiangiogenic Activity

Components from *L. stoechas* essential oil potentially displayed a higher grade of interaction with matrix metalloproteinase (MMP)-2 and MMP-9 in vitro (Zeidán-Chuliá et al. 2012). Although antibacterial and growth inhibitory effects of essential oils on the tested periodontopathogens were limited, *L. stoechas* inhibited MMP-2 and

MMP-9 in vitro at concentrations of 1 and 5 µL/mL. MMP-inhibiting concentrations of essential oils were not cytotoxic against keratinocytes. The authors proposed that essential oil of *L. stoechas* may be useful therapeutic agents as MMP inhibitors through a mechanism possibly based on their antioxidant potential.

Hypotensive Activity

Crude extract of *L. stoechas* produced a fall in blood pressure and heart rate in anesthetized NMT rats (Gilani et al. 2000). Pretreatment of atropine abolished the cardiovascular responses, suggesting that the antihypertensive and bradycardia effects of the crude extract may be mediated through mechanism(s) similar to that of acetylcholine.

Anticonvulsant and Antispasmodic/Spasmogenic Activity

The isolation of a smooth muscle relaxant principle identified as 7-methoxycoumarin from *Lavandula stoechas* was reported by Aftab et al. (1998). The aqueous-methanolic extract of *L. stoechas flowers* (600 mg/kg) significantly reduced the severity and increased the latency of convulsions induced by pentylenetetrazole (PTZ) in mice and reduced PTZ's lethality (Gilani et al. 2000). The extract up to a dose of 600 mg/kg was found devoid of any hypnotic effect in mice; however, animals were found to be dull, calm and relaxed. The sedative effect of lavender extract was confirmed, as it prolonged the pentobarbital sleeping time in mice similar to that of diazepam. In isolated rabbit jejunum preparations, the extract caused a dose-dependent (0.1–1.0 mg/mL) relaxation of spontaneous contractions. The extract also inhibited K(+)-induced contractions in a similar dose range, thereby suggesting calcium channel blockade which was confirmed when pretreatment of the jejunum preparation with the extract produced a dose-dependent shift of the Ca(2+) dose–response curve to the right, similar to the effect of verapamil, a standard calcium channel blocker. The data indicated that lavender extract exhibited anticonvulsant and antispasmodic activities and that its calcium channel blocking property may be mechanistically related to these activities.

In vitro studies showed that *Lavandula stoechas* crude extract (1–10 mg/mL) caused atropine-sensitive spasmogenic effect in guinea pig ileum (Jabeen et al. 2007). In spontaneously contracting rabbit jejunum, the extract (0.03–1 mg/mL) caused a transient spasmogenicity followed by relaxation at higher doses. The extract relaxed high K^+-induced contractions at the similar dose range (0.03–1 mg/mL), suggesting that the spasmolytic effect was mediated through calcium channel blockade. Activity-directed fractionation revealed that the spasmolytic effect was concentrated in the petroleum fraction while the spasmogenic effect was more evident in the aqueous fraction. The data indicated the presence of both spasmogenic and spasmolytic components mediated through muscarinic receptor activation and calcium channel blockade, respectively. The data may also explain some of its medicinal uses in gut disorders, like constipation and spasm.

Anti-inflammatory Activity

French Lavender (*Lavandula stoechas*) extract exhibited inhibitory activity in the paw oedema induced by carrageenan (38 % at 3 h) but had no effect on the TPA-induced ear oedema (Amira et al. 2012). The extract also showed antioxidant activity. Lavender extract at 200 µg/mL decreased proinflammatory cell viability by 63 % after 3 h of incubation. Neutrophil elimination through apoptosis could be implicated in the resolution of acute inflammation in the case of lavender, whereas the reduction of reactive oxygen species produced by neutrophils, such as the superoxide anion and the hydroxyl radical, could be implicated in the overall reduction of inflammation.

Insecticidal Activity

The essential oils of both *L. stoechas* and *L. angustifolia* exhibited insecticidal effects against *Drosophila auraria* flies (Konstantopoulou et al.

1992). Extracts of *Myrtus communis* were found to be the most toxic against fourth instar larvae of the mosquito *Culex pipiens molestus*, followed by those of *Origanum syriacum*, *Mentha microcorphylla*, *Pistacia lentiscus* and *Lavandula stoechas*, with LC_{50} values of 16, 36, 39, 70 and 89 mg/L, respectively (Traboulsi et al. 2002). Among the components of the oils tested, thymol, carvacrol, (1R)-(+)-α-pinene and (1S)-(−)-α-pinene were the most toxic (LC_{50} = 36–49 mg/L), while menthone, 1,8-cineole, linalool and terpineol (LC_{50} = 156–194 mg/L) were less toxic. The essential oils of *Lavandula stoechas* and *Eucalyptus globulus* were toxic to the cigarette beetle *Lasioderma serricorne* with LC_{50} = 0.379 μL/cm^2 and LC_{50} = 0.216 μL/cm^2, respectively, in contact toxicity (Ebadollahi et al. 2010). In fumigation toxicity, lavender oil had an LC_{50} = 3.835 μL/L air and the eucalyptus oil LC_{50} = 11.222 μL/L air at 24 h time of exposure. A direct relationship between mortality rate and dose was detected.

Genotoxic Activity

Studies showed that aqueous extracts of *L. stoechas* flowers reduced mitotic index of *Allium cepa* root tip meristem cells, but significantly induced chromosome aberrations and mitotic aberrations in comparison with water control (Çelik and Aslantürk 2007). Aqueous extracts induced breaks, stickiness, pole deviations and micronuclei. Furthermore, these effects were related to extract concentrations. The results showed *L. stoechas* aqueous extracts had cytotoxic and genotoxic effects.

Contraindication

A case of poisoning by ingestion of tea made from *Lavender stoechas* herb was reported (Acikalin et al. 2012). The patient was admitted to the emergency department with supraventricular tachycardia due to anticholinergic syndrome triggered by drinking lavender tea. On electrocardiography, a narrow QRS complex tachycardia was evident. After carotid sinus massage, the patient immediately returned to sinus rhythm.

Traditional Medicinal Uses

Polat and Satıl (2012) found that *Hypericum perforatum*, *Lavandula stoechas*, *Salvia tomentosa*, *Origanum onites*, *Origanum vulgare* and *Teucrium polium* were the most commonly used plant species for medical purposes by the local people of Edremit Gulf, located in the western region of Turkey. The traditional medicinal plants have been mostly used for the treatment of abdominal and stomach pain (17 %), cough and cold (12 %), diabetes (6 %), kidney ailments (5 %) and wounds (4 %). Most of the medicinal plants used in the Marmaris district of south-west Anatolia, Turkey, belong to the families Lamiaceae (13 species) and Asteraceae (four species); among the Lamiaceae was *Lavandula stoechas* (Gürdal and Kültür 2013). *Lavandula stoechas* oil is extensively used in aromatherapy as a holistic relaxant (Evans 1996). In Morocco, *L. stoechas* in decoction is used for catarrh of the upper respiratory tract, sneezing, cough, asthma, bronchitis, abdominal pains, colds, rheumatism, lumbago, etc. (Bellakhdar 1997). In the Middle Atlas, North Africa, *L. stoechas* is used to aromatize the Lben (skim milk) (IUCN 2005). An infusion of flowering tips is used as a tonic, resolvent, stomachic, vulnerary, diaphoretic, pectoral, diuretic, antispasmodic and antirheumatic and for headache, cases of irritability, epilepsy and blennorrhagia (Grieve 1971; Chopra et al. 1986; Bown 1995; IUCN 2005).

Other Uses

This lavender is grown as a medicinal plant in western India, as an ornamental and for essential oil elsewhere. All the forms of lavender including this lavender are much visited by bees and provide good sources of honey. From this lavender, an essential oil is extracted and used for air fresheners, deodorants, disinfectants, insecticides

(IUCN 2005), soaps, perfumes and medicines (Uphof 1968; Usher 1974). The aromatic leaves and flowers are used in potpourri and as an insect repellent in the linen cupboard (Polunin and Huxley 1967; Bown 1995). After the removal of the flowers for use in potpourri, the flowering shoots can be tied in small bundles and burnt as incense sticks (Genders 1994).

Comments

This lavender can be propagated by softwood cuttings or seeds. The species is a declared weed species in Victoria and Western Australia.

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Salvia elegans

Scientific Name

***Salvia elegans* Vahl**

Synonyms

Salvia camertonii Regel, *Salvia elegans* var. *sonorensis* Fernald, *Salvia incarnata* Cav. [Illeg.], *Salvia longiflora* Sessé & Moc., *Salvia microcalyx* Scheele, *Salvia microculis* Poir., *Salvia punicea* M. Martens & Galeotti, *Salvia rutilans* Carrière

Family

Lamiaceae

Common/English Names

Pineapple Sage, Pineapple Scented Sage, Honey Melon Sage, Tangerine Sage

Vernacular Names

Finnish: Ananassalvia
French: Sauge Ananas
German: Ananas-Salbei, Honigmelonen-Salbei
Mexico: Flor del Cerro, Limoncillo, Mirto, Perritos Rojos (Spanish)
Portuguese: Sábio Abacaxi
Swedish: Ananassalvia

Origin/Distribution

Pineapple Sage is indigenous to Mexico and Guatemala.

Agroecology

In its native range, Pineapple Sage grows naturally in oak and pine scrub forests at high elevations from 2,438 to 3,048 m.

The plant prefers full sun and thrives in well-drained, humus-rich, fertile loamy or sandy-loam soils with regular watering. It is sensitive to drought. Although frost tolerant, it will die down in deep frost but will sprout again in spring.

Edible Plant Parts and Uses

Pineapple Sage leaves and flowers are edible (Morton 1976; Facciola 1990; Roberts 1993, 2000; Coyle 1999; Hanson 2001; Newman and O'Connor 2009; Anonymous 2013). Pineapple Sage imparts a pineapple-like fragrance to food, but its only real use in cooking is as a fresh edible flower (Anonymous 2013). The flowers are redolent of honeysuckle and make a colourful sparkle when scattered in salads, fruit cocktails, fruit puddings, dessert or any garnish. They are particularly attractive when scattered with yellow or green bell pepper. They can be sugared and used to garnish cakes or cookie platters or infused to make a tea. Minced leaves and flowers can be

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mixed in cream cheese to afford a delightful fruity spread. The leaves can be kneaded into raisin dough bread. Pineapple Sage herbal sugar can be prepared by layering leaves in sugar and allowing it to infuse for a week. Fresh leaves can be steep in hot apple juice and the juice used to make jelly with Pineapple Sage flavour. Leaves can also be brewed into tea or make into a refreshing summer drink. The fresh or dried leaves can be added to savoury dishes to impart a pineapple-like flavour. Other recipes for flowers and leaves reported include sweet banana smoothie, fritters, salsa, ginger chicken with fresh Pineapple Sage and Pineapple Sage pound cake.

Botany

A perennial semi-woody, subshrub 1–1.5 m high with an open-branched habit, pubescent, squarish stems and roots extending underground to form a large clump. The leaves are opposite, simple, softly pubescent, pale green, elliptic, 5–10 cm long, with acute to acuminate tip and obtuse to cordate base, sunken-veined and finely serrated to cuneate margin on 3 cm pubescent petioles (Plate 1). Flowers are arranged in 4-flowered whorls on 20 cm long terminal spikes. Flowers ruby red, 2.5–5 cm long, calyx tubular and hairy; corolla tubular, two-lipped, pubescent, with upper hoodlike lip and lower spreading lip 3-lobed; stamens 2 short, staminodes 2 small; style bi-cleft (Plate 2). Nutlet glabrous ovoid.

Nutritive/Medicinal Properties

Twenty-eight volatile aroma components were identified in Pineapple Sage (Makino et al. 1996). Among them, monoterpenoids and sesquiterpenoids such as *trans*-ocimene, linalool, β-caryophyllene, germacrene D and spathulenol; aliphatic alcohols such as 2-propanol and 3-octanol; and *trans*-3-hexenal were predominant components. Also, *cis*-jasmone was found as a minor component. The contents of the predominant terpenoids, such as *trans*-ocimene, linalool and β-caryophyllene, found in the

Plate 1 Opposite pubescent leaves and stems

Plate 2 Tubular red flowers

preflowering stage were lower in ether extract of the full flowering stage.

Essential oil composition of *S. elegans* aerial parts harvested at full flowering stage comprised mainly monoterpenes (68.2 %) made up of oxygenated compounds (62.7 %) and monoterpene hydrocarbons (5.5 %), with total sesquiterpenes amounting to 24.0 % (20.9 % sesquiterpene hydrocarbons and 3.1 % of oxygenated sesquiterpenes) and only 0.7 % of phenolic compounds (De Martino et al. 2010). *cis*-Thujone (38.7 %) and geranyl acetate (6.9 %) were the most abundant among oxygenated monoterpenes, while geraniol (6.5 %) and camphor (4.6 %) were present in less amount. The most abundant sesquiterpene hydrocarbons were δ-cadinene (11.5 %), bicyclogermacrene (2.5 %) and α-muurolene (1.8 %). The other components included (*Z*)-β-ocimene (2.2 %), α-terpinene (1.7 %), α-terpineol (1.6 %), γ-cadinene (1.5 %), τ-muurolol (1.4 %), limonene (1.1 %), geranial (1 %), bornyl acetate (1 %), τ-cadinol (0.9 %), β-pinene (0.7 %), neral (0.7 %), terpinen-4-ol (0.7 %), carvacrol (0.6 %), α-guaiene (0.5 %), valencene (0.5 %), β-elemene (0.4 %), b-phellandrene (0.4 %), 1,8-cineole (0.4 %), sabinene (0.3 %), α-humulene (0.3 %), α-cadinene (0.3 %), *allo*-aromadendrene (0.2 %), cubebol (0.2 %), germacrene D (0.2 %), tricyclene (0.2 %), spathulenol (0.2 %), β-oplopenone (0.2 %), 1-*epi*-cubenol (0.2 %), camphene (0.2 %), *cis*-β-guaiene (0.2 %), neryl acetate (0.2 %), β-caryophyllene (0.2 %), cadina-1,4-diene (0.1 %), aromadendrene (0.1 %), *cis*-calamenene (0.1 %), *o*-cymene (0.1 %), (*E*)-β-ocimene (0.1 %), γ-terpinene (0.1 %), *cis*-sabinene hydrate (0.1 %), *trans*-linalool oxide (0.1 %), *cis*-*p*-menth-2-en-1-ol (0.1 %), *p*-cymen-8-ol (0.1 %), δ-elemene (0.1 %), α-cubebene (0.1 %), (Z)-isoeugenol (0.1 %), γ-muurolene (0.1 %), β-himachalene (0.1 %) and α-gurjunene (0.1 %).

Anxiolytic and Antidepressant Activity

Salvia elegans (leaves and flowers) hydroalcoholic (60 %) extract, administered orally to mice, increased the percentage of time spent and the percentage of arm entries in the open arms of the elevated plus maze, as well as increased the time spent by mice in the illuminated side of the light–dark test, and decreased the immobility time of mice subjected to the forced swimming test (Herrera-Ruiz et al. 2006). The same extract was not able to modify the spontaneous locomotor activity measured in the open-field test. These results indicated the potential antidepressant and anxiolytic activity of *Salvia elegans*. Intraperitoneal administration of *Salvia elegans* leaf hydroalcoholic (60 % ethanol) extract (3.12, 12.5, 25 and 50 mg/kg) to male Sprague-Dawley rats caused a significant decrease in total motility, locomotion, rearing and grooming behaviour (Mora et al. 2006). Only the dose of 12.5 mg/kg increased the exploration of the elevated plus-maze test open arms in a similar way to that of diazepam (1 mg/kg). In the forced swimming test, all doses of the extract induced a reduction of immobility, in a similar way to that of fluoxetine (10 mg/kg) and imipramine (12.5 mg/kg), along with a significant increase in the time spent in swimming behaviour. Acquisition of active avoidance responses was disrupted by pretreatment with the extract, but retention of a passive avoidance response was not significantly modified. The results suggested that some of the components of the hydroalcoholic extract of *Salvia elegans* had psychotropic properties.

Antihypertensive Activity

Administration of *S. elegans* hydroalcoholic extract significantly decreased systolic blood pressure of mice; the antihypertensive effect was greater than that treatment with losartan (Jiménez-Ferrer et al. 2010). The extract decreased the E(max) of the angiotensin II hypertensive effect by about 20 % in both systolic and diastolic pressures; treatment with losartan also decreased the same parameter between 6 % and 8 % for systolic and diastolic pressures, respectively. Fractions SeF8 and SeF8-8 of the extract showed similar levels of angiotensin II ED_{50} for both pressures compared with losartan; these fractions

were found to contain major compounds typical of flavonoids. The extract also inhibited angiotensin-converting enzyme activity (50.27 %). SeBuOH fraction and SeF8-22 fraction exhibited greater ACE inhibitory activity 78.40 % and 82.61 % compared to lisinopril (87.18 %). The main compounds of the fractions SeBuOH and SeF8-22 were found to be flavonoid and phenyl propanoid types. The results suggested the antihypertensive effect of *Salvia elegans* was attributed to the angiotensin II antagonism and inhibition of angiotensin-converting enzyme.

Cholinergic Activity

Of plant extracts tested for CNS act acetylcholine receptor activity traditionally used to improve failing memory, *Melissa officinalis*, three *Salvia* species and *Artemisia absinthium* ethanol extracts were found to be the most potent with IC_{50} concentrations of <1 mg/mL (Wake et al. 2000). The plant extracts were able to displace [3H]-(N)-nicotine and [3H]-(N)-scopolamine from nicotinic receptors and muscarinic receptors, respectively, in homogenates of human cerebral cortical cell membranes. *M. officinalis* displayed the highest [3H]-(N)-nicotine displacement value and *Salvia elegans* the highest [3H]-(N)-scopolamine displacement value. Choline, a weak nicotinic ligand ($IC_{50} = 3 \times 10^{-4}$ M), was found in extracts of all plants studied at concentrations of 10^{-6} to 10^{-5} M. These concentrations could not account for not more than 5 % of the displacement activity observed.

Insecticidal Activity

The essential oils of *S. elegans* and *S. splendens* Blue Ribbon exhibited excellent inhibitory larvicidal effect against fourth instar larvae of *Aedes albopictus* mosquito, and their LC_{50} values at 24 h were 46.4 and 59.2 ppm, and LC_{90} values 121.8 and 133.0 ppm, respectively (Mathew and Thoppil 2011). The main components of *S. elegans* essential oil were spathulenol (38.73 %) and caryophyllene (10.32 %) and that of *S. splendens* were β-cubebene (22.9 %) and caryophyllene (12.99 %).

Traditional Medicinal Uses

S. elegans is widely used in Mexican traditional medicine to alleviate central nervous system ailments, especially anxiety (Herrera-Ruiz et al. 2006; Mora et al. 2006). The plant is widely used in Mexico for healing purposes and also as antihypertensive treatment for lowering blood pressure (Jiménez-Ferrer et al. 2010). The purported health benefits of this herb include calming the nervous system, serving as a general tonic, improving the digestive system and treating heartburn.

Other Uses

Pineapple Sage is used as a medicinal plant, a flavourful herb for garnishing dishes and an ornamental specimen plant for avid gardeners. The decorative, fragrant leaves are employed in bouquets, and the scarlet flowers are used in potpourris. Entire flowering stems can be dried for use in herbal wreaths.

Studies found that *S. elegans* essential oil has allelopathic activity and can control germination of unwanted or competitive plants. The oils of *S. elegans*, *S. greggii* and *S. munzii* were active inhibitors of germination and radical elongation of *Raphanus sativus* and *Lepidium sativum* (De Martino et al. 2010). The germination of garden cress was completely inhibited by *S. elegans*, *S. greggii* and *S. munzii* oils, at the highest doses (1.25, 0.625 µg/mL) used. *S. elegans* essential oil at the almost all doses tested inhibited significantly the radical elongation of both radish and garden cress.

Comments

Pineapple Sage is easily propagated from stem cuttings rooted in potting soil or a mixture of sand and peat moss. The red flowers are attractive to hummingbirds and butterflies.

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Sideritis scardica

Scientific Name

***Sideritis scardica* Griseb.**

Synonyms

Navicularia scardica (Griseb.) Soják, *Siderits florida Boiss*. & Heldr., *Sideritis raeseri* subsp. *florida* (Boiss. & Heldr.) Papan. & Kokkini, *Sideritis scardica* subsp. *longibracteata* Papan. & Kokkini

Family

Lamiaceae

Common/English Names

Balkan Sideritis, Bulgarian Viagra, Ironwort, Greek Mountain Tea, Mountain Tea, Pirin Tea, Mursalski Tea, Shepherd's Tea

Vernacular Names

Albanian: Çaj Mali
Crete: Malotira
French: Crapaudine
German: Bergtee, Griechischer Bergtee
Greece: Τσάι Του Βουνού
Slovaščina: Šarplaninski Čaj
Spanish: Rabogatos, Garranchuelos, Zahareñas
Turkish: Adaçayi, Daçayi, Dalli

Origin/Distribution

Sideritis scardica is indigenous to the Balkan and occurs in south-west Albania, Macedonia, Bulgaria, Serbia, Greece and Turkey (Heywood 1973; Petrova and Vladimirov 2010).

Agroecology

Sideritis scardica grows in the subalpine and alpine vegetation belts accompanied by high-mountain, mostly chasmophytic plants. The plant is frost tolerant, surviving low temperatures to −10 °C. In its native range, it occurs in open, dry, stony places, on limestone, on shallow and eroded soil. It is a robust, hardy plant that is adapted to survive with little water and little soil.

Edible Plant Parts and Uses

Sideritis scardica is used for the preparation of a popular drink throughout Eastern and Central Europe (Danesi et al. 2013). *Sideritis* species including *S. sideritis* have been traditionally used as teas for feeding, flavouring agents and in folk medicine (González-Burgos et al. 2011). *Sideritis scardica* and *Sideritis raeseri* are very popular in Macedonia, Bulgaria and Greece as well as

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throughout the Eastern Mediterranean as refreshment but also herbal cure for common cold (Qazimi et al. 2010). Its inflorescences and leaves are used. The tea is sometimes enhanced with cinnamon and honey.

Botany

A perennial, densely greyish-white, tomentose, herb 15–40 cm high and woody at the base. Leaves, opposite, basal leaves, oblong-lanceolate, crenate, mucronate or subobtuse and attenuate to a short petiole, 40–80 by 7–10 mm, middle and upper leaves subsessile, linear-lanceolate, acute 30–60 by 6–8 mm. Floral leaves reduced to bracts. Bracts ovate, white lanate with curled, eglandular hairs outside and acuminate tip, 12–20 mm long, twice longer than flowers. Inflorescence 4–9 cm long, verticillasters 2-many-flowered, clustered in a terminal spike (Plates 1, 2 and 3). Flowers small; calyx narrowly campanulate, densely hairy, shortly toothed, corolla lemon-yellow, 12–14 mm long, glandular, 2-lipped, upper lip 2-lobbed, lower lip 3-lobed, stamens 4, style with bifid stigma. Nutlets ovoid.

Plate 1 Mass of ironwort inflorescences

Plate 2 Verticillastered inflorescences

Plate 3 Close-up of verticillaster with numerous flowers

Nutritive/Medicinal Properties

The *n*-hexane extracts of aerial parts of *Sideritis scardica* and *S. raeseri* from Albania and Macedonia contained more than 90 components, dominated by diterpenes and hydrocarbons (Karapandzova et al. 2013). The most abundant components were hentriacontane, nonacosane and heptacosane and two other components both with *MW* = 286, probably diterpenes, which were not fully identified. The most abundant minerals were K > Ca > Mg > P > Fe > Al > Na. The microelement and toxic element contents were found in the following order: Zn > Mn > B > Ba > Cu > Sr > Li > Ni > Cr > Co and Cd > Pb > As.

Over 100 constituents of *n*-hexane extracts of the aerial plant parts of *Sideritis scardica* were identified, belonging to several classes of components (Qazimi et al. 2010): diterpenes (- (+)-beyrene; pimara-8-(14), 15-diene; kaur-15-en; manonyl oxide; 3-α-hydroxymanool; 7-ethenyl-1,2,3,4,4a,5,6,7,9,10,10a-dodecahydro-1,1,4a,7-tetramethyl-2-phenathrenol, unidentified M346, M286 and M306), hydrocarbons (heptadecane; octadecane; nonadecane; eicosane; heneicosane; docosane; tricosane; tetracosane; pentacosane; hexacosane; heptacosane; octacane; nonacosane; octacosen; triacontane; hentriacontane; dotriacontane; tritriacontane), dominantly present in each of the extracts, followed by fatty acids (dodecanoic acid; tetradecanoic acid; octadecanoic acid; 9,12-octadecadienoic acid; 9,12,15-octadecatrienoic acid), esters (benzyl benzoate, isopropyl tetradecanoate; di-isobutyl phthalate; methyl hexadecanoate; hexadecanoic acid ethyl ester; isopropyl; hexadecanoate; methyl octadecanoate; 9,12-octadienoic acid ethyl ester), aliphatic and aromatic alcohols (2,4-di-tert-butylphenol; tetradecanol; phytol (isomer); 2-hexadecen-1-ol; oleyl alcohol; octadecanol), sterols ((−)-cholesterol; 22,23-dihydrobrassicasterol; stigmasterol; γ-sitosterol) triterpenes (squalene; β-amyrin; α-amyrin; triterpene alcohol) and monoterpenes and sesquiterpenes (α-pinene; camphene; β-pinene; β-myrcene; D-limonene; β-phellandrene; *trans*-pinocarveol; *trans*-sabinol; myrtenol; (−)-verbenone; α-cubebene; α-copaene; *cis*-muurola-4(14),15-diene; *trans*-muurola-3,5-diene; *trans*-caryophyllene; α-humulene; germacrene D; bicyclogermacrene; δ-cadinene; *trans*-cadina-1,4-diene; (−)-spathulenol; caryophyllene oxide; viridiflorol; α-cadinol; τ-muurol; valeranone) and a miscellaneous compound, hexahydrofarnesyl acetone, which were found in much smaller amounts or only in traces. Most abundant was an unidentified diterpene M286 and large amounts of nonacosane (1.7–12.22 %) and hentriacontane (4.48–20.79 %).

Besides flavonoids, *S. scardica* was also reported to contain tannins (Evstatieva 2002). *S. scardica* was found to contain the following flavones: isoscutellarein, chryseriol, apigenin and 3′-methyl ether of hypolaetin (Janeska et al. 2007). Three new phenylethanoid glycosides, alyssonoside, echinacoside, and forsythoside, were detected for the first time in Balkan *Sideratis* species (*S. scardica*, *S. raeseri*, *S. taurica*, *S. syriaca* and *S. perfoliata*), along with two known phenylethanoid glycosides, verbascoside and leucoseptoside A (Petreska et al. 2011a, b). Three hydroxycinnamic acids, such as, 3-caffeoylquinic acid, 5-caffeoylquinic acid and feruloylquinic acid; five flavonoid 7-*O*-diglycosides, namely, isoscutellarein 7-*O*-allosyl-(1 → 2)glucoside, hypolaetin 7-*O*-allosyl-(1 → 2)glucoside, luteolin 7-*O*-allosyl-(1 → 2)glucoside, 3′-*O*-methylhypolaetin 7-*O*-allosyl-(1 → 2) glucoside and 4′-*O*-methyl isoscutellarein 7-*O*-allosyl-(1 → 2)glucoside; and 11 acetylated flavonoid 7-*O*-diglycosides, viz., hypolaetin 7-*O*-[6‴-*O*-acetyl]-allosyl(1 → 2)glucoside, apigenin 7-*O*-[6″-*O*-acetyl]-allosyl(1 → 2)glucoside, isoscutellarein 7-*O*-[6″-*O*-acetyl]-allosyl(1 → 2) glucoside,3′-*O*-methylhypolaetin7-*O*-[6‴-*O*-acetyl]-allosyl(1 → 2)glucoside, isoscutellarein 7-*O*-[2‴, 6‴-diacetyl]-allosyl(1 → 2)glucoside, hypolaetin 7-*O*-[2‴,6‴-di-*O*-acetyl]-allosyl(1 → 2)glucoside, 4′-*O*-methylisoscutellarein 7-*O*-[6‴-*O*-acetyl]-allosyl (1 → 2)glucoside,isoscutellarein7-*O*-[6‴-*O*-acetyl]-allosyl (1 → 2)-[6″-*O*-acetyl]-glycoside, 3′-*O*-methylhypolaetin 7-*O*-[2‴,6‴-di-*O*-acetyl]-allosyl (1 → 2)glucoside and 4′-*O*-methylisoscutellarein 7-*O*-[6‴-*O*-acetyl]-allosyl(1 → 2)-[6″-*O*-acetyl]-glucoside were isolated. Acylated flavonoid glycosides isoscutellarein 7-*O*-[6‴-*O*-acetyl]-allosyl (1 → 2)-[6″-*O*-acetyl]glucoside and 4′-*O*-methylisoscutellarein 7-*O*-[6″-*O*-acetyl]-glycosyl(1 → 2)-

[6″-*O*-acetyl]glucoside had been previously reported by Sattar et al. (1993, 1995).

The major components in Bulgarian *S. scardica* essential oil were β-caryophyllene (18.8 %) and nerolidol (12.1 %) (Todorova et al. 2000). The major constituents of the water-distilled essential oil from aerial parts of *Sideritis scardica* subsp. *scardic*a were β-pinene (17.91 %), carvacrol (14.78 %) and α-pinene (7.26 %) (Başer et al. 1997). The essential oils of *S. scardica* from different locations differed significantly: In the Macedonian sample, α-cadinol (20 %) predominated, while in the oil of Bulgarian samples, the main components were diterpenic compounds and octadecenol (over 20 %) (Kostadinova et al. 2007).

In *S. scardica* essential oil (EO) sample obtained by hydrodistillation, about 111 compounds were identified; oxygenated monoterpenes (30.01 %) were the major constituents, but with significant amount of oxygenated sesquiterpenes (25.54 %) and fatty acids with their esters (15.96 %) (Tadić et al. 2012a). The most abundant compounds were hexadecanoic acid (12.92 %), myristicin (5.23 %), menthol (4.90 %), caryophyllene oxide (4.84 %), τ-muurolol (3.62 %), followed by (*E*)-anethole (2.89 %), 2-(*E*)-tridecanol acetate (2.50 %) and valeranone (2.15 %). In the EO obtained by supercritical carbon dioxide at 10 MPa and at 40 °C, 34 compounds are found; fatty acids with their esters (41.16 %) and diterpenes (33.75 %) predominated. The main components were hexadecanoic acid (18.59 %), dihydroxy derivative of sandaracopimar-8(14),15-diene (14.89 %), (*E*)-ferruginol acetate (11.82 %), ethyl hexadecanoate (11.73 %), followed by (octadecanol 6.20 %) and caryophyllene oxide (2.44 %). In the EO obtained by supercritical carbon dioxide at 30 MPa and at 40 °C, 17 compounds were obtained; fatty acids (71.07 %) and diterpenes (26.81 %) predominated The major compounds were hexadecanoic (43.22 %) and linoleic acids (24.80 %) and diterpenes—the dihydroxy derivative of sandaracopimar-8(14),15-diene (11.49 %) followed by (*E*)-ferruginol acetate (11.22 %) and pimaradiene (2.84 %). Fraction A from solvent extraction contained 13 compounds mainly hexadecanoic acid (46.57 %), dodecanoic acid (17.05 %), dihydroxy derivative of sandaracopimar-8(14),15-diene (10.79 %), (*E*)-ferruginol acetate (8.25 %), (*Z*)-ferruginol acetate (4.26 %), ethyl hexadecanoate (4.13 %) and cyclopentadecanolide (4.01 %). Fraction B contained 12 compounds mainly diterpenes, which were not detected in the extracts C (10 compounds) and D (8 compounds). The main components in fraction B were (*E*)-ferruginol acetate (65.47 %), hexadecanoic acid (8.53 %), dodecanoic acid (6.96 %) and the dihydroxy derivative of sandaracopimar-8(14),15-diene (6.25 %). Fractions C and D were the fractions abundant in fatty acids and their esters (66.48 and 54.59 %, respectively), with differences in the type of fatty acids and their esters present in greatest quantity as determined; hexadecanoic acid (29.89 %) and dodecanoic acid (25.56 %) were the major components in C followed by cyclopentadecanolide (15.35 %), (*E*)-coniferyl alcohol (11.81 %) and ethyl hexadecanoate (7.64 %). In fraction D, dodecanoic acid (35.78 %), decyl acetate (12.54 %) and (*E*)-coniferyl alcohol (18.69 %) were most abundant followed by decanoic acid (5.47 %) and (*Z*)-chrysanthenyl acetate (4.58 %).

Thirty-seven components, representing 73.1–79.2 % of the total oil content, were identified in the essential oil of six native Bulgarian populations of *Sideritis scardica* (Trendafilva et al. 2013). Among them, α-pinene (4.4–25.1 %), β-pinene (2.8–18.0 %), oct-1-en-3-ol (2.3–8.0 %), phenylacetaldehyde (0.5–9.5 %), β-bisabolene (1.3–11.0 %), benzyl benzoate (1.1–14.3 %) and m-camphorene (0.3–12.4 %) were the main compounds. Other compounds found were sabinene (tr (trace): 1.8 %), myrcene (tr: 1.2 %), α-phellandrene (nd (not detected): 2.1 %), δ-car-3-ene (nd: 2.8 %), limonene (0.4–3.7 %), benzyl alcohol (tr: 2.4 %), γ-terpinene (nd: 0.5 %), (*E*)-oct-2-en-1-ol (tr: 1.2 %), terpinolene (nd: 0.4 %), linalool (0.4–1.8 %), nonanal (tr: 0.8 %), 2-phenylethyl alcohol (0.2–5.1 %), terpinen-4-ol (tr: 1.0 %), α-terpineol, bicycloelemene (nd: 1.0 %), eugenol (tr: 6.8 %), α-copaene (tr: 2.2 %), β-elemene (tr: 0.6 %), β-caryophyllene (2.8–5.5 %), *trans*-β-farnesene (tr: 1.7 %),

germacrene D (0.6–4.7 %), bicyclogermacrene (0.6–3.4 %), δ-cadinene (tr: 3.9 %), spathulenol (0.5–1.3 %), 2,6-dimethyl-10-(p-tolyl)undeca-2,6-diene (0.4–3.5 %), 7 α-hydroxymanool (tr: 3.4 %), caryophyllene oxide (0.6–1.0 %), sandaracopimaradien-3b-ol (0.1–3.6 %) and two unidentified diterpenes ($M = 288$). All samples were characterized by low contents of oxygenated mono- and sesquiterpenes (≤1.6 and 2.3 %, respectively).

The chemical components found in *Sideritis* genus included terpenes, flavonoids, essential oil, iridoids, coumarins, lignanes and sterols, among others (González-Burgos et al. 2011). Diterpenes, flavonoids and essential oil were found in almost every species and were the main compounds responsible for the observed in vivo and in vitro pharmacological activities which are elaborated below.

Antioxidant Activity

Although *Sideritis scardica* extract had a lower phenolic concentration and total antioxidant capacity than tea, *Camellia sinensis* extract, their cellular antioxidant effects were similar (Danesi et al. 2013). The different phenolic pattern of the extracts suggested that the protective activity was not limited to catechins. Total phenol contents ranged up to 50.8 and up to 48.9 mg gallic acid/g for *S. scardica* and *S. raeseri*, respectively, and DPPH radical scavenging activity in terms of IC_{50} values ranged from 3.2–8.9 mg/mL to 7.6–12.6 mg/mL for *S. scardica* and *S. raeseri*, respectively (Karapandzova et al. 2013).

Anti-inflammatory Activity

Oral administration of the *S. scardica* extracts caused a dose-dependent anti-inflammatory effect in a model of carrageenan-induced rat paw oedema (Tadić et al. 2012b). The diethyl ether and *N*-butanol plant extracts at doses of 200 and 100 mg/kg exhibited about the same effect, 53.6 and 48.7 %, 48.4 and 49.9 %, respectively, compared to the effect of the positive control, the anti-inflammatory drug indomethacin (4 mg/kg), which produced a 50 % decrease in inflammation.

Gastroprotective Activity

S. scardica extracts produced dose-dependent gastroprotective activity with the efficacy comparable to that of the reference drug ranitidine when evaluated using the ethanol-induced acute stress ulcer in rats (Tadić et al. 2012b).

Anticancer Activity

The diethyl ether extract of *S. scardica* showed significant dose-dependent cytotoxicity on murine melanoma B16 cells and human leukaemia HL-60 cells, decreasing cell growth to 51.3 and 77.5 % of control, respectively, when used at 100 μg/mL (Tadić et al. 2012b). It appeared that phenolic compounds (apigenin, luteolin and their corresponding glycosides) were responsible for the diethyl ether extract cytotoxic effect. It also appeared that induction of oxidative stress might be involved in its cytotoxicity, since B16 and HL-60 cells increased their ROS production in response to treatment with diethyl ether extract. Results of in vitro studies revealed that diethyl ether and ethyl acetate extracts of *S. scardica* exerted a cytotoxic effect on C6 rat glioma cells (Jeremic et al. 2013). Diethyl ether extract induced an increase in reactive oxygen species production, leading to apoptotic and autophagic cell death, while ethyl acetate extract induced G2 M cell cycle arrest and autophagy. None of the tested extracts were cytotoxic to rat astrocytes in primary culture. Cytotoxic effects of *S. scardica* extracts were found to be partly mediated by their flavonoid constituents, apigenin and luteolin, that, when applied alone, induced cell cycle arrest, apoptosis and autophagy.

Antimicrobial Activity

S. scardica extracts and essential oil exhibited a strong to a moderate antibacterial activity in vitro

against tested microorganisms (Tadić et al. 2012a). Gram-positive bacteria *Streptococcus pyogenes*, *Streptococcus canis*, *Moraxella catarrhalis*, *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus*, *Corynebacterium pseudotuberculosis* and *Enterococcus faecalis* were found to be more susceptible in comparison to Gram-negative bacteria *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, with the exception of *Pasteurella multocida* and *Haemophilus* sp. *Sideritis scardica* essential oil exhibited the strongest activity against *Corynebacterium pseudotuberculosis* and *Haemophilus* sp. with MIC values of 640 µg/mL, while moderate activity was determined against *Staphylococcus pyogenes*, *Moraxella catarrhalis* and *Pasteurella multocida*. The strongest antibacterial activity was determined against *Haemophilus* sp. for the solvent extraction, extracts C and D, with MIC values of 40 and 80 µg/mL, respectively. The same extracts exhibited strong antimicrobial activity against *Corynebacterium pseudotuberculosis*, with MIC values of 80 µg/mL.

Central Nervous System Activity

S. scardica extracts inhibited the uptake of all three monoamines serotonin, noradrenaline and dopamine into rat brain synaptosomes by their respective transporters, the alcoholic extracts being more effective than the water extract (Knörle 2012). EC_{50} values were in the range of 30–40 µg/mL. Inhibition of the human serotonin transporter in human JAR cells by the methanol extract was even more effective (EC_{50} 1.4 µg/mL). The pharmacological profile of *S. scardica* extracts as triple monoamine reuptake inhibitors suggested their potential use in the phytochemical therapy of mental disorders associated with a malfunctioning monoaminergic neurotransmission, such as anxiety disorders, major depression, attention-deficit hyperactivity disorder, mental impairment or neurodegenerative diseases.

In a pharmacological classification of herbal extracts based on spectral EEG signatures induced by synthetic drugs in the freely moving rat, *Rhodiola rosea* root and *Sideritis scardica* herb extracts developed similar EEG frequency patterns comparable to a psychostimulant drug (methylphenidate) as well to an antidepressive drug (paroxetine) (Dimpfel 2013).

Pharmacokinetic Studies

Flavonoid and phenolic acid metabolites excreted in the urine of 10 human volunteers after ingestion of *Sideritis scardica* decoction were identified (Stanoeva and Stefova 2013). Thirty-one different metabolites of hypolaetin, methylhypolaetin, isoscutellarein, methylisoscutellarein and apigenin and 32 phenolic acid metabolites were detected. The urinary excretion of polyphenol metabolites corresponded to 5 % (n/n) of the intake of polyphenols from the *Sideritis* decoction. Flavonoid metabolites were dominant in urine samples with 87–94 % of total polyphenolic metabolite content. The most abundant metabolites were methyl hypolaetin and methyl isoscutellarein glucuronides. Urinary excretion of isoscutellarein (35.61 %) was 10 times higher than that of hypolaetin (3.67 %). Apigenin also showed high urinary excretion (32.46 %).

Traditional Medicinal Uses

Sideritis species including *S. scardica* have been traditionally used as teas for feeding, flavouring agents and in folk medicine as anti-inflammatory, antiulcerative, antimicrobial, vulnerary, antioxidant, antispasmodic, anticonvulsant, sedative, antitussive, analgesic, stomachic and carminative agents (Kirimer et al. 2004; González-Burgos et al. 2011), especially in the treatment of coughs due to colds and for curing gastrointestinal disorders (Kirimer et al. 2004). In ancient times *Sideritis* was a generic reference for plants capable of healing wounds caused by iron weapons during battles.

Sideritis scardica and *Sideritis raeseri* are very popular in Macedonia, Bulgaria and Greece as well as throughout the Eastern Mediterranean as refreshment but also herbal cure for common

cold (Qazimi et al. 2010). The herbs are often used to prepare teas widely believed to alleviate sinus congestion, aches, pains and viruses including flu and common cold. In Bulgaria, the infusion of the aerial parts of *S. scardica*, known as 'Pirin mountain tea' or 'Mursalitza tea', is employed largely as an expectorant for the treatment of bronchitis and bronchial asthma, cold, pulmonary emphysema and angina pectoris (Ivancheva and Stancheva 2000; Evstatieva and Koleva 2000; Tadić et al. 2012a, b). *Sideritis scardica* has also been used in traditional medicine in the treatment of gastrointestinal complaints, inflammation and rheumatic disorders in the Balkan Peninsula (Tadić et al. 2012a, b).

Other Uses

Studies reported that stratification of *S. scardica* seeds with a chemical solution (gibberellic acid and copper sulphate) enhanced seed germination by 80 % compared to a low germination rate of 5 % under natural conditions (Evstatieva and Koleva 2000).

Comments

S. scardica is limitedly distributed in Bulgaria and has been included in the Red Book of Bulgaria (1984) as a rare and protected plant (Evstatieva and Koleva 2000).

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Lilium lancifolium

Scientific Name

Lilium lancifolium Thunberg

Synonyms

Lilium lancifolium var. *flaviflorum* Makino, *Lilium lancifolium* var. *fortunei* (Standish) V. A. Matthews, *Lilium lancifolium* var. *splendens* (Van Houtte) V. A. Matthews, *Lilium leopoldii* Baker, *Lilium lishmannii* T. Moore, *Lilium tigrinum* Ker Gawler., *Lilium tigrinum* var. *fortunei* Standish, *Lilium tigrinum* var. *plenescens* Waugh, *Lilium tigrinum* var. *splendens* Van Houtte

Family

Liliaceae

Common/English Names

Devil Lily, Easter Lily, Garden Lily, Japanese Show Lily, Kentan, Lance-Leaf Tiger Lily, Martagon, Tiger Lily

Vernacular Names

Brazil: Lírio-De-Tigre (Portuguese)
Chinese: Juan-Dan, Chuan-Tan (Recurved Red Lily), Bai-He, Pai-Ho (Hundred Union), Suan-Nao-Shu (Garlic Head Bulb)
Czech: Lilie Tygrovaná
Danish: Tiger-Lilje
Dutch: Tijgerlelie
Finnish: Tiikerililja
French: Lis Elegant
German: Tiger-Lilie
India: Liliyama Lancifolium (Hindu)
Italian: Giglio Cinese, Giglio Tigrino
Japanese: Oni-Yuri
Korean: Chamnari
Norwegian: Tigerlilje
Polish: Lilia Tygrysia
Portuguese: Laço De Ouro, Laço De Prata, Lírio Tigrino
Russian: Lilija Tigrinaja
Spanish: Lirio De Tigre
Swedish: Sen Tigerlilja, Tigerlilja
Turkish: Kaplan Zambağı, Türk Zambağı, Zambak
Vietnamese: Hoa Lo Kèn Vằn; Loa Kèn Vằn; Quyển Đơn

Origin/Distribution

Tiger lily is native to eastern temperate Asia—China (Anhui, Gansu, Guangxi, Hebei, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Jilin, Qinghai, Shaanxi, Shandong, Shanxi, Sichuan, Xizang, Zhejiang), Japan and Korea. The species has also

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naturalized in other temperate regions of the world (e.g. northern and eastern USA, Canada and New Zealand). It has been introduced and grown as ornamental in subtropical and temperate areas elsewhere.

Agroecology

A cool climate species, occurring in woods, thickets, river banks, grassy slopes in lowlands, hillsides and mountains, from 400 to 500 m elevation in its native range. The plant grows well in full sun, in well-drained, humus-rich loamy soil.

Edible Plant Parts and Uses

Tiger lily bulbs and flowers (with stamens removed) are edible (Grieve 1971; Tanaka 1976; Facciola 1990; Hu 2005). The flower is used either fresh or cooked in salads, soup rice dishes or dried and used as spice for seasoning. The flowers add a delicate flavour to salad and other dishes. Fleshy scales of the bulb are eaten fresh or cooked in Chinese cooking. They are traditionally eaten in the summer season and are deemed to have a cooling effect. The starch-rich bulbs may also be baked, grated or ground into flour. The bulb is also pickled.

Botany

A herbaceous perennial scaly bulb. Bulb ovate to spherical, 4–8 cm across, scales broadly ovate, 2 cm long and wide, unsegmented. Stems 0.8–1.5 m, erect, unbranched, white-lanate, purplish, scabrous. Leaves alternate, cauline, linear-lanceolate, 3–8 cm long. 1.5–2 cm wide, distal leaves bearing purplish black bulbils at axils (Plates 1 and 2. Flower showy, 3–6(−20) in a nodding raceme, to 12 cm across, subtended by leafy bracts, orange-red spotted purple black, perianth segments 6 funnelform, strongly reflexed, each with a vasal nectar-bearing gland; stamens 6, anthers versatile (Plates 1 and 2). Fruit a 3-valved, loculicidal capsule, 3–4 cm across, the margins of valves flat; seeds many, flat, in 2 rows in each cell.

Plate 1 Flowers, buds and leaves

Plate 2 Close view of flowers

Nutritive/Medicinal Properties

Phytochemicals in Aerial Parts

Crystalline flavonoid pigments I and II were isolated from *Lilium lancifolium* pollens with yields of 0.056 and 0.036 %, respectively (Togasawa et al. 1966). The pigments I and II were confirmed to be rutin (quercetin-3-rutinoside) and narcissin (isorhamnetin-3-rutinoside), respectively. Vitamin C, β-carotene, vitamin B2, riboflavin, pantothenic acid, biotin and choline were detected in *L. lancifolium* pollens (Togasawa et al. (1967a). *L. lancifolium* pollens were found to contain Na, K, Mg, Ca, Sr, Zn, Mn, Fe, Al, Cu, B, Si, P, Ni and Cr (Togasawa et al. 1967b). P was also found in the form of acid-soluble P, phospholipid-P, RNA-P, phosphoprotein-P and insoluble-P.

A glycerol glucoside, lilioside C, was isolated from the leaves and stems of *L. lancifolium* (Kaneda et al. 1982).

Phytochemicals in the Bulb

Two steroidal saponins were identified from *L. lancifolium* bulbs: ophiopogonin D with the structure diosgenin3–*O*–{*O*–α-L-rhamnopyranosyl-(1 → 2)–*O*–[β-D-xylopyranosyl (1 → 3)]-β-D-glucopyranoside} and lililancifoloside A with the structure diosgenin 3-*O*-{*O*-α-L-rhamnopyranosyl-(1 → 2)-*O*—[α-L-arabinopyranosyl(1 → 3)]-β-D-glucopyranoside} (Yang et al. 2002). Ten compounds were identified fresh fleshy scale leaf of *Lilium lancifolium*: regaloside A; regaloside C; methyl-α-D-mannopyranoside; methyl-C-α-D-glucopyranoside; (25R, 26R) -26-methoxyspirost-5-ene-3p-yl-*O*-C-α-L-rhamnopyranosyl-(1 → 2)-[β-D-glucopyranosyl-(1 → 6)]-β-D-glucopyranoside; (25R)-spirost-5-ene-3β-yl-*O*-α-L-rhamnopyranosyl-(1 → 2)-[β-D-glucopyranosyl-(1 → 6)]-β-D-glucopyranoside; (25R, 26R)-17α-hydroxy-26-methoxyspirost-5-ene-3β-yl-*O*-α-L-rhamnopyranosyl-(1 → 2β-D-glucopyranosyl-(1 → 6)]-β-D-glucopyranoside; daucosterol; adenoside; and berberine (Hu et al. 2007). Ultrasonic wave extraction of flavonoids from the bulb of *Lilium lancifolium* yielded 99.25 % rate (Niu et al. 2007). The phenolic composition of *L. lancifolium* (in mg/100 g dw) comprised gallic acid (1.26 mg), rutinoside not detected (nd), (+)-catechin (1.06 mg), chlorogenic acid (nd), (−)-epicatechin (1.48 mg), myricetin (0.81 mg), rutin (2.36 mg), *p*-coumaric acid (4.51 mg), quercetin (2.38 mg), phloridzin (1.92 mg) and kaempferol (8.03 mg). Total phenolic content of *L. lancifolium* was 2827.25 GAE (gallic acid equivalent)mg/100 g, total flavonoid content was 227.24 rutin equivalent/100 g and total flavanol content was 112.12 catechin equivalent mg/100 g (Jin et al. 2012).

A phenolic glycerol glucoside regaloside F with the structure (2*S*) = 1-*O*-feruloyl-3-*O*-feruloyl-3-*O*-β-D-glucopyranosylglycerol was isolated from *L. lancifolium* fresh bulbs (Shimomura et al. 1989). The following phenylpropenoid glycerides were identified from bulbs of *Lilium lancifolium:* 1-*O*-feruloylglycerol; 1-*O*-*p*-coumaroylglycerol; 1-*O*-caffeoyl-3-*O*-*p*-coumaroylglycerol; 1,2-*O*-diferuloylglycerol; 1,3-*O*-diferuloylglycerol; 1-*O*-feruloyl-3-*O*-*p*-coumaroylglycerol; and 1,3-*O*-di-*p*-coumaroylglycerol (Luo et al. 2012).

A mucous polysaccharide, named Lilium-La-glucomannan, with molecular weight 417,000 was isolated from *Lilium lancifolium* bulbs (Tomoda et al. 1976). It comprised D-mannose and D-glucose in the molar ratio of 5:2. The polysaccharide was mainly composed of β-1 → 4 linked aldohexopyranose residues with D-Mannose units occupying non-reducing terminal positions and branch points linked through positions 2 and 3. Fermentation of tiger lily bulb powder with *Saccharomyces cerevisiae* to remove protein impurities afforded non-starch polysaccharides (NSP) with experimental yield of 8.81 % (You et al. 2010).

More than 50 components were identified in *L. lancifolium* bulb oil, including C12-C13 alkanes, C6-C18 alcohols and aldehydes, C10-C18 acids and esters and mono- and sesquiterpenes (Kameoka and Sagara 1988). The predominant compounds were sandaracopimaradiene, 1-carboxmethoxy-4-(1,5-dimethyl-3-oxohexyl)-1-cyclohexene, 2-ethylhexyl adipate, 2-phenyl-4,4-dimethyldecane and 2- and 3-phenyltetradecane. Also a number of organochloro compounds were also found in the oil.

A trypsin inhibitor (LTI-II-4) with a molecular weight of 21,000 was purified from *L. lancifolium* bulb (Asao et al. 1998). The amino acid composition was characterized by high contents of glycine, aspartic acid and serine. The inhibitor contained 4 half cystines in its constituent amino acids. The reactive site amino acid of LTI-II –4 was assumed to be lysine. The inhibitor did not inhibit elastase and subtilisin. From these results, the inhibitor LTI-II-4 was assumed to belong to the Kunitz soybean trypsin inhibitor family.

Antioxidant Activity

Studies demonstrated inhibitory activities of various aqueous extracts of food constituents on the chemiluminescence of hydroxyl radicals generated by Fenton's reagents with the order of scavenging efficiencies being *Prunus mume* > *Cordyceps sinensis* > *Lilium lancifolium* > *Astragalus membranaceu*s (Tsai et al. 2001).

All bulb extracts of six *Lilium* spp. (*L. regale, L. concolor, L. pumilum, L. leucanthum, L. davidii* var. *unicolor* and *L. lancifolium*) exhibited antioxidant activities, which generally correlated positively with the total phenolic contents ($R^2 = 0.68$ to 0.94), total flavonoid contents ($R^2 = 0.51$ to 0.89) and total flavanol contents ($r = 0.54$ to 0.95) (Jin et al. 2012). *L. lancifolium, L. leucanthum* and *L. davidii* var. *unicolor* were clustered in the third group with low phenolic content and weak antioxidant activity. Total phenolic content of *L. lancifolium* was 2827.25 GAE (gallic acid equivalent)mg/100 g, total flavonoid content was 227.24 rutin equivalent/100 g and total flavanol content was 112.12 catechin equivalent mg/100 g. The highest antioxidant activity (DPPH radical scavenging activity) was found for the bulb extract of *L. regale* (600.33 TE μmol/100 g), followed by *L. pumilum*, *L. lancifolium* (541.27 TE μmol/100 g), *L. leucanthum* and *L. concolor*, while *L. davidii* var. *unicolor* (404.48 TE μmol/100 g) yielded the lowest antioxidant capacity. In the ABTS-scavenging activity the ranking order was *L. regale* (*1173.28* TE μmol/100 g) > *L. concolor* > *L. pumilum* > *L. lancifolium* (*1075.51* TE μmol /100 g) > *L. leucanthum* > *L. davidii* var. *unicolor* (848.49 TE μmol/100 g). In the cupric-reducing potential assay, the ranking was as follows: *L. regale* (1,438.01 μmol TE/100 g dw) > *L. pumilum* > *L. concolor* > *L. lancifolium* (1,075.51 TE μmol/100 g) > *L. leucanthum* > *L. davidii* var. *unicolor* only 595.61 μmol TE/100 g dw). In the hydroxyl radical scavenging activity (HRSA) expressed as the percentage of free radical scavenging activity (%), the ranking order was *L. regale* (53.22 %) > *L. concolor* > *L. pumilum* > *L. leucanthum* > *L. lancifolium* (26.85 %) > *L. davidii* var. *unicolor* (22.45 %). Three phenolic acids (gallic acid, *p*-coumaric acid and chlorogenic acid), five flavonols (rutinoside, myricetin, rutin, quercetin and kaempferol), two monomeric flavanols [(+)-catechin and (−)-epicatechin] and one chalcone (phloridzin) were quantified. Rutin and kaempferol were the major phenolic components in the extracts.

The following phenylpropenoid glycerides were identified from bulbs of *Lilium lancifolium:* 1-*O*-feruloylglycerol (1), 1-*O*-*p*-coumaroylglycerol (2),1-*O*-caffeoyl-3-*O*-*p*-coumaroylglycerol(3),1,2-*O*-diferuloylglycerol (4), 1,3-*O*-diferuloylglycerol (5), 1-*O*-feruloyl-3-*O*-*p*-coumaroylglycerol (6) and 1,3-*O*-di-*p*-coumaroylglycerol (7) (Luo et al. 2012). The trend in antioxidant capacity was similar in all the three assays, namely, DPPH radical scavenging activity, ABTS radical cation scavenging activity and ferric-reducing antioxidant power (FRAP), with 3 > 1, 4, 5, 6 > 2, 7.

Anti-inflammatory Activity

Methanol root extracts from *Lilium lancifolium* exhibited anti-inflammatory effects which were attributable to downregulation of iNOS and COX-2 via suppression of NF-kappaB activation and nuclear translocation as well as blocking of ERK and JNK signalling in LPS-stimulated Raw264.7 cells (Kwon et al. 2010).

Cat Toxicity

A case of renal failure in a castrated male domestic short hair that consumed tiger lily flowers was reported by Berg et al. (2007).

Traditional Medicinal Uses

The bulb is anti-inflammatory, diuretic, emmenagogue, emollient and expectorant (Chopra et al. 1986; NPRI-SNU 1998). They are employed to relieve heart diseases, pain in the cardiac region and angina pectoris and prescribed for the treatment of myopic astigmatism and to strengthen the eyelid muscles. In Korea, they are used in traditional medicine to treat coughs, sore throats, palpitations and boils (NPRI-SNU 1998) and also commonly used to treat bronchitis, pneumonia, etc (Kwon et al. 2010). It has a sedative influence and is used for cough and tuberculosis (Yamaguchi et al. 1996). The flowers are carminative (Chopra et al. 1986). A tincture made from the flowering plant, harvested when in full flower, is used in the therapy of uterine neuralgia, congestion, irritation

and the nausea of pregnancy (Grieve 1971). It relieves the bearing-down pain accompanying uterine prolapse and is an important remedy in ovarian neuralgia.

Other Uses

Tiger lily is cultivated as a popular ornamental plant and as a medicinal plant.

Comments

Modern cultivars of edible lily bulb in Hokkaido were assumed to have been derived from a hybrid between *Lilium leichtlinii* var. *maximowiczii* ('Maximowicz's lily') and *Lilium lancifolium* Thunb. ('tiger lily') (Yamaguchi et al. 1996). The tiger lily, a triploid species, was monomorphic in cpDNA haplotype (I). It was assumed that the contributors to the modern cultivars were two landraces derived from wild populations of the Maximowicz's lily in Honshu of Japan and that the tiger lily contributed rarely as a cytoplasmic donor.

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Tulip gesneriana

Scientific Name

***Tulip gesneriana* L.**

Synonyms

Tulipa acuminata Vahl ex Hornem., *Tulipa acutiflora* DC. ex Baker [Illeg.], *Tulipa armena* f. *galatica* (Freyn) Raamsd., *Tulipa aurea* Raf., *Tulipa aximensis* E.P. Perrier & Songeon, *Tulipa baldaccii* Mattei, *Tulipa bicolor* Raf., *Tulipa billietiana* Jord., *Tulipa bonarotiana* Reboul, *Tulipa campsopetala* Delaun. ex Loisel., *Tulipa connivens* Levier, *Tulipa connivens* var. *luteoguttata* Levier, *Tulipa connivens* subsp. *luteoguttata* (Levier) K. Richt., *Tulipa connivens* var. *obtusata* Levier, *Tulipa connivens* subsp. *obtusata* (Levier) K. Richt., *Tulipa cornuta* Delile, *Tulipa coronaria* Salisb. [Illeg.], *Tulipa didieri* Jord., *Tulipa didieri* var. *billietiana* (Jord.) Baker, *Tulipa didieri* subsp. *billietiana* (Jord.) Nyman, *Tulipa didieri* var. *flavicans* Levier, *Tulipa didieri* subsp. *flavicans* (Levier) K. Richt., *Tulipa didieri* var. *mauriana* (Jord. & Fourr.) Baker, *Tulipa didieri* var. *planifolia* (Jord.) Baker, *Tulipa didieri* subsp. *platystigma* (Jord.) Nyman, *Tulipa elegans* Baker, *Tulipa etrusca* Levier, *Tulipa fransoniana* Parl., *Tulipa fransoniana* subsp. *mauriana* (Jord. & Fourr.) Nyman, *Tulipa fulgens* Baker, *Tulipa galatica* Freyn, *Tulipa gesneriana* var. *spathulata* (Bertol.) Nyman, *Tulipa grengiolensis* Thommen, *Tulipa hortensis* Gaertn., *Tulipa laciniata* Fisch. ex Bellerm., *Tulipa lurida* Levier, *Tulipa lutea* Freyn, *Tulipa marjolletii* E.P. Perrier & Songeon, *Tulipa mauriana* Jord. & Fourr., *Tulipa maurianensis* Didier, *Tulipa mauritiana* Jord., *Tulipa media* C. Agardh ex Schult. & Schult.f., *Tulipa montisandrei* J. Prudhomme, *Tulipa neglecta* Reboul, *Tulipa neglecta* var. *atroguttata* Levier, *Tulipa neglecta* subsp. *atroguttata* (Levier) K. Richt., *Tulipa passeriniana* Levier, *Tulipa perrieri* Marj. ex P. Fourn. [Illeg.], *Tulipa planifolia* Jord., *Tulipa platystigma* Jord., *Tulipa pubescens* Willd., *Tulipa repens* Fisch. ex Sweet, *Tulipa retroflexa* Baker, *Tulipa saracenica* E.P. Perrier, *Tulipa scabriscapa* Fox-Strangw., *Tulipa scabriscapa* var. *bonarotiana* (Reboul) Nyman, *Tulipa scabriscapa* var. *hawardeniana* Bertol., *Tulipa scabriscapa* var. *mixta* Fox-Strangw., *Tulipa scabriscapa* var. *neglecta* (Reboul) Nyman, *Tulipa scabriscapa* var. *primulina* Fox-Strangw., *Tulipa scabriscapa* var. *rebouliana* Bertol., *Tulipa scabriscapa* var. *sommieri* (Levier) Nyman, *Tulipa scabriscapa* var. *strangulata* (Reboul) Fox-Strangw., *Tulipa scardica* Bornm., *Tulipa segusiana* E.P. Perrier & Songeon, *Tulipa serotina* Reboul, *Tulipa serotina* var. *etrusca* (Levier) Nyman, *Tulipa sommieri* Levier, *Tulipa spathulata* Bertol., *Tulipa stenopetala* Delaun. ex Loisel., *Tulipa strangulata* Reboul, *Tulipa strangulata* var. *bonarotiana* (Reboul) Levier, *Tulipa strangulata* subsp. *bonarotiana* (Reboul) K. Richt., *Tulipa strangulata* subsp. *obtusa* K. Richt., *Tulipa strangulata* var. *obtusata* Levier, *Tulipa strangulata* var. *variopicta* (Reboul) Levier, *Tulipa strangulata* subsp. *variopicta* (Reboul) K. Richt., *Tulipa stricta* Stokes, *Tulipa suaveolens*

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var. *passeriniana* (Levier) Nyman, *Tulipa turcica* var. *media* (C. Agardh ex Schult. & Schult.f.) Regel, *Tulipa unguiculata* Raf., *Tulipa variopicta* Reboul, *Tulipa viridiflora* auct., *Tulipa vitellina* auct.

Family

Liliaceae

Common/English Names

Tulip, Didier's Tulip, Garden Tulip, Tall Garden Tulip

Vernacular Names

Brazil: Tulipa-De Jardim
Chinese: Yu Jin Xiang
Czech: Tulipán Zahradní
Danish: Havetulipan
Eastonian: Aedtulp
French: Tulipe De Gesner, Tulipe Des Jardins
German: Garten-Tulpe, Gesners Tulpe, Zucht-Tulpe
Icelandic: Garðatúlípani
India: Tyūlipa (Hindi)
Italian: Tulipano Di Gessner
Japanese: Chūrippu
Korean: Tyullib
Persian: Thoulyban
Portuguese: Tulipa
Russian: Tyul'pan
Serbian: Lala
Spanish: Tulipán
Swedish: Tulpan
Turkish: Tulbend, Turban
Vietnamese: Cây Uất Kim Hương

Origin/Distribution

Tulipa gesneriana is an early hybrid of uncertain, complex origin from which most of the cultivated forms of tulips are derived. *T. gesneriana* thus represents the collective name given to a large number of tulip cultivars. The genus *Tulipa* has a native range that stretches west to the Iberian Peninsula, through North Africa to Greece, the Balkans, Turkey, throughout the Levant (Syria, Israel, Palestine, Jordan) and Iran, north to the Ukraine, southern Siberia and Mongolia and east to the northwest of China (Christenhusz et al. 2013). Tulip's centre of diversity had been reported to be in central Asia—in Pamir, Hindu Kush and Tien Shan mountains (King 2005).

Agroecology

T. gesneriana is a cool temperature climatic crop. Its bulbs are planted out in autumn after chilling treatment, for its spring blooms. Bulbs of *T. gesneriana* need low temperature chilling requirement for shoot elongation following the completion of the floral organ formation (Moe and Wickstrøm 1973; Le Nard 1980; Le Nard and De Hertogh 1993; Inamoto et al. 2000). Le Nard (1980) found that after lifting the bulbs followed by immediate storage for 1, 3 or 5 weeks at 30 °C and then at 20 °C or 15 °C until the completion of flower differentiation, stage G and followed by either planting at 14–16 °C or cooled at 5 °C for 12 weeks before planting at 14–16 °C is beneficial to subsequent flower differentiation, rooting and flowering of tulip bulbs. The duration of bulb chilling greatly influences forcing duration and cut flower quality. Moe and Wickstrøm (1973) found that 12–14 weeks of low temperature treatment (5 °C) are optimal to obtain satisfactory shoot growth and flowering after planting. Cold areas will not require as many weeks chilling. Based on the shoot fresh weight and its perianth length, the best cut flower was obtained from the bulbs chilled at 2 °C for 12 weeks; longer chilling lowered cut flower quality (Inamoto et al. 2000).

Tulips prefer full sun to very light shade. It does best in well-drained, moist, friable, fertile soil. Top dressing with a complete fertilizer after planting and watering in has been recommended for crop establishment.

Edible Plant Parts and Uses

Tulip bulbs are edible (Uphof 1968; Usher 1974; Tanaka 1976). The bulbs can be used as a substitute for onion in cooking. They can be dried, powdered and added to cereals or flour for making bread. Tulip flowers are also edible (Roberts 2000; Wilson 2013). Cooking with tulips dates back to the late sixteenth century when unopened flower buds were cooked with peas or finely cut green beans. The petals have little taste but can be used to garnish a dish, chop a few petals and mixed them in a salad, or the entire flower (minus the pistil and stamens) used for a fruit bowl. The petals can be sugared and used to decorate a cake or eaten with syrup as a dessert. Some of the recipes with tulip flowers listed by Roberts (2000) included tulip syrup, tulips stuffed with chicken mayonnaise and three-bean salad with tulips. During the recent Chelsea Flower Show, Chef Pascal Aussignac used tulip flowers as the base for a unique starter, stuffing them with a mixture of mushrooms, tapioca and parmesan and surrounding them with a pea puree (Wilson 2013).

Botany

A bulbose, scapose to sub-scapose, perennial herb with papery to coriaceous, tunicate, often stoloniferous bulbs. Leaves 2–6(−12), cauline, alternate, distally reduced; lamina linear to narrow oblong, weakly fleshy (Plates 1, 2 and 3). Inflorescences 1(−4)-flowered. Flowers: perianth campanulate to cup-shaped; tepals 6, distinct, caducous, petaloid, variously coloured white, yellow, orange, pink, red, maroon, purple, variegated and with coloured streaks, often blotched near base (Plates 1, 2, 3, 4, 5, 6 and 7). Stamens 6, distinct, with filaments shorter than tepals, basally dilated; anthers basifixed, linear to narrowly elliptic, introrse. Ovary superior, 3-locular; style very short or absent; stigma prominently 3-lobed. Fruits, ellipsoid to subglobose, 3-angled, leathery capsules dehisces loculicidally. Seeds flat, numerous in 2 rows per locule.

Plate 1 Tulip flowers and foliage

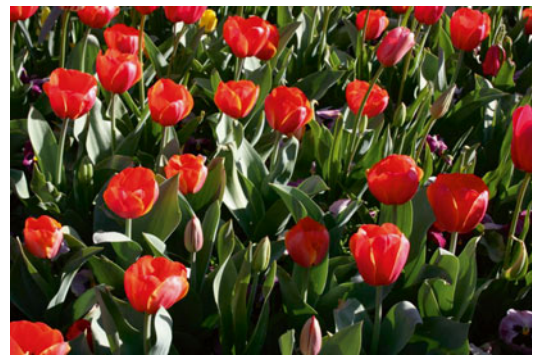

Plate 2 Orangey red tulip flower

Plate 3 Red tulip flowers

Nutritive/Medicinal Properties

Tulips were found to contain carotenoids, delphinidin, cyanidin, pelargonidin and flavonols in varying amounts (Van Eijk et al. 1987). For delphinidin, cyanidin and pelargonidin, a moderate

Plate 4 Yellow-orange variegated tulips

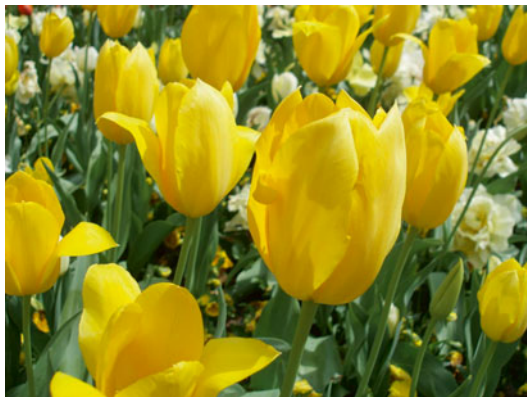

Plate 5 Yellow tulip flowers

Plate 6 Yellow tulip with fringed petals

Plate 7 White tulip showing the ovary and stigma

variation was found among 500 cultivars tested, and for carotenoids a rather large variation. For flavonols there was almost no variation. White cultivars contained only flavonols, or also low carotenoid concentrations. Yellow cultivars generally only contained carotenoids in addition to flavonols. Most pink and red cultivars contained cyanidin and pelargonidin and no delphinidin. Besides anthocyanidin, orange cultivars mostly contained high carotenoid concentrations and purple and violet cultivars contained delphinidin and cyanidin. A clear correlation was found between pigment composition and tulip flower colour (van Raamsdonk 1993). Anthocyanidins appeared to be absent in white and yellow flowers, while carotenoids were abundant in yellow, orange and red flowers. The main classes in the flower colour range were orange and red for pelargonidin; orange, red and pink for cyanidin; and purple for delphinidin.

Shibata (1956) and Shibata and Sakai (1958) isolated crystalline delphinidin 3-rhamnoglucoside and cyanidin 3-rhamnoglucoside from tulip flowers. Six anthocyanins were found in tulip flowers: keracyanin (cyanidin-3-glucorhamnoside), chrysanthemin (cyanidin-3-monoglucoside), tulipanin (delphinidin-3-glucorhamnoside), delphin (delphinidin-3,5-diglucoside), delphinidin-3-monoglucoside and pelargonidin-3-glucorhamnoside (Shibata and Ishikura 1959). Tulipanin was the major pigment in purplish varieties, keracyanin in dark red varieties and the unnamed pelargonidin-3-glucorhamnoside in orange-red varieties. Shibata and Ishikura (1960) in a chromatographic examination of 107 tulip varieties identified at least 6 anthocyanins, as well as various minor pigments including delph-

inidin 3-glucoside and delphinidin 3,5-diglucoside in tulip flowers, and most red to dark purple varieties contain two to four anthocyanins. *T. gesneriana* var. "Bishop" flowers contained four anthocyanins approximately in the following proportion: delphinidin (1 part), tulipanin (delphinidin-3-glucorhamoside) 7 parts), keracyanin (cyanidin-3-glucorhamnoside) (2 parts) and pelargonidin glucorhamnoside (trace) and var. Parrot Pierson flower contained three anthocyanins: keracyanin (4 parts), pelargonidin glucorhamnoside (4.5 parts) and tulipanin (1.5 parts) (Shibata and Sakai 1961).

Petals of tulip var. "Smiling Queen" contained cyanidin 3-glucoside (chrysanthemin), cyanidin-3-rhamnoglucoside (antirrhinin), pelargonidin 3-glucoside (callistephin) and pelargonidin 3-rhamnoglucoside (Halevy and Asen 1959). The petals of var. "Pride of Haarlem" also contained the 4 anthocyanins and delphinidin-3-rhamnoglucoside.

Five anthocyanins were identified from petals of tulip var. "President Eisenhower": delphinidin 3-glucoside, delphinidin 3-rhamnoglocoside, pelargonidin 3-glucoside, pelargonidin 3-rhamnoglucoside and a new isomer of pelargonidin 3-rhamnoglucoside (Halevy 1962). A yellow colouring pigment isolated from the flower of a garden variety "Golden Harvest" (cottage tulip strain with large deep lemon yellow flowers) was identified as rutin (quercetin-3-rutinoside) in a yield of 1 % on dry weight basis (Kawase and Shibata 1963). Its presence was also confirmed in a garden variety "Athleet" (Mendel tulip strain with pure white flowers).

Two anthocyanins, delphinidin 3–*O*–(6–*O*–(2–*O*–acetyl-α-rhamnopyranosyl)-β-glucopyranoside) and delphinidin 3–*O*–(6–*O*–(3–*O*–acetyl-α-rhamnopyranosyl)-β-glucopyranoside), were identified from the anthers of *Tulipa gesneriana* (Nakayama et al. 1999). These and delphinidin 3–*O*–(6–*O*–(α-rhamnopyranosyl)-β-glucopyranoside) made up over 80 % of the anthocyanin content in the dark purple anthers. Four major anthocyanins in orange-red *Tulipa* "Queen Wilhelmina" were identified as pelargonidin 3–*O*–[6″-*O*–(2‴-*O*–acetyl-α-rhamnopyranosyl)-β-glucopyranoside] (34 %) and cyanidin 3-*O*–[6″-*O*–(2‴-*O*–acetyl-α-rhamnopyranosyl)-β-glucopyranoside] (11 %) in addition to pelargonidin 3-*O*–(6″-*O*–α-rhamnopyranosyl-β-glucopyranoside) (29 %) and cyanidin 3-*O*–(6″-*O*–α-rhamnopyranosyl-β-glucopyranoside) (15 %) (Torskangerpoll et al. 1999).

Pelargonidin 3-rutinoside, cyanidin 3-rutinoside and their 2‴-acetyl esters pelargonidin 3-(2‴-acetylrutinoside) and cyanidin 3-(2‴-acetylrutinoside) were major anthocyanins in perianthes of the red, orange and pink tulip cultivars with their variant composition ratios (Nakayama et al. 2004). Cyanidin 3-rutinoside and delphinidin 3-rutinoside were major anthocyanins in the dark purple perianth bottoms. Delphinidin 3-rutinoside and its acetyl esters delphinidin 3-(2‴-acetylrutinoside) and delphinidin 3-(3‴-acetylrutinoside) were present in the dark purple anthers and pollens of several cultivars. Five anthocyanins in tulip flowers were identified as the 3-*O*-(6″-*O*-α-rhamnopyranosyl-β-glucopyranoside) of delphinidin (1), cyanidin (2) and pelargonidin (3) and the 3-*O*-[6″-*O*-(2‴-*O*-acetyl-α-rhamnopyranosyl)-β-glucopyranoside] of cyanidin (4) and pelargonidin (5) (Torskangerpoll et al. 2005). Tepals with blue nuances contained 1 as the major anthocyanin and no or just traces of pelargonidin derivatives. Those with 'magenta nuances' showed similar anthocyanin content with increased relative proportions of 2 at the expense of 1. Orange-coloured tepals were to a large extent correlated with high relative proportions of the pelargonidin derivatives 3 and 5. Within section *Tulipa* (subgenus *Tulipa*), considerable anthocyanin variation was observed. The anthocyanin and flavonol compositions in both purple- and blue-coloured tulip protoplasts were the same: delphinidin 3-*O*-rutinoside and major three flavonol glycosides manghaslin, rutin and mauritianin (Shoji et al. 2007). The Fe^{3+} content in the blue protoplast was ~9.5 mM, which was 25 times higher than that in the purple protoplasts. In further studies they identified a vacuolar iron transporter in *T. gesneriana* (TgVit1) that played an essential role in blue coloration as a vacuolar iron transporter in tulip petals (Momonoi et al. 2009).

The perianths of *Tulipa gesneriana* yielded 3-glucosides, 3-gentiobiosides and 3-rutinosides of 7-*O*-glucuronosylquercetin and 7-*O*-glucuronosylkaempferol (Budzianowski 1991). Isovitexin and 3-glucosides of kaempferol and quercetin were also detected. A mixture of flavonoid glucuronides, consisting of 7-*O*-glucuronides of kaempferol and quercetin 3-*O*-rutinosides, 3-*O*-gentiobiosides and 3-*O*-glucosides, was isolated from the perianths of *Tulipa gesneriana* L. var. "Paradae" (Budzianowski et al. 1999). During tulip bulb cooling, the leaf content of quercetin and kaempferol (after hydrolysis) substantially increased (in comparison to uncooled bulbs stored at 17 °C) (Saniewski and Horbowicz 2005). The anther content of quercetin and apigenin greatly increased during storage of bulbs at high temperature and was low in cooled bulbs.

Tuliposides, the glucose esters of 4-hydroxy-2-methylenebutanoate and 3,4-dihydroxy-2-methylenebutanoate, are major secondary metabolites in tulip (*Tulipa gesneriana*) (Bergman and Beijersbergen 1968; Tschesche et al. 1968, 1969; Slob and Varekamp 1977; Christensen and Kristiansen 1999; Nomura et al. 2012). All parts of tulip plants, such as bulbs, roots, stems, leaves, petals, stamens and pistils, accumulate large amounts (approximately 0.2–2 % [w/fresh weight]) of tuliposides, whereas tulipalins are far less abundant than tuliposides and sometimes barely detectable (Beijersbergen and Lemmers 1972; Christensen and Kristiansen 1999). Christensen and Kristiansen (1999) reported that tulips contained tuliposides: 1-tuliposide A, 6-tuliposide A, tuliposide D, tuliposide B, 1-tuliposide B, 6-tuliposide B and tuliposide F, and tulipans: tulipalin A and (−)-tulipalin B and (−)-tulipalin B The predominant compounds were 6-tuliposide A (1.5 %) and B (1.3 %) of fresh weight. 6-Tuliposide A and tulipalin A appeared to be the major allergens in tulips, although tuliposide D and F may also contribute to the allergenic properties. Tulipalin A and (−)-tulipalin B occur in intact tulips and are not only produced in response to microbial attack or after excision of the plants. The changes in tulipalin A (α-methylene-γ-butyrolactone) and its precursor tuliposide A contents were measured in tissue culture of tulip explants (van Rossum et al. 1998). Relatively large amounts of free tulipalin A were found to be present in the scale tissue and a small amount of tuliposide A. In young developing shoots, the situation was reversed: tuliposide is the main component but the concentration is much lower. During the tissue culture period (10 weeks), an increase was found in both tulipalin A and tuliposide A. Nomura et al. (2012) purified a lactone-forming carboxylesterase: tuliposide-converting enzyme (TCE) from tulip bulbs that catalysed the conversion of tuliposides to tulipalins, the lactonized aglycons of tuliposides, tulipalins, which function as defensive chemicals due to their biological activities. They named the enzyme tuliposide A-converting enzyme (TCEA) and verified that TgTCEA catalysed the conversion of 6-tuliposide A to tulipalin A. Earlier, Christensen and Kristiansen (1999) reported that tulips contained tuliposides: 1-tuliposide A, 6-tuliposide A, tuliposide D, tuliposide B, 1-tuliposide B, 6-tuliposide B and tuliposide F, and tulipans: tulipalin A and (−)-tulipalin B and (−)-tulipalin B. The predominant compounds were 6-tuliposide A (1.5 %) and B (1.3 %) of fresh weight. 6-Tuliposide A and tulipalin A appeared to be the major allergens in tulips, although tuliposide D and F may also contribute to the allergenic properties. Tulipalin A and (−)-tulipalin B occur in intact tulips and are not only produced in response to microbial attack or after excision of the plants. Kato et al. (2009a) purified and characterized a tuliposide-converting enzyme from bulbs of *Tulipa gesneriana* that converted 6-tuliposide into tulipalin. The enzyme appeared to be a dimer, with molecular mass of each subunit being 34,900; it had maximum activity and stability at neutral pH and moderate temperature. The enzyme preferentially acted on such glucose esters as 6-tuliposides, and to a lesser extent on p-nitrophenyl acetate.

DNA synthesis-inhibiting proteins, designated tulipin 1 and 2, were isolated from the bulbs of *Tulipa* sp. (Gasperi-Campani et al. 1987). Tulip bulb was found to contain chitinase-1 and -2 (TBC-1 and -2) (Yamagami and Ishiguro 1998). Both consisted of 275 amino acid residues and had molecular masses of 30,825 and 30,863,

respectively, and shared 247 identical residues (= 90 %) identity. TBC-1 and –2 were found to be class IIIb chitinases. Novel antimicrobial peptides (AMP), designated Tu-AMP 1 and Tu-AMP 2, were purified from the bulbs of tulip (*Tulipa gesneriana*) (Fujimura et al. 2004). Tu-AMP 1 and Tu-AMP 2 had molecular masses of 4,988 and 5,006 Da and were thionin-like antimicrobial peptides; they bind to chitin in a reversible way. Half of all amino acid residues of Tu-AMP 1 and Tu-AMP 2 were occupied by cysteine, arginine, lysine and proline.

Antimicrobial Activity

The concentrations of antimicrobial peptides from tulip bulb, designated Tu-AMP 1 and Tu-AMP 2 peptides required for 50 % inhibition (IC_{50}) of the growth of plant pathogenic bacteria and fungi were 2–20 μg/mL (Fujimura et al. 2004).

Tuliposides had been reported to exhibit antimicrobial activities (Tschesche et al. 1968, 1969; Shoji et al. 2005). Through extensive structure–activity relationship studies using synthetic analogues of tuliposides and tulipalins, it was clearly demonstrated that the glucose moiety of tuliposides was not indispensable for their inhibitory activities and that the formation of tulipalins played a key role in antimicrobial action (Shigetomi et al. 2010, 2011). A fungitoxic substance isolated from extracts from the white skins of tulip bulbs, from the fleshy bulb scales and from the flower pistils was identified as α-methylene butyrolactone (tulipan A) (Bergman 1966; Bergman et al. 1967). It was found to be fungitoxic to *Fusarium oxysporum*, inhibiting its growth (Bergman 1966; Bergman and Beijersbergen 1968). Extracts of pistils, white bulb skins and outer bulb scales of tulip were found to contain a precursor of the fungitoxic substance tulipalin A (α-methylene butyrolactone) (Beijersbergen and Lemmers 1972). The findings demonstrated that, in vitro, the precursor must be split chemically or enzymically to yield the fungitoxic tulipalin A. Fungitoxic lactones tulipalin A and B were extracted from crude extracts of various parts of the tulip (Beijersbergen 1972). Kato et al. (2009b) developed a facile method of enzyme-mediated conversion of 6-tuliposide to α-methylene-γ-butyrolactone (tulipalin) from tulip tissues. Strong antimicrobial activity was observed in water extracts of tulip anthers (Kazuaki et al. 2005; Shoji et al. 2005). The bioactive compound isolated was 6-tuliposide B (6-*O*-((*S*)4′, 5′-dihydroxy-2′-methylenebutyryl)-D-glucopyranose). It showed a strong growth inhibition against Gram-positive and Gram-negative bacteria and certain fungicide tolerant fungal strains except for a yeast. Tulipalins and tuliposides were found to be inhibitors of the enzyme MurA, an essential enzyme in peptidoglycan biosynthesis in bacteria and therefore a target for the discovery of novel antibacterial compounds (Mendgen et al. 2010). Shigetomi et al. (2010) also found bacterial MurA to be one of the major molecular targets of 6-tuliposide B using a broad panel of bacterial strains. Tuliposides and tulipalins showed antifungal activities against most of the strains tested at high concentrations (2.5 mM), while *Botrytis tulipae* was resistant to tuliposides (Shigetomi et al. 2011). Tulipalin A showed higher inhibitory activity than 6-tuliposide B and tulipalin B. Both the tuliposides and tulipalins showed pigment-inducing activity against *Gibberella* zeae and inhibitory activity against *Fusarium oxysporum* f. sp. *tulipae*.

DNA Synthesis-Inhibiting Activity

Inhibition of DNA synthesis by tulipalin, isolated from the bulb, varied in intact cells according to the cellular types studied, with a minimum ID_{50} (concentration giving 50 % inhibition) of 400 ng/mL in neuroblastoma cells. The effect was reversible. No effect was obtained in cell lysate. RNA and protein synthesis were unaffected. The acute toxicity, evaluated in Swiss mice, gave an LD_{50} of 6.1 mg/kg body weight.

Wound Healing Activity

A mixture of flavonoid glucuronides, consisting of 7-*O*-glucuronides of kaempferol and quercetin

3-*O*-rutinosides, 3-*O*-gentiobiosides and 3-*O*-glucosides, isolated from the perianths of *Tulipa gesneriana* showed protective activity (59.8 %) against the increased (both chloroform and histamine) skin vascular permeability in rabbits compared to 45.5 % with troxerutin (Budzianowski et al. 1999).

Agglutinating/Mitogenic Activity

A lectin of molecular mass 67,000, which agglutinated specifically the yeast cells of the *Saccharomyces* genus, was isolated from tulip bulbs (*Tulipa gesneriana*) (Oda and Minami 1986). Another agglutinin with molecular mass of 40,000 which agglutinated animal erythrocytes was purified from the tulip bulbs (Oda et al. 1987). This agglutinin agglutinated mouse and rat erythrocytes at a minimum concentration of 2 and 30 μg/mL, respectively, but did not agglutinate erythrocytes from other animals and yeasts even at a concentration of 1,000 μg/mL. *Tulipa gesneriana* agglutinin (TGA) showed novel carbohydrate-binding specificity and preferentially recognized triantennary oligosaccharides with galactose residues at non-reducing termini and a fucose residue linked through alpha (1–6) linkage at chitobiose portion of the reducing termini but not tetraantennary carbohydrates (Nakajima et al. 2004).

Modification of lysine, tyrosine, histidine, aspartic acid and glutamic acid residues did not affect the agglutinating activity of the *Tulipa gesneriana* lectin (TGL) (Oda et al. 1989). Modification of two arginine residues per subunit in the lectin with either 2,3-butanedione or phenylglyoxal and modification of tryptophan with *N*-bromosuccinimide or 2-hydroxy-5-nitrobenzyl bromide led to an almost complete loss of activity. *Tulipa gesneriana* lectin-erythrocyte (TGL-E) which agglutinates mouse erythrocytes showed a potent mitogenic activity on mouse spleen cells and human peripheral blood lymphocytes, but exhibited only slight mitogenic activity on mouse thymus cells (Oda et al. 1991). Its subunit alpha with a molecular weight (MW) of about 26,000 showed a potent mitogenic activity as did that of native lectin, but subunit beta with a MW of about 14,000 showed no activity, indicating that the mitogenic activity of TGL-E originates from subunit alpha. The other lectin in tulip bulbs, *Tulipa gesneriana* lectin yeast, showed no mitogenic activity on mouse spleen, thymus cells or human peripheral blood lymphocytes.

Mutagenic Activity

Crude extracts from *Tulipa gesneriana* bulbs were found to activate promutagenic 7,12-dimethylbenz[a]anthracene (DMBA) in the *Salmonella* mutagenicity assay (Pánková et al. 1986). The frequency of his + revertants increased in relation to both the promutagenic dose and the amount of bulb extract in the mixture and, under optimal conditions, was more than 50 times higher than the value found after the action of the promutagen alone. The addition of NADP and glucose 6-phosphate to the incubation mixture did not seem to be obligatory.

Traditional Medicinal Uses

Soothing poultice of the petals used for burns, skin rashes, insect bites and bee stings (Roberts 2000). In the seventeenth century, young girls crushed red tulip petals and rubbed on cheeks so that the petals impart their colour and the juice would help clear up any spots. Crushed petals and juice from the flower base are used to soothe scratches and rough skin on work-worn hands of tulip growers in Holland.

Other Uses

Tulips are the world's most popular spring ornamental bulb flowers and are widely grown in temperate areas. They make beautiful flower gardens, beds and borders in parks and house gardens and also as potted plants. Tulips make excellent and long-lasting cut flowers in lovely and beautiful flower arrangements. They can be used for bridal

bouquets, table centrepieces and general wedding decor. They are also a great choice for a baby shower or as a gift for a new baby.

Comments

Commercial tulip production occurs in some 15 countries worldwide, with the largest production area in the Netherlands with 10,800 ha (88 %), followed by the next five major countries—Japan (300 ha, 2.5 %), France (293 ha, 2.4 %), Poland (200 ha, 1.6 %), Germany (155 ha, 1.3 %) and New Zealand (122 ha, 1 %) (Buschman 2005). The Netherlands produces 4.32 billion tulip bulbs, of which 2.3 billion (53 %) are used as the starting material for the cultivation of cut flowers. No fewer than 1.3 billion of these (57 %) are grown in the Netherlands as cut flowers. The remainder are exported to countries within the European Union (0.63 billion) and outside the European Union (0.37 billion). The tulips cultivated in the Southern Hemisphere are scheduled for autumn flowering (October–December) in the Northern Hemisphere and are exported to the United States, the Netherlands, Japan and Canada.

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Limnocharis flava

Scientific Name

***Limnocharis flava* (L.) Buchenau**

Synonyms

Alisma flava L., *Damasonium flavum* Mill., *Limnocharis emarginata* Humb. & Bonpl. nom. illeg., *Limnocharis laforesti* Duchass., *Limnocharis plumieri* Richard nom illeg.

Family

Limnocharitaceae also placed in Butomaceae

Common/English Names

Hermit's Waterlily, Limnocharis, Sawah-Flower Rush, Sawah Lettuce, Velvetleaf, Velvet Leaf, Yellow Burrhead, Yellow Burhead

Vernacular Names

Brazil: Barata
Chinese: Huang Hua Lin
India: Kalmi, Kengkong (Bengali), Manja Payal (Malayalam)
Dutch: Gele Sawahsla
Indonesia: Bengok, Berek, Gènjèr, Gunda Wehehan, Tempujung, Timpujung, Tjèntongan, Chengtongan, Wewean, Wewehan (Javanese), Echeng (Malay), Endjer (Madurese), Bang-Eng, Gèndjèr, Gendot, Saber (Sundanese)
Japanese: Kibana Omodaka
Laos: Kaanz Choong Phak Khan Chong
Malaysia: Emparuk (Sarawak), Kakatung, Balehir (Sabah), Èt jèng, Paku Rawan, Jinjir
Philippinese: Cebolla De Chucho (Tagalog)
Spanish: Cebolla De Chucho
Thai: Bonchin, Talapatrusi, Nangkwak
Vietnamese: Cù Nèo, Kèo Nèo

Origin/Distribution

The species is native to Tropical America—Southern Mexico and Antilles to Peru and Central Brazil. It has now naturalized in south-east Asia.

Agroecology

Limnocharis is found in warm tropical and subtropical areas. It is an aquatic, erect, clump-forming and rapidly spreading herb that is generally found growing rooted in fertile, muddy or marshy conditions. It is common in rice fields, ditches, waterways and ponds.

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Edible Plant Parts and Uses

Limnocharis flava is a very popular and common vegetable in India, Vietnam, Thailand, Laos, Cambodia, Malaysia and Indonesia (Burkill 1966; Ochse and Bakhuizen van den Brink 1980; Voon et al. 1988; Van den Bergh 1993; Tanaka and Nguyen 2007; Maisuthisakul et al. 2008). Young leaves, petioles, open and unopened flowers and stalks are consumed as vegetables (Plates 2, 3 and 4). In Vietnam, the leaves, flower and petiole are eaten as vegetables commonly by dipping in steam boat dishes with other vegetables. In Sabah, they are boiled and eaten as salad or fried with shrimp paste or boiled with other vegetables. In Sarawak, similar parts are blanched in hot water or slightly heated over a fire before being eaten as ulam. It is also prepared as a cooked vegetable and eaten like spinach. In Thailand, young inflorescences are collected and eaten fresh with chilli sauce and as side dish together with other hot and spicy dishes. In Indonesia, the young leaves, petioles and inflorescences are eaten as lalab or sepan.

Botany

Perennial herb arsing to 1 m high from a short thick erect rhizome and rooting in mud (Plate 1), strongly tillering. The scapes erect, 20–40 cm high; leaves erect or ascending, not floating, often exceeding the scapes, long-petiolate up to 85 cm, the petiole triangular vaginate bearing pale green leaves; lamina velvety up to 28 cm long and 20 cm wide with 11–15 parallel veins, variable in shape, lanceolate to oblong-elliptic when young and becoming oval with age (Plates 1 and 2). Inflorescence umbelliform, 3–15 flowered, peduncle 50–70 cm long, erect; flower in the axils of membranous bracts; pedicel 2–5 cm long. Sepals 3, ca. 2 cm long, thin, ovate-elliptic, yellow (Plates 1, 4 and 5). Petals 3, ovate to orbicular, 1.5–2.5 cm long, yellow. Stamens many, surrounded by a whorl of staminodes. Ovary superior, many-carpelled, densely crowded and laterally compressed, stigmata sessile and linear. Fruit compound, stalk down-curved, composed of the ripe carpels forming together a globose or broadly ellipsoid head, 1.5–2 cm in diameter, enclosed by the sepals. Seed numerous small dark brown, horse-shoe shaped seed, 1–1.5 mm across with thin transverse ridges.

Plate 1 Plant habit growing in mud in a ditch

Plate 2 Leaves and petioles on sale in a local market

Plate 3 Flower buds and stalks on sale in a local market

Plate 4 Flower, buds and stalks harvested as vegetables

Plate 5 Close up of flower

Nutritive/Medicinal Properties

Nutrient composition of the edible parts comprising young shoots and inflorescence (per 100 g) was reported by Saupi et al. (2009) as follows: moisture 79.34 %, energy 343.26 kJ, carbohydrate 14.56 %, crude protein 0.28 %, crude ft 1.22 %, crude fibre 3.81 %, K 4,202.50 mg, Ca 770.87 mg, Mg 228.10 mg, Na 107.72 mg, Zn 0.66 mg and Cu 8.31 mg.

Leaves of *Limnocharis flava* contain the following nutrients per 100 g edible portion (Leung et al. 1972): energy 33 kJ, moisture 90 %, protein 1.7 g, fat 0.2 g, total carbohydrates 7.7 g, ach 0.4 g, Ca 62 mg, P 33 mg, Fe 2.1 mg, β-carotene equivalent 2,280 ug, thiamin 0.07 mg and ascorbic acid 54 mg.

Nutrient composition of the leaves (per 100 g edible portion) analysed in Thailand was reported as follows: energy 341.9 Kcal, protein 11.3 g, carbohydrate 55.4 g, fat 8.4 g, ash 11.4 g, dietary fibre 52.6 g, Ca 452.8 mg, Fe 285.8 mg and vitamin c 452.8 mg (Maisuthisakul et al. 2008). The concentration of plant extract necessary to decrease DPPH radical scavenging activity by 50 % (EC_{50}) was expressed as antiradical activity (1/EC50) which was found to be 0.1; the total phenolic content was 5.4 mg GAE/g dry weight and total flavonoids 3.7 mg RE (rutin equivalent)/g dry weight basis. Antioxidant activity correlated with phenolic and flavonoid contents.

Other Uses

Its foliage is used as pig feed and green manure. Slime from the plant is used as soap. The plant is also grown as ornamentals in ponds.

Comments

Limnocharis flava is deemed a major noxious weed in many countries as it forms dense, choking infestations that obstruct water flow. It is a serious weed of rice fields, waterways, lakes and irrigation canals.

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Magnolia denudata

Scientific Name

Magnolia denudata **Desrousseaux**

Synonyms

Gwillimia yulan (Desf.) Kostel., *Lassonia heptapeta* Buc'hoz, *Magnolia alexandrina* Steud., *Magnolia citriodora* Steud., *Magnolia conspicua* Salisb., *Magnolia conspicua* var. *rosea* Pamp., *Magnolia cyathiformis* Rinz ex K. Koch, *Magnolia denudata* var. *angustitepala* T.B. Chao & Z.S. Chun, *Magnolia denudata* var. *pyriformis* T.D. Yang & T.C. Cui, *Magnolia heptapeta* (Buc'hoz) Dandy, *Magnolia precia* Corrêa ex Vent. [Invalid], *Magnolia purpurea* var. *denudata* (Desr.) Loudon, *Magnolia spectabilis* G. Nicholson [Invalid], *Magnolia superba* G. Nicholson [Invalid], *Magnolia triumphans* G. Nicholson [Invalid], *Magnolia yulan* Desf., *Michelia yulan* (Desf.) Kostel., *Yulania conspicua* (Salisb.) Spach, *Yulania denudata* (Desr.) D.L. Fu, *Yulania denudata* subsp. *pubescens* D.L. Fu, et al., *Yulania pyriformis* (T.D. Yang & T.C. Cui) D.L. Fu

Family

Magnoliaceae

Common/English Names

Hsin-I, Jade Lily, Jade Orchid, Lily Tree, White Magnolia, White Yulan, Yulan, Yulan Magnolia, Yulan Tree

Vernacular Names

Brazil: Magnolia
Chinese: Bai Yu Lan, Pai Yu Lan, Yu Lan Hua Pian, Yu Lan Hua P'ien
Czech: Šácholan Obnažený, Šácholan Olysalý
Estonian: Sile Magnolia
French: Magnolia Denude, Magnolia Yulan, Yulan
German: Yulan-Magnolie
Japanese: Haku-Mokuren
Korean: Bag Mok Ryeon
Polish: Magnolia Naga
Swedish: Yulanmagnolia

Origin/Distribution

White Magnolia is native to central and eastern China, Korea and Japan.

Agroecology

In its native range, it occurs in mixed forests of evergreen broad-leaved trees and deciduous broad-leaved trees, woods, thickets and open

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areas at elevations of 500–1,000 m and can withstand cold winters. They do best in a wind-protected, warm location in full sun or morning shade with afternoon sun.

Edible Plant Parts and Uses

Fresh petals of partially opened flowers are dipped in batter and deep fried and served hot as delicacy (Hu 2005). The flowers, after removal of the calyx, are also pickled and used for flavouring rice (Facciola 1990).

Botany

A deciduous upright, sparsely branched tree 6–18 m high with an ovate crown, grey-brown bark and stout pilose branches becoming glabrous with age. Leaves are alternate, coriaceous, obovate-oblong or broadly elliptic 10–18 cm by 6–10 cm with acute apex and cuneate base, entire margin, dark green, glabrous above and pale silvery-green and puberulous lower surface. Flowers solitary, bisexual, large, usually fragrant, 10–15 cm across, appearing before leaves; tepals 6–12 in 3–4 whorls, subequal, spatulate, ivory-white (Plates 1 and 2) or base tinged pink; stamens numerous red, caducous, with flat filaments and introse anthers; carpels numerous, spirally arranged, with 2 ovules per carpel, style curved outward and stigma papillate. Fruit is aggregated to form a cylindrical follicetum, reddish-brown, 8–12 cm long with many 2-seeded follicles. Seeds red, fleshy and oily.

Nutritive/Medicinal Properties

Magnolia species including *M. denudata* were reported to contain various compounds, including alkaloids, terpenoids, lignans and neolignans (Noshita et al. 2009).

The yields of *M. denudata* essential oils were 0.03–0.05 % in the fresh leafy shoots (branchlets and leaves), 0.04–0.05 % in the leaves, 0.29–0.67 % in the flower buds and 0.08–0.09 % in the opened flower in full bloom (Fujita et al. 1977). The main components of essential oils of the fresh leaves were β-caryophyllene (15.3–18.4 %), (+)-*trans*-nerolidol (21.9–25.9 %) and α-humulene (3.5–8.4 %); those of the branchlets were 1,8-cineole (17.6 %), (+)-terpinen-4-ol (18.2 %) and (−)-α-terpineol (10.9 %); those of the barks were 1,8-cineole (43.5 %), (+)-terpinen-4-ol (8 %) and (−)-α-terpineol (7.3 %); those of the flowers were 1,8-cineole (34–36.1 %), β-pinene and sabinene (12–30 %), *n*-pentadecane (4–9.1 %) and (−)-α-terpineol (4.4–7.6 %); and those of the flower buds were 1,8-cineole (49–57.2 %), β-pinene and sabinene (4–11.5 %) and (−)-α-terpineol (6.2–8.3 %).

Other minor identified constituents of the opened flower oil included α-pinene (2.3–4.1 %), camphene (0.3 %), β-myrcene (0.1–0.5 %), limonene

Plate 1 Profuse flowering yulan magnolia

Plate 2 Side view of yulan magnolia flowers

(0.9–1.5 %), *p*-cymene (1.2–1.4 %), *cis*-3-hexen-1-ol (0.1 %), *trans*-linalool oxide (0.1–0.2 %), *cis*-linalool oxide (0.5–1.7 %), α-copaene (0.3–0.8 %), β-bourbonene (0.9 %), (+)-terpinen-4-ol (1.8–2 %), (−)-bornylacetate (1–2 %), β-caryophyllene (1.1–1.9 %), α-humulene (0.3–0.4 %), γ-muurolene (0.1 %), germacrene-D (2.1–2.6 %), α-citronellyacetate (0.7–1 %), α-muurolene (0.2–0.3 %), β-selinene (0.2 %), gerany lacetate (0.2–0.3 %), δ-cadinene (0.8–1.1 %), γ-cadinene (0.1 %), *n*-nonadecane (0.1–0.6 %), caryophylleneoxide (0.3–1.1 %), (+)-*trans*-nerolidol (1–2.9 %), elemol (0.3–0.8 %), T-muurolol (0.1 %), β-eudesmol 2.2–5.5 %, *p*-cymen-8-ol (trace), α-cadinene (trace) and calamenene (trace). The flower oil also contained 89.2 % of $C_{15}H_{32}$ and 3.7 % of $C_{19}H_{40}$ paraffins. The main components found in the essential oil of flowers from three kinds of Xinyi (*Magnolia biondii, Magnolia denudata* and *Magnolia sprengeri*) were 1,8-cineole, sabinene, β-pinene, α-pinene and *trans*-caryophyllene (Wu 2000). Eleven marker lignan components were identified in *Magnolia* flowers including *M. denudata*: eudesmin (1), magnolin (2), lirioresinol dimethyl ether (3), epimagnolin (4), aschantin (5), kobusin (6), fargesin (7), burchellin (8),5-allyl-5-methoxy-3-methyl-2-piperonyl-2,3,5,6-tetrahydro-6-oxobenzofuran (9), ((1S,5S,6S,7S)-5-allyl-6-methyl-3-methoxy-7(3′,4′-dimeth oxyphenyl)-bicyclo[3.2.1]oct-3en-2,8-dione (10) and (2R,3S,3aR)-3a-allyl-5-methoxy-3-methyl-2-piperonyl 2,3,3a,6-tetrahydro-6-oxobenzofuran (11) (Xu et al. 2003). Compounds 8–11 were commonly found and the most abundant markers in *M. denudata and M. denudata* var. *purpurascens* were burchellin (1.1–2.5 %) and (2*R*,3*S*,3a*R*)-3a-allyl-5-methoxy-3-methyl-2-piperonyl2,3,3a,6-tetrahydro-6-oxobenzofuran (1.8–4.9 %).

Naphthalene was isolated from the ether extract of the petals and gynoecium of *M. denudata* flowers (Azuma et al. 1996). The lignin, licarin was isolated from the flower bud (Kwon et al. 1999). A new tricyclo[4.2.0.0(2,8)]octane-type neolignan, 6-allyl-7-(3,4-dimethoxyphenyl)-2,3-dimethoxy-8-methyl-tricyclo[4.2.0.0(2,8)]oct-3-en-5-one, together with 15 known tetrahydrofuran-type and bis-tetrahydrofuran-type lignans and neolignans were isolated from the flower buds of *Magnolia denudata* (Li et al. 2005). The known lignans and neolignans were identified as veragensin (1), galgravin (2), a lignan (3), fargesone B (4), lariciresinol (5), a lignan (6), fargesin (7), (−)-methylpiperitol (8), magnolone (9), (−)-galbacin (10), licarin B (11), acuminatin (12), hancinone (13), burcellin (14) and a neolignan (15). Six melanin biosynthesis inhibitory compounds identified as asfargesin, kobusin, aschantin, magnolin, rel-[7s,8s,8′s]-3,4,3′,4′-tetra-methoxy-9,7′-dihydroxy-8.8′,7.O.9′-lignan and oplodiol were isolated from the methanol extract of *M. denudata* flowers (Xu et al. 2004). In *Magnolia denudata* flowers, several quercetin glycosides, and particularly rutin, were converted to coloured substances via *o*-quinones by the action of phenolase (Sato et al. 1992). *Magnolia denudata* 'Feihuang' flowers emitted the following major volatile organic compounds: perillene (62.46 %), *cis*-linalool oxide (9.56 %) and *cis*-verbenone (7.54 %) making a total of 79.6 % (Ding et al. 2013).

Machilin G and four neolignans denudatin A and B, denudadione B and fargesone A were isolated from young fruits of *Magnolia denudata* (Noshita et al. 2008). Two new phenolic derivatives, named denudalide and denudaquinol and a known neolignan compound (denudatin A), were isolated from the mature fruit (Noshita et al. 2009).

New neolignans, denudatin A and B (hydrobenzofuranoids) and denudatone [spiro(5,5) undecanoid], together with three known neolignans, veraguesin, futoenone and burchellin, were isolated from the aerial parts (Iida et al. 1982). The ethyl acetate fraction of the methanol extract of powdered twigs of *M. denudata* afforded seven new neolignan derivatives, named denudanolides A, B, C and D; denudadiones A, B and C; along with 18 known lignan and known neolignan compounds identified as (1S,5S,6S,7S)-5-allyl-6-methyl-3-methoxy-7(3,4-methylendioxyphenyl)-bicyclo[3.2.1]oct-3-en-2,8-dione; denudatin B; denudatin A; neolignan; kadsurin A; neolignan; neolignan; burcellin; neolignan; mirandin A; licarin B; acuminatin; veraguensin; grandisin; yangambin; syringresinol; isodihydrofutoquinol A; and isodihydrofutoquinol B (Kuroyanagi et al. 2000).

Twenty compounds were isolated from *Magnolia denudata* leaves including 16 lignans, which belong to 6 structural types (Du et al. 2001). Except for (7R, 8S, 1′S)-δ-8′ -1′, 4′- dihydro-5′-methoxy-3,4-methylenedioxy-4′-oxo-7.0.2′, 8.1′-neolignan; magliflonenone; 2, 5′-diene-2′, 8′-epoxy-5′-methoxy-8-methyl-4′-oxo-3,4-methylenedioxy-spiro (5, 5)-undecane; veraguensin; and β-sitosterol; the other 15 compounds were obtained from this species for the first time. Compound 2 was shown to have significant inflammation inhibition effect on mice hind paw oedema induced by carrageenan. An alkaloid, tyramine was isolated from the leaves (Matsutani and Shiba 1975). The alkaloids armepavine, asimilobine, liriodenine, *N*-norarmepavine, nornuciferine and roemerine were isolated from the leaves (Furmanowa and Jozefowicz 1980).

Alkaloids were found in the green and yellow leaves and also in the branches of *M. denudata* (Ziyaev et al. 1999).

Alkaloids salicifoline chloride and magnocurarine were isolated from the root bark (Tomita and Nakano 1952). A quaternary alkaloid, magnoflorine, was identified from *Magnolia denudata* root (Nakano 1956). A chloroform extract of the root bark of *Magnolia denudata* afforded sesquiterpenes parthenolide and costunolide; three phenylpropanoids, myristicine aldehyde, *trans*-isomyristicine and deacyllaserine; and four lignans viz. sesamin, kobusin, eudesmin and pinoresinol (Funayama et al. 1995).

Antioxidant Activity

At doses of 100 and 200 mg/kg, the ethanol flower extract showed significant inhibition on both change in paw volume and vascular permeability (Lim and Park 2005). The extract at 100 mg/kg significantly inhibited PAR2 agonist-induced myeloperoxidase (MPO) activity in paw tissue. These results indicate that ethanol flower extract had anti-inflammatory activity in PAR2-mediated paw oedema.

The ethyl acetate fraction of the ethanol flower extract of *M. denudata* showed strong 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity with a 50 % inhibition concentration (IC_{50}) of 0.20 mg/mL, and total antioxidant activity was 0.90 mg AA (ascorbic acid) eq/100 mg (Nho et al. 2009). The ethyl acetate fraction contained the highest phenolic and flavonoid contents of 427.10 mg garlic acid eq/g and 356.05 mg catechin eq/g, respectively.

Methanol (MeOH) and dichloromethane (CH_2Cl_2) extracts of *M. denudata* flower buds inhibited dose-dependently generation of reactive oxygen species (ROS) in HT 1,080 cells (Seo 2010). MeOH and CH_2Cl_2 extracts were combined and fractionated with *n*-hexane, 85 % aqueous MeOH and *n*-butanol (*n*-BuOH). Both *n*-hexane-soluble and 85 % aqueous-soluble fractions showed strong radical scavenging activity in the cellular system and further afforded five known lignans, namely, (+)-eudesmin, (+)-magnolin, (+)-epimagnolin A, (+)- fargesin and (7S*,8S*, 8′S*)-3,4,3′,4′-tetramethoxy-9,7′-dihydroxy-8.8′,7.0.9′-lignan, all of which exhibited significant radical scavenging effect on intracellular ROS in a dose-dependent manner. The total phenolic contents of the methanolic extracts of white-coloured (*Magnolia denudata*, WME) and violet-coloured (*M. denudata* var. *purpurascens*, VME) flowers were 85.80 and 80.96 mg/g gallic acid equivalents, respectively (Jo et al. 2012). DPPH radical scavenging activity at 1 mg/mL was 87.74 and 75.05 % and for 2,2-azino-bis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical scavenging activity at 1 mg/mL was 88.24 and 85.98 %, respectively. There was no significant difference between WME (1.094) and VME (1.081) in reducing power.

Anticancer Activity

A chloroform extract of the root bark of *Magnolia denudata* showed strong cytocidal activity against P388 leukaemia cells, and parthenolide and costunolide were isolated as active principles (Funayama et al. 1995). In the MTT assay the chloroform fraction of ethanol flower extract of *M. denudata* showed the highest cytotoxic effect against HCT116, NCL-H460 and HepG2 human cancer cells (IC_{50} value: 0.14, 0.37 and

0.41 mg/mL, respectively) (Nho et al. 2009). Denudalide and denudaquinol isolated from mature fruit showed cytotoxicity against the serum-free mouse embryo (SFME), and r/mHM-SFME-1 cell lines, the latter with highly metastatic potential in host animal, were derived from ras/mycSFME (Noshita et al. 2009).

Antiplatelet Activity

The lignin, licarin which was isolated from the flower bud was found to have acyl-CoA cholesterol acyltransferase (ACAT) inhibitory activity in the rat liver (Kwon et al. 1999).

The neolignan derivative denudanolide A and neolignan denudatin B isolated from the twigs exhibited moderate antiplatelet activity factor activity, 50 % inhibition at 50 and 100 μg/mL, respectively (Kuroyanagi et al. 2000).

Anti-inflammatory Activity

Nitrate synthesis inhibitory effect of ethanol flower extract of *M. denudata* and its solvent fractions on nitric oxide synthase activity in LPS-stimulated RAW 264.7 cells were decreased in dose-dependent manners, and IC_{50} value of hexane and chloroform fractions were 0.39 and 0.49 mg/mL, respectively (Nho et al. 2009). Machilin G and four neolignans denudatins A and B, denudadione B and fargesone A which were isolated from young fruits of *Magnolia denudata* exhibited inhibitory effects on nitric oxide (NO) production in the lipopolysaccharide plus interferon-gamma activated-murine macrophage cell line J774.1 (Noshita et al. 2008). Some but not all of the inhibition of NO production by machilin G and denudatin A and B was apparently through the decreased expression of the inducible NO synthase (iNOS) gene.

Skin Whitening Activity

Tyrosinase inhibitory activities of the methanolic extracts of white-coloured (*Magnolia denudata*, WME) and violet-coloured (*M. denudata* var. *purpurascens*, VME) flowers were 17.48 and 8.63 %, respectively (Jo et al. 2012).

Allergy Modulatory Activity

Studies showed that flower buds of *Magnolia denudata* induced apoptosis of mast cells (Kim et al. 2003). Changes in cell morphology, generation of DNA fragmentation, cell cycle arrest, activation of caspase-3 and PARP and DFF degradations were demonstrated. The reduction of mitochondrial membrane potential (MMP) and the release of cytochrome C to cytosol were also shown. Bax protein content was increased, and Bax was translocated from cytosol into mitochondria at early time points after Magnolia treatment. The results suggested that the clinical effect of Magnolia flower may depend on their pharmacological efficacy in regulating mast cell apoptosis.

Ethanolic extracts of *Magnolia biondii, M. denudata, M. kobus, M. liliflora, M. sargentiana* and *M. sprengeri* produced a concentration-dependent inhibition of compound 48/80-induced histamine release in rat peritoneal mast cells (Shen et al. 2008). The rank order of the IC_{50} values was *M. biondii* < *M. kobus* < *M. liliflora* < *M. denudata* < *M. sprengeri* < *M. sargentiana.* The marker compound magnolin, but not fargesin, only slightly inhibited histamine release. The contents of magnolin and fargesin varied significantly among the species. Magnolin was found in *M. biondii, M. kobus* and *M. liliflora*, but not in *M. denudata*, *M. sprengeri* and *M. sargentiana*, while fargesin was only found in *M. biondii* and *M. kobus*.

Antiobesity Activity

Among the fractions of the crude extracts of the flower buds of *Magnolia denudata*, *n*-hexane and 85 % aqueous methanol fractions effectively reduced the lipid accumulation and the regulation of the adipogenic transcription factor (Kong et al. 2011). Both n-hexane and 85 % aqueous methanol fractions afforded four lignans (A–D).

In comparative analysis, the presence of the lignans during adipogenic differentiation reduced the absorbance values of eluted Oil Red O solution in the order of potency C > D > B > A. Also, lignans C and D effectively downregulated SREBP1, PPARγ and C/EBPα.

Traditional Medicinal Uses

The plant is anodyne, sedative and tonic (Kunkel 1984; Duke and Ayensu 1985). The flower buds are antifungal, astringent, cytotoxic, hypotensive and a uterine stimulant (NPRI 1998). The flower buds and seed are regarded as diaphoretic and carminative (Duke and Ayensu 1985), and in Korea they are used in the therapy of headaches, nasal obstruction and sinusitis (NPRI 1998). The flowers are dried and used for the treatment of nasal disorder in Korea (Kunkel 1984; Lim and Park 2005).

Other Uses

Yulan magnolia is a popular ornamental and has been cultivated in Chinese Buddhist temple gardens since 600 AD where its flowers were regarded as a symbol of purity in the Tang dynasty. It was also planted in the grounds of the Emperor's palace and summer palace. It is the official flower of the city of Shanghai.

Comments

Magnolia grandiflora is readily propagated from softwood cuttings and also from seeds, layering and grafting/budding.

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Magnolia grandiflora

Scientific Name

***Magnolia grandiflora* L.**

Synonyms

Magnolia angustifolia Millais, *Magnolia elliptica* (W.T.Aiton) Link, *Magnolia exoniensis* Millais, *Magnolia ferruginea* W.Watson, *Magnolia ferruginea* Z. Collins ex Raf., *Magnolia foetida* (L.) Sarg., *Magnolia foetida* f. *margaretta* Ashe, *Magnolia foetida* f. *parvifolia* Ashe, *Magnolia galissoniensis* Millais, *Magnolia glabra* P.Parm., *Magnolia gloriosa* Millais, *Magnolia grandiflora* var. *angustifolia* Loudon, *Magnolia grandiflora* var. *elliptica* W.T.Aiton, *Magnolia grandiflora* var. *exoniensis* Loudon, *Magnolia grandiflora* var. *ferruginea* Sims, *Magnolia grandiflora* f. *galissoniensis* K.Koch, *Magnolia grandiflora* var. *lanceolata* Aiton, *Magnolia grandiflora* f. *lanceolata* (Aiton) Rehder, *Magnolia grandiflora* var. *obovata* W.T.Aiton, *Magnolia grandiflora* var. *praecox* Loudon, *Magnolia grandiflora* var. *rotundifolia* Sweet ex Loudon, *Magnolia hartwegii* G.Nicholson (Inval.), *Magnolia hartwicus* G.Nicholson (Inval.), *Magnolia lacunosa* Raf., *Magnolia lanceolata* (Aiton) Link, *Magnolia longifolia* Sweet, *Magnolia maxima* Lodd. ex G.Don, *Magnolia microphylla* Ser. (Inval.), *Magnolia obovata* (W.T.Aiton) Link (Illeg.), *Magnolia obtusifolia* (Inval.), *Magnolia praecox* Millais, *Magnolia pravertiana* Millais, *Magnolia rotundifolia* Millais, *Magnolia stricta* G.Nicholson (Inval.), *Magnolia tardiflora* Ser. (Inval.), *Magnolia tomentosa* Ser. (Inval.), *Magnolia umbrella* var. *maxima* (Lodd. ex G.Don) P.Parm., *Magnolia virginiana* var. *foetida* L., *Magnolia virginiana* var. *grisea* L.

Family

Magnoliaceae

Common/English Names

Big Laurel, Bull Bay, Great Laurel Magnolia, Large-Flower Magnolia, Laurel-Leaved Magnolia, Southern Magnolia, Evergreen Magnolia, Loblolly Magnolia

Vernacular Names

Catalan: Magnòlia
Chinese: Guang Yulan, He hua mu lan, Hou po, Yang yulan
Czech: Šácholan velkokvětý
Danish: Storblomstret Magnolie
Dutch: Zuidelijke magnolia
Eastonian: Suureõieline magnolia
Finnish: Kuningasmagnolia
French: Laurier Tulipier, Magnolia à grandes fleurs, Magnolia toujours vert
German: Großblütige Magnolie, Immergrüne Magnolie, Riesenlorbeer

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Hungarian: Örökzöld liliomfa
India: Andachampa, Him champa (Hindi), Oothambal (Manipuri)
Japanese: Taisan-Boku
Polish: Magnolia wielkokwiatowa
Portuguese: Magnólia, Magnólia-Branca, Magnólia-de-flores-grandes, Magnólia-sempre-verde
Slovaščina: Magnolija velecvetna
Spanish: Laurel Tulipan, Lauro-Tulipan, Magnòlia, magnolia de Los Jardines, Magnolia lorandi, Magnolier, Magnoliera, Magnolio
Swedish: Kungsmagnolia
Turkish: Büyük çiçekli manolya
Vietnamese: Hoa Mộc Lan

Origin/Distribution

The species is native to the south-eastern United States: from Virginia south to central Florida, and western to eastern Texas and Oklahoma. The plant is widely cultivated in subtemperate areas around the world.

Agroecology

The species is found growing on the margins of ponds and swamps, ravines, hummocks and wooded floodplains on a rich fertile, moist, well-drained soil in its native range. It does not tolerate inundation and frost.

Edible Plant Parts and Uses

The flowers are pickled in some parts of England and are considered to have an exquisite flavour (Hedrick 1972; Facciola 1990). They are also said to be used as a spice and a condiment (Facciola 1990).

Botany

Magnolia grandiflora is a medium to large evergreen, typically straight and erect tree (up to 30 m high) with spreading branches that form a dense, broadly pyramidal crown. The trunk attains a diameter of 1.8 m and has a grey-brown, thinly scaly, fissured bark. Twigs, vegetative buds, petioles, densely brown to greyish brown and shortly tomentose. Leaves are alternate, simple, stiff, leathery, broadly ovate, large (12–20 cm long × 6–12 cm wide), with smooth margins and tapering at both ends, dark green above and tomentose underneath with yellow-brown pubescence (Plates 1 and 2). Flowers large, showy, fragrant, lemon citronella-scented, 15–30 cm across, with 6–12 white, waxy, fleshy, obovate tepals emerging on stout, pubescent pedicels from the tips of twigs (Plate 1). Stamens about 2 m long, with purple filaments and introrse anthers. Gynoecium ellipsoid, densely long tomentose with 1–1.5 cm, ovoid carpels and reclinate styles. Fruit cylindrical to ovoid, 7–10 by 4–5 cm, densely brown to pale greyish yellow tomentose containing bright red, glossy, ovoid seeds 1.4×0.6 cm.

Plate 1 Showy white flower and dark green glossy foliage

Nutritive/Medicinal Properties

Various classes of compound such as sesquiterpenoids (El-Feraly 1984; El-Feraly and Chan 1978; Yang et al. 1994; Luo et al. 2001; Ganzera et al. 2001; Hong et al. 2007), coumarins (Yang et al. 1994), phenylpropanoids (Clark et al. 1981), lignans (Schühly et al. 2009), glycosides (Rao 1975; Rao and Juneau 1975), alkaloids (Rao 1975; Ziyaev et al. 1999), and other compounds (Azuma et al. 1997a, b; Fan et al. 2009; Wang et al. 2009; Luo et al. 2012) had been

Plate 2 Lower leaf surface tomentose with yellow-brown pubescence

reported from this plant. Two cytotoxic germacranolide hydroperoxides peroxycostunolide (verlotorin) and peroxyparthenolide were isolated from *M. grandiflora* (El-Feraly et al. 1977, 1979b) and cyclocolorenone, a sesquiterpene ketone of the aromadendrane class (Rao and Davis 1982a; Jacyno et al. 1991).

Flower Phytochemicals

Volatile floral substances of *Magnolia* species including *M. grandiflora* comprised primarily of monoterpenoids and sesquiterpenoids produced by the mevalonate pathway, acetogenins by the acetate–malonate pathway and phenylpropanoids by the shikimate pathway (Yasukawa et al. 1992). Sporopollenin in mature pollen grains of *M. grandiflora* was shown by x-ray analysis to have a simple aliphatic polymer as the main structure (Kawase and Takahashi 1995). In subsequent studies, they found that sporopollenin possessed organosilicon compounds elucidated as 1,1,1, 5, 7, 7, 7-heptamethyl-3,3-bis (trimethylsiloxy) tetrasiloxane and 1, 1, 1, 3, 5, 7, 7, 7-octamethyl-3, 3-bis-(trimethylsiloxy) tetrasiloxane and also organic compound 1, 2-benzenedicarboxylic acid butyl 2-ethylhexyl ester (Kawase and Takahashi 1996). A sesquiterpene, vulgarenol, isolated from *Magnolia grandiflora* flower petals (Del Valle-Mondragón et al. 2007, 2009).

Twenty-eight constituents were present in the flower essential oil in which three were monoterpene hydrocarbons (3.9 %), 14 sesquiterpene hydrocarbons (80 %), 7 oxygenated sesquiterpenes (13.5 %) and 4 long-chain compounds (2.7 %) (Garg and Kumar 1999). Among them, 17 constituents were identified; β-caryophyllene (34.8 %) was the major constituent of the oil. The most abundant components of *M. grandiflora* floral essential oil were cyclocolorenone (up to 39.6 %), bicyclogermacrene (1.2–25.2 %), germacrene D (2.3–23.8 %), isobornyl acetate (trace to 16.0 %), methyl myristate (up to 15.3 %), β-pinene (3.3–14.6 %), β-elemene (3.3–12.8 %), (2Z,6E)-farnesol (up to 15.0 %) and (2E,6E)-farnesol (up to 12.5 %) (Davé et al. 2011).

Sixty-seven and thirty-four components were obtained by simultaneous distillation–extraction (SDE) and headspace–solid-phase microextraction (SPME) from flowers of *Magnolia grandiflora* growing in Cuba, respectively (Báez et al. 2012). β-Pinene (10.5 %), geraniol (7.4 %) and germacrene D (6.2 %) were the main constituents of the volatile oil isolated by SDE, while (E)-β-ocimene (24.6 %), geraniol (18.9 %), β-elemene (11.2 %) and germacrene D (9.9 %) were the most abundant in the headspace of the flowers, respectively. In *M. grandiflora* flower essential oil sample, (E,E)-farnesol (18 %) and 2-phenylethanol (10 %) were found as main constituents, whereas germacrene D (17 %) and β-bisabolene (17 %) were the main components of the headspace flower extract sample (Faraq and Al-Mahady 2013).

Fruit and Seed Phytochemicals

Biphenyls magnolol and honokiol were isolated from *M. grandiflora* seeds (El-Feraly and Li 1978).

Five neolignan compounds were obtained from *M. grandiflora* crude seed oil extract: honokiol (3′,5-di-2-propenyl-[1,1′-biphenyl]-2,4′-diol), magnolol(5,5′-di-2-propenyl-[1,1′-biphenyl]-2,2′-diol),4-*O*-methylhonokiol(3′,5-di-2-propenyl-4′-methoxy-[1,1′-biphenyl]-2-ol), 5,5′-di-2-propenyl-3-methoxy-[1,1′-biphenyl]-2,2′-diol (4) and grandiflora lignan (4α,9β-dihydro-8,9β-di-2-propenyl-(4H)-dibenzofuran-3-one) (Schühly et al. 2009). Biphenyl neolignans magnolol, honokiol and 4′-*O*-methylhonokiol (MH) were isolated from *M. grandiflora* seed oil (Schuehly et al. 2011). MH is only a minor secondary metabolite in Asian *Magnolia* species, but it is the major constituent of *M. grandiflora* seeds. In *M. grandiflora* seeds, 4-*O*-methylhonokiol was found to be the major neolignan (10 % in the crude seed extract), followed by magnolol, honokiol and 4-mono-*O*-methylhonokiol (Rao and Davis 1982b).

Sixteen types of compounds were identified, including 40.91 % oxygen-containing terpene derivatives, 19.51 % terpenes, 13.97 % esters, 13.05 % nitrogenous compounds and 3.64 % acids from *M. grandiflora* seed essential oil (Luo et al. 2012). Major components were 13-ethyl-3-hydroxy-(14*β*)-gona-1,3,5,7,9-pentaen-17-ketone (21.19 %); caryophyllene (19.36 %); *N*-(6-oxo-9,10,11,12-tetrahydro-6H-5-oxa-8-aza-benzo[C] phenanthren-7-yl)-propionamide (13.04 %); eucalyptol (10.7 %); 6,9,12,15-docosatetraenoic acid, methyl ester (8.74 %); equilenin (8.02 %); tetradecanoic acid (3.64 %); and (*Z*)-2-hydroxy-1-(hydroxymethyl)-9-octadecenoic acid ethyl ester (3.26 %). Other minor components included hexadecanoic acid,2-hydroxy-1-(hydroxymethyl)-ethyl ester (1.41 %); androsta-1,4,6-triene-3,17-diketone (0.62 %); 2,3-dihydroxyantioleic acid ester (0.56 %); 4-(2-proprnyl)-phenol (0.27 %); 1,2,3,4-tetrahydro-1,6-dimethyl-4(1-methylethyl)-(*1S-cis*)-naphthalene (0.07 %); α-cubebene (0.04 %); 1,6-dimethyl-4-(1-methylethyl)-naphthalene (0.04 %); and 4-(1,4,5,7-tetramethyl-pyrrolo[3,4-d]pyridazin-6-yl)-phenylamine (0.01 %). The following major essential oil constituents were found in seeds with aril: 8.8 % β-caryophyllene, 7.3 % β-phellandrene, 6.2 % octanol and 5.5 % *p*-cymene; deseeded unripe fruit: 12.9 % β-elemene, 12.7 % β-pinene, 7.9 % β-caryophyllene and 5.1 % α-terpineol; deseeded mature fruit: 12.2 % 1,8 cineole, 7.2 % caryophyllene oxide, 6.9 % β-pinene and 5.7 % β-elemene; leaves: 23.0 % β-pinene, 13.6 % β-elemene and 6.3 % α-pinene (Rehman et al. 2013).

Leaf Phytochemicals

From the leaves the alkaloids anonaine and liriodenine (Tomita and Kozuka 1967) and magnoflorine, lanuginosine, liriodenine and anonaine were isolated (Mohamed et al. 2010). The germacranolide sesquiterpene lactones costunolide, parthenolide and costunolide diepoxide were isolated from *M. grandiflora* leaves (El-Feraly and Chan 1978). Two isomeric melampolides, melampomagnolide A and melampomagnolide B, were isolated from the newly formed leaves of *Magnolia grandiflora* (El-Feraly 1984). The leaves of *Magnolia grandiflora* afforded in addition to costunolide diepoxide and parthenolide, a guaianolide named magnograndiolide (Halim et al. 1984). Five sesquiterpenes were found in *M. grandiflora* (Ganzera et al. 2001). Quantitative analysis of different *M. grandiflora* samples showed parthenolide as the most dominant sesquiterpene lactone in all specimens, with concentrations ranging from 0.019 % in fruits to 0.335 % in leaves (w/w). The alkaloids remerine and liriodenine were isolated from mature leaves and liriodenine from young branches (Ziyaev et al. 1999). Three sesquiterpenoids were isolated from the leaves and determined as 6α,11-dihydroxy-12, 13-diacetoxyelem-1,3,diene;4α,6α,10α-trihydroxy-13-acetoxyguia-11-ene; and 12,13-diacetoxy-guaia-4α,6α,10α,11-tetraol; also isolated was the known sesquiterpenoid magnograndiolide (Luo et al. 2001). Magnograndiolide was isolated earlier by Yang et al. (1994). The bioactive sesquiterpene lactones parthenolide and costunolide and the tricyclic sesquiterpene cyclocolorenone were extracted from the leaves of *Magnolia grandiflora* (Castaneda-Acosta et al. 1995). Two sesquiterpenoids, 4,5-epoxy-13-methoxy-1(10)-germacren-12,6-olide and 4,5-epoxy-13-acetoxy-1(10)-germacren-12,6-olide, were isolated from the leaves, together with six known compounds, 2α-hydroxy-dihydroparthenolide, parthenolide,

costunolide, syringaresinol, (+) medioresinol and 6,7-dimethoxycoumarin (Wu et al. 2001). Sesquiterpene lactones costunolide, parthenolide and costunolide diepoxide were isolated from the leaves (El-Feraly and Chan 1978). Sesquiterpene lactones costunolide, parthenolide and 1,10-epoxyparthenolide were isolated from the leaves (Ahmed and Adeglegaleil 2005).

The volatiles (in μg/12 h/100 cm^2 leaf area) emitted from artificially damaged leaves of the evergreen *M. grandiflora* were dominated by sesquiterpenes, especially β-elemene (7.65), α-bisabolene (6.23), bicyclogermacrene (7.65), caryophyllene (2.73), γ-cadinene (2.50) and (*E*)-4,8-dimethyl-l,3,7-nonatriene (2.48). In contrast, undamaged leaves did not appear to emit these terpene compounds in appreciable amounts. Other minor volatiles included monoterpenes: β-myrcene (0.24), limonene (0.09), aliphatic, namely, (*Z*)-3-hexenol (0.30) and 4 unknowns (Azuma et al. 1997a). Azuma et al. (1997b) reported the floral scent to be dominated (in relative amounts) by geraniol (19.7 %), β-myrcene (12.7 %), (*E*)-β-ocimene (14.4 %), limonene (9.9 %) and verbenone (5.1 %). Other compounds (relative amounts) detected in the volatiles of detached flowers included sabinene and α-pinene (3.3 %), terpinolene (2.1 %), perillene (1.5 %), β-pinene (1.5 %), α-terpineol (1.0 %), isopinocamphone (1.0 %), (*Z*)-β-ocimene (0.7 %), nerol (0.7 %), linalool (0.6 %), neral (0.6 %) and (*E*)-4,8-dimethyl-l,3,7-nonatriene (0.5 %). The overall terpene profile differed between attached and detached flowers. Overall, less volatile were released from the intact flowers than those detached. Hong et al. (2007) isolated a sesquiterpene from the leaves, 4,5-epoxy-1(10)E,11(13)-germacradien-12,6-olide, that exhibited nematicidal property.

Forty-eight constituents were separated and identified from the volatile constituents of *Magnolia grandiflora* fresh leaves (Wang et al. 2009). The main constituents included γ-elemene (15.67 %), 2,6-dimethyl-6-bicyclo[3.1.1]hept-2-ene (11.60 %), caryophyllene (9.03 %), isocaryophyllene (4.92 %) and spathulenol (6.51 %). Forty-eight volatile compounds were separated and identified from the fresh leaves of *Magnolia grandiflora* (Fan et al. 2009). Identified major compounds included γ-elemene (16.67 %); 2,6-dimethyl-6-bicyclo[3,1,1]hept-2-ene (11.64 %); caryophyllene (9.03 %); 1,2,3,4a,5,6,7,8a-octahydronaphthalene (7.91 %); spathulenol (6.52 %); isocaryophyllene (4.92 %). Minor components were 3,7,11-trimethy-1,6,10-dodecatrien-3-ol (2.60 %); ledene alcohol (2.34 %); 1,4-dimethyl-3-[2-methyl]-1-cycloheptene-(2.30 %); α-cadinol (2.29 %); α-farnesene (2.23 %); 1,2,3,5,6,7,8,8a-octahydronaphthalene (2.10 %); caryophyllene oxide (2.04 %); 2,5,5-trimethyl-1,3,6-heptatriene (2.01 %); β-panasisene (1.98 %); 1,2,3,5,6,8a-hexahydro-4,7-naphthalene (1.90 %); 4,8a-dimethyl-6-isopropenyene (1.64 %); 1H-cycloprop[e]azulen-7-ol (1.58 %); dicyclohexyl-propanedinitrile (1.58 %); dihydrocarveol (1.55 %); α-caryophyllene (1.5 %); copaene (1.14 %); furfural (1.12 %); germacrene D (0.93 %); 5-methyl-2-furancarboxaldehyde (0.89 %); 2-methyl-4-bromo-1-butene (0.89 %); isoaromadendrene epoxide (0.82 %); hydroxymethyl-1-methylidene (0.82 %); heptadecane (0.81 %); 3,7-dimethyl-1,6-octadien-3-ol (0.79 %); 3,7,11-trimethyl-1,36,10-datecatetranene (0.75 %); α-copaene-8-ol (0.74 %); *n*-hexadecanoic acid (0.61 %); 2,4-decadienal (0.51 %); 1-undecen-3-yne (0.49 %); hexadecanoic acid ethyl ester (0.49 %); phytol(0.39 %); *trans*-Z-α-bisabolene epoxide (0.36 %); β-humulene (0.33 %); linoleic acid ethyl ester (0.29 %); camphor (0.28 %); benzeneacetaldehyde (0.25 %); 2-hexyl-furan (0.25 %); 1,4-methanoazulene (0.22 %); 2,3-dimethylanisole (0.20 %); hexadecanoic acid methyl ester (0.17 %); isopropyl palmitate (0.11 %) and tricosane (0.09 %). Twenty-eight compounds from *M. grandiflora* leaf essential oil were identified (representing 93.6 % of the total area of the gas chromatogram), with the major component being bornyl acetate (20.9 %) (Guerra-Boone et al. 2013). The major constituents found in the leaf essential oil were 23.0 % β-pinene, 13.6 % β-elemene and 6.3 % α-pinene (Rehman et al. 2013).

Stem/Root Phytochemicals

Since the 1950s a number of alkaloids were isolated from *M. grandiflora*: from the roots quaternary alkaloids salicifoline, candicine from the roots (Nakano 1954a); magnoflorine from bark

which was quite identical with corytuberine methiodide of the aporphine type (Nakano 1954b, c); from the trunk wood the alkaloids anolobine, anonaine, *N*-nornuciferine and liriodenine were isolated (Tomita and Kozuka 1967). Magnoflorine and salicifoline were also found in the plant (Tomita et al. 1961). The root bark of *M. grandiflora* yielded costunolide together with the two eudesmanolides, santamarine and reynosin (El-Feraly and Chan 1978). Rao and Davis (1982c) isolated menisperine (also called chakranine and isocorydinium cation) a toxic phenolic quaternary principle from the alcoholic extract of the wood. The compound exhibited toxicity to mice when injected by the i.p. route. Three crystalline glycosides magnolidin, magnolenin and magnosidin and the known alkaloids magnoflorine and candicine were isolated from the bark (Rao 1975). Magnolidin was the major glycoside of the bark. It consisted of two moles of rhamnose and each of glucose, caffeic acid and 3,4-dihydroxyphenethanol (Rao and Juneau 1975). Sesquiterpene lactones costunolide, parthenolide and 1,10-epoxyparthenolide were isolated from the stem bark (Ahmed and Adeglegaleil 2005), and two eudesmanolides santamarine and reynosin were isolated from the root bark (El-Feraly and Chan 1978). An unknown γ-isomer of the two eudesmanolides santamarine and reynosin was detected in the root bark of *M. grandiflora* and designated magnolialide (El-Feraly et al. 1979a).

Lee et al. (2010) isolated seven compounds from the wood of *M. grandiflora*: erythro-1-C-syringylglycerol; 2,3-dihydroxypropyltetracosanoate; 2,3-dihydroxypropyl-24′-hydroxytetracosanoate; 3-hydroxy-4,5-dimethoxyphenyl-β-D-glucopyranoside; daucosterol; syringic acid; and syringaldehyde.

Recently, many investigators reported the anticancer, antistress, antianxiety, antidepressant, antioxidant, anti-inflammatory and hepatoprotective effects as well as toxicities and pharmacokinetics data of the bioactive compound of magnolia, namely, magnolol, honokiol and 4-*O*-methylhonokiol (Lee et al. 2011). Also, studies had found honokiol and magnolol to have antioxidative, anti-inflammatory, antitumour, antidiabetic, anti-neurodegeneration, antidepressant, pain control, hormone, gastrointestinal and uterus modulation, antimicrobial, cardiovascular and liver protective properties in preclinical models, without appreciable toxicity (Shen et al. 2010).

Antioxidant Activity

In in-vitro cell studies, all *M. grandiflora* seed essential oil concentration (6.9, 13.8, 27.7, 55.5, 111.0, and 222.0 μg/ml) increased cell proliferation by 26 % or more (26.0 %, 38.8 %, 44.8 %, 40.2 %, 35.8 % and 30.4 %, respectively, in the MTT assay) (Luo et al. 2012). In in-vivo studies, SD rats orally administered the essential oil at 50, 100 and 200 mg/kg per day exhibited 38.62 %, 61.68 % and 62.86 % rise in glutathione-peroxisome (GSH-Px) activity, respectively, with 29.56 %, 24.30 % and 36.93 % reduction in malondialdehyde (MDA) content, respectively, but no significant difference in superoxide dismutase activity was found. The results showed that the essential oil had strong antioxidant activity, without dose effect within the concentration range.

Lin et al. (1995) reported that magnolol at 10^{-9} to 10^{-7} M significantly suppressed FeSO4-induced lipid peroxidation and significantly reversed the FeSO4-suppressed sperm tail beat frequency. Magnolol significantly inhibited the generation of malondialdehyde (MDA), the end product of lipid peroxidation, in sperm. Thus, magnolol protected sperm motility by inhibiting lipid peroxidation in sperm. Intraperitoneal injection of magnolol (30 mg/kg) significantly inhibited the formylmethionyl-leucyl-phenylalanine (fMLP)-induced respiratory burst in rat whole blood ex vivo (Wang et al. 1999). Magnolol also inhibited the $0^{2\text{-}}$* generation with an IC_{50} of 15.4 μM and O^2 consumption in rat neutrophils in vitro. Magnolol weakly inhibited the $O^{2\text{-}}$* generation in the xanthine–xanthine oxidase system, decreased cellular cyclic AMP level and weakly inhibited neutrophil cytosolic protein kinase C activity. Magnolol also attenuated fMLP-induced protein tyrosine phosphorylation and the phosphorylation of mitogen-activated protein kinase p42/44. In the presence of NADPH, the arachidonate-activated NADPH oxidase activity

in a cell-free system was weakly suppressed by magnolol. These results suggested that the inhibition of respiratory burst in fMLP-activated neutrophils by magnolol was probably attributable mainly to the attenuation of protein tyrosine phosphorylation and p42/44 mitogen-activated protein kinase activation and partly to the suppression of protein kinase C and NADPH oxidase activities.

In a separate study, magnolol was found to be an effective antioxidant in suppressing lipid peroxidation in rat liver mitochondria (Chiu et al. 1999). It was 470 times more potent than α-tocopherol in inhibiting oxygen consumption and 340 times more potent than α-tocopherol in inhibiting MDA formation. Also magnolol could be used as a rinsing solution in protecting transplanted organs from lipid peroxidation during reperfusion. Magnolol enhanced survival ratio of H460 cells after oxidative agent tert-butyl hydroperoxide (TBHP)-induced injury (Li et al. 2007). Magnolol was effective against DNA single strand break formation, cytotoxicity and lipid peroxidation induced by TBHP, and its effects on p53 phosphorylation, PTEN and Akt phosphorylation were due to its antioxidative function, and partially via a p53-dependent mechanism in this protective effect. The protective action of magnolol was more efficacious than that of *N*-acetylcysteine, a putative antioxidant.

The antioxidant effects of magnolol and honokiol were 1,000 times higher than that of α-tocopherol in isolated rat heart mitochondria lipid peroxidation induced with ADP and ferrous sulphate (Lo et al. 1994). The IC_{50} values of magnolol and honokiol for inhibition of oxygen consumption were 8.0×10^{-8} M and 1.0×10^{-7} M, respectively, while that of α-tocopherol was 1.0×10^{-4} M. Magnolol at 0.5 μM inhibited 71.4 % of oxygen consumption and 59.3 % malondialdehyde (MDA) production. At the same concentration, honokiol inhibited 78.1 % of oxygen consumption and 86.9 0 % of MDA production. Of the conjugated diene formation, 48.4 % and 53.1 % were inhibited by 0.5 μM magnolol and honokiol, respectively. Also both magnolol and honokiol exhibited free radical scavenging activities as shown by the diphenyl-p-picrylhydrazyl (DPPH) assay but they were less potent than α-tocopherol. In another study, honokiol and magnolol were found to inhibit microsomal lipid peroxidation induced by Fe(III)-ADP/NADPH and mitochondrial lipid peroxidation induced by Fe(III)-ADP/NADH (Haraguchi et al. 1997). These neolignans protected mitochondrial respiratory chain enzyme activity against NADPH-induced peroxidative stress and protected red cells against oxidative haemolysis. The antioxidative activity of honokiol was more potent than that of magnolol. Lee et al. (2005) using DPPH and SOD activity assays showed both magnolol and honokiol exhibited antioxidant activities; honokiol had relatively stronger antioxidant activities than magnolol (Lee et al. 2005). For DPPH assay, % of DPPH bleaching were 19.8 % and 67.3 % for magnolol and honokiol, respectively. For SOD assay, SOD activity were 53.4 % and 64.3 % for magnolol and honokiol, respectively. Honokiol was found to be a potent scavenger of superoxide and peroxyl radicals (Dikalov et al. 2008). Honokiol efficiently scavenged superoxide radicals in xanthine oxidase and cytochrome P-450 cell-free systems with the rate constant similar to reactivity of ascorbic acid but 20 times higher than reactivity of vitamin E analogue trolox. Honokiol potently scavenged intracellular superoxide within melanoma cells. Further, honokiol scavenged peroxyl radicals generated by 2,2′-azo-bis(2-amidinopropane hydrochloride).

In an earlier study, the relative mutagenic activity (the mutation frequency of treated cells divided by the mutation frequency of control cells times 100 %) at concentrations of 5 μg per plate for magnolol and honokiol was 62 as tested in *Salmonella typhimurium* TA102 (Fujita and Taira 1994). These values indicated that low concentrations of these biphenyl compounds effectively suppressed UV-induced mutagenesis. Also, these compounds acted as effective antimutagens in a dose-dependent manner (0.00005-5 μg per plate). These compounds were also effective hydroxyl radical scavengers. Thus, the results suggested that these compounds could inhibit against UV-induced mutations by scavenging of OH generated by UV irradiation.

Antityrosinase Activity

Studies by Huang et al. (2012) showed that *M. grandiflora* flower extract inhibited mushroom tyrosinase activity (IC_{50} = 11.1 %; v/v); the flower extract also effectively suppressed intracellular tyrosinase activity (IC_{50} = 13.6 %; v/v) and decreased the amount of melanin (IC_{50} = 25.6 %; v/v) in a dose-dependent manner in B16F10 cells. Protein expression level of tyrosinase and tyrosinase-related protein 1 (TRP-1) was also decreased by the flower extract. The flower extract also showed antioxidant capacities and depleted cellular reactive oxygen species (ROS). The results suggested that *M. grandiflora* flower extract could be applied as a type of dermatological whitening agent in skin care products.

Anti-inflammatory Activity

Reynosin, found in *M. grandiflora, Ambrosia confertiflora* and *Saussurea lappa*, exhibited a dose-dependent inhibition on CINC-1(cytokine-induced neutrophil chemoattractant-1) induction in LPS-stimulated rat kidney epithelioid NRK-52E cells, where 50 % of inhibitory effect was determined at the concentration of about 1 μM (Jung et al. 1998). Sesquiterpene lactones, costunolide, and parthenolide, from *M. grandiflora*, both potently inhibited LPS-induced NF-kappa B activation (Koo et al. 2001). Costunolide, which showed more potent inhibition than parthenolide, strongly suppressed nitric oxide (NO) production in LPS-stimulated RAW 264.7 cells. Costunolide also significantly inhibited LPS-induced DNA-binding activity of NF-kappa B, LPS-induced phosphorylation of I kappa B-alpha as well as the LPS-induced degradation of I kappa B-alpha and B-beta. In the rat carrageenan inflammation model, i.p. injection of rats with parthenolide (20 mg/kg), from *M. grandiflora*, significantly blocked the hyperalgesic response and significantly attenuated the oedema response suggesting that parthenolide may be useful in the treatment of inflammatory pain (Feltenstein et al. 2004).

Wang et al. (1993) demonstrated the inhibitory effect of magnolol on the plasma leakage in passive cutaneous anaphylactic reaction, neurogenic inflammation, dorsal skin and ear oedema in mice. The inhibitory effect of magnolol was found to be probably mediated through a nonselective inhibition on vascular tissue to prevent the permeability change caused by various mediators. The inhibitory effect of magnolol was more marked than that of diphenhydramine combined with methysergide. Separate animal studies showed that magnolol altered the course of endotoxin tolerance and provided early protection against endotoxin challenge following sublethal haemorrhage in rats by inducing an anti-inflammatory response (Shih et al. 2004). However, magnolol attenuated the protraction of endotoxin tolerance and inhibited late protection against endotoxin challenge following sublethal haemorrhage. Magnolol suppressed lipid peroxidation but not the SOD activity after sublethal haemorrhage.

Studies showed that the production of interleukin-8 (IL-8) and tumour necrosis factor-alpha (TNF-alpha) induced by *Propionibacterium acnes* in THP-1 cells, a human monocytic cell line, was reduced by magnolol and honokiol (Lee et al. 2005). Cyclooxygenase-2 (Cox-2) activity was also suppressed by them. It was found that magnolol and honokiol exerted their anti-inflammatory effects by inhibiting downstream pathway of MEKK-1 in NF-kappaB activation signalling in Cox-2, IL-8 and TNF-alpha promoters. The results suggested that magnolol and honokiol may be introduced as possible acne-mitigating agents.

Studies by Schühly et al. (2009) demonstrated that the neolignans honokiol, magnolol, 4-*O*-methylhonokiol and 5,5′-di-2-propenyl-3-methoxy-[1,1′-biphenyl]-2,2′-diol isolated from *Magnolia* seeds inhibited COX-2 enzyme activity in activated macrophages (RAW 264.7 cells), and they were able to inhibit the conversion of exogenous arachidonic acid to PGE2 in a dose-dependent manner, without causing any cytotoxic effects in RAW 264.4 and VERO cells. The anti-inflammatory activity of magnolol and honokiol as well as of methylhonokiol could be

explained by their inhibitory effects on the prostaglandin biosynthesis in the cyclooxygenase metabolism through COX-2 inhibition. In vitro studies showed that magnolol inhibits LPS-induced expression of iNOS gene by obstructing activation of NF-κB/Rel and p38 kinase signalling in RAW 264.7 cells (Li et al. 2010).

Honokiol strongly inhibited various inflammatory responses, such as (1) the up-regulation of nitric oxide (NO), prostaglandin E2 and TNF-alpha production and costimulatory molecule CD80 induced by lipopolysaccharide (LPS); (2) the functional activation of beta1-integrin (CD29) assessed by U937 cell–cell and cell–fibronectin adhesions; (3) the enhancement of lymphocytes and CD8+CTLL-2 cell proliferation stimulated by LPS, phytohemagglutinin A (PHA) and concanavalin A or interleukin (IL)-2; and (4) the transcriptional up-regulation of inducible NO synthase, TNF-alpha, cyclooxygenase-2, IL-12 and monocyte chemoattractant protein (MCP)-1 in various cell lines and primary cells (U937, RAW264.7, CTLL-2 cells and splenic lymphocytes) (Kim and Cho 2008). These anti-inflammatory effects of honokiol appeared to be mediated by interrupting the early activated intracellular signalling molecule phosphoinositide 3-kinase (PI3K)/Akt pathway. Studies by Li et al. (2011) showed that honokiol inhibited LPS-induced maturation and inflammatory response of human monocyte-derived dendritic cells. The anti-inflammatory actions of honokiol on LPS-induced dendritic cells were associated with the NF-κB and mitogen-activated protein kinase (MAPK) signalling pathways.

Animal studies by Lee et al. (2012b) suggested that 4-*O*-methylhonokiol inhibited LPS-induced amyloidogenesis via anti-inflammatory mechanisms and could be used as an agent against neuroinflammation-associated development or the progression of Alzheimer disease. Oral administration of AD mice with 4-*O*-methylhonokiol ameliorated LPS-induced memory impairment in a dose-dependent manner and prevented the LPS-induced expression of inflammatory proteins, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) as well as activation of astrocytes (expression of glial fibrillary acidic protein; GFAP) in the brain. In in-vitro study, they found that 4-*O*-methylhonokiol suppressed the expression of iNOS and COX-2 as well as the production of reactive oxygen species, nitric oxide, prostaglandin E_2, tumour necrosis factor-α and interleukin-1β in the LPS-stimulated cultured astrocytes. 4-*O*-methylhonokiol also inhibited LPS-induced Aβ1-42 generation, β- and γ-secretase activities and expression of amyloid precursor protein (APP), BACE1 and C99 as well as activation of astrocytes and neuronal cell death in the brain, in cultured astrocytes and in microglial BV-2 cells.

Magnolol inhibited mouse hind-paw oedema induced by carrageenan, compound 48/80, polymyxin B and reversed passive Arthus reaction (Wang et al. 1992). Magnolol also suppressed acetic acid-induced writhing response. The lethality of endotoxin challenge was reduced by pretreatment with magnolol. The recovered myeloperoxidase activity in oedematous paw was significantly decreased in mice pretreated with magnolol and BW755C. Suppression of oedema was demonstrated not only in normal mice but also in adrenalectomized animals. The action of magnolol was proposed to be dependent on reducing the level of eicosanoid mediators. Further studies by Wang et al. (1995) suggested that magnolol, like BW755C, might be a dual cyclooxygenase and lipoxygenase inhibitor. The inhibitory effect of magnolol on the A23187-induced pleurisy was proposed to be, at least partly, dependent on the reduction of the formation of eicosanoids mediators in the inflammatory site. A23187-induced protein leakage in mice was reduced by magnolol (10 mg/kg, i.p.), indomethacin (10 mg/kg, i.p.) and BW755C (30 mg/k, i.p.). A23187-induced polymorphonuclear (PMN) leucocyte infiltration in the pleural cavity was suppressed by magnolol and BW755C, while enhanced by indomethacin. Like BW755C, magnolol reduced both prostaglandin E2 (PGE2) and leukotriene B4 (LTB4) levels in the pleural fluid of A23187-induced pleurisy, but increased LTB4 formation. In the rat-isolated peripheral neutrophil suspension, magnolol (3.7 μM) and BW755C (10 μM) also suppressed the A23187-induced thromboxane B2 (TXB2) and LTB4 formation.

In vitro studies using human U937 promonocytes cells suggested that magnolol may have potential anti-inflammatory action by dose-dependently suppressing NF-kappaB activation and NF-kappaB -regulated gene expression through inhibition of IkappaB kinase activation (Tse et al. 2007). Intravenous administration with magnolol at 0.3–1 mg/kg protected against ischaemic limb damage in male Sprague-Dawley rats (Chen et al. 2009a). Relative to controls, rats treated with magnolol (0.3 and 1 mg/kg) had attenuated muscular inflammation, oedema and damage. Magnolol (0.3–1 mg/kg) also effectively reduced postischaemic rises in the nitrite/nitrate, malondialdehyde and myeloperoxidase levels. Thus the observed cytoprotection may be attributed to its antioxidant, anti-nitrosative and anti-inflammatory actions.

Studies showed that honokiol and magnolol did not produce analgesia in tail-flick, hot-plate, paw-shaking and neurogenic phase of the overt nociception induced by intraplantar injection of formalin (Lin et al. 2007). However, honokiol and magnolol reduced the inflammatory phase of formalin-induced licking response. Additionally, honokiol and magnolol significantly decreased formalin-induced c-Fos protein expression in superficial (I-II) laminae of the L4–L5 lumbar dorsal horn. However, honokiol and magnolol did not elicit motor incoordination and memory dysfunction at doses higher than the analgesic dose. These results demonstrated that honokiol and magnolol effectively alleviated the formalin-induced inflammatory pain without motor and cognitive side effects, suggesting their therapeutic potential in the treatment of inflammatory pain.

In a recent study, magnolol inhibited the expression of tumour nuclear factor TNF-α, interleukins IL-6 and IL-1β in LPS-stimulated RAW264.7 cells in a dose-dependent manner (Fu et al. 2013). Magnolol also suppressed LPS-induced nuclear factor-κB (NF-κB) activation, inhibitory kappa B (IκBα) protein degradation, phosphorylation of extracellular signal-regulated kinase (ERK), c-Jun *N*-terminal kinase (JNK) and P38. Magnolol could significantly downregulate the expression of Toll-like receptor 4 (TLR4) stimulated by LPS. Further, magnolol suppressed LPS-induced IL-8 production in mTLR4/mMD2 co-transfected HEK293 cells.

Anti-allergic/Antiasthmatic Activity

In vitro studies showed that magnolol inhibited production of leukotrienes in intact rat basophilic leukaemia (RBL)-2H3 cells by inhibiting cytosolic phospholipase A2, 5-lipoxygenase, leukotrienes LTC4 synthase and LTA4 hydrolase which were essential for leukotriene synthesis (Hamasaki et al. 1999). Thus, magnolol may have an anti-allergic effect by blocking leukotriene synthesis. In another study, magnolol, one of the bioactive compound in Saiboku-To, a herbal medicine for bronchial asthma (Homma et al. 1992), was found to inhibit concanavalin A-induced human lymphocyte blastogenesis in vitro and picryl chloride-induced mouse ear swelling in vivo (Taniguchi et al. 2000). Oral administration of Saiboku-To and magnolol inhibited picryl chloride-induced ear swelling significantly by 23.5 % and 23.6 %, respectively, indicating an antiasthmatic effect of Saiboku-To through suppression of type IV allergic reaction. Magnolol was found to be the most potent chemical constituents of Saiboku-To, a herbal remedy for steroid-dependent bronchial asthma, on the inhibition of the enzyme 11 beta-hydroxysteroid dehydrogenase, with IC_{50} of 1.8×10^{-4} M (Homma et al. 1994). The results suggested that magnolol might contribute to the inhibitory effects of Saiboku-To on prednisolone metabolism through inhibition of 11 beta-hydroxysteroid dehydrogenase. The five phenolic active compounds contained in Saiboku-To, magnolol, dihydroxydi hydromagnolol, baicalein, medicarpine and davidigenin, were found to exert a marked inhibition on leukotrienes LTB4- and LTC4-release from human polymorphonuclear leukocytes with IC50 values of 0.7–15.3 μM (Homma et al. 2000). The results suggested that the phenolic compounds contributed to the anti-allergic effects of Saiboku-To through suppression of leukotriene release from polymorphonuclear leukocytes. Studies by Niitsuma et al. (2001) found baicalein and magnolol were 5–10 times more potent than azelastine, an anti-allergic drug, and significantly

suppressed leukotriene C4 release by polymorphonuclear leukocytes obtained from asthmatic patients, as compared with healthy subjects. Suppression of leukotriene C44 release by these compounds may play an important role in the clinical efficacy of Saiboku-To. Magnolol and honokiol inhibited C48/80-induced histamine release from mast cells (Ikarashi et al. 2001). The potency of magnolol (IC_{50} = 1.04 μg/ml) was greater than that of honokiol (IC_{50} = 2.77 μg/ml).

Magnolol and honokiol potently inhibited passive cutaneous anaphylaxis reactions in mice induced by IgE-antigen complex as well as compound 48/80-induced scratching behaviours (Han et al. 2007). Both compounds exhibited not only potent inhibitory activity on the degranulation of RBL-2H3 cells induced by IgE-antigen complex, with IC_{50} values of 45 and 55 μM, respectively, but also the protein expressions of IL-4 and TNF-alpha. The findings suggested that magnolol and honokiol may improve IgE-induced allergic diseases.

Studies showed that in addition to the presence of antioxidative activity, magnolol was found to be potent in stimulating BK(Ca) channel activity in human tracheal smooth muscle cells (Wu et al. 2002). The direct stimulation of these BK(Ca) channels by magnolol may contribute to the underlying mechanism by which it acts as an antiasthmatic compound. In separate studies, magnolol and honokiol (0.1–100 μM) inhibited carbachol- and high K^+-induced muscle contractions in porcine trachea in a concentration-dependent fashion, but did not affect basal muscle tension (Ko et al. 2003). Magnolol and honokiol also concentration-dependently decreased the Ca^{2+}-dependent muscle contraction induced by high K^+ depolarization. The relaxant effects of magnolol and honokiol on porcine tracheal smooth muscle suggested an association with the blockade of Ca^{2+} influx through voltage-operated Ca^{2+} channels instead of Ca^{2+} release from intracellular Ca^{2+} stores. The magnolol- and honokiol-induced inhibitions on tracheal smooth muscle contraction may be relevant to the claimed therapeutic effects of the extract from magnolia bark and may contribute to their pharmacological effects by acting as antiasthmatic agents.

Antiseptic/Anti-shock Activity

Studies showed that magnolol attenuated peroxidative damage and improved survival of rats with sepsis (Kong et al. 2000). When one cecal puncture was performed, a moderately evolving type of sepsis was induced, and the survival rate of affected rats was significantly improved by pretreatment with 10^{-7} g/kg magnolol. The beneficial effect was partially retained if magnolol was administered 6 h after onset of sepsis when a higher dose (10^{-5} g/kg) was used. The intensity of lipid peroxidation in plasma, liver and lung of septic rats was also attenuated in a treatment-dependent manner. The methanol extract of *Magnolia obovata* stem bark afforded two inhibitors, magnolol and honokiol, of nitric oxide (NO) production in lipopolysaccharide (LPS)-activated macrophages by the suppression of i-NOS expression (Son et al. 2000). Their IC_{50} values were 16.8 and 6.4 μM, respectively. They also inhibited the production of tumour necrosis factor-alpha (TNF-alpha) in LPS-activated macrophages. The results indicated that these compounds may be possible candidates for the development of new drugs to treat endotoxemia accompanied by the overproduction of NO and TNF-alpha. Shih et al. (2003) found that magnolol treatment reduced the elevated levels of TNF-alpha in plasma and tissue of rats after haemorrhagic shock and sepsis. Magnolol-treated rats had decreased pulmonary permeability after the onset of sepsis and survival rate was significantly higher in magnolol-treated group. It was concluded that magnolol modified the cytokine response after haemorrhagic shock and resuscitation and suppressed the proinflammatory cytokine response. The modified cytokines response induced by magnolol may result in decreased tissue injury and increased survival in subsequent intra-abdominal sepsis.

Antitumour Activity

The petroleum ether extract of the stem and leaves showed inhibitory activity against human epidermoid nasopharynx carcinoma KB9 cells in vitro; the active principle was isolated and identified

as parthenolide (Wiedhopf et al. 1973). *M. grandiflora* flower essential oil was found to be active against human lung carcinoma and breast carcinoma cell lines, even at concentrations higher than 200 μg/ml (Faraq and Al-Mahady 2013). An extract of powdered *M. grandiflora* was found to induce apoptosis in chlorambucil-resistant B-cell chronic lymphocytic leukaemia (B-CLL) cells in vitro (Marin and Mansilla 2010). The results suggested a potentially effective repertoire for B-CLL treatment.

The ethanol bark extract exhibited inhibitory effect on human fibrosarcoma HT-1080 cell invasion in a reconstituted basement membrane (Nagase et al. 2001). The active components magnolol and honokiol inhibited HT-1080 cell migration at a high concentration (100 μM). Magnolol and honokiol inhibited the activity of matrix metalloproteinase (MMP)-9 secreted by HT-1080 which degraded the extracellular matrix as a part of the invasive process.

Bai et al. (2003) used the transformed endothelial cell line SVR as an effective screen of natural product extracts to isolate anti-angiogenesis and antitumour compounds. They found that aqueous extracts of *Magnolia grandiflora* exhibited potent activity in SVR proliferation assays. Honokiol, the active principle of magnolia extract, exhibited potent antiproliferative activity against SVR cells in vitro. In vivo, honokiol was highly effective against angiosarcoma in nude mice. The preclinical data suggested honokiol to be a systemically available and nontoxic inhibitor of angiogenesis with potential chemotherapeutic activity. Honokiol induced caspase-dependent apoptosis in B-cell chronic lymphocytic leukaemia (B-CLL) cells and was more toxic towards B-CLL cells than to normal mononuclear cells, suggesting greater susceptibility of the malignant cells (Battle et al. 2005). B-CLL cells pretreated with interleukin-4 (IL-4), a cytokine known to support B-CLL survival, underwent apoptosis when subsequently incubated with honokiol, indicating that honokiol could also overcome the prosurvival effects of IL-4. Further, honokiol enhanced cytotoxicity induced by fludarabine, cladribine or chlorambucil. These data indicated honokiol to be a potent inducer of apoptosis in B-CLL cells and should be examined for further clinical application either as a single agent or in combination with other anticancer agents.

In an in vitro proliferation assay, 100 μM of magnolol inhibited the proliferation of B16-BL6, THP-1, BAE and HT-1080 tumour cells, but 30 μM of magnolol did not affect cell proliferation (Ikeda and Nagase 2002). Additionally, 100 μM of magnolol induced apoptotic cell death within 24 h in three tumour cell lines, B16-BL6, THP-1 and HT-1080, not BAE cells, and then up-regulated the activity of caspase-3 and caspase-8. In another study, magnolol inhibited cell proliferation and induced apoptosis of CGTH W-2 thyroid carcinoma cells (Huang et al. 2007). The results showed that magnolol initiated apoptosis via the cytochrome c/caspase 3/PARP/AIF and PTEN/Akt/caspase 9/PARP pathways and necrosis via PARP activation. In vitro studies showed that magnolol induced apoptosis in HCT-116 colon cancer cells, migration and invasion of HCT-116 cells through activation of AMP-activated protein kinase (AMPK) (Park et al. 2012). Magnolol downregulated expression of the anti-apoptotic protein Bcl2, up-regulated expression of pro-apoptotic protein p53 and Bax and caused the release of mitochondrial cytochrome C. Magnolol inhibited proliferation of human leukemic HL-60 cells and Jurkat T leukaemia cells via inducing apoptosis in a dose- and time-dependent manner (Zhong et al. 2003). Activation of caspase-9, -3 and -2 and the proteolytic cleavage of poly(ADP-ribose) polymerase were found during apoptosis induced by magnolol. Further, magnolol did not cause apoptosis in neutrophils and peripheral blood mononuclear cells of healthy donors. The results suggested that magnolol could be a potentially effective drug for leukaemia with low toxicity to normal blood cells. In another study, intraperitoneal (i.p.) administration of 2 or 10 mg/kg of magnolol to mice significantly suppressed liver and spleen metastasis or lung metastasis (Ikeda et al. 2003). In the spontaneous lung metastasis model using B16-BL6 melanoma, multiple i.p. administrations of 10 mg/kg of magnolol after and before tumour inoculation significantly suppressed lung metastasis and primary tumour growth. In addition,

magnolol significantly inhibited B16-BL6 cell invasion of the reconstituted basement membrane without affecting cell growth. The data from the in vivo experiments suggested that magnolol possessed strong antimetastatic ability. Magnolol inhibited proliferation of human malignant melanoma A375-S2 cells (You et al. 2009). It induced oligonucleosomal fragmentation of DNA in A375-S2 cells and increased caspase-3, 8, 9 activities followed by the degradation of caspase-3 substrates, inhibitor of caspase-dependent DNase and poly-(ADP-ribose) polymerase. The results indicated that magnolol induced apoptosis by activation of both mitochondrial and death receptor pathways in A375-S2 cells.

In vitro studies showed magnolol and honokiol to have potential differentiation enhancing activity, allowing the use of low doses of 1,25-dihydr oxyvitamin D3 (VD3) and all-trans-retinoic acid (ATRA)in the treatment of acute promyelocytic leukaemia (Fong et al. 2005). Both compounds enhanced HL-60 human leukaemia cell differentiation induced by 1,25-dihydroxyvitamin D3 and retinoic acid. Magnolol and honokiol were found to possess antitumour activity by targeting the apoptosis pathways such as death receptor-mediated pathway, mitochondria-mediated pathway, caspase-mediated common pathway and regulation of apoptosis-related proteins which have been considered as targets for cancer therapies (Xu et al. 2011).

Liu et al. (2008) demonstrated that treatment of different human breast cancer cell lines with honokiol resulted in a time- and concentration-dependent growth inhibition in both estrogen receptor-positive and estrogen receptor-negative breast cancer cell lines, as well as in drug-resistant breast cancer cell lines such as adriamycin-resistant and tamoxifen-resistant cell lines. The inhibition of growth was associated with a G1-phase cell cycle arrest and induction of caspase-dependent apoptosis. Combination of honokiol with the mTOR inhibitor rapamycin presented synergistic effects on induction of apoptosis of breast cancer cells. The data suggested that honokiol, either alone or in combination with other therapeutics, could serve as a new, promising approach for breast cancer treatment. Honokiol had been demonstrated to combat cancer through mechanisms including inhibition of angiogenesis and induction of apoptosis (Xu et al. 2006). It was further shown that honokiol downregulated the expression of P-glycoprotein at mRNA and protein levels in MCF-7/ADR, a human breast MDR cancer cell line. Fried and Arbiser (2009) reported that honokiol, a multifunctional antiangiogenic and antitumour agent, had two major mechanisms of chemotherapeutic action: firstly, by blocking signalling in tumours with defective p53 function and activated ras by directly blocking the activation of phospholipase D by activated ras and secondly by inducing cyclophilin D, thus potentiating the mitochondrial permeability transition pore and causing death in cells with wild-type p53. Pretreatment of female SKH-1 mice with honokiol, at concentrations in micrograms per application compared with milligram applications of other potential chemopreventive agents, prevented UVB-induced skin cancer development (Chilampalli et al. 2010). This chemopreventive action was possibly by activating pro-apoptotic proteins (caspase-3, caspase-8, caspase-9, poly ADP-ribosepolymerase (PARP) and p53) through both intrinsic and extrinsic pathways leading to the induction of DNA fragmentation and apoptosis. In another study, treatment of human breast cancer cells (MCF-7) and murine mammary cancer cells (4T1) with honokiol resulted in a dose-dependent inhibition of migration of these cells, which was associated with a reduction in nitric oxide (NO) levels (Singh and Katiyar 2011). Honokiol also inhibited the levels of cyclooxygenase-2 (COX-2) and prostaglandin (PG) E2 and activation of nuclear factor κB (NF-κB) in 4T1 cells. The study by Nagalingam et al. (2012) provided in vitro and in vivo evidence of the integral role of the liver kinase B1 (LKB1)-AMP-activated protein kinase (AMPK) axis in honokiol-mediated inhibition of the invasion and migration of breast cancer cells. They concluded that honokiol treatment could potentially be a rational therapeutic strategy for breast carcinoma.

In prostate cancer (PCa) cells honokiol induced apoptosis via the activation of caspases 3, 8 and 9 and the cleavage of poly-adenosine

diphosphate ribose polymerase in a dose- and time-dependent manner (Shigemura et al. 2007). Honokiol was shown to inhibit the growth and depress serum prostate-specific antigen (PSA) in mice harbouring C4-2 xenografts in the skeleton, and the combination with docetaxel showed additive effects that inhibited further growth without evidence of systemic toxicity. The combination of honokiol and low-dose docetaxel may be used to improve patient outcome in androgen-independent prostate cancer with bone metastasis. Treatment of prostate cancer PC-3 cells for 24 h with magnolol (60 μM) induced apoptotic cell death in a dose- and time-dependent manner (Lee et al. 2009). A sustained inhibition of the major survival signal, Akt (protein kinase B), occurred in magnolol-treated cells. The apoptotic cell death by magnolol was associated with significant inhibition of pEGFR (phosphorylated epidermal growth factor receptor), pPI3K (phosphorylated phosphatidylinositol 3-kinase) and pAkt (phosphorylated Akt). The results suggested that one of the mechanisms of the apoptotic activity of magnolol involved its effect on epidermal growth factor receptor (EGFR)-mediated signalling transduction pathways. Interestingly, at similar concentrations (60 μM), magnolol treatment did not affect the viability of normal human prostate epithelial cell (PrEC) line.

Topical treatment of SKH-1 hairless mice with honokiol in a hydrophilic cream-based topical formulation before or after UVB (180 mJ/cm^2) irradiation resulted in a significant protection against photocarcinogenesis in terms of tumour multiplicity and tumour volume per tumour-bearing mouse (Vaid et al. 2010). Honokiol also inhibited and delayed the malignant progression of papillomas to carcinomas. Treatment with honokiol significantly inhibited UVB-induced expression of cyclooxygenase-2, prostaglandin E(2), proliferating cell nuclear antigen and proinflammatory cytokines, such as tumour necrosis factor-α, interleukin (IL)-1β and IL-6 in the skin as well as in skin tumours. Also, honokiol (1) inhibited the levels of cyclins D1, D2 and E and associated cyclin-dependent kinases (CDKs)2, CDK4 and CDK6, (2) up-regulated Cip/p21 and Kip/p27 and (3) inhibited the levels of phosphatidylinositol 3-kinase and the phosphorylation of Akt at Ser(473) in UVB-induced skin tumours.

Honokiol exerted growth inhibitory effects on two pancreatic cancer cell lines, MiaPaCa and Panc, by causing cell cycle arrest at G_1 phase and induction of apoptosis (Arora et al. 2011). Honokiol also potentiated the cytotoxic effects of gemcitabine, in part, by restricting the gemcitabine-induced nuclear accumulation of NF-κB in the treated pancreatic cancer cell lines. In separate studies, honokiol inhibited the growth and proliferation of oral squamous cell carcinoma cells in vitro in a time- and dose-dependent manner (Chen et al. 2011b). Its inhibitory effect was associated with the cell apoptosis. The inhibition or apoptosis mediated by 15 μg/ml or 20 μg/ml of honokiol were stronger than that of 20 μg/ml 5-fluorouracil suggesting honokiol to be a promising compound that can be potentially used as a novel treatment agent for human oral squamous cell carcinoma. Honokiol exhibited significant antiproliferative activity in a dose-dependent manner on HEI 193 human cells schwannoma (Lee et al. 2012a). Significant apoptosis was detected on schwannoma cells with 7 mg/ml (IC_{50}) honokiol. Western blot analysis showed significant inhibition of extracellular signal-regulated kinase (ERK) phosphorylation. The results suggested that honokiol could be evaluated as a chemotherapeutic agent for vestibular schwannoma. In a separate study, honokiol was reported to be a potent inhibitor of hypoxia-inducible-factor (HIF) pathways as well as hypoxia-induced expression of histone lysine demethylases (KDMs) in a number of cancer and retinal pigment epithelial cell lines (Vavilala et al. 2012). Treating the cells with honokiol led to inhibition of KDM-mediated induction of pro-angiogenic genes (adrenomedullin and growth differentiation factor 15) under hypoxic conditions. The results suggested therapeutic benefits with honokiol for treatment of pathological neovascularization in retinal ischaemic diseases and cancers.

In their review, Arora et al. (2012) reported that honokiol targeted multiple signalling pathways

including nuclear factor kappa B (NF-κB), STAT3 (signal transducers and activator of transcription 3), EGFR (epidermal growth factor receptor) and m-TOR (mammalian target of rapamycin), which have great relevance during cancer initiation and progression. They also reported that recent studies had demonstrated anti-inflammatory, antiangiogenic, antioxidative and anticancer properties of honokiol in in-vitro and in preclinical models. Recent studies showed that honokiol induced apoptosis of cancer cells due to endoplasmic reticulum stress by binding with glucose-regulated protein 78 (GRP78) (Martin et al. 2013). With respect to cell death, honokiol exhibited synergistic effects on melanoma and glioblastoma cells with the endoplasmic reticulum stress inducers fenretinide or bortezomib, but only additive (fenretinide) or inhibitory (bortezomib) effects on neuroblastoma cells.

Magnolol and honokiol exhibited cytotoxic activity in vitro against OVCAR-3 (ovarian adenocarcinoma), HepG2 (hepatocellular carcinoma) and HeLa (cervical epithelioid carcinoma) cell lines (Syu et al. 2004). The CD_{50} values for compounds 1–3 were in the range of 3.3–13.3 μg/ml. Studies showed that honokiol, magnolol and 4-*O*-methylhonokiol downregulated the expression of P-glycoprotein (P-gp) in a concentration- and time-dependent manner in NCI/ADR-RES cells (Han and Van Anh 2012). Furthermore, pretreatment with honokiol, magnolol or 4-*O*-methylhonokiol significantly increased the susceptibility of cancer cells to daunorubicin-induced cytotoxicity in NCI/ADR-RES cells. The results suggested all three could be promising agents for reducing the multidrug resistance of cancer cells to anticancer drugs via the down-regulation of P-gp expression. In other studies, treatment of human epidermoid squamous carcinoma A431 cells with honokiol significantly decreased cell viability and cell proliferation in a concentration- and time-dependent manner (Chilampalli et al. 2011a). Pretreatment of A431 cells with honokiol induced cycle arrest at G0/G1 phase, DNA fragmentation and apoptosis. Similarly they reported that magnolol pretreatments prevented UVB-induced skin cancer development in mice by enhancing apoptosis, causing cell cycle arrest at G2/M phase and affecting various signalling pathways Chilampalli et al. (2011b). They suggested that magnolol could be a potentially safe and potent anticarcinogenic agent against skin cancer.

Costunolide was shown to induce apoptosis in human promonocytic leukaemia U937 cells by depleting the intracellular thiols (Choi et al. 2002). Costunolide treatment rapidly depleted the intracellular reduced glutathione (GSH) and protein thiols, and this preceded the occurrence of apoptosis. Overexpression of Bcl-2 significantly attenuated the effects of costunolide. The results suggested that the costunolide-induced apoptosis depended on intracellular thiol contents, which were modulated by Bcl-2. Costunolide, exhibited significant inhibition on the farnesylation process of human lamin-B by farnesyl-protein transferase (FPTase), in a dose-dependent manner in vitro (IC_{50} value = 20 μM) (Park et al. 2001). Costunolide also inhibited proliferation of cultured human tumour cells, namely, A549 (non-small-cell lung), SK-OV-3 (ovary), SK-MEL-2 (melanoma), XF498 (central nerve system) and HCT-15 (colon), in vitro.

Four aporphine alkaloids, magnoflorine, lanuginosine, liriodenine and anonaine, isolated from the methanol leaf extract, exhibited cytotoxic activity (Mohamed et al. 2010). Magnoflorine was more cytotoxic (IC_{50} 0.4 μg/ml) than lanuginosine (IC_{50}2. μg/ml) against HEPG2 (hepatocellular carcinoma cell line) in comparison with the standard doxorubicin (IC_{50} 0.27 μg/ml). In addition, magnoflorine and lanuginosine exhibited cytotoxicity against U251 (brain tumour cell line), with IC_{50} of 7 and 4 μg/ml, respectively. The two compounds were found to be inactive against the Hela cancer cell (cervix tumour cell line).

Antiviral Activity

Magnolol and honokiol were found to be inhibitors of Epstein–Barr virus early antigen (EBV-EA) activation induced by 12-*O*-tetradecanoylphorbol-13-acetate (Konoshima et al. 1991). Magnolol exhibited remarkable inhibitory effects on mouse

skin tumour promotion in an in vivo two-stage carcinogenesis test. Honokiol inhibited hepatitis C virus (HCV) infection in vitro by targeting cell entry and replication and, only at a concentration >30 μM, internal ribosome entry site (IRES)-mediated translation of HCV life cycle (Lan et al. 2012). Based on its high therapeutic index (LD_{50}/EC_{90} = 5.4), honokiol may be a promising drug for the treatment of hepatitis C virus infection. The methanol leaf extract showed high antiviral activity against the herpes simplex virus (HSV-1) 76.7 % inhibition at 1.1 μg/ml, but exhibited a moderate antiviral activity against poliovirus type-1 (47 % inhibition at the same concentration) (Mohamed et al. 2010).

Antidiabetic Activity

Magnolol inhibited 11beta-hydroxysteroid dehydrogenase (11beta-HSD) without increases in the blood concentration of corticosterone and in thymocyte apoptosis in mice (Horigome et al. 2001). Magnolol inhibited the enzyme activity in kidney and thymus, while the activity in liver was not affected so that the blood concentrations of corticosterone could not exceed the control level. Excess of corticosteroids such as corticosterone can have a detrimental impact on glucose control, blood pressure and lipid levels. Studies showed that in magnolol-treated non-obese type 2 diabetic Goto-Kakizaki (GK) rats, fasting blood glucose, plasma insulin, urinary protein and creatinine clearance were significantly decreased, and the pancreatic islets also showed strong insulin antigen positivity (Sohn et al. 2007). The overproduction of renal sorbitol, advanced glycation end products (AGEs), type IV collagen and TGF-beta1 mRNA were significantly reduced in magnolol-treated GK rats. The results suggested that the use of magnolol could result in good blood glucose control and prevent or retard development of diabetic complications such as diabetic nephropathy. Studies demonstrated that high glucose (25 mM) or S100b (a specific receptor of advance glycation end products ligand) (5 μg/ml) induced increases in transforming growth factor-beta1 (TGF-beta1) and fibronectin expression in human retinal pigment epithelial cells, but this increased expression was inhibited by magnolol via the extracellular signal-regulated kinase (ERK)/mitogen-activated protein kinase (MAPK)/Akt activation signalling pathway in human retinal pigment epithelial cells under diabetic conditions (Kim et al. 2007).

Choi et al. (2011) found that treatment of 3T3-L1 preadipocytes with honokiol promoted adipocyte differentiation via increased expression of PPARγ2 mRNA and potentiation of insulin signalling pathways such as the Ras/ERK1/2 and phosphoinositide-3-kinase (PI3K)/Akt signalling pathways. In other studies, Choi et al. (2012) found that honokiol and magnolol dose-dependently and acutely stimulated glucose uptake without synergistic effects of combined administration in L6 myotubes by activating Akt phosphorylation, a key element in the insulin signalling pathway. The results suggested that honokiol and magnolol may have beneficial effects on glucose metabolism. In diabetic KKAy mice, oral application of honokiol prevented hyperglycaemia and suppressed weight gain (Atanasov et al. 2013). While honokiol stimulated basal glucose uptake to a similar extent as pioglitazone, it did not induce adipogenesis in contrast to pioglitazone. They found that honokiol acted as a partial non-adipogenic peroxisome proliferator-activated receptor gamma (PPARγ) agonist that could clinically be used to counteract hyperglycaemia.

Antimicrobial Activity

Three phenolic constituents magnolol, honokiol and 3.5′-diallyl-2′-hydroxy-4-methoxybiphenyl isolated from *Magnolia grandiflora* were shown to possess significant antimicrobial activity against Gram-positive and acid-fast bacteria and fungi (Clark et al. 1981). Magnolol and honokiol exhibited antimicrobial activity against periodontopathic microorganisms, *Porphyromonas gingivalis, Prevotella gingivalis, Actinobacillus actinomycetemcomitans, Capnocytophaga gingivalis* and *Veillonella dispar*, and had a relatively low cytotoxic effect on human gingival cells (Chang et al. 1998). However, magnolol and

honokiol were less potent than chlorhexidine. They suggested that magnolol and honokiol may have a potential therapeutic use as a safe oral antiseptic for the prevention and the treatment of periodontal disease. Magnolol was found to have potent inhibitory effect on the growth of *Helicobacter pylori* (Bae et al. 1998). In another study, honokiol and magnolol exhibited marked antimicrobial effect (MIC = 25 μg/ml) against *Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, Prevotella intermedia, Micrococcus luteus* and *Bacillus subtilis* but did not show antimicrobial activity (MIC > or = 100 μg/ml) for *Shigella flexneri, Staphylococcus epidermidis, Enterobacter aerogenes, Proteus vulgaris, Escherichia coli* and *Pseudomonas aeruginosa* (Ho et al. 2001). The results indicated that honokiol and magnolol, although less potent than tetracycline, displayed a significant antimicrobial activity for periodontal pathogens. Magnolol and honokiol exhibited antibacterial activities against vancomycin-resistant enterococci and methicillin-resistant *Staphylococcus aureus* at minimum inhibitory concentrations (MIC) in the range of 6.25–25 μg/ml (Syu et al. 2004). Honokiol and magnolol showed strong antibacterial activities against both acne-causing bacteria *Propionibacterium acnes* and *Propionibacterium granulosum*, and the minimum inhibitory concentrations (MIC) of honokiol and magnolol were 3–4 μg/ml (11.3–15 μM) and 9 μg/ml (33.8 μM), respectively (Park et al. 2004). It was further found that magnolol and honokiol killed *P. acnes* rapidly, with 10(5) organisms/ml eliminated within 10 min of treatment with either 45 μg (169.2 μM) of magnolol or 20 μg (75.2 μM) of honokiol per ml. In the 3-(4,5-dimetyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay using two animal cell lines, human normal fibroblasts and HaCaT, magnolol exhibited lower cytotoxic effects than honokiol at the same concentration. Further they both reduced secretion of interleukin-8 and tumour necrosis factor-alpha (TNF-alpha) induced by *P. acnes* in THP-1 cells indicating their anti-inflammatory effects. When applied topically, neither of the phenolic compounds induced any adverse reactions in a human skin primary irritation test. Therefore, based on these results, the scientists suggested the possibility that magnolol and honokiol may be considered as attractive acne-mitigating candidates for topical application. Honokiol and its synthesized derivatives honokiol-acetate, honokiol-succinic acid, honokiol-glycerol, honokiol-glycine, honokiol-glucose and honokiol-mannose exhibited antimicrobial activity (Kim et al. 2010). Among the tested compounds, honokiol-glycine showed improved water solubility and antibacterial activities against *Escherichia coli* and *Pseudomonas aeruginosa* when compared to honokiol.

M. grandiflora leaf essential oil displayed antifungal activity against five dermatophyte strains and had antimicrobial activity against *Staphylococcus aureus* and *Streptococcus pyogenes*, which cause skin infections that potentially may lead to sepsis (Guerra-Boone et al. 2013). However, the antioxidant activities of all oils were small (half maximal effective concentration values >250 μg/ml).

Cyclocolorenone, a sesquiterpene ketone isolated from *Magnolia grandiflora,* exhibited both antibacterial and antifungal activities in vitro (Jacyno et al. 1991). It also inhibited growth of wheat coleoptiles and was phytotoxic to greenhouse grown tobacco plants. Two neolignan compounds, magnolol (5,5′-diallyl-2,2′-dihydroxy biphenyl, 1) and honokiol (5,5′-diallyl-2,4′-dihydroxybiphenyl, 2), isolated from the stem bark, showed significant inhibitory activities against various human pathogenic *Trichophyton mentagrophytes, Microsporum gypseum, Epidermophyton floccosum, Aspergillus niger, Cryptococcus neoformans* and *Candida albicans* with minimum inhibitory concentrations (MIC) in a range of 25–100 μg/ml (Bang et al. 2000).

Anticonvulsant Activity

The ethyl ether and hydroalcoholic extract of *Magnolia grandiflora* seeds, orally administered to adult male wistar rats in a single dose of 250 mg/kg (calculated on lipidic base) and 200 mg/kg, exhibited abolition of the extensor reflex of maximal electric-induced seizure test in 50 and 40 % of the experimental animals,

respectively (Bastidas Ramírez et al. 1998). The results suggested that the chemical constituents in the seeds could be useful in the treatment of epileptic patients presenting convulsive seizures.

Studies showed that both honokiol and magnolol significantly increased the *N*-methyl-D-aspartate (NMDA)-induced seizure thresholds and honokiol was more potent than magnolol (Lin et al. 2005). These results demonstrated that magnolol and honokiol have differential effects on NMDA and non-NMDA receptors, suggesting that the distinct therapeutic applications of these two compounds for neuroprotection should be considered. Magnolol at doses of 40 and 80 mg/kg significantly delayed the onset of myoclonic jerks and generalized clonic seizures and decreased the seizure stage and mice mortality compared with those of the vehicle-treated animals (Chen et al. 2011a). The inhibitory effects of magnolol on epileptiform activity were mediated by the GABA(A)/benzodiazepine receptor complex.

Vasodilatory/Muscle Relaxant Activity

Magnolol (75 mg/kg, i.p.) completely inhibited the extensor reflex in 40 min after the injection while honokiol elicited almost the same effect on spinal reflex, but a higher dose (150 mg/kg, i.p.) (Watanabe et al. 1975). The results indicated that magnolol and honokiol are a distinct and long-lasting muscle relaxant activity than mephenesin (50 mg/kg, i.p.), with as much shorter duration of action. Magnolol, 5,5′-diallyl-2,2′-dihydroxydiphenyl, produced potent inhibitory effects of gradual onset and of long duration on grip strength in mice and spinal reflexes in young chicks (Watanabe et al. 1983a). Position of allyls and hydroxyls in honokiol, 5,3′-diallyl-2,4′-dihydroxydiphenyl, was different from magnolol, although the pharmacological characteristics were quite similar to magnolol. The results suggested that a hydroxyl accelerated the onset and shortened the muscle relaxant activity of diphenyl and an allyl impacted the activity in the opposite direction. Both radicals appear to intensify the activity.

The aqueous extracts of flowers and leaves have been reported to exhibit cardiovascular effects (Mellado et al. 1980). *Magnolia grandiflora* extracts were found to have positive inotropic and vasodilatory effects in isolated and perfused male guinea pigs hearts (Del Valle Mondragón et al. 2004). Vulgarenol and 2-p-hydroxyphenyl-2-hydroxy-ethylamine were isolated and identified and were found to be responsible for its positive inotropic and vasodilatory effects being complemented by magnograndiolide and tyramine. A sesquiterpene, vulgarenol, isolated from *Magnolia grandiflora* flower petals caused a statistically significant decrease in coronary vascular resistance and increased nitric oxide release and cyclic guanosine monophosphate accumulation in left ventricular tissue samples in the Langendorff isolated and perfused heart model when compared to control (Del Valle-Mondragón et al. 2007, 2009). Pretreatment with 3 μm gadolinium chloride hexahydrate, 100 μm Nω-nitro-L-arginine methyl ester hydrochloride and 10 μm 1H-[1,2,4]oxadiazolo[4,2-a]quinoxalin-1-one significantly abolished the vulgarenol-induced coronary vascular resistance decrease, nitric oxide increased release and cGMP accumulation in left ventricular tissue samples. The results supported the fact that nitric oxide and cyclic guanosine monophosphate were likely involved in the endothelium-dependent coronary vasodilation.

Studies showed that magnolol relaxed vascular smooth muscle in the rat thoracic aorta by releasing endothelium-derived relaxing factor (EDRF) and by inhibiting calcium influx induced by high potassium or norepinephrine through voltage-gated calcium channels (Teng et al. 1990). Pretreatment of rat aortic rings with magnolol reduced vascular tension induced by the thromboxane A_2 agonist U46619, sodium fluoride (NaF) and the α_1-adrenoceptor agonist phenylephrine in both endothelium-intact and endothelium-denuded rings (Seok et al. 2012). The magnitudes of the relaxation effects of magnolol on the contraction induced by each of the drugs were similar. Magnolol reduced vascular contraction by inhibiting the RhoA/Rho kinase pathway in endothelium-denuded rat aorta.

Magnolol (75 mg/kg, i.p.) completely inhibited the extensor reflex in 40 min after the injection while honokiol elicited almost the same effect on spinal reflex, but a higher dose (150 mg/kg, i.p.) (Watanabe et al. 1975). The results indicated that magnolol and honokiol are a distinct and long-lasting muscle relaxant activity than mephenesin (50 mg/kg, i.p.), with as much shorter duration of action.

Studies suggested that magnolol caused a depression of the ascending activating systems as well as of the spinal cord (Watanabe et al. 1983b). Magnolol and honokiol produced sedation, ataxia, muscle relaxation and a loss of the righting reflex with an increase in dose of 50–500 mg/kg i.p. Magnolol and honokiol at a dose of 50 mg/kg suppressed spinal reflexes in young chicks in a similar manner, but with a much longer duration of action than mephenesin. Pretreatment of mice with magnolol 100 mg/kg inhibited tonic extensor convulsions and death produced by an intracerebroventricular injection of penicillin G potassium 50 μg. In rats, after an intraventricular injection of penicillin G 400 μg, magnolol suppressed the incidence of spike discharge, but not seizure discharge. Magnolol produced spindle discharges in sensory and motor cortex electroencephalograms and inhibited midbrain reticular formation- and hypothalamus-stimulated responses in the neo- and palaeo-cortex electroencephalograms, respectively.

Studies by Jeong et al. (2009) found that magnolol differently regulated the spontaneous gastrointestinal motility according to the region of the rat gastrointestinal tracts and orientation of smooth muscles. Magnolol (0.3–30 μM) dose-dependently stimulated the tone and amplitude of spontaneous contractions in ileum longitudinal muscles. Magnolol at 3 μM significantly increased the contractions of jejunum longitudinal and colon circular muscles, but not the longitudinal muscle contractions in fundus, antrum and colon. The magnolol-induced regulation of smooth muscle contractions in rat gastrointestinal strips was likely to be mediated, at least in part, by activation of acetylcholine and 5-HT receptors, possibly the M(3) and/or 5-HT(4) receptors.

Cardioprotective Activity

Studies in male Sprague-Dawley rats found that magnolol may protect the myocardium against ischaemic injury and suppress ventricular arrhythmia during ischaemia and reperfusion (Hong et al. 1996). The incidence and duration of ventricular tachycardia and ventricular fibrillation during 30 min coronary ligation were significantly reduced by magnolol. Ventricular arrhythmias during 10 min reperfusion after the relief of coronary ligation were also reduced. In rats subjected to 4 h, coronary ligation magnolol significantly reduced infarct size. Similar results were obtained with honokiol at similar concentrations, and they concluded that honokiol may protect the myocardium against ischaemic injury and suppress ventricular arrhythmia during ischaemia and reperfusion (Tsai et al. 1996). Studies demonstrated that pretreatment of rats with magnolol (0.2 and 0.5 μg/kg, i.v. bolus) before 45 min of left coronary artery occlusion significantly suppressed the incidence of ventricular fibrillation and mortality when compared with the control group (Lee et al. 2001). Magnolol (0.2 and 0.5 μg/kg) also significantly reduced the total duration of ventricular tachycardia and ventricular fibrillation. After 1 h of reperfusion, pretreatment with magnolol (0.2 and 0.5 μg/kg) caused a significant reduction in infarct size. Additionally, magnolol (0.2 μg/kg) significantly reduced superoxide anion production and myeloperoxidase activity, an index of neutrophil infiltration in the ischaemic myocardium. Further, pretreatment with magnolol (0.2 and 0.5 μg/kg) suppressed ventricular arrhythmias elicited by reperfusion following 5 min of ischaemia. In in-vitro studies magnolol (5, 20 and 50 μM) significantly suppressed *N*-formylmethionyl-leucyl-phenylalanine (fMLP; 25 nM)-activated human neutrophil migration in a concentration-dependent manner. The finding suggested that pronounced cardioprotective activity of magnolol may be mediated by its antioxidant activity and by its capacity for neutrophil inhibition in myocardial ischaemia–reperfusion. Neutrophil adhesion had been reported to play a crucial process during the inflammatory response in cardiac ischaemia–reperfusion injury.

Studies by Shen et al. (1998) found that magnolol inhibited neutrophil adhesion which accounted for its anti-ischaemia–reperfusion injury effect. They found that the inhibitory effect of magnolol on neutrophil adhesion to the extracellular matrix is mediated, at least in part, by inhibition of the accumulation of reactive oxygen species, which in turn suppressed the up-regulation of Mac-1 essential for neutrophil adhesion. A pertussis toxin-insensitive inositol trisphosphate signalling pathway was found to be involved in the magnolol-induced [Ca2+]i elevation in rat neutrophils (Wang and Chen 1998).

Magnolol (5–20 μM) concentration-dependently induced significant rat vascular smooth muscle cells (VSMCs) apoptosis in vitro (Chen et al. 2003). Magnolol increased caspase-3 and caspase-9 activities significantly and reduced the mitochondrial potential (Deltapsi(m)). The levels of B-cell leukaemia/lymphoma-2 (Bcl-2), but not those of Bcl-2-associated X protein (Bax) or Bcl-x(L), were downregulated concentration dependently by magnolol. In an animal model, balloon angioplasty-induced neointima formation was inhibited significantly by magnolol and Bcl-2 protein levels were reduced. The results showed that magnolol-induced apoptosis in VSMCs via the mitochondrial death pathway was found to be mediated through downregulation of Bcl-2 protein levels, both in vivo and in vitro. Magnolol thus shows potential as a novel therapeutic agent for the treatment of atherosclerosis and restenosis. The pathological mechanism of percutaneous transluminal coronary angioplasty-induced restenosis had been attributed to outgrowth of vascular smooth muscle cells, and magnolol had been shown to inhibit rat smooth muscle cell proliferation (Wu et al. 2005). Magnolol (0.05 mg/ml) caused an approximate 61 % reduction of smooth muscle cells progressing to the S-phase, a significant reduction (73 %) of DNA synthesis and protein level of the proliferating cell nuclear antigen was suppressed by approximately 48 %. Further, malondialdehyde formation was significantly inhibited by 0.05 mg/ml of magnolol supporting the antioxidant effect of magnolol. Magnolol had exhibited approximately 1,000 times more potent antioxidant effects than alpha-tocopherol. The study suggested that magnolol might be a potential pharmacological reagent in preventing balloon injury-induced restenosis. Studies showed that magnolol inhibited urotensin-II-induced cell proliferation, endothelin-1 protein secretion and extracellular signal-regulated kinase (ERK) phosphorylation in rat cardiac fibroblasts by interfering with reactive oxygen species generation (Liou et al. 2009).

The cardiovascular protective effects of magnolol were reported to be cell-type specific and dose related (Ho and Hong 2012). Magnolol under low and moderate dosage was reported to possess the ability to protect heart from ischaemic/reperfusion injury, to reduce atherosclerotic change, to protect endothelial cell against apoptosis and to inhibit neutrophil–endothelial adhesion. Magnolol was reported to induce apoptosis in vascular smooth muscle cells at moderate concentration and to inhibit proliferation at moderate and high concentration. High concentration of magnolol also abolished platelet activation, aggregation and thrombus formation and served as smooth muscle relaxant at high concentration.

Cholesterol Homeostasis Activity

Honokiol was found to be an activator of the ABCA1 promoter by binding to retinoid X receptor beta as a ligand (Jung et al. 2010). It was found that honokiol also increased ABCA1 mRNA and protein expression levels in a dose-dependent manner in U251-MG cells without significant cell death and also increased ABCA1, ABCG1 and apolipoprotein E (apoE) expression levels in THP-1 macrophages. ABCA1, a member of the ATP-binding cassette transporter family, was found to regulate high-density lipoprotein (HDL) metabolism and reversed cholesterol transport.

Hepatoprotective Activity

Honokiol was found to exhibit in vitro and in vivo protective effects on rat liver from peroxidative

injury (Chiu et al. 1997). The inhibitory effect of honokiol on oxygen consumption and malondialdehyde formation during iron-induced lipid peroxidation in liver mitochondria showed obvious dose-dependent responses with a concentration of 50 % inhibition being 2.3×10^{-7} M and 4.96×10^{-7} M, respectively, that is, 550 times and 680 times more potent than alpha-tocopherol, respectively. They found that the dose-dependent protective effect of honokiol on ischaemia–reperfusion injury was 10–100 μg/Kg body weight. They found honokiol to be a strong antioxidant and may have clinical implications for protection of hepatocytes from ischaemia–reperfusion injury. Honokiol and magnolol were found to have protective effect n hepatocyte injury induced by either tertiary butyl hydroperoxide (tBH)- or D-galactosamine (GalN) (Park et al. 2003). Treatment with honokiol or magnolol significantly inhibited lipid peroxidation in cells and media, the generation of intracellular reactive oxygen species (ROIs) and intracellular glutathione (GSH) depletion induced by tBH. The hepatoprotective effects of honokiol and magnolol were attributed to their antioxidant activity. Studies showed that treatment of rats with magnolol exerted an anti-hepatotoxic activity induced by acetaminophen (*N*-acetyl-p-aminophenol/APAP) (Chen et al. 2009b). Elevated levels of aspartate aminotransferase, alanine aminotransferase and lactate dehydrogenase induced by APAP were reduced by treatment with magnolol lipid peroxidation (thiobarbituric acid-reactive substance/TBARS), and glutathione depletion in liver tissue induced by APAP were also restored by magnolol treatment. However, separate studies showed that magnolol could not protect liver grafts from cold ischaemia–reperfusion injury (Kao et al. 2010). High concentration of magnolol under serum-reduced conditions attenuated NF-kappaB-mediated signalling and induced intrinsic apoptotic pathway, thereby inducing in vitro hepatotoxicity.

The therapeutic goal in liver fibrosis is the reversal of fibrosis and the selective clearance of activated hepatic stellate cells (HSCs) by inducing apoptosis (Park et al. 2005). Honokiol, at concentrations of 12.5–50 μM, was found to induce apoptotic death in activated rat HSCs, while causing no cell viability change in hepatocytes. Apoptosis was induced via cytochrome c release and caspase activation in activated rat hepatic stellate cells.

Neuroprotective Activity

Studies demonstrated that magnolol protected neurons against chemical hypoxic damage or necrotic cell death in cortical neuron-astrocyte mixed cultures (Lee et al. 1998). Treatment with magnolol (10 and 100 μM) significantly reduced chemical hypoxia KCN-induced lactate dehydrogenase release in a concentration-dependent manner. In another study, magnolol (20 or 40 mg/kg, i.v.) significantly attenuated the heatstroke-induced hyperthermia, arterial hypotension, intracranial hypertension, cerebral ischaemia and neuronal damage and increased free radical formation and lipid peroxidation in the rat brain (Chang et al. 2003). The extracellular concentrations of ischaemic (e.g. glutamate and lactate/pyruvate ratio) and damage (e.g. glycerol) markers in the corpus striatum were increased after the onset of heatstroke. Magnolol significantly attenuated the increase in striatal ischaemia and damage markers associated with heatstroke.

Studies showed that honokiol at the doses of 10^{-7} or 10^{-6} g/kg ameliorated cerebral infarction from ischaemia–reperfusion injury in rats (Liou et al. 2003a). The neuroprotective effect of honokiol may be related to its antioxidant effect and antiplatelet aggregation activity. The protective effects of honokiol against focal cerebral ischaemia–reperfusion injury in rats were related to its antioxidant effect leading to a reduction in reactive oxygen species production by neutrophils (Liou et al. 2003b).

Administration of *N*-methyl-D-aspartic acid (NMDA) to mice caused a lethality of approximately 60 %, which resulted in a significant decrease of total glutathione (GSH) level and increase of thiobarbituric acid-reactive substances (TBARS) value in brain tissue (Cui et al. 2007). Oral administration of honokiol (> or = 3 mg/kg)

for 3 days reduced the lethality (60 %) in NMDA-treated group to 10 % level and alleviated the behavioural signs of NMDA neurotoxicity. Further, honokiol pretreatment restored the levels of total glutathione (GSH) and thiobarbituric acid-reactive substances (TBARS) in the brain tissue to control levels. Additionally, GSH peroxidase activity in cytosolic portion of brain homogenate was also restored significantly, whereas GSH reductase activity was not. Based on these results, oral intake of honokiol was suggested to prevent oxidative stress in the brain of mice.

Reactive oxygen species produced by neutrophils contributed to the pathogenesis of focal cerebral ischaemia–reperfusion injury and signal the inflammatory response. In a recent study, honokiol microemulsion (50 μg/kg, i.v. at 0, 1 or 3 h after reperfusion) significantly reduced neurological deficit, infarct volume and brain water content in rats subjected to cerebral ischaemia–reperfusion (Hu et al. 2013). Honokiol (0.1–10 μM) significantly attenuated oxygen-glucose deprivation- or glutamate-induced injury of fetal rat cortical neurons. They found that honokiol cerebral protective effect may be in part ascribed to the disruption of the PSD95-nNOS interaction leading to the inhibition of neurotoxic NO production.

Pulmonary Protective Activity

Studies showed that pretreatment of mice with magnolol protected against lipopolysaccharide (LPS)-induced acute lung injury (Fu et al. 2012). Magnolol markedly attenuated the histological alterations in the lung; reduced the number of total cells, neutrophils and macrophages in the bronchoalveolar lavage fluid; decreased the wet/dry weight ratio of lungs in the bronchoalveolar lavage fluid; downregulated the level of proinflammatory mediators and inhibited Toll-like receptor-4 (TLR4)-mediated NF-κB signalling pathways. The results suggested that magnolol may be a promising potential therapeutic reagent for acute lung injury treatment.

Antiplatelet Activity

Magnolol and honokiol were found to inhibit the activity of acetyl-CoA:1-alkyl-sn-glycero-3-phosphocholine acetyltransferase, a key enzyme in the biosynthesis of platelet-activating factor (PAF, 1-alkyl-2-acetyl-sn-glycero-3-phospho choline) (Yamazaki et al. 1994). The inhibitory action of magnolol and honokiol was reversible and similar to or higher than that of nordihydroguaiaretic acid. PAF production in human polymorphonuclear leukocytes stimulated by the ionophore A23187 was also suppressed dose dependently by magnolol and honokiol. Magnolol inhibited phorbol 12-myristate 13-acetate (PMA)-activated rat neutrophil aggregation in a concentration-dependent manner with an IC_{50} of 24.2 μM (Wang et al. 1998). Magnolol suppressed the enzyme activity of neutrophil cytosolic and rat brain protein kinase C and attenuated [3H] phorbol 12,13-dibutyrate binding to neutrophil cytosolic protein kinase C. The results suggested that the inhibition of PMA-induced rat neutrophil aggregation by magnolol may be attributable, at least in part, to the direct suppression of protein kinase C activity through blockade of the regulatory region of protein kinase C. The antiplatelet activity of honokiol was comparable to acetyl salicylic acid (Pyo et al. 2002). Hsu et al. (2004) demonstrated that magnolol suppressed thromboxane B2 (TXB2) and leukotriene B4 (LTB4) formation in A23187-stimulated rat neutrophils. Maximum inhibition was obtained with about 10 microM magnolol. Magnolol was more effective in the inhibition of cyclooxygenase (COX) activity than in the inhibition of 5-lipoxygenase (5-LO) activity. Magnolol alone stimulated cytosolic phospholipase A2 (cPLA2) phosphorylation and the translocation of 5-LO and cPLA2 to the membrane and evoked arachidonic acid (AA) release. The results indicated that magnolol inhibited the formation of prostaglandins and leukotrienes in A23187-stimulated rat neutrophils, probably through a direct blockade of COX and 5-LO activities. The stimulatory effects of magnolol at high concentration on the membrane association of 5-LO and cytosolic phospholipases A2 (cPLA2) were attributable to the elevation of

[Ca2+]i, and on the AA release was likely via activation of cPLA2 and Ca2+-independent PLA2 (iPLA2).

Magnolol and syringin showed only very mild inhibitory effects to all the stimulators. Studies by Zhang et al. (2007) showed that honokiol inhibited arterial thrombosis through stimulation of prostacyclin (PGI2) generation by up-regulating prostacyclin synthase protein expression and endothelial cell protection by inhibiting endothelial cell apoptosis. A recent study by Shih and Chou (2012) demonstrated that the antiplatelet and antithrombotic activities of magnolol in mice were modulated by up-regulation of peroxisome proliferator-activated receptor (PPAR)-β/γ-dependent pathways. Magnolol (20–60 μM) dose-dependently enhanced the activity and intracellular level of PPAR-β/γ in platelets.

Antihypertensive Activity

Results of studies suggested that chronic treatment with honokiol exerted an antihypertensive effect in spontaneously hypertensive rats (SHR) and its vasorelaxant action and antioxidant properties may contribute to reducing the elevated blood pressure (Zhang et al. 2010). Long-term administration of honokiol (400 mg/kg/day) to SHR significantly decreased systolic blood pressure. Honokiol (200, 400 mg/kg/day) enhanced the aortic relaxation in response to acetylcholine after a 49-day treatment and induced significant reductions in the elastin bands and media thickness in the aorta. Also, oral administration of honokiol significantly increased the plasma level of NO^{2-}/NO^{3-}, but lowered the level of malondialdehyde in the liver of SHR compared with the control vehicle.

Photoprotective Activity

Tanaka et al. (2007) found that *Magnolia obovata* extract inhibited NF-kappaB-mediated gene expression and demonstrated that external swabbing with magnolia extract preventing skin photoaging processes through keratinocyte hyperproliferation and degradation of collagen fibres in mice skin. Magnolol was identified as the solely responsible active compound in magnolia extract; it effectively inhibited the NF-kappaB-dependent transcription. The results suggested that Magnolia extract and its active component magnolol could be used to prevent the skin photoaging via inhibiting NF-kappaB by external topical application.

Antipyretic Activity

Studies suggested that intraperitoneal administration of magnolol decreased body temperature (due to increased heat loss and decreased heat production) by reducing 5-hydroxytryptamine release in rat hypothalamus in normothermic rats and in febrile rats treated with interleukin-1 beta (Hsieh et al. 1998).

Anxiolytic Activity

The use of the elevated plus-maze experiment and activity and traction tests in mice showed that seven daily treatments with 0.2 mg/kg and higher doses of honokiol had an anxiolytic effect without change in motor activity or muscle tone (Kuribara et al. 1998, 1999). The maximum effect was observed for doses of 0.5 mg/k. Honokiol at any dose in both single and repeated administration schedules caused neither change in motor activity nor disruption of traction performance. Diazepam, 1 mg/kg, had the same anxiolytic potential as 0.2 mg/kg honokiol but induced muscle relaxation. The results suggested that, in contrast with diazepam, honokiol selectively induced an anxiolytic effect with less liability of eliciting motor dysfunction and sedation or disinhibition. In another study, Honokiol and magnolol were shown to increase the number of [3H] muscimol binding sites threefold in rat forebrain membranes in vitro using a filtration assay by allosterically increasing the affinities of low-affinity sites (Squires et al. 1999). The potentiation of GABAergic neurotransmission by honokiol and magnolol was suggested to be

probably involved in the anxiolytic and central depressant effects. In a more recent study, mice treated with 7 daily injection of honokiol (1 mg/kg, p.o.) caused anxiolytic action which was similar to that was induced by 7 daily injection of diazepam (2 mg/kg, p.o.) in the elevated plus-maze test (Ku et al. 2011). The anxiolytic activity of honokiol may be mediated by altering the synthesis of glutamic acid decarboxylase (GABA synthesized enzymes) GAD(65) and GAD(67) in the brain of mice.

Neurotrophic Activity

Honokiol and magnolol had been demonstrated to increase choline acetyltransferase activity, inhibit acetylcholinesterase, promote potassium-function in in-vitro studies (Hou et al. 2000). Further studies showed that a high dose (10^{-4} M) of honokiol or magnolol may enhance in vivo hippocampal acetylcholine release in conscious, freely moving rats.

Antiosteoporotic/ Antiosteoclastogenic Activity

Studies by Hasegawa et al. (2010) suggested that honokiol inhibits osteoclast differentiation by suppressing the activation of p38 mitogen-activated protein kinase (MAPK), extracellular signal-regulated kinase (ERK) and c-Jun *N*-terminal kinase (JNK), decreasing the expressions of c-Fos and nuclear factor of activated T cells-c1 and attenuated bone resorption by disrupting the actin rings in mature osteoclasts. Therefore, honokiol could prove useful for the treatment of bone diseases associated with excessive bone resorption. In another study, honokiol caused a significant elevation of cell growth, alkaline phosphatase activity, collagen synthesis, mineralization, glutathione content and osteoprotegerin release in osteoblastic MC3T3-E1 cells (Choi 2011). Further, honokiol significantly decreased the production of osteoclast differentiation-inducing factors such as TNF-α, IL-6 and receptor activator of nuclear factor-kB ligand (RANKL) in the presence of antimycin A. The results demonstrated that honokiol may have positive effects on skeletal structure by stimulating osteoblast function and inhibiting the release of bone-resorbing mediators. Yamaguchi et al. (2011) showed honokiol to be a potent inducer of in vitro osteoblast differentiation by virtue of its capacity to suppress basal and tumour necrosis factor-alpha (TNF-α)-induced NF-κB activation and to alleviate the suppressive action of TNF-α on bone morphogenetic protein (BMP)-2-induced Smad activation. Their data confirmed that honokiol may have considerable promise as a dual anabolic/anti-catabolic agent for the amelioration of multiple osteoporotic diseases.

Separate studies showed that magnolol had a protective effect against antimycin A-induced cell damage in osteoblastic MC3T3-E1 cells by its antioxidant effects and the attenuation of mitochondrial dysfunction (Choi 2012). The data indicated that magnolol may reduce or prevent osteoblast degeneration in osteoporosis or other degenerative disorders. Kwak et al. (2012) found that magnolol caused a significant elevation of cell growth, alkaline phosphatase activity, collagen synthesis, mineralization and glutathione content in osteoblastic MC3T3-E1 cells. Skeletal turnover is orchestrated by a complex network of regulatory factors. Magnolol significantly decreased the production of osteoclast differentiation-inducing factors such as RANKL, TNF-α and IL-6 in the presence of antimycin A suggesting that magnolol may be used as an agent in the prevention of osteoporosis.

The natural biphenyl neolignan 4′-*O*-methyl honokiol (MH), from *M. grandiflora* seed oil, was found to be a cannabinoid CB_2 receptor-selective antiosteoclastogenic lead structure (Schuehly et al. 2011). MH exhibited an intriguing nonspecific heteroactive behaviour at the CB_2 receptor, i.e. acting as inverse agonist at $G_{i/o}$ and full agonist at $[Ca^{2+}]_i$, thus providing a novel type of functionally nonspecific CB_2 receptor ligand. The most active inverse agonists from a library of MH derivatives inhibited osteoclastogenesis in RANK ligand-stimulated RAW264.7 cells and primary human macrophages. Moreover, these ligands potently inhibited the osteoclastogenic

action of endocannabinoids. The results indicated methylhonokiol to be an easily accessible and apparently nontoxic CB_2 receptor ligand with potential for the development of therapeutics for diseases such as osteoarthritis, neuroinflammation, pain and chronic bowel disease in which the CB_2 receptor may play a role.

Antityrosinase/Skin Whitening Activity

Studies demonstrated that *M. grandiflora* flower extract decreased the expression of tyrosinase and tyrosinase-related protein 1 (TRP-1) and then inhibited melanogenesis in a dose-dependent manner in B16F10 cells (Huang et al. 2012). The flower extract also showed antioxidant capacities and depleted cellular reactive oxygen species. The authors concluded that *M. grandiflora* flower extract could be applied as a type of dermatological whitening agent in skin care products.

Sleep Enhancement Activity

Studies showed that magnolol prolonged the sleeping time induced by pentobarbital (Ma et al. 2009). The expression of the GABA(A) receptor alpha subunit was increased selectively by magnolol and magnolol increased chloride influx in primary cultured cerebellar granule cells. The results suggested that magnolol may enhance pentobarbital-induced sleeping behaviours through the activation of GABAergic systems. Studies showed that magnolol administered i.p. at a dose of 5 or 25 mg/kg could significantly shorten the sleep latency and increase the amount of non-rapid eye movement (non-REM, NREM) and rapid eye movement (REM) sleep for 3 h after administration with an increase in the number of NREM and REM sleep episodes in mice(Chen et al. 2012). The sleep-promoting effects and changes in c-Fos induced by magnolol were reversed by flumazenil, an antagonist at the benzodiazepine site of the GABA(A) receptor. The results indicated that magnolol increased NREM and REM sleep via the GABA(A) receptor.

Larvicidal Activity

All essential oils of the leaves, seeds with arils, deseeded unripe fruit and deseeded mature fruit showed larvicidal and biting deterrent activity against *Aedes aegypti* (Rehman et al. 2013). The LD_{50} values of three of essential oils ranged between 51.5 and 54.7 ppm against first instar larvae. Biting deterrent activity of one of the essential oils was equivalent to DEET with proportion not biting value of 0.94 versus 0.90, respectively.

Eryptosis Activity

Studies found that honokiol triggered suicidal erythrocyte death or eryptosis, a suicidal death characterized by cell shrinkage and by breakdown of cell membrane phosphatidylserine asymmetry with phosphatidylserine exposure at the erythrocyte surface (Zbidah et al. 2013). The effect at least in part was attributed to stimulation of Ca^{2+} entry and ceramide formation. Honokiol further induced slight but significant haemolysis. Eryptosis may be a mechanism of defective erythrocytes to escape haemolysis.

Allergy Problem

A patient who developed severe allergic reaction to *M. grandiflora* was reported (Guin et al. 1990). The condition was a chronic lichenified dermatitis that was unresponsive to treatment but cleared with protective measures.

Traditional Medicinal Uses

The bark, wood and other plant parts have been featured in American Indian medicine and listed in the United States Pharmacopoeia and pharmacognosy text as bitter tonics, antimalarials and diaphoretics (Rao and Davis 1982a, b, c). *Magnolia grandiflora* is widely used as a traditional medicine for the treatment of diarrhoea, abdominal diseases, rheumatic arthritis, heart

disturbances, high blood pressure, epilepsy, infertility and fever (Schühly et al. 2001). *M. grandiflora* seeds have been used in traditional Mexican medicine to treat different ailments such as spasms, infertility, epilepsy and inflammatory diseases (Mellado et al. 1980).

The plant is also used in traditional Chinese medicine for treatment of cold, headache and stomach ache (Wu et al. 1988). Extracts from its leaves are used to reduce blood pressure and as a raw material in Chinese herbal medicines, including use as a substitute for *M. officinalis* (Li et al. 2013). The bark of the root and stem of various *Magnolia* species has been used in traditional Chinese medicine to treat a variety of disorders including anxiety and nervous disturbances (Squires et al. 1999).

Other Uses

M. grandiflora has economic value, as well as strong resistance to wind and toxic gases such as sulphur dioxide (Li et al. 2013). It has beautiful flowers with a fragrant smell and is regarded as an important ornamental and horticultural species. Southern magnolia is a very popular ornamental tree throughout the south-eastern United States and California. It is also grown in Central and South America, Australia as well as parts of Asia. The leathery green leaves and beautiful flowers are used in decorating and floral arrangements.

The timber is hard and heavy and has been used commercially to make furniture, pallets and veneer.

M. grandiflora has nematicidal, antialgal and antifungal activities. The ethanol leaf extract of *Magnolia grandiflora* exhibited the strongest nematicidal activity against both nematodes, *Bursaphelenchus xylophilus* (Steiner & Buhrer) Nickle and *Panagrellus redivivus* (L.) Goodey, causing 73 % and 100 % mortality, respectively, within 48 h at 5 mg/ml (Hong et al. 2007). A new nematicidal sesquiterpene was obtained and determined to be 4,5-epoxy-1(10)*E*,11(13)-germacradien-12,6-olide. The median lethal concentrations (LC_{50}) of the compound against *B. xylophilus* and *P. redivivus* were 71 and 46 mg/l, respectively at 48 h.

Among the sesquiterpene lactones, costunolide and parthenolide and 1,10-epoxyparthenolide isolated from the dichloromethane extracts of leaves and the stem bark, costunolide showed the strongest antifungal activity against three fungi, *Nigrospora* spp., *Rhizoctonia solani* and *Helminthosporium* spp., with EC_{50} values of 0.48, 2.92 and 2.96 µg/mL, respectively, while parthenolide exhibited the highest antifungal activity against *Alternaria alternata* and *Fusarium culmorum* (EC_{50} = 4.07 & 50.27 µg/ml, respectively) (Ahmed and Adeglegaleil 2005). The three sesquiterpene lactones showed higher antifungal activity than a reference fungicide, thiophanate-methyl, against *Helminthosporium* spp.

Magnolia grandiflora n-butanol leaf extract (8 g/l) exhibited inhibitory activity (97.4 %) against the freshwater cyanobacteria *Microcystis aeruginosa*, which forms harmful algal blooms (Dong et al. 2011). The antialgal substances found in the extract were mainly small molecule substances such as alcohols, ketones and esters.

Comments

The tree is propagated using fresh, cold-stratified seeds or semi-hardwood cuttings.

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Abutilon indicum

Scientific Name

***Abutilon indicum* (L.) Sweet**

Synonyms

Abutilon albidum (Willd.) Sweet, *Abutilon albidum* (Willd.) Hook. & Arn., *Abutilon album* Hill (Inval.), *Abutilon arborescens* Medik., *Abutilon asiaticum* (L.) Sweet, *Abutilon asiaticum* (L.) G. Don, *Abutilon asiaticum* (L.) Guill. & Perr., *Abutilon asiaticum* var. *subasperum* Fosberg, *Abutilon asiaticum* var. *supraviride* Fosberg, *Abutilon australe* var. *malvifolium* (Benth.) Baker f., *Abutilon cavaleriei* H. Lév., *Abutilon croizatianum* Moscoso, *Abutilon cunninghamii* Benth., *Abutilon cysticarpum* Hance ex Walp., *Abutilon elongatum* Moench (Illeg.), *Abutilon frutescens* Medik., *Abutilon grandiflorum* G. Don, *Abutilon hirsutissimum* Moench (Illeg.), *Abutilon indicum* var. *albidum* (Willd.) Baker f., *Abutilon indicum* var. *asiaticum* (L.) Griseb., *Abutilon indicum* var. *microphyllum* Hochr., *Abutilon indicum* var. *populifolium* (Lam.) Wight & Arn. ex Mast, *Abutilon indicum* var. *populifolium* (Lam.) Wight & Arn., *Abutilon indicum* var. *welwitschii* Baker f., *Abutilon leiospermum* Griseb., *Abutilon malvifolium* (Benth.) J.M. Black, *Abutilon malvifolium* (Benth.) Domin, *Abutilon oxycarpum* var. *malvifolium* Benth., *Abutilon populifolium* (Lam.) Sweet, *Abutilon populifolium* (Lam.) G. Don, *Abutilon pubescens* (Cav.) Urb. (Illeg.), *Abutilon subpapyraceum* Hochr., *Abutilon vesicarium* (Cav.) Sweet, *Beloere cistiflora* Shuttlew. ex A. Gray, *Sida albida* Willd., *Sida asiatica* L., *Sida beloere* L'Hér., *Sida coronata* Scop., *Sida doniana* D. Dietr., *Sida eteromischos* Cav., *Sida guilleminiana* Steud., *Sida hookeri* D. Dietr., *Sida indica* L., *Sida meridionalis* Salisb., *Sida polycarpa* D. Dietr., *Sida populifolia* Lam., *Sida pubescens* Cav., *Sida vesicaria* Cav.

Family

Malvaceae

Common Names

Chinese Bellflower, Country Mallow, Indian Abutilon, Indian Lantern Plant, Indian Mallow Abutilon, Monkey Bush, Moon Flower, Twelve O'Clock Flower

Vernacular Names

Arabic: Khitmi Hindi
Bangladesh: Potari (Bengali)
Brazil: Abutilão (Portuguese)
Burmese: Thama-Khyoke
Chamorro: Malbas, Matbas
Chinese: Dong Kui Zi, Mi Lan Cao, Mo Pan Cao
Czech: Mračňák Indický
French: Fausse Guimauve, Guimauve, Herbe De Douze Heures, Mauve Du Pays

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German: Indische Samtpappel
Greek: Avutilon To Indikon
Guadeloupe: Guimauve
I Kiribati: Te Kaura, Te Kaura Ni
India: Bellpaku (Andhra Pradesh), Jhapa (Assamese), Potary, Mirubaha, Atibala, Petari, Potari (Bengali), Atibala, Tara Kanchi, Itawari, Jhili, Debi, Kanghi, Tara-Kanchi (Hindi), Gidutingi, Hetakisa, Hettukisu, Hettutti, Hetutti, Kisangi, Shrimudri, Srimudre, Tutti, Urki (Kannada), Belocre, Katturam, Katturan, Katuram, Pettekaputti, Pitikkapattu, Tatta, Tutti, Tuvatti, Uram, Velluram (Malayalam), Akakai, Kansuli, Karandi, Madmi, Mudra, Mudrika, Petaari, Pidari, Vikankati, Petari (Marathi), Biley, Phulo (Oriya), Atibala (Sanskrit), Ottuttutti, Tutti, Paniyaratutti, Perundhuthi, Tutti-P-Pattai, Kakkati, Kikkaci, Tuttikkirai, Thuththi, Tuti (Tamil), Adavibenda, Adivibenda, Botlabenda, Dudi, Muttavaciribenda, Noogoobenda, Nugoobenda, Nugubenda, Peddabenda, Thellabenda, Tootieakoc (Telugu)
Indonesia: Belangan Sumpa (Sumatra), Bunga Sore, Cemplok (Javanese), Kecil (Maluku)
Italian: Abutilone, Fiore Di Dodici Ore
Japanese: Takasago Ichibi
Kampuchea: Dok Toc Lai
Korean: Eo-Jeo-Gwi
Laos: Houk Phao Ton
Malaysia: Bunga Kisar, Kembang Lubok, Kembang Lohor, Malba, Malva
Naru: Ekaura, Inen Kaura
Nepal: Poti (Majhi), Kangiyo (Nepali)
Philippines: Daluapng, Palis, Pilis, Taratakopes (Bisaya), Lulupau, Luplupao, Malvas (Iloko), Takbitakbi (Sulu), Malbas, Giling-Giliñgan, Kuakuakohan, Malis, Marbas, Tabing (Tagalog)
Polish: Zaślaz
Portuguese: Abutilo
Russian: Kanatnik Indijskij
Spanish: Boton De Oro, Malva Amarilla
Sri Lanka: Beheth Anoda, Wal Anoda (Sinhala), Thuththi (Tamil)
Taiwan: Mopan Cao;
Thai: Phong Phaang (Eastern), Khrop Chak Krawaan, Krop Fan See (Central), Ma Kong Khao (Northern)
Vietnam: Cối Xay, Giằng Xay, Quỳnh Ma, Kim Hoa Thảo, Ma Mãnh Thảo, Nhĩ Hương Thảo, Co To Ép (Thái), Phao Tôn (Tày)

Origin/Distribution

Indian abutilon is native to the Old World tropics—south Asia and Southeast Asia; it is now widespread as a weed pantropically.

Agroecology

It occurs in sunny locations, in disturbed sites and waste ground in the warm, humid tropics usually below 800 m (−1,500 m) elevation. The plant is drought resistant and is commonly found in dry sites in upland fields, waste lands and roadsides at low elevations in its native range.

Edible Plant Parts and Uses

The raw flowers are eaten in Arabia (Hedrick 1972) and are cooked and eaten as vegetable in Andhra Pradesh, India (Reddy et al. 2007). The leaves contain a large quantity of mucilage.

Botany

An erect, branched, 1–2 m high, pubescent shrub. Stem green or somewhat purplish. Leaves are simple, alternate, long petiolate with suborbicular to cordate, pubescent lamina, 2.5–10 cm by 2.7,5 cm wide, with coarsely crenate–serrate margins (Plates 1 and 2). Flowers are solitary in axils, long pedicellate (4–7 cm) with yellow to orange yellow, imbricate, deltoid–obovate petals and a hirsute staminal tube (Plates 1 and 2). Fruit is a circular capsule, densely pubescent with 11–20 radiating carpels (mericarp) forming conspicuous and horizontally spreading beaks (Plates 1 and 2). Each mericarp is flattened and boat shaped. Seed is reniform, tuberculate and pubescent with minutely stellate hairs.

Plate 1 Yellow flowers, circular capsules (fruit) and leaves

Plate 2 Close view of flower, fruit and leaves

Nutritive/Medicinal Properties

Flower Phytochemicals

The flowering tops of *Abutilon indicum* afforded 0.15 % of an essential oil, which contained several terpenes: 'alpha'-pinene (0.1 %), 1,8-cineole (1 %), caryophyllene (11.6 %), borneol (0.6 %), geraniol (13 %), geraniol acetate (2 %), caryophyllene oxide (2 %), eudesmol (22 %) and farnesol (2.8 %) (Geda and Gupta 1983). Flavonoids found in four Malvaceous plants including *Abutilon indicum* (petals) were quercetin, gossypetin and kaempferol (Subramanian and Nair 1972).

The flowers were reported to contain flavonoid compounds: luteolin, chrysoeriol, luteolin 7-*O*-β-glucopyranoside, chrysoeriol 7-*O*-β-glucopyranoside, apigenin 7-*O*-β-glucopyranoside, quercetin 3-*O*-β-glucopyranoside and quercetin 3-*O*-α-rhamnopyranosyl (1 → 6)-β-glucopyranoside (Matlawska and Sikorska 2002).

Leaf Phytochemicals

The flowers and leaves were found to contain quercetin; leaves contained 72 % more quercetin than the flowers (Rajalakshmi and Senthil 2009). Quercetin-3-rutinoside was isolated from the leaves (Matlawska et al. 2007). Tocopherols and β-sitosterol were isolated from leaves (Baxi and Parikh 1980). Eudesmic acid, ferulic acid and caffeic acid were isolated from the methanol leaf extract (Rajput and Patel 2012).

Abutilon indicum plant extract was found to contain alkaloids, flavonoids, tannins, glycosides, and saponins (Krisanapun et al. 2009). The ethanol leaf extract of *A. indicum* was found to contain terpenes, fatty acids, ketones, aldehydes and vitamin E (Ramasubramaniaraja 2011). Fifty-seven compounds were identified in the ethanol leaf extract: *N,N*-dimethylglycine; heptanoic acid; 3-hexenoic acid; 2-hexenoic acid;1-gala-1-ido-octose; 2-cyclopenten-1-one, 3-ethyl-2-hydroxy-; nonanal; 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-; isoborneol, dL-glyceraldhye diethylacetal; (−)-*trans*-pinocarvyl acetate; 1H-indene, 1-methylene-; 2-methoxy-4-vinylphenol; propane, 1,1-diethoxy-2-methyl-; 1-decene; (+)-2-carene, 10-(acetylmethyl)-, bicyclo[4.1.0]heptan-2-ol, 1-phenyl-, endo-; naphthalene, 1,4-dimethyl-; 4-(2,6,6-trimethylcyclohexa-1,3-dienyl)but-3-en-2-one; tetradecane; nonanoic acid, 9-oxo-, ethyl ester; β-copaen-11-ol; β-D-glucopyranose, 4-*O*-β-D-galactopyransoyl-; 2(4H)-benzofuranone, 5,6,7α-tetrahydro-4,4,7α-trimethyl-; erucic acid; dodecanoic acid, 1-methylethyl ester; 3-hydroxy-β-damascone; acetic acid, 3-hydroxy-6-isopropenyl-4,8α-dimethyl-1,2,3,5,6,7,8,8α-octahydronapthalen-2-yl ester; 2-methyl-4-(2,6,6-trimethylcyclohex-2-enyl) but-3-en-2-ol-; 3,5-heptadienal, 2-ethylidene-6-methyl-; α-copaen-11-o; 9.12-octadeinoyl chloride (*Z,Z*)-; β-citrylideneethanol; 1-{2-[3-)2-acetyloxiran-2-yl)-1,1-dimethylpropyl]cyclo-prop-2-enyl}ethanone;1-[1-methoxy-3,3-dimethyl-

2-(3-methylbuta-1,3-dienyl)cyclopentyl]ethanone; 2-octenoic acid, 4-isopropylidene-7-methyl-6-methylene-, methyl ester; acetic acid, 2(2,2,6-tromentyl-7-oxa-bicyclo[4.1.0]hep-1-yl]-propenyl ester; 2-pentacedanone, 6,10,14-trimethyl-; 2,2-dimethyl-6-methylene-1-[3,4-dihydroxy-1-pentenyl]cyclohexan-1-perhydrol; 7-(1,3-dimethyl-buta-1,3-dienyl)-1,6,6,-trimethyl-3,8-dioxatri-cylco[5.5.0.092,4)]octane; hexadecanoic acid, ethyl ester; 9.12-octadecadienoic acid, ethyl ester; linolenic acid, ethyl ester; octadecanoic acid ethyl ester; oleic acid, palmitin,-2-mono-, dodecanal; 9-octadecenaide, (*Z*)-; 9,12-octadedi-enoyl chloride, (*Z,Z*)-; stearin, 1,3-di-; linolenin, 1-mono-; lup-2-(29)-en-3-one; 2,2,4-trimethyl-3-(3,8,12,16-tetramethyl-heptadeca-3,7,11,15-tetraenyl)-cyclohexanol; betulin; linoleic acid ethyl ester; β-sitosterol; and vitamin E.

Seed Phytochemicals

A water-soluble galactomannan containing D-galactose and D-mannose in 2:3 M ratio was isolated from *Abutilon indicum* seeds (Singh et al. 1997). The seed gum was found to have a branched structure consisting of linear chain β-D(1 → 4)-linked mannopyranosyl units, some of which were substituted at *O*-6 by two α-D(1 → 6) galactopyranosyl units mutually linked glycosidically as end groups.

Gupta and Saharia (1950) reported the isolation of approximately 5 % oil in the seeds of *Abutilon indicum*. The unsaponifiable matter (1.77 %) contained sitosterol and acetyl derivative.

Gambhir and Joshi (1952) reported the presence of linolenic, linoleic, palmitic, oleic, stearic acids and raffinose from *Abutilon indicum*. Dry seeds were extracted with petroleum ether and pale yellow oil (9.21 %) was obtained. Alcoholic extract of the fat extracted residue contained 1.61 % raffinose.

The seed oil was found to contain oleic acid (14.3 %), linoleic acid (11.0 %), palmitic acid (53.9 %) stearic acid (33.7 %) and linolenic acid (1.4 %) (Badami et al. 1975). The seed oil of *Abutilon indicum* was found to contain three HBr-reactive fatty acids: *cis*-12,13-epoxyoleic (vernolic) acid (1.6 %), 9,10-methylene-octadec-9-enoic (sterculic) acid (0.9 %) and 8,9-methylene-heptadec-8-enoic (malvalic) acid (2.3 %) (Babu et al. 1980). Amino acid profile of seed proteins (31 %) contained threonine, glycine, serine, glutamine, lysine, methionine, isoleucine, proline, alanine, cysteine, tyrosine, phenylalanine, leucine, asparagine, histidine, valine and arginine (Prakash et al. 1988).

The proximate nutrient composition of *A. indicum* seeds were reported as moisture (5.9 %), ash (2.3 %), crude fibre (25.1 %), crude protein (22.4 %), crude carbohydrate (22.92 %) and minerals (mg/100 g): aluminium (4.02), cadmium (0.01), calcium (237.32), iron (3.13), lead (0.08), magnesium (176.50), phosphorus (212.15), potassium (261.01) and zinc (1.94) (Kashimiri et al. 2009). Lipids extracted from the finely ground seeds were fractionated into polar (3.7 %) and nonpolar (95.2 %) lipids comprising hydrocarbons (1.4 %), sterol esters (8.3 %), triglycerides (70.3 %), free fatty acids (2.8 %), diglycerides (3.2 %), sterols (2.7 %) and monoglycerides (6.5 %). Triglyceride was found to be the major fraction (70.3 %) among neutral lipids. The lipids of *Abutilon indicum* were rich in unsaturated fatty acids and their composition was in general comparable to the fatty acid composition of the family Malvaceae. Oleic acid and linoleic acids were found to be the predominant fatty acids in most of the lipids.

Root Phytochemicals

Gallic acid (Sharma et al. 1989) and fixed oil (Bagi et al. 1984) were detected in the roots.

Plant Phytochemicals

The unsaponifiable matter of fraction A of the petroleum ether extract of *Abutilon indicum* aerial parts was found to contain *n*-alkane mixture (C22-C34), an alkanol fraction and β-sitosterol (Gaind and Chopra 1976). In fraction B of the residual plant material, vanillic, *p*-coumaric,

p-hydroxybenzoic, caffeic and fumaric acids and, in fraction C, *p*-β-D-glucosyloxybenzoic acid and gluco-vanilloyl glucose were isolated and identified. In fractions D and F, fructose, galactose, glucose, leucine, histidine, threonine, serine, glutamic acid and aspartic acid were identified. In fraction E, a mucilage, the acid hydrolysate showed galactose and galacturonic acid. Jain et al. (1982) reported the presence of β-pinene, eudesmol, farnesol and borneol besides geraniol, β-caryophyllene and their derivatives in *A. indicum*. Two sesquiterpene lactones alantolactone and isoalantolactone were isolated from *Abutilon indicum* (Sharma and Ahmad 1989) and eugenol (Ahmed et al. 2000). The plant also contained abutilon A and (R)-*N*-(1′-methoxycarbonyl-2′-phenylethyl)-4-hydroxybenzamide as well as 28 known compounds: 1-methoxycarbonyl-β-carboline; 3-hydroxy-β-damascone; 3-hydroxy-β-ionol; 3,7-dihydroxychromen-2-one; 4-hydroxy-acetophenone; 4-hydroxybenzaldehyde; 4-hydroxybenzoic acid; 4-hydroxybenzoic acid ester; 4-hydroxyphenylacetic acid methyl ester; adenine; adenosine; aurantiamide acetate; benzamide derivative; benzoic acid; coumaric acid; methylindole 3 carboxylate; 4-hydroxybenzamide; *n*-feruloyltyrosine; *p-coumaric* acid; riboflavin; scoparone; scopoletin; sitosterol; stigmasterol; syringaldehyde; thymine; vanillic acid; and vanillin (Kuo et al. 2008). Yasmin (2008) isolated and characterized five new and four known compounds from *A. indicum*: 3,5,7-trihydroxy-4′,6-dimethoxy-flavone; 3,5′,5-trihydroxy-4′-methoxyflavone-7-*O*-E-D-glucopyranoside; vasicine; lupeol and methyl triacontanoate and known compounds gallic acid; β-sitosterol; β-amyrin and 4-hydroxy benzoic acid. Seven compounds were isolated from *A. indicum* and six of them were identified as β-sitosterol; oleanic acid; (24R)-5α-stigmastane-3,6-dione; daucosterol; 2,6-dimethoxy-1,4-benzoquinone; and vanillic acid (Liu et al. 2009). The tannin content in leaves, stems and roots of *Abutilon indicum* were determined to be 0.34, 0.16 and 0.27 % GAe (gallic acid equivalent), respectively (Zhang et al. 2010). The following compounds were also isolated from the plant: *p*-β-D-glucosyloxybenzoic acid, *p*-hydroxybenzoic and caffeic acid (Pandey et al. 2011). Gallic acid and quercetin were validated to be effective biomarker compounds for *A. indicum* herbal plant extracts (Hussain et al. 2012).

The pharmacological properties of the various plant parts studied are elaborated below.

Antioxidant Activity

Abutilon indicum seed was found to contain potent antiradical and antioxidant components (Kashimiri et al. 2009). TEAC (trolox equivalent antioxidant capacity) values of *A. indicum* seed oil were 14.006 and 21.375 as determined by $ABTS^+$ (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) and FRAP (ferric reducing power of plasma) methods, respectively. The total phenolic content of the extract obtained from the seed oil was 13.770 mg/g seed oil. The ethanol plant extract showed dose-dependent antioxidant and free radical scavenging effects when tested by reducing power assay and DPPH free radical scavenging method (Kaushik et al. 2010). Aqueous extract of *A. indicum* stem showed a potent total phenolic content and possessed significant DPPH (2, 2-diphenyl-1 picrylhydrazyl) scavenging activity (Chakraborthy and Ghorpade 2010). The TEAC ranged from 3.019 to 10.5 muM for *n*-hexane and butanol fractions of *Abutilon indicum* in the ABTS assay (Yasmin et al. 2010). The FRAP assay showed reducing powers of the fractions in the order of butanol > ethyl acetate > chloroform > *n*-hexane and butanol > chloroform > hexane > ethyl acetate. The antioxidant/radical scavenging capacity of the extracts was found to be a dose-dependent activity. The reaction kinetics with the free radical DPPH indicated the presence of both slow-reacting and fast-reacting antioxidant components in the plant extracts.

Among the various extracts (petroleum ether, chloroform, ethyl acetate, *n*-butanol, ethanol and water) of *A. indicum,* the ethyl acetate extract showed maximum free radical scavenging activity (Srividya et al. 2012). Correlation between total antioxidant capacity and total phenolic content was not significant.

Antimicrobial Activity

Studies by Mehta et al. (1997) reported that the hexane plant extract was inhibitory to *Staphylococcus aureus* and *Pseudomonas aeruginosa* and fungi *Aspergillus terreus, A. ochraceus, A. flavus* and *A. oryzae*. The menthol extract was active against *Aspergillus oryzae* and *A. ochraceus*, while the chloroform and ethyl acetate extracts were active against most bacteria. Among the various leaf extracts, maximum antibacterial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Salmonella typhi* was exhibited by the ethanol extract followed by the chloroform extract, while the aqueous extract showed no activity (Poonkothai 2006). *Abutilon indicum* leaf extract displayed enhanced antibacterial activity against Gram-negative bacteria, *Salmonella typhimurium*, and Gram-positive bacteria, *Bacillus licheniformis* (Yasmin et al. 2008). Root extracts showed low MIC value (239 μg/mL) against *Escherichia coli* which could be attributed to the presence of β-hydroxyl groups in the extract. The antifungal activity of the leaf and stem extracts was negligible but the root extract showed good activity (MIC; 640 μg/L) against *Aspergillus niger*. The best activity (MIC; 235 μg/L) was observed by the root extract against *Trichoderma viride. Abutilon indicum* seed oil which inhibited the growth of both Gram-positive (*Bacillus licheniformis, Bacillus subtilis, Micrococcus luteus* and *Nocardia asteroides*) and Gram-negative (*Escherichia coli* and *Proteus mirabilis*) bacteria in vitro (Kashimiri et al. 2009). However, *Salmonella typhimurium* was resistant. The methanolic leaf extract of *Abutilon indicum* exhibited marked antifungal activity against *Trichophyton rubrum*; quercetin was isolated from the extract (Vairavasundaram and Senthil 2009).

Among all the plant extracts tested, the ethanolic leaf extract showed significant antibacterial activity in vitro comparable to the standard penicillin potassium and streptomycin sulphate against selected Gram-positive and Gram-negative bacteria (Prabahar et al. 2009). The ethanolic plant extract of *Abutilon indicum* was found to be most effective against Gram-positive bacteria *Staphylococcus aureus* followed by *Bacillus subtilis* and Gram-negative bacteria, *Escherichia coli*, followed by *Pseudomonas aeruginosa* (Kaushik et al. 2010). The antibacterial activity of the extract against *S. aureus* and *B. subtilis* was comparable to that of standard drug ciprofloxacin. Also, the ethanolic extract showed higher inhibitory activity against *Candida albicans* than that of standard drug, amphotericin B.

The carbon tetrachloride fraction of the methanol leaf extract of *Abutilon indicum* exhibited mild-to-moderate activity in vitro against Gram-positive (*Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Staphylococcus aureus, Sarcina lutea*) and Gram-negative bacteria (*Escherichia coli, Pseudomonas aeruginosa, Salmonella paratyphi, Salmonella typhi, Shigella boydii, Shigella dysenteriae, Vibrio mimicus, Vibrio parahaemolyticus*) and fungi (*Candida albicans, Aspergillus niger* and *Saccharomyces cerevisiae*) (Abdul et al. 2010). The average zone of inhibition produced by the carbon tetrachloride extract was 6–10 mm at a concentration of 400 μg/disc. The chloroform extract exhibited no antibacterial activity except against *Sarcina lutea* (8.4 mm). Separate studies showed that the petroleum ether and methanol extracts of *Abutilon indicum* had potent antibacterial activity against the pathogenic strains of *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Klebsiella pneumoniae* (Gurumurthy et al. 2011). Moderate activity was found against *Escherichia coli*. The chloroform leaf extract of *Abutilon indicum* exhibited antimicrobial activity against only Gram-positive bacteria, namely, *Staphylococcus aureus, Micrococcus luteus, Bacillus subtilis* and *Bacillus pumilus* (Ranjit et al. 2013).

Analgesic Activity

Fixed oil isolated from the petroleum ether root extract exhibited dose-dependent analgesic activity in rats using analgesiometer and in mice against acetic acid-induced writhing test (Bagi et al. 1984). The fixed oil exhibited analgesic effect at a dose of 400 mg/kg s.c. LD_{50} of the

fixed oil in mice was 2357.9 mg/kg p.o. and 933.3 mg/kg s.c. Gallic acid isolated from the roots showed analgesic activity in rats at a dose of 0.1 g/kg i.p. within 30–45 min of administration (Sharma et al. 1989). Eugenol (4-allyl-2-methoxyphenol), isolated from *A. indicum*, was found to possess significant analgesic activity (Ahmed et al. 2000). At doses of 10, 30 and 50 mg/kg body weight, eugenol exhibited 21.30, 42.25 and 92.96 % inhibition of acetic acid-induced writhing in mice, respectively. At a dose of 50 mg/kg body weight, eugenol showed 33.40 % prolongation of tail flicking time determined by the radiant heat method. The petroleum ether leaf extract and benzene leaf extracts were found to possess very good analgesic property (Lakshmayya et al. 2003).

The petroleum ether and ethanol root extracts of *A. indicum* exhibited significant analgesic activity in both animal models: acetic acid-induced writhing method (for peripheral analgesic activity) in Swiss albino mice and the tail-flick method and the tail immersion method (for central analgesic activity) (Goyal et al. 2009). The petroleum ether extract showed higher analgesic activity. The results suggested that the analgesic activity may be related to the central mechanism or may be due to the peripheral analgesic mechanisms. In another study, the petroleum ether, chloroform, methanol and aqueous plant extracts showed analgesic activity at a dose of 400 mg/kg body weight in rats when tested by the tail-flick method (Saraswathi et al. 2011).

Anti-inflammatory Activity

Studies found that the methanolic extract of aerial parts of *A. indicum* had significant mast cell stabilizing effect against compound 48/80 and egg albumin induced rat peritoneal mast cell degranulation (Paranjape and Mehta 2008). Also, *A. indicum* showed significant anti-inflammatory activity using the carrageenan-induced rat paw oedema model. The results indicated that possible mechanism of action of *A. indicum* in the treatment of bronchial asthma involved its mast cell stabilizing and anti-inflammatory activity. In another study, *Abutilon indicum* alcohol extract inhibited mouse auricular swelling induced by xylol indicating its anti-inflammatory effects (Chen et al. 2009). The ethanolic, chloroform and aqueous leaf extracts exhibited anti-inflammatory activity when tested using the human red blood cell (HRBC) membrane stabilization method (Rajurkar et al. 2009). The prevention of hypotonicity-induced HRBC membrane lysis was taken as a measure of anti-inflammatory activity. All three extracts showed a biphasic effect on the membrane stabilization. Their activities were comparable to that of standard drug diclofenac sodium. The petroleum ether, chloroform, methanol and aqueous plant extracts showed anti-inflammatory activity at a dose of 400 mg/kg body weight in rats when determined by the carrageenan-induced paw oedema method in rats (Saraswathi et al. 2011). The ethanolic extract of *A. indicum* showed predominantly significant anti-inflammatory activity in a dose-dependent manner using the carrageenan-induced paw oedema in healthy Wistar albino rats which was comparable to the reference standard ibuprofen (Tripathi et al. 2012).

Antidiabetic Activity

Alcohol and water extracts of *Abutilon indicum* leaves (400 mg/kg, p.o.) showed significant hypoglycaemic effect in normal rats 4 h after administration (23.10 and 26.95 %, respectively) (Seetharam et al. 2002). It was also observed that different leaf extracts (petroleum ether, benzene, methanol, ethanol, aqueous) exhibited significant hypoglycaemic activity at 400 mg/kg dose, but the aqueous leaf extract was most potent in reducing the blood glucose levels, but the aqueous extract was most potent in reducing the blood glucose levels (Lakshmayya et al. 2003). Administration of *A. indicum* plant aqueous extract (0.5 and 1 g/kg body weight) in an oral glucose tolerance test elicited a significant reduction in plasma glucose levels in 30 min after the administration in moderately diabetic rats, as compared with untreated rats (Krisanapun et al. 2009), and this was at a faster rate than the use of

an antidiabetic drug, glibenclamide. The extract at a dose of 0.156–5 mg/mL inhibited glucose absorption through the small intestine in a dose–response manner. The maximum response was observed at a dose of 2.5 mg/mL. The promotion of the extract on insulin secretion was confirmed by incubating beta cell of pancreatic islets and INS-1E insulinoma cells with the extract at 1–1,000 μg/mL. The results suggested that the aqueous *A. indicum* plant possessed antidiabetic properties, which inhibited glucose absorption and stimulated insulin secretion. Phytochemical screening also revealed that the extract contained alkaloids, flavonoids, tannins, glycosides and saponins that could account for the observed pharmacological effects of the plant extract. In a subsequent study, they found that the aqueous extract of the entire plant (leaves, twigs and roots) of *A. indicum* exhibited antidiabetic effect on postprandial plasma glucose in diabetic rats (Krisanapun et al. 2011). The study suggested that the extract may be beneficial for reducing insulin resistance through its potency in regulating adipocyte differentiation through PPARγ agonist activity and increasing glucose utilization via GLUT1. In another study, single oral administration of methanol leaf extract at a dose of 500 mg/kg significantly decreased the blood glucose concentrations in both normal and streptozotocin-induced diabetic rats after 2 h administration (Adisakwattana et al. 2009). The postprandial elevation in the blood glucose concentrations at 30 min after the plant administration of sucrose with the extract was significantly suppressed when compared with the control group. No significant change in blood glucose concentrations was observed in maltose-loading rats. In an in vitro study, *A. indicum* extract inhibited α-glucosidases, the disaccharide-digesting enzyme in the small intestine. The extract showed a potent sucrase inhibitory activity with IC_{50} of 2.45 mg/mL while the extract was less potent on the maltase inhibition. The extract was found to contain phenolic compounds (1.04 mg/g) and flavonoid compounds (59.92 μg/g extract). The results suggested that *A. indicum* extract would be effective for lowering and suppressing elevation of blood glucose.

Patel et al. (2011) found that the use of atibalamula (*Abutilon indicum*) 10 g twice a day for 30 days in the patients of diabetic neuropathy could revert the diminished sensory perception and could reduce diabetic symptoms significantly.

Hepatoprotective Activity

The aqueous extract of the leaves of *A. indicum* exhibited significant hepatoprotective activity at 100 and 200 mg/kg dose levels in carbon tetrachloride-treated rats (Dash et al. 2000); CCl_4-induced changes were significantly reduced in the *A. indicum*-treated animals. Another animal study showed that juice from fresh *A. indicum* leaves used in combination with the liquid extract of *Allium cepa* was effective against paracetamol- and carbon tetrachloride-induced hepatotoxicity (Porchezhian and Ansari 2000). They reported that the significant hepatoprotective activity exhibited by *Abutilon indicum* aqueous extract in reducing carbon tetrachloride- and paracetamol-induced changes in biochemical parameters in rats could be attributed to its antioxidant activity (Porchezhian and Ansari 2005).

Administration of *A. indicum* leaf extract to rats at the doses of 100 and 200 mg/kg body weight/day, p.o., for 21 days dose dependently reduced peroxidative damage in both liver and serum (Singh and Gupta 2008). The extract improved hepatic antioxidant status by enhancing the decreased levels of the enzymatic and nonenzymatic antioxidants such as superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, glutathione-S-transferase, glutathione, vitamin C, vitamin E, ceruloplasmin and β-carotene in the liver and serum caused by alcohol.

Anticancer/Cytotoxicity Activity

A decrease in the growth of human brain glioblastoma-astrocytoma cancer (U-87 MG) cells was observed with increasing concentrations of the methanol leaf extract of *A. indicum*

and its chloroform and ethyl acetate fractions (Khan et al. 2011). The crude methanol extract showed 44.2 % growth inhibition at 50 µg/mL. While, the chloroform fraction showed highest inhibition of 61.02 % at 50 µg/mL, and the ethyl acetate fraction showed 57.48 % inhibition at the same concentration. The results were compared to the reference compound, quercetin, which showed 28.9 % growth inhibition at 30 µg/mL.

In the brine shrimp lethality bioassay for cytotoxicity, the LC_{50} obtained from the best-fit line slope were 0.419, 3.01, 5.62,1.51 for *n*-hexane, carbon tetrachloride, chloroform and aqueous fractions of the methanol leaf extract of *Abutilon indicum*, respectively, and 11.20 µg/mL for positive control (vincristine sulphate) (Abdul et al. 2010). The cytotoxicity exhibited by chloroform soluble fraction of methanol extract was promising.

Antidiarrhoeal Activity

The methanolic extract and aqueous extract of *A. indicum* leaves exhibited significant antidiarrhoeal activity in castor oil-induced diarrhoea and prostaglandin E2-induced diarrhoea in rats, compared to the control group (Chandrashekhar et al. 2004). *Abutilon indicum* showed significant antidiarrhoeal activity as compared to loperamide.

Diuretic Activity

Abutilon indicum alcohol extract markedly increased the rat urinary output within 6 h compared to the control, indicating its diuretic effects (Chen et al. 2009).

Aqueous extract of *A. indicum* at 200 and 400 mg/kg produced significant diuresis and increased sodium elimination but not potassium in rats (Balamurugan et al. 2010). The results suggested the aqueous extract of *A. indicum* to possess significant diuretic and natriuretic effect but not a potassium-sparing effect.

Antifertility Activity

The methanol plant extract of *A. indicum* was found to have oestrogenic/antioestrogenic potential when tested on uterotrophic and uterine peroxidase activities in ovariectomized rats (Johri et al. 1991).

Antihypertensive Activity

The water, acetone and ethanol root extracts of *A. indicum* inhibited angiotensin converting enzyme by 18, 9 and 1 %, respectively (Hansen et al. 1995). Inhibition was measured from the enzymatic cleavage of the chromophore–fluorophore-labelled substrate dansyltriglycine into dansylglycine and diglycine.

CNS Depressant Activity

All leaf extracts (petroleum ether, benzene, methanol, ethanol, aqueous) showed CNS depressant activity but none of them could elicit narcosis (Lakshmayya et al. 2003).

Anticonvulsant Activity

Abutilon indicum leaf ethanol extract exhibited anticonvulsant activity when administered orally to Wistar rats; it gave significant protection against pentylenetetrazole and maximal electroshock-induced convulsions (Golwala et al. 2010).

Antihyperlipidemic Activity

The ethanol and aqueous leaf extracts of *Abutilon indicum* at 400 mg/kg dose levels inhibited the elevation in serum cholesterol and triglyceride levels on Triton WR 1,339 administration rats (Giri et al. 2003). The extracts at the same dose level significantly attenuated the elevated serum total cholesterol and triglycerides with an increase in high-density lipoprotein cholesterol in high-fat-diet-induced hyperlipidemic rats.

Immunomodulatory Activity

Oral administration of ethanolic and aqueous leaf extracts of *A. indicum* in mice elicited a significant increase in the production of circulating haemagglutination antibody (HA) titre in response to sheep red blood cells (SRBCs) (Dashputre and Naikwade 2010). A significant increase in both primary and secondary HA titre was observed when compared to control group, whereas in cyclophosphamide-treated group, *A. indicum* showed significant increase in HA titre. *A. indicum* also significantly potentiated the delayed-type hypersensitivity reaction by facilitating the footpad thickness response to SRBCs in sensitized mice. Further, *A. indicum* evoked a significant increase in percentage neutrophil adhesion to nylon fibres and phagocytic activity. The results suggested that *A. indicum* triggered both specific and nonspecific responses.

Wound Healing Activity

Roshan et al. (2008) reported that ethanolic extract of *A. indicum* at a dose of 400 mg/kg exhibited significant wound healing activity. Ganga Suresh et al. (2011) found that the petroleum ether plant extract of *A. indicum* elicited greater wound healing activity than the ethanol plant extract in Wistar albino rats. In two different models, namely, excision and incision models, there were significant wound closure rates. The wound healing activity was postulated to be due to an increase in collagenation deposition, better alignment and maturation.

Libido Enhancement Activity

Methanol extract of *Abutilon indicum* aerial parts exhibited libido enhancement activity in female rats in the automated runway methodology and copulatory behaviour models (Khadabadi and Bhajipale 2011). The results revealed significant reduction in runtime and increase in core proximity time for the male targets in oestrous *A. indicum-treated* females.

Antiurolithiatic Activity

The ethanolic extract of *A. indicum* was found to have antiurolithiatic activity when evaluated by calcium oxalate calculi induction by employing CPD (calculi-producing diet; 5 % ammonium oxalate in rat feed) and gentamicin (40 mg/kg, s.c.) (Kumar et al. 2011). The preventive and curative rats showed a significant decrease in the deposition and excretion of calcium oxalate urinary stones. The ethanolic extract of *A. indicum* was found to be safe at 2,000 mg/kg p.o. The ethanolic extract also showed antioxidant properties.

Larvicidal Activity

Among the five medical plants studied, the petroleum ether extract of *A. indicum* exerted highest larval mortality on the early fourth instar larvae of *Culex quinquefasciatus* (Abdul Rahuman et al. 2008). The bioactive principle was isolated and identified as β-sitosterol. β-sitosterol showed larvicidal effect with LC_{50} values of 11.49, 3.58 and 26.67 ppm against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus*, respectively. The hexane, chloroform, ethyl acetate and methanol of *A. indicum* exhibited mortality of third instar larvae of the filarial vector, *Culex quinquefasciatus*, with LC_{50} values of 204.18, 155.53, 166.32 and 111.58 ppm, respectively (Kovendan et al. 2012). Maximum larvicidal activity was observed in the methanolic extract followed by the ethyl acetate, chloroform and hexane extracts.

Anthelmintic Activity

The alcoholic stem extract of *Abutilon indicum* showed good anthelmintic activity against *Pheretima posthuma* (Ranjit et al. 2013). The alcoholic stem extract showed time taken for paralysis of 11 min and time taken for death of 15 min, compared to the standard drug albendazole for paralysis of worms of 13 min and time taken for death of 19 min at 80 mg/mL concentration.

Traditional Medicinal Uses

The plant is traditionally used in India, Pakistan, China and the Philippines for treatment of several diseases like bronchitis, body ache, toothache, jaundice, diabetes, fever, piles, leprosy, ulcers, cystitis, gonorrhoea, diarrhoea, asthma, etc. (Goyal et al. 2009). The plant is used in traditional medicine for inflammation, piles and gonorrhoea treatment and as an immune stimulant; root and bark are used as aphrodisiac, antidiabetic, nervine tonic and diuretic; seeds are used as aphrodisiac and in urinary disorders (Giri et al. 2003). *Abutilon indicum* is an Asian phytomedicine traditionally used to treat several disorders, including diabetes mellitus (Krisanapun et al. 2011). This medicinal plant plays an important role in folk medicine; in Thailand, it has been used as a blood tonic, carminative, antipyretic, anti-cough, diuretic, anti-inflammatory, laxative and antidiabetic (Chuakul et al. 1997). In India and China, it has been used for urinary disease, gonorrhoea, jaundice, rheumatism, high fever, mumps, pulmonary tuberculosis, bronchitis, lack of urination and some nervous and ear problems (Abdul Rahuman et al. 2008; Deokule and Patale 2002). The leaves of *Abutilon indicum* were traditionally used to treat bronchitis and gonorrhoea and as mouthwash in toothache (Lakshmayya et al. 2003). However local practitioners have claimed that the leaves are highly useful in controlling diabetes mellitus. *Abutilon indicum* is employed for haemorrhoids by Siddha medical practitioners in Tirunelveli District, Tamil Nadu, India (Chellappandian et al. 2012), and by traditional healers in Mayiladumparai block of Theni District, Tamil Nadu, India (Pandikumar et al. 2011). The Irula tribe in Chittoor district of Andhra Pradesh used the leaves for dysentery, leucorrhoea, piles and psoriasis and the roots as galactagogue (Vedavathy et al. 1997).

According to Burkill (1966), the plant leaves rich in mucilage are widely used as demulcent in Malaysia and India. The leaves after boiling and mixed with glutinous rice are applied as plaster to the body for fevers and on ulcers. In Palembang, Sumatra, a lotion is made from the plant and used warm for rheumatism. A poultice of the roots is applied to the gum for toothache and used as ear drops for earache. In India, root infusion is used as a cooling medicine. The seeds are laxative and demulcent and enter into Indian and Chinese medicine for their diuretic properties.

In Vietnamese traditional medicine, the plant (stems, shoots, leaves, fruits) is used to treat influenza, coryza, headache and dysuria (Le and Nguyen 1999). Sap from pounded fresh leaves and seeds is administered orally for furunculosis and snake bites; the residue is utilized as poultice. The leaves and stems are used as an ingredient in a herbal recipe for treating rheumatism and arthrodynia accompanied by fever. A decoction of its dried leaves along with *Adenosma caeruleum* and *Premna integrifolia* is prescribed for postpartum jaundice.

Other Uses

In India (kashi-fibre) and E. Africa, *Abutilon indicum* is cultivated as a fibre plant, the fibre is used to make cordage or woven into fabrics as it takes dyes well (Burkill 1966). The seeds provide an oil source. *Abutilon indicum* is also used as an ornamental and medicinal plant, often as an indoor house plant or as a bonsai plant.

Comments

Abutilon indicum is readily propagated from seeds.

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Abutilon megapotamicum

Scientific Name

***Abutilon megapotamicum* (A. Spreng.) *A.* St. Hil. & Naudin.**

Synonyms

Abutilon inflatum Garcke & K. Schum., *Abutilon vexillarium* E. Morren, *Periptera megapotamica* (A. Spreng.) G. Don, *Sida leopoldii* Voss, *Sida megapotamicum* A. Spreng.

Family

Malvaceae

Common/English Names

Brazilian Bell Flower, Candy Corn Plant, Chinese Bell Flower, Chinese Lantern, Flowering Maple, Lantern Flower, Trailing Abutilon

Vernacular Names

Brazil: Chapéu-De-Cardeal, Lantana-Japonêsa, Lanterna-Chinesa, Sininho
Danish: Japanlugte
Dutch: Belgische Vlag
French: Abutilon De Rio Grande
German: Ballonmalve, Kriechende Samtpappel, Rio-Grande-Schönmalve
Polish: Zaślaz
Portuguese: Linterna China
Slovenian: brazilski slezinec
Spanish: Linterna China
Swedish: Lyktmalva

Origin/Distribution

The species is native to Brazil and has been introduced to other tropical, subtropical and mild temperate areas around the world as an ornamental.

Agroecology

The plant is naturally found growing in rain-forests on well-drained, moderately fertile, organic rich moist soils in Brazil. It prefers a wind-protected, partial-shaded to full-sun position and is drought and frost tender. It has been grown in the mildest areas of Britain, tolerating temperatures down to between −5 and −10 °C when provided protection of a south or south-west-facing wall.

Edible Plant Parts and Uses

Flowers are usually cooked as a vegetable (Lovelock 1973; Facciola 1990; Fern 1997) and are said to have a pleasant sweet flavour and

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delicious to eat raw (Fern 1997). The flowers produce nectar all the time they are open.

Botany

A medium-sized, semi-deciduous shrub, growing to 2 m high with slender branches. Leaves simple, ovate to shallowly three-lobed, with cordate bases, acute tips and dentate margin margins, 5–8 cm long (Plates 1 and 2). Flowers solitary, axillary, bisexual, pendulous, bell-shaped or lantern-shaped, attractive (Plates 1 and 2). Calyx large, campanulate, red with 5 free, greenish apical lobes. Corolla of 5 yellow petals. Staminal column divided apically into numerous yellow filaments that mature to dark brown, protruding about 2 cm from the yellow petals. Ovary 5-loculed, each with 3–9 ovules; style branches as many as loculi, filiform to clavate, stigmatose only at apex.

Plate 1 Flowers and leaves

Plate 2 Close view of flowers and leaves

Nutritive/Medicinal Properties

No medicinal uses and nutritive properties have been reported.

Other Uses

Trailing *Abutilon* is a popular ornamental plant, excellent for a hanging basket, looks graceful when grown in the ground and can even be grown as a house plant.

Comments

The plant is propagated from seeds and softwood stem cuttings.

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Alcea rosea

Scientific Name

***Alcea rosea* L.**

Synonyms

Alcea biennis Winterl, *Alcea ficifolia* Nyman, *Althaea caribaea* Sims, *Althaea chinensis* Wall., *Althaea coromandeliana* Cav., *Althaea flexuosa* Sims, *Althaea meonantha* Link, *Althaea mexicana* Kunze, *Althaea rosea* (L.) Cav., *Althaea rosea* var. *sinensis* (Cav.) S.Y. Hu, *Althaea sinensis* Cav., *Althaea sinensis* Blanco, *Malva florida* Salisb., *Malva hortensis* Schimp. & Spenn., *Malva rosea* Garsault (inval).

Family

Malvaceae

Common/English Names

Common Garden Hollyhock, Common Hollyhock, Derives, Garden Hollyhock, Garden Mallow, Hollyhock

Vernacular Names

Brazil: Malva Da Índia
Arabic: Khatmae
Chinese: Shi Kui, Zhu Kui
Czech: Proskurník Růžový, Topolovka Růžová
Danish: Almindelig Stokrose, Have-Stokrose**,** Stokrose
Dutch: Stokroos
Estonian: Harilik Tokkroos
Esperanto: Aed-Tokkroos, Alceo, Alteo Alta, Rozalteo
Finnish: Salkoruusu, Tarhasalkoruusu
French: Passe Rose, Rose Papale, Rose Tremière
German: Bauerneibisch, Baummalve, Baumrose, Chinesische Stockrose, Garten-Stockrose, Gartenmalve, Gewöhnliche Stockrose, Herbstrose, Pappelrose, Roseneibisch, Schwarze Malve, Stockmalve, Stockrose, Winterrose
Hungarian: Fekete Mályvarózsa. Festőmályva, Kerti Mályvarózsa, Kertimályva, Mályvarózsa
Icelandic: Stokkrós
Italian: Malva Rosa, Malvarosa, Malvone, Malvone Roseo, Rosone, Rosoni
Japanese: Hana-Ao, Tachi-Aoii
Korean: Jeop-Si-Kkot;
Norwegian: Hagestokkrose, Praktstokkrose, Vinterstokkrose
Pakistan: Gulekhera
Polish: Malwa, Malwa Ogrodowa, Malwa Różowa, Prawoślaz Różowy, Prawoślaz Wysoki
Russian: Štockrosa
Slovaščina: Sleznik Rožlin
Slovencina: Ibiš Ružový, Topoľovka Ružová
Spanish: Alcea, Cañamera Real, Malva De Las Indias, Malva Isabela, Malva Loc, Malva Reial, Malva Rósea, Malvaloca, Malvarrosa, Vara De San José

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Swedish: Stockros
Turkish: Gü'hatmi, Gül Hatmi, Gülhatmi
Welsh: Hocysen Fendigaid

Origin/Distribution

Alcea rosea originated in the south-western provinces of China and has been grown in Europe since at least the fifteenth century (Tang et al. 2007). It is not known from any truly wild situations. It is cultivated as an ornamental and is used medicinally. Today hollyhock is distributed and naturalized in the northern temperate regions.

Agroecology

A temperate species but will grow in the highlands in the tropics. Hollyhocks prefer rich, well-drained and fertile loamy soil and full sun. Light shade is tolerated but wet soil is not.

Edible Plant Parts and Uses

Flowers, leaves, stem and roots have edible uses (Hedrick 1972; Lust 1974; Tanaka 1976; Kunkel 1984; Kasumov 1984; Facciola 1990; Roberts 2000; Lauderdale and Evans 1999; Newman and O'Connor 2009). Today hollyhock is used mainly for the dark red pigment, which is produced from the flowers, for food purposes. *Alcea rosea* petals afford a red pigment found suitable for colouring confectionery products, fruit berry jams and jellies, non-alcoholic beverages, wine, sausages and other foods (Kasumov 1984). The pigment can be used instead of $NaNO_3$ in sausage manufacture. It is thermostable and does not alter the organoleptic properties of foods.

Flower petals and flower buds are eaten raw in salads. A refreshing herbal tea is made from the flower petals. Young leaves can be consumed raw or cooked as potherb. They can also be finely chopped and added to salads. The inner portion of young stems can be eaten raw. A nutritious starch is obtained from the root.

Botany

An erect, slender, sparsely branched herbaceous biennial or short-lived perennial growing to 1.5–2 m high. The stem is terete, light green and pubescent. Leaves are orbicular in outline, 7–15 cm across, palmately lobed with 5–7 shallow lobes, medium green, bases cordate, margins crenate (Plates 1 and 2); petioles 2–5 cm long and pubescent. Inflorescence–terminal or axillary spike-like raceme. Flowers occur individually or in small clusters along the rachis. Flowers are large and showy, 7–12 cm across when fully opened, funnelform, in a range of colours—pink, red (Plates 1 and 2), mauve, white, yellow and purple—and maybe double petalled. Flower has 6–9 green, hairy bracts; 6 ovate, green sepals; 5 overlapping petals forming a funnel; a central columnar structure bearing numerous stamens towards the tip and numerous thread-like stigmas below. Fruit is schizocarp containing 15–20 small, oval, flattened seeds.

Nutritive/Medicinal Properties

As a result of the investigations performed, it was found that the sources of natural food dyes which are of greatest value were the red double form of the hollyhock, the hybrid Hibiscuses, the cotton plant and the pressing residues of dark varieties of grape and mulberry, which were distinguished by a high content of anthocyanin pigments (Karimdzhanov et al. 1995). Quantitative analysis of the plants studied for their total content of anthocyanins showed that it ranged over wide limits (0.5–12 %). *Alcea rosea* petals were twice extracted with acetone–water and distilled to give a dry product (60 g) containing 12–13 % red pigment suitable for colouring confectionery products, fruit berry jams and jellies, non-alcoholic beverages, sausages and other foods (Kasumov 1984). The pigment cyanidin-3-glucoside, delphinidin-3-glucoside and malvidin-3,5-diglucoside.

Studies showed that the high molecular weight acidic polysaccharides (HMWAP) mucilages from *A. rosea* flowers were superior to mucilages

Plate 1 Flowers and leaves

Plate 2 Leaves, flower buds and flowers

from its leaves and leaves or flowers from *Malva sylvestris* (Classen and Blaschek 1998). The molecular weight of all HMWAPs was in a range of 1.3–1.6 × 10(6) Dalton. HMWAPs were found to be composed mainly of glucuronic acid, galacturonic acid, rhamnose and galactose. Highly esterified pectic substances were obtained from *Alcea rosea* flowers (Rakhimov et al. 2007). The pectic substances had molecular weight of 30,000 from red flowers and 40,000 from black flowers.

Double-petalled black hollyhock flower was found to contain mucilaginous polysaccharide, a food dye and pectin (Atkhamova et al. 1995). The polysaccharide had a molecular mass of 40,000 and contained N (0.7 %) and protein (3.5 %); the latter included lysine 0.3 %, histidine 0.2 %, valine 0.1 %, glycine 0.4 %, serine 0.1 %, threonine 0.1 %, glutamic acid 0.6 % and aspartic acid 0.5 %. The polysaccharide comprised of galactose, glucose, mannose, arabinose, xylose and rhamnose in the ratio of 2:1.2:1.7:7.4: traces, respectively, and of GalUA and GlcUA. The predominant monosaccharides were rhamnose and arabinose. The flower pigments comprised of anthocyanidin glycosides: cyanidin, peonidine, delphinidin and malvidin. The predominant monosaccharides were rhamnose and arabinose. The residual meal yielded 11 % of pectin substance with molecular mass of 37,000, with 58 % content of uronic acid and 5.89 % O–Ch_3 content. The pectic substance contained neutral sugars in addition to uronic acid—rhamnose, arabinose, xylose (11:3.5:1) and trace amounts of mannose, glucose and galactose—thus, confirming it to be a highly esterified pectin. The amount of hemicelluloses in the flower was 3.5 % comprising GalUA, galactose, glucose, arabinose and rhamnose. The dark violet flowers of *Althaea rosea* var. *nigra* were found to have the following phenolic acids: ferulic (*cis* and *trans*), vanillic, syringic, *p*-coumaric (*cis* and *trans*), *p*-hydroxybenzoic, *p*-hydroxyphenylacetic and caffeic acids (*cis* and *trans*) (Dudek et al. 2006). From among the phenolic acids analyzed, the syringic, *p-hydroxybenzoic* and *p*-coumaric acids were dominant.

The dark violet flowers of *Althaea rosea* var. *nigra* were found to have flavonoids, mainly derivatives of kaempferol, quercetin, luteolin and myricetin (Matławska et al. 1992). Kaempferol 3-*O*-(6-*O*-*trans*-*p*-coumaroyl)-β-glucopyranoside (*trans* tiliroside), luteoline 4′-*O*-β-glucopyranoside and flavone apigenin glycoside were also found in other Malvaceous species. The dark violet flowers of *Althaea rosea* var. *nigra* were found to have the following phenolic acids: ferulic (*cis* and *trans*), vanillic, syringic,

p-coumaric (*cis* and *trans*), *p*-hydroxybenzoic, *p*-hydroxyphenylacetic and caffeic acids (*cis* and *trans*) (Dudek et al. 2006). From among the phenolic acids analyzed, the syringic, *p-hydroxybenzoic* and *p*-coumaric acids were dominant.

Elaioplasts observed in *A. rosea* were found to exhibit all the features characteristic of lipotubuloids earlier described in *Ornithogalum umbellatum* (Kwiatkowska et al. 2010). Lipotubuloids are cytoplasmic domains containing aggregates of lipid bodies connected with microtubules. Tubulin was found to be present in this domain. *Alcea rosea* seed oil was found to be a rich source of ricinoleic acid (61.7 %) and also contain other fatty acids such as myristic (1.1 %), palmitic (25.3 %), stearic (2.6 %) and oleic (9.3 %) (Daulatabad and Jamkhandi 2000). *Alcea rosea* seed oil was found to contain 5.25 % oil and the oil contained 8.97 % cyclopropenoid acid (Sherwani et al. 2012). The cyclopropenoid moiety was resolved into two components: malvalic and sterculic acids. Other fatty acids present included myristic, palmitic, stearic, oleic, linoleic and linolenic acids.

An acidic polysaccharide rhamnoglucouronan with molecular weight of 39,000 was isolated from *A. rosea* stem (Atkhamova et al. 2001). The main polysaccharide chain was branched and consisted of α-1 → 2 and α-1 → 4 bound rhamnopyranoses and uronic. Pectinic substances isolated from *A. rosea* stem gave a yield of 4.3 % and comprised of rhamnose, arabinose, xylose, glucose, galactose in the ratio of 4.5:1.0:trace:trace:4.2 and uronic acid (Azizov et al. 2007). Pectinic substance isolated from roots gave a yield of 2.3 % and comprised of rhamnose, arabinose, xylose, glucose, galactose in the ratio of 18:3:trace:trace: 1.0 and uronic acid. Microelements (mg/kg) from the stem dry extract comprised of 30.1 mg Pb, 0.67 mg Cd, 30.0 mg Cu, 93.6 mg Zn, 23.21 mg Sn, 106 mg Fe and 196 mg Cr. Microelements (mg/kg) from the root dry extract comprised of 26.1 mg Pb, 0.0.83 mg Cd, 24.2 mg Cu, 37.5 mg Zn, 18.5 mg Sn, 79 mg Fe and 200.5 mg Cr. Amino acid composition of proteins of dry extract from stems comprised of asparagine 5.7 %, threonine 3.0 %, serine 2.1 %, glutamine 11.3 %, proline 3.2 %, glycine 1.1 %, alanine 3.4 %, cysteine 2.7 %, valine 3.5 %, isoleucine 0.2 %, leucine 8.8 %, tyrosine 2.3 %, phenylalanine 3.5 %, histidine 1.8 %, lysine 7.7 % and arginine 3.4 %. Amino acid composition of proteins of dry extract from roots comprised of asparagine 8.2 %, threonine 3.4 %, serine 2.2 %, glutamine 11.5 %, proline 3.0 %, glycine 1.2 %, alanine 3.2 %, valine 3.2 %, methionine 0.6 %, isoleucine 1.4 %, leucine 5.5 %, tyrosine 2.6 %, phenylalanine 3.6 %, histidine 1.9 %, lysine 6.8 % and arginine 3.5 %. The extract obtained from roots called Alceum was approved as 0.2-g tablets for medical use as an expectorant. The dry extract of stems was sent for preclinical pharmacological investigations as an antiulcer agent to treat stomach and small intestine ulcers.

Antiurolithiatic Activity

Administration of the hydroalcoholic extract of *Alcea rosea* roots to rats with ethylene glycol-induced kidney calculi significantly reduced the number of kidney calcium oxalate deposits compared to ethylene glycol group (Ahmadi et al. 2012). The extract also reduced the elevated urinary oxalate due to ethylene glycol. This effect was attributed possibly to diuretic and anti-inflammatory effects or presence of mucilaginous polysaccharides in the plant. The results indicated *Alcea rosea* to have a beneficial effect in preventing and eliminating calcium oxalate deposition in the rat kidney.

Immunomodulatory and Antiulcerogenic Activity

Alcea rosea contains polysaccharides which possess antiulcer and immunomodulatory properties. Recent studies reported that aqueous extracts of polysaccharides from *A. rosea* exhibited immunomodulatory activity (El Ghaoui et al. 2008). The polysaccharide extract appeared to boost the antibody response to egg albumin and acted as a B-lymphocyte polyclonal activator but had no effect on interleukin-4 and γ-interferon gene transcription. *Alcea rosea* was also found to be a

source of polysaccharides with antiulcer property (Barnaulov et al. 1985).

Antimicrobial Activity

Extracts of *A. rosea* (leaf and flower) were found to have antibacterial activity against *Pseudomonas aeruginosa, Listeria monocytogenes, Staphylococcus epidermidis, Staphylococcus aureus, Klebsiella pneumoniae, Salmonella typhi, Bacillus cereus, Bacillus anthracis, Escherichia coli,* and *Strepto-coccus pyogenes* (Seyyednejad et al. 2010). *Escherichia coli* was the most resistant strain.

The *n*-hexane, methanol, ethanol, ethyl acetate and water extracts of *Alcea rosea* flowers were found to possess an activity against *Escherichia coli* ATCC 29998, *Escherichia coli* ATCC 11230, *Staphylococcus aureus* ATCC 6538, *Staphylococcus aureus* ATCC 29213, *Staphylococcus epidermidis* ATCC 12228, *Salmonella typhimurium* CCM 5445, *Pseudomonas aeruginosa* ATCC 27853 and *albicans* ATCC 10239 by disc diffusion method (Mert et al. 20100). *E. Coli* 25922, *Enterobacter cloacae* 13047, *Enterococcus faecalis* 29212 and *Candida albicans* 10239 were found to be resistant. There was no significant activity difference between extracts. But all of the extracts were found to be slightly active against tested microorganisms than ceftazidime.

Anticancer/Cytotoxicity Activity

Seven phenolic compounds, scopoletin (1), *p*-hydroxyphenethyl trans-ferulate (2), 1-(α-l-rhamnosyl(1 → 6)-β-D-glucopyranosyloxy)-3,4,5-trimethoxybenzene (3), benzyl α-L-rhamnopyranosyl(1 → 6)-β-D-glucopyranoside (4), suberic acid (5), sebacic acid (6) and scopolin (7) were isolated from the methanol extract of *Althaea rosea* roots (Kim et al. 2007). The compounds were weakly cytotoxic in vitro to human cancer cell lines A549 (lung carcinoma), SK-OV-3 (ovary malignant ascites), SK-MEL-2 (skin melanoma) and HCT-15 (colon adenocarcinoma) with ED_{50} values >30 μg. The ethyl acetate flower extract showed cytotoxic activity against brine shrimp (Mert et al. 2010).

Studies showed that the methanol extracts from *A. rosea* and *Plantago major* significantly suppressed neoplastic cell transformation by inhibiting the kinase activity of the epidermal growth factor receptor (EGFR) in JB6 P + mouse epidermal cells (Choi et al. 2012). The activation of EGFR by EGF was suppressed by both extracts in EGFR+/+ cells, but not in EGFR−/− cells. Moreover, both extracts inhibited EGF-induced cell proliferation in EGFR-expressing murine embryonic fibroblasts (EGFR+/+). The results strongly indicated that EGFR targeting by both plant extracts may be a good strategy for chemopreventive or chemotherapeutic applications.

Analgesic and Anti-inflammatory Activity

The ethanolic extract of the flower of *Althaea rosea* was found to inhibit significantly the acetic acid-induced twisting of mice and the heat-induced (tail) flicking of rats, the acetic acid-induced increase in permeability of abdominal blood capillaries, the oedema of the rat paw induced by carrageenan or dextran and the release of PGE from inflammatory tissue (Wang et al. 1989). The results indicated *A. rosea* flower extract to possess analgesic and anti-inflammatory properties.

Antiulcer Activity

Polysaccharides from *A. rosea* stem possessed resorptive and coating properties and were effective in reducing forestomach lesions in rats following the ligature of the pylorus when administered enterally, intraperitoneally or intravenously (Barnaulov et al. 1985).

Antioestrogenic Activity

Studies showed that rats drinking aqueous hollyhock flower extract for 30 days manifested

marked increase in the 3-β-hydroxysteroid dehydrogenase (3β-HSD), glucose-6-phosphate dehydrogenase (G6PD) and nicotinamide adenine dinucleotide phosphate (NADP) activities and in the Khanolkar reaction intensity in Leydig cells which also increased in volume and nuclei (Papiez 2001). In group 2 given the extract for 180 days, Leydig cells manifested statistically insignificant changes in the G6PD and NADPD activities; however, the significant increase in the 3β-HSD activity and the Khanolkar reaction intensity indicated compensatory changes. The statistically significant elevation of the androgen level accompanied by a decrease in oestrogen content in homogenates of group A2 testes pointed to weak antioestrogenic effect of the extract. Papiez et al. (2002) further showed that the weak antioestrogenic activity of flavonoid compounds present in the hollyhock extract was mediated through aromatase and oestrogen receptor beta rather than by oestrogen receptor alpha in the rat testicular cells.

In subsequent studies, rats given hollyhock flower extract at a dose of 100 mg/day for 7 weeks manifested statistically significant increases in glucose-6-phosphate dehydrogenase (G6PDH) and δ(5)β-hydroxysteroid dehydrogenase (δ(5) βHSD) activities in the Leydig cells (Papiez 2004). There were no significant changes in either the diameter of seminiferous tubules or the height of seminiferous epithelium after hollyhock administration. Further, only a small amount of hyperplasia of the interstitial tissue was observed. The morphological and histoenzymatic changes in the Leydig cells indicated that the methanolic hollyhock extract had a direct but small influence on rat testes. The insignificant changes in testicular testosterone and estradiol content suggested that the extract did not disturb steroidogenesis.

Traditional Medicinal Uses

Hollyhock is an old medicinal plant. All parts of the plant have been used in traditional medicine (Grieve 1971; Duke and Ayensu 1985; Chopra et al. 1986; Tsarong 1994: Choi et al. 2012). Since ancient times in Asia, *Althaea rosea* and *Plantago major* have been used as powerful nontoxic therapeutic agents that inhibit inflammation (Choi et al. 2012). Hollyhock is an old medicinal plant. It has been used in folk medicine as an anti-inflammatory, astringent, demulcent, diuretic, emollient and febrifuge. It is used to control inflammation and to stop bedwetting and as a mouthwash in cases of bleeding gums. The flowers are regarded to be demulcent, diuretic and emollient. Flowers have been used in the treatment of chest complaints, and a decoction is used to improve blood circulation and for the treatment of constipation, dysmenorrhoea and haemorrhage.

The shoots have been employed to ease difficult labour. The root is astringent and demulcent. Pulverized roots are applied as a poultice to ulcers and used internally as a medicine for dysentery. In Tibetan medicine, roots and flowers are deemed to have a sweet, acrid taste and a neutral potency. They are employed in the therapy of inflammations of the kidneys and womb, vaginal and seminal discharge. The roots on their own are used to rectify loss of appetite. The seed is demulcent, diuretic and febrifuge.

Other Uses

Alcea rosea is mainly planted as an ornamental. Hollyhocks are especially well suited for growing along a wall or fence; they are often used in mixed borders, especially near the rear. Today many cultivated ornamental races exist. The flower colour varies extremely (from white to rose, mauve, purple to blackish red, also yellow). Most of them have spotted flowers. Double-flower cultivars also exist.

The red anthocyanin constituent of the flowers is used as a litmus. A brown dye is obtained from the petals. Flowers have been utilized as an ingredient of ‘Quick Return’ herbal compost activator. This is a dried and powdered mixture of several herbs that can be added to a compost heap in order to enhance bacterial activity and reduce the time needed to make the compost. The seed contains 12 % of a drying oil. The stem fibres have been employed in the past for paper manufacture.

Studies showed the two ornamental plants *Calendula officinalis* and *Althaea rosea* to have promised to be used for phytoremediation of cadmium contaminated soils (Liu et al. 2008). *A. rosea* in particular could be regarded as a potential Cd-hyperaccumulator through applying chemical agents.

Comments

Hollyhock is readily propagated from seeds.

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Hibiscus mutabilis

Scientific Name

***Hibiscus mutabilis* L.**

Synonyms

Abelmoschus mutabilis (Linnaeus) Wallich ex Hasskarl, *Abelmoschus venustus* Walp., *Hibiscus immutabilis* Dehnh. ex Walp., *Hibiscus immutabilis* Dehnh., *Hibiscus javanicus* Weinm., *Hibiscus malvarosa* Noronha, *Hibiscus mutabilis* f. *plenus* S. Y. Hu, *Hibiscus sinensis* Miller, *Ketmia mutabilis* (Linnaeus) Moench

Family

Malvaceae

Common/English Names

Changeable Rose, Changing Rose, Chinese Rose, Common Rose Mallow, Confederate Rose, Cotton Rose, Cotton Rosemallow, Dixie, Dixie Rose Mallow, Rose Mallow, White Mallow

Vernacular Names

Chinese: Fu Rong Hua, Fu Yong, Mu Fu Rong, Chong Ban Mu Fu Rong (double-flowered variety)
Estonian: Muutlik Hibisk
French: Caprice De Femme
French Polynesia: Akaimhe, Rakauhai, Rap
German: Filziger Roseneibisch
India: Sthal Padma, Thul Padma (Bengali), Sthalkamal (Hindi), Neladavare (Kannada), Chinappratti (Malayalam), Semburuti (Tamil), Gul-E-Ajaib (Urdu)
Indonesia: Waru Landak (Javanese), Saya Ngalingali (Ternate)
Japanese: Fuyô, Fuyou
Korean: Bu Yong
Malaysia: Baru Landak, Botan, Bunga Waktu Besar Mati Laki Mati Bini, Laki pukul Bini
Philippines: Amapola, Mapula (Tagalog)
Portuguese: Amor-De-Homem, Amor-Dos-Homens, Aurora, Inconstante Amante, Firmeza Dos Homens, Mimo-De-Vênus, Papoila, Papoula-De-Duas-Cores, Rosa-Branca, Rosa Da China, Rosa-De-Jericó, Rosa-De-São-Francisco, Rosa-Louca, Rosa-Paulista
Sierra Leone: Bokichal-Ie (Bulom), Chenjis-Ov-Laif (Krio), Ndopa-Ne (Mende)
Spanish: Malva Rosa, Rosa Algodón
Swedish: Föränderlig Hibiscus
Taiwan: Shan Fu Rong
Thai: Phuttan
Vietnamese: Đại Diệp Phù Dung, Địa Phù Dung, Mộc Liên, Phù Dung, Sương Giáng Hoa, Tam Biến Hoa, Thất Tinh Hoa, Túy Tửu Phù Dung

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Origin/Distribution

Hibiscus mutabilis is native to Southeast China and was domesticated a long time ago. It is now cultivated throughout the world and has occasionally become naturalized elsewhere, e.g. in Japan and Southeast Asia.

Agroecology

In its native range, it is found in thickets along streams. The plant is frost sensitive and thrives best in frost-free, warm areas. It is drought tolerant and grows on well-drained and slightly acidic soils. It flowers well in full sun or light shade.

Edible Plant Parts and Uses

Flowers are edible and provide food colourant (Puckhaber et al. 2002). The seeds were found to be a good source of phospholipids with potential to be used as supplements or formulated into functional foods for the nutraceutical market (Holser and Bost 2002). The leaves are edible (Kunkel 1984) and are rich in rutin (Xie et al. 2011), and rutin is a bioactive compound used as preservative in foods (Kondo and Shibara 2008). In China, the leaves are boiled and then eaten with oil and salt (Read 1946). The roots are edible but very fibrous and mucilaginous without much flavour (Cribb and Cribb 1976).

Botany

Hibiscus mutabilis is a deciduous, erect, branched, bushy, large shrub or small multi-stemmed tree, 2–5 m tall. All aerial parts are densely stellate pubescent. Leaves are papery, bright green, broadly ovate to orbicular ovate, 7–15 cm across, 5–7 lobed, with acute tips, cordate base and obtusely serrated margin on 3–10 cm long petioles and with small linear-lanceolate stipules (Plate 1). Flowers are axillary, solitary, large, single or double flowered on 5–8 cm pedicel on the upper branches. Calyx -5-lobed, ovate with acute tips; corolla 8 cm across, white to pink, becoming dark red in the evening (Plate 1); petals 4–6 cm long and broad, obovate, pubescent outside, claw with ciliate margin; staminal column 2.5–3 cm, glabrous; styles 5, pilose. Fruit is a flattened globose capsule, 2.5 cm across, yellowish and woolly. Seeds are numerous, 2–2.5 mm long, reniform, dark brown and hairy.

Plate 1 Flowers, buds and leaves

Nutritive/Medicinal Properties

Cyanidin pigments were found in the flowers (Yeh et al. 1958). The following anthocyanins cyanidin 3-xylosylglucoside (ilicicyanin) and cyanidin 3-glucoside and flavanol glycosides of quercetin and kaempferol were isolated from the red petals of *H. mutabilis* (Ishikura 1973). Five additional flavonol glycosides were isolated from the ethyl acetate extract of petals and identified as quercetin 3-sambubioside, isoquercitrin (quercetin 3-glucoside), hyperin (quercetin 3-galactoside), guaijaverin (quercetin 3-α-L-arabopyranoside), kaempferol + glucose + galactose + xylose (Ishikura 1982). Cyanidin 3-sambubioside was the most common floral anthocyanin in 14 Malesian *Hibiscus* species including *H. mutabilis* (Lowry 1976). Also cyanidin 3-glucoside was detected. Flavonoid aglycones (mg.g fresh tissues) found in the fresh flowers of *H. mutabilis* included quercetin 80 mg, kaempferol 8 mg, cyanidin 5 mg and total pigment 93 mg (Puckhaber et al. 2002). A new flavonol triglycoside,

quercetin 3-*O*-[β-D-xylopyranosyl(1 → 2)-α-L-rhamnopyranosyl(1 → 6)]-β-D-galactopyranoside (mutabiloside), was isolated, and the four known flavonols identified as quercetin 3-*O*-[β-D-xylopyranosyl(1 → 2)]-β-D-galactopyranoside (1) and kaempferol 3-*O*-[β-D-xylopyranosyl (1 → 2)]-β-D-galactopyranoside (2), quercetin (3) and hyperoside (4) were isolated from the methanol petal extract of *H. mutabilis* after fractionation (Iwaoka et al. 2009). The following phytochemicals had been reported from the flowers: quercetin, quercemeritrine, quercetin-3-d-xyloside, quercetin-3-sambubioside, isoquercetin, meratrin, hybridin, kaempferol, hyperin, guaijaverin, cyanidine-3-xlosyl glucose, cyanidin-3-monoglucoside, hibiscones and hibiscoquinones (Barve et al. 2010).

The seed oil yields found in *H. mutabilis* 'single pink' (8.87 %) and *H. mutabilis* 'double pink' (9.06 %) were low compared to other *Hibiscus* species (Holser and Bost 2002). The seed oil of *H. mutabilis* single pink flowers and *H. mutabilis* double pink flowers contained the following non-polar fatty acid methyl esters (mole%): c16: (palmitic acid) 19.93 %, 19 %; c18:0 (stearic acid) 2.88 %; c18:1 (oleic acid) 17.83 %, 16.30 %; c18:2 (linoleic acid) 61.35 %, 64.90 %, total % fatty acid 79.18 %, 81.20 %, respectively. However, the seeds could be a significant source of phospholipids that could be recovered by a selective extraction and the products used as supplements or formulated into functional foods for the edible nutraceutical market. The polar phospholipid profiles of *H. mutabilis* single pink flowers and *H. mutabilis* double pink flowers contained monogalactosyldiacylglycerol 21.5 %, 14.5 % (as % diacylglycerol detected); digalactosylacylglycerol 78.5 %, 85.5.5 %; phosphatidylethanolamine 4.45, 4.45; phosphatidic acid 2.7 %, 0 %; phosphatidylserine 9.2 %, 0 %; phosphatidylcholine 17.6 %, 56.5 %; lysophosphatidylcholine 66.2 %, 39 % (% total phospholipids), respectively.

Nine compounds isolated from *H. mutabilis* leaves were identified as tetracosanoic acid, β-sitosterol, daucosterol, salicylic acid, emodin, rutin, kaempferol-3-*O*-β-rutinoside, kaempferol-3-*O*-β-robinobinoside and kaempferol-3-*O*-β-D-(6-*E*-*p*-hydroxycinnamoyl)-glucopyranoside (Yao et al. 2003). A hexameric 150-kDa galactonic acid-binding lectin was isolated from dried *Hibiscus mutabilis* seeds (Lam and Ng 2009). The hemagglutinating activity of the lectin, which was stable at pH 4–7 and up to 50 °C, could be inhibited by 25 mM galactonic acid. The following phytochemicals had been reported from the leaves: β-sitosterol, β-carotene and quercetin (Barve et al. 2010). Rutin (quercetin-3-rutinoside), one of the most bioactive flavonoid glycosides, was isolated by mechanochemical-assisted extraction from the leaves (Xie et al. 2011). Rutin is used as preservative in various foods (Kondo and Shibara 2008), and animal studies had shown it to reduce the risk of cardiovascular diseases (Annapurna et al. 2009) and kidney diseases (Hu et al. 2009).

A flavanone glycoside, naringenin 5,7-dimethyl ether 4′-*O*-β-D-xylopyranosyl-β-D-arabino-pyrano-side was isolated from the stem (Chauhan et al. 1979). A new diterpenoid named hibtherin A was isolated from the stem (Ma et al. 2009). The following phytochemicals had been reported from the stems: naringenin-5,7-dimethyl ether,4′-β-D-xylopyranosyl-β-D-arabinopyranoside and eriodictyol-5,7-dimethyl ether-4′-β-D-arabinopyranoside (Barve et al. 2010).

Antioxidant Activity

The ethanol leaf extracts of four Bangladeshi medicinal plants including *Hibiscus mutabilis* exhibited significant dose-dependent NO scavenging activity of 78.60 % with IC_{50} value of 147.64 μg/mL (Saha et al. 2008). Leaves of *H. mutabilis* ranked second to *H. tiliaceus* in terms of antioxidant potential with ascorbic acid equivalent antioxidant capacity (AEAC) value of 877 mg ascorbic acid/100 g fw and total phenolic content (TPC) of 861 mg gallic acid equivalent (GAE)/100 g (Wong et al. 2009, 2010). The flowers had lower AEAC value of 562 mg and ferric-reducing power (FRP) of 2.4 mg GAC/g and total phenolic content (TPC) of 495 mg GAE/100 g and total anthocyanin content (TAC) of 16 mg cyanidin-3-glucoside equivalent (CGE)/100 g. Anthocyanin content of red flowers was 3 times that of pink flowers and 8 times that of white

flowers (Wong et al. 2009). There was a significant increase in phenolic content with colour change. Overall ranking of antioxidant potential of *H. mutabilis* flowers was red > pink > white. The red flowers remain on plants for several days before they abort (Wong et al. 2009). Weight of a single detached flower was 15.6 g when white, 12.7 g when pink and 11.0 g when red.

Antityrosinase Activity

Of four species of *Hibiscus* tested, ranking of antityrosinase activity was *H. tiliaceus* > *H. mutabilis* (25 %) > *H. rosa-sinensis* (11 %) = *H. sabdariffa* (5 %) (Wong et al. 2010). Leaves of *H. tiliaceus* (42 %) had the strongest antityrosinase activity comparable to leaves of *P. guajava* (41 %) as positive control.

Analgesic Activity

The methanol, ethyl acetate and petroleum ether extracts of *H. mutabilis bark* showed significant analgesic activity at 50 mg/kg, i.p. dose in mice (Ghogare et al. 2007). Analgesic activity was comparable with standard drug pentazocine. Among all the extracts, petroleum ether extract of *H. mutabilis* showed highest increase in reaction time. At dose of 100 mg/kg, i.p., all the extracts significantly attenuated the number of writhing and stretching induced by intraperitoneal injection of 0.1 mL 0.6 % acetic acid. Methanol extract showed more inhibitory effect on writhing induced by acetic acid as compared to other extracts as well as the standard drug paracetamol. Result showed that peripheral analgesic activity in descending order was methanol, ethyl acetate and petroleum ether. Tannins, flavonoids and sterols were detected in the above extracts.

Antidiabetic Activity

The methanol leaf extract of *H. mutabilis* was found to inhibit α-glucosidase (Kumar et al. 2012). Ferulic acid and caffeic acid were identified as the α-glucosidase inhibitors present in the extract. The results suggested the potential use of the leaf extract for management of diabetes.

Anti-allergic Activity

Among the flavonol derivatives isolated from the methanol petal extract of *H. mutabilis*, quercetin 3-*O*-[β-D-xylopyranosyl(1 → 2)-α-l-rhamnopyranosyl(1 → 6)]-β-D-galactopyranoside (mutabiloside), and quercetin 3-*O*-[β-D-xylopyranosyl (1 → 2)]-β-D-galactopyranoside showed significant allergy-preventive effects (Iwaoka et al. 2009).

Anti-inflammatory Activity

The ethyl acetate leaf extract exhibited comparable anti-inflammatory activity when compared with standard drug nimuselide (Barve et al. 2010). The extract had 64.52 % inhibition of carrageenan-induced paw oedema in rats as compared to nimuselide which showed 70.22 %.

Anthelmintic Activity

The crude methanol leaf extract of *H. mutabilis* and ferulic acid, the active molecule from the ethyl acetate fraction, showed significant microfilaricidal as well as macrofilaricidal activities against the microfilaria (L_1) and adult of *Setaria cervi* by both a worm motility and MTT reduction assays (Saini et al. 2012). Ferulic acid was found to exert its antifilarial effect through induction of apoptosis and by downregulating and altering the level of some key antioxidants (GSH, GST and SOD) of the filarial nematode *S. cervi*. Ferulic acid caused an increased pro-apoptotic gene expression and decreased expression of anti-apoptotic genes simultaneously with an elevated level of ROS and gradual dose-dependent decline of parasitic GSH level. They also observed a gradual dose-dependent elevation of GST and SOD activity in the ferulic acid-treated worms.

Antiviral/Antiproliferative Activities

The aqueous extract of *H. mutabilis* was one of the ten effective plant extracts that exhibited anti-HSV-II (Herpes simplex virus II) activity (Zheng 1989). A hexameric 150-kDa galactonic acid-binding lectin isolated from the seeds potently inhibited HIV-1 reverse transcriptase with an IC_{50} of 0.2 μM (Lam and Ng 2009). It exhibited weak antiproliferative activity towards both hepatoma HepG2 cells (40 % inhibition) and breast cancer MCF-7 cells (50 % inhibition) at 100 μM concentration of the lectin.

Antibacterial Activity

Of all solvents, the 70 % alcohol leaf extract elicited the best antibacterial activity against *Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Staphylococcus aureus* and *Enterococcus faecalis* (Li et al. 2009). The MIC value to *E. coli, P. vulgaris* and *E. faecalis* was 0.25 mg/mL. Both methanolic and ethyl acetate leaf extracts elicited good in vitro inhibitory activity against *Bacillus subtilis, Proteus vulgaris, Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus* and *Salmonella typhi* (Barve et al. 2010).

Traditional Medicinal Uses

Flowers and leaves have been employed in traditional herbal medicine (Burkill 1966; Stuart 2012; Dasuki 2001). They are considered to be emollient, cooling, expectorant, pectoral, analgesic and antidote to various kinds of poison. Flower infusions have been used for chest and pulmonary complaints; for treating nasopharyngeal carcinoma, persistent coughs, menorrhagia and dysuria; and also as a stimulant. Leaves and flowers are used as poultices for swellings, skin infections and wounds like burns and scalds. Leaves are used as a component in Chinese herbal medicine for treating tuberculosis lymphadenitis. Mucilage from flowers and leaves is used by midwives to facilitate delivery during labour.

Other Uses

The plant is planted as ornamentals in gardens, roadsides and parks.

Comments

The plant is readily propagated from stem cuttings which root well at any time of the year.

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Hibiscus rosa-sinensis

Scientific Name

***Hibiscus rosa-sinensis* L.**

Synonyms

Hibiscus arnottii Griff. ex Mast., *Hibiscus cooperi* hort. ex Fl. de Serres, *Hibiscus festalis* Salisb., *Hibiscus fragilis* DC., *Hibiscus fulgens* hort. ex W.W. Baxt., *Hibiscus javanicus* Mill., *Hibiscus rosiflorus* Stokes

Family

Malvaceae

Common/English Names

China Rose, Chinese Hibiscus, Hawaiian Hibiscus, Hibiscus, Hibiscus Flower, Jamaica Flower, Rose Mallow, Rose of China, Shoeblack Plant Hibiscus, Shoeflower

Vernacular Names

Arabic: Angharae-Hindi, Angharaehindi, Angharae-Hindi
Brazil: Hibisco, Mimo-Chinês, Rosa Da China, Mimo De Vênus (Portuguese)
Burmese: Khaung-yan
Chinese: Zhu Jin, Da Hong Hua, Tai Hua Fa, Chijin, Riji, Fusang, Fosang, Hongfusang, Hongmujin, Sangjin, Huohonghua, Zhaodianhong, Songjin, Erhonghua, Huashanghua, Tuhonghua, Jiamudan, Zhongguoqiangwei
Colombia: Pejo
Cook Islands: Hibiscus, Kaute, Kaute 'Enua, Kaute Kula, Kaute Kumu, Kaute Kura
Czech: Ibišek čínská růže
Danish: Hawaiiblomst, Kinesisk Rose
Dutch: Chinese Roos
Estonian: Rooshibisk
Fiji: Kauti, Loloru, Senitoa Yaloyalo, Senicikobia
French: Hibiscus De Chine, Hibiscus Rose De Chine, Rose De Chine
German: Chinesischer Roseneibisch, Roseneibisch
Japanese: Fusou, Haibisukasu
Malaysia: Baru Landak, Botan, Bunga Waktu Besar, Bunga Raya, Mati Bini, Mati Laki, Laki Pukul Bini
India: Dusanna (Andhra Pradesh), Jaba (Assamese), Jiwa, Joba, Oru (Bengali), Jasunt, Jasvua (Gujarati), Gudhal, Gurhal, Guthur, Jassoon, Jasum, Jasun, Jasund, Jasut, Java, Odhul, (Hindi), Dasavala (Malayalam), Dasavala (Kannada), Aimparutti, Ain-Pariti, Ayamparutti, Cemparatti, Cemparutti, Champarutti, Chebarathi, Chemburuthi, Chemparutti, Himbarathi, Jampa, Japa, Schem-Pariti, Shemparatti, Schempariti (Malayalam), Jubakushum (Manipuri), Darshan, Dasindachaphula, Jaasavand, Jasavanda, Jasund, Jassvandi, Jasvand (Marathi), China Pangpar, Chinnpang-Par, Midumpangpar (Mizoram), China Pangpar, Mandar, Midumpangpar, Mondaro

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(Oriya), Jaipushpa, Jasum, Gurhal (Punjabi), Arkapriya, Aruna, Aundrapuspa, Harivallabha, Japa, Japaapushpa, Japapushpa, Japapushpam, Java, Joba, Odhrapushpa, Odrapuspa, Ondrakhya, Ondrapuspi, Oundrapuspa, Pratika, Raktapushpi, Rogapuspi, Rudhrapushpa, Trisandhya (Sanskrit), Sapattuu, Semparathai, Semparuthi, Semparutti, Shamberattai, Tacanapu, Tacanpu, Tamalomaya, Tarupaka, Tiruttikkiritam, Uruttiraputpam (Tamil), Cembarattamu, Chimabarathamu, Daanachettu, Dasana, Dasanipu, Daasaana Chettu, Daasaani, Daasanamu, Dasana, Dasanamu, Dasani, Dasanie, Japa, Japapushpamu, Javapushpamu, Mandara, Madarapuvvu, Nandara (Telugu), Gul-E-Gurhal, Gul Gurhal Taza (Urdu)

Indonesia: Woro-Wari (Javanese), Kembang Wera (Sundanese), Kembang Sepatu

Italian: Rosa Della Cina

Laotian: Dok Deng, May

Marquesas Islands: Koute

Mexico: Bis, Gallarde, Lamparilla, Sùchel, Tulipán

Nepalese: Baarhmaase Phuul, Gudahal, Japaa Kusum, Japa Puspii, Rakta Puspi

Niue: Kaute

Panama: Clavel Japonés, Hibiscus De Los Jardines, Papo, Palo De La Reina, Tapo

Papua New Guinea: Banban (Hisiu, Central Province), Gelegwaugwau (Rigo, Central Province), Ovaova Vava'a (Vanapa, Central Province), Hibiscus (Waiwa, Central Province)

Persian: Angarae-Hindi, Angaraehindi, Angharae-Hindi

Philippines: Kayanga (Bikol), Antalongan, Gumamela, Kayanga, Tapuranga, Tarokanga (Bisaya), Saysayam (Bontok), Kayanga (Iloko), Aratangan, Gumamela, Tapolanga, Tarokanga (Pampangan), Taukangga (Sulu) Antalongan, Gomamela, Gumamela, Tapolanga (Tagalog)

Polish: Hibiskus róza chinska, Ketmia Róza-Chinska

Portuguese: Rosa-Da-China

Rarotonga: Kaute

Samoa: 'Aute

Spanish: Clavel Japonés, Rosa china, Rosa de la China, Tulipán

Sri Lanka: Wada Mal (Sinhalese)

Swedish: Hibiskus, Kinaros

Tahiti: 'Aute

Taiwan: Fo Sang, Fu Sang

Thai: Chaba

Tuvalu: 'Aute

Vietnam: Bụp, Râm Bụp, Dâm But

Origin/Distribution

It is believed to have originated in East Asia—China. It is now widely distributed and cultivated in the tropics and subtropics.

Agroecology

Tropical or subtropical in requirements, Hibiscus is commonly cultivated as a garden ornamental from sea level to 500 m altitude. It is frost sensitive and will freeze in mild winters but will resprout from the base in spring. A good cover of loose mulch before winter will help reduce severe winter injury. It does best in full sun in well-drained fertile soil high in organic matter.

Edible Plant Parts and Uses

Flower petals and young leaves are edible (Hedrick 1972; Tanaka 1976; Facciola 1990; Duke 2012; French 1986; Johansson 1989; Reddy et al. 2007; Wongwattanasathien et al. 2010). The slightly acidic petals are used sparingly in salads or as garnish. Flowers are reported eaten as pickles and the young leaves are eaten cooked in Papua New Guinea. The flowers are eaten in salad in the Pacific Islands. In Andhra Pradesh, India, the flowers are pounded into a paste and used as chutney (Reddy et al. 2007). The flowers are also used in herbal teas and as food colouring. In some areas in Africa, the young leaves are gathered for relish. Hibiscus flowers have a tart, cranberry-like flavour and should be used sparingly (Wilson 2013). The Lecture Room and Library at Sketch has created a wonderful dish of rhubarb, brie and gingerbread with hibiscus syrup and celery for the 2013 Chelsea Flower Show.

Plate 1 (**a**, **b**) Flowers and leaves of common Hibiscus

Botany

Erect, much-branched, glabrous, evergreen shrub, 1–3 m tall. Leaves alternate, papery, dark green, broadly or narrowly ovate, 4–9×2–5 cm, base rounded or cuneate, margin serrate-dentate, apex acuminate; stipules linear, 5–10 mm long; petiole 0.5–2 cm long (Plate 1a, b). Flowers solitary, axillary on upper branches, large, simple or double, usually pendulous on 1–8 cm long pedicels. Epicalyx lobes 6–9, linear or linear-lanceolate. Calyx campanulate with 5 ovate to lanceolate, stellate puberulent, lobes. Corolla white, rosy red, reddish or orange-yellow or purplish, funnel-shaped, 6–10 cm in diameter (Plates 1a, b, 2 and 3), often double; petals 5 obovate, imbricate, pilose abaxially, apex obtuse or irregularly lobed. Staminal column exserted, glabrous, antheriferous near the apex, style 5-fid each branch crowned by stigma. Fruit a dehiscent, ovoid capsule, 2.5 cm, glabrous with beaked apex splitting into 5. Seeds small, black.

Plate 2 Golden yellow-pink variegated-flowered cultivar

Nutritive/Medicinal Properties

Chemical constituents of *Hibiscus rosa-sinensis* isolated and identified from various plant parts include taraxeryl acetate, beta-sitosterol, campesterol, stigmasterol, ergosterol, lipids, arachidic acid, behenic acid, oxalic acid, palmitic acid, octanoic acid, stearic acid, sterculic acid, tricosanoic

Plate 3 Orangey-red variegated cultivar

acid, tridecanoic acid, undecanoic acid, citric acid, tartaric, fructose, glucose, sucrose, flavonoids and flavonoid glycosides, chrysanthemin, quercetin, hibiscetin, alkanes, hentriacontane, cyanidin, cyanidin chloride and cyanin glucosides (Shrivastava 1974; WHO 1998, 2009; Lee 2008).

Flower Nutrients and Phytochemicals

The edible portion of the flower (61.6 %) was reported to have the following nutrient composition (per 100 g): moisture 89.8 %, nitrogen 0.064 %, fat 0.36 %, crude fibre 1.56 %, calcium 4.04 mg, phosphorus 26.68 mg, iron 1.69 mg, thiamin 0.031 mg, riboflavin 0.048 mg, niacin0.61 mg and ascorbic acid 4.16 mg (CSIR 1959). Petals of *Hibiscus rosa-sinensis* were reported to contain quercetin-3-di-*O*-β-D-glucoside; quercetin-3-7-di-*O*-β-D-glucoside; quercetin-3-*O*-β-D-sophorotrioside; and kaempferol and kaempferol-3-*O*-β-D-xylosyl-glucoside (Subramanian and Nair 1972). The major anthocyanin contained in the red flowers of *H. rosa-sinensis* was cyanidin-3-sophoroside (Lowry 1976; Nakamura et al. 1990). Red-petalled varieties of *H. rosa-sinensis* were found to have more number of anthocyanin bands compared with that observed in yellow–yellow orange varieties (Shobha et al. 1999). The varieties in the different coloured groups differed in the quantitative distribution of anthocyanins, leucoanthocyanins, flavonol and carotenoids. Flavonoid aglycones found in the flowers (per g fresh tissues) included quercetin 7 mg and cyanidin 36 mg (Puckhaber et al. 2002).

The flowers were also reported to contain the following flavones: quercetin-3,5-diglucoside; quercetin-3,7-diglucoside; cyanidin-3,5-diglucoside and cyanidin-3-sophoroside-3-5-glucoside from deep yellow and white flowers and from ivory white flowers is kaempferol-3-xylosylglucoside (Joshi 2004). Khare (2004) reported the following from the flowers: quercetin-3,5-diglucoside; quercetin-3,7-diglucoside; quercetin-3-sophorotrioside; kaempferol-3-xylosylglucoside and cyanidin-3-sophoroside-5-glucoside. Five compounds were isolated from the chloroform extract of *H. rosa-sinensis* flower, *n*-nonacosan-13-one, *n*-triacontane, *n*-dotetracontane, *n*-nonacosan-4-ol-18-one and *n*-hentriacontan-4-one-10-ol (Siddique et al. 2005), and five compounds were isolated from the hydroalcoholic flower extract, *n*-docosane; henicos-11-ene-9-one; stigmast-5-ene-3β, 4α-diol; stigmast-5-ene-3β-benozyloxy-12β-ol; and *n*-pentacos-4-en-3-one-18, 23-diol (Siddique et al. 2006).

The following chemicals were isolated from the ethanol extract of the flowers: hexadecanoic acid, hexanedioic acid and squalene (Bhaskar et al. 2011). Polyphenolic compound isolated from the flowers included quercetin-7-*O*-galactoside; kaempferol-7-*O*-[6‴-O-*p*-hydroxybenzoyl-β-D-glucosyl-(1 → 6)-β-D-glucopyranoside] and scutellarein-6-*O*-α-L-rhamnopyranoside-8-*C*-β-D-glucopyranoside (Salib et al. 2011). The flowers were also reported to contain cyclopeptide alkaloids (Khokhar and Ahmad 1992).

Leaf Phytochemicals

The following fatty acids, fatty alcohols and hydrocarbons were identified from *Hibiscus rosa-sinensis* leaves: undecanoic acid, tridecanoic acid, tricosanoic acid, tricosan-1-ol, triacontan-1-ol, tartaric acid, stearic acid, pentadencanoic acid, pentacosanoic acid, pentacosan-1-ol, palmitic acid, octanoic acid, octadecadienoic acid, octacosanoic acid, octacosan-1-ol, *N*-tricosane, *N*-triacontane, *N*-triacontan-1-ol, *N*-pentacosane, nonanoic acid, nonadecanoic acid, *N* octadecane, *N*-octacosane, *N*-nonadecane, *N*-nonacosane,

N-hexadecane, *N*-hexacosane, *N*-heptadecane, *N*-heptacosane, *N*-heneicosane, *N*-eicosane, *N*-dotriacontane, *N*-docosane, myristic acid, montanyl alcohol, margaric acid, lignoceric acid, lauric acid, isotriacontan-1-ol, iso-octacosan-1-ol, hexacosanoic acid, hexacosan-1-ol, heptacosanoic acid, heptacosan-1-ol, heneicosanoic acid, heneicosan-1-ol, docosan-1-ol, decanoic acid, behenic acid and arachidic acid (Srivastava et al. 1976). Two cyclic acids, sterculic (2-octyl-l-cyclopropene-l-octanoic acid) and malvalic (2-octyl-l-cyclopropene-l-heptanoic acid), were also identified.

A representative mucilage, named Hibiscus-mucilage RL, was isolated from *H. rosa-sinensis* leaves (Shimizu et al. 1993). Its major constituent was an acidic polysaccharide composed of L-rhamnose: D-galactose: D-galacturonic acid: D-glucuronic acid in the molar ratio of 5:8:3:2. Its main structural features including a unique backbone chain composed of alpha-1,4-linked D-galactosyl alpha-1,2-linked L-rhamnosyl alpha-1,4-linked D-galacturonic acid units. The mucilage showed considerable anti-complementary activity.

Stem and Root Phytochemicals

The aliphatic compounds methyl 10-oxo-11-octadecynoate, methyl 8-oxo-9-octadecynoate, methyl 9-methylene-8-oxoheptadecanoate and methyl 10-methylene-9-oxooctadecanoate (Nakatani et al. 1986) were isolated from the stem bark and methyl (*E*)-11-methoxy-9-oxo-10-nonadecenoate and (*E*)-10-methoxy-8-oxo-9-octadecenoate from the root bark (Nakatani et al. 1994). 8-Nonynoic, 9-decynoic acids and their methyl esters were isolated from *H. rosa-sinensis* and found to inhibit germination of lettuce seeds (Nakatani et al. 1995).

Various parts of *Hibiscus rosa-sinensis* plant have been reported to exhibit various pharmacological activities.

Antioxidant Activity

Total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) of *H. rosa-sinensis* leaves were 301 mg gallic acid equivalent (GAE)/100 g and 96 mg ascorbic acid/100 g, respectively (Wong et al. 2010). Leaves of *H. schizopetalus*, *H. sabdariffa* and *H. rosa-sinensis* had better FIC (ferrous iron chelating) ability than those of *H. mutabilis*, *H. tiliaceus* and *H. taiwanensis.* Leaves of species with higher TPC and AEAC had lower FIC ability for *H. tiliaceus* and *H. mutabilis* and vice versa for *H. schizopetalus* and *H. rosa-sinensis*. The results suggested the presence of compounds in leaves of *H. schizopetalus* and *H. rosa-sinensis* with relatively weak radical scavenging activity but good metal chelating ability that could prevent the generation of hydroxyl radicals via Fenton's reaction. Flowers of *H. rosa-sinensis* had 735 mg GAE/100 g total phenolic content (TPC), 284 mg cyanidin-3-glucoside equivalent (CGE)/100 g total anthocyanin (TAC), 640 mg AA/100 g ascorbic acid equivalent antioxidant capacity (AEAC) and 4.0 mg GAE/g ferric reducing power (FRP). Based on TPC, ranking was *H. tiliaceus* > *H. rosa-sinensis* > *H. taiwanensis* ~ *H. schizopetalus* ~ *H. mutabilis* > *H. sabdariffa.* The red flowers of *H. rosa-sinensis* and *H. schizopetalus*, which yielded the highest TAC, displayed high FIC ability and lipid peroxidation inhibition (LPI) activity (Wong et al. 2009, 2010). Species with low TAC such as *H. mutabilis* and *H. sabdariffa* displayed low or no FIC ability and LPI activity. TAC appeared to be positively correlated with FIC ability and LPI activity in flowers of *Hibiscus* species. The extract ethanolic extract *of Hibiscus rosa-sinensis* flowers was found to contain large amounts of phenolic compounds and flavonoids (Bhaskar et al. 2011). The extract exhibited a concentration-dependent scavenging activity. Additionally, the reducing power (capacity to reduce Fe^{3+} to Fe^{2+}) and the capacity to scavenge hydrogen peroxide, superoxide radicals and nitric oxide were also determined. *Hibiscus rosa-sinensis* crude extract was found to have radical scavenging and antioxidant activity (Mandade et al. 2011). The crude extract of the aerial parts inhibited 94.58 % peroxidation of linoleic acid emulsion at 20 µg/mL concentration, while the standard antioxidants BHA (butylated hydroxyanisole), BHT (butylated hydroxytoluene) and α-tocopherol exhibited an inhibition of 93.75, 96.66 and 83.33 % at 60 µg/mL concentration, respectively. The crude

Hibiscus extract showed 51.9 % hydrogen peroxide radical scavenging activity compared to 38.2 % for BHA, 36.3 % for BHT and 41.2 % for α-tocopherol. The Hibiscus extract exhibited 68.2 % superoxide scavenging activity compared to 76.4 % for BHA, 72.2 % for BHT and 24.1 % for α-tocopherol. The crude extract of *H. rosa-sinensis* contained high level of phenols 49.44 mg/g tannic acid equivalent, proanthocyanidins 9.15 mg/g catechin equivalent, flavonols 5.5 mg/g quercetin equivalent and flavonoids 4.8 mg/g quercetin equivalent. The high phenol content might account for the strong activity observed against ABTS + radical cation(s) and H_2O_2 radicals.

The total antioxidant capacity of *H. rosa-sinensis* extract (500 μg/mL) was nearly twofold higher than that of butylated hydroxytoluene (BHT) that was used as a standard with the same concentration (Abdel Ghaffar and El-Elaimy 2012). The scavenging ability of the extract was very close to that of butylated hydroxyanisole (BHA) for the superoxide anion radical (60.4 % for extract vs. 61.4 % for BHA) and for NO (36.3 % for extract vs. 37.3 % for BHA) while the extract was lower for hydrogen peroxide (48.55 % for extract vs. 65.8 % for BHA). The co-incubation of Fe^{+3}/ascorbate with Hibiscus extract inhibited lipid and protein oxidative damage by nearly 31 % at 500 μg/mL. The phenolic content of *H. rosa-sinensis* leaf extract was determined to be 48.40 mg catechol equivalent/g of dry sample while the flavonoid content was 24.26 mg quercetin equivalent/g of dry sample. The extract also contained carbohydrates and/or glycosides, steroids and/or triterpenes, flavonoids and tannins. The in vitro antioxidant and scavenging activities were attributed to its phenolic and flavonoid contents.

Antityrosinase Activity

Of four species of *Hibiscus* tested, leaves of *H. tiliaceus* (42 %) had the strongest antityrosinase activity (Wong et al. 2010). Ranking of antityrosinase activity was *H. tiliaceus* > *H. mutabilis* > *H. rosa-sinensis* = *H. sabdariffa*.

Cognitive Enhancing and Anti-amnesic Activity

The results of animal study suggested that *H. rosa-sinensis* had a protective role against age and scopolamine-induced amnesia, indicating its utility in management of cognitive disorders (Nade et al. 2011). The ethyl acetate-soluble fraction of the methanol extract of *H. rosa-sinensis* (EASF) attenuated amnesia induced by scopolamine and aging. Pretreatment with EASF significantly increased the discrimination index in the object recognition test which was significantly lowered in the aged mice and scopolamine group. In passive avoidance test, scopolamine-treated mice exhibited significantly shorter step-down latencies; EASF treatment showed a significant increase in shorter step-down latencies in young, aged as well as in scopolamine-treated animals. EASF administration significantly reduced lipid peroxidation and reversed the decrease in brain superoxide dismutase (SOD) and glutathione reductase (GSH) levels caused by scopolamine treatment. The administration of *H. rosa-sinensis* improved memory in amnesic mice and prevented the oxidative stress associated with scopolamine.

Hibiscus rosa-sinensis plant extract attenuated the ischaemic reperfusion-induced increase in lipid peroxidation and fall in superoxide dismutase (SOD), catalase (CAT) and glutathione reductase (GSH) levels (Nade et al. 2010). The cerebral hypoperfusion caused a propensity towards anxiety and was accompanied by deficits of learning and memory. The extract ameliorated anxiety and there was improvement of learning and memory. They postulated that neuroprotection afforded by *H. rosa-sinensis* may be due to cerebral adaptation, through augmentation of cellular antioxidants such as GSH, SOD and CAT. They added that the results indicated the beneficial role of *H. rosa-sinensis* in cerebrovascular insufficiency states and dementia.

Anti-dyskinesia Activity

Nade et al. (2009) found that reserpine-treated rats significantly developed vacuous chewing

movements and tongue protrusions; however, co-administration of *Hibiscus rosa-sinensis* root extract (100, 200 and 300 mg/kg, per orally) attenuated the effects. Biochemical analysis of brain revealed that the reserpine treatment significantly increased lipid peroxidation and decreased levels of superoxide dismutase (SOD), catalase (CAT) and glutathione reductase (GSH), an index of oxidative stress process. Co-administration of extract significantly reduced the lipid peroxidation and reversed the decrease in brain SOD, CAT and GSH levels. The results suggested that *Hibiscus rosa-sinensis* had a protective role against reserpine-induced orofacial dyskinesia and oxidative stress.

Antifertility Activity

H. rosa-sinensis flowers were found to have anti-oestrogenic activity (Kholkute and Udupa 1976). The benzene extract of the flowers was found to disrupt the oestrous cycle of female albino rats (Kholkute et al. 1976). Treatment for 30 days resulted in a significant reduction in the weight of the ovaries, uterus and pituitary gland. Ovarian follicular atresia and uterine atrophy were observed. Treatment dose-dependently damaged the pituitary resulting in degranulated gonadotrophs. The post-coital antifertility properties of benzene hot extracts of *Hibiscus rosa-sinensis* flowers, leaves and stem barks were also investigated in female rats (Kholkute et al. 1977). Only extracts from the flowers of the plant were 100 % effective in preventing pregnancy. They also found that the benzene extracts of flowers collected from *Hibiscus mutabilis, Hibiscus schizopetalus* and *Malvasicus grandiflorus* did not markedly affect pregnancy. Ethanolic extracts (50 %) and the benzene extracts of *H. rosa-sinensis* dose-dependently and significantly reduced the glycogen contents in the uterus of adult rat (Prakash 1979). Of the two, benzene extract appeared to be more potent. The results were attributed to the antioestrogenic nature of the extracts. The benzene extract of *Hibiscus rosa-sinensis* flowers exhibited the most effective antifertility activity on female albino rats (Singh et al. 1982). The ether-soluble portion of the water-insoluble fraction of the benzene extract showed significant anti-implantation and abortifacient activities.

Kabir et al. (1984) found that with an increase in the dosage of the *Hibiscus rosa-sinensis* benzene extract, the percentage of implantation failure increased. At the dose level of 1 g/kg body weight, the extract led to failure of implantation in 93 % of the mice. The effect was accompanied by adversely altered uterine weight, its protein content and alkaline and acid phosphatase activity. They also found that the extract exerted neither inhibitory nor stimulatory influence on uterine progesterone uptake in untreated castrated mice, but the oestrogen-induced increase in the uptake level was significantly inhibited by the extract. Failure of uterine bed preparation due to antioestrogenic potentiality of the extract was suggested as the plausible cause of implantation failure. Further, they found that the benzene *Hibiscus* flower extract administered during day 1–4 of gestation exerted anti-implantation effect without affecting the tubal transport of zygote. On day 4, normal number of blastocyst was present in the uterus, but they did not implant (Pal et al. 1985). Ovarian structure exhibited signs of luteolysis. Inadequate progestational development of the endometrium due to interference with the conditioning of the uterus with progesterone during prenidatory phase of pregnancy was suggested as the plausible cause of the extract-induced implantation failure. In another paper, they reported that oral administration of the benzene *Hibiscus* flower extract at a dose level of 1 g/kg body weight/day from day 5–8 of gestation led to termination of pregnancy in about 92 % of the animals (Pakrashi et al. 1986). The effect was associated with a significant decline in peripheral level of progesterone and increase in uterine acid phosphatase activity, as measured on day 10. The ovary exhibited signs of luteolysis and the corpus luteal δ-5-3 β-hydroxysteroid dehydrogenase activity decreased considerably. In unilaterally pregnant mouse having trauma-induced deciduomata in the sterile horn, the extract caused resorption of the fetuses and regression of the deciduomata accompanied by reduction in weight

of the ovaries. Luteolysis may be due to interference with the luteotropic influence, and a consequent fall in plasma level of progesterone was suggested as the plausible cause of termination of pregnancy. *Hibiscus* flowers were found to have significant antifertility effect in rats (Sethi et al. 1986). Treating ovariectomized, pregnant and cyclic rats separately with 50 % ethanol or benzene extracts of *Hibiscus rosa-sinensis* flowers did not elicit any significant changes in the concentration of Na+ in uterine flushings and of Na+ and K+ of serum (Prakash et al. 1990). Murthy et al. (1997) found that the benzene *Hibiscu*s flower extract administered intraperitoneally at the dose levels of 125 and 250 mg/kg body weight to adult mice resulted in an irregular oestrous cycle with prolonged estrus and metestrus. The increase in the atretic follicles and the absence of corpora lutea indicated the antiovulatory effect of the extract. The extract also showed oestrogenic activity in immature mice by early opening of the vagina, premature cornification of the vaginal epithelium and an increase in uterine weight. They postulated that the antiovulatory effect may be due to an imbalance in the hormonal environment, as there may be an increase in the endogenous secretion of oestrogen by atretic follicles, and also to the oestrogenicity of *Hibiscu*s flower extract.

Recent scientific studies supported ancient literature in Ayurvedic and Unani texts that described the use of a number of the plant preparations for fertility regulation. Nivsarkar et al. (2005) found that *Hibiscus rosa-sinensis* leaf extract also possessed antifertility and abortifacient activity. No implantation sites were observed in pregnant female mice treated with the aqueous leaf extract from days 1 to 6 of pregnancy. A sharp rise in superoxide anion radical and a sharp decline in superoxide dismutase (SOD) activity, as seen in the endometrium from control animals, were altered in extract-treated animals. The extract also exhibited antioestrogenic activity, as indicated by increase in uterine weight.

Vasudeva and Sharma (2008) reported that ethanolic extract of the roots of *Hibiscus rosa-sinensis* exhibited potent anti-implantation (inhibition 100 %) and uterotropic activities which were observed at the dose level of 400 mg/kg body weight. Oral administration of the ethanol extract increased the uterine weight and stimulated uterine growth, suggesting oestrogenic activity. The pregnancy interceptive effect of the ethanol extract of *Hibiscus rosa-sinensis* root could be interpreted as due to the oestrogenic nature of the plant. Histological studies confirmed this effect. Preliminary phytochemical studies indicated the presence of steroids, amino acids and carbohydrates in the ethanol extract. Both the methanolic extract of *H. rosa-sinensis* flowers and its water-soluble fraction showed significant inhibitory effects on alkaline phosphatase enzyme activity in vitro (Salib et al. 2011). Its high inhibitory activity was attributed to the presence of quercetin-7-*O*-galactoside which showed a high potent inhibition of the enzyme activity, reaching 100 % at 100 mg/mL reaction mixture.

Folkloric medicinal information collected on traditional herbal treatments to control fertility from different parts of Assam, India, showed that plants used for temporary methods of birth control included *Cissampelos pareira* in combination with *Piper nigrum*, root of *Mimosa pudica* and *Hibiscus rosa-sinensis* (Tiwari et al. 1982). Plants used for permanent sterilization included *Plumbago zeylanica, Heliotropium indicum, Salmalia malabarica, Hibiscus rosa-sinensis, Plumeria rubra* and *Bambusa arundinacea.* Abortion was achieved through use of *Osbeckia nepalensis* or *Carica papaya* in combination with resin from *Ferula narthex.* In a review of Indian plants investigated for fertility regulation based on published literature of the country and unpublished data of the Central Drug Research Institute (CDRI), located in Lucknow, India, the following plants were excluded from consideration for follow-up on the basis of preliminary toxicity data on their extract/compounds: *Aristolochia indica, Artemisia scoparia, Hibiscus rosa-sinensis, Laccardia lacca* and *Plumbago zeylanica* (Kamboj and Dhawan 1982). The hormonal profiles revealed oestrogenic activity in active extracts/fractions/compounds from *Artabotrys odoratissimus, Datura quercifolia, Daucus carota, Embelia ribes, Hibiscus rosa-sinensis, Pueraria tuberosa* and *Tabernaemontana heyneana* which excluded them from follow-up.

Antispermatogenic and Androgenic Activities

Studies conducted in Singapore found that aqueous and alcoholic extracts of flowers of *H. rosa-sinensis* did not affect the reproductive organs of males (Tan 1983). The organ weights were unaffected by the extracts; weights of the testis, epididymis, ventral prostate and seminal vesicle of the treated animals were not significantly different from those of the controls. The testis and epididymis of the rats also showed normal histological features, irrespective of treatment. No apparent toxicity of the extracts was discernible. In contrast, Reddy et al. (1997) found that the benzene, chloroform and alcoholic extracts of H. rosa-sinensis flowers had antispermatogenic and androgenic activities. Administration of the extracts at two different dose levels of 125 and 250 mg/kg body weight to adult male albino mice for 20 days elicited a decrease in the spermatogenic elements of testis and epididymal sperm count. High content of testicular cholesterol may be due to lowered androgen synthesis. The increase in the weight of accessory reproductive organs indicated the androgenicity of the plant extract itself, which was confirmed in their study by testing the benzene extract in immature mice. Olagbende-Dada et al. (2007) found that rats treated for 8 weeks with cold aqueous extract, hot aqueous and alcohol extract of *H. rosa-sinensis* leaves gained 15, 18 and 22 % in body weights, respectively, compared to 8 % for untreated. The increases in the weight of testis, epididymis, seminal vesicle and prostate of the alcoholic extract-treated rats were 19, 30, 31 and 40 %, respectively. The results confirmed the androgenic effect of the leaf extracts of *H. rosa-sinensis*.

Hypolipidemic Activity

Hibiscus rosa-sinensis flower petal extract was found to lower lipids in monosodium glutamate (MSG)-induced obese rats (Gomathi et al. 2008). Feed intake, body weight gain and levels of free fatty acids, triglycerides (TG), phospholipids, total cholesterol (TC), low-density lipoprotein (LDL) cholesterol and very low-density lipoprotein (VLDL) cholesterol were increased while high-density lipoprotein (HDL) cholesterol level was decreased in MSG obese rats. After administration of *H. rosa-sinensis*, the feed intake and body-weight gain were normalized, and also the levels of free fatty acids, TG, phospholipids, TC, VLDL cholesterol, LDL cholesterol and HDL cholesterol were reverted to near normal. They also reported that MSG-induced obese rats showed a significant increase in the activities of glucose metabolizing enzymes like hexokinase, phosphoglucoisomerase, glucose-6-phosphatase, fructose-1,6-bisphosphatase, glucose-6-phosphate dehydrogenase, succinate dehydrogenase and in the level of glycogen and significantly lower activities of enzymes isocitrate dehydrogenase and lactate dehydrogenase (Gomathi and Malarvili 2009). *H. rosa-sinensis* administration to obese rats reversed the above changes in a significant manner. They concluded that administration of *H. rosa-sinensis* flower regulated the blood sugar levels in MSG-induced obesity in rats and not only maintained the blood glucose homeostasis but also altered the activities of carbohydrate metabolizing enzymes.

Oral administration of 500 mg/kg body weight of the ethanolic extract of *Hibiscus rosa-sinensis* flowers exhibited a significant reduction in serum lipid parameters, total cholesterol, triglycerides, low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) and increase in high-density lipoprotein (HDL) in triton-induced and atherogenic diet-induced hyperlipidemic rats (Sikarwar Mukesh and Patil 2011). *Hibiscus rosa-sinensis* root extract was found to have hypolipidemic activity (Kumar et al. 2009). In triton WR-1339-induced hyperlipidemia, feeding rats with root extract (500 mg/kg body wt/day p.o.) exerted lipid-lowering effect, as assessed by reversal of plasma levels of total cholesterol (TC), phospholipids (PL) and triglycerides (TG) and reactivation of post-heparin lipolytic activity (PHLA) of plasma. Supplementation of cholesterol-rich high-fat diet-induced models of hyperlipidemia also caused lowering of lipid levels in plasma and liver homogenate and reactivation of plasma PHLA and hepatic total lipoprotein lipase activity. Histopathological findings in rat liver supported

the protective role of *H. rosa-sinensis* root extract in preventing cholesterol-rich HFD-induced hepatic steatosis.

Cardioprotective Activity

Studies by Gauthaman et al. (2006) found that *Hibiscus rosa-sinensis* flower extract (250 mg/kg) augmented the levels of endogenous antioxidant compounds superoxide dismutase, reduced glutathione and catalase levels of the rat heart and also prevented the myocardium from isoproterenol-induced myocardial injury. In contrast, significant rise in myocardial thiobarbituric acid-reactive substances and loss of superoxide dismutase, catalase and reduced glutathione (suggestive of increased oxidative stress) occurred in the vehicle-treated hearts subjected to in vivo myocardial ischaemic reperfusion injury. The study supported the traditional medicinal use of the flowers of *Hibiscus rosa-sinensis* in treating disorders of the heart. In another study, administration of *H. rosa-sinensis* plant extract at concentrations of 180 and 360 µg/mL in Langendorff-perfused rat hearts prior to global ischaemia/reperfusion (I/R) increased left ventricular developed pressure (LDVP) (21 and 55 %, respectively) and coronary flow (Khandelwal et al. 2010). The extract significantly improved post-ischaemic recovery of LVDP and dose-dependently reduced the numbers of ectopic beats, duration of ventricular tachycardia and the infarct size. The results indicated that *H. rosa-sinensis* plant extract elicited vasodilation and positive inotropic and cardioprotective effects.

Hypotensive Activity

Agarwal and Shinde (1967) reported that powdered *Hibiscus rosa-sinensis* leaves exhibited blood pressure lowering activity. *Hibiscus* flowers were found to be effective in the treatment of arterial hypertension (Dwivedi et al. 1977). Zakaria and Ali Mohd (2010) reported that the glycoside constituents in *H. rosa-sinensis* plant exhibited hypotensive effects (lower the blood pressure) in dogs at dosages 40–80 mg/kg for 1–2 h. Compounds isolated were quercetin-3-diglucoside, quercetin-3,7-diglucoside, cyanidin-3,5-diglucoside and cyanidin-3-sophoroside-5-glucoside. Hydroalcoholic extract of *H. rosa-sinensis* flower was found to have prominent hypotensive activity compared to the standard minoxidil followed by the chloroform extract in normotensive rats using the tail and cuff method (Siddique et al. 2005). Five compounds isolated from the chloroform extract of flower, *n*-nonacosan-13-one, *n*-triacontane, *n*-dotetracontane, *n*-nonacosan-4-ol-18-one and *n*-hentriacontan-4-one-10-ol, showed moderate activity. The results suggested that the synergistic action of the constituents in the crude extract could be responsible for the hypotensive activity. They also reported that the hydroalcoholic flower extract exhibited prominent activity when compared to the reference standard minoxidil (Siddique et al. 2006). Five new phytoconstituents were isolated *n*-docosane; henicos-11-ene-9-one; stigmast-5-ene-3β, 4α-diol; stigmast-5-ene-3β-benozyloxy-12β-ol; and *n*-pentacos-4-en-3-one-18, 23-diol. Of these isolated novel constituents, the compound stigmast-5-ene-3β-benzyloxy-12β-ol (SM-4) showed highest hypotensive activity. In contrast, the hypotensive activity shown by the ethanol–water (7:3) extract was greater when compared to the isolated constituent SM-4. These findings suggested that there must be synergistically acting constituent(s) present in the crude extract, responsible for its hypotensive activity, and these compounds were only effective in combination with each other, and not alone.

Studies by Imafidon and Okunrobo (2010) found that administration of 200 mg/kg of crude extract of *H. rosa-sinensis* significantly reduced blood pressure in normal and hypertensive rats. The extract increased urea, alanine transaminase, aspartate aminotransferase and Na^+ concentrations in normal and hypertensive rats compared with normal control. There was a significant increase in Ca^{2+} level in the hypertensive rats administered with the crude extract compared with normal control. Total protein level was not significantly affected in the test rats compared

with control. Potassium ions were significantly reduced in hypertensive control rats compared with normal control. The results showed that although *H. rosa-sinensis* leaf extract reduced blood pressure, the integrity of the kidney may be compromised when this plant is used for the treatment of hypertension.

Anticancer Activity

H. rosa-sinensis extract was found to exert a protective effect against the tumour promotion stage of skin cancer development in mice skin (Sharma and Sultana 2004). Combination of a single topical application of benzoyl peroxide (20 mg/0.2 mL/animal) followed by ultraviolet radiations (0.420 J/m^2/s) was used to induce hyperproliferation and oxidative stress. Pretreatment of *H. rosa-sinensis* extract (3.5 mg and 7 mg/kg b.wt.) partly restored the levels of cellular protective enzymes. Besides, malondialdehyde formation and hydrogen peroxide content were statistically significantly reduced at both doses. The ornithine decarboxylase activity and thymidine incorporation in DNA were also reduced dose-dependently by the plant extract. The results suggested an ameliorative potential of *Hibiscus rosa-sinensis* against the tumour promotion stage of cancer development. The scientists also found that gentisic acid, a chemical constituent in *Hibiscus rosa-sinensis* extract, played a role in the inhibition of tumour promotion response and oxidative stress induced by 7,12-dimethyl benz(a)anthracene (DMBA)/croton oil-mediated and 12-*O*-tetradecanoyl phorbol-13-acetate (TPA)-induced carcinogenesis in mouse skin (Sharma et al. 2004). Pretreatment of *H. rosa-sinensis* extract (3.5 mg and 7 mg/kg body weight) and gentisic acid (2.0 µg and 4.0 µg/0.2 mL acetone per animal) restored the levels of glutathione (GSH) and its metabolizing and antioxidant enzymes. There was also a statistically significant reduction in malondialdehyde formation and H_2O_2 content at both doses. The study showed that gentisic acid had a role in the tumour modulatory activity of *H. rosa-sinensis* extract.

Antimutagenic Activity

The dichloromethane, methanol and water extract of *Hibiscus rosa-sinensis* flowers were found not to be mutagenic for *Salmonella typhimurium* strains TA 98 and TA 100 without metabolic activation (Wongwattanasathien et al. 2010). However, after being treated with sodium nitrite in acid solution, the dichloromethane and water extract of *Hibiscus rosa-sinensis* were mutagenic on both tester strains, suggesting that consumers who consume these flowers should avoid any nitrite-containing food items.

Antidiabetic Activity

Administration of *H. rosa-sinensis* flower extract lowered the elevated levels of blood glucose, carbohydrate metabolizing enzymes, TBARS, enzymatic and non-enzymatic antioxidants and lipid profiles in streptozotocin-induced diabetic rats (Sankaran and Vadivel 2011). Among the three doses (125, 250 and 500 mg/kg body weight), 250 mg/kg showed the best result. Two fractions of the ethanolic extract of *H. rosa-sinensis* leaves (100 and 200 mg/kg body weight) fed orally to non-obese diabetic mice demonstrated insulinotropic nature and protective effect and may contain potential oral hypoglycemic agent (Moqbel et al. 2011).

Leaf and flower extracts of *Hibiscus rosa-sinensis* were found to have hypoglycemic activity. Studies in glucose-located rats showed that the average hypoglycemic activity after repeated administration of 250 mg/kg Hibiscus leaf extract was 81 %, and under similar conditions average activity of tolbutamide was 96 % (Sachdewa and Khemani 1999). At 250 mg/kg the efficacy of the extract was found to be 84 % of tolbutamide (100 mg/kg). Repeated treatment of animals either with tolbutamide a sulphonylurea or *H. rosa-sinensis* caused a 2–3-fold improvement in glucose tolerance as compared to those receiving only once. The data suggested that the leaf extract acted like tolbutamide. They also reported that in streptozocin-induced diabetic rats, the hypoglycemic activity of *H. rosa-sinensis*

leaf extract is comparable to tolbutamide and not to glibenclamide treatment (Sachdewa et al. 2001a). The scientists in another paper reported a comparable hypoglycemic effect from research data obtained after 7 and 21 days of oral administration of the ethanol flower extract and glibenclamide (Sachdewa and Khemani 2003). Maximal reduction in blood glucose (41–46 %) and insulin level (14 %) was observed after 21 days. The extract lowered the total cholesterol and serum triglycerides by 22 and 30 %, respectively. The increase in HDL cholesterol was much higher (12 %) under the influence of the extract as compared to that of glibenclamide (1 %). The hypoglycemic activity of the ethanol flower extract was comparable to that of glibenclamide but was not mediated through insulin release.

Studies showed that glucose-induced hyperglycaemic rats administered either *Aegle marmelos* or *H. rosa-sinensis* alcoholic leaf extracts for seven consecutive days at an oral dose equivalent to 250 mg/kg showed significant improvements in their ability to utilize the external glucose load (Sachdewa et al. 2001b). Average blood glucose lowering caused by *A. marmelos* and *H. rosa-sinensis* was 67 and 39 %, respectively, improving the glucose tolerance curve. The results suggested that both extracts had a hypoglycemic effect.

Hepatoprotective Activity

Pretreatment of Wistar rats with the anthocyanin fractions from *H. rosa-sinensis* petals reduced the levels of alanine transferase activity value and liver: body weight gain ratio and, hence, the degree of liver damage induced by carbon tetrachloride, though with varying magnitudes (Onyesom et al. 2008). The lead precipitated, non-slimy red fraction possessed the greatest hepatoprotective property on the rat liver when compared with the other anthocyanin fractions tested.

Hair Growth Stimulation Activity

Extracts of *Hibiscus rosa-sinensis* aerial parts were found to have stimulatory growth effect on hairs (Adhirajan et al. 2003). In in-vivo studies, it was found that the leaf and flower petroleum ether extract-treated groups produced a significant hair stimulatory growth effect with respect to the placebo and control in the shaved skin of albino rats after 30 days. However, in the leaf extract-treated group, the length of hair was significantly higher than that of the flower extract-treated group. There was also a marked difference in the different cyclic phases (anagen and telogen) of hair follicles in treated and controlled rats. On 10th day, nearly 40 % of the follicles were in anagen phase in all the groups, and at the end of the course, the leaf extract-treated groups showed the maximum number of anagen follicles (67 %) when compared to flower, placebo and control. The flower extract also produced a higher value than the placebo and control, but to a lesser extent than the leaf extract. In in-vitro studies of hair follicles from albino rat neonates, the leaf extract-treated groups produced a greater effect on the length of hair when compared to other groups being 17 mm at the end of the course, compared to 13.6 mm in the control and 14.5 mm in the placebo. They concluded that the leaf extract of *Hibiscus rosa-sinensis* had a potential effect on maintaining the hair growth in in vivo and in vitro methods and suggested that the leaf extract of *Hibiscus rosa-sinensis* could be included as a constituent in the hair growth formulations.

Wound Healing Activity

Animals treated with the ethanol extract of *H. rosa-sinensis* flower exhibited an 86 % reduction in the wound area compared with water controls, which exhibited a 75 % reduction (Shivananda Nayak et al. 2007). The extract-treated rats were found to epithelize their wounds significantly faster than controls and exhibited significantly higher skin-breaking strength than controls. The dry and wet weight of granulation tissues and hydroxyproline content were also increased significantly when compared with controls. The reported observations indicated that *H. rosa-sinensis* promoted wound healing in the rat model.

Anticonvulsive Activity

The ethanolic extracts of flowers of *Hibiscus rosa-sinensis* was found to exhibit anticonvulsant activity in experimental animals (Kasture et al. 2000). The anticonvulsant activity was found in the methanolic fraction of the acetone-soluble part of ethanolic flower extract. The fraction protected mice from maximum electroshock-, electrical kindling-, lithium-pilocarpine- and pentylenetetrazole-induced convulsions in mice. However, it failed to protect animals from strychnine-induced convulsions. The fractions antagonized the behavioural effects of D-amphetamine and potentiated the pentobarbitone-induced sleep and raised brain contents of gamma-aminobutyric acid (GABA) and serotonin. The fraction was found to be anxiogenic and general depressant of central nervous system.

Antimicrobial Activity

The petroleum ether extract from *H. rosa-sinensis* leaves, stems and flowers and methanol extract from the leaves inhibited growth of methicillin-resistant *Staphylococcus aureus* (MRSA) in vitro (Arullappan et al. 2009). Overall, the petroleum ether extract from flowers at concentrations of 4 and 2 mg/disc displayed the strongest inhibition zones of 18.6 and 18.5 mm, respectively, as compared to vancomycin (30 μg/mL), 18.0 mm size.

Extracts of *Hibiscus rosa-sinensis* (leaf and flower) were found to have antibacterial activity against *Pseudomonas aeruginosa, Listeria monocytogenes, Staphylococcus epidermidis, Staphylococcus aureus, Klebsiella pneumoniae, Salmonella typhi, Bacillus cereus, Bacillus anthracis, Escherichia coli* and *Streptococcus pyogenes* (Seyyednejad et al. 2010). *Escherichia coli* was the most resistant strain.

Volatiles extracted from the stem leaves and flowers of *H. rosa-sinensis* cv. red flower and cv. white flower exhibited antifungal activity in vitro (Boughalleb et al. 2005). The extracts of cv. white flower were inhibitory to *Alternaria solani*, *Fusarium oxysporum* f. sp. *niveum, F. solani* f. sp. *cucurbitae*, *Verticillium dahliae*, *Botrytis cinerea* and *Rhizoctonia solani* but not *Pythium ultimum*. The extracts of cv. red flower were inhibitory to *Alternaria solani*, *Fusarium oxysporum* f. sp. *niveum, F. solani* f. sp. *cucurbitae*, *Verticillium dahliae*, *Botrytis cinerea* but not *Pythium ultimum*, and the stem extract was not inhibitory to *Rhizoctonia solani.*

Anti-inflammatory, Analgesic and Antipyretic Activities

The ethanolic extract of the flowers of *Hibiscus rosa-sinensis* was found to exhibit anti-inflammatory activity as evaluated by the carrageenan-induced paw oedema, cotton pellet-induced granuloma and xylene-induce mice ear oedema tests in rats (Birari et al. 2009).

The extract also exhibited analgesic activities using the formalin and writhing tests. The extract also demonstrated antipyretic effect in pyrexia induced by brewer's yeast in rats.

Antiulcerogenic Activity

Oral administration of aqueous and alcohol extracts (250 and 500 mg/kg) of *H. rosa-sinensis* roots resulted in highly significant and dose-dependent antiulcer activity in albino rats with pyloric ligation-induced gastric ulcer. (Anita Gnana Kumari et al. 2010). Preliminary phytochemical screening of *H. rosa-sinensis* roots revealed the presence of sterols, glycosides, proteins, mucilage and flavonoids.

Antimutagenic Activity

The dichloromethane of *H. rosa-sinensis* flowers inhibited the mutagenicity of the reaction product of 1-aminopyrene nitrite model in the absence of metabolic activation on both *Salmonella typhimurium* strains TA 98 and TA 100, while the methanol flower extract exerted similar effect on TA 98 (Wongwattanasathien et al. 2010). The water flower extract exhibited antimutagenic activity on both tester strains. The results indicate

the flowers are safe if they are consumed and partially satisfy the first step in using the extracts for any purpose in food product development.

Cytotoxicity Activity

In the *Allium cepa* assay for cytotoxicity, *Hibiscus rosa-sinensis* flower decoction was found toxic on root output and root length and reduced the mitotic index significantly (Ali 2010). The results suggested that *Hibiscus rosa-sinensis* flowers contained antimitotic constituents which halted cell division cycle.

Larvicidal Activity

Water, hot water, acetone, chloroform, methanol leaf, stem bark and flower extracts of *H. rosa-sinensis* at 1,000 ppm showed moderate larvicidal effects against the larvae of the filarial vector, *Culex quinquefasciatus* after 24 h of exposure (Rahuman et al. 2009).

Traditional Medicinal Uses

Various parts of *H. rosa-sinensis* are used for various ailments in traditional medicine. *H. rosa-sinensis* has been reported to possess antioestrogenic, anti-implantation, abortifacient, antipyretic, antispasmodic, CNS depressant, hypotensive, antispermatogenic, embryotoxic, hypothermic, insect attractant, analgesic, antifungal and anti-inflammatory properties.

In the Philippines, the flower buds, pounded into a paste, are applied as a poultice to boils, cancerous swellings and mumps. In Malaysia, Chinese women used to use the juice from the petals for blackening their eyebrows, and so did people in India. A decoction of flowers has been used as an expectorant in bronchitis. The flower infusion after a night's exposure to dew may be used for gonorrhoea. The Chinese and Annamese employ the flowers against paralysis and dysmenorrhoea. A decoction of the flowers has been reported effective for coughs. In Indonesia, the red flowers are believed to regulate menstruation and sometimes said to cause abortion and also used for sprue. In India, the flowers, fried in ghee, are given in menorrhagia; the dark-red petals are administered in the form of a mucilaginous infusion in ardor-urinae, strangury, cystitis and other irritable conditions of the genito-urinary tract. This infusion is also a refrigerant drink in fevers and a demulcent in coughs. Oil made by mixing the juice of the fresh petals and olive oil in equal proportions and boiling is useful as a stimulating application for increasing the growth and improving the colour of the hair. In the Philippines, the leaves and flower buds are mashed and applied on swellings externally, and that the same mixture with lime hastens maturation of tumours. The flowers, leaves, barks and roots in decoction are used as an emollient.

In India, the seeds, pounded into a pulp and mixed with water, were used effectively for gonorrhoea. The expressed juice of the leaves is also given. In Malaysia, a decoction of the leaves has been used as a lotion for fevers and an infusion or a poultice of the leaves for headache; the leaves have also been used for boils. In Indonesia, it was very common to poultice swellings with the leaves. Midwives applied the mucilage during labour, at the same time giving draughts of the juice of the leaves. The juice of the leaves among with that of *Vernonia cinerea* is used by midwives to stimulate the expulsion of the afterbirth. In China, leaves are employed as an emollient, an anodyne and a gentle aperient. In Samoa, a preparation from the leaves is used to treat postpartum relapse sickness, to treat boils, sores and inflammations.

In Malaysia, the Malays used a decoction of the root as an internal medicine. A decoction from the roots of red- and white-flowered plants is a Kelantan antidote for poisons. This decoction is also drunk for venereal diseases and fevers. An infusion of the root is also used for glands in the neck. An application of the root of the white-flowered plant was also used for carbuncles, a decoction being drunk at the same time. A decoction of the root may be dropped into sore eyes. In India the root is regarded valuable for coughs. The Chinese and Annamese use the bark as an emmenagogue.

Plate 4 Red-orangey-flowered hybrid

Plate 5 Pink-flowered hybrid

Other Uses

A very popular and widely planted ornamental, planted as hedges and for fence or in median strips of avenues, as garden plants and in parks. Outside the tropics and subtropics, it is also a popular indoor plant. In India and China, the plant is sometimes used as a fibre source. A black pigment is extracted from the flowers. Hibiscus flower and leaf preparations are used for hair care. The petals are used to blacken shoes and eyebrows in parts of India, as well as for the worship of the Hindu deity, Devi.

Comments

Hibiscus rosa-sinensis is a very popular flowering shrub or garden plant with many great cultivars and hybrids with flower colours ranging from white

Plate 6 Double-petal red-flowered hybrid

through yellow and orange to scarlet and shades of pink, purple with both single and double sets of petals (Plates 2, 3, 4, 5 and 6). Plants with double sets of petals have been named as var. *rubroplenus* Sweet. *Hibiscus rosa-sinensis* was nominated as the national flower of Malaysia in 1960.

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Hibiscus sabdariffa

Scientific Name

***Hibiscus sabdariffa* L.**

Synonyms

Abelmoschus cruentus Bertol, *Abelmoschus cruentus* Walp., *Hibiscus acetosus* Noronha, *Hibiscus cannabinus* Linn., *Hibiscus digitatus* Cav., *Hibiscus fraternus* L., *Hibiscus gossypiifolius* Mill., *Hibiscus rosella* hort., *Hibiscus palmatilobus* Baill., *Hibiscus sanguineus* Griff., *Sabdariffa digitata* Kostel., *Sabdariffa rubra* Kostel

Family

Malvaceae

Common/English Names

Florida Cranberry, Guinea Sorrel, Hibiscus, Indian Sorrel, Jamaican Sorrel, Jamaica tea flower, Java Jute, Jelly Okra, Karkadé, Natal Sorrel, Nubia tea, Pink Lemonade, Queensland Jelly Plant, Red Sorrel, Red Tea, Rosella, Roselle, Royal Roselle, Rozelle, Rozelle Hemp, Sorrel, Sour-Sour

Vernacular Names

Arabic: Bissap, Carcadé, Karkadé, Karkady
Africa: Ufuta, Ufuta Dume, Vinagreira
Angola: (U)Tetia (Ganguela), (U)Se (Kimbundu), Azedas (Portuguese)
Benin: Bissap, Malcavene Bean
Botswana: Karkadeh
Brazil: Caruru-Azedo, Carurú-De-Guiné, Hibsico, Quiabo De Angola, Quiabo-Azedo, Quiabo-Róseo, Quiabo-Roxo, Rosella, Vinagreira (Portuguese)
Burkina Faso: Bito (Mooré), Bissap
Burmese: Chin Baung
Cameroon: Folere (Fulfulde)
Caribbean: Sorelle
Central African Republic: Kokpo (Banda), Zima (Gbaya), Zima Mbele (Manja)
Chinese: Mei Gui Qie, Luo Shen Hua, Luo Shen Kui, Shan Qie Zi
Congo: Abuya, Bissap, Ibuya, Inkulu
Danish: Hibiscus, Rosella
Dutch: Amerikaansch Zuur, Roselle, Zuring
Egypt: Karkade, Karkareeh
Finnish: Malvatee, Rosella-Tee, Teehibiskus
French: Karkadé, L'oiselle, Groseille Pays, Oseille De Guinée, Oseille Rouge, Roselle, Thé Rose D'abyssinie
Gabon: Bo-Kolo (Eviya)
Gambia: Wonjo

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German: Afrikanische Malve, Afrikanischer Eibisch, Hibiscus-Tee, Hibiskus-Tee, Karkade, Karkade-Tee, Malven-Tee, Rosella, Roselle, Rosselahanf, Rote, Rote Malve, Sabdariffa-Eibisch
Ghana: Bissap
Guinea Bissau: Baquitche, Bissap
Guinea Conakry: Folere Boleyo, Folere Badi (Foula And Fouta-Djalon), Da (Malinke), Santon Belli (Soussou)
Hungarian: Hibiszkuszvirág, Rozella
India: Chukiar, Tengamora (Assamese), Chukar, Chukor, Lal-Mista (Bengali), Mesta Tenga, Mwitha Tenga Mora (Bodo, Assam), Thakhlao Maikhri (Dimasa, Assam), Vai An Thur Avarpa (Hmar, Assam), Nkiaie (Zeme Naga, Assam), Ginguru, Gongura, Laalambaar, Lal Lambari, Lal-Ambari, Patwa (Hindi), Kempupundrike, Plachakiri, Pundi, Pundibija (Kannada), Lalchatni, Kutrum, Mathipuli (Kerala), Polechi, Puli-Cheera, Puilichcha (Malayalam), Silo-Sougree (Manipuri), Ambadi, Laal-Ambaari, Tambdi-Ambadi (Marathi), Lekhar-Anthur (Mizo), Ambasthaki (Sanskrit), Pulicha Keerai, Simaikkasuru, Sivappukkasuru, Shimai-Kashuruk-Kirai (Tamil), Erragomgura, Erragonkaya, Ettagomgura, Gongura, Yerra Gogu (Telugu) Alambari, Sabdriqal (Urdu)
Indonesia: Gamet Walanda (Sundanese), Kasturi Roriha, Rosela
Iran: Chaye-Torosh
Italian: Ibisco, Karkadè
Japanese: Rohzelu, Roozera, Roozeru, Rozerusou
Khmer: Slok Chuu
Laotian: Som Phor Dee, Somz Ph'oox Dii
Madagascar: Divay, Voamahomhazaha
Malaysia: Asam Belanda, Asam Susur, Asam Paya
Mali: Anjukooro, Anje, Bissap, Dah, Dah Bleni
Mexico: Flor De Jamaica, Jamaica, Rosa De Jamaica, Rosa Jamaica
Myanmar: Chin Baung
Namibia: Omutete
Nepalese: Blechanda
Nicaragua: Hamaiga
Niger: Bissap
Nigeria: Yakuwa, Zo'barodo, Barekata (Hausa), Isapa (Ogun State), Amukan, Amukan-Zobo, Isapa, Zobo (Yoruba)
Norwegian: Hibisk, Hibiskus, Jamaicahibisk, Roselle
Panama: Saril
Paraguay: Grosella
Philippines: Roselle, Kubab, Talingisag
Polish: Hibiskus Szczawiowy, Ketmia Szczawiowa
Popular Republic of Congo: Bakoumou (Bambara), Oseille De Guinée (French)
Portuguese: Azeda De Guiné, Azedinha, Rosela, Vinagreira
Russian: Роселла
Samoan: Uaina
Senegal: Dakumu (Bambara), Bassap (Niominka), Folere, Folérébadi (Peulh), Bissap (Wolof), Basap (Serere), Lomoda (Socé), Kaekade, Oseille De Guinée, Thé Rose D' Abyssinie (Local French)
Sierra Leone: Sour Sour (Krio), Satoi (Mende), Kapan Thorr (Temne), Salui
Spanish: Acedera De Guinea, Agrio De Guinea, Caruru Azedo, Flor De Jamaica, Gamakiya, Hibisco, Jamaica, Karkadé, Quetmia Ácida, Quiabeiro Azedo, Quimbombó Chino, Rosa De Jamaica, Serení, Viña, Viñuela
Sudan: Karkade
Swedish: Hibiskus, Rosellhibiskus
Switzerland: Karkadé
Tanzania: Rozi (Ngindo)
Thailand: Krachiap-Daeng, Krachiap-Prieo, Kachieb Priew, Phakkengkheng
Togo: Anyagha (Ewé), Oseille De Guinée (French)
Turkish: Afrika Bamyası, Hibiskus
Uganda: Musayi (Bulamogi Country), Musayi (Rutooro), Kalabi
Vietnam: Bụp Giấm, Lá Giấm, Rau Chua
Zambia: Lumanda (Cibemba), Katolo (Kikaonde), Wusi (Chilunda)

Origin/Distribution

Roselle is probably native to Africa and now widely naturalized in tropical and subtropical regions of the world particularly in India and Southeast Asia. It is widely cultivated in Africa, Asia, Papua New Guinea and the Pacific. China and Thailand are the leading producers and dominate much of the world supply. Mexico, Egypt, Senegal, Tanzania, Mali and Jamaica are also

important suppliers, but production is mostly used domestically.

Agroecology

In its native range, *H. sabdariffa* is found growing on river levees and cleared agricultural land, in disturbed and undisturbed natural vegetation and on bare areas from sea level to 600 m elevation. Roselle prefers a warm and humid tropical climate and is susceptible to damage from frost and fog. Roselle can be cultivated in the tropical and subtropical zones with annual temperature range from 12 to 30 °C and with well-distributed annual rainfall of 1,500–2,000 mm. It does best in a well-drained, friable sandy loam soil rich in humus but is adaptable on many soils types—from sandy to clayey soils from pH of 4.5–8.0—and can tolerate short periods of flooding. It prefers full sun as it is not shade tolerant.

Edible Plant Parts and Uses

All parts of roselle plant are edible and useful. The most valued and widely used plant part is the fleshy flower calyx (Burkill 1966; Tanaka 1976; Duke 1983; Chopra et al. 1986; Morton 1987; Facciola 1990; Boonkerd et al. 1994; Rao 1996; Roberts 2000; Woodward 2000; Duke et al. 2002; Mohamad et al. 2002, 2012; Hu 2005; Tanaka and Nguyen 2007; Wikipedia 2013). The fleshy flower calyces are rich in citric acid (3.74%) (Rao 1996), pectin, anthocyanin pigments and vitamins and are used fresh in salad and for making roselle wine, syrup, gelatin, refreshing beverages, puddings, chutneys, pickles, cakes, herbal teas, jellies, marmalades, ices, ice cream, sherbets, butter, pies, sauces, tarts and other desserts. In Pakistan, roselle has been recommended as a source of pectin for the fruit-preserving industry. The calyces are used for food colouring in America, Asia and Europe. The calyces are used to colour and flavour rum in the Caribbean and to add colour and flavour to herbal teas and beverages. In the Caribbean, a drink is made from the fresh fruit, and it is considered an integral part of Christmas celebration. In Mexico and Central America, *aguas frescas*, inexpensive beverages, are commonly consumed and are typically made from fresh fruits, juices or extracts. A refreshing and very popular beverage can be made by boiling the calyx, sweetening it with sugar and adding ginger. In East Africa, the calyx infusion, called 'Sudan tea', is taken to relieve coughs. In Africa, especially the Sahel, roselle calyces are commonly used to make a sugary herbal tea that is commonly sold on the street. In Mali and Senegal, calyces are used to make cold, sweet drinks popular in social events, often mixed with mint leaves, dissolved menthol candy, and or various fruit flavours. In Trinidad and Tobago, the Carib Brewery Trinidad Limited produces a Shandy Sorrel in which roselle tea is combined with beer. In Mexico and Central America, *agua de Jamaica* (water of roselle) is most often home-made and drank chilled, and *Jamaica Ipa* is another popular drink in Mexico and Central America, which is made from calyces of the roselle. Roselle calyces are sold in bags usually labelled *Flor de Jamaica* in health food stores in the United States for making a tea that is high in vitamin C, an anthocyanin. In addition to being a popular home-made drink, *Jarritos*, a popular brand of Mexican soft drinks, makes a Jamaica-flavoured carbonated beverage. Imported *Jarritos* is commonly available in the United States

In Senegal the green leaves are used as spinach in a fish and rice dish called *thiéboudieune*. In Myanmar, the green leaves form the main ingredient in making *chin baung kyaw* curry. In Assam, leaves and calyces are acidic, eaten as cooked vegetable, good with fermented fish and pork (Medhi and Borthakur 2012; Patiri and Borah 2007). Jelly is prepared from calyces. Tender young leaves and stems are eaten raw or cooked in salads; as a potherb and as a seasoning in curries; they have an acid, rhubarb-like flavour. The calyx is rich in citric acid and pectin and so is useful for making jams, jellies, etc. It is also used to add a red colour and to flavour to herb teas (Mungole and Chaturvedi 2011). Using marinades of roselle calyx extract for fried beef

patties was found to reduce the formation of carcinogenic heterocyclic aromatic amines (Gibis and Weiss 2010). In Nigeria the calyces are gathered for sale either fresh or dried; they are whole in preparing melon soup together with other soup ingredients and in the production of roselle jams (Nnam and Onyeke 2003). A pleasantly flavoured beverage produced as an infusion from the calyx has been widely appreciated in Nigeria and is used for refreshment and entertainment in home and public gatherings and also sold as a local drink. Traditionally, the calyx has been chewed to alleviate thirst on long desert tracks of Moslems. In Sudan, the dry calyx is used to produce a flavoursome and healthy drink rich in vitamin C, and dried calyces are used for tea (known as kakkady in Arabic), jelly, marmalade, ices, ice cream, sorbets, butter, pies, sauces, tarts and other desserts (Mohamed et al. 2012). Iced red hibiscus tea is drunk daily in Sudan; in Spain it is called 'quimbombe chino'. Roselle herbal tea is commonly drunk in Thailand on its own or mixed with normal tea to reduce cholesterol. In Malaysia, roselle calyces are harvested fresh to produce pro-health drink due to high contents of vitamin C and anthocyanins (Mohamad et al. 2002). In Malaysia, young leaves and shoots cooked as vegetables and the calyces used to flavour fish and in curries (Saidin 2000). In Vietnam, young leaves, stems, calyx and fruits are used for cooking fish or eel (Tanaka and Nguyen 2007). Tender young leaves and stems eaten raw or cooked in Nepal and elsewhere (Duke 1983; Kunkel 1984; Manandhar and Manandhar 2002). In Angola, leaves used as food complement (Bossard 1996).

The seeds have been reported to be eaten in some parts of Africa (Burkill 1966; Rao 1996). *Furundu*, a meat substitute, is traditionally prepared by cooking *Hibiscus sabdariffa* seed and then fermenting it for 9 days (Yagoub et al. 2004). *Yanyanku* and *Ikpiru*, made by the fermentation of *Hibiscus sabdariffa* seeds, are used to produced food condiments in Benin (Agbobatinkpo et al. 2013). The seeds are roasted, ground into a powder and used in oily soups and sauces (Kunkel 1984; Facciola 1990). The roasted seeds have been used as a coffee substitute that is said to have aphrodisiac properties (Duke 1983; Duke et al. 2002; Facciola 1990; Mohamed et al. 2012).

The roots are edible but very fibrousy, mucilaginous and rather bland, lacking flavour (Cribb and Cribb 1987).

Botany

A broad-leaved, erect and branched annual herb, up to 1.1 m high with a deep penetrating tap root. Stem reddish with sparse, simple, bulbous, spiny hairs. Leaves are alternate, glabrous, simple, stipulate, petiolate; petiole 20–50 mm long; stipules 6–8 mm long, filiform; lamina broadly ovate and not lobed in the lowermost part, in the upper part deeply dissected 3–7 partite (Plates 1, 2, and 3), base tapering, margins serrate or dentate, and

Plate 1 Roselle plant habit

Plate 2 Roselle leaves

Plate 3 Roselle plant with buds and flowers opening

Plate 4 Harvested roselle floral buds enveloped in red fleshy calyces

apex acute, variously coloured, dark green to red. Flowers axillary, solitary, predominantly yellow and red, regular, pedicellate; epicalyx of about 12 reddish bracts, connate at base, 10–12 mm long; calyx 15–30 mm long (enlarging in fruit to 40 mm), 5 reddish, large, accrescent, fleshy sepals, all sepals fused at base (Plates 1, 3, and 4); corolla 15–25 mm long, 5 free petals; stamens 100 (numerous), adnate to the perianth (at the base), coherent to each other (filaments fused in a column surrounding the style); anthers dehiscing via longitudinal slits; ovary syncarpous, superior, 5-celled, hairy with numerous ovules; style a five-fid. Fruit a dehiscent, 5-valved, non-fleshy, bright red ovoid capsule, 18–20 mm long by 15–18 mm wide. There is a green form known as the white sorrel, with greenish-white fruits.

Nutritive/Medicinal Properties

Flower/Flower Tea Phytochemicals

Analyses carried out in the United States reported that raw roselle (minus 39 % seed pods and stem) had the following nutrient composition (per 100 g edible portion): water 86.58 g, energy 49 kcal (205 kJ), protein 0.96, total lipid 0.64 g, ash 0.51 g, carbohydrates 11.31 g, Ca 215 mg, Fe 1.48 mg, Mg 51 mg, P 37 mg, K 208 mg, Na 6 mg, vitamin C 12.0 mg, thiamin 0.011 mg, riboflavin 0.028 mg, niacin 0.310 mg and vitamin A 287 IU (USDA 2013).

Nnam and Onyeke (2003) reported the nutrient composition of dry red and yellow roselle calyces, respectively, as follows: crude protein (6.40, 9.08 %), carbohydrate (79.25, 76.69 %), fat (5.13, 4.92 %), crude fibre (2.70, 2.95 %), ash (6.52, 6.08 %), minerals and vitamins per 100 g sample Ca (3.0, 3.0 mg), Mg (1.0, 1.07 mg), Fe (833.00, 800.67 mg), P (22.0, 23.33 mg), Na (15.33, 16.01 mg), Zn (1.17, 1.37 mg), Cu (0.70, 0.78 mg), β-carotene (285.29, 281.28 RE (retinol equivalent)), thiamin (24.67 mg, trace), riboflavin (0.95, 0.96 mg), ascorbic acid (53.0, 56.83 mg). Mohamed et al. (2012) reported chemical composition of dried roselle calyces (red and white), respectively, as follows: moisture (11.0, 9.3 %), crude protein (7.88,7.53 %), crude fibre (10.16, 0.12 %), ash (10.60, 9.50 %), total carbohydrates (57.16, 61.55 %), ascorbic acid (11.0,15.5 %), total soluble solids (5.5, 5.5 %), titratable acidity (9, 11 mg/100 g), Ca (60, 50 mg/100 g) and Fe (25, 20 mg/100 g).

Roselle was found to contain per 100 g basis 141.09 mg ascorbic acid, 1.88 mg ß-carotene, 164.34 µg lycopene, glucose (1.28 g) as the major sugars, organic acids with a predominance of succinic acid (0.51 g) and oxalic acid and delphinidin-3-sambubioside and cyanidin-3-sambubioside as the main anthocyanins (Wong et al. 2002). Roselle was found to be rich in malic acid, anthocyanins, ascorbic acid and minerals, especially Ca and Fe, but low in glucose (Jung et al. 2013). More than 18 volatile

compounds were identified. From the flower petals, hibiscitrin was isolated as the main component; its aglycone, hibiscetin, a hexahydroxy flavonol, formed a heptaacetyl derivative on acetylation (Rao and Seshadri 1942a). Gossypitrin and sabdaritrin were also isolated from the flowers (Rao and Seshadri 1942b). On boiling with dilute sulphuric acid, it yielded a new hydroxyflavone called sabdaretin. Hibiscitrin was confirmed to be a 3-glucoside of hibiscetin (Rao and Seshadri 1948a, b). A new glycoside, gossytrin, was isolated from the petals (Seshadri and Thakur 1961).

Perkins (1909) isolated a yellow pigment gossypetin from the flower calyces. The major pigment, hisvicin, which was formerly isolated from roselle calyx and bract by Yamamoto and Osima (1932), was reported to have the structure of delphinidin pentosido-glucoside. Re-examination studies by Shibata and Furukawa (1969) found its structure to be delphinidin-3-xylosido-glucoside (daphniphyllin) and not hisvicin. Small amounts of minor pigments delphinidin-3-monoglucoside, cyanidin 3-monoglucoside (chrysanthemin) and delphinidin were also isolated. Hibiscus acid, (2*S*,3*R*)-hydroxycitric acid, was found in roselle calyces (Griebel 1939). Two major anthocyanins, delphinidin-3-sambubioside and cyanidin-3-sambubioside, and two minor ones, cyanidin-3-monoglucoside and delphinidin-3-monoglucoside, were isolated (Du and Francis 1973). Two main anthocyanins (delphinidin-3-sambubioside or hibiscin and cyanidin-3-sambubioside or gossypicyanin) were isolated from methanol extracts of calyces of *H. sabdariffa* (Pouget et al 1990). The genins and sugars were also identified as delphinidin and cyanidin and as glucose, xylose and fructose. The main colouring pigment in dry roselle calyces was delphinidin-sambubioside and its structure was elucidated as delphinidin-3-[*O*-β-D-xylopyranosyl–(1→2)–β-D-glucopyranoside] (Sato et al. 1991). Roselle calyx extract was found to contain flavonoid constituents including chrysanthemin, delphinidin-3-*O*-sambubioside, myricetin and hibiscitrin and phenylpropanoid compounds such as *O*-coumaric acid, *p*-coumaric acid and ferulic acid (Abbas et al. 1993).

Dried calyces of *Hibiscus sabdariffa* were found to contain anthocyanidins, delphinidin-3-sambubioside and cyanidin-3-sambubioside had been detected as main components and cyanidin-3-*O*-rutinoside, delphinidin-3-*O*-glucoside and cyanidin-3,5-diglucoside, and chlorogenic acid as minor constituents (Segura-Carretero et al. 2008), two major anthocyanins delphinidin-3-sambubioside and cyanidin-3-sambubioside (Juliani et al. 2009) and anthocyanins delphinidin-3-*O*-sambubioside and cyanidin-3-*O*-sambubioside (Ojeda et al. 2010). Total phenolics were better extracted with hot water that also resulted in a higher antioxidant capacity in roselle extracts (Ramirez-Rodrigues et al. 2011b). Similar polyphenolic profiles were observed between fresh and dried roselle extracts. Hydroxybenzoic acids, caffeoylquinic acids, flavonols and anthocyanins constituted the polyphenolic compounds identified in roselle extracts. Two major anthocyanins were found in both cold and hot extracts: delphinidin-3-sambubioside and cyanidin-3-sambubioside. Hibiscus acid and two derivatives were found in all extracts. In general, both cold and hot extractions yielded similar phytochemical properties; however, under cold extraction, colour degradation was significantly lower and extraction times were 15-fold longer. The aqueous roselle extract was found to contain 32.4 mg/g delphinidin-3-*O*-sambubioside, 11.5 mg/g cyanidin-3-*O*-sambubioside, 11.5 mg/g quercetin and chlorogenic acid 2.7 mg/g (Jiménez-Ferrer et al. 2012). The yield of *Hibiscus sabdariffa* aqueous extraction was 28.3 % and the chemicals obtained from 1 g of extract were 56.5 mg delphinidin-3-*O*-sambubioside, 20.8 mg/g cyanidin-3-*O*-sambubioside, 3.2 mg/g quercetin, 2.1 mg/g rutin and 2.7 mg/g chlorogenic acid (Alarcón-Alonso et al. 2012). The concentration of anthocyanin in four pigmented *H. sabdariffa* varieties ranged from 17.3 to 32.2 mg of cyanidin 3-glucoside/g dry weight, while volatile compounds analysis showed that geraniol was the main compound in extracts (Camelo-Méndez et al. 2013). Aqueous extract from the Rosa variety afforded high contents of geraniol, ethanol, menthol, 2-nonanol, benzaldehyde, linalool, γ-undecalactone and

ethyl methylphenylglycidate, compared with the other varieties.

Decoction process of roselle calyces extracted part of soluble carbohydrates, ashes and some extractable polyphenols (Sáyago-Ayerdi et al. 2013). Some calyces components were partially transferred to beverage during the decoction process and others remained in decoction residues. However, the major part of these foods components was retained in the decoction residues. Dietary fibre content changed in dried residues that afforded a high dietary fibre material with a high proportion of soluble dietary fibre (about 20 % from total dietary fibre) with a considerable antioxidant capacity. These by-products could be used as an antioxidant dietary fibre source. Of ten medicinal herbs tested, *Hibiscus sabdariffa* was found to be the richest in phytoestrogens quercetin and daidzein, whereas *Cyperus conglomeratus* had the highest concentrations of kaempferol and genistein (Saeed et al. 2013).

Chemical composition of roselle flower tea marketed in Sudan was reported as follows: moisture content 15 % max, extract content 41 % min, protein content 5 % max, ash and mineral salts 7 % max, impurities 2 % max, vitamin C 80–100 mg/100 g, natural pigment >1.5 mg/100 g, reducing sugar 12 % max, fibre 15 % min and total acids 25–305 (Mohamed et al. 2012). Ni was found to be present in its divalent ionic form in the infusion of roselle flower tea with a pH of 2.7(Ščančar et al. 2013). Total concentrations of Ni in dry leaves of white, green, oolong and black tea (*Camellia sinensis*) and flowers of herbal chamomile (*Matricaria chamomilla*) and roselle (*Hibiscus sabdariffa*) ranged from 1.21 and 14.4 mg/kg.

More than 37 volatiles compounds were characterized in differently treated roselle samples: untreated, frozen, hot-air-dried at 50 °C and hot-air-dried at 75 °C (Chen et al. 1998). They were classified into four groups: fatty acid derivatives, sugar derivatives, phenolic derivatives and terpenes. Large amounts of the aliphatic C_6 lipid derivative, imparting green note aromas, were in the fresh roselle, while only trace amounts were found in the frozen and air-dried samples. In the air-dried roselles, significant amounts of furfural and 5-methyl-2-furfural were formed, while only minimal amounts were detected in the fresh samples. There were no obvious changes in phenolic derivatives (eugenol) among the four samples. Terpenoid and oxide could also be isolated after distillation extraction. The drying process reduced them dramatically, especially the amount of α-terpineol, linalool oxide and limonene. A combination of the terpene derivatives with fragrance notes and the sugar derivatives with a caramel-like odour were responsible for the roselle aroma.

Totals of 28, 25, 17 and 16 volatiles were identified in the dried hot extract (DHE), dried cold extract (DCE), fresh hot extract (FHE) and fresh cold extract (FCE) roselle calyces samples, respectively (Ramírez-Rodrigues et al. 2011a). Nonanal, decanal, octanal, and 1-octen-3-ol were among the major volatiles in all four roselle beverage types. Thirteen volatiles were common to all four teas. Furfural and 5-methyl furfural were detected only in dried roselle beverages whereas linalool and 2-ethyl-1-hexanol were detected only in beverages from fresh roselle. Seventeen, 16, 13 and 10 aroma-active volatiles were detected for DHE, DCE, FHE and FCE samples, respectively. The most intense aroma volatiles were 1-octen-3-one and nonanal with a group of 4 aldehydes and 3 ketones common to all samples. Dried samples contained dramatically higher levels of lipid oxidation products such as hexanal, nonanal, and decanal. In fresh roselle extracts, linalool (floral, citrus) and octanal (lemon, citrus) were among the highest intensity aroma compounds, but linalool was not detected in any of the dried roselle extracts.

Eighty-one volatiles were identified in the aroma concentrate of roselle tea in which linalool and α-terpineol were the major constituents (Pino et al. 2006). The volatile constituents (mg/kg) were 2,3-dimethybutane <0.01 mg, isobutanol 0.15 mg, 2-pentanone <0.01 mg, 2-methylbutanal 0.06 mg, 3-methyl-1-butanol 0.14 mg, 2-methyl-1-butanol 0.06 mg, isobutanoic acid 0.01 mg, 2-ethylfuran 0.03 mg, hexanal 0.12 mg, 2-furfural 0.13 mg, 2-methylbutanoic acid 0.02 mg, (*E*)-2-hexenal 0.02 mg, 2-furfuryl alcohol 0.02 mg, (*Z*)-3-hexen-1-ol 0.02 mg, α-angelica lactone

0.04 mg, *p*-xylene <0.01 mg, heptanal 0.02 mg, 2-acetylfuran 0.02 mg, (*E*)-2-heptena 0.03 mg, benzaldehyde 0.03 mg, 5-methyl-2-furfural <0.01 mg, 2,2,6-trimethyl-6-vinyltetrahydrofuran 0.13 mg, pentyl propanoate 0.02 mg, methyl-2-furoate 0.03 mg, 1-octen-3-ol 0.05 mg, 6-methyl-5-hepten-2-one 0.02 mg, octanal 0.03 mg, α-terpinene 0.01 mg, *p*-cymene 0.02 mg, limonene 0.07 mg, (*Z*)-β-ocimene 0.02 mg, 1-propylbenzene 0.05 mg, (*E*)-β-ocimene 0.06 mg, acetophenone <0.01 mg, octanol 0.03 mg, *cis* linalool oxide 0.36 mg, m-cymenene <0.01 mg, *trans* linalool oxide 0.29 mg, linalool 0.58 mg, nonanal 0.16 mg, 2-phenethyl alcohol 0.01 mg, myrcenol 0.03 mg, *cis*-β-terpineol 0.03 mg, (*E*)-2-nonenal 0.05 mg, ethyl benzoate 0.01 mg, terpinen-4-ol 0.08 mg, *p*-cymen-8-o 0.06 mg, α-terpineol 0.55 mg, methyl salicylate 0.06 mg, decanal 0.05 mg, *p*-menthen-9-al 0.08 mg, thymoquinone 0.14 mg, geraniol 0.10 mg, decanol 0.03 mg, (*E*)-anethole 0.06 mg, 1-methylnaphthalene 0.02 mg, indole 0.04 mg, undecanal 0.02 mg, 4-vinylguaiacol 0.04 mg, (*E,E*)-2,4-decadienal 0.03 mg, methyl decanoate 0.02 mg, methyl anthranilate 0.02 mg, 1,2-dihydro-2,5,8-trimethylnaphthalene 0.02 mg, eugenol 0.23 mg, methyl eugenol 0.07 mg, 2-6-dimethyl naphthalene 0.04 mg, β-caryophyllene 0.04 mg, α-humulene 0.02 mg, geranyl acetone 0.02 mg, β-santalene 0.02 mg, α-calacorene 0.07 mg, (*E*)-nerolidol 0.15 mg, dodecanoic acid 0.15 mg, γ-eudesmol 0.12 mg, tetradecanoic acid 0.13 mg, pentadecanoic acid 0.04 mg, methyl hexadecanoate 0.04 mg, (*Z*)-9-hexadecenoic acid 0.19 mg, (*E*)-phytol 0.04 mg, hexadecanoic acid 0.21 mg and (*E*)-phytol-acetate 0.09 mg. The exotic aroma character of roselle tea comprised the interaction of terpenoids with floral notes (linalool, α-terpineol and linalool oxides), fatty acids with acidic notes and the sugar degradation products with a caramel-like odour.

Three water-soluble polysaccharides were isolated from *Hibiscus sabdariffa* flower buds (HIB 1,2,3) (Müller and Franz 1992). The neutral polysaccharides (HIB 1 and 2) were composed of arabinans and arabinogalactans of low relative molecular mass; the major fraction was shown to be a pectin-like molecule ($Mw = 10^5 D$). The main chain was composed of alpha-1,4-linked GalA and alpha-1,2-linked Rha. Side chains comprised Gal and Ara connected to the main chain via C-4 of every third Rha.

Using a PARAFAC model (a mathematical fluorescence excitation emission model), in the pH range from 1 to 13, seven degraded species of anthocyanins extracted from roselle calyces were identified: flavylium cation, carbinol, quinoidal base, *E*- and *Z*-chalcones and *E*- and *Z*-ionized chalcones (Marco et al. 2005).

Seed Phytochemicals

Chemical composition of unextracted and extracted roselle seeds were, respectively, as follows: moisture content 7.58 %, 8.18 %; crude protein 23.95 %, 29.04 %; ether extract 22.34 %, 0.69 %; nitrogen-free extract 23.81 %, 32.86 %, crude fibre 15.30 %, 20.04 %; ash 7.02 %, 9.19 %; Ca 0.31 %, 0.41 %; P 0.60 %, 0.79 %; and S 0.35 %, 0.37 % (Samy 1980). The digestible crude protein, total digestible nutrients, starch value and calculated metabolizable energy for the unextracted roselle seeds were 15.36 %, 75.81 %, 84.06 % and 3,184 kcal/kg, respectively; the corresponding values for the extracted seeds were 27.50 %, 68.83 %, 64.23 % and 2,891 kcal/kg. Iodine number, saponification number and Reichert–Meissl and Polenske values for the roselle seed oil were 15.63, 258 and 1.75 and 1.14 respectively. Al-Wandawi et al. (1984) reported that roselle seeds contained 25.20 % protein, 21.10 % lipids, 18.30 % crude fibre, 2.25 % starch, 5.19 % ash, 26.57 % total carbohydrate, 5.57 % moisture and traces of free and bound gossypol. They also reported that the amino acid (g/16 g nitrogen) profile comprised glutamic acid 23.45 g, arginine 10.75 g, aspartic acid 10.16 g, lysine 5.56 g, histidine 1.87 g, tryptophan 0.68 g, threonine 2.94 g, serine 4.37 g, proline 3.29 g, glycine 5.08 g, alanine 4.09 g, cysteine 2.50 g, valine 3.85 g, methionine 1.35 g, isoleucine 3.21 g, leucine 6.31 g, tyrosine 3.45 g and phenylalanine 5.20 g. Most limiting amino acids were tryptophan, valine, isoleucine and threonine while the most abundant essential

amino acids were leucine, lysine and phenylalanine. Oleic acid was the most predominant fatty acid followed by palmitic and stearic acids. K, Na, Ma and CA were the major elements. Gossypol was found in traces.

Two varieties of roselle seeds were found to have high contents of protein (18.8–22.3 %), fat (19.1–22.8 %) and dietary fibre (39.5–42.6 %), and also phosphorus 596–672 mg/100 g, calcium 119–128 mg/100 g and magnesium 369–393 mg/100 g (Rao 1996). The seeds had 6.7–8.6%moisture, 5.5 %, ash, 11.2–12.1 % soluble fibre and per 100 g edible portion: zinc 4.4.3 mg, manganese 5.9–7.4 mg, copper 2.8–3.1 mg, chromium 0.08–0.18 mg, riboflavin 0.36–0.51 mg and nicotinic acid 0.9–1.0 mg. The seed oil was found to be rich in unsaturated fatty acids (70 %), of which linoleic acid constituted 44 %. Roselle seeds were found to contain 0.8 % myristic acid, 9.2 % palmitic acid, 2.4 % stearic acid, 4.1 % arachidic acid, 33.5 % oleic acid, 44.2 % linoleic acid 0.5 % linolenic acid, 1.1 % arachidonic acid and 7.3 % adrenic acid. The amino acid composition (g/16 g nitrogen) of the seeds comprised 3.3–4.3 g lysine, 2.4–2.5 g histidine, arginine 9.9–10.2 g, aspartic acid 8.3–9.1 g, threonine 3.8–4.2 g, serine 5.5 g, glutamic acid 21.6–21.8 g, proline 4.6–5.2 g, glycine 5.1–6.4 g, alanine 4.2–6.1 g, cystine 1–4.2 g, valine 4.8–5.0 g, methionine 1.2–1.9 g, isoleucine 3.7–5.0 g, leucine 5.9–6.5 g, tyrosine 2.7–3.2 g, phenylalanine 4.7–4.8 g and tryptophan 1.2–1.4 g. Their study found that food intake of rats receiving raw roselle seed diets was significantly lower than those receiving cooked seed diets as well as the casein control diet. Protein and dry matter digestibilities of raw and cooked roselle seed diets were lower than that of casein control diet. Cooking improved dry matter and protein digestibility of roselle seed diets and improved food intake and gain in body weight. Their results indicated cooked roselle seed protein to be of relatively good quality. Animal studies showed that rats fed on boiled roselle seed powder for 4 weeks had significantly higher food intake and weight gain compared to dry seed powder (Nazri et al. 2007). There was no significant difference in protein efficiency ratio (PER) and net protein ratio (NPR) of boiled compared to dried seeds, but it was significantly different with casein. True nitrogen absorption and nitrogen balance (NB) of boiled seed group was significantly higher than the dried seed group. However, apparent digestibility, true digestibility and biological value for both diets were not significantly different. The study showed that the protein quality of dried roselle seeds was similar to the roselle seeds boiled at 100 °C for 30 min.

Roselle seed oil was found to contain myristic (2.1 %), palmitic (35.2 %), palmitoleic (2.0 %), stearic (3.4 %), oleic (34.0 %), linoleic (14.6 %) and three unusual HBr-reacting fatty acids: *cis-12*,13-epoxy-*cis*-9-octadecenoic (12,13-epoxyoleic), 4.5 %; sterculic, 2.9 %; and malvalic, 1.3 % (Ahmad et al. 1979). Acetolysis of epoxide in the presence of cyclopropenes was effected by room temperature treatment with acetic acid and 10 % sulphuric acid. Roselle seed oil, like cottonseed oil, was found to contain cyclopropenoid fatty acids (2.9 %) and epoxy fatty acids (2.6 %) in addition to normal fatty acids found in vegetable oils (Rukmini et al. 1982). Roselle seeds had been reported to be rich in dietary fibre, oil and proteins (El-Adawy and Khalil 1994; Ismail et al. 2008). Chemical composition of three roselle varieties, light red, early dark red and late dark red, was reported, respectively, as follows: moisture 9.25 %, 11.66 %, 11.45 %; protein 31.02 %, 30.11 %, 30.94 %; ash, 6.89 %, 5.80 %, 6.52 %; fat 21.60 %, 22.53 %, 23.26 %; total carbohydrate 36.37 %, 38.12 %, 38.05 %; and crude fibre 4.12 %, 3.44 %, 1.23 % (El-Adawy and Khalil 1994). The predominant amino acids were lysine, arginine, leucine, phenylalanine and glutamic acid, and the most limiting amino acids were valine, isoleucine and tryptophan. The major fatty acids were linoleic, oleic, palmitic and stearic acids. The protein quality of roselle seed powder prepared from dried and boiled seeds was reported to be similar. The most predominant inorganic elements in roselle seed were found to be K, Na, Mg and Ca. Roselle seeds exhibited high digestibility by a trypsin–pancreatin system. Analysis of tannins and physic acid in roselle seed revealed low levels. Raw freeze-dried, sun-dried and boiled sun-dried roselle seeds

contained 6.81 %, 9.9 %, 9.8 % moisture; 35.4 %, 33.5, 30.6 % protein; 27.2 %, 22.1 %, 29.6 % lipids; 2.3 %, 13.0 %, 4.0 % available carbohydrate; 25.5 %, 18.3 %, 19.2 % total dietary fibre; and 7.4 %, 7.5 %, 6.6 % ash, respectively (Hainida et al. 2008b). The carbohydrate, protein, lipids and moisture of raw freeze-dried roselle seeds were significantly different from sun-dried roselle seeds and boiled sun-dried roselle seeds. The predominant minerals in roselle seeds were potassium (99–109 mg/100 g), magnesium (26–28 mg/100 g) and calcium (24–31 mg/100 g). The total dietary fibre of the seeds was within the acceptable range, with soluble and insoluble fibre ratios ranging from 1.2 to 3.3. Roselle seeds contained 17 essential and non-essential amino acids. The seeds were rich in lysine (14–15 g/100 g), arginine (30–35 g/100 g), leucine (15.4–18.6 g/100 g), phenylalanine (11–12 g/100 g) and glutamic acid (21–24 g/100 g). The study indicated that roselle seeds may serve as a potential source of functional ingredients. Nutrient composition of roselle seed oil reported by Nzikou et al. (2011) was as follows: moisture content 6.48 %, crude protein 21.85 %, ether extract 27.78 % and per 100 g edible portion crude fibre 16.44 g, ash 6.2 g, total carbohydrate 21.35 g, energy 326.53 Kcal, K 13.29 mg, Ca 647 mg, P 510 mg, Mg 442 mg and Na 659 mg. The oil had a refractive index of 1.467. The saponification value suggested the potential use of this oil in liquid soap, shampoo and oil-based ice cream production.

Roselle seeds were found to be a good source of lipid-soluble antioxidants, particularly γ-tocopherol (Mohamed et al. 2007). Roselle seed oil was found to have the following physicochemical parameters: acidity, 2.24 %; peroxide index, 8.63 meq/kg; extinction coefficients at 232 (k(232)) and 270 nm (k(270)), 3.19 and 1.46, respectively; oxidative stability, 15.53 h; refractive index, 1.477; density, 0.92 kg/L; and viscosity, 15.9 cP. Roselle seed oil was characterized as belonging to the linoleic/oleic category, its most abundant fatty acids being C18:2 linoleic (40.1 %), C18:1 oleic (28 %), C16:0 palmitic (20 %), C18:0 stearic (5.3 %) and C19:1 nonadecanoic (1.7 %). Sterols included β-sitosterol (71.9 %), campesterol (13.6 %), Δ-5-avenasterol (5.9 %), cholesterol (1.35 %) and clerosterol (0.6 %). Total tocopherols were detected at an average concentration of 2,000 mg/kg, including α-tocopherol (25 %), γ-tocopherol (74.5 %) and δ-tocopherol (0.5 %). *H. sabdariffa* seeds were found to contain 17.35 % oil, 18.52 % palmitic, 25.16 % oleic, 3.52 % vernolic, 4.31 % stearic, 44.72 % linoleic and 1.57 % dihydrosterculic acids (Wang et al 2012).

Roselle seed protein showed a maximum foaming capacity at pH 12 and 1.6 M NaCl, a maximum emulsification capacity at pH 11 and 1.8 M NaCl and a weaker foam stability at neutral pH than at acidic or alkaline pH, with a better foam stability at alkaline pH (Salah and Hayat 2009). The foam stability was considerably improved by treatment with 1.6 M NaCl.

More than 25 volatiles mainly unsaturated hydrocarbons, alcohols and aldehydes predominating from C_8 to C_{13} were identified in roselle seed oil (Jirovetz et al. 1992). Total yield of seed oil was 23 %. Volatile constituents included 2,2-dimethyl-3-propyloxirane 0.5 %, 2-methyl-5-methoxypentan-2-ol 0.2 %, 5-mehtyltetrahydro-2-furanmethnaol 1.3 %, 2-octen-1-ol 0.3 %, octanoic acid 0.2 %, 2,4-dimethylheptan-1-ol 0.7 %, 1,4-nonadiene 0.2 %, 2-nonen-1-ol 0.3 %, nonanal 0.4 %, nonanoic acid 0.1 %, camphor 0.2 %, linalool 0.1 %, decano 0.3 %, 2,4-decadienal 0.4 %, 2,4-dimethylnonane 0.2 %, dodecane 0.1 %, dodecanol 0.3 %, 2-ethyl-1-decanol 0.1 %, 1,13-tetradecadiene 0.1 %, 2-(1.mehtylheptyl) cyclohexanone 0.2 %, 7-dexadedene 0.1 %, heptadecane 0.2 % and 1-heptadecene 0.1 %. Roselle seed oil was found to contain triacylglycerols belonging to trisaturated (1.0–2.1) disaturated–monounsaturated (12.3–20.9), monosaturated–diunsturated (42.3–46.6) and triunsaturated (30.1–44.2) types of triacylglycerols (Fiad 1991a). Roselle seed oil contained 20 % oil and 1.3 % phospholipid such as cephalins, lecithin (phosphatidylcholine) and some of their lysoforms (Fiad 1991b). Different proportions of three common fatty acids, palmitic, oleic and linoleic were found in the six glycerophospholipids.

Karkade protein isolate had lower free and total gossypol than did the whole seed and

defatted flour (Abu-Tarboush and Ahmed 1996). The in vitro protein digestibility of karkade defatted flour and protein isolate was lower than that of casein. Phytic acid was higher in karkade defatted flour than in soybean defatted flour. Undefatted roselle seed flour contained 27.32 and 39.24 % of protein and carbohydrates, respectively, but were both elevated significantly to 36.39 and 46.03 % after defatting (Tounkara et al. 2013). The fat content was 20.83 % for undefatted and 1.36 % for deffated, and likewise the ash content was 4.47 % and 5.58 %, respectively. Roselle seed comprised 31.18 % of total protein, followed by albumin (16.47 %), glutelin (10.20 %) and prolamin (5.57 %). The protein content was 91.50, 93.77, 81.55, 71.30 and 40.83 % for roselle seed protein isolate (RSPI), globulin, albumin, glutelin and prolamin, respectively. RSPI, globulin, albumin, glutelin and prolamin all contained the following essential and non-essential amino acids in varying amounts (g/100 g protein) essential amino acids: lysine, histidine, leucine, isoleucine, phenylalanine, methionine, cysteine, valine, threonine, tryptophan; non-essential amino acids: glycine, aspartic acid, glutamic acid, serine, arginine, alanine, tyrosine and proline. Glutelin possessed the highest water-holding capacity and albumin the lowest. The oil-holding capacity ranged from 3.47 to 7.23 mL/g and the emulsifying capacity from 95 to 18 mL/g. Glutelin had the higher foam capacity, while RSPI showed the more stable foam.

Furundu (cooked and fermented roselle seeds) preparation resulted in significant changes in seed major nutrients (Yagoub et al. 2004). Total polyphenols and phytic acid were also reduced. The increase in total acidity and fat acidity coupled with a decrease in pH indicated microbial hydrolysis of the major nutrients, proteins, carbohydrates and fats during fermentation. In vitro digestibility of the seed proteins reached the maximum value (82.7 %) at the sixth day of fermentation, but thereafter it significantly decreased. The foaming capacity from the flour of raw seed decreased as a result of cooking. Fermentation for 9 days significantly increased the foaming capacity of the cooked seed, restoring the inherent value. In water, the emulsion stability from the fermented samples was significantly higher than that of the raw seed flour. Addition of 1 M NaCl significantly decreased the emulsion stability of the fermented samples. Roselle and soybean oils were found to impact on the quality characteristics of pork patties (Jung and Joo 2013). It was found that reduction in thickness, pH and L* and b* values decreased; however, water-holding capacity, reduction in diameter and a* values increased, respectively, as the amount of roselle increased. The preference of colour, tenderness, juiciness and overall quality depended on the addition of roselle and soybean oil. The maximum overall quality score (5.42) was observed when 12.5 g of soybean oil and 0.7 g of roselle extract were added.

Leaf Phytochemicals

Leaves were found to have 86.2 % moisture, 1.7–3.2 % protein, 1.1 % fat, 10 % fibre, 1 % ash, 0.18 % Ca, 0.04 % P and 0.0054 % Fe (Mahadevan and Kamboj 2009). Seven glycosides were isolated from roselle dietary leaves: kaempferol 3-*O*-rutinoside; kaempferol 3-*O*-glucopyranoside; quercetin-3-*O*-rutinoside; citrusin C; 2,3-dihydro-2-(4′-hydroxy-3′-methoxyphenyl)-3-β-D-glucopyranosylmethyl-7-hydroxy-5-benzofuranpropanol; corchoionoside C; and *trans*-carveol 6-*O*-β-glucopyranoside (Sawabe et al. 2005). β-sitosteryl-β-D-galactoside was found in the leaves (Osman et al. 1975).

Other Plant Parts' Phytochemicals

Phenols, alkaloids, tannins, flavanoids, saponins were found in the leaves, stem and root of roselle plant (Mungole and Chaturvedi 2011). Phenolics were higher in the leaves 0.125 mg/g than stem and roots. In leaf flavonoid content was found to be highest, i.e. 0.230 mg/g, followed by stem and then by root. The calyx is rich in citric acid and pectin. Cellulose microfibres extracted from roselle fibres had higher α-cellulose content and lower lignin and hemicelluloses (Sonia and

Dasan 2013). Thermal characterization showed enhanced thermal stability of celluloses microfibres compared to raw fibres.

The edible shoots were reported to contain per 100 g edible portion: moisture 85 g, protein 3.3 g, fat 0.3 g, carbohydrate 9 g, fibre 1.6 g, Ca 213 mg, P 93 mg, Fe 4.8 mg, carotene 4.1 mg, thiamin 0.17 mg, riboflavin 0.45 g, niacin 1.2 mg and vitamin C 45 mg, while the fruit contained 94.5 g moisture, 1.7 g protein, 1.0 g fat and 12 g carbohydrate and the calyx contained 4 % citric acid (Saidin 2000).

Roselle essential oil from Yunnan was found to be dominated by esters (31.42 %) such as tributyl phosphate (18.63 %), benzyl benzoate (3.40 %) and1,2-benzenedicarboxylic acid diisooctyl ester (3.37 %) (Zhang and Wang 2007). It also contained alkyls (29.19 %), acids (9.85 %), aromatic compounds (9.34 %), ketones (9.32 %), hydroxyketone (4.91 %), alkene (2.04 %) and aldehyde (0.93 %). Other compounds above 2 % included nonacosane 11.84 %; heneicosane 8.62 %; 1,2-dimethoxy-4-(2-propenyl)-benzene 7.97 %; eugenol 4.62 %; 2-tridecanone 3.24 %; 2-pentadecanone 2.01 %; and *n*-hexadecanoic acid 2.23 %. Other components <2 % included 2 α-isophoron; benzoic acid; nonanoic acid; 2-isopropenyl-5-methyl-4-hexenal; 2-undecanone; citronellic acid; isopropyl ester salicylic acid; 2,3,5,8-tetramethyl-decane; geranic acid; *n*-decanoic acid; 4-methyl-1-undecene; 6,10-dimethyl-5,9-undecadien-2-one; 1,2,3-trimethoxy-5-2(2-propenyl)-benzene; 4-dihexylcarbamoyl-butyric acid; 3,8-dimethylundecane; diethyl phthalate; tetradecanal; 1-methyldodecyl acetate; 2,6,10,14-tetramethyl-pentadecane; heptadecane; 8-cotadecenal; tetradecanoic acid; 10,14-trimethyl-2-pentadecanone; 2-phenylethyl ester benzoic acid; bis(2-methylpropyl) ester 1,2-benzenedicarboxylic acid; nonadecane; farnesyl acetone; 3,7-dimethylproponate 6-octen-1-ol; dibutyl phthalate; eicosane; (*Z,Z*)-9,12-octadecadienoic acid; octadecanoic acid; docasane; (*Z*)-9-tricosane, tetracosane; 1-pentacosanol and pentacosane.

H. sabdariffa had been reported to possess antihypertensive, antioxidant, anticancer, anticlastrogenic, hypolipidaemic, hepatoprotective, antistress, antispasmodic, diuretic and antidiarrhoeal activities (Joshi and Parle 2006). Numerous studies had demonstrated that *H. sabdariffa* aqueous flower extracts (HES), *H. sabdariffa* polyphenol-rich extracts (HPE), *H. sabdariffa* anthocyanins (HAs), and *H. sabdariffa* protocatechuic acid (PCA) exerted many biologic effects (Lin et al. 2011). PCA and HAs protected against oxidative damage induced by tert-butyl hydroperoxide (*t*-BHP) in rat primary hepatocytes. Animal and human experimental studies suggested that roselle extracts could be used as atherosclerosis chemopreventive agents as they inhibit LDL oxidation, foam cell formation as well as smooth muscle cell migration and proliferation. The extracts also afforded hepatoprotection by influencing the levels of lipid peroxidation products and liver marker enzymes in experimental hyperammonemia. PCA had also been shown to inhibit the carcinogenic action of various chemicals in different tissues of the rat. HAs and HPE were demonstrated to cause cancer cell apoptosis, especially in leukaemia and gastric cancer. More recent studies investigated the protective effect of HSE and HPE in streptozotocin-induced diabetic nephropathy.

Antioxidant Activity

Studies showed that the antioxidant capacity of roselle extract increased when extraction time or weight of petals increased (Tsai et al. 2002). The ferric-reducing ability of plasma (FRAP) assay showed a linear relationship with anthocyanin. Comparisons between FRAP, radical absorbance capacity (ORAC) and total antioxidant status (TAS) antioxidant assays gave a linear relation. The results suggested anthocyanin to be the major source of antioxidant capacity in roselle extract. Studies showed that the antioxidant capacity of roselle extract increased when extraction time or weight of petals increased (Tsai et al. 2002). The ferric-reducing ability of plasma assay showed a linear relationship with anthocyanin. Comparisons between FRAP, ORAC and TAS antioxidant assays gave linear relations. The

results suggested anthocyanin to be the major source of antioxidant capacity in roselle extract. Studies indicated that the roselle extract showed stronger antioxidant properties than butylated hydroxyanisole (BHA) or α-tocopherol in the linoleic acid model system (Tee et al. 2002). A total of 200 ppm of the extract inhibited more than 85 % of diene-conjugated compounds after 7 days of incubation at 40 °C. The total phenolic compound was found to be 2.96 mg/g calyx as gallic acid equivalent. The results indicated roselle to be a good source of natural antioxidants which may protect the body from damage by free radicals and lipid peroxidation. The protective effect was effected probably through the action of highly bioavailable ascorbic acid, ß-carotene and phenolic compounds, especially the anthocyanins. After heating roselle, FRAP activity, monomeric and copigmented anthocyanins decreased, while degradation index polymeric anthocyanins and 2,2-diphenyl-1-picryl hydrazine (DPPH) scavenging effect increased after heating (Tsai and Huang 2004). On fractionation of roselle anthocyanin, they found that the contribution percentage of DPPH scavenging effect of fraction II increased after being heated, while the contribution in FRAP activity of fraction III dropped. This suggested that fractions II and III might be the major contributors for DPPH scavenging ability and FRAP activity, respectively.

Studies demonstrated that the dried roselle calyx extracts exhibited strong antioxidant activity in Cu^{2+}-mediated oxidation of LDL in vitro (Hirunpanich et al. 2005). The inhibitory effect of the extracts on LDL oxidation was dose dependent at concentrations ranging from 0.1 to 5 mg/mL. Moreover, 5 mg/mL of roselle inhibited TBARS formation with greater potency than 100 μM of vitamin E. The results demonstrated the potent antioxidant effect of roselle in vitro. Another study estimated the total antioxidant activity of roselle ethanol flower extracts to be 4.6 and 8.6 mM of vitamin C for the chloroform and ethyl acetate fractions, respectively (Farombi and Fakoya 2005). Both extracts scavenged hydrogen peroxide (H_2O_2) (79–94 %) at 500 μg dose and inhibited (70–80 %) superoxide anion radicals (O_2^{-*}) at 1,000 μg. The concentrations required for a 50 % scavenging of hydroxyl radical (OH) (IC_{50}) were 380 and 200 μg for chloroform and ethyl acetate fractions, respectively. Both extracts were better scavengers of superanion, hydroxyl and hydrogen peroxide as compared to BHA, quercetin and α-tocopherol. At a concentration of 25 μg/mL chloroform and ethyl acetate fractions exhibited 32 and 38 % inhibition on CCl_4-NADPH-induced lipid peroxidation, respectively, while both extracts exhibited 80 and 89 % inhibitory effects at 100 μg/mL. Pretreatment of rats with *H. sabdariffa* extracts orally with 100 and 250 mg/kg simultaneously with intraperitoneal injection $FeCl_2$–ascorbic -acid–ADP mixture reduced the formation of malondialdehyde content.

Suboh et al. (2004) found that *H. sabdariffa* extract protected erythrocytes against lipid peroxidation. Studies showed that *H. sabdariffa* anthocyanins may be used to inhibit low-density lipoprotein (LDL) oxidation and oxLDL-mediated macrophage apoptosis and thus serve as a chemopreventive agent (Chang et al. 2006). The antioxidative activity of *H. sabdariffa* anthocyanins was confirmed by relative electrophoretic mobility of oxLDL (decrease of 50 % at 2 mg/mL), fragmentation of Apo B (inhibition of 61 % at 1 mg/mL) and thiobarbituric acid relative substances (TBARS) assay (IC_{50}: 0.46 mg/mL) in the Cu^{2+}-mediated oxidize LDL. Further, the addition of >0.1 mg/mL of roselle anthocyanins could scavenge over 95 % of free DPPH radicals, of roselle anthocyanins showed strong potential in inhibiting LDL oxidation induced by copper. MTT assay, leukostate staining analysis and Western blot revealed that roselle anthocyanins could inhibit oxLDL-induced apoptosis.

Roselle anthocyanin extract effectively scavenges DPPH radical, 92 % at a concentration of 2.0 mg/mL, and produced a 69 and 90 % scavenging effect on superoxide ion and hydrogen peroxide, respectively, at 1.0 mg/mL, which compared favourably with the synthetic antioxidant (butylated hydroanisole and α-tocopherol) (Ajiboye et al. 2011). Roselle anthocyanin extract also exhibited reducing power that was approximately twofold that of the synthetic antioxidant,

butylated hydroanisole as evaluated using $K_3[Fe(CN)_6]$. Roselle anthocyanin extract produced a significantly increase and completely attenuated the CCl_4-mediated decrease in antioxidant enzymes (e.g. catalase, superoxide dismutase, glutathione peroxidase and glutathione reductase) in the rat's liver. However, the level of nonenzymatic antioxidant molecules (i.e. vitamins C and E) were significantly preserved by roselle anthocyanin extract. There was an induction of phase II drug-detoxifying enzymes: glutathione S-transferase, NAD(H)/quinone oxidoreductase and uridyl diphosphoglucuronosyl transferase by 65, 45, and 57 %, respectively. The results indicated that *Hibiscus sabdariffa* anthocyanin extract could act as a prophylactic by intervening as a free radical scavenger both in vitro and in vivo as well as inducing the phase II drug-detoxifying enzymes.

The decoction preparation protocol of dried roselle flowers afforded the highest nutritional value and the polyphenol content accounted for the antioxidant capability of *H. sabdariffa*-based beverages (Prenesti et al. 2007). *H. sabdariffa-based* drinks could be considered as protective beverages, and a regular consumption of roselle might be proposed to ensure protection against free radicals. *Hibiscus sabdariffa* flowers were found to contain important amount of dietary fibre that endowed it with high antioxidant capacity (Sáyago-Ayerdi and Goñi 2010). The infusion obtained by decoction of flowers had been extensively studied due to its wholesome health-related properties. Roselle flower was found to contain dietary fibre as the largest component (33.9 %) and was rich in phenolic compounds (6.13 %) (Sáyago-Ayerdi et al. 2007). Soluble dietary fibre was 0.66 g/L in roselle beverage, and 66 % of total extractable polyphenols contained in roselle flower were passed to the beverage and showed an antioxidant capacity of 335 μmol trolox equivalents/100 mL beverage measured by ABTS [2,2′-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid)]. The data suggested that roselle flower beverage intake in the Mexican diet may contribute around 166 and 165 mg/serving to the intake of dietary fibre and polyphenols, respectively.

Methanol extract of roselle calyces gave the highest DPPH inhibition (78 %) and was significantly different from acetone and water extracts (Anokwuru et al. 2011). Ethanol roselle extract gave the highest inhibition to lipid peroxidation (26 %) but was not significantly different from the other solvent extracts. Methanol extracted the highest total phenolic content (29.2 mg GAE/g DW) and the acetone extract extracted the highest flavonoid content (53.6 mg QE/g DW) There was a stronger correlation obtained between total phenolic content and inhibition of DPPH ($R^2 = 0.969$) compared to total flavonoid content and DPPH ($R^2 = 0.742$). The study showed that methanol and ethanol were better solvents for the extraction of phenols of *Hibiscus sabdariffa* calyx compared to water and acetone. It also showed that phenols contributed more to the antioxidant activity of *H. sabdariffa* calyx compared to flavonoids.

Results of studies found that incorporation of roselle extract in *Lactobacillus casei* incorporated probiotic yoghurt had a beneficial effect: it improved the total antioxidant property and organoleptic qualities and decreased the exudation of whey proteins (Syneresis) (Rasdhari et al. 2008). Yeast and mould counts were negligible in the roselle yoghurts. Roselle seed extracts were found to have the highest antioxidant activity and strongest radical-scavenging activity of all plants tested (Mohd-Esa et al. 2010). Methanol extracts showed a positive correlation between phenolic content and antioxidant activity, as measured by β-carotene bleaching assay and DPPH radical-scavenging activity. In a whole food system investigated patties treated with roselle seeds had reduced lipid oxidation compared to patties treated with BHT. The study suggested that roselle seeds possessed potential to be used as food antioxidants. Using marinades of roselle extract for fried beef patties was found to reduce the formation of carcinogenic heterocyclic aromatic amines (Gibis and Weiss 2010). Four heterocyclic aromatic amines, namely, 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx) (0.3–0.6 ng/g), 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) (0.02–0.06 ng/g), co-mutagenic norharmane (0.4–0.7 ng/g) and harmane (0.8–1.1 ng/g), were found

at low levels. The concentration of MeIQx was reduced by about 50 and 40 % by applying marinades containing the highest amount of roselle extract compared to sunflower oil and control marinade, respectively. The antioxidant capacity (TEAC assay/Folin–Ciocalteu assay) was determined as 0.9, 1.7, 2.6 and 3.5 μmol Trolox antioxidant equivalents, and total phenolic compounds were 49, 97, 146 and 195 μg/g roselle marinade. In sensory-ranking tests, marinated and fried patties were not significantly different to control samples.

In a randomized, open-label, two-way crossover study of eight healthy humans, roselle extract caused significantly higher plasma areas under the curve (AUC) of FRAP, an increase in Ae(0-24) of FRAP, ascorbic acid and hippuric acid, whereas malondialdehyde excretion was reduced in human volunteers (Frank et al. 2012). Further, the main hibiscus anthocyanins as well as one glucuronide conjugate could be quantified in the volunteers' urine (0.02 % of the administered dose). The results suggested that roselle extract enhanced the systemic antioxidant potential and reduced the oxidative stress in humans.

Leaves of *H. sabdariffa* were found to have total phenolic content (TPC) of 523 mg GAE (gallic acid equivalent)/100 g and ascorbic acid equivalent antioxidant capacity (AEAC)of 351 mg AA/100 g (Wong et al. 2010). Based on TPC and AEAC, ranking was as follows: *H. tiliaceus* > *H. mutabilis* > *H. sabdariffa* > *H. taiwanensis* > *H. schizopetalus* ~ *H. rosa-sinensis.* Leaves of *H. schizopetalus*, *H. sabdariffa* and *H. rosa-sinensis* had better ferrous ion-chelating (FIC) ability than those of *H. mutabilis*, *H. tiliaceus* and *H. taiwanensis*. Flowers of *H. sabdariffa* with TPC, AEAC and FRP values of 264 mg GAE/100 g, 230 mg AA/100 g and 141.5 mg GAE/g, respectively, were significantly lower than all other species (Wong et al. 2010). Based on flower TPC, ranking was as follows: *H. tiliaceus* > *H. rosa-sinensis* > *H. taiwanensis* ~ *H. schizopetalus* ~ *H. mutabilis* > *H. sabdariffa.* Species with low total anthocyanin content (TAC) such as *H. mutabilis* (16 mg CGE (cyanidin-3-glucoside equivalent)/100 g) and *H. sabdariffa* (43 mg CGE/100 g) displayed low or no ferrous ion-chelating ability and lipid peroxidation-inhibiting activity.

Anti-hyperammonemic Activity

Oral administration of roselle extract (250 mg/kg body weight) to hyperammonemic rats (induced by daily intraperitoneal injections of ammonium chloride at a dose of 100 mg/kg body weight for 45 days) decreased levels of tissue lipid peroxidation and increased antioxidant levels (Essa et al. 2006a). Roselle significantly normalized the levels of ammonia, urea, uric acid, creatinine and nonprotein nitrogen in the blood and significantly reduced brain levels of lipid peroxidation products such as thiobarbituric acid and reactive substances (TBARS) and hydroperoxides (Essa and Subramanian 2007). Roselle significantly increased the levels of antioxidants such as catalase, superoxide dismutase, glutathione peroxidase and reduced glutathione in brain tissues of hyperammonemic rats. Treatment of hyperammonemic rats with roselle extract significantly decreased the elevated levels of the ammonium chloride-induced circulatory ammonia, urea, aspartate transaminase, alanine transaminase, alkaline phosphatase, TBARS and hydroperoxides induced by ammonium chloride (2006b). The results suggested that roselle extract afforded hepatoprotection by influencing the levels of lipid peroxidation products and liver markers in experimental hyperammonemia, and this could be due to its free radical-scavenging property and the presence of natural antioxidants.

Antimicrobial Activity

Roselle calyx extract and protocatechuic acid (PCA) inhibited the growth of methicillin-resistant *Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Acinetobacter baumannii* in vitro (Liu et al. 2005). The antibacterial activity of PCA was significantly higher than roselle calyx. Further, heat treatment did not affect the antibacterial activity of roselle calyx and protocatechuic acid against

all test pathogens. PCA exhibited concentration-dependent antibacterial activities in broth and human plasma; however, PCA acid showed less inhibitory activity in human plasma than in broth. Based on their lower MIC values, heat tolerance and concentration-dependent antibacterial activity, PCA and roselle extract may be useful in clinical infection prevention or therapy.

Gossypetin (3,5,7,8,3,′ 4′-hexahydroxy flavone) isolated from *Hibiscus sabdariffa* flowers exhibited antibacterial activity in vitro against *Escherichia coli, Staphylococcus aureus, Bacillus subtilis, Bacillus pumilus* and *Pseudomonas aeruginosa* (Mounnissamy et al. 2002). Methanol and aqueous roselle extracts exhibited antibacterial activity against cariogenic *Streptococcus mutans* with minimum inhibitory concentration (MIC) of 2.5 mg/mL (Afolabi et al. 2008). At 1 mg extract/disc, roselle leaves were found to inhibit Gram-positive bacteria *Bacillus cereus*, *Micrococcus luteus* and *Staphylococcus aureus* (Wong et al. 2010). At 2 mg extract/disc, roselle leaves inhibited both Gram-positive and Gram-negative bacteria of *Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella choleraesuis*.

Studies showed that methanol roselle calyx extracts at concentrations of 10, 5, and 2.5 % were effective in inhibiting *Escherichia coli* isolates from food, veterinary and clinical samples in vitro (Fullerton et al. 2011). In a recent study, the inhibition of the roselle ethanol extract against *Bacillus subtilis* and *Staphylococcus aureus* was slightly higher than that of water extract in vitro, but this difference was not significant (Jung et al. 2013). However, *Escherichia coli* was strongly inhibited by the roselle water extract at concentrations of 25 and 50 mg/mL.

Anticancer Activity

Studies showed that protocatechuic acid (PCA) isolated from *H. sabdariffa* possessed potential as a cancer chemopreventive agent against tumour promotion (Tseng et al. 1998). Topical application of PCA (5, 10 or 20 µmol) 5 min prior to TPA (12-O-tetradecanoylphorbol-13-acetate) (15 nmol) treatment twice weekly for 20 weeks to female CD-1 mice which were initiated with benzo[a]pyrene (B[a]P) inhibited the incidence of tumours in mice to 81.3, 62.5 and 56.3 %, respectively, while all mice in the TPA-treated group developed tumours. PCA significantly suppressed TPA-induced hyperplasia in the skin and oedema of mouse ears by 65 and 73 % at doses of 10 and 20 µmol, respectively. The same doses (5, 10 or 20 µmol) of PCA also reduced the formation of hydrogen peroxide in the mouse skin when compared with that of the TPA-treated group. However, Nakamura et al (2000) demonstrated not only the lack of an inhibitory effect but also significant enhancement of mouse skin tumour promotion by pretreatment with a high dose of PCA 3 h before TPA induction. The possibility that metabolism by tyrosinase activity of PCA to certain compound(s) without antioxidative properties and/or with tumour promotional potency was also suggested.

Hibiscus protocatechuic acid was found to inhibit the survival of human promyelocytic leukaemia HL-60 cells by induction of apoptosis in a concentration- and time-dependent manner (Tseng et al. 2000). Protocatechuic acid caused an increase in the level of hypophosphorylated retinoblastoma and a decline in hyperphosphorylated retinoblastoma. It also reduced Bcl-2 protein expression and increased Bax protein expression. The anticarcinogenicity of protocatechuic acid was postulated to be related, in part, to its specific suppression of neoplastic hyperproliferation (Babich et al 2002). In in-vitro studies in non-tumorigenic S-G gingival epithelial cells, and malignant HSG1 cells derived from the salivary gland, exposure to protocatechuic acid induced oxidative stress, presumably through its bioactivation by a tyrosinase pathway. A brief exposure to 25 mM protocatechuic acid lowered the levels of intracellular glutathione and potentiated Fe^{2+}-induced lipid peroxidation of the cells. Preexposure of the S-G and HSG1 cells to a non-toxic level of protocatechuic acid (2.5 mM) enhanced their sensitivity to a subsequent exposure to tert-butyl hydroperoxide. Studies showed that roselle anthocyanin could cause human promyelocytic leukaemia HL-60 cancer cell apoptosis in a dose- and time-dependent manner

(Chang et al. 2005). Also there was increased phosphorylation in p38 and c-Jun, cytochrome c release and expression of Bid, Fas and FasL in the roselle-treated HL-60 cells. The results suggested that roselle anthocyanin mediated HL-60 apoptosis via the p38-FasL and Bid pathway. Delphinidin-3-sambubioside (Dp3-Sam), isolated from dried roselle calyces, induced a dose-dependent apoptosis of human leukaemia cells (HL-60) as characterized by cell morphology; DNA fragmentation; activation of caspase-3, caspase-8 and caspase-9; and inactivation of poly(ADP-ribose) polymerase (PARP) (Hou et al. 2005). The results showed that that Dp3-Sam might induce apoptosis in HL-60 cells through a reactive oxygen species (ROS)-mediated mitochondrial dysfunction pathway.

In vitro studies showed that roselle polyphenol-rich extracts induced cell death of eight kinds of cell lines in a concentration-dependent manner (Lin et al. 2005). Among them human gastric carcinoma (AGS) cells were the most susceptible. Their results revealed that AGS cells underwent DNA fragmentation and had an increase in the distribution of hypodiploid phase (apoptotic peak) after a 24-h treatment with roselle extract (2.0 mg/mL). This effect was found to be mediated via p53 signalling and p38 MAPK/FasL cascade pathway. Another in vitro study also showed that roselle extract exerted chemopreventive effect on human gastric adenocarcinoma cells via apoptosis induction and JNK/p38 MAPK signalling activation (Lin et al. 2007a).

Antiurolithiatic Activity

In a study of 36 healthy men, the urine consumption of roselle juice showed a decrease of creatinine, uric acid, citrate, tartrate, calcium, sodium, potassium and phosphate but not oxalate in urinary excretion (Kirdpon et al. 1994). They found that a low dose of roselle juice (16 g/day) caused more significant decrease in salt output in the urine than a high dose (24 g/day). The urinary changes were similar to the observations on villagers with and without stones in northeastern Thailand. *Hibiscus sabdariffa* and *Phyllanthus amarus* decreased calcium crystal deposition in the kidneys of rats with glycolate-diet-induced hyperoxaluria (Woottisin et al. 2011). The antilithic effect of *Hibiscus sabdariffa* may be related to decreased oxalate retention in the kidney and more excretion into urine while that of *Phyllanthus amarus* may depend on increased urinary citrate. Supplementation of aqueous extract *of H. sabdariffa* calyces at different doses (250, 500 and 750 mg/kg body weight) significantly lowered the deposition of stone-forming constituents in the kidneys and serum of urolithiatic male albino rats induced by a mixture of 0.75 % ethylene glycol and 2 % ammonium chloride (Laikangbam and Damayanti Devi 2012). Roselle extract was found to be safe without lethal or genotoxic effects. Results of in vivo genotoxicity testing showed no significant chromosomal aberrations in the bone marrow cells of ethylene glycol-induced rats.

Uricosuric Activity

In a human study of nine subjects with no history of renal stones (non-renal stone, NS) and nine with a history of renal stones (RS), after consumption of roselle tea, the trend was an increase in oxalate and citrate in both groups and uric acid excretion and clearance in the NS group (Prasongwatana et al. 2008). In the RS group, both uric acid excretion and clearance were significantly increased. The values for excretion of uric acid were clearly increased in both the NS and RS groups after the intake of roselle tea and returned to baseline values in the washout period. The results demonstrated a uricosuric effect of roselle calyces.

Antihypertensive Activity

Hibiscus sabdariffa decoctions and infusions of calyxes, and on occasion leaves, are used in at least 10 countries worldwide in the treatment of hypertension and hyperlipidaemia with no reported adverse events or side effects (Hopkins et al. 2013). Animal studies had consistently

shown that consumption of roselle extract reduced blood pressure in a dose-dependent manner. In randomized clinical trials, the daily consumption of a tea or extract produced from roselle calyxes significantly lowered systolic blood pressure (SBP) and diastolic blood pressure (DBP) in adults with pre- to moderate essential hypertension and type 2 diabetes. Further, roselle tea was as effective at lowering blood pressure as the commonly used blood pressure medication Captropril, but less effective than Lisinopril. Roselle extracts were reported to have a low degree of toxicity with a LD_{50} ranging from 2,000 to over 5,000 mg/kg/day. There had been no evidence of hepatic or renal toxicity as the result of roselle extract consumption, except for possible adverse hepatic effects at high doses.

Antioxidant activity using a model liposome system was the highest overall in the red roselle varieties compared to the white with methanol extracts showing the highest activity (Christian et al. 2006). The methanol and ethyl acetate extracts of the varieties showed higher COX-1 enzyme inhibition than COX-2 and therefore had high potential to decrease blood viscosity. The findings supported the ethnomedicinal use of *H. sabdariffa* in Africa and the Caribbean for the treatment of cardiovascular disease and hypertension. A crude methanolic extract roselle calyces relaxed, concentration-dependently, KCl (high K^+)- and phenylephrine-precontracted aortic rings from spontaneously hypertensive rats, with a greater potency against the alpha(1)-adrenergic receptor agonist (Ajay et al. 2007). It was found that these effects were probably mediated through the endothelium-derived nitric oxide-cGMP-relaxant pathway and inhibition of calcium (Ca^{2+}) influx into vascular smooth muscle cells. The data further supported previous in vivo findings and the traditional use of roselle as an antihypertensive agent. The anthocyanins delphinidin-3-*O*-sambubioside and cyanidin-3-*O*-sambubioside, isolated from roselle calyces, exhibited angiotensin-converting enzyme (ACE) inhibitor activity in vitro with IC_{50} values of 84.5 and 68.4 μg/mL, respectively (Ojeda et al. 2010). This activity accorded well with the folk medicinal use of *Hibiscus sabdariffa* calyces as antihypertensive.

Animal Studies

Intravenous injection of aqueous extract of roselle calyces to anaesthetized cats lowered the blood pressure in a dose-response manner (Ali et al. 1991). The inhibitory effects were resistant to a number of standard receptor blockers, but the hypotensive influence was partially blocked by atropine and the tonic effects on rat uterus were partially reduced by hydrocortisone and indomethacin. Pretreatment of rats with 20 mg/kg roselle calyx extract in anaesthetized rats did not have a significant effect on increase in blood pressure induced by bilateral carotid occlusion (Adegunloye et al. 1996). The cumulative addition of roselle to noradrenaline precontracted aortic rings produced dose-dependent relaxation of the rings. The maximum relaxation response was 86.96 % observed at the dose of 1.70 mg/mL. The results suggested that the antihypertensive effect of roselle extracts was not mediated through inhibition of the sympathetic nervous system, but it could be mediated through acetylcholine-like and histamine-like mechanisms as well as via direct vasorelaxant effects. Roselle calyx infusion was found to lower significantly both systolic and diastolic pressure in spontaneously hypertensive and normotensive Wistar–Kyoto rats at tested doses of 500 and 1,000 mg/kg body weight (Onyenekwe et al. 1999). The reduction in blood pressure in both groups was positively correlated with weight. Continuous consumption of the infusion at 1,000 mg/kg was found to lead to sudden death in spontaneously hypertensive rats but not in Wistar–Kyoto rats. The water intake in the treated spontaneously hypertensive and normotensive rats was not different from the corresponding control groups. However, the urine output of the treated spontaneously hypertensive rats was significantly higher. A significant decrease in serum creatinine, cholesterol, and glucose in the treated rats compared with the control as well as a significant increase in serum uric acid was observed.

Administration of roselle extract to 2 K-1C (2-Kidney, 1-Clip renovascular) hypertensive rats, caused a reduction in systolic blood pressure

compared to untreated 2 K-1c rats and a reduction in heart rat compared to the sham-operated control rats (Odigie et al. 2003). The hearts of the untreated 2 K-1C rats were heavier than those of 2 K-1C + roselle extract. The results suggested that roselle extract exhibited antihypertensive and cardioprotective effects in vivo. Separate studies found that the blood pressure and heart rate fell dose-dependently in both the hypertensive and normotensive rats after intravenous injection of 1–125 mg/kg of roselle calyx extract, suggesting that roselle extract possessed antihypertensive, hypotensive and negative chronotropic effects (Mojiminiyi et al. 2007). The fall in mean arterial pressure was significantly pronounced in the hypertensive rats (salt-induced; l-NAME-induced) than in the normotensive control rats. Results of studies suggested that aqueous roselle calyx attenuated the development of salt-induced hypertension in Sprague-Dawley rats and this attenuation may be associated with its high K + content or high potassium/sodium ratio and not with altered pressor/depressor response to noradrenalin or acetylcholine (Mojiminiyi et al. 2012). Also the effects of roselle and furosemide on mean arterial blood pressure were comparable. Inuwa et al. (2012) found that roselle ingestion by spontaneously hypertensive rats (SHR) significantly reduced systolic and diastolic blood pressures and left ventricle mass in a dose-dependent fashion but did not affect heart rate. Roselle extract significantly increased surface area and length density of myocardial capillaries by 59 %, 65 % and 86 % and length density by 57 %, 77 % and 57 %, respectively. Myocyte nuclear volume was significantly decreased in extract-treated rats. The changes suggested that the observed beneficial effect of roselle on high blood pressure in SHRs could be mediated through a reduction in the diffusion distance between capillaries and myocytes, as well as new vessel formation. It was concluded that these effects might be beneficial in restoring myocyte normal nutritional status compromised by the hypertrophic state of hypertension.

Clinical Studies

In a study of patients with moderate essential hypertension, consumption of roselle tea resulted in 11.2 % lowering of the systolic blood pressure and a 10.7 % decrease of diastolic pressure in the experimental group 12 days after beginning the treatment, as compared with the first day (Haji Faraji and Haji Tarkhani 1999). The difference between the systolic blood pressures of the roselle treated and control groups was significant, as was the difference of the diastolic pressures. In a randomized, double-blind, placebo-controlled clinical trial involving 65 pre-hypertensive and mildly hypertensive adults, age 30–70 years, not taking blood pressure (BP)-lowering medications, daily consumption of roselle tisane in an amount readily incorporated into the diet lowered blood pressure (McKay et al. 2010). Participants with higher systolic blood pressure (SBP) at baseline showed a greater response to hibiscus treatment for SBP change. A month long daily administration of roselle calyx infusion were compared with captopril (twice a day) for antihypertensive effects in a controlled and randomized clinical trial involving 75 patients, 30–80 years old, with diagnosed hypertension and without antihypertensive treatment for at least 1 month (Herrera-Arellano et al. 2004). *H. sabdariffa* reduced systolic blood pressure (BP) from 139.05 to 123.73 mmHg and the diastolic BP from 90.81 to 79.52 mmHg. However, at the end of the study, there were no significant differences between the BP detected in both treatment groups. The rates of therapeutic effectiveness were 0.7895 and 0.8438 with *H. sabdariffa* and captopril, respectively, while the tolerability was 100 % for both treatments. In a separate randomized, double-blind lisinopril-controlled clinical trial of 193 patients, 25–61 years old with hypertension stage I or II, treatment with dried roselle calyces exerted important antihypertensive effectiveness with a wide margin of tolerability and safety, while it also significantly reduced plasma angiotensin-converting enzyme activity and demonstrated a tendency to reduce serum sodium (Na) concentrations without modifying potassium (K) levels (Herrera-Arellano et al. 2007). However,

blood pressure reductions and therapeutic effectiveness were lower than those obtained with lisinopril. In a double-blind randomized controlled trial of 60 type II diabetic patients with mild hypertension, consumption of roselle tea and black tea were found to have positive lowering effects on blood pressure indicating the antihypertensive effects of both teas (Mozaffari-Khosravi et al. 2009b).

Review Studies

A systemic review of four randomized controlled studies by Wahabi et al. (2010) found no reliable evidence to support recommending *Hibiscus sabdariffa* for the treatment of primary hypertension in adults.

Hypocholesterolemic/ Hypolipidaemic/ Antiatherosclerotic Activities

In Vitro Studies

A crude hydroalcoholic extract from roselle calyces showed in vitro an appreciable enzyme-inhibiting activity towards the angiotensin-converting enzyme (ACE) I, but weak inhibiting activities towards elastase, trypsin and alpha-chymotrypsin (Jonadet et al. 1990). Studies by Lee et al. (2002) found that both protocatechuic acid and esculetin exhibited strong potency to inhibit oxidative low-density lipoprotein (LDL) induced by copper or an NO donor. Both compounds demonstrated remarkable ability to rescue the cholesterol degradation and Apo B fragmentation. Additionally, their nontoxic characteristics raised the possibility for their use in the daily diet to help prevent atherosclerosis. The angioprotective activity in vivo, also important, was attributed to flavones and anthocyanins. In vitro studies found that roselle anthocyanins could inhibit serum-stimulated proliferation of smooth muscle cell and result in cell apoptosis via p38 and p53 pathway (Lo et al. 2007). In consequence, the rate of atherosclerotic formation was retarded, and its progress was suppressed.

Studies showed that anthocyanin-rich roselle extract decreased low-densitylipoprotein (oxLDL)-mediated macrophage-derived foam cell formation (Kao et al. 2009b) Oxidative modification of oxLDL had been reported to be involved in the pathogenesis of atherosclerotic lesions through the formation of macrophage-derived foam cells. The enhanced expression of CD36 in oxLDL-treated J774A.1 cells was decreased both at the mRNA as well as protein level after roselle treatment. Treatment of J774A.1 cells with oxLDL significantly increased PPAR-gamma protein levels in nuclear extracts while treatment with roselle resulted in significant decreases in nuclear PPAR-gamma protein levels. The results suggested that roselle extract inhibited the macrophage uptake of oxLDL and this may involve CD36 downregulation.

Hibiscus sabdariffa extract was shown to lower the plasma lipid level and reduce the liver damage (Yang et al. 2010). *Hibiscus sabdariffa* polyphenols exhibited higher potency to decrease plasma cholesterol and LDL cholesterol than the crude roselle extract and increased HDL cholesterol dose-dependently. It decreased the lipid content of hepatocyte through the activation of AMPK (5′ adenosine monophosphate-activated protein kinase) and reduction of SREBP-1(sterol regulatory element-binding transcription factor 1), thus inhibiting the expression of fatty acid synthase and HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl-CoA reductase). Low-density lipoprotein receptor (LDLR) and LDL binding of HepG2 cells were enhanced when treated with roselle extract. The results suggested roselle polyphenols could be developed as an adjunctive for hepatic lipid control and hypolipidaemic therapy. The potency of roselle extract at 100 μg/mL was found to be similar to 0.4 μg/mL pravastatin in inhibiting HMG-CoA reductase and possibly reduced cholesterol biosynthesis (Duangjai et al. 2011).

Aqueous polyphenol-rich roselle extracts were up to 100 times more efficient in inhibiting triglyceride accumulation in a model of adipogenesis from 3T3-L1 cells and in hypertrophic and insulin-resistant adipocytes when devoid of fibre and polysaccharides (Herranz-López et al. 2012). Significant differences were also observed in reactive oxygen species generation and adipokine

secretion. When polyphenols were fractionated and isolated, the benefits of the whole extract were greater than the sum of its parts, which indicated a previously unnoticed synergism. Roselle leaf polyphenolic extract demonstrated potential in reducing foam cell formation and intracellular lipid accumulation in oxidized-LDL (ox-LDL)-induced macrophage J774A.1 cells under non-cytotoxic concentrations (Chen et al. 2013). The results implied that roselle extract up-regulated the LXRα (liver × receptor alpha)/ABCA1 (ATP-binding cassette transporter A)1 pathway, which in turn led to stimulation of cholesterol removal from macrophages and delayed atherosclerosis.

Animal Studies

Consumption of roselle extract had been found to lower total cholesterol, low-density lipoprotein cholesterol (LDL-C) and triglycerides in the majority of normolipidaemic, hyperlipidaemic and diabetic animal models, whereas high-density lipoprotein cholesterol (HDL-C) was generally not affected (Hopkins et al. 2013). Over half of the RCTs showed that daily consumption of roselle tea or extracts had favourable influence on lipid profiles including reduced total cholesterol, LDL-C, triglycerides as well as increased HDL-C.

Studies found that feeding weanling rats for up to 12 weeks with alkali refined roselle seed oil that was heated and dehydrogenated to remove cyclopropene fatty acids resulted in serum and liver composition of total lipids, cholesterol and phospholipids comparable to those fed with peanut oil (Sarojini et al. 1985). However, the food intake and weight gain were found to be less in the refined roselle oil group compared to the peanut group. The liver architecture did not show any abnormalities with roselle oil feeding.

Administration of roselle extract to male albino rats fed on a mixture of cholesterol and cholic acid for 12 weeks to induce hypercholesterolemia elicited significant lowering effect in the level of different lipid fractions in spite of the continued cholesterol and cholic acid loading during the treatment (El-Saadany et al. 1991). However, blood phospholipids were increased after roselle administration. Although the administration of roselle at 5 and 10 % induced a significant decrease in the activity of serum glutamic oxaloacetic transaminase and glutamic pyruvic transaminase, alkaline and acid phosphatase as well as total serum protein, the values reverted to the initial levels after 9 weeks of roselle administration.

Animal studies showed that the levels of triglyceride, cholesterol and low-density lipoprotein cholesterol (LDL-C) were lower in the serum of rabbits fed on high-cholesterol diet (HCD 3 % lard oil) plus roselle extract than in the serum of rabbits fed HCD (Chen et al. 2003). Feeding roselle extract (0.5 and 1 % in the diet) to rabbits significantly reduced severe atherosclerosis in the aorta. Roselle reduced foam cell formation and inhibited smooth muscle cell migration and calcification in the blood vessel of rabbits. The results suggested that roselle extract exhibited antiatherosclerotic activity by inhibiting serum lipid increases. Another animal study revealed an inhibitory effect of roselle flower extract on Cu^{2+}-mediated relative electrophoretic mobilities and thiobarbituric acid-reactive substances (TBARS) (Chen et al. 2004). Roselle extract exhibited a remarkable ability to reduce cholesterol degradation and ApoB fragmentation. It exhibited a high potency to inhibit the production of oxidized LDL induced by copper and, specifically, to reduce serum triglycerides in high-fructose diet (HFD)-fed rats and serum cholesterol in high-cholesterol diet (HCD)-fed animals. The levels of LDL and the ratio of LDL cholesterol (LDL-C) to HDL cholesterol (HDL-C) were reduced by the extract in both hyperlipidaemic models. The study suggested that roselle extract may be used to inhibit LDL oxidation and to prevent various types of hyperlipidaemia in HFD- or HCD-fed rats.

The chronic administration of aqueous extracts of both petals of red and green *Hibiscus sabdariffa* for 28 days resulted in significant decreases in the plasma total cholesterol levels at 1.5 mg/kg body weight while the extracts led to significant decreases in LDL cholesterol levels at both 1.0 and 1.5 mg/kg body weight only in rats (Olatunji et al 2005). In contrast, the administration of the extracts did not have any significant effect on HDL cholesterol, triglycerides, haema-

tocrit, haemoglobin, red blood cell count, white blood cell count and platelet count values when compared with the controls. The results indicated that the lowered plasma total cholesterol concentrations induced by aqueous extracts of either red or green *Hibiscus sabdariffa* petals was strongly associated with decreased LDL cholesterol concentrations. Carvajal-Zarrabal et al. (2005) found that 4 week supplementation of *H. sabdariffa* ethanol extract at 5, 10, and 15 % levels to Sprague-Dawley rats fed on a basal high-cholesterol diet was found to reduce the lipid profile. Five percent roselle extract addition showed the best results in the reduction of serum lipids—total lipids, total cholesterol (TC), triacylglycerols (TAG) and LDL levels. No significant results were found in any group in the cases of either phospholipid or HDL levels. A hypothesis of hibiscus acid racemization, (+)-HCA to (−)-HCA, mediated by intestinal flora enzymes was proposed to elucidate the significant triacylglycerol decrease in all experimental groups. VLDL, the precursor of LDL, comprising predominantly of triacylglycerols, suggested that the significant decrease in LDL was related to observed triacylglycerol synthesis inhibition. In another study, administering dried roselle calyx extracts at doses of 500 and 1,000 mg/kg together with continuous cholesterol feeding to hypercholesterolemic rats for 6 weeks significantly decreased serum cholesterol level by 22 % and 26 %, respectively; serum triglycerides level by 33 % and 28 %, respectively; and serum LDL level by 22 % and 32 %, respectively (Hirunpanich et al. 2006). However, serum HDL level was not affected. Six-week treatment with 250, 500 and 1,000 mg/kg of the extracts significantly decreased thiobarbituric acid-reactive substances (TBARS) formation while the formation of conjugated dienes during the oxidation of LDL induced by $CuSO_4$ was also reduced. The results suggested that the aqueous extracts of dried roselle calyx possessed both antioxidant effects against LDL oxidation and hypolipidaemic effects in vivo.

The ethanol roselle calyx extract at the dose of 200 mg/kg significantly attenuated the elevated blood glucose concentration by 57 % of alloxan-induced diabetic rats and reduced the alloxan-induced increases in cholesterol, very low-density lipoprotein cholesterol (VLDL-C), low-density lipoprotein cholesterol (LDL-C) and atherogenic index by 29 %, 36 %, 40 %, and 32 %, respectively (Farombi and Ige 2007). The extract attenuated the alloxan-induced decrease in the activities of superoxide dismutase (SOD), catalase (CAT) and the level of glutathione (GSH) by 36, 44 and 64 % in the liver and by 20, 43, and 85 % in the rat kidney. The extract significantly decreased the alloxan-mediated increase in malondialdehyde (MDA) and protein carbonyl levels in the liver by 44 % and 43 % and in the kidneys by 45 % and 38 %, respectively. The extract also normalized the activity of phosphatidate phosphohydrolase in the liver. Their data demonstrated that roselle possessed strong hypolipidaemic as well as antioxidant properties in alloxan-induced diabetic rats and could be useful in preventing the development of atherosclerosis and possible related cardiovascular pathologies associated with diabetes. Hainida et al. (2008a) found the addition of 50 g/kg or 150 g/kg of defatted dried roselle powder to the diet of Sprague-Dawley male rats with induced hypercholesterolemia significantly lowered plasma total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels.

Studies by Ochani and D'Mello (2009) suggested that the ethanolic leaf and calyx extracts of roselle containing polyphenols and flavanols possessed significant antioxidant and antihyperlipidaemic activities. Highest antioxidant activity was exhibited by the ethanolic calyx extract followed by ethanolic leaf extract and the aqueous leaf extract. In cholesterol-induced hyperlipidaemic model, groups of rats treated with extracts of roselle calyces and leaves showed a significant decrease in the serum TC, LDL-C, VLDL-C, TAG values along with an increase in serum HDL-C levels. The treated groups also showed significant decrease in the atherogenic index, LDL-C:HDL-C risk ratios, and in the levels of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase activities compared to cholesterol-induced hyperlipidaemic control group. Significant antihyperlipidaemic

activity was shown by ethanolic extract of calyces, followed by ethanolic extract of leaves. It was observed from the histopathological findings that rats fed with roselle extracts showed decrease in granular degeneration caused by cholesterol feedings.

Results of animal studies demonstrated the hypolipidaemic and antioxidant activities of roselle extract and suggested its therapeutic potential in disorders of lipid metabolism and cardiovascular events associated with hypercholesterolemia (Ekor et al. 2010). Roselle extract significantly attenuated the alteration in lipid levels and antioxidant status induced by high cholesterol intake in rabbits. Both serum and tissue levels of low-density lipoprotein cholesterol, triglycerides, phospholipids, and total cholesterol decreased with increase in high-density lipoprotein- cholesterol except in the heart, following treatment with roselle extract in cholesterol-fed rabbits when compared with the untreated group. Similarly, roselle extract prevented cholesterol-induced depletion of enzymic (superoxide dismutase, catalase) and nonenzymatic (reduced glutathione, vitamin C) antioxidants with the attendant increases in lipid peroxidation and xanthine oxidase activity in rabbits.

Administration of roselle leaf extract (200 and 300 mg/kg) together with continuous cholesterol feeding of hyperlipidaemic Wistar rats for 4 weeks showed significant reduction in serum cholesterol level by 18.5 % and 22 %; serum triglyceride level by 15.6 % and 20.6 %; serum LDL level by 24 % and 30 % and serum VLDL level by 15.5 % and 20.5 %, respectively, as compared to cholesterol group (Gosain et al. 2010). However, no significant change in HDL level was observed. Roselle extract 300 mg/kg was more effective than 200 mg/kg dose but less effective than the standard drug, atorvastatin. The results indicate that roselle exhibited the hypolipidaemic effect and that 300 mg/kg dose had the best hypolipidaemic effect.

Clinical Studies

In a clinical study of 42 volunteers, 18–75 years old, with a cholesterol level of 175–327 mg/dL, ingestion of two capsules of roselle extract (with meal) for a month, was found to significantly lower the serum cholesterol level (Lin et al. 2007b). In a sequential randomized controlled clinical trial of 60 patients with diabetes, consumption of roselle tea or black tea had a positive effect on lipid profile (Mozaffari-Khosravi et al. 2009a). Those given roselle tea had significant increase in high-density lipoprotein cholesterol (HDL-C) and significant decrease in the mean of total cholesterol, low-density lipoprotein cholesterol, triglycerides and Apo-B100 at the end of the study. Changes in apolipoprotein-A1 and lipoprotein (a) were not significant. In the black tea group only HDL-C showed significant change at the end of the study and changes in the other parameters were not statistically significant.

Ninety hypertensive patients were randomly assigned to receive *Hibiscus sabdariffa* tea or black tea for 15 days in a randomized clinical trial (Mohagheghi et al. 2011). There was no significant differences between pre- and post-experiment values within the two groups. An upward trend in total cholesterol, HDL cholesterol and LDL cholesterol was evident in both groups. The increase in total and HDL cholesterol in both groups relative to their initial values was significant. No significant harmful changes in cholesterol, triglyceride, BUN (blood urea nitrogen), serum creatinine, Na and K levels were observed within 15 days after the discontinuation of the medication.

In a double-blind, placebo-controlled, randomized trial conducted in India involving 60 subjects with serum LDL values in the range of 130–190 mg/dL and with no history of coronary heart disease, daily consumption of roselle leaf extract (1 g/day) did not appear to have a blood lipid-lowering effect (Kuriyan et al. 2010). Body weight, serum LDL cholesterol and triglyceride levels decreased in both groups; there were no significant differences between the experimental and placebo group.

Antiobesity Activity

Roselle extract inhibited the adipocyte differentiation of 3T3-L1 preadipocytes induced by insulin,

dexamethasone and isobutylmethylxanthine (IBMX) in a dose-dependent manner (Kim et al. 2003). Its inhibitory effect was found to be partly via its suppression on the expression of adipogenic transcription factors, including CCAAT element-binding protein (C/EBP)-alpha and peroxisome proliferator-activated receptor (PPAR)-gamma. Seven Brazilian plant species including *Hibiscus sabdariffa* afforded preclinical data that indicated a potential role in the control of certain conditions associated with obesity, such as hyperlipidaemia (Dickel et al. 2007). In vitro studies showed that roselle extract inhibited adipocyte differentiation through the modulation of PI3-K/Akt and ERK pathways that played pivotal roles during adipogenesis in 3T3-L1 preadipocytes (Kim et al. 2007). Further, the phosphorylation and expression of MEK-1/ERK known to regulate the early phase of adipogenesis were clearly decreased with the addition of hibiscus extract.

Oral administration of *Hibiscus sabdariffa* aqueous extract, containing 33.64 mg of total anthocyanins, significantly reduced body weight gain in obese mice and increased liquid intake in healthy and obese mice (Alarcon-Aguilar et al. 2007). Alanine aminotransferase levels were significantly increased on the 15th and 45th day in obese mice, but aspartate aminotransferase levels did not show significant changes. Triglycerides and cholesterol levels showed nonsignificant reductions in animals treated with roselle. The data confirmed the antiobesity effect of *Hibiscus sabdariffa* reported by the Mexican population. Rats fed on a basal diet supplemented with roselle calyx extract (15 %) showed a significant decrease in weight, food consumption and efficiency compared with control rats fed on the basal diet but not at 5 % (Carvajal-Zarrabal et al. 2009). The 10 % extract-treated responses were similar to the 15 % with the exception of food consumption.

In a follow-up study carried out in a factorial, randomized design, patients with metabolic syndrome (MeSy) orally treated with *Hibiscus sabdariffa* extract powder (HSEP) had significantly reduced glucose and total cholesterol levels, increased HDL-C levels and an improved TAG/HDL-C ratio, a marker of insulin resistance (Gurrola-Díaz et al. 2010). Additionally, a triglyceride-lowering effect was observed in MeSy patients treated with roselle-powdered extract plus diet and in individuals without MeSy treated with HSEP. Significant differences in total cholesterol, HDL-C and triacylglycerols/HDL-C ratio were found when the means of absolute differences among treatments were compared.

Roselle extract had been reported to show therapeutic promise in the prevention of metabolic syndrome, an obesity-associated collection of disorders, each of which contributed to cardiovascular risk in patients; its effect was probably due to its polyphenol content (Pérez-Torres et al. 2013a). Further animal studies suggested that alteration in fatty acid metabolism in metabolic syndrome (MS) rats caused impaired vascular reactivity but treatment with roselle infusion ameliorated this condition (Pérez-Torres et al. 2013b). Body mass, intra-abdominal fat, triglycerides, insulin, blood pressure, saturated, monounsaturated FA, NEFAs (nonesterified fatty acids), Δ9-, Δ6-desaturases and vasoconstriction were increased, while vasorelaxation, polyunsaturated FA, endothelial nitric oxide and NO_3/NO_2 ratio decreased in MS but roselle infusion modified it and increased Δ5-desaturase. Villalpando-Arteaga et al. (2013) found that oral administration of aqueous roselle extract reduced fat tissue accumulation, diminished body weight gain and normalized the glycemic index as well as reduced dyslipidaemia compared to the obese mice group that did not receive roselle treatment. Further, roselle treatment attenuated liver steatosis, downregulated sterol regulatory element-binding protein-1C (S)REBP-1c and peroxisome proliferator-activated receptor gamma (PPAR-γ); blocked the increase of IL-1, TNF-α mRNA and lipoperoxidation; and increased catalase mRNA. The results suggested that the antiobesity, antilipidaemic and hepatoprotective effects of roselle extract were related to the regulation of PPAR-γ and SREBP-1c in the liver.

Seventy-two obese Iranian youths (mean age of 14.21 ± 1.6, 35 boys) completed a triple blind randomized placebo-controlled clinical trial to evaluate the effect of *Hibiscus sabdariffa* calyces

in controlling dyslipidaemia (Sabzghabaee et al. 2013). Serum total cholesterol, low-density lipoprotein cholesterol and serum triglyceride showed a significant decrease in roselle-treated group, but high-density lipoprotein cholesterol level was not changed significantly. The two arms of the study (treated and controls) were not statistically different in terms of age, gender, weight, body mass index (BMI) and lipid profile before the trial. The authors concluded that *Hibiscus sabdariffa* calyces powder may have significant positive effects on lipid profile of adolescents which may be attributed to its polyphenolic and antioxidant content.

Hepatoprotective Activity

The chloroform-soluble fraction of roselle flower ethanol extract showed the greatest capacity of scavenging 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical (EC_{50} = 0.017 mg/mL) and the strongest inhibitory effect on xanthine oxidase activity (Tseng et al. 1997). The chloroform, ethyl acetate and residual fractions were found to inhibit significantly the unscheduled DNA synthesis induced by *tert*-butyl hydroperoxide (*t-BHP*) at a concentration of 0.20 mg/mL. The chloroform and ethyl acetate fractions also decreased the leakage of lactate dehydrogenase (LDH) and the formation of malondialdehyde (MDA) induced by *t*-BHP (tert-butyl hydroperoxide) markedly at a concentration of 0.10 and 0.20 mg/mL in the rat primary hepatocyte cultures. The results indicated that the dried flower of *H. sabdariffa* L. protected rat hepatocytes from *t*-BHP-induced cytotoxicity and genotoxicity by different mechanisms. (Tseng et al. 1996) showed that roselle protocatechuic acid at concentrations of 0.05 and 0.10 mg/mL significantly decreased the leakage of lactate dehydrogenase and alanine transaminase and the formation of malondialdehyde induced by treatment with *t-BHP* in primary cultured rat hepatocytes. Roselle protocatechuic acid also attenuated t-BHP-induced mitochondrial depolarization and effectively quenched DPPH radicals. They concluded that roselle protocatechuic acid protective effects against cytotoxicity and genotoxicity of hepatocytes induced by *t*-BHP may possibly be associated with its free radical-scavenging ability.

Studies showed that *Hibiscus sabdariffa* anthocyanins had hepatoprotective effect against *t*-BHP-induced cytotoxicity in primary hepatocytes and hepatotoxicity in rats (Wang et al. 2000). The extract was found to quench DPPH free radicals in a preliminary study. The extract at the concentrations of 0.10 and 0.20 mg/mL significantly decreased the leakage of lactate dehydrogenase and the formation of malondialdehyde induced by a 30-min treatment of *t*-BHP (1.5 mM). The in vivo investigation showed that the oral pretreatment of roselle (100 and 200 mg/kg) for 5 days before a single dose of *t*-BHP (0.2 mmol/kg, i.p.) significantly lowered the serum levels of hepatic enzyme markers (alanine and aspartate aminotransferases) and reduced oxidative liver damage. The histopathological evaluation of the liver revealed that hibiscus pigments reduced the incidence of liver lesions including inflammatory, leucocyte infiltration and necrosis induced by *t*-BHP in rats.

Studies showed that pretreatment of rats with protocatechuic acid (PCA), a polyphenolic compound from *Hibiscus sabdariffa* (50–100 mg/kg), by gavage for 5 days before a single dose of t-BHP (ip; 0.2 mmol/kg) significantly lowered serum levels of the hepatic enzyme markers, lactate dehydrogenase, alanine aminotransferase and aspartate aminotransferase, and reduced oxidative stress of the liver by evaluating malondialdehyde and glutathione (Liu et al. 2002). Histopathological evaluation of the rat livers revealed that PCA reduced the incidence of liver lesions, including hepatocyte swelling, leukocyte infiltration and necrosis induced by *t*-BHP. Further, PCA inhibited *t*-BHP-induced tyrosine phosphorylation, an implication of the activation of a stress signal pathway, in the liver. The results indicated that PCA protected against *t*-BHP-induced hepatotoxicity by its antioxidant and anti-inflammatory characteristics accompanied by blocking of stress signal transduction. Four week administration of roselle extract (but not for 2 or 3 weeks) significantly improved liver function of paracetamol-induced hepatotoxicity

in rats, but did not alter the histology of the paracetamol-treated rats or the pentobarbitone-induced sleeping time (Ali et al. 2003). At a dose of 200 mg/Kg, the hepatic histology and the biochemical indices of liver damage were restored to normal but lower doses were ineffective. Dahiru et al. (2003) found that oral administration of roselle calyx extract following a single dose of carbon tetrachloride promoted healing of oxidative liver damage as determined by serum aminotransferases ALT, AST levels and liver thiobarbituric acid-reactive substance levels. Studies by Lin et al. (2003) showed that pretreatment of rats with protocatechuic acid (PCA) for 5 days exhibited inhibitory potential on iNOS and hepatic damage induced by lipopolysaccharide (LPS). PCA significantly decreased the serum levels of the hepatic enzyme markers alanine and aspartate aminotransferase (ALT, alanine aminotransferase; AST, aspartate aminotransferase) induced by the 6-h treatment with LPS. It also reduced the incidence of liver lesions induced by LPS, including neutrophil infiltration, congestion, and liver cell swelling. In another study, pretreatment of rats with any of three herbal plants (*H. sabdariffa*, rosemary and sage) was found to have a protective effect against azathioprine-induced hepatotoxicity (Amin and Hamza 2005). Animals pretreated with water extracts from any of the three herbs not only failed to show necrosis of the liver after azathioprine administration but also retained livers that, for the most part, were histologically normal. Further, these herbs blocked the induced elevated levels of alanine aminotransferase and aspartate aminotransferase in serum. The azathioprine-induced oxidative stress was relieved to varying degrees by the three herbal extracts.

Roselle extract significantly and dose-dependently reduced the liver damage including steatosis and fibrosis in rats with carbon tetrachloride-induced fibrosis (Liu et al. 2006). In addition, the extract significantly decreased elevation in plasma aspartate aminotransferase and alanine aminotransferase, restored the decrease in glutathione content and inhibited the formation of lipid peroxidative products during CCl_4 treatment. Roselle extract also significantly inhibited the activation of the hepatic stellate cells. Pretreatment of rats with aqueous roselle extract resulted in significantly less hepatotoxicity than with cadmium alone as measured by plasma alanine aminotransferase and liver L-alanine and L-aspartate aminotransferases activities (Asagba et al. 2007). The extract also protected the rats against Cd-induced liver, prostate and testis lipoperoxidation as evidenced by significantly reduced malondialdehyde values in these organs, as well as reduced prostatic acid phosphatase activity in the prostate, when compared to the Cd-only exposed rats. The data suggested that *H. sabdariffa* might be protective in cadmium toxicity.

Studies showed that roselle extract could increase the antioxidant defence systems and may probably protect animals from gamma radiation-induced liver damage (Adaramoye et al. 2008). Treatment with roselle reduced gamma radiation-induced increases in serum alanine transferase after 24 h and decreased the levels of unconjugated bilirubin 5 weeks after irradiation. Also treatment with roselle (400 and 800 mg/kg) significantly elevated the levels of reduced glutathione (GSH) by 41 % and 44 %, respectively, at 5 weeks. Another study demonstrated that aqueous roselle extract could protect BALB/c mouse liver from acetaminophen-induced injury and that the protective mechanism might involve decreasing oxidative stress; decreasing expression of pJNK, Bax and tBid in the liver; and reducing cell death (Liu et al. 2010a, b).

Recent studies showed that pretreating BABL/c mice with *H. sabdariffa* polyphenol extract increased the level of glutathione (GSH), decreased the level of lipid peroxidation and increased catalase activity in the liver (Lee et al. 2012). Histopathological evaluation showed that roselle extract could decrease acetaminophen (AAP)-induced liver sterosis accompanied by a decreased expression of AIF, Bax, Bid and p-JNK in the liver. An in vitro assay revealed that roselle extract could reduce AAP-induced death of BABL/c normal liver cells (BNLs), reverse the lost mitochondrial potency and improve the antioxidative status, similarly to the results of the in vivo assay.

Anti-inflammatory Activity

Studies showed that polyphenols extracted from *Hibiscus sabdariffa* reduced 94.6 % of xanthine oxidase activity in vitro and decreased nitrite and prostaglandin PGE(2) secretions in lipopolysaccharide (LPS)-induced RAW264.7 cells (Kao et al. 2009a). In LPS-treated rats, the extract significantly decreased the serum levels of alanine and aspartate aminotransferase. In the liver, lipid peroxidation and liver lesions decreased, and catalase activity and glutathione increased. The results suggested that inhibition of lipopolysaccharide-induced hepatic inflammation by roselle extract was attained by improving antioxidative conditions and downregulation of cyclooxygenase-2 (COX-2), p-c-Jun N-terminal kinase (p-JNK) and p-P38.

The ethanol roselle calyx extract showed significant dose-related inhibition of ear oedema formation in xylene-induced ear oedema in mice compared with the blank control (Ali et al. 2011). Aqueous roselle extract rich in anthocyanins and other phenolic compounds including hydroxycitric and chlorogenic acids was found to effectively protect cultured peripheral blood mononuclear cells from the cellular death induced by H_2O_2 and a significant role in the production of inflammatory cytokines (Beltrán-Debón et al. 2010). It stimulated the production of interleukin IL-6 and IL-8 and decreased the concentration of monocyte chemoattractant protein-1 (MCP-)1 in supernatants in a dose-dependent manner. In humans, the ingestion of an acute dose of the extract (10 g) was well tolerated and decreased plasma MCP-1 concentrations significantly without further effects on other cytokines. This effect was not due to a concomitant increase in the antioxidant capacity of plasma but probably involved a direct inhibition of inflammatory and/or metabolic pathways responsible for MCP-1 production and may be relevant in inflammatory and chronic conditions.

Antidiabetic Activity

Roselle tea extract was found to have high inhibitory activity against porcine pancreatic α-amylase. Hibiscus acid and its 6-methyl ester were respectively isolated as active principles from the 50 % methanol and acetone extracts of roselle tea (Hansawasdi et al. 2000). In subsequent study, hibiscus acid was found to show weak inhibition of starch digestion in the Caco-2 model system and the methyl ester derivatives showed even weaker or no activity (Hansawasdi et al. 2001). The IC_{50} values of roselle inhibitory activity against pancreatic α-amylase occurred at concentration of 3.52 mg/mL, against intestinal maltase at >5 mg/mL and intestinal sucrose at >5 mg/mL (Adisakwattana et al. 2012). Total phenolic content of roselle flowers was 460 mg/g dried extract and flavonoid content amounted to 50.29 mg/g dried extract. Combining roselle, chrysanthemum, and butterfly pea extracts with mulberry extract showed additive interaction on intestinal maltase inhibition. Combination of chrysanthemum, mulberry, or bael extracts together with roselle extract produced synergistic inhibition, whereas roselle extract showed additive inhibition when combined with butterfly pea extract against pancreatic α-amylase. The results could be useful for developing functional foods by combination of plant-based foods for treatment and prevention of diabetes mellitus. Aqueous extracts of red and white roselle varieties caused inhibition of α-amylase and α-glucosidase activities in vitro (Ademiluyi and Oboh 2013). The IC_{50} revealed that the red variety (25.2 μg/mL) exhibited higher α-glucosidase inhibitory activity than the white variety (47.4 μg/mL), while the white variety (90.5 μg/mL) exhibited higher α-amylase inhibitory activity than the red variety (187.9 μg/mL). However, the α-glucosidase inhibitory activities of both calyces were higher than that of their α-amylase. Additionally, the red variety possessed higher antioxidant capacity as exemplified by the (•)OH scavenging abilities, Fe^{2+}-chelating ability and inhibition of $Fe^{(2+)}$-induced pancreatic lipid peroxidation in vitro. It was concluded that inhibition of α-amylase and α-glucosidase, coupled with strong antioxidant properties, could be the possible underlying mechanism for the antidiabetes properties of *H. sabdariffa* calyces; however, the red variety appeared to be more potent.

Studies showed that roselle polyphenol extract dose- and time-dependently reduced the high-glucose-stimulated vascular smooth muscle cell proliferation and migration and suppressed the proliferating cell nuclear antigen (PCNA) level and matrix metalloproteinase (MMP)-2 activation (Huang et al. 2009). Further, the expressions of connective tissue growth factor (CTGF) and receptor of advanced glycation end product (RAGE) enhanced by high glucose were prominently suppressed by roselle extract. The results suggested that roselle polyphenols potentially could be a promising adjuvant herbal therapy for diabetic patients. In another study, *H. sabdariffa* polyphenolic extract was shown to inhibit high glucose-stimulated cellular changes (Peng et al. 2011). At least 18 phenolic compounds were found in the extract. Treatment with the extract reduced hyperglycemia and hyperinsulinemia, especially at the dose of 200 mg/kg, and decreased serum triacylglycerol, cholesterol, and the ratio of low-density lipoprotein/high-density lipoprotein (LDL/HDL). Diabetes promoted plasma advanced glycation end product (AGE) formation and lipid peroxidation, while roselle extract significantly reduced these elevations. Immunohistological observation revealed that roselle extract inhibited the expression of CTGF and RAGE, which were increased in type 2 diabetic aortic regions. In addition, roselle extract reverted the weight loss found in type 2 diabetic rats. The study demonstrated the anti-insulin resistance properties of roselle polyphenolic extract and its effect on hypoglycemia, hypolipidaemia and antioxidation. The results suggested that it had potential to be an adjuvant for diabetic therapy. Ethanolic roselle calyx extract 1.0 g/kg/day significantly decreased the blood glucose level by 38 % in streptozotocin-induced diabetic rats but not in normal rats (Wisetmuen et al. 2013). In normal rats, treatment with 1.0 g/kg extract increased the basal insulin level significantly as compared with control normal rats. Interestingly, diabetic rats treated with 1.0 g/kg extract also showed a significant increase in basal insulin level as compared with the control diabetic rats. The results suggested that the antidiabetic activity of roselle extract may be partially mediated via the stimulating effect on insulin secretion. Ethanolic roselle calyx extract 1.0 g/kg/day significantly decreased the blood glucose level by 38 % in streptozotocin-induced diabetic rats but not in normal rats (Wisetmuen et al. 2013). In normal rats, treatment with 1.0 g/kg extract increased the basal insulin level significantly as compared with control normal rats. Further, diabetic rats treated with 1.0 g/kg extract also showed a significant increase in basal insulin level as compared with the control diabetic rats. The results suggested that the antidiabetic activity of roselle extract may be partially mediated via the stimulating effect on insulin secretion.

Haematological Activity

After 14 days of roselle calyx aqueous extract administration, significant elevations were observed in haematocrit and haemoglobin in the groups of rats administered doses of 200 and 400 mg/kg while the groups given higher doses revealed significant reductions in the haematocrit but not in haemoglobin (Adigun et al. 2006). The presence of some nutrients, e.g. protein, mineral elements (potassium) and vitamin C in the calyx, was confirmed. The results suggested that aqueous extract of *Hibiscus sabdariffa* calyx had beneficial effects on the red cells at low doses (200–400 mg/kg) which may not be sustained at higher doses.

Antispasmodic Activity

Addition of an aqueous extract of roselle calyces (2.5 mL/bath approximately 125 mg of starting crude material) inhibited the tone of various isolated muscle preparations (rabbit aortic strip, rhythmically contracting rat uterus, guinea pig tracheal chain and rat diaphragm) (Ali et al. 1991). Studies suggested that roselle aqueous extract relaxed vascular smooth muscle in isolated rat aorta via a mechanism associated with an inhibition of Ca^{2+} influx through receptor-operated channels and also on inhibition of Ca^{2+} release from intracellular stores (Owolabi et al. 1995).

Hibiscus sabdariffa methanol extract exhibited a significant dose-dependent relaxant effect (IC_{50} = 350 μM) on rat ileal strip comparable to the effect shown by nifedipin and papaverine as reference compounds (Salah et al. 2002). Similarly, the extract when administered intraperitoneally significantly reduced the intestinal transit (13–35 %) in rats (IC_{50} = 250 μM). The extracts (40 %) and nifedipin (51 %) also potentiated the diarrhoea-inducing effect of castor oil (IC_{50} = 350 μM). It was postulated that these effects were possibly generated by constituents such as quercetin and eugenol via a Ca^{2+} channel-modulated mode of action. Roselle calyx extract increased micturition thresholds in a dose-dependent manner in rats after bladder inflammation and after bilateral hypogastric neurectomy (Fouda et al. 2007). Neither atropine (0.1 mg/kg) nor propranolol (0.4 mg/kg) had significant effects on cystometric parameters. They also did not affect the responses obtained by roselle extract on cystometric parameters. Roselle extracts inhibited both the rate and amplitude of uterine contractions in a dose-dependent manner as with bladder response. A slight, but significant, reduction of contraction amplitude by roselle extract in the oxytocin precontracted uteri was only noted at a dose of 500 mg/kg.

In the concentration range of 0.02–7.68 mg/mL, roselle petal aqueous extract did not exhibit a measurable contractile effect on the rat aorta ring; contrariwise, in tissues with noradrenaline-induced tone, vasorelaxation was observed with cumulative concentrations of roselle extract and reached a mean of 91 % at a concentration of 1.70 mg/mL, with an EC_{50} of 0.53 mg/mL (Obiefuna et al. 1993). This relaxation response was significantly attenuated by removal of the endothelium. Sarr et al. (2009) found that roselle calyx crude extracts induced mainly endothelium-dependent relaxant effects in isolated thoracic aorta of male Wistar rats. The biological efficiency of the various studied extracts, in term of vasorelaxant capacity, showed that butanol extract > crude extract > residual marc > ethyl acetate extract. The results suggested that the strong activity of the butanolic extract was primarily due to the presence of anthocyans.

Aflatoxin Production Inhibition Activity

H. sabdariffa calyx extract at concentrations of 5, 7.5, 10 and 12.5 g/100 mL inhibited aflatoxin B1production by 91.5–97.9 % and 87.1–93.3 % for *Aspergillus flavus* and *A. parasiticus*, respectively, but had no significant effect on growth of either *Aspergillus* species (El-Nagerabi et al. 2012).

Antityrosinase and Cosmeceutical Activities

The aglycones of kaempferol-3-*O*-rutinoside and quercetin-3-*O*-rutinoside, from roselle leaves, were found to have good tyrosinase inhibitory activity 90.1 % and 95.4 % and 50.1 % and 73 % inhibition of DOPA (dihydroxyphenylalanine) oxidation, respectively (Sawabe et al. 2005). The 1-butanol leaf extract was found to be promising as a cosmetic agent. Of four species of *Hibiscus* tested, leaves of *H. sabdariffa* (5 %) had the weakest antityrosinase activity (Wong et al. 2010) Ranking of antityrosinase activity was *H. tiliaceus* > *H. mutabilis* > *H. rosa-sinensis* ~ *H. sabdariffa*.

Studies showed that liposome formulations containing roselle calyx extracts had good stability, high entrapment efficacy, increased skin permeation and low skin irritation and may have potential for development as active ingredients in cosmetic products (Pinsuwan et al. 2010). Studies showed that liposome-capsulated anthocyanin (LCA) from *Hibiscus sabdariffa* may be suitable as a photoprotective agent for the skin (Hwang et al. 2013). Overexposure to UV radiation could lead to the formation of free radicals and trigger inflammation and hyperpigmentation of the skin. Anthocyanin exhibited scavenging activity on DPPH radical with the inhibitory rate of 11 and 24 % at 20 and 50 mg/mL concentration treatment, respectively, and inhibitory effects on melanin production by 8, 14, 23 and 30 % at 5, 10, 20 and 50 mg/mL concentration treatment, respectively. However, LCAs enhanced DPPH scavenging activity (64 and 76 % at 20 and 50 mg/mL

concentration treatment, respectively) and inhibitory effects against melanin synthesis (23, 35, 43 and 60 % at 5, 10, 20 and 50 mg/mL concentration treatment, respectively). Anthocyanin-inhibited melanin synthesis was found to occur through the inhibition of tyrosinase enzymatic activity and suppression of the protein expression of tyrosinase and microphthalmia-associated transcription factor (MITF). Liposome encapsulation was found to increase the stabilization of anthocyanin and the inhibition of melanogenesis.

Immunomodulatory Activity

All fractions of neutral water-soluble polysaccharides isolated from roselle flower buds showed immune-modulating activity (Müller and Franz 1992). Roselle calyx infusion decreased mitogen-induced blastogenesis of human T lymphocytes in vitro but did not affect the level of spontaneous proliferation (Rapavi et al. 2006). The results suggested that roselle infusion may alleviate overstimulated condition of the immune system in hypersensitivity conditions.

The water and alcohol extracts (including its fractions) of the dried roselle calyx at doses of 50 mg/kg were found to possess higher immunostimulatory activities in mice in comparison with levamisole (positive control), with significant effects when compared with the vehicle-treated group (Fakeye 2008; Fakeye et al. 2008a). Increased activity was observed with increase in doses of the 50 % ethanol and absolute ethanol extracts. The insoluble fraction exhibited a significant dose-dependent immunostimulatory activity, while the residual water-soluble fraction exhibited activity at 100 mg/kg body weight. The production of tumour necrosis factor-alpha (TNF-alpha) was low in all the roselle extract groups tested, while the production of interleukin 10 (IL-10) was high compared with the control. The insoluble fraction exhibited a profound dose-dependent immunostimulatory activity higher than the positive control at 100 mg/kg. The ethyl acetate-soluble fraction exhibited a significant dose-dependent immunostimulation higher than that observed for levamisole (positive control). The results established the immuno-enhancing properties of the extracts of this plant confirming that the immunomodulatory activity is cell mediated and humoral.

Anxiolytic/Sedative Activity

Aqueous roselle calyx (100, 200 and 400 mg/kg, i.p.) exerted a remarkable dose-dependent decrease in spontaneous motor activity in mice and increased the duration of pentobarbital (40 mg/kg, i.p.) induced sleep in rats (Amos et al. 2003). Roselle extract significantly reduced the exploratory behaviour in mice. The extract significantly inhibited the intensity of apomorphine (1 mg/kg, s.c.) induced stereotypic behaviour and attenuated climbing in the mice dose-dependently. Similarly, chlorpromazine (3 mg/kg, i.p.) blocked apomorphine-induced stereotype behaviour significantly. The results suggested that the aqueous roselle extract may contain psychoactive substances that accounted for its use in traditional medicine as a sedative.

Animal studies using the elevated-plus maze and ketamine-induced sleep in animal models showed that roselle aqueous, hydroalcoholic and ethanolic extracts possessed anxiolytic and sedative effects which became more pronounced with administration of repeated doses of the extracts (Fakeye et al. 2008b). The extracts exhibited a dose-dependent increase in the time spent in the open arm with ethanol extracts having the best anxiolytic activity. The fractions of the hydroalcoholic extracts showed no significant anxiolytic activity. Neither the extracts nor the fractions significantly reduced or increased latency to sleep after a single dose except hydroalcoholic at 300 mg/kg. There was significant reduction in onset of sleep and increase in sleeping time with multiple doses of aqueous and hydroalcoholic extracts. A reduction in sleeping time after several daily doses of ethanol extracts doses was observed.

Anticlastogenic Activity

A crude aqueous roselle extract was found to have anticlastogenic effects against sodium arsenite-induced micronuclei formation in Swiss albino mice (Adetutu et al. 2004) Administration of a crude roselle extract evoked a significant reduction of micronuclei in polychromatic erythrocytes.

Nephroprotective Activity

Studies showed that roselle polyphenol extract reduced kidney mass induced by streptozotocin significantly, as well as improving hydropic change of renal proximal convoluted tubules in the rats (Lee et al. 2009). The extract also significantly reduced serum triglyceride, total cholesterol and LDL in streptozotocin-induced rats and significantly increased the activity of catalase and glutathione and reduced lipid peroxidation (thiobarbituric acid-reactive substances, TBARS). The results highlighted the beneficial effects of roselle polyphenols on STZ-induced diabetic nephropathy including pathology, serum lipid profile and oxidative marker in the rat's kidney. Another study showed that roselle aqueous extract was capable of reducing lipid peroxidation, increasing catalase and glutathione activities significantly in diabetic kidney and decreasing the plasma levels of triglyceride, low-density lipoprotein (LDL) and increasing high-density lipoprotein (HDL) value (Wang et al. 2011). Roselle extract improved hyperglycemia-caused osmotic diuresis in renal proximal convoluted tubules in diabetic rats. The results showed that roselle extract ameliorated diabetic nephropathy via improving oxidative status and regulating Akt/Bad/14-3-3γ signalling. Recent animal studies showed that treatment with roselle polyphenol extract had the potential to be an adjuvant for diabetic nephropathy by reducing angiotensin II receptors (AT)-1 and transforming growth factor β1 (TGF-β1) evoked by high glucose and recovered the increased vimentin and decreased *E*-cadherin (Yang et al. 2013). Roselle extract decreased fibronectin, thus avoiding epithelial to mesenchymal transition (EMT) and accompanying fibrosis. Another recent study showed that aqueous roselle extracts attenuated the progression of chronic kidney disease in 5/6 nephrectomy rats; systolic blood pressure (SBP) and serum levels of malondialdehyde were significantly lower at week 7 (Seujange et al. 2013). Roselle treated 5/6 nephrectomy rats had fewer renal injuries as measured by blood urea nitrogen, serum creatinine, creatinine clearance and renal pathology when compared with untreated group.

Wound-Healing Activity

Creams containing *H. sabdariffa* extract showed significant and concentration-dependent wound-healing activities in rats with superficial skin excision wounds (Builders et al. 2013). There was also evidence of synergism with creams containing a combination of gentamicin and *H. sabdariffa* extract. The extract demonstrated antioxidant properties with a total flavonoid content of 12.30 mg/g.

Antinociceptive Activity

In acetic acid-induced writhing test, the ethanol roselle calyx extract significantly inhibited writhing in mice compared with the blank control (Ali et al. 2011).

Antipyretic Activity

Hibiscus sabdariffa aqueous extract had no effect on paw oedema but had an inhibitory effect on yeast-induced pyrexia and a significant effect on the hot plate reaction time (Dafallah and Al-Mustafa 1996). Among the phytoconstituents found in both plants, flavanoids, polysaccharides and organic acids may be mainly responsible for these pharmacological activities. In another study, oral administration of the ethanol and the vacuum-dried extract of *H. sabdariffa* calyces (200–800 mg/kg, p.o.) decreased the yeast-induced fever in rats (Reanmongkol and Itharat

2007). Oral administration of the ethanol extract at the dose of 800 mg/kg significantly decreased the number of contortions and stretchings induced by acetic acid in mice. The aqueous extract had no effect on this test. Neither the ethanol nor aqueous extract had an effect in the formalin and hot plate tests in mice. The *H. sabdariffa* extract had no effect on carrageenin-induced paw oedema in rats. The results suggested that the ethanol and aqueous extract (vacuum dry) of *H. sabdariffa* calyces possessed antipyretic action through mechanisms that were different from that of aspirin.

Antidiarrhoeal Activity

Rats administered roselle calyces and *Ocimum gratissimum* leaf extracts experienced an increase in transit time indicating that both plant extracts could be useful at appropriate doses in the control of diarrhoea (Owulade et al. 2004). Roselle was more effective in this regard. Ali et al. (2011) found that the ethanol roselle calyx extract exerted a significant antidiarrhoeal activity against castor oil-induced diarrhoeal in mice in which it decreased the frequency of defecation and increased the mean latent period at the doses of 250 and 500 mg/kg body weight.

Diuretic/Naturetic Activity

Aqueous roselle petal extract was found to have diuretic activity (Mojiminiyi et al. 2000). Studies by Jiménez-Ferrer et al. (2012) found that the diuretic, natriuretic and potassium-sparing effects of *Hibiscus sabdariffa* aqueous extract were partly due to modulation of aldosterone activity by anthocyanins, flavonoids and chlorogenic acid present in the extract. *Hibiscus sabdariffa* aqueous extract showed a dose-dependent diuretic and natriuretic effect (Alarcón-Alonso et al. 2012). The pharmacological constants of natriuretic effect was $ED_{50} = 86$ mg/kg and Emax = 0.9 mEq/100 g/5 h. It was observed that renal filtration increased 48 % with the aqueous roselle extract and an additive effect was obtained when perfused with furosemide. Quercetin present in the extract had effect on the vascular endothelium causing oxide nitric release, increasing renal vasorelaxation by increasing kidney filtration. Therefore, they concluded the diuretic effect of *Hibiscus sabdariffa* may be mediated by nitric oxide release.

Nootropic Activity

The aqueous roselle calyx extracts (100 and 200 mg/kg, p.o.) significantly attenuated amnestic deficits induced by scopolamine (0.4 mg/kg, i.p.) and natural aging in mice (Joshi and Parle 2006). Roselle extract decreased the transfer latencies and increased step-down latencies significantly in the aged mice and scopolamine-induced amnesic mice as compared with piracetam (200 mg/kg, i.p.). Roselle was found to significantly decrease acetyl cholinesterase activity in mice. The results indicated that aqueous roselle extract may prove to be a useful memory restorative agent in the treatment of dementia in the elderly.

Immunoprotective Activity

The anthocyanin-rich roselle calyx extract significantly and dose-dependently increased the lowered viability of cadmium-treated U937 cells and cadmium-mediated activation of U937-derived macrophages (Okoko and Ere 2012). The extract also reduced the cadmium-mediated production of the markers of macrophage activation when compared to quercetin dihydrate. The results showed roselle to possess immunoprotective effect that could be exploited for pharmacological and neutraceutical advantages.

Antiprotozoal Activity

Animal studies showed that consumption of roselle extract ameliorated the pathological changes in blood and organs of *Trypanosoma congolense*-infected rats (Umar et al. 2009).

After 2 weeks of infection the roselle extract and vitamin C kept the parasitaemia significantly lower than the untreated infected group. The anaemia in the untreated infected group was significantly more severe than that of the corresponding roselle extract- or vitamin-treated groups. *Trypanosoma congolense* infection caused significant decreases in serum total proteins and albumin, serum and organ ascorbic acid as well as significant elevation of serum alanine amino transferase levels in untreated rats. Consumption of roselle extract or vitamin C, however, prevented these disease-induced anomalies in the treated infected rats. Consumption of roselle extract also significantly retarded the rate of weight gain in both healthy and infected rats.

Antimutagenic/Mutagenic Activity

The 80 % ethanol extract of roselle reduced about 60–90 % of the mutagenicity induced by 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) and other heterocyclic amines: 2-amino-3-methylimidazo[4,5-f]quinoline (IQ); 2-amino-3,4-dimethylimidazo[4,5-f]quinoline(MelQ);2-amino-3,8-dimethylimidazo-[4,5-f]quinoxaline(MelQx); 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1); 3-amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P-2); 2-amino-6-methyldipyrido[1,2-a:3′,2′-d]imidazole (Glu-P-1); and 2-aminodipyrido[1,2-a:3′,2′-d]imidazole (Glu-P-2), at a concentration of 12.5 mg/plate in the *Salmonella* mutation assay (Chewonarin et al. 1999). The extract showed no mutagenicity and no antibacterial activity below this dose. Mutagenicity of methylazoxymethanol (MAM) acetate, a colon carcinogen, was also efficiently inhibited by the roselle extract. In a colon carcinogenesis model in F344 rats, the roselle extract decreased the number of azoxymethane AOM- and PhIP-induced 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine aberrant crypt focus (ACF) formation in the initiation stage, although it rather increased the number of ACF in the post-initiation stage. Treatment of rats with chloroform and ethyl acetate fractions of roselle ethanol flower extract and vitamin C (standard antioxidant) significantly inhibited the induction of micronucleated polychromatic erythrocytes by sodium arsenite (2.5 mg/kg) after 24 h by 60, 70 and 50 %, respectively indicating that extract of *H. sabdariffa* showed strong antimutagenic activity (Farombi and Fakoya 2005). In another study, roselle extract dose-dependently inhibited the mutagenicity of 1-nitropyrene in microsuspension assay and dose-dependently decreased proliferation of transformed human HeLa cells (Olvera-García et al. 2008). These effect were attributed probably to its phenolic acids composition as its hot aqueous extract was found to contain 22.27 mg of protocatechuic acid per gram of lyophilized dried extract.

Quercetin but not kaempferol was found to be the mutagen in roselle colour as determined by mutagenicity test with *Salmonella typhimurium* TA98 (Takeda and Yasui 1985).

Keratinocyte-Stimulating Activity

Raw polysaccharides isolated from roselle flowers and all acidic subfractions caused a strong stimulation of proliferation of human keratinocytes (HaCaT) of up to 40 %, while the neutral polymers were ineffective (Brunold et al. 2004). While mitochondrial activity was not influenced, raw polysaccharides induced early differentiation of primary natural human keratinocytes, as determined by involucrin formation

Antiparasitic Activity

Hibiscus sabdariffa was one of five plants that showed toxic activity against cercariae and miracidia of *Schistosoma mansoni* at 50–100 ppm concentration (Elsheikh et al. 1990).

Reproductive Hormonal Activity

The aqueous roselle calyx extract at a dose of 500 mg/kg i.p. induced an oestrogen-like activity in immature female rats (Ali et al. 1989). The activity of roselle on the increase of the uterine

weight was about 1/3 of that of oestradiol at the dose of 2 mg/kg s.c. Studies showed that subchronic administration of aqueous roselle calyx extract induced testicular toxicity in rats (Orisakwe et al. 2005). There was no significant change in the absolute and relative testicular weights; however, there was a significant decrease in the epididymal sperm counts in the 4.6 g/kg group, compared to the control. The 1.15 g/kg dose group showed distortion of tubules and a disruption of normal epithelial organization, while the 2.3 g/kg dose showed hyperplasia of testis with thickening of the basement membrane and 4.6 g/kg dose group showed disintegration of sperm cells. Studies showed that aqueous roselle extract consumption during lactation significantly decreased maternal fluid and food intake, increased postnatal weight gain and delayed the onset of puberty in the female Sprague-Dawley rat offspring (Iyare and Adegoke 2008a). The increased postnatal weight gain, delayed puberty onset and elevated body mass index at onset of puberty in the offspring of rats that consumed roselle during pregnancy were found to be associated with elevated maternal plasma Na ion and corticosterone levels during pregnancy (Iyare and Adegoke 2008b). Studies found that that consumption of aqueous roselle extract during the juvenile–pubertal period (21–42 postnatal days) decreased fluid and food consumption, increased weight gain and delayed puberty onset in rats (Iyare and Nwagha 2009). In another study, they found decreased maternal fluid and food intake and an increased maternal plasma Na(+) and corticosterone concentration in roselle-treated female Sprague-Dawley dams with delayed puberty (Iyare et al. 2010). They ascribed the effects and delayed puberty in roselle-treated female offsprings may be through increased corticosterone and decreased leptin delivery through breast milk.

Studies by Mahmoud (2012) demonstrated that aqueous extracts from dried calyx of *H. sabdariffa*, either cold or boiled, altered normal sperm morphology and testicular ultrastructure and adversely influenced the male reproductive fertility in albino mice. However, recent studies by Ali et al. (2012) found that neither the *H. sabdariffa* aqueous extract nor its anthocyanins significantly altered either rat testicular weight and histology or uterus weight. Plasma concentrations of the three hormones, testosterone, luteinizing hormone and oestradiol, studied; the testicular concentrations of protein; reduced glutathione and total cholesterol; and superoxide dismutase activity were all insignificantly affected by either the extract or the anthocyanins, except for a slight, but statistically significant, decrease in testicular protein concentration caused by the 15 % aqueous extract when compared with controls. The results suggest that *H. sabdariffa* exerted no adverse effect on the male reproductive system. Consumption of *H. sabdariffa* aqueous extract inhibited the growth of the rats compared with the controls. Another study found that both *H. sabdariffa* and *Zingiber officinale* treatment increased the activities of testicular antioxidant enzymes (superoxide dismutase, reduced glutathione and catalase), reduced sperm abnormality, and restored level of malondialdehyde (lipid peroxidation marker) and sperm motility of cisplatin-treated male albino rats (Amin and Hamza 2006).

Pharmacokinetic Studies

Studies of six healthy volunteers found that within 7 h of consumption of a single oral dose of 150 mL of *H. sabdariffa* extract yielding 62.6 mg of cyanidin-3-sambubioside, 81.6 mg of delphinidin-3-sambubioside and 147.4 mg of total anthocyanins (calculated as cyanidin equivalents), the urinary excretion of cyanidin-3-sambubioside, delphinidin-3-sambubioside and total anthocyanins (i.e. the sum of all quantifiable anthocyanidin glycosides) was 0.016 %, 0.021 %, and 0.018 % of the administered doses, respectively (Frank et al. 2005). The dose-normalized plasma area under the curve estimates was 0.076, 0.032, and 0.050 ng × h/mL/mg for cyanidin-3-sambubioside, delphinidin-3-sambubioside and total anthocyanins, respectively. The dose-normalized C(max) estimates were 0.036, 0.015, and 0.023 ng/mL/mg in the same sequence. The urinary excretion of intact anthocyanins was fast and appeared to be monoexponential.

Seventeen polyphenols and metabolites were detected in rat plasma after acute ingestion of a polyphenol-enriched aqueous *Hibiscus sabdariffa* extract (Fernández-Arroyo et al. 2012). Although phenolic acids were found in plasma without any modification in their structures, most flavonols were found as quercetin or kaempferol glucuronide conjugates. Flavonol glucuronide conjugates were proposed to contribute to the observed lipid peroxidation inhibitory activity in the cellular membranes. By contrast, phenolic acids appeared to exert their antioxidant activity through ferric ion reduction and superoxide scavenging at shorter times.

Proteinase Inhibitory Activity

Karkade defatted flour and protein were found to have chymotrypsin inhibitory activity which was almost half that of trypsin (Abu-Tarboush and Ahmed 1996). The trypsin inhibitory activity of the protein isolate was 70 % of that of the defatted flour extracts. Heating the extract in boiling water for 10 min destroyed 66.1 % of the trypsin inhibitor activity.

Plant/Drug Interaction Activity

Studies showed that intake of roselle drink by six healthy male volunteers 1.30 h prior to administration of acetaminophen did not change acetaminophen absorption parameters $t_{1/2a}$, Ka, T_{max}, C_{max} and $AUC_{0}.\alpha$ (Kolawole and Maduenyi 2004). However, statistically significant changes in Kβ and $t_{1/2}\beta$ of acetaminophen when administered after roselle drink were observed. This also resulted in 11.69 % increase in Cl_T.

Co-administration of roselle extract with hydrochlorothiazide, a diuretic drug, caused a significant increase in the volume of urine excreted and resulted in a decrease in the pH of urine and the concentrations of sodium, bicarbonate and chloride ions in rabbits (Ndu et al. 2011). Co-administration of both materials increased and prolonged the plasma concentration, the mean area under the concentration–time curve and the volume of distribution of hydrochlorothiazide achieved over the 24-h sampling period. The results revealed a possible herb–drug interaction involving hydrochlorothiazide and roselle, used as an ingredient in medicinal or refreshing drinks in many countries.

In a controlled study in healthy human volunteers, ingestion of aqueous roselle calyx beverage after administration of diclofenac was found to reduce the quantity of diclofenac excreted in the urine compared to control (Fakeye et al. 2007).

Toxicity Studies

Rats-fed mesta seed oil had inferior growth and reproductive performance and also had altered liver metabolism (Rukmini et al. 1982). The authors asserted that raw or refined mesta oil may not be suitable for human consumption. Studies showed that prolonged usage of roselle extract at 15-dose level of 250 mg/kg each could cause liver injury while the effect was mild at small dose levels (1–10) in Wistar albino rats (Akindahunsi and Olaleye 2003). The group with 15 doses had their serum level of albumin significantly increased. Though the average consumption of 150–180 mg/kg per day appeared safe, the extract should be taken with caution bearing in mind that higher doses could affect the liver. Studies showed that the aqueous roselle calyx extract administered for 12 weeks induced testicular toxicity in rats (Orisakwe et al. 2005). The 1.15 g/kg dose group showed distortion of tubules and a disruption of normal epithelial organization, while the 2.3 g/kg dose showed hyperplasia of testis with thickening of the basement membrane. The 4.6 g/kg dose group showed disintegration of sperm cells and a significant decrease in the epididymal sperm counts compared to the control.

Among several herbal tea plant infusions, highest concentrations of Al, B, Cu, Fe, P, K, Mn, Ni and Zn were detected in those prepared from roselle petals (Malik et al. 2013). The total Al allowance (up to 1.2 mg/L) suggested that no more than 1 L of the roselle infusion should be consumed per day by sensitive individuals

including pregnant women and should be completely excluded from the diet of children under 6 months of age and children with chronic renal failure.

Another toxicity studies showed that death of albino rats was preceded by a severe loss in weight, accompanied with diarrhoea when given oral administration of 2,000 mg/kg dose of water and alcohol extracts of dried roselle calyx for 90 days (Fakeye et al. 2009). Significant reductions in the erythrocyte count with no difference in total leucocyte count were observed. The activity of aspartate aminotransferase was enhanced by the administration of aqueous and 50 % ethanol extract with a significant increase in its level at higher doses. Alanine aminotransferase and creatinine levels were significantly affected by all the extracts at the different dose levels. However, aqueous extracts exhibited a significant increase in creatinine levels at higher doses. No significant histopathological changes were observed, although there was a significant reduction in the weight of the spleen of the animals administered with ethanol and water extracts when compared with the control.

Traditional Medicinal Uses

Roselle flowers, leaves and to a lesser extent seeds and roots have been used in traditional medicine in the tropics as antiseptic, aphrodisiac, astringent, cholagogue, demulcent, digestive, diuretic, emollient, purgative, antipyretic, refrigerant, resolvent, sedative, mild laxative, stomachic and tonic and as a folk remedy for abscesses, bilious conditions, cancer, cough, debility, dyspepsia, dysuria, fever, hangover, heart ailments, hypertension, neurosis, scurvy and strangury (Perry 1980; Duke 1983; Chopra et al. 1986; Bown 1995, Duke et al 2002). Roselle drink made by placing, the calyx in water, is said to be a folk remedy for cancer. Medicinally, leaves are emollient and are much used in Guinea as a diuretic, refrigerant and sedative; fruits are antiscorbutic; leaves, seeds and ripe calyces are diuretic and antiscorbutic; and the succulent calyx, boiled in water, is used as a drink in bilious attacks; flowers contain gossypetin, anthocyanin and glucoside hibiscin, which may have diuretic and choleretic effects, decreasing the viscosity of the blood, reducing blood pressure and stimulating intestinal peristalsis (Duke et al. 2002). In Burma, the seeds are used for debility and the leaves as emollient. Taiwanese regard the seed as diuretic, laxative and tonic. Angolans use the mucilaginous leaves as an emollient and as a soothing cough remedy. Roselle is an aromatic, astringent, cooling herb that is much used in the Tropics (Mungole and Chaturvedi 2011). The leaves are antiscorbutic, emollient, diuretic, refrigerant and sedative (Mungole and Chaturvedi 2011). In the Philippines, the bitter root is used as an aperitif and tonic (Perry 1980).

Hibiscus sabdariffa is also a traditional Chinese rose tea and has been effectively used in folk medicines for treatment of hypertension and inflammatory conditions (Lin et al. 2011). *Hibiscus sabdariffa*, a local soft drink material and medicinal herb, is usually used effectively in native medicines against hypertension, pyrexia and liver disorders (Chen et al. 2003). *Hibiscus sabdariffa* popularly known in Mexico as 'Jamaica', 'flor de Jamaica', has been widely used in Mexican Traditional Medicine as antihypertensive and diuretic (Alarcón-Alonso et al. 2012), The beverages of the calyces are widely used in Mexico as diuretic, for treating gastrointestinal disorders, liver diseases, fever, hypercholesterolemia and hypertension (Ojeda et al. 2010). In folk medicine, the calyx extracts are used for the treatment of several complaints, including high blood pressure, liver diseases and fever (Ali et al 2005). In the Ayurvedic literature of India, different parts of this plant have been recommended as a remedy for various ailments like hypertension, pyrexia and liver disorders. In traditional medicine, roselle has been used as antidotes to poisonous chemicals (acids, alkali, pesticides) and venomous mushrooms (Chifundera et al. 1994). In Assam, leaves are sometimes used as medicine in dysentery of man and domestic animals (Patiri and Borah 2007).

In Brazzaville, powdered calyces is used as an aphrodisiac on the penis (Adjanohoun et al. 1988),

leaf juice is used as eye drop and oxytocic and pulp of the roots is used as local application for abscess and administered for bronchitis (Bouquet 1969). In Togo, finely powdered dried fruit is applied to sores and wounds (Adetutu et al. 2011). In Sudan, an infusion of the calyx is used to treat haematuria and headache and decoction used for snake bite and scorpion sting (El-Kamali 2009). In Dogonland, Mali, powdered roselle fruit mixed with powdered tamarind bark is used as local application for old wounds; powdered macerated roselle flowers are similarly used (Inngjerdingen et al. 2004). In Saloun Island, Senegal, roselle tea is used as a diuretic, cholagogue and diaphoretic (Kerharo and Adam 1964). Tea from crushed leaves soaked in water is taken orally for epilepsy in Temeke district, Tanzania (Moshi et al. 2005). In Uganda, a decoction of fresh leaves is taken orally for anaemia (Namukobe et al. 2011). In Ogun State, Nigeria, the leaves are used for tuberculosis (Ogbole and Ajaiyeoba 2010). In Senegal, an infusion of roselle calyx is taken orally for urinary problems and to treat colibacillosis (Pousset 1989); roots are used as a purgative or laxative, dried leaves used as sudorific and leaf decoction is used for measles, roots pulped and used as poultice to mature abscesses and for bronchitis (Potel 2002). In Madagascar, juice from pounded leaves is used as coagulant with latex (Pernet 1957). In Sierra Leone, a macerated and pounded leaves, flower concoction is taken orally for scurvy and heated leaves used externally for sand-crack feet (Sawyerr 1983). In Egypt, a decoction or infusion of roselle flowers are administered for hypertension and also used as an antimicrobial (Abouzid and Mohamad 2011). In Cameroon, roselle flowers are used in traditional treatment of malaria (Saotoing et al. 2011). In Bulamogi county, Uganda, roselle leaf decoction is used to treat anaemia (Tabuti et al. 2003). In Central African Republic, leaf decoction is used as mouth gargle (Vergiat 1969). In Burkina Faso, crushed seeds are used as veterinary medicine (Tamboura et al. 1998). *H. sabdariffa* aqueous extract, rich in several polyphenols, is commonly and effectively used in native medicines against hypertension, diabetes and liver disorders (Pérez-Torres et al. 2013a). A study of the prevalence of herbal medicine use in a cohort of patients with chronic kidney disease, dyslipidaemia and hypertension in Jordan found that the most common herbal product used was *H. sabdariffa* (22.5 %) (Wazaify et al. 2013).

Other Uses

Roselle is an annual multi-use crop used in food, animal feed, nutraceuticals, cosmeceuticals and pharmaceuticals. The strong bast fibre obtained from the stem (called India rosella hemp, rosella fibre, rosella hemp, rozelle hemp, Pusa hemp) (Crane 1949) is used for various household purposes including making sackcloth, gunnies, twine, ropes, cord and cordage and as a substitute for jute in the manufacture of burlap (Crane 1949; Rao 1996; Mungole and Chaturvedi 2011). Roselle fibre may be as good or even better than fibre of *H. cannabinus* (Burkill 1966). A yellow dye is obtained from the petals and used in medicine, etc. The seeds are fed to cattle in some parts of Africa (Burkill 1966) and poultry. The seed yields 20 % oil which is useful as a lubricant.

Studies showed that anthocyanin dye extracted from roselle flowers, the commercially available textile dye Remazole Red RB-133, could be used in dye-sensitized solar cells (DSSCs) because of their high stability (Abdou et al. 2013). The stability results favoured selecting anthocyanin as a promising sensitizer candidate in DSSCs based on natural products.

Comments

There are two botanical varieties in *Hibiscus sabdariffa*: var. *sabdariffa* is mainly cultivated as food and var. *altissima* Wester grown commercially as a jute substitute (Morton 1987). *H. sabdariffa* var. *sabdariffa* comprised dwarf, bushy plants and has been categorized into four groups, *albus, intermedius, ruber* and *bhagalpuriensis,* based on pigmentation patterns in various plant parts (Howard and Howard 1911).

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Hibiscus schizopetalus

Scientific Name

***Hibiscus schizopetalus* (Dyer ex Masters) J. D. Hooker**

Synonyms

Hibiscus rosa-sinensis Linnaeus var. *schizopetalus* Dyer ex Masters

Family

Malavaceae

Common/English Names

Chinese Lantern, Coral Hibiscus, East-African Hibiscus, Fringed Rose Mallow, Fringed Hibiscus, Japanese Hibiscus, Japanese Lantern, Pagoda Flower, Schizopetalus, Skeleton Hibiscus, Waltzing Ladies.

Vernacular Names

Brazil: Lanterninha (Portuguese)
Chinese: Diao Deng Fu Sang, Diao-Deng-Hua, Tiao-Tneh-Hua, Deng-Long-Hua, Teng Lung Hua, Lie Ban Zhu Jin, Lieh-Pan-Chu-Chin
Columbia: Arana, Canastilla (Choco), Waitutu (Cuna)
Cook Islands: Kaute Verevere, Kaute Very (Maori)
German: Hängender Roseneibisch
Hawaiian: Aloalo Ko'ako'a, Kulapepeiao
India: Jhumko Jaba (Bengali)
Indonesian: Kembang Sepatu Sungsang
Japanese: Aka-Bana, Butusouge, Furin-Busoge, Husso-Kwa
Malaysia: Tanglong (Malay)
Naruan: Dorot
Nukuoro: Keleunleng, Pern Tikitik, Ros
Panama: Paraguita China
Pohnpeian: Kaanth, Keleun Wai, Koloun Wai
Samoan: 'Aute, Aute, 'Aute, 'Aute Tipi, 'Aute Tipi
Thai: Phu Ra Hong
Tongarevan: Kaute

Origin/Distribution

The species is a native of tropical East Africa—Kenya, Tanzania and Mozambique.

Agroecology

A tropical species but will also grow in the sub-tropics. It does well in full sun or light shade. The plant thrives in well-drained, moist sandy loam soil, rich in organic matter. The plant is intolerant of drought.

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Edible Plant Parts and Uses

The flower petals are edible. Flowers have been used in food in Taiwan (Hu 2005).

Botany

A glabrous, evergreen to semi-deciduous, erect shrub, 3 m high with slender branchlets. Stipules subulate, 2 mm, usually caducous; petiole 1–2 cm. Leaves elliptic or oblong, 4–7 cm by 1.5–4 cm, acute or shortly acuminate apex, obtuse base, basal half of margin entire, distal half serrate (Plate 1). Flowers solitary, axillary on upper branchlets, pendulous and elegant on 10–14 cm long pedicel. Epicalyx 8, small and ciliate; calyx spatulate, tubular, shallowly 5-toothed; petals 5, red or pink, 5 cm, deeply pinnatifid, strongly reflexed; staminal tube 9–10 cm long, slender, glabrous; style 5-fid and glabrous (Plate 1). Capsule oblong-cylindrical, 4 cm long by 1 cm across, glabrous. Seeds smooth.

Nutritive/Medicinal Properties

No published reports are available on the nutritive value of the flowers.

Two triterpene esters, named 22-hydroxytaraxeryl acetate 1 and 22-hydroxytaraxeryl-*cis-p*-coumarate 2, were isolated from the leaves of *Hibiscus schizopetalus* (Jose and Vijayan 2006). Cyanidin-3-sambusophoroside was found as the major anthocyanin found in *H. schizopetalus* flowers (Lowry 1976).

Some pharmacological properties of the leaves and flowers reported include the following.

Antioxidant Activity

Total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) of *H. schizopetalus* leaves were 336 mg gallic acid equivalent(GAE)/100 g and 94 mg ascorbic acid/100 g, respectively (Wong et al. 2010).

Plate 1 Leaves and pendent flowers

Leaves of *H. schizopetalus*, *H. sabdariffa* and *H. rosa-sinensis* had better FIC (ferrous iron chelating) ability than those of *H. mutabilis*, *H. tiliaceus* and *H. taiwanensis.* Leaves of species with higher TPC and AEAC had lower FIC ability for *H. tiliaceus* and *H. mutabilis* and *vice versa* for *H. schizopetalus* and *H. rosa-sinensis*. The results suggested the presence of compounds in leaves of *H. schizopetalus* and *H. rosa-sinensis* with relatively weak radical scavenging activity but good metal chelating ability that could prevent the generation of hydroxyl radicals via Fenton's reaction. Flowers of *H. schizopetalus* had 516 mg GAE/100 g total phenolic content (TPC), 192 mg cyanidin-3-glucoside equivalent (CGE)/100 g total anthocyanin (TAC), 520 mg AA/100 g ascorbic acid equivalent antioxidant capacity (AEAC) and 3.0 mg GAE/g ferric reducing power (FRP). Based on TPC, ranking was *H. tiliaceus* > *H. rosa-sinensis* > *H. taiwanensis* ~ *H. schizopetalus* ~ *H. mutabilis* > *H. sabdariffa.* The red flowers of *H. rosa-sinensis* and *H. schizopetalus*, which yielded the highest TAC, displayed high FIC ability and lipid peroxidation inhibition (LPI) activity (Wong et al. 2009, 2010). Species with low TAC such as *H. mutabilis* and *H. sabdariffa* displayed low or no FIC ability and LPI activity. TAC appeared to be positively correlated with FIC ability and LPI activity in flowers of *Hibiscus* species.

Anti-inflammatory Activity

The chloroform, methanol and petroleum ether extracts of *H. schizopetalus* leaf exhibited significant anti-inflammatory activity as evaluated by the carrageenan-induced paw oedema assay in Wistar albino rats (Pal et al. 2011). The methanol extract was found to be the most potent followed by the chloroform and petroleum ether extracts, respectively.

Analgesic Activity

The oral administration of the methanol flower and methanol leaf extract of *H. schizopetalus* (50, 100, 200 mg/kg, body weight) to mice caused significant prolongation of the reaction time after 30 min administration tail-flick test when compared to the control group (Zahid et al. 2012). The prolongation in the reaction time indicated central analgesic activity of the extracts. In the tail immersion test, both extracts produced significant dose-dependent analgesic effect at all the tested doses when compared to the control group.

Antipyretic Activity

The subcutaneous injection of brewer's yeast to mice markedly increased the rectal temperature after 19 h of administration (Zahid et al. 2012). The oral administration of methanol flower extract of H. *schizopetalus* (50, 100, 200 mg/kg, body weight) significantly reversed yeast-induced hyperthermia in a non-dose-dependent manner, while a dose-dependent antipyretic response was observed with the leaf extract when compared with the standard drug aspirin (100 mg/kg, body weight).

Traditional Medicinal Uses

In Malaysia, the Malays do not distinguish it from *H. rosa-sinensis* since it hybridizes freely with the latter and so are liable to use it medicinally as for *H. rosa-sinensis* (Burkill 1966). The flower has been used as eye medicine by the Cuna Indians, and the flower infusion is used to treat cold and cough in Columbia (Duke 2012).

Other Uses

The species is widely cultivated as an ornamental plant in house gardens and parks. The Choco Indians in Columbia use the flowers for garlands.

Comments

The plant is readily propagated by stem cuttings.

Selected References

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Hibiscus syriacus

Scientific Name

***Hibiscus syriacus* L.**

Synonyms

Althaea frutex Mill., *Hibiscus acerifolius* Salisb., *Hibiscus floridus* Salisb., *Hibiscus rhombifolius* Cav., *Hibiscus syriacus* var. *micranthus* Y.N. Lee & K.B. Yim, *Ketmia arborea* Moench, *Ketmia syriaca* (L.) Scop., *Ketmia syrorum* Medik

Family

Malvaceae

Common/English Names

Althaea, Bush Hollyhock, Common Hibiscus, Mallow, Rose Althea, Rose Mallow, Rose Althea, Rose Of Sharon, Rosemallow, Shrub Althea, Shrubby Althaea, St Joseph's Rod, Syrian Hibiscus, Syrian Ketmia, Syrian Rose

Vernacular Names

Brazil: Altéia-Arbustiva, Hibisco Hibisco-Colunar, Hibisco-Da-Síria, Rosa-De-Sharão (Portuguese)
Chinese: Mu Jin, Mu Jin Hua
Czech: Ibišek Syrský
Danish: Havehibiscus, Syrisk Rose, Syrisk Hibiskus
Dutch: Althaeastruik
Estonia: Süüria Hibisk
French: Althéa, Hibiscus De Syrie, Ketmie Des Jardins, Ketmie De Syrie, Mauve De Syrie, Mauve En Arbre
German: Echter Roseneibisch, Garten-Hibiscus, Roseneibisch, Syrischer Eibisch, Syrischer Rosen-Eibisch
Italian: Ibico Syraicus
Japanese: Hachisu, Mokukinka, Mukuge
Korean: Moo Goong Hwa, Mugunghwa
Mexico: Flor De Una Hora, Tulipán
Philippines: Gumamelang Asul (Tagalog)
Polish: Hibiskus, Hibiskus Syryjski, Ketmia Syryjska
Slovaščina: Oslez
Slovencina: Ibištek Sýrsky
Spanish: Hibisco, Rosa De Siria
Swedish: Frilandshibisku
Thai: Chaba Chin

Origin/Distribution

Despite its scientific name, this *Hibiscus* species is a native of China, and it is found wild in Anhui, Guangdong, Guangxi, Jiangsu, Sichuan, Taiwan, Yunnan and Zhejiang; it is cultivated since ancient times in Fujian, Guizhou, Hainan, Hebei, Henan, Hubei, Hunan, Jiangxi, Shaanxi, Shandong and Xizang (Ya et al. 2007). It was introduced into Korea, Japan and Asia Minor and from the latter made its way into European gardens where

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it has naturalized in southern Europe. Today, it is popularly cultivated in Korea, Japan and in other warm temperate and subtropical areas around the world as ornamental plants and hedges. The plant has also been grown in Malaysia but is more suited for the higher cooler altitude.

Agroecology

In its native range, the plant is found on mountain slopes, sea cliffs, hillsides, along streams and roadsides and is also extensively cultivated below 1,200 m elevation. The plant is hardy, and it withstands brief light frost, high temperatures and brief period of drought. The plant is not fastidious of soil types but thrives best in free-draining, near neutral pH loams. It does best in full sun but will tolerate light shade.

Edible Plant Parts and Uses

Young leaves and flowers are edible raw or cooked (Hedrick 1972; Kunkel 1984; Tanaka 1976; Reid 1977; Hu 2005; Facciola 1990; Deane 2007–2012). In China, the leaves are also used as a substitute for tea, and the petals of a white cultivar are eaten as vegetable. In Korea, since ancient times, the leaves are brewed for a tisane and the flowers eaten. Flowers have commercialization potential of flower teas, vinaigrettes, bulk dried petals and concentrated edible petal pigment extracts. (Puckhaber et al. 2002; Bost 2004)

Botany

A deciduous, erect shrub, 2–4 m high with smooth grey-brown bark. Stipules filiform-subulate and pilose; petioles 0.5–2.5 cm long. Leaf alternate, simple, rhomboid to triangular-ovate or broadly lanceolate, variously 3-lobed, 3–10×2–4 cm, papery, puberulent abaxially, glabrous adaxially, green above, paler green below, veins 3–5 palmate veins, margin irregularly serrated, apex obtuse to subacute, base cuneate (Plates 1 and 2).

Plate 1 Flowers, buds and leaves

Plate 2 Deltoid-rhomboid leaves with serrated margins

Flowers large, attractive, hermaphrodite, solitary, axillary on upper branches, on 4–14 mm puberulent pedicels. Epicalyx 6–8 free, filiform lobes; calyx campanulate with 5 puberulent deltoid lobes, corolla 5–6 cm across, campanulate, with 5 obovate pilose lobes, 3.5–4.5 cm, blue-purple, violet, white, pink or reddish, sometimes with darker centre; staminal column 3 cm; style glabrous (Plates 2 and 3). Capsule ovoid-globose, 12 mm across, densely puberulent. Seeds reinform with yellowish white hairs.

Nutritive/Medicinal Properties

Phytochemicals in Flowers

Ten carotenoids were found in the leaf, bud and flower of *H. syriacus* (Hanny et al. 1972). Most abundant in buds and leaves were β-carotene and

Plate 3 Close-up of flower

lutein while lutein 5,6 epoxide predominated in the flowers. Carotene hydrocarbon comprised 19 % of total carotenoids in the flowers, with 37 % in the buds and 33 % in the leaves. *H. syriacus* contained lower percentage of the colourless phytoene precursors to the carotenoids than cotton. Main pigments contributing to the colour of *H. syriacus* petals were identified by Egolf and Santamour (1975) as 3-glucosides of cyaniding, petunidin, delphinidin and malvidin. Three carotenoids were found in were present in *H. syriacus* cryptoxanthin, antheraxanthin and chrysanthemaxanthine. Methanolic formic acid extract of *H. syriacus* petals yielded 3-*O*-malonylglucosides of delphinidin, cyanidin, pentunidin, pelargonidin, peonidin and malvidin (Kim et al. 1989a). Predominant pigments in petals of *H. syriacus* were found to be cyanidin 3-glucoside and 3-malonylglucoside (Kim et al. 1989b). Kim and Fujieda (1991) found the flower of *H. syriacus* to contain peonidin and pelargonidin 3 glucosides and unidentified labile anthocyanins determined as malonated pigments of six common anthocyanidin 3 glucosides. Flavonoid aglycones found in the flowers (mg per g fresh tissues) of *H. syriacus* 'purple red' and *H. syriacus* 'the blues' were total pigments 15 mg, 10 mg; kaempferol 3 mg, 6 mg; delphinidin 3 mg, 1 mg; cyanidin 1 mg,1 mg; petunidin 3 mg,1 mg; and malvidin 15 mg, 10 mg, respectively (Puckhaber et al. 2002).

Good recovery rates of over 90 % for aliphatic polyamines (PAs) and 76–97 % for 1-aminocyclopropane-1-carboxylic acid (ACC) were obtained from *H. syriacus* petal, sepal, ovary and style with stigma (+stamen) collected at two different stages (flower opening and flower senescence showing complete petal in-rolling) (Seo et al. 2007). Both ACC and ACC-conjugate, which were generally associated with tissue senescence, were consistently detected in all organs even immediately after flower opening, but their concentrations, especially that of the ACC-conjugate in the ovary, greatly increased in the senescent flowers. As regards the free PA levels, a high concentration of spermidine was found in the ovary, and its level was maintained even when the petals wilted. PA-conjugates bound to small molecules decreased in the ovaries of senescent flowers, while the PA-conjugates bound to macromolecules remained very low in all organs at the two different flower stages.

A representative mucilage, named Hibiscus-mucilage SF, was isolated from the white flower buds of *Hibiscus syriacus* (Tomoda and Ichikawa 1987). It was mainly composed of partially acetylated acidic polysaccharide of molecular weight 1,050,000 and is composed of L-rhamnose : D-galactose: D-galacturonic acid : D-glucuronic acid in the molar ratio of 36:36:33:22.

The mature pollen grains of *Magnolia grandiflora* and *Hibiscus syriacus* were found to contain sporopollenin (Kawase and Takahashi 1996). The following organosilicon compounds were extracted from sporopollenin after oxidative degradation: 1, 1, 1, 5, 7, 7, 7-heptamethyl-3,3-bis(trimethylsilox)tetrasiloxane and 1, 1, 1, 3, 5, 7, 7, 7-octamethyl-3, 3- bis(trimethylsiloxy) tetrasiloxane. 1,2-benzendicarboxylic acid butyl 2-ethylhexyl ester was also detected.

Phytochemicals in Seeds

The seed oil of *Hibiscus syriacus* was found to contain 16.87 % of the cyclopropenoid acids, malvalic acids and sterculic acids: 0.31 % C:14 (myristic), 18.32 % C16:0 (palmitic acid), 1.25 % C16:1, 2.74 % C18:0, 18.90 % C18:1, 40.59 % C18:2, 1.83 % C18:3 (Chernenko et al. 1973). The only monocarboxylic acid found was pelargonic. The unsaponifiable matter of the seed oil was found to comprise 0.27 % free sterol

(β-sitosterol and campesterol) and 0.24 % bound sterols and β-tocopherol and δ-tocopherol (Chernenko and Umarov 1974). Alpha-carotene, β-carotene and 3,4-dihydroxy-β-carotene were also found in the oil. Alpha-carotene and β-carotene were also found in the leaves and root of the plant (Hanny et al., 1972). Among the 65 identified components of the essential oil of *Hibiscus syriacus*, a hitherto unknown compound phenethyl-3-methylbut-2-enyl ether or 2-methyl-7-phenyl-5-oxahept-2-ene was found (Andreev and Bibicheva, 1985.)

Phytochemicals in Leaves

A representative mucilage, named Hibiscus-mucilage SF, was isolated from the leaves of *Hibiscus syriacus* (Shimizu et al. 1986). The following flavonoids were isolated from the leaves: taxifolin 3-*O*-B-D-glucopyranoside; herbacetin 7-B-D-glucopyranoside; kaempferol 3-a-L-arbinoside 7-a-L-rhamnoside; saponaretin; and saponarin (saponaretin 7-*O*-B-D-glucopyranoside) (Bandyukova and Ligai, 1990). *Hibiscus syriacus* was found to contain Ty3-gypsy-like elements (Jeung et al. 2005). The sequence heterogeneity and ubiquity of the Ty3-gypsy-like elements in *H. syriacus* genomes could provide reliable DNA markers for line identification as well for the analysis of genetic diversity in *H. syriacus*. The contents of tyrosine, phenylalanine and tryptophan in *Hibiscus syriacus* leaves determined by alternating penalty trilinear decomposition algorithm coupled with excitation-emission matrix fluorometry afforded coefficients of variation of 0.84, 0.36 and 1.59 % and recoveries of 101.0–92.7 %, 106.5–93.0 % and 103.0–95.0 %, respectively, for the three amino acids (Xiao et al. 2007).

Phytochemicals in Stems and Roots

Two compounds oil A and B, with antifungal activity, were isolated from *H. syriacus* bark (Yokota et al. 1978). Oil A was a mixture of lauric, myristic and palmitic acid, and B was canthin-6-one (6H-indolo [3,2,1-d, e] [1,5] naphthyridin-6-one).

Seven constituents (I–VII) were isolated from the bark of *Hibiscus syriacus* and identified as nonanedioic acid (I), suberic acid (II), 1-octarcosanol (III), beta-sitosterol (IV), 1,22-docosanediol (V), betulin (VI) and erythrotriol (VII) (Zhang et al. 1993). Three new naphthalenes, designated as syriacusins A–C, were isolated from the root bark of *Hibiscus syriacus* and identified as 2,7-dihydroxy-6-methyl-8-methoxy-1-naphthalenecarbaldehyde;2-hydroxy-6-hydroxymethyl-7,8-dimethoxy-1-naphthalenecarbaldehyde; and 1-carboxy-2,8-dihydroxy-6-methyl-7-methoxynaphthalenecarbolactone (1 → 8), respectively (Yoo et al. 1998). Cyclic peptides designated as hibispeptin A and designated as hibispeptin B isolated from the root bark of *Hibiscus syriacus* and their structures determined as *cyclo*[-Ahabpa(-pyro-Glu)-Pro-Leu-Phe-] and *cyclo*[-Ahabpa(-pyro-Glu)-Pro-Leu-Leu-], respectively. Hibispeptin B possessed a unique amino acid unit assigned as 2-amino-3-(2-hydroxy-5-aminoacetylbenzyl)pentanoic acid (Ahabpa) in cyclic core (Yun et al. 1998a, b). A new lignan named hibiscuside, (+)-pinoresinol 4-*O*-[β-glucopyranosyl (1 → 2)-α-rhamnoside], and a known lignan syringaresinol were isolated from the root bark of *Hibiscus syriacus* together with two feruloyltyramines (3,4) *E*-*N*-feruloyl tyramine and *Z*-*N*-feruloyl tyramine and three known isoflavonoids 6″-*O*-acetyldaidzin, 6″-*O*-acetylgenistin and 3-hydroxydaidzein (Lee et al. 1999). Two new triterpene caffeates were isolated from the root bark of *Hibiscus syriacus* and determined as 3β,23,28-trihydroxy-12-oleanene 23-caffeate and 3β,23,28-trihydroxy-12-oleanene 3β-caffeate (Yun et al. 1999). A previously undescribed coumarin and a new coumarino-lignan, together with the known compounds scopoletin and cleomiscosins A, C and D were isolated from the root bark of *Hibiscus syriacus* (Yun et al. 2001). Hydroxyhibiscone A, a new furanosesquiterpenoid, together with hibiscone D, was isolated from the root bark of *Hibiscus syriacus* (Ryoo et al. 2010). Nonanoic acid was isolated from the roots (Jang et al. 2012).

Antioxidant Activity

Three new naphthalenes, designated as syriacusins A–C, isolated from the root bark of *Hibiscus syriacus,* inhibited lipid peroxidation with IC_{50} values of 0.54, 5.90 and 1.02 μg/mL, respectively (Yoo et al. 1998). Among several phenolic compounds isolated from the root bark, 6″-*O*-acetyldaidzin, 6″-*O*-acetylgenistin and 3-hydroxydaidzein with IC_{50} values of 8.2, 10.6 and 4.1 μM, respectively, significantly inhibited lipid peroxidation in rat liver microsomes. Hibiscuside, *E-N*-feruloyl tyramines and *Z-N-feruloyl* tyramines exhibited moderate antioxidant activity (Lee et al. 1999). Two new triterpene caffeates 3β,23,28-trihydroxy-12-oleanene 23-caffeate and 3β,23,28-trihydroxy-12-oleanene 3β-caffeate isolated from the root bark of *Hibiscus syriacus* showed lipid peroxidation activity (Yun et al. 1999). The coumarin analogue and scopoletin isolated from the root bark inhibited monoamine oxidase with moderate IC_{50} values (Yun et al. 2001). The new coumarino-lignan and cleomiscosin C showed lipid peroxidation inhibitory activity comparable to vitamin E. The extracts of *Hibiscus syriacus* stems and roots heat-treated at 100 °C for 24 h were more effective than those of non-treated *Hibiscus syriacus* in reducing the stable free radical 1,1-dipheny 1-2-picrylhydrazyl (DPPH) (Kwon et al. 2003).

Anticancer Activity

Syriacusin A showed cytotoxicity against some human cancer cell lines with an ED_{50} of 1.5–2.4 μg/mL (Yoo et al. 1998). Two new triterpene caffeates 3β,23,28-trihydroxy-12-oleanene 23-caffeate and 3β,23,28-trihydroxy-12-oleanene 3β-caffeate isolated from the root bark showed significant cytotoxicity against a panel of human cancer cell lines (Yun et al. 1999).

The root bark of *Hibiscus syriacus* was found to have antiproliferative effects on human lung cancer cells (Cheng et al. 2008). The acetone root bark extract exhibited a higher cytotoxic effect on lung cancer cells than its methanol extract or water extract. The IC_{50} values of on A549 (adenocarcinoma), H209 (squamous cell carcinoma) or H661 (large cell carcinoma) lung cancer cells ranged from 14 to 22 μg/mL after 48 h of treatment. After 48 h of exposure, the extract (15 μg/mL) induced A549 cell apoptosis to 48 % of the control. The extract appeared to suppress the expression of caspase-p53 and apoptosis-induced factor. The results of in vivo study showed the extract suppressed growth in A549 subcutaneous xenograft tumours.

Antimicrobial Activity

The methanolic root extract of *H. syriacus* Ggoma exhibited four times higher antifungal activity than its parent type against *Trichophyton mentagrophytes* (Jang et al. 2012). The antifungal principle was identified as nonanoic acid.

Wound Healing Activity

Both 5 and 10 % ointment concentrations of the methanol extract of *H. syriacus* flower showed significant responses in both the wound types tested when compared with the control group (Umachigi et al. 2010). The effect produced by the extract ointment, in terms of wound contracting ability, wound closure time, regeneration of tissues at wound site, tensile strength of the wound and histopathological characteristics, was comparable to those of a standard drug nitrofurazone ointment. The results showed *H. syriacus* flower extract had wound healing properties and supported its use in folkloric medicine in India.

Anti-aging Activity

Hydroxyhibiscone A and hibiscone D isolated from the root bark were found to possess significant anti-aging properties on the human neutrophil elastase (HNE) assay, exhibiting HNE inhibitory activities with IC_{50} values of 5.2 and 4.6 μM, respectively (Ryoo et al. 2010).

Antiulcer Activity

H. syriacus was one of 15 plants whose methanol and aqueous extracts exhibited antiulcerogenic activity when assayed by the indomethacin-, aspirin- and the water-immersion stress-induced ulcer models (Muto et al. 1994).

Traditional Medicinal Uses

A decoction or infusion of the flowers is used as a diuretic, ophthalmic and stomachic (Burkill 1966; Stuart 1979; Duke and Ayensu 1985; Fogarty 1990), for treatment of itches and other skin aliments (Burkill 1966), for dizziness, for bloody stools with much gas (Fogarty 1990) and for dysentery in Indo China (Burkill 1966). The leaves are also used as a diuretic, expectorant and stomachic (Chopra et al. 1986; Duke and Ayensu 1985). A decoction of the root bark is antiphlogistic, demulcent, emollient, febrifuge, haemostatic and vermifuge and used as a remedy for diarrhoea, dysentery, abdominal pain, leucorrhoea, dysmenorrhoea and dermaphytosis (Duke and Ayensu 1985, Chopra et al. 1986; Fogarty 1990). In Korea, the roots have been used for treatment of fungal diseases such as tinea pedis (athlete's foot) (Jang et al. 2012). In Japan, white flower bud is used as an oriental drug *Mokukinka* as a demulcent and antidiarrhoeic (Tomoda and Ichikawa 1987).

Other Uses

Rose of Sharon is grown mainly as an ornamental landscape or hedge plant. It is also cultivated as garden and medicinal plant. The leafy, flowering shoots make interesting vase cuttings remaining green for a long time, and the flowers may open from more mature buds. A low quality fibre is obtained from the stems used for making cordage and paper. A hair shampoo is made from the leaves. A blue dye is obtained from the flowers and an oil is obtained from the seeds.

Comments

Hibiscus syriacus is the national flower of South Korea and its Korean appellation *Mugunghwa* means immortality.

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Hibiscus taiwanensis

Scientific Name

***Hibiscus taiwanensis* S.Y. Hu**

Synonyms

No synonym recorded

Family

Malvaceae

Common/English Names

Dog's Head Lotus, Formosan Hibiscus, Mountain Cotton Rose, Taiwan Cotton Rose, Taiwan Hibiscus, Thousand Faces Beauty, Thousand Pretty Women, Sour Cotton Rose

Vernacular Names

Chinese: Tai Wan Fu Rong
Indonesia: Viluwaq

Origin/Distribution

The species is indigenous to Taiwan.

Agroecology

The ecological distribution area of *Hibiscus taiwanensis* is anywhere below the altitude of 1,200 m all over Taiwan. It can also be found in Lanyu. The plant has been distributed elsewhere in Southeast Asia.

Edible Plant Parts and Uses

Its blossom is not only attractive/decorative but also edible. It is delicious whether mixed in salad, cooked or fried (Anonymous 2012).

Botany

A deciduous tree or shrub, erect, 3–8 m high, densely strigose and scabrous, with bristlelike stiff hairs, not stellate. Leaves alternate, suborbicular, papery, lobes 3–5, broadly deltoid, serrate or dentate on 14–17 cm long petioles (Plate 1). Flowers solitary, axillary on upper branches on 11–13 cm pedicels; epicalyx lobes 8, filiform, 8–12 × 1.5–2 mm, stellate puberulent, apex acute; calyx campanulate, 5-lobed, lobes deltoid, 10 mm long, 8 mm wide, acute at apex, stellate- tomentose; corolla white or creamy-yellow, with deep brown or purple centre, broadly subcampanulate, 6–9 cm across petals nearly orbicular, connate at base, villous, claw bearded (Plates 1 and 2). Capsules globose, 2 cm across, pubescent.

T.K. Lim, *Edible Medicinal and Non Medicinal Plants: Volume 8, Flowers*,
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Plate 1 Flower and leaves

Plate 2 Close view of flower

Nutritive/Medicinal Properties

Three phenylpropanoid esters, (7S,8S)-demethylcarolignan E and hibiscuwanin A and hibiscuwanin B, were isolated from the stem in addition to eight known ones (Wu et al. 2004). Fifty-six compound were isolated from *H. taiwanensis* stems and identified as hibicuslide A; hibicuslide B; hibicuslide C; hibicutaiwanin; hibicusin; hibicuwanin A; hibicuwanin B; (7*S*,8*S*)-demethylcarolignanE;*threo*-carolignanE;*erythro*-carolignan E; *threo*-1-*C*-syringylglycerol; 9,9′-*O*-feruloyl-(−)-secoisolaricinresinol; dihydro-coni feryl alcohol; boehmenan, (−)-syringaresinol; cleomiscosin A; cleomiscosin C; mansonone E; mansonone H; hibiscone C; isohemigossypol-1-methyl ether; gossyvertin; *N-trans*-feruloylty ramine; *N-cis*-feruloyltyramine; 2-(2-hydroxy tricosanoylamino)-1,3,4-hexadecanetriol; myricerol; myriceric acid A; myriceric acid B; myriceric acid C; uncarinic acid A; uncarinic acid B; 3-oxo-olean-12-en-28-oic acid; scopoletin; scoparone; 4-hydroxy-benzoic acid; ferulic acid; methyl *trans*-ferulate; methyl *cis*-ferulate; lignocerylferulate; caffeic acid; methyl caffeate; hexacosanyl caffeate; vanillin; vanillic acid; methyl vanillate; benzoic acid; *p*-coumaric acid; methyl *p*-coumarate; *p*-formylbenzoic acid; methyl *p*-formylbenzoate; syringic acid; syringaldehyde; sinapinaldehyde; ficusol; a mixture of β-sitosterol and stigmasterol; and β-sitosteryl-β-D-glucoside (Wu et al. 2005).

Antioxidant Activity

Total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) values for methanol leaf extract of *H. taiwanensis* were 403 mg GAE (gallic acid equivalent)/100 g and 233 mg AA(ascorbic acid)/100 g, respectively (Wong et al. 2010). Based on TPC and AEAC values, antioxidant ranking was *H. tiliaceus* > *H. mutabilis* > *H. sabdariffa* > *H. taiwanensis* > *H. schizopetalus* ~ *H. rosa-sinensis*. Leaves of *H. schizopetalus*, *H. sabdariffa* and *H. rosa-sinensis* had better FIC (ferrous ion chelating) ability than those of *H. mutabilis*, *H. tiliaceus* and *H. taiwanensis*. TPC, TAC (total anthocyanin content), AEAC and FRP (ferric reducing power) values of flowers of *Hibiscus taiwanensis* were 580 mg GAE/100 g, 92 mg CGE (cyanidin-3-glucoside equivalent)/100 g,

761 mg AA/100 g and 3.6 mg GAE/g, respectively. Based on TPC in flowers, ranking was *H. tiliaceus* > *H. rosa-sinensis* > *H. taiwanensis* ~ *H. schizopetalus* ~ *H. mutabilis* > *H. sabdariffa.*

Anticancer Activity

In cytotoxicity evaluation of the compounds from the stem, 9,9′-*O*-feruloyl-(−)-secoisolaricinresinol displayed strong cytotoxic activity against human lung carcinoma and breast carcinoma cell lines in an in vitro cytotoxicity assay with EC_{50} values of 1.8 and 3.9 μg/mL, respectively (Wu et al. 2004;2005). The triterpenoids, myriceric acid C and uncarinic acid A, exhibited marginal cytotoxicity.

Antiviral Activity

Of the compounds isolated from the stem, the naphthoquinone mansonone H and triterpenoid uncarinic acid A inhibited HIV replication in H9 lymphocyte cells with EC_{50} values of 16.58 and 1.53 mg/mL, and their therapeutic indices (IC_{50}/EC_{50}) were 1.50 and 12.95, respectively (Wu et al. 2005).

Antidiabetic Activity

Studies suggested that *Hibiscus taiwanensis* had a hypoglycaemic activity by increasing glucose utilization and insulin sensitivity to lower plasma glucose in streptozotocin-induced diabetic rats (Huang et al. 2013). The bioactive compound syringaldehyde was identified. Syringaldehyde exhibited antihyperglycaemic activity in a dose-dependent manner in streptozotocin-induced diabetic rats (Huang et al. 2012). Syringaldehyde was also found to increase glucose utilization and insulin sensitivity to lower plasma glucose in diabetic rats. Stems of *Hibiscus taiwanensis* were more effective than other parts to decrease the plasma glucose in a dose-dependent manner in streptozotocin-induced diabetic rats (Wang et al. 2013). Oral administration of the extract three times daily for 3 days into STZ-diabetic rats increased the sensitivity to exogenous insulin showing an increase in insulin sensitivity and produced a marked reduction of phosphoenolpyruvate carboxykinase expression in liver and an increased expression of glucose transporter subtype 4 (GLUT 4) in skeletal muscle.

Anti-inflammatory Activity

The aqueous extract of *Hibiscus taiwanensis* was found to have anti-inflammatory activity in lipopolysaccharide (LPS)-stimulated mouse macrophage RAW264.7 cells and carrageenan-induced mouse paw oedema model (Liu et al. 2012). When RAW264.7 macrophages were treated with the extract together with LPS, a concentration-dependent inhibition of nitric oxide (NO), tumour necrosis factor (TNF-α) and prostaglandin E2 (PGE(2)) level productions were found. In the in vivo test, the extract decreased mouse paw oedema at the 4th and the 5th hour after administration, and it increased the activities of catalase, superoxide dismutase and glutathione peroxidase in the paw tissue. The extract also decreased NO, TNF-α and PGE2 levels on the serum level at the 5th hour after the carrageenan injection.

Traditional Medicinal Uses

The stem and root of *H. taiwanensis* have been used as anti-inflammatory, analgesic, antifungal, antipyretic and anthelmintic agents in traditional Chinese medicine (Gan 1965). The whole plant can clear lungs and cease coughing, cool blood and resolve toxin. The plant is used to treat pulmonary heat-induced coughing, ulcers and pyrogenic infections (Huang 2009).

Other Uses

The plant is cultivated as an ornamental. The wood is white, light textured and soft and is used for making clogs. The stem fibres are used for ropes for hiking and camping.

Comments

The plant is propagated from seeds or stem cuttings.

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Hibiscus tiliaceus

Scientific Name

***Hibiscus tiliaceus* L.**

Synonyms

Hibiscus boninensis Nakai, *Hibiscus tiliaceus* var. *abutiloides* (Willd.) Hochr., *Hibiscus tiliaceus* var. *heterophyllus* Nakai, *Hibiscus tiliaceus* var. *tortuosus* (Roxb.) Mast., *Hibiscus tiliifolius* Salisb., *Hibiscus tortuosus* Roxb., *Pariti boninense* (Nakai) Nakai, *Pariti tiliaceum* (L.) A. Juss., *Pariti tiliaceum* var. *heterophyllum* (Nakai) Nakai, *Paritium abutiloides* (Willd.) G. Don, *Paritium elatum* var. *abutiloides* (Willd.) Griseb., *Paritium tiliaceum* (L.) Wight & Arn., *Paritium tiliaceum* (L.) A. Juss.

Family

Malvaceae

Common/English Names

Beach Hibiscus, Bladder Ketmia, Coast Hibiscus, Coastal Hibiscus, Coast Cottonwood, Coastal Cottonwood, Cottonwood Hibiscus, Green Cottonwood, Hawaiian Tree Hibiscus, Lagoon Hibiscus, Linden Hibiscus, Mahoe, Mahuat, Mountain Mahoe, Native Hibiscus, Norfolk Hibiscus, Native Rosella, Kurrajong, Sea Hibiscus, Sea Rose Mallow, Tree Hibiscus, Yellow Mallow Tree

Vernacular Names

Afrikaans: Kusvuurblom, Wildekatoenboom
Bangladesh: Bhola
Brazil: Algodão Da Praia, Guaxima-Do-Mangue (Portuguese)
Chinese: Huang Jin
Chuuk: Kilife
Cook Islands: ‘Au
Czech: Ibišek Lípovitý
Estonian: Pärnhibisk
Fiji: Vau, Vaundamu, Vaundamundamu, Vaundina, Vauleka, Vaundra
French: Bourao
French Polynesia: Purau
Guam: Pago
Hawaiian: Hau, Hau Ka‘Eka‘E
India: Pola (Hindi), Bilipatta, Kaark Bendu, Samudra Theeradatthi (Kannada), Nirparatthi, Nirparatti, Nirparuthi, Nirparutti, Paratti, Pariti, Paritti, Paroottee, Parutti, Talipparutti (Malayalam), Baelsing, Belipata, Bellipata, Belpata, Bhotee, Kharikapusi, Mothi Potaare, Varadhaa, Varanga (Marathi), Bala (Sanskrit), Attuparuthi, Nirparathi, Nirparutti, Nirpparutti, Potari (Tamil), Cherigogu, Erragogu, Ettagogu (Telugu)

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Indonesia: Waru, Waru Laut (Javanese), Baru (Malay)
Japanese: Oo-Hamaboo, Yama-Asa
Kiribati: Te Kiaiai, Te Rau
Kosrae: Lo
Laos: Hou Sua, Ta Sua
Malaysia: Akar Seregang, Baru, Baru-Baru, Baru Laut, Bebaru, Embaru, Dedap Laut, Mebaru (Malay), Kelaut, Selaut (Sakai)
Marquesas: Fau Toui, Fau Maoi
Marshall Islands: Lo
Myanmar: Thin Ban
New Caledonia: Vo, Vole
Niue: Fou
Palau: Ermall
Panama: Algondoncillo, Hibisco Marítimo, Majagua, Mahoe
Papua New Guinea: Varvar (E. New Britain), Bang (Gaikorovi, Sepik Province), Pow (Lomeoi, Manus Island), Valu (Hula, Central Province)
Philippines: Laogo (Bagobo), Majagua, Malubago, Mayambago (Bikol), Balibago, Ragindi (Bisaya), Bago (Bontok), Mayambago (Cebu Bisaya), Bauan, Marakapas (Ibanag), Malabagu (Iloko), Hanot (Ivatan), Mulabago (Maguindanao), Malibago (Panay Bisaya), Balabago, Malabago (Samar–Leyte Bisaya), Danglog, Malibago, Lambagu (Sulu), Dangliu, Malabago, Malubago (Tagalog)
Pohnpei: Kalau
Samoa: Fau
Solomon Islands: Ayiwo, Fa'Alo, Fa'Ola, Fakasu, Kwara'Ae
Spanish: Emajagua
Sri Lanka: Beli Patta (Sinhalese)
Swedish: Strandhibiskus
Tahitian: Purau
Thai: Khamin Naang Matsee (North-eastern Thailand), Po Na, Pho Thale (Bangkok), Po Fai (Central Thailand)
Tonga: Fau
Tuvalu: Fautu'u
Vanuatu: Burao, Var
Vietnamese: Tra Bụp, Bụp Tra, Tra Làm Chèo, Tra Làm Chiếu
Yap: Gaal'

Origin/Distribution

Hibiscus tiliaceus is indigenous to the tropical shores of the Pacific and Indian oceans. Today it is cultivated or naturalized throughout the tropical and subtropical regions of the world.

Agroecology

The plant occurs at elevations from sea level to 800 m in areas that receive 900–2,500 mm of mean annual rainfall in the tropics. It is common on beaches, by rivers and streams and in mangrove swamps. The plant thrives in a coastal and riparian environment but can also be found in inland areas and valleys in its native range. It is well adapted to saline and water-logged conditions. It grows well in coral sand, quart sand, marl and limestone in weakly acidic to alkaline soils (pH 5–8.5).

Edible Plant Parts and Uses

The flowers, young leaves and roots are edible (Burkill 1966; Morton 1977; Cribb and Cribb 1987; Bhargava 1983; Facciola 1990; Deane 2007–2012). The flowers are eaten as potherb or dipped in batter and fries. Tender young leaves are eaten cooked or boiled in salt water to prepare a beverage called Onge tea. Tender young leaves are also used to ferment soybean pulp into a sauce used as a substrate for tempeh starter culture. The roots are edible when cooked, and the inner bark, the cambium, can be suckled of its moisture and nutrients.

Botany

H. tiliaceus is a large, stout, open-branched shrub or a small evergreen tree with a trunk of up to 60 cm bole, pale greyish-brown or greyish-white bark and low spreading branches. It grows to a height of 3–10 m. Young branches, buds and

Plate 1 Yellow flowers, buds and leaves

Plate 2 Pink flowers and leaves

Plate 3 Close view of yellow flower

Plate 4 Close view of pink flower

flowers densely covered with short soft hairs. Leaves are spirally arranged, simple, suborbicular to broadly ovate with cordate base, 8–15 × 8–15 cm, leathery with 5–9 prominent veins from the base, olive green and glabrescent adaxially, velvety white to greyish and densely and finely tomentose abaxially (Plates 1, 2 and 3). Stipules foliaceous and caducous. Inflorescence a 1 to few-flowered cyme, terminal or axillary; peduncle 4–5 cm. Flowers large, conspicuous, bisexual and bright yellow in the early morning, turning reddish or reddish purple before dropping off in the evening (Plates 1, 2, 3 and 4). Pedicel 1–3 cm, with 1 pair of stipule-like bracteoles at base. Epicalyx lobes 7–10, connate at lower 1/3–1/2, free lobes 2–2.5 mm, triangular–acuminate with slightly rounded sinuses, puberulent. Calyx 1.5–2.5 cm, connate proximally for 1/4–1/3 of length, lobes 5, lanceolate, puberulent and persistent. Corolla yellow with dark purple centre and campanulate, 6–7.5 cm across; petals obovate, 4–4.5 cm, yellow and puberulent abaxially. Filament tube 3 cm, glabrous and light yellow. Style branches 5, slender, with glandular hairs, stigmas deep crimson purple. Capsule subglobose to ovoid, 2 cm, obscurely beaked, densely fascicled–hirsute, valves 5, woody. Seeds reniform, smooth, glabrous and black or dark brown.

Nutritive/Medicinal Properties

Flower Phytochemicals

Flowers were found to contain gossypetin, kaempferol and quercetin and 3-*O*-galactosides of kaempferol and quercetin (Subramanian and Swamy 1960), and anthers were found to contain gossypetin glucosides, gossypitrin and gossytrin (Nair et al. 1961). Cyanidin-3-glucoside was found to be the major anthocyanin

found in flowers of *H. tiliaceus* (Lowry 1976). Some saturated hydrocarbons, fatty acids, fatty acid methyl esters, phytosterols and vitamin E were identified in *H. tiliaceus* methanol flower extracts (Melecchi et al. 2006).

Fruit Phytochemicals

Gossypol, mansonones D and F, gossypetin glycoside, hibiscones and hibiscoquinones A and D were found in the fruit (Subramanian and Nair 1973).

Leaf Phytochemicals

In *H. tiliaceus* leaves, nicotinamide was converted to nicotinic acid and utilized for trigonelline (N-methylnicotinic acid) synthesis (Ashihara et al. 2012). Fifty-four compounds were identified from the volatile oil of *H. tiliaceus* leaves; the major compounds were as follows: pyrrole (6.34 %), furan (9.78 %), phenol (19.32 %), aldehyde ketone (25.59 %), alcohol(15.85 %) and indole (4.06 %) (Li et al. 2011). Thirteen compounds were identified from the fatty acids of the leaves, which contained abundant hexadecanoic acid (30.11 %) and octadecadienoic acid (10.11 % of fatty acids). Fourteen compounds were isolated from the twigs and leaves of *Hibiscus tiliaceus* and identified as friedelin, β-sitosterol, vanillin, syriacusin A, hibiscolactone, scopoletin, cleomiscosin C, fumaric acid, kaempferol, quercetin, daucosterol, azelaic acid, succinic acid and rutin (Zhang et al. 2012).

Stem/Bark Phytochemicals

The heartwood was found to contain sesquiterpenoid ketones, hibiscones A–D, and *O*-naphthoquinones, hibiscoquinones A–D and lapachol, and the roots (from Brazil) contained gossypol and mansonones D and F (Ali et al. 1980). Gmelofuran was the other name for the furanodiketone, hibiscone C (Fereira et al. 1980). A coumarin, hibiscusin, and an amide, hibiscusamide, together with 11 known compounds including vanillic acid, *p*-hydroxybenzoic acid, syringic acid, *p*-hydroxybenzaldehyde, scopoletin, *N-trans*-feruloyltyramine, *N-cis*-feruloyltyramine, a mixture of β-sitosterol and stigmasterol and a mixture of β-sitostenone and stigmasta-4,22-dien-3-one were isolated from the stem wood of *Hibiscus tiliaceus* (Chen et al. 2006). From the stem and bark, a friedelane-type triterpene named 27-oic-3-oxo-28-friedelanoic acid together with eight known triterpenoids involving five friedelane-type derivatives was isolated (Li et al. 2006). Six friedelane-type triterpenoids were isolated from the bark of *Hibiscus tiliaceus* collected from Hainan province, and nine oxygenated sesquiterpenoids (mansonones) were isolated from the heartwood (Zhang 2013).

Unidentified Plant Part Phytochemicals

Contrary to earlier claim, studies found that *H. tiliaceus*, *Abelmoschus esculentus* and *H. sabdariffa* did not contain gossypol (Jaroszewski et al. 1992). Eleven compounds were isolated from *H. tiliaceus*: coniferaldehyde; methyl 3,4-dihydroxybonate; pinoresinol; syringaresinol; gramrione; astragalin; phytol; cholest-5-ene-3β,7α-diol; cholest-5-ene-3β,7β-diol; cholesterol; and β-daucosterol (Feng et al. 2008b). Three new triterpenoids with the rarely occurring nigrum skeleton, namely, (20*E*)-22-hydroxynigrum-20-en-3-one, 21*β*-hydroxynigrum-22(29)-en-3-one and 21α-hydroxynigrum-22(29)-en-3-one, were isolated from *Hibiscus tiliaceus* (Feng et al. 2008a). Additionally, five known triterpenoids including friedelin; 12-oleanen-3*β*-ol (**5**), 3*β*-hydroxy-12-oleanen-28-oic acid; 20(29)-lupen-3*β*,28-diol and cucurbita-5,23-diene-3*β*,25-diol were also isolated and identified. Ten compounds were isolated from *H. tiliaceus* and identified as friedelin; pachysandiol; glutinol; lupeol; germanicol; stigmast-4-en-3-one; stigmast-4, 22-dien-3-one; ergosta-4, 6, 8; 22-tetraen-3-one; β-sitosterol; and stigmasterol (Wang et al. 2011).

Antioxidant and Antimutagenic Activities

Of nine coastal plant species, screened, the highest antioxidant activity (DPPH radical scavenging activity) was recorded in young leaves of *Hibiscus tiliaceus* (76 %), followed by *Syzygium corymbosa* (71 %), *Calophyllum inophyllum* (68 %) and *Colubrina asiatica* (55 %) (Nivas et al. 2010). These plant species also possessed appreciable reductive potential. The leaves of these species were found to be rich in flavanoids (6.03–16.63 mg/g of dry weight) and total polyphenol (12.12–26.23 mg/g of dry weight), and these compounds mainly contributed the antioxidant potential of these plants.

H. tiliaceus flower extract exhibited significant reducing power and free radical scavenging effect on hydroxyl, superoxide and hydrogen peroxide radicals (Kumar et al. 2008). The high antioxidant potential could be attributed to the phenolic and flavonoid content of the flowers. Treatment with *H. tiliaceus* methanolic flower extract protected several *Saccharomyces cerevisiae* strains defective in antioxidant defences against the mutagenic action of hydrogen peroxide and tert-butyl hydroperoxide cytotoxicities, showing a clear antioxidant activity (Rosa et al. 2006). The effect was the same for all strains used, independent of the antioxidant defence disrupted, suggesting that protection may be due to molecules that acted as versatile and wide spectrum nonenzymatic antioxidants, such as vitamins (vitamin E) or phytosterols (stigmasterol derivatives) present in the extract. *H. tiliaceus* methanolic flower extract was not mutagenic in either *Salmonella typhimurium* or *Saccharomyces cerevisiae* and showed a significant antimutagenic action against oxidative mutagens in *S. cerevisiae*. At concentrations ranging from 0.001 to 0.1 mg/mL, the methanol flower extract was not cytotoxic, genotoxic or mutagenic (Rosa et al. 2007). Treatment with non-cytotoxic concentrations of the extract increased V79 cell survival after of hydrogen peroxide and tert-butyl hydroperoxide exposure and prevented DNA damage. Pretreatment with the extract also was able to decrease the mutagenic effect of these genotoxins, evaluated using the micronucleus test. The extract prevented the increase in lipid peroxidation and decrease in glutathione content in response to the oxidative challenge.

Of the six *Hibiscus* species, leaves and flowers of *H. tiliaceus* had the strongest antioxidant properties (AOP) (Wong et al. 2009, 2010). Leaves of *H. tiliaceus* showed outstanding AOP with total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) values of 2,080 mg GAE (gallic acid equivalent)/100 g and 2,370 mg AA (ascorbic acid)/100 g, respectively. Values were 2.4 and 2.7 times higher than those of *H. mutabilis* which ranked second. Based on TPC and AEAC, ranking was *H. tiliaceus* > *H. mutabilis* > *H. sabdariffa* > *H. taiwanensis* > *H. schizopetalus* ~ *H. rosa-sinensis*. Leaves of *H. schizopetalus*, *H. sabdariffa* and *H. rosa-sinensis* had better ferrous ion-chelating (FIC) ability than those of *H. mutabilis*, *H. tiliaceus* and *H. taiwanensis*. Leaves of species with higher TPC and AEAC had lower FIC ability for *H. tiliaceus* and *H. mutabilis* and vice versa for *H. schizopetalus* and *H. rosa-sinensis*. Flowers of *H. tiliaceus* with TPC, AEAC and FRP (ferric reducing power) values of 2,420 mg GAE/100 g, 3,180 mg AA/100 g and 14 mg GAE/g, respectively, were significantly higher than all other species. Based on TPC, ranking was *H. tiliaceus* > *H. rosa-sinensis* > *H. taiwanensis* ~ *H. schizopetalus* ~ *H. mutabilis* > *H. sabdariffa*. There was no distinct variation between AOP of coastal and inland populations of *H. tiliaceus* for both leaves and flower despite the greater UV radiation in the coastal areas (Wong and Chan 2010).

Antitumour Activity

Among the compounds isolated from the stem bark, the amides hibiscusamide, *N-trans*-feruloyltyramine and *N-cis*-feruloyltyramine exhibited cytotoxicity (IC_{50} values <4 μg/mL) against P-388 and/or HT-29 cell lines in vitro (Chen et al. 2006). All three compounds were more active against p-388 cell line than HT-29 cell line. *N-trans*-feruloyltyramine was the most

cytotoxic, with IC_{50} values of 1.7 μg/mL and 3.8 μg/mL, respectively, against P-388 and HT-29 cell lines. A significant enhancement of mean survival time of *H. tiliaceus*-treated Dalton's ascitic lymphoma (DAL)-bearing mice was found with respect to the control group (Sunilson et al. 2008). *H. tiliaceus* treatment was found to enhance peritoneal cell counts. When these *H. tiliaceus*-treated animals underwent intraperitoneal (i.p.) inoculation with DAL cells, tumour cell growth was found to be inhibited. The results indicated that *H. tiliaceus*-treated group was able to reverse the haematological parameters, protein and packed cell volume (PCV) consequent to tumour inoculation within 14 days after the transplantation. The methanol leaf extract of *H. tiliaceus* exhibited selective cytotoxicity against breast cancer cells MDA-MB-435S (IC_{50} 1.14 mg/mL) and had no toxicity against healthy mouse fibroblasts (Uddin et al. 2011). The aqueous leaf extract from *Hibiscus tiliaceus* showed potent cytotoxicity with significantly lower IC_{50} values, especially against gastric (IC_{50} 0.25 mg/mL) and colon cancer cells (IC_{50} 0.8 mg/mL).

Tyrosinase Inhibitory Activity

Of 39 plant species screened, the methanol leaf extract of *Hibiscus tiliaceus* exhibited displayed strong free radical scavenging activity and the highest tyrosinase inhibition activity (Masuda et al. 1999; 2005). Of four species of *Hibiscus* tested, leaves of *H. tiliaceus* (42 %) had the strongest antityrosinase activity (Wong et al. 2010). Values were comparable to leaves of *P. guajava* (41 %) as positive control. Ranking of antityrosinase activity was *H. tiliaceus* > *H. mutabilis* > *H. rosa-sinensis* ~ *H. sabdariffa*. With strong antioxidant properties and antityrosinase activity, leaves of *H. tiliaceus* may have potential to be developed into functional food and skin care products.

Antidepressant Activity

Methanol flower extract of *H. tiliaceus* significantly decreased the duration of immobility of mice in both animal models of antidepressant activity, forced swimming and tail suspension tests (Vanzella et al. 2012). The extract did not potentiate the effect of ketamine-induced hypnosis, as determined by the time to onset and duration of sleeping time indicating lack of a sedative effect.

Antinociceptive and Anti-inflammatory Activities

Oral administration of the methanolic, petroleum ether and chloroform leaf extracts of *Hibiscus tiliaceus* (250 and 500 mg/kg, orally) exhibited significant anti-inflammatory activity on carrageenan-induced paw oedema in rat at the second and third hour (Narender et al. 2009). All the extracts significantly inhibited the acetic acid-induced abdominal contractions in mice in the order methanolic > chloroform > petroleum ether extract. The extracts also showed significant antinociceptive activity at similar doses at 60 min after extract administration. No acute toxicity was observed in mice after oral administration of the methanolic, petroleum ether and chloroform extracts of *Hibiscus tiliaceus* leaves at the dose of 5 g/kg. The methanolic wood extract of *Hibiscus tiliaceus* exhibited anti-inflammatory activity in experimental acute and chronic inflammatory animal models (Borhade et al. 2012). The percentage inhibition increase of paw oedema was increased with time and gave maximum effect at 2 h. Only the 200 and 4,000 mg/kg body weight extracts exhibited significant result

Immunomodulatory Activity

Oral administration of methanolic leaf extract of *H. tiliaceus* to Wistar rats exerted a significant increase in the production of circulating haemagglutination antibody titre in response to sheep red blood cells (SRBCs) (Rajeswari et al. 2013). The extract significantly potentiated the delayed type hypersensitivity reaction by facilitating the footpad thickness response to SRBCs in sensitized rats. Also the extract evoked a significant increase in

percentage neutrophil adhesion to nylon fibres and phagocytic activity. It also enhanced the production of RBC, WBC and haemoglobin. It did not affect the biochemical parameters. The results suggested that *H. tiliaceus* had a significant effect on both humoral and cellular immunity in experimental animals, and this may be attributed to the polyphenols and flavonoid content of the plant extract.

Antimicrobial Activity

H. tiliaceus leaf extract was found to inhibit Gram-positive bacteria of *Bacillus cereus*, *Micrococcus luteus* and *Staphylococcus aureus* but was not inhibitory to Gram-negative bacteria (Wong et al. 2010). MIC (minimum inhibitory concentration) values of leaf extracts of *H. tiliaceus* was 0.5 mg/disc for *M. luteus*, 0.25 mg/disc for *S. aureus* and 1 mg/disc for *B. cereus.*

Analgesic Activity

The methanolic wood extract of *Hibiscus tiliaceus* exhibited analgesic activity in experimental acute and chronic analgesic animal models (Sopan et al. 2012). The percentage increase in reaction time at 90 min was 21.02, 79.96 and 158.05 % for extract at a dose of 100, 200 and 400 mg/kg body weight, respectively, in the acetic acid-induced writhing method when compared with control. The percentage inhibition of writhes or protection was found to be 64.09, 78.56 and 81.45 % for extract at a dose of 100, 200 and 400 mg/kg body weight, respectively, in Eddy's hot plate method when compared with control.

Antiulcerogenic Activity

Albino rats pretreated with doses of 150 and 250 mg/kg of methanol, petroleum ether and chloroform leaf extract of *H. tiliaceus* showed significant reduction in gastric ulcer lesion index, total affected area and percentage of ulcer lesion in comparison with control group in the cold-restraint stress-induced ulcer and pylorus ligation models (Sharma et al. 2010).

Antidiabetic Activity

Significant reduction in blood glucose levels was observed in streptozotocin-induced diabetic Wistar rats treated with methanol flower extract of *H. tiliaceus* (500 mg/kg) for 21 days. The extract elicited significant antidiabetic activity with significant improvement in body weight. Daily oral treatment with the extract for 21 days also resulted in significantly reduction serum cholesterol and triglycerides. HDL cholesterol level was found to be improved as compared to diabetic control group.

Traditional Medicinal Uses

The flowers, roots and barks serve as herbal medicines in the Pacific (Gutmanis 1979; Weiner 1984; Kepler 1984; Abbott 1992; Whistler 1992; Cambie and Ash 1994; Elevitch and Thomson 2006), south (Uddin et al. 2011) and Southeast Asia (Burkill 1966). In Fiji, the leaves are wrapped around fractured limbs and sprained muscles, and leaf juice is used for gonorrhoea. Sap from the bark is used to induce menstruation in delayed menstrual period. Such usage is also found in Tahiti where the flowers are used in making a salve. In Tahiti, Cook Islands and the Marquesas Islands, the flowers are used in a paste as a poultice for sores, cuts, boils and swellings. In the Cook Island the bark is employed together with coconut bark or husk to make an infusion used for bathing fractures. In Wallis and Futuna, the leaves or shoots are used to treat recurring sickness. In Tonga, the bark and the young leaves are employed for skin diseases. The bark is used as a therapy for eye infections and injuries and stomach aches. Leaf infusion is utilized as an aid in the delivery of a child and to alleviate postpartum discharges. In the Solomon Islands, parts of the plant are employed for cuts, tuberculosis and conjunctivitis. In New Guinea, the bark is used as a cough remedy and also used for tuberculosis. The leaves are used in treating coughs, sore throats and open wounds. A preparation made from the leaves, roots and bark is administered for fever.

According to Burkill (1966) in Amboina, root infusion is taken for fever and a decoction taken for fever in Java and Pahang, Malaysia. Leaves boiled with sugar are used for coughs and bronchitis in Java. Boiled leaves are rubbed over swellings and applied hot to boils and used for the hair in Java. Flowers are boiled in milk for use to treat earache in the Philippines. The bark is emetic. Young leaves are used medicinally as substitute for the European 'folia althaeae' and flowers likewise for 'flores malvae'. The roots are used as an antifebrile and emetic, and the leaves and bark are used for the treatment of cough and bronchitis in Chinese folk medicine (Kan 1997). In Bangladesh, the leaves are employed in traditional medicine for fever, coughs and dry throat and the flowers for bronchitis, ear infections, dysentery and chest congestion (Uddin et al. 2011).

In Hawaii, the bark is said to have contraceptive effect, which produces slimy mucus that is thought to have spermicidal effect, and hot leaf infusion is introduced into vagina to cause abortion (Gutmanis 1979). The leaves are used to alleviate fevers and soothe coughs, the bark as a therapy for dysentery and ear infections, flowers to treat abscesses and bark and flower as a mild laxative (Kepler 1984; Abbott 1992; Elevitch and Thomson 2006). For babies and young children, the flower buds are used. The leaf buds are chewed/swallowed for dry throat. Hawaiians use the slimy sap from the inner bark as an enema (internal lubricant) to facilitate the passage of a fetus through the birth canal, and flowers are thought to aid in digestion. The inner bark (with sap) is soaked and drunk for labour pains and rubbed on stomach (Chun 1994). In Melanesia flowers are said to be smoked with tobacco for antifertility (Bronegaard 1973).

Other Uses

Hibiscus tiliaceus is grown throughout the tropics mainly as an ornamental tree for landscaping and avenue planting. Sea hibiscus is widely used in Asian countries as a subject for the art of bonsai, especially in Taiwan.

The stems and branches are long and flexuous and are used as living fence posts and fish kraals. The fibres from the bark make excellent string and rope and are used for hut building, cordage, fishing nets, coarse bags and caulking boats. The bark is used for making paper. The wood is used for light boat and canoe construction, planking, firewood, wood carvings, fishing nets, household implements, carts and canoe floats, sailing spars and axe handles. The leaves are fed to cattle.

Comments

H. tiliaceus can be propagated from seeds and from tips or hardwood cuttings or grafting.

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Malva sylvestris

Scientific Name

***Malva sylvestris* L.**

Synonyms

Althaea godronii Alef., *Althaea mauritiana* Alef., *Malva ambigua* Guss., *Malva erecta* C. Presl, *Malva grossheimii* Iljin, *Malva mauritiana* L., *Malva sylvestris* var. *mauritiana* (L.) Boiss., *Malva sylvestris* subsp. *mauritiana* (L.) Boiss.

Family

Malvaceae

Common/English Names

Blue Mallow, Blue Malva, Cheese Cake, Cheese Flower, Cheeses, Common Mallow, Country Mallow, Forest Mallow, High Mallow, Mallow, Marsh Mallow, Pick-Cheese, Round Dock, Tall Mallow, Wild Mallow, Wood Mallow, Zebrina Mallow

Vernacular Names

Albanian: Mullaga
Arabic: Khobbiza
Basque: Ziga, Zigiña
Brazil: Malva, Malva Silvestre
Catalan: Malva, Vauma, Malva De Cementiri
Corsican: Malba
Croatian: Sljez Crni, Sljez Divlji
Czech: Sléz Lesní, Erdei Mályva
Danish: Almindelig Katost
Dutch: Groot Kaasjeskruid, Groot Kaasjeskruid Soort
Estonian: Mets-Kassinaeris
Esperanto: Malvo Granda
Finnish: Kiiltomalva, Maurinmalva, Metsämalva
French: Fausse Guimauve, Fouassier, Fromageon, Grande Mauve, Mauve Des Bois, Mauve Sauvage, Mauve Sylvestre, Mauve Des Bois, Petit-Fromage, Petite Mauve, P'tite Mauve
Gaelic: Lus Na Meall Muire
German: Algiermalve, Gartenpappel, Grosse Käsepappel, Hanfpappel, Hasenpappel, Kultur-Käsepappel, Malve, Mauretanische Malve, Ross-Malve, Rosspappel, Waldmalve, Wilde Malve
Hungarian: Erdei Mályva, Mályva, Papsajt
India: Gul-Khair, Gurchanti, Kunzi, Socholi, Vilayatiikangai (Hindi), Sanna Bindige Gida, Seeme Bende (Kannada), Hobbejza tar-raba (Malayalam), Kubaajee (Marathi), Gul-E-khair, Gul-e-khubazi, Khubbazi (Urdu)
Iran: Panirak
Italian: Malva, Malva Selvatica, Malva Silvestre, Malva Sylvestris Méiba, Nalba, Riondella
Japanese: Usenbeni-Aoi, Zeni-Aoi
Kashmiri: Sotsal
Korean: Dang-A-Uk, Dangaug
Maltese: Hobbejza Tar-Raba

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Norwegian: Apotekerkattost, Kattost
Polish: Ślaz Dziki
Portuguese: Malva, Malva-Comum, Malva-Das-Boticas, Malva-Maior, Malva-Mourisca, Malva-Selvagem, Malva-Silvestre
Romanian: Nalba De Culturä, Nalba De Padure
Russian: Mal'va Leanaja, Prosvirnik Lesnoj
Sardinian: Mamarutza, Marmaredda, Marva, Narbedda
Serbian: Crni Slez
Slovašcina: Gozdni Slezenovec, Slezenovec Gozdni
Slovencina: Slez Lesný
Spanish: Alboeza, Malva, Malva Alta, Malva Común, Malva Silvestre, Malva Sylvestris
Swedish: Rød Kattost, Rödmalva, Vanlig Rödmalva, Vildmalva
Turkish: Lus Na Meall Muire
Welsh: Hocysen Gyffredin, Glyf Gyffredin, Hocys Cyffredin, Meddalon, Meddalon Gyffredin, Melotai, Melotai Gyffredin, Rhocos, Rhwygo yn Llaprau, Rhwygo yn Llarpiau

Origin/Distribution

The species occurs wild from temperate Europe to the Mediterranean/north Africa region. The species is widely distributed from Western Europe to the Himalayas and Siberia in Central Asia. It has been introduced elsewhere and has naturalized in many temperate regions, probably escape from cultivation in eastern Australia, the United States, Canada and Mexico.

Agroecology

A temperate species growing from near sea level to 2,400 m altitude. The Common Mallow is a nitrophilous species; it is commonly found in pastures, fallow ground, waste grounds, crop fields, field verges, paths and roadsides. It thrives in full sun in moist, well-drained, neutral to alkaline soils.

Edible Plant Parts and Uses

Young leaves and shoots, flowers, immature fruit and seeds are edible and eaten in several parts of Europe (Hedrick 1972; Facciola 1990; Pardo de Santayana 2004; Carvalho 2005; Neves et al. 2009). Young leaves are eaten raw in salad; leaves and shoots are eaten as boiled vegetables or consumed in soups, acting as thickeners because of their mucilaginous nature. Leaves, flowers and roots can be used to make tea. Flowers are added to salads or used as garnish. Immature fruits are sucked or chewed by children, shepherds and hunters as snacks; seeds are used for flavouring. The flower pigments (anthocyanins) are used as a natural colourant for food stuff.

Botany

An erect or decumbent, usually biennial pubescent to glabrescent herb, up to 1.5 m high and sparingly branching basally. Leaves alternately arranged, 2–4 cm by 2–5 cm wide, orbicular, maybe be shallowly 3–5 (-7) lobed, cordate with irregularly serrated margin, deep green and downy; stipule lanceolate and scarious, petiole 2–6 cm, pilose (Plate 1). Flowers bisexual, pentamerous, in 2–4-flowered axillary fascicles on 2 cm long pedicels. Epicalyx segments, ovate; calyx free to the middle, glabrescent, lobes broadly deltoid, 2–3 mm across; petals reddish purple, or bright pinkish purple with dark stripes, obovate, 1 cm wide, apical margin emarginate and ciliate, reticulate wrinkled on the back; stamens 3 mm long, stellate pubescent (Plate 1). Fruit glabrous, 5–6 mm in diameter, with 10–12 coherent reticulate mericarps, each mericarp with a single seed. Seeds brown, 2.5 mm long and broad, shaped like a cheese wheel.

Nutritive/Medicinal Properties

Nutrients and Phytochemical in the Plant

Malva sylvestris was found to contain 10–30 µg/g dry weight scopoletin (Tosi et al. 1995). The content was found to be higher in the aqueous extract compared with the methanol extract of the same sample. Sulphite oxidase was isolated and partially characterized from *Malva sylvestris* leaves (Ganai et al. 1997). Eleven compounds were isolated from the aqueous extract of *M. sylvestris*:

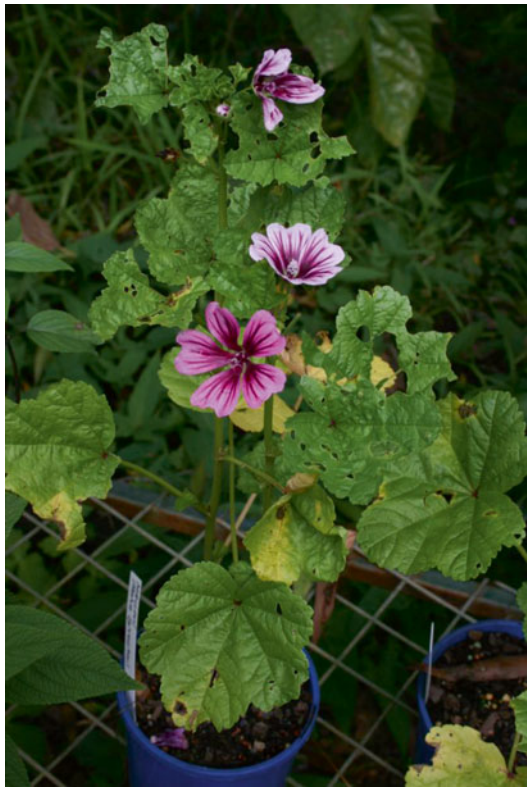

Plate 1 Flowers and leaves

4-hydroxybenzoic acid; 4-methoxybenzoic acid; 4-hydroxy-3-methoxybenzoic acid; 4-hydroxycinnamic acid; ferulic acid; methyl 2-hydroxydihydrocinnamate;scopoletin;*N-trans*-feruloyl tyramine; a sesquiterpene, (3*R*,7*E*)-3-hydroxy-5,7-megastig-madien-9-one; and (10*E*, 15*Z*)-9,12,13-trihydro-xyoctadeca-10,15-dienoic acid. Chlorophyll a, chlorophyll b, xanthophylls and carotenoids were extracted from the acetone extract of the plant (Redzić et al. 2005).

A phytoalexin, malvone A (2-methyl-3-methoxy-5,6-dihydroxy-1,4-naphthoquinone), induced in *Malva sylvestris* by the plant pathogen *Verticillium dahliae* was isolated (Veshkurova et al. 2006). In a turbidimetric assay for toxicity to *V. dahliae*, it had an ED_{50} value of 24 μg/mL. A sesquiterpene and a tetrahydroxylated acyclic diterpene as well as two known monoterpenes, 6 C(13)nor-terpenes and 11 aromatic compounds were isolated from the aqueous extract *of Malva sylvestris* (Cutillo et al. 2006).

The major fatty acids found in the leaves, flowers, immature fruits and leafy flowered stems were α- linolenic (C18:3), linoleic (C18:2) and palmitic acid (C16:0). In all the samples, polyunsaturated fatty acids (PUFA) predominated over monounsaturated fatty acids (MUFA) due to the significant contribution of α-linolenic and linoleic acids; leaves presented the highest levels of UFA (~84 %), while fruits and flowers revealed the highest contents of saturated fatty acids (SFA) (~37 %). In all the cases unsaturated fatty acids (UFA) predominated over SFA, ranging from 63 to 84 %, palmitic acid being the main SFA found, followed by tricosanoic acid (C23:0). Twenty-two fatty acids were identified and quantified: caproic acid (C6:0); caprylic acid (C8:0); capric acid (C10:0); lauric acid (C12:0); myristic acid (C14:0); myristoleic acid (C14:1); pentadecanoic acid (C15:0); palmitic acid (C16:0); palmitoleic acid (C16:1); heptadecanoic acid (C17:0); 572 stearic acid (C18:0); oleic acid (C18:1n9c); linoleic acid (C18:2n6c); γ-linolenic acid (C18:3n6) (not detected in leaves, flowers and immature fruits); α-linolenic acid (C18:3n3); arachidic acid (C20:0); eicosenoic acid 574 (C20:1c); *cis*-11, 14-eicosadienoic acid (C20:2c); *cis*-11, 14, 17-eicosatrienoic acid (C20:3n3); heneicosanoic acid (C21:0); behenic acid (C22:0); tricosanoic acid (C23:0); and lignoceric acid (C24:0) (Barros et al. 2010).

An arabinogalactan protein (AGP) was isolated from suspension cell culture of *Malva sylvestris* (Classen and Blaschek 2002). AGP comprised a high amount of polysaccharide with a ratio of galactose to arabinose of 1.9:1, some uronic acids and a small protein moiety with the main amino acids serine, alanine and hydroxyproline. The molecular weight was estimated to be 1.3×10(6) Da. AGP was composed of a highly branched core polysaccharide of 3-, 6- and 3,6-linked Galp residues with terminal Araf, GlcAp and Galp.

Nutrients and Phytochemicals in the Leaves

An acidic polysaccharide mucilage, designated as MSL-M, with molecular weight about 6.0×10^6.was isolated from the leaves of *Malva sylvestris* var. *mauritiana* (Tomoda et al. 1989). It was composed of L-rhamnose/D-galactose/D-galacturonic acid/D-glucuronic acid in the molar

ratio of 6:3:2:2. An acidic polysaccharide preparation with a molecular weight of 11,000 was isolated from the leaves of *Malva sylvestris* var. *mauritiana* (Gonda et al. 1990). It was composed of L-rhamnose, D-galactose, D-galacturonic acid and D-glucuronic acid in the molar ratio of 22:6:22:11 and contained 7.7 % peptide.

Four 8-hydroxyflavonoidglucuronides gossypetin 3-glucoside-8-glucuronide; hypolaetin 4′-methyl ether 8-glucuronide; hypolaetin 8-glucuronide and isoscutellarein 8-glucuronide were isolated from the leaves of *Malva sylvestris* (Billeter et al. 1991). Terpenoids, phenolic acids and anthocyanins were identified in the aqueous leaf extract of the plant (Cutillo et al. 2006). Elemental analysis of the leaves was conducted using inductively coupled plasma optical emission spectrometry (ICP-OES), and the mean values (mg/kg) for large and small leaves were found as follows, respectively: aluminium 42.90, 47.62 mg; boron 0.360, 0.200 mg; barium 13.60, 8.64 mg; calcium 15 936, 11,761 mg; chromium 0.26, 1.08 mg; copper 8.30, 8.70 mg; iron 88.62, 75.24 mg; potassium 288.66, 290.54 mg; magnesium 2039, 1,833 mg; manganese 26.78, 22.98 mg; lead 1.54, 1.42 mg; silicon 27.16, 27.84 mg; strontium 31.38, 31.38 mg; titanium 0.68, 0.66 mg; and zinc 19.90, 2.03 mg (Hiçsönmez et al. 2009).

Nutrient composition (g/100 g fresh weight (fw)) of mallow leaves was moisture 76.30 g, carbohydrates 71.46, proteins 12.15 g, fat 2.76 g, ash 13.53 g, reducing sugars 6.22 g and energy 356.72 Kcal/100 g (dry weight (dw)); The sugar composition and tocopherol content (g/100 g dw) were as follows: total sugars 11.61 g, fructose 1.82 g, glucose 3.15 g, sucrose 3.97 g, trehalose 2.67 g and raffinose not detected (nd) and total tocopherols 106.52 mg, α-tocopherol 83.70 mg, β-tocopherol 1.48 mg, γ-tocopherol 20.05 mg and δ-tocopherol 1.29 mg (Barros et al. 2010). Leaves were found to contain the highest (mg/g extract) phenolics 386.45 mg, flavonoids 210.81 mg and carotenoids 0.19 mg among the aerial plant parts but were low in ascorbic acid 0.17 mg. Leaves were also the richest in PUFA (80.03 %) particularly in α-linolenic acid (C18:3n3) (67.79 %) and lowest in SFA (16.32 %) and MUFA (3.65 %).

Nutrients and Phytochemicals in the Flowers

Two anthocyanins were isolated from the aqueous alcoholic extract of *M. sylvestris* flowers: malvidin 3,5-*O*-diglucoside (malvin) and malvidin 3-*O*-(6″-*O*-malonylglucoside)-5-*O*-glucoside (Farina et al. 1995). A new malonated anthocyanin, malvidin 3-(6′-malonylglucoside)-5-glucoside, was isolated from the flowers of both wild and cultivated forms of *M. sylvestris* (Takeda et al. 1989). The total anthocyanin concentration in the flowers was significantly increased to about 180.08 % by UVB radiation compared to untreated sample (Jayalakshmi et al. 2011). Fractionation of acidified methanolic extract of flowers afforded two anthocyanidins, viz., malvidin and delphinidin. The plant could be used for the extraction of anthocyanins intended to be employed as food colourant and antioxidant agent by the food, pharmaceutical and cosmetic industries.

High molecular weight acidic polysaccharide (HMWAP) mucilages were isolated from *Malva sylvestris* flowers and leaves (Classen and Blaschek 1998). The molecular weight of all HMWAPs was in a range of $1.3–1.6 \times 10^6$ Da. HMWAPs were found to be composed mainly of glucuronic acid, galacturonic acid, rhamnose and galactose A neutral heteropolysaccharide with molecular weight $0.05–1.5 \times 10^6$ and consisting of D-galactose (23.4 %), L-arabinose (34.3 %) and L-rhamnose (42.2 %) was isolated from the mucilage of the flowers of *Malva mauritiana* (Capek et al. 1999). It possessed a 3,6-linked D-galactopyranose, 5-linked L-arabinofuranose as well as 4-linked and terminal L-rhamnopyranose residues as the main building units.

Nutrient composition (g/100 g fw) of mallow flowers was moisture 72.49 g, carbohydrates 78.12, proteins 8.50 g, fat 2.48 g, ash 10.54 g, reducing sugars 13.95 g and energy 372.01 Kcal/100 g (dw), and sugar composition and tocopherol content (g/100 g dw) were as follows: total sugars 20.02 g, fructose 8.72 g, glucose 7.36 g, sucrose 2.47 g, trehalose 1.47 g and raffinose nd and total tocopherols 17.37 mg, α-tocopherol 14.03 mg, β-tocopherol 0.57 mg, γ-tocopherol 2.53.mg and

δ-tocopherol 0.24 mg (Barros et al. 2010). Flowers were found to contain 285.65 mg phenolics, 46.55 mg flavonoids, 1.11 mg ascorbic acid, 0.03 mg carotenoids, 57.33 % PUFA, 6.84 % MUFA and 35.83 % SFA. α-linolenic acid (C18:3n3) content was 33.50 % and γ-linolenic acid (C18:3n6) was not detected in the flowers.

Nutrients and Phytochemicals in the Fruits

Six new steroidal lactones and a homomonoterpenic glucoside along with β-sitosterol-3-β-D-glucopyranoside were isolated from the extract of defatted fruits of *Malva sylvestris* (Mustafa and Ali 2011). Their structures were elucidated as cholest-5-en-3a-ol-18(21)-olide (sylvestrosterol A), cholest-9(11)-en-3α-ol-18(21)-olide (sylvestrosterol B), cholest-4,6,22-trien-3α-ol-18(21)-olide (sylvestrosterol C), 2-methyl-6-methylene-n-decan-2-olyl-3β-D-glucopyranoside (malvanoyl glucoside), cholest-7-en-18(21)-olide-3α-olyl-3β-D-glucopyranoside (sylvestrogenin A), cholest-9(11)-en-18(21)-olide-3α-olyl-3β-D-glucopyranoside (sylvestrogenin B) and cholest-5-en-8(21)-olide-3α-olyl-3β-D-glucopyranoside (sylvestrogenin C).

Nutrient composition (g/100 g fw) of immature fruits was moisture 45.60 g, carbohydrates 74.96, proteins 3.26 g, fat 8.96 g, ash 12.83 g, reducing sugars 2.09 g and energy 393.45 Kcal/100 g dw, and sugar composition and tocopherol content (g/100 g dw) were as follows: total sugars 2.30 g, fructose 0.40 g, glucose 1.52 g, sucrose 0.11 g, trehalose nd and raffinose 0.26 g and total tocopherols 2.61 mg, α-tocopherol 2.07 mg, β-tocopherol 0.26 mg, γ-tocopherol 0.28 mg and δ-tocopherol nd (Barros et al. 2010). Immature fruits were found to contain 56.76 mg phenolics, 25.35 mg flavonoids, ascorbic acid 0.27 mg, carotenoids 0.01 mg, 56.69 % PUFA, 6.52 % MUFA and 36.79 % SFA. α-Linolenic acid (C18:3n3) content in the immature fruit was low (10.33 %), and γ-linolenic acid (C18:3n6) was not detected in the immature fruits.

Nutrients and Phytochemicals in Leafy Flowered Stems

Nutrient composition (g/100 g fw) of leafy flowered stems was moisture 77.26 g, carbohydrates 71.89, proteins 14.26 g, fat 3.09 g, ash 10.76 g, reducing sugars 10.46 g and energy 372.43. Kcal/100 g dw, and sugar composition and tocopherol content (g/100 g dw) were as follows: total sugars 14.67 g, fructose 3.52 g, glucose 3.30 g, sucrose 3.09 g, trehalose nd and raffinose 14.67 g and total tocopherols 34.92 mg, α-tocopherol 28.40 mg, β-tocopherol 0.57 mg, γ-tocopherol 5.93 mg and δ-tocopherol 0.02 mg (Barros et al. 2010). Leafy flowered stems were found to contain 317.93 mg phenolics, 143.40 mg flavonoids, ascorbic acid 0.20 mg, carotenoids 0.11 mg, 71.90 % PUFA, 3.48 % MUFA and 0.95 % SFA. α-Linolenic acid (C18:3n3) content in the leafy flowered stems was 53.09 %, and γ-linolenic acid (C18:3n6) content was 2.23 %.

Nutrients and Phytochemicals in Seeds

Total oil content of *M. sylvestris* was 9.60 %. Lipid percentage and fatty acid composition of *M. sylvestris* seed oil were reported as follows: 9.60 % lipid, myristic acid (14:0) 0.46 %, palmitic acid (16:0) 24.29 %, margaric acid (17:0) 0.19 %, stearic acid (18:0) 3.68 %, behenic acid (22:0) 0.44 %, lignoceric acid (24:0) 0.27 %, total SFA 29.33 %, palmitoleic acid (16:1) 0.33 %, oleic acid (18:1) 13.66 %, total MUFA 13.99 %; linoleic acid (18:2) 44.16 %, linolenic acid (18:3) 0.77 %, total PUFA 45.65 %, dihydromalvalic acid (18:ca) 0.59 %, dihydrosterculic acid (19:ca) 0.82 %, malvalic acid (18:ce) 0.85 %, sterculic acid (19:ce) 0.52 %, total cyclopropenoid fatty acids (CPEFA) 2.78 %, 10-ketostearic acid 1.11 % and total fatty acids 91.94 % (Tešević et al. 2012). Sterols (mg/g) found in the seeds were campesterol 3.278 mg, stigmasterol 3.975 mg, β-sitosterol 17.34 mg, fucosterol 4.021 mg, gramisterol 0.307 mg, cycloartenol 1.107 mg, avenasterol 0.587 mg, 3β-cholest-5ene-3,25-diol 0.250 mg,

9,19-cyclolanostan-3-ol 0.923 mg and two identified compounds.

Antioxidant Activity

Some greens including *Malva sylvestris* (Blue Mallow) used as traditional dishes in Mediterranean diet exhibited radical scavenging and iron chelating activities (El and Karakaya 2004). All samples showed antioxidant activity as a radical scavenger in the DPPH* radical assay. Greens also possessed antioxidative activity towards H_2O_2. Especially, greens exhibited a marked scavenging effect on H_2O_2 at 0.2 g/mL concentration. The Fe^{2+} ion chelating activities of the samples except jointed glasswort (*Salicornia europaea*) were greater than 70 %. High-fat albino rats were fed with different dosages of anthocyanin from *Malva sylvestris*; results showed that total cholesterol was decreased by 19.7 % at an anthocyanin of 0.04 g/day and triglyceride was decreased by 34.4 % at an anthocyanin of 0.05 g/day (Wang 2005). Further, the scavenging rate of free radical reached 43.46 % when the content of anthocyanin was 0.20 mg/mL and the inhibition rate of lipid peroxidation reached 18.82 % when anthocyanin content was 0.5 mg/mL.

Antioxidant capacity of the aqueous extract of *Malva sylvestris* was measured by its ability to scavenge the DPPH and superoxide anion radicals and to induce the formation of a phosphomolybdenum complex (DellaGreca et al. 2009). Eleven compounds were isolated and the antioxidant activities of all these compounds were reported. The seed oil had weak antioxidant activity in the DPPH assay with an EC_{50} value of 52.8g mg/mL which was 28–53 times weaker than that of BHT (Tešević et al. 2012).

Antimicrobial Activity

Anthocyanin extracted from *Malva sylvestris* dose-dependently (6–30 g/L) inhibited the growth in vitro of *Staphylococcus aureus* but not *Escherichia coli* and *Aspergillus niger* (Cheng and Wang 2006). Extracts from ten plants including Malva sylvestris exhibited an $IC_{50} < \text{or} = 32$ µg/mL for biofilm inhibition of methicillin-resistant *Staphylococcus aureus*, a common cause of skin and soft tissue infection (Quave et al. 2008b). *Malva sylvestris* leaves exhibited very strong antioxidant properties including radical scavenging activity ($EC_{50} = 0.43$ mg/mL), reducing power ($EC_{50} = 0.07$ mg/mL) and lipid peroxidation inhibition in liposomes (β-carotene bleaching inhibition) ($EC_{50} = 0.04$ mg/mL) and brain cell homogenates (TBARS inhibition) ($EC_{50} = 0.09$ mg/mL) (Barros et al. 2010). Leaves were also the richest in nutraceuticals such as powerful antioxidants (phenols, flavonoids, carotenoids and tocopherols), unsaturated fatty acids (e.g. α-linolenic acid) and minerals measured in ash content. The antioxidant activities (EC_{50} value mg/mL) of other aerial plant parts were DPPH scavenging activity (flowers 0.55 mg, immature fruits 4.47 mg, leafy flowered stems 0.59 mg), reducing power (flowers 0.17 mg, immature fruits 1.00 mg, leafy flowered stems 0.10 mg), β-carotene bleaching inhibition (flowers 0.11 mg, immature fruits 0.68 mg, leafy flowered stems 0.10 mg) and TBARS inhibition (flowers 0.12 mg, immature fruits 0.85 mg, leafy flowered stems 0.05 mg).

Both flowers and leaves of *M. sylvestris* methanol extracts exhibited strong antibacterial effects against *Erwinia carotovora*, a plant pathogen, with MIC value of 128 and 256 µg/mL, respectively (Razavi et al. 2011). The flower extract also showed high antibacterial effects against some human pathogen bacteria strains such as *Staphylococcus aureus*, *Streptococcus agalactiae* and *Enterococcus faecalis*, with an MIC value of 192, 200 and 256 µg/mL, respectively. Among all extracts, ethanol extracts of both *Malva sylvestris* and *Malva neglecta* especially *M. sylvestris* exhibited the best antibacterial activity against wound bacteria *Streptococcus pyogenes* with MIC of 0.4 mg/mL followed by aqueous extracts (Zare et al. 2012). All extracts were active against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Proteus vulgaris*. Aqueous and chloroform extracts had better antifungal activity. The best of antifungal MIC values was 0.6 mg/mL for *M. sylvestris* aqueous extract against *Aspergillus niger*. All extracts had activity against *A. niger*, *Aspergillus fumigatus* and *Candida albicans*.

Wound and Eczema Healing Activity

Alloxan-induced diabetic Wistar rats treated with diethyl ether extract of *M. sylvestris* and *Punica granatum* flowers showed significant reduction in the wound area when compared with control (Pirbalouti et al. 2010). Also, histological studies of the tissue showed that the extract of *M. sylvestris* increased well-organized bands of collagen, more fibroblasts and few inflammatory cells. The findings demonstrated that the extract of *M. sylvestris* effectively stimulated wound contraction as compared to control group and other groups. *M. sylvestris* accelerated wound healing in rats and thus supported its traditional use.

In a randomized clinical trial involving 50 patients with hand eczema, treatment with 4 % *M. sylvestris* ointment was found to be efficacious at 3 and 6 weeks of treatment compared to the placebo group (Barikbin et al. 2010). The researchers found *M. sylvestris* to be a safe and effective therapeutic modality for the treatment of hand eczema and could be used as an optimal substitute for corticosteroids and antihistamines

Anti-aging Activity

Talbourdet et al. (2007) compared the in vitro anti-aging activities of *Malva sylvestris* extract with those of all-*trans* retinoic acid (RA), a well-established topical therapy for photodamage and wrinkles. The genes studied were known to be modified by RA. The cDNA macro-array technology experiment with the reconstructed human epidermis model showed that some genes modulated by treatment with the *Malva sylvestris* extract were also regulated by RA treatment indicating a similar transcriptional activity at the mRNA level.

Immunomodulatory Activity

In studies with egg albumin-immunized and egg albumin-non-immunized Balb/c mice, water extracts of *Malva sylvestris* treatment appeared to have no effect on anti-egg albumin antibody production, but enhanced interleukin-12 and gamma-interferon gene transcription (El Ghaoui et al. 2008). The extract appeared to switch off interleukin-4 transcription. The results indicated *M. sylvestris* extract to be macrophage and T helper 1 (Th1) activators.

Cytotoxicity Activity

M. sylvestris methanol extracts exhibited relatively high cytotoxic activity against McCoy cell line, indicating its potential as a chemopreventive or a chemotherapeutic agent (Razavi et al. 2011).

Nephroprotective Activity

Malva sylvestris decoction was found to have a protective effect against ammonium metavanadate-induced nephrotoxicity in rats (Marouane et al. 2011). In 80 rats exposed to ammonium metavanadate (0.24 mmol/kg body weight in drinking water) for 90 days, a significant increase in the formation of free radicals and antioxidant enzyme activities was observed. Additionally, histological examination of kidney revealed a structural deterioration of the renal cortical capsules and a shrinking of the Bowman space. In animals intoxicated by metavanadate but also given a *Malva sylvestris* decoction (0.2 g dry mallow/kg body weight), no such pathologic features were observed: lipid peroxidation levels, antioxidant enzyme activities and histological features appeared normal as compared to control rats.

Anti-inflammatory and Antitussive Activity

In the digestive tract, the fruit mucilage could be used to heal and soothe inflammations such as gastritis, peptic ulcers, enteritis and colitis (Yeole et al. 2010). The flowers and leaves of *M. sylvestris* var. *mauritiana* had been used in the treatment of catarrhs of the respiratory system and various inflammations of the nasal and oral cavities (Tešević et al. 2012). Capek et al. (1999) found that

the mucilage isolated from the flowers exhibited cough-suppressing activity.

Traditional Medicinal Uses

All parts of the plant have medicinal uses. Common Mallow is considered to have diuretic, laxative, emollient, demulcent, spasmolytic, lenitive, choleretic, bronchodilatory, expectorant, antitussive, antidiarrhoeal and anti-inflammatory properties (CSIR 1962; Grieve 1971; Bown 1995; Chevallier 1996; Foster and Duke 1998; Camejo-Rodrigues et al. 2003; Novais et al. 2004; Pardo de Santayana 2004; Carvalho 2005; Ferreira et al. 2006; Natale and Pollio 2007; Quave et al. 2008a; DellaGreca et al. 2009; Leporatti and Ghedira 2009; Neves et al. 2009; Barros et al. 2010). Roots, shoots, leaves, flowers, fruits and seeds are applied in infusions, decoctions, poultices, liniments, lotions, salves, tisane baths and gargles. Traditionally, mallow has been employed to treat specified disorders of several systems of the body, such as the digestive, the respiratory, the genitourinary, the muscular, the skeletal systems, and renal lithiasis, as well as skin disorders and injuries. It is also highly recommended for acne and skin care and as antiseptic, emollient and demulcent. The plant is an excellent laxative for young children. Roots are used for toothache, genital tract infections and dermatitis. Shoots are employed to treat toothache, genital tract infections, haemorrhoids and constipation. Leafy flowered stems are employed for cold, cough, throat pain, tonsils and bladder problems. Seeds/mericarps are used to treat inflamed or injured skin and as a demulcent, emollient and diuretic. Young leaves are use for burns, skin injuries, diarrhoea, pectoral and rheumatism. The demulcent properties of leaves and flowers make them valuable as a poultice for bruise, inflammations, insect bites, etc., or they can be taken internally in the treatment of respiratory system diseases and problems with the digestive tract. Flowers are used for acne, skin problems, eyes, throat pain and cough. In tisanes, the flowers and leaves are used to help heal internal wounds, lesions of the mucous membranes and stomach ulcers. The flowers and immature fruits are efficacious to cure whooping cough and are official in French and Swiss pharmacopoeias (CSIR 1962). The German Commission E Monographs, a therapeutic guide to herbal medicine, approved *Malva sylvestris* for cough, bronchitis and inflammation of the mouth and pharynx (Rister et al. 1998). The edible *Malva sylvestris* is used as folkloric medicine for cough and bladder ulcer in Samahni Valley (Azad Kashmir), Pakistan (Ishtiaq et al. 2007).

Other Uses

Malva sylvestris was one of the six species (*Cichorium intybus*, *Eryngium creticum*, *Foeniculum vulgare*, *Malva sylvestris*, *Thymus syriacus* and *Gundelia tournefortii*) found popular for their edible uses as well as their health and/or medicinal benefits in north-east Lebanon (Jeambey et al. 2009). *Malva sylvestris* mucilage could be used as a suspending agent; it was found to have a low rate of sedimentation, high viscosity and slightly basic pH and was easily redispersible (Yeole et al. 2010).

Cream, yellow and green dyes can be obtained from the plant and the seeds/mericarps. In former times, the flowers were spread on doorways and made into garland or chaplets for celebrating May Day. A tincture of the flowers affords a very sensitive test for alkalis. A fibre obtained from the stems is useful for cordage, textiles and paper manufacture.

Comments

In some temperate areas, the plant has become a weed after introduction.

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Malvaviscus arboreus

Scientific Name

Malvaviscus arboreus Cav.

Synonyms

Achania coccinea Salisb., *Achania malvaviscus* Sw., *Achania mollis* Aiton, *Hibiscus coccineus* Walter, *Hibiscus malvaviscus* L., *Hibiscus nutans* Sessé & Moc., *Hibiscus pilosus* (Sw.) Fawc. & Rendle, *Malvaviscus acapulcensis* Kunth, *Malvaviscus arboreus* var. *lobatus* A. Robyns, *Malvaviscus arboreus* var. *sagraeanus* (A. Rich.) Baker f., *Malvaviscus arboreus* var. *sepium* (Schltdl.) Schery, *Malvaviscus balbisii* DC., *Malvaviscus ciliatus* DC., *Malvaviscus coccineus* Medik., *Malvaviscus lanceolatus* Rose, *Malvaviscus mollis* (Aiton) DC.

Family

Malvaceae

Common/English Names

Bootblack Flowers, Cardinal's Hat, Drummond's Wax-Mallow, Firecracker, Firecracker Hibiscus, Hibiscus-Piment, Ladies Teardrop, Mexican Turks Cap, Old Man's Apple, Pepper Hibiscus, Scotchman's Purse, Sleepy Hibiscus, Sleepy Mallow, Texas-Mallow, Turk's Cap, Turk's Turban, Turkcap, Wax Mallow, White Moho, Wild Apple

Vernacular Names

Belize: Catusa, Tulipán, Tulipan Del Monte, Tulipancia, Tulipancillo, Tulipanoia (Spanish), Old Man's Apple, White Moho, Wild Apple (English)
Bolivia: Malvavisco Arborescente
Brazil: Malvaisco (Portuguese)
Chinese: Xio Xuan Ling Hua
Cook Islands: Kaute, Kaute Moe, Kaute Makatea, Kaute ʻŌporo (Maori)
Costa Rica: Amapola, Amapolilla
Cuba: Majaguilla
Danish: Kræmmerhusmalva, Søvnig Hawaiiblomst
Estonian: Pehme Malvavisk
El Salvador: Manzanita Quesillo
French: Calalou Diable Hibiscus Dormant, Malvaviscus Arboré Du Mexique
French Guyana: Calalou-Diable
German: Beerenmalve, Gewöhnliche Beerenmalve, Mexikanische Beerenmalve, Wachsmalve
Guatemala: Clavel Encarnado, Estrella De Panama
Hawaiian: Aloalo Pahupahu
India: Lanka Jaba (Bengali), Mottu Chemparathi (Malayalam), Juba Kusum (Manipuri)

T.K. Lim, *Edible Medicinal and Non Medicinal Plants: Volume 8, Flowers*,
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Malaysia: Bunga Raya Kuncup
Mayan: Amapola, Amapollila, Arito, Bizil, Capuchito, Capuyito, Chillilo, Civil, Flor De Arito, Mahoe Rose, Malvito, Manzana, Mapola, Managuillo, Obelisco De La Sierra, Papito De Monte, Pico De Gorion, Polvo De Monte, Poro,Quesito, Resucitado De Monte, Sobon, Tamanchich
Mexico: Civil, Manzanilla, Manzanita, Mazapan, Monacillo, Moanacillo Coloradol
Nicaragua: Quesillo
Peru: Cucarda Caspi, Malvavisco,Pinon Ceqeati
Pukapukan: Kaute
Spanish: Flor De Santos, Manzanillo, Monacillo, Obelisco De La Sierra, Tripa De Buey, Tulipancillo
Swedish: Bärmalva
Thai: Chaba
Tuamotuan: Aute'Umoa
Vietnamese: Bụp Giàn Xay, Bụp Kín

Origin/Distribution

The plant is indigenous to the Southeastern United States, Mexico, Central America and South America. Introduced to other tropical and subtropical areas in Africa, Asia, Australia and the Pacific Islands.

Agroecology

A lowland tropical/subtropical species. A robust plant that thrives best in a diverse range of well-drained, moist soils, in full sun or partial shade.

Edible Plant Parts and Uses

The plant is a both a culinary and medicinal herb, used for salad, herbal tea and herbal dyes (Hamburg 2011). It produces a red dye. The flowers and fruit make a good herbal tea, and the young tender leaves, fruits and flowers are edible raw or cooked. They can be used as a culinary herb or salad herb. When the fruit is cooked, it will produce a good jelly or syrup. In Thailand, the flowers are eaten in salad or in light curries (Kaisoon et al. 2011).

Botany

A spreading perennial, erect shrub, 1–2 m high. Stem and branchlets sparsely villous to glabrate. Leaves on 2–12 cm long petioles, lamina broadly cordate to ovate–cordate, usually 3-lobed, sometimes entire, 6–12×2.5–10 cm, nearly glabrous or stellate pilose on both surfaces, basal veins 3 or 5, base broadly cuneate to nearly rounded or cordate, margin crenate-serrate, apex acuminate (Plate 1). Stipules lanceolate, deciduous. Flowers on 3–20 mm long pedicels, axillary, solitary, pendulous, tube shaped expanding slightly at the apex, 2.5–5 cm. Epicalyx lobes spatulate 7–9, connate at base, green, hirsute, adnate to calyx. Calyx tubular, 5-lobed, teeth ciliate, greenish-cream. Petals 5 scarlet-red, 2.5–5 cm (Plates 2 and 3). Staminal column 5–7 cm exceeding corolla tube. Style 10-fid with capitate stigmas. Fruit bright red when ripe, depressed-globose, 3–4 seeded.

Nutritive/Medicinal Properties

The soluble phenol acids (per g dry weight) identified in *Malvaviscus arboreus* flower extract were gallic acid 23.2 µg, protocatechuic acid 2.2 µg, *p*-hydroxy benzoic acid 52.0 µg, chlorogenic acid 14.8 µg, *p*-coumaric acid 5.6 µg,

Plate 1 Leaves and young flower buds (S. Wee)

Plate 2 Pendulous bright red flowers with protruding 10-fid styles (S. Wee)

Plate 3 Close view of pendulous flower showing the green epicalyx and cream calyx lobes (S. Wee)

ferulic acid 11 μg, sinapic acid 7.9 μg and total phenolic acid 116.7 μg (Kaisoon et al. 2011). The flowers contained 234.4 μg total bound phenolic acid made up of gallic acid 77.5 μg, protocatechuic acid 4.4 μg, *p*-coumaric acid 7.3 μg, ferulic acid 20.9 μg and sinapic acid 214.3 μg. The flowers contained 69.5 μg total soluble flavonoid made up of rutin 27.7 μg, myricetin 5.05 μg, quercetin 33.6 μg and kaempferol 3.18 μg and bound flavonoid 34.8 μg made up of quercetin 9.1 μg and apigenin 25.7 μg. The DPPH radical scavenging activity (% inhibition) of soluble and bound phenolic fraction of the flower was 31.39 % and 21.03 %, respectively. Bound phenolics exhibited lower antioxidant activity than soluble ones. The reducing potential of the soluble phenolic fraction of the flower as evaluated by FRAP (ferric reducing antioxidant power) assay (mmol $FeSO_4$/100 g dry weight) was 27.13 mmol.

Flavonoid aglycones found in the flowers (mg per g fresh tissues) of *M. arboreus drummondii* and *M. arboreus mexicana* were total pigments 53 mg, 56 mg; quercetin 41 mg, 42 mg; cyanidin 2 mg, 3 mg; and pelargonidin 10 mg, 11 mg, respectively (Puckhaber et al. 2002).

The fatty acids, 17-methyl-5,9-octadecadienoic acid, 16-methyl-5,9-octadecadienoic acid and 5,9-nonadecadienoic acid were identified in the phospholipid (mainly phosphatidylcholine) extract of *M. arboreus* (Carballeira and Cruz 1998).

Antimicrobial Activity

Aqueous extract from leaves of *Malvaviscus arboreus penduliflorus* showed in vitro activity against both *Escherichia coli* and *Staphylococcus aureus* giving a MIC value of 16.6 mg/mL and 15.8 mg/mL, respectively (Selvaraj et al. 2010). Volatiles extracted from the stem leaves and flowers of *M. arboreus* exhibited antifungal activity in vitro (Boughalleb et al. 2005). The extracts were inhibitory to *Alternaria solani*, *Fusarium oxysporum* f. sp. *niveum, F. solani* f. sp. *cucurbitae* and *Rhizoctonia solani*. The stem and flower extracts were not inhibitory on *Verticillium dahliae*, while the flower extract was not inhibitory to *Botrytis cinerea*. All extracts were not inhibitory towards *Pythium ultimum*.

Insect Repellent Activity

Malvaviscus arboreus was found to contain a dominant sesquiterpenoid, caryophyllene epoxide, that exhibited high repellency against attine ant (Hubbell et al. 1984). The caryophyllene epoxide was 20 times more repellent in bioassay than its biological precursor, caryophyllene.

Traditional Medicinal Uses

The plant has been used in traditional medicine in Central America and Haiti (Duke et al. 2009). Costa Ricans use the leaf decoction for cystitis,

diarrhoea and gastritis. Cubans use a flower decoction as gargle for sore throat. Dominicans apply the leaf juice to lice, seborrhoea and wounds, and a flower decoction is given to nursing infants with cold. Haitians and Mexicans drink the flower decoction for bronchitis, diarrhoea, thrush and tonsillitis. Hondurans drink the leaf decoction for fever.

Other Uses

The plant is used as landscape and garden plants especially in shady localities and also as potted house plants.

Comments

The flowers do not open fully and help attract butterflies and hummingbirds. The plant is readily propagated from stem cuttings.

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Azadirachta indica

Scientific Name

***Azadirachta indica* A. Juss**

Synonyms

Azadirachta indica var. *minor* Valeton, *Azadirachta indica* var. *siamensis* Valeton, *Azadirachta indica* subsp. *vartakii* Kothari, Londhe & N.P. Singh, *Melia azadirachta* L., *Melia indica* (A. Juss.) Brandis

Family

Meliaceae

Common/English Names

Azadirachta, Bead Tree, Burmese Neem Tree, Chinaberry, Cornucopia, Indian Azadirach, Indian Cedar, Indian-Lilac, Indian Lilac, Margosa, Margosa Tree, Neem, Neem Tree, Nim, Nimba, Nimtree, Pride of China

Vernacular Names

Amharic: Kinin
Angola: mbombolo, mbobola (Umbundu)
Arabic: azad, darkhtu Hind, Margosa, Neeb, Nim, sabah-bah, Sherish, Shereesh
Bangladesh: Nim
Brazil: Nim
Burmese: Bowtamaka, Tamabin, Tamaka, Tamar, Tamarkha, Thinboro
Cambodia: Sadao, Sdao
Cameroon: gagné (Fulfulde)
Chamorro: Sdau
Chinese: Lian Shu, Ku Lian, Lian Zao Zi, Yin Du Ku Lian
Cote D'Ivoire: Djokouadjo- Brou (Dioula)
Creole: Nim
Czech: Zederach Hladký
Dutch: Margosier
Estonian: India Neemipuu
Ethiopia: Kinina (Oromo), Nib (Tiigrinya)
Fiji: Neem
Finnish: Neem
French: Azadirachta De l'Inde, Huile De Neem, Margosier, Margousier, Neem, Nim Des Indes
German: Burma-Nimbaum, Indischer Zadrach, Grossblaettiger Zedrach, Neem, Neembaum, Niem, Niembaum, Nimbaum
Ghana: Kintsi, Kinsto (Adangbe), Akagyatia (Lobi), Nim (Southern region)
Guinea Conarky: kassia kunkhuri
Hungarian: Indiaiorgona
India: Mahanim, Neem, Nim (Assamese), Bim, Neem, Nim, Nimgach, Nimun (Bengali), Nim (Dogri), Limbo (Gujarati), Balnimb, Dinkan, Leemba, Leemda, Limbada, Neem, Neemda, Neemdi, Neemdo, Neemro, Nim, Nimb, Nimgachh, Ninb (Hindi), Baalanthi Baevu, Baemu, Baevina Mara, Baevu, Bemu, Beorunara, Bevina, Bevina Mara, Bevina-Mara,

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Bevu, Beysdunara, Isabaevu, Kaayabaevu, Kahi Baevu, Kahi Bevu, Kahi Nimba, Kahibevu, Kaybevu, Kayibevu, Kaypebevu, Kaypebivu, Keibevu, Lemalo, Nimba, Olle-Bevu, Ollebevu, Vevina (Kannada), Kodu Nimb (Konkani), Aria-Bepou, Ariabepou, Ariya-Veppa, Aruveppu, Aryatikta, Aryaveppu, Arytikta, Kaippanveppu, Nimbam, Picumarddam, Pisumarddam, Rajaveppu, Vembu, Veppa, Veppu, Veppuu, Vepu (Malayalam), Seizrak (Manipuri) Balantanimba, Balanthanimba, Kadu Khajur, Kadukhajur, Kadunimb, Limb, Limba, Limba Chajhada, Limbachajhada, Nimb, Nimbay (Marathi), Hnahkha, Nim, Nimthing Nim (Mizoram), Hnahkha, Nim, Nimthing Nim, Vranasodhakari (Oriya), Arishta, Arista, Aristah, Arkapadapa, Chhardana, Chhardighna, Hingu, Hinguniryasa, Kaitarya, Kakaphala, Kireshta, Kitaka, Malaka, Neta, Nimba, Nimbah, Nimbaka, Nimbavrikshaha, Niryasa, Niyamana, Pakvakrita, Paribhadhraka, Paribhadrakah, Pichumanda, Picumanda, Picumandah, Picumarda, Pitasara, Prabhadra, Prabhadrah, Pukamalaka, Puyari, Rajabhadraka, Ravipriya, Sarvatobhadra, Shirshaparna, Shita, Shukrapriya, Subhadra, Sumana, Varatvacha, Vishirnaparna, Vranasodhakari, Yavaneshta (Sanskrit), Acutakimaram, Akaluti, Akappalamakkiyacatti, Akuluti, Ammapattini, Ammapattiri, Aracankanni, Aricu, Aristakam, Aritam, Arittam, Arkkapatavam, Arukkapatavam, Arulaci, Arulundi Kaduppagai, Arulupati, Aruluruti, Arunati, Aruttakam, Aruttam, Atipam, Cakarakam, Cakatam, Cakatamaram, Cakatamuli, Cankumaru, Cankumarutam, Cankumarutamaram, Carutopattiri, Carvacatakam, Catapalacitti, Catapalacittimaram, Cavamuli, Cenkumaru, Cippuratimuli, Cirilipannan, Cirinapannam, Cirinapanni, Cirinapannimaram, Cirinapattiram, Cirnaparam, Cirnapattiram, Civam, Civamatukam, Civamatukamaram, Iravippiriyam, Kacappi, Kacappu, Kacappuppacitam, Kacappuppacitamaram, Kacappuvaruti, Kacappuvarutimaram, Kaitariyam, Katippakai, Kecamutti, Kinci, Kincika, Kinji, Kiruminacamaram, Kosaram, Kotakapaciyam, Kotakapaciyamaram, Kotaravali, Kotaravalimaram, Malakai, Malakam, Malugam, Malukam, Maturakkacappi, Mutikam, Nalatampumaram, Nattuvempu, Nim, Nimpakam, Nimpamaram, Nimpataru, Ninpam, Niriyacam#, Niriyacam, Niriyasam, Nitarpam, Niyacam, Niyamanam, Niyamanamaram, Niyaracam, Niyaratam, Niyatam, Pacumantam, Paripattiram, Pariyam, Parvatam, Peranimpam, Perunimpam, Picacappiriyam, Picacappiriyam, Picacappiriyam, Picacuppiriyam, Picaram, Picavappiriyam, Picumantam, Picumantam, Picumattam, Pirapattiram, Pisidam, Piyacukam, Puyari, Puyarikam, Sengumaru, Tittai, Tittai, Tuttai, Ukkirakantam, Ukkirakanti, Ukkragandam, Varuttam, Vembu, Vempu, Vempumaram, Venipam, Vepa, Veppam, Veppamaram, Veppan, Veppu, Vicimikini, Vicumantam, Vicumikini, Vicumini, Viruttamaram, Visapatcani (Tamil), Nimbamu, Taruka, Tharuka, Vaepa, Vemu, Vepa, Vepa-Chettu, Vepachettu, Vepu, Vempu, Vepa, Yaapa Chettu, Yapa, Yeppa (Telugu), Burg Neem, Burge Neem, Gul Neem, Maghz Tukhm Neem, Maghz Tukhm-E-Neem, Neem, Neem Ke Khusk Pattay, Neem Ki Namontian, Poast Darakht Neem, Poast Darakht Nim, Poast Neem, Roghan Neem, Roghan Nim (Urdu)

Indonesia: intaran, mimba (Balinese), imba, mimba (Javanese), membha, mempheuh (Madurese)

Iran: Azad Darakth E Hind, Neeb, Nib

Kenya: mkilifi (Digo); Arubaine, Dwele, Muarubaini (Luo), arubaine (Suba)

Laos: Kadao

Madagascar: traimpilga, voandelaka

Malaysia: Baypay, Intaran, Mambu, Sadu, Veppam

Nepalese: Nim

Niger: Dogo'n (Hausa), Turi Forta (Zarma), Neem (French)

Nigeria: darbejiya, dogon yaro, yaro (Hausa), dogogaro (Igbo); afoforo oyimbo, igi-oba (Yoruba)

Norwegian: Neem, Nim

Pakistan: Limbi, Nimmi, Nimuri

Papua New Guinea: Neem

Persian: Azad Dirakht, Azad-Darakhte-Hindi, Azaddarachtehindi, Neeb, Nib

Portuguese: Margosa, Nimbo
Senegal: Nivaquine (Diola), Emdepanda (Peul), Dim U Tubab, Neem, Nim, Dimi Buki (Wolof)
Singapore: Kohumba, Neem, Nimba
South Africa: Umsilinga (Northern Maputaland, KwaZulu-Natal province)
Spanish: Lila De La India, Lila De Persia, Paraiso De India, Lilaila, Pasilla
Sri Lanka: Kohomba (Sinhala), Nimbu-nimbagaha
Sudan: Neem
Swahili: Mkilifi, Mwarobaini, Mwarubaini Kamili
Swedish: Margosa, Neem, Nim
Taiwan: Yin Du Lian Shu
Tanzania: mwarobaini
Thai: Cha-Tang, Khwinin, Kwinin, Sadao, Sadao India
Tibetan: Ni Mba, Ni-Mba
Togo: Kiniti, Liliti, Sabuléti (Ewé), Kiniti (Mina)
Turkish: Nem Ağacı
Vietnamese: Sầu Đâu, Xoan Ấn Độ
Yemen: Meraimarah

Origin/Distribution

Neem tree is indigenous to the dry forests of South and Southeast Asia. It is widely distributed in Pakistan, India, Sri Lanka, Nepal, Bangladesh, Myanmar, Thailand and Indonesia. Its exact origin is obscured by widespread cultivation and is thought to be native to Myanmar and Assam region in north-east India. Neem has been introduced and established throughout the tropics and subtropics, especially in drier areas in Southeast Asia, the Pacific Islands, Australia, South and Central America, the Caribbean, Africa and the Middle East.

Agroecology

In its native range in the tropics and subtropics, neem inhabits dry deciduous mixed forests. It thrives in subarid and subhumid areas from sea level to 700 m elevation and up to 12,000 m asl as in India. Mean annual temperatures within its natural range are typically 21–32 °C, although it can tolerate high temperatures to 45 °C and low temperatures to 10 °C and is frost intolerant. It thrives in areas with mean annual rainfall of 450–1,200 mm but will grow in areas with mean annual rainfall as low as 150 mm when groundwater is available. Once established, neem is very drought resistant, surviving up to 7 months of dry periods. It is also resistant to termites. Neem prefers full sun but will grow in partial shade.

Neem thrives best on deep, permeable, sandy soils. It is robust and adaptable to many types of soil including difficult sites where other species do not thrive well. It will grow on rocky, dry, shallow, infertile soils but abhors waterlogged or seasonally inundated soils and saline soils. It prefers a soil pH in the 6.2–7.0 range, but can grow within a range of 5.0–8.0 pH.

Edible Plant Parts and Uses

Tender leafy shoot, young leaves, flower and fruits are edible. The tender shoots, leaves and flowers are eaten as a vegetable in India, Myanmar, Thailand, Cambodia and Vietnam. Young shoots and young inflorescences are popular and highly priced vegetables in Thailand; normally available during the end of rainy season, they are harvested and eaten raw or steamed and dipped in a sweet, sour and hot sauce (Pongpangan and Poobrasert 1985; Rojanapo and Tepsuwan 1992; Kusamran et al. 1998a, b; Maisuthisakul et al. 2008; Maisuthisakul 2012). In Vietnam, young bitter leaves and flowers are eaten raw with other vegetables in salads (Tanaka and Nguyen 2007). In Myanmar, young neem leaves and flower buds are boiled with tamarind fruit to soften its bitterness and eaten as a vegetable. Pickled neem leaves are also eaten with tomato and fish paste sauce in Myanmar.

In Tamil Nadu, India, neem flowers are used with tamarind, turmeric, salt and sugar in a soup-like dish called 'Veppam poo rasam' (Wikipedia 2013) . In West Bengal, young neem leaves are fried in oil with tiny pieces of eggplant, turmeric, salt and sugar in a crispy fried neem leaves/brinjal dish called 'neem begun'. In Andhra Pradesh, neem flowers are used in a souplike pickle called 'Ugadi Pachadi' on Ugadi day, and

in Karnataka, neem flowers (bitter) and jaggery (sweet) are consumed on Ugadi day, the Karnataka New Year, signifying the bitter and sweet things in life. In Maharashtra, a small quantity of neem juice or paste is consumed on Gudhi Padva, the New Year's day to herald the start of festivities. Neem fruits are eaten fresh or cooked or prepared as a dessert or lemonade-type drink (Stoney 1997).

According to Watt (1908), neem tree exude sap which can also be tapped and fermented to give 'nim toddy' which is consumed more for medicinal purposes. Neem gum is used as a bulking agent and for the preparation of special purpose food (those for diabetics) and has potential as food additives (Stoney 1997).

Botany

An evergreen, perennial, deep-rooted, glabrous tree up to 20 m (rarely to 35 m) with a short, straight bole, whitish-grey to reddish-brown, fissured or scaly bark and with a rounded much-branched crown of alternately arranged, shiny dark green pinnately compound 20–30 cm long leaves on short 70–90 mm petioles (Plate 1). Very young leaves are copper–bronze colour (Plate 2). Each leaf has 12–18 obliquely falcate–lanceolate, serrate leaflets with cuneate base, acuminate apex, 7 by 2.5 cm. The odd terminal one is often missing. Inflorescence an axillary, many-flowered thyrse, up to 30 cm long; bracts minute and caducous. Flowers bisexual or male on the same tree, actinomorphic, small, pentamerous, white or pale yellow, slightly sweet scented (Plate 3); calyx lobes imbricate, broadly ovate and thin, puberulous inside; petals free, 5–11 mm long, imbricate, spatulate, spreading; stamens 10, filaments fused into a 10-lobed staminal tube, anthers sessile; disc annular, fused to the base of the ovary; ovary superior, style slender, stigma capitate, 3 lobed. Drupes are ovoid–oblong, 1–2 cm long, smooth, thin skinned, indehiscent, greenish (Plate 4), greenish-yellow to yellow or purple when ripe and usually one seeded. Seed ovoid or spherical, apex pointed, testa thin and brown.

Plate 1 Leaves with serrated margins

Plate 2 Mature and juvenile leaves

Plate 3 Flowers and buds (G.F. Chung)

Plate 4 Developing fruits

Nutritive/Medicinal Properties

More than 150 compounds had been isolated from various parts of neem tree since the isolation of nimbin and nimbinin; these included isoprenoids such as protomeliacins, meliacins (limonoids or tetranortriterpenoids, tetratetranortriterpenoid-γ-hydroxybutenolides, ring C-seco-tetranortriterpenoid and ring C-seco-tetranortriterpenoid-γ-hydroxybutenolides), pentanortriterpenoids, a hexanortriterpenoid and nontriterpenoidal constituents (Siddiqui et al. 1988c, 2008). Other isoprenoid-derived constituents from neem included diterpenoids and stereols. The non-isoprenoids included phenols (flavonoids and coumarins), carbohydrates, proteins, hydrocarbons and fatty acids and their esters. These compounds isolated from leaves, flowers, seeds, fruits, roots and bark of neem tree had been reported to have a vast array of pharmacological properties such as immunomodulatory, anti-inflammatory, antihyperglycaemic, antiulcerogenic, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic, hepatoprotective, anticarcinogenic, antiparasitic, diuretic, antipyretic, neuroprotective, anxiolytic, analgesic and cardiovascular beside imparting insecticidal and pesticidal activities. *A. indica* can be regarded as a valuable plant source for the rationalization of its use in traditional medicine and for modern drug development (van der Nat et al. 1991a).

Flower Phytochemicals

From the flowers were isolated: flavonol monoglycosides quercetin-3-galactoside (or hyperin), kaempferol-3-glucoside(astragalin)andmyricetin-3′-*O*-L-arabinoside (melicitrin A) (Subramaniam and Nair 1972); pentacosane, heptacosane and octacosane (Siddiqui et al. 1988b); neeflone, a new tetranortriterpenoid (Nanduri and Banstola 1995); four prenylated flavanones (5,7,4′-trihydroxy-8-prenylflavanone (1), 5,4′-dihydroxy-7-methoxy-8-prenylflavanone(2),5,7,4′-trihydroxy-3′,8-diprenylflavanone (3) and 5,7,4′-trihydroxy-3′,5′-diprenylflavanone (4)) (Nakahara et al. 2003); two new flavanones (flowerine (=5-hydroxy-7,4′-dimethoxy-8-(3-methylbut-2-enyl)flavan-4-one) and flowerone (=5,7,8,4′-tetrahydroxy-3′-(3-methylbut-3-enyl)flavan-4-one)); two new triterpenoids (*O*-methylazadironolide (=7α-(acetoxy)-23ε-methoxy-21,23-epoxy-24,25,26,27-tetranorapotirucalla-1,14,20(22)-trien-3,21-dione) and diepoxyazadirol (=(20*S*,23*S*,24*R*)-7-α-(acetoxy)-25-hydroxy-21,24:23,24-diepoxyapotirucalla-1,14-dien-3-one)), along with the known triterpenoid trichilenone acetate (=7α-(acetoxy)-14,15:21,23-diepoxy-24,25,26,27-tetranorapotirucalla-1,20,22-trien-3-one); two known flavanones nimbaflavone (=5,7-dihydroxy-4′-methoxy-8,3′-bis(3-methylbut-2-enyl)-flavan-4-one) and 3′-prenylnaringenin(=5,7,4′-trihydroxy-3′-(3-methylbut-2-enyl) flavan-4-one)); 7); 4-(2-hydroxyethyl)-phenol (Siddiqui et al. 2003b); and a flavanone namedazharone(5,7,4′-trihydroxy-3′-(3″-methyl-2″,3″-epoxybutyl)flavan-4-one) along with azadirone and isoazadironolide (Siddiqui et al. 2006). Forty-one compounds were identified in nonpolar to less polar fraction n-hexane-soluble fraction of fresh neem flowers as well as in essential oil (Siddiqui et al. 2009b). The compounds identified included 5 sesquiterpenes, 3 aromatics, 17 fatty acids, 5 fatty acid esters, 3 steroids and 8 hydrocarbons, many of which had been previously reported from different parts of the tree (Siddiqui et al. 1989). Some compounds identified included hydrocarbons (tricosane, pentacosane, heptacosane, hentriacontane, heneicosane, octacosane, nonacosane and nonadecane); steroids

(α-sitosterol, α-sitosterol acetate and lanosterol); sesquiterpenoids 1*S*,2*S*,5*R*-1,4,4-trimethyl-tricyclo [6.3.1.0 (2,5)]dodec-8-ene; decahydro-1,1,3a-trimethyl-7-methylene-[1a*S*-(1aa′,3aa′,7aa′,7ba)]-1H-cyclopropa[a]naphthalene; 1,1,4,8-tetramethyl-*cis*-*cis*,*cis*-4,7,10-cycloundecatriene; germacrene and α-himachalene; fatty acids and fatty acid esters (dodecanoic acid, heptadecanoic acid or margaric acid, hexacosanoic acid or cerotic acid, 15-methylheptadecanoic acid, 12-methyltridecanoic acid or isomyristic acid, nonanedioic acid, octacosanoic acid, octadecanoic acid, 9-oxanonaoic acid or azelaldehydic acid, 4-oxooctanoic acid, pentacosanoic acid and 9-methyltetradecanoic acid); and palmitic, myristic, behenic, lauric acid, 17-hydroxystearic acids and their methyl esters.

Fruit Phytochemicals

Compounds isolated from the fruit included the following: melianone and nimolinone (Lavie et al. 1967); salannin and nimbin (Pachapurkar et al. 1974); 17-hydroxyazadiradion (Siddiqui et al. 1978); a tetranortriterpenoid nimolicinol with structure elucidated as 17α-hydroxy-14,15-deoxy-17-epi-gedunin (Siddiqui et al. 1984a); limonoids (deacetylazadirachtinol, azadirachtin, salannin, 6-*0*-acetylnimbandiol and 3-desacetylsalannin) (Kubo et al. 1986); a meliacin and nimocin, along with the known azadirone, gedunin, epoxyazadiradione, 7-deacetyl-7-benzoylazadiradione, azadiradione, 17-hydroxyazadiradione and β-sitosterol (Siddiqui et al. 1986c); two triterpenoids (isonimolicinolide and nimolicinoic acid) (Siddiqui et al. 1987b); three triterpenoids azadironolide [24,25,26, 27-tetranorapoeupha-7α-acetoxy-23xi-hydroxy-21,23-epoxy-1,14, 20(22)-trien-3,21-dione]; isoazadironolide [24,25,26, 27-tetranorapoeupha-7α-acetoxy-21xi-hydroxy-21,23-epoxy-1,14, 20(22)-trien-3,23-dione] and azadiradionolide [24,25,26,27-tetranorapoeupha-7α-acetoxy-21,23-epoxy-1,14,20(22)-trien-3, 16,21-trione] (Siddiqui et al. 1990a); five terpenoids (tirucalla-7,24-dien-16β-o1 (limocinol), tirucalla-8,24-dien-16-one (limocinone), 24,25,26,27-tetranorapotirucalla-7 α-acetoxy-21,23-epoxy-21α-methoxy-1,14-dien-3-one (limocin A), kulactone and azaridol, an apotirucallol (apoeuphol) derivative with the C-8 side chain uncyclized) (Siddiqui et al. 1991a); 24,25,26,27-tetranorapotirucalla-7α-acetoxy-21,23-epoxy-23ε-methoxy-1,14-dien-3-one (limocin B) and 24,25,26,27-tetranorapotirucalla (24,25,26,27-tetranorapoeupha)-7α-benzoylox-21,23-epoxy-20ε-hydroxy-23ε-methoxy-1, 14-dien-3-one (limocinin) (Siddiqui et al. 1991b); a protolimonoid, naheedin and azadirachtol; four hydrocarbons (icosane, docosane, 2-methyltricosane and docosene) (Siddiqui et al. 1992b); three degraded triterpenoids (desfurano-azadiradione, 5α,13α-androstone and 5α,13α-17-oxa-androstone derivatives) (Siddiqui et al. 1992a); four tetracyclic triterpenoids (salimuzzalin [24,25,26, 27-tetranorapotirucalla (apoeupha)-7α-hydroxy-21ε,23ε-diacetoxy-21,23-epoxy-1,14, 20(22)-trien-3-one], azadirolic acid [26,27-dinorapotirucalla (apoeupha)-6β-acetoxy-7α-hydroxy-1,14,20(22)-trien-3-one-25-oic acid], azadiradionol[26,27-dinorapotirucalla(apoeupha)-7α-acetoxy-24ε-hydroxy-1,14-dien-3,16 dione] and azadironol [4,4,8-trimethyl-5α-(13αMe)-androst-17α-hydroxy-1-en-7α-(*p*-methoxy, *m*-hydroxy *trans* cinnamoyloxy)-3-one] (Siddiqui et al. 1998); two triterpenoids (26,27-dinor-17-oxa-1, 14,20(22)-trien-3, 16-dioxo-7α-acetoxy-17β-methoxy-4,4,8-trimethyl(5α, 13α)-cholane(meliacinin)and24,25,26,27-tetranor-apotirucalla(-apoeupha)-7α-acetoxy-1,14,20(22)-trien-3-oxo-23-oic acid (azadironic acid)) (Siddiqui et al. 2000b); 16 *n*-alkanes (*n*-pentadecane, *n*-hexadecane, *n*-heptadecane, *n*-octadecane, *n*-nonadecane, *n*-icosane, *n*-heneicosane, *n*-docosane, *n*-tricosane, *n*-tetracosane, *n*-pentacosane, *n*-hexacosane, *n*-heptacosane, *n*-octacosane, *n*-nonadecane and *n*-hentriacontane); three aromatics (2,6-bis-(1,1-dimethylethyl)-4-methyl phenol, 2-(phenylmethylene)-octanal or α-hexylcinnamaldehyde and 1,2,4-trimethoxy-5-(1Z-propenyl)-benzene or β-asarone); three benzopyranoids (3,4-dihydro-4,4,5,8-tetramethylcoumarin, 3,4-dihydro-4,4,7,8-tetramethylcoumarin-6-ol and1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethyl-cyclopenta[g]-2-benzopyran or galoxolide); one sesquiterpene, methyl-3,7,11-trimethyl-2E,6E,

10-dodecatrienoate or methyl (2*E*,6*E*)-farnesoate; three esters of fatty acids (methyl 14-methylpentadecanoate, ethyl hexadecanoate or ethyl palmitate and ethyl 9Z-octadecenoate or ethyl oleate); and one monoterpene, 3,7-dimethyl-1-octen-7-ol or dihydromyrcenol (Siddiqui et al. 2004b). Fully mature fruit (yellow fruits) kernels contained the highest concentration of azadirachtin, nimbin and salannin, whereas the concentration of azadiradione and epoxyazadiradione was high in the unripe green berries (Siddiqui et al. 2009a). Antiplasmodial triterpenoids were isolated from the fruits of neem, *Azadirachta indica*.

Seed Phytochemicals

Compounds isolated from the seed included the following: desacetylnimbin (Narayanan and Iyer 1967); six tetranortriterpenoids (1α-methoxy-1,2-dihydroepoxyazadiradione, 1β,2β-diepoxyazardiradione, 7-acetylneotrichilenone, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylepoxyazadiradione and 7-desacetyl-7-benzoylgedunin) (Kraus et al. 1981); 4-epinimbin, a meliacin (Devakumar and Mukerjee 1985); azadiradione, 7-deacetylazadiradione (Siddiqui et al. 1986d); two limonoids (3-deacetyl-3-cinnamoylazadirachtin and 1-tigloyl-3-acetyl-11-methoxyazadirachtinin in addition to azadirachtin); 22,23-dihydro-23β-methoxyazadirachtin and 3-tigloylazadirachtol (Kraus et al. 1987a); tetranortriterpenoid lactams salannolactam-(21) and salannolactam-(23) (Kraus et al. 1987b); a meliacin named salannolide (Garg and Bhakuni 1984b); a tetranortriterpenoid of the limonoid type, 7-deacetyl-17β-hydroxyazadiradione, and the known compound azadiradione (Lee et al. 1988); salannin (Yamasaki et al. 1988); nimbin, epinimbin, desacetylnimbin, salannin, desacetylsalannin, azadirachtin and two unidentified compounds—a salannin derivative and a nonterpenoid (Singh et al. 1988); 1,3-diacetyl-11,19-deoxa-11-oxomeliacarpin, a possible intermediate in the biosynthesis of azadirachtin (Kraus et al. 1989); two tetranortriterpenoids (an aldehyde named nimbanal and the 3-acetyl derivative of salannol, i.e. salannol-3-acetate) (Rojatkar et al. 1989); a tetranortriterpenoid nimbinol (Bokel et al. 1990); triterpenoid limbolide (Siddiqui et al. 1990b); azadirachtin (Govindachari et al. 1990); azadirachtins A, B, D, H and I (Govindachari et al. 1991, 1992a); azadirachtin K (Govindachari et al. 1992b), a meliacarpin 1-tigloyl-3-acetyl-11-hydroxy-4β-methylmeliacarpin (Rojatkar and Nagasampagi (1992); meliacin, 11α-hydroxy-12-norazadirachtin (Rojatkar and Nagasampagi 1994); tetranortriterpenes 11-epi-azadirachtin H (Ramji et al. 1996) and 11-epi-azadirachtin D (1-tigloyl-3-acetyl-11α-hydroxy-4β-methylmeliacarpin) (Ramji et al. 1998); limonoids (nimbolide, epoxyazadiradione, salannin, nimbin, deacetylnimbin and azadirachtin) (Cohen et al. 1996); four limonoids, 11-hydroxyazadirachtin-B,1-tigloyl-3-acetylazadirachtinin,1,2-diacetyl-7-tigloyl-12-hydroxyvilasinin and 23-desmethyllimocin-B (Kumar et al. 1996); a tetranortriterpenoid, 13,14-desepoxyazadirachtin-A (Govindachari and Gopalakrishnan 1997); two azadirachtin derivatives, namely, 29-oxymethylene-11-demethoxycarbonyl-11α-hydroxyazadirachtin (azadirachtin M) and 22,23-dihydro-23α-hydroxy-3-tigloyl-11-deoxyazadirachtinin (azadirachtin N) together with known compounds 11-*epi*-azadirachtin H (Luo et al. 1999) triterpenoid, 1α,7α-diacetoxyapotirucall-14-ene-3α,21,22,24,25-pentaol and odoratone and 2β,3β,4β-trihydroxypregnan-16-one (Luo et al. 2000); seven bioactive tetranortriterpenoids, azadirachtin A, azadirachtin B, azadirachtin H, desacetylnimbin, desacetylsalannin, nimbin and salannin (Silva et al. 2007); 31 nortriterpenoids, including 28 limonoids, azadiradione, 7-benzoyl-nimbocinol, 15-hydroxyazadiradione, 17-hydroxyazadiradione, 7-benzoyl-17-hydroxynimbocinol, epoxyazadiradione, 7-deacetyl-7-benzoylepoxyazadiradione, 17-epiazadiradione,17-epi-17-hydroxyazadiradione,7-acetyl-16,17-dehydro-16-hydroxyneotrichilenone, azadiradionolide, 23-deoxyazadironolide, limocin E, 23-epilimocin E, 20,21,22,23-tetrahydro-23-oxoazadirone, 3-acetyl-7-tigloylvilasinin lactone, gedunin, 7-deacetylgedunin, 7-deacetyl-7-benzoylgedunin, nimolicinol, azadirachtin B, 11-epiazadirachtin D, vepaol, 23-eipvepaol, 3-acetyl-11-methoxy-1-tigloylazadirachtinin, nimbin, 6-deacetylnimbin, 6-deacetylnimbandiol

and degraded limonoids, α-nimolactone, β-nimolactone, desfuranoazadiradione and one diterpenoid, 7α-acetoxy-3-oxoisocopala-1,13-dien-15-oic acid arbutin (Akihisa et al. 2009); and 35 limonoids, including 15 of the azadiradione type, five of the gedunin type, four of the azadirachtin type, nine of the nimbin type and two degraded limonoids (Kikuchi et al. 2011). Seventeen limonoids (tetranortriterpenoids, azadiradione,17-epiazadiradione,17-hydroxyazadiradione, 17-epi-17-hydroxyazadiradione, azadiradionolide, desfuranoazadiradione, nimbin, 3-diacetylvilasinin,6-deacetylnimbin,6-acetylnimbandiol, 28-deoxonimbolide, ohchinin acetate, salannin, 2′,3′-dihydrosalannin, 3-deacetylsalannin, 17-defurano-17-oxosalannin and nimolicinol, and gedunin) and fatty acids, myristic (14:0) 0.7 %, palmitic (16:0) 17.6 %, palmitoleic (16:1, *n*-7) 0.1 %, stearic (18:0) 18.6 %, oleic (18:1, *n*-9) 50.2 %, *cis*-vaccenic acid (18:1, *cis*-11) 0.4 %, elaidic (18:1, *trans*-9) 0,2 %, linoleic (18:2, *n*-6) 9.4 %, α-linolenic (18:3, *n*-3) 0.2 %, arachidic (20:0) 1.6 %, behenic (22:0) 0.3 %, erucic (22:1, *n*-9) 0.2 % and lignoceric (24:0) 0.3 %,were isolated from the n-hexane extract of neem seeds (Akihisa et al. 2011).

A tetranortriterpene nimbidinin obtained from the neutral fraction of nimbidin, the amorphous bitter principle of *Azadirachta indica* seed kernel, was shown to be biogenetically related to salannin. The crystalline acidic constituent nimbidic acid had been found to be identical to salannic acid, derived from salannin (Mitra et al. 1971). Azadirachtins A and B (Rembold et al. 1984) were obtained from seeds; out of 27 kg neem seed, amounts of 3.5 g and 0.7 g, respectively, were obtained after extensive chromatographic purifications (Rembold et al. 1987; Forster 1988), and several minor azadirachtins C–G were isolated (Rembold 1987 citing Forster). Three limonoids, 1-benzoyl-3-deacetyl-1-detigloyl salannin, 7-tigloyl-12-oxo vilasini and azadiralactone, and a triterpenoid azadirahemiacetal, along with three known constituents, nimbin, 3-deacetylsalannin and 6-deacetylnimbin, were isolated from the dried kernels (after extracting azadirachtin) of *Azadirachta indica* (Wang et al. 2013b).

Neem seed was found to contain about 45 % of a brownish-yellow of fixed oil, mainly constituted by oleic acid (50–60 %), palmitic acid (15–19 %), stearic acid (14–19 %) and linoleic acid (8–16 %) and characterized by an acrid taste and a persistent and unpleasant odour (Mongkholkhajornsilp et al. 2005). The major components of *A. indica* oil from neem seeds were hexadecanoic acid (34.0 %), oleic acid (15.7 %), 5,6-dihydro-2,4,6-triethyl-(4H)-1,3,5-dithiazine (11.7 %), methyl oleate (3.8 %) and eudesm-7(11)-en-4-ol (2.7 %) (Kurose and Yatagai 2005). The major components of *A. indica* oil were hexadecanoic acid (34.0 %), oleic acid (15.7 %), 5,6-dihydro-2,4,6-triethyl-(4H)-1,3,5-dithiazine (11.7 %), methyl oleate (3.8 %) and eudesm-7(11)-en-4-ol (2.7 %).

Other compounds found in neem oil included the following: three bitter compounds (nimbin, nimbinin and nimbidin) (Siddiqui 1942); meliantriol (Lavie et al. 1967); meldenin and nimbinin (Connolly et al. 1968); a tetranorterpenoid, vepinin (Narayanan et al. 1969); pentanortriterpenoids (nimbinene, 6-deacetylnimbinene, 6-*O*-acetylnimbandiol and nimbandiol) (Kraus and Cramer 1981b); three insect antifeedant tetranortriterpenoids (3-deacetylsalannin, salannol and 1,3-diacetylvilasinin) (Kraus and Cramer 1981a); an insect antifeedant and ecdysis inhibitor, deacetylazadirachtinol (Kubo et al. 1984); nimbocinol and 17-epinimbocinol (Gaikwad et al. 1990); mahmoodin, a limonoid, was isolated from neem oil, along with seven known tetranortriterpenoids (azadirone, epoxyazadiradione, nimbin, gedunin, azadiradione, deacetylnimbin and 17-hydroxyazadiradione) (Siddiqui et al. 1992b); deacetylgedunin, salannin, gedunin, 17-hydroxyazadiradione, nimbandiol, azadiradione, deacetylsalannin, deacetylnimbin, epoxyazadiradione, 17-epiazadiradione and nimbin were isolated from the methanol extract of neem oil (Ishida et al. 1992); azadirachtins A, B, D, H and I (Govindachari et al. 1996); tetranortriterpenoids, 1α,2α-epoxy-17β-hydroxyazadiradione, 1α,2α-epoxynimolicinol and 7-deacetylnimolicinol; and epoxyazadiradione, 17β-hydroxyazadiradione, gedunin, nimbin and nimolicinol (Hallur et al. 2002) and a tetrahydrofuranyl diester (Zhang et al. 2010).

Leaf Phytochemicals

Compounds isolated from the leaves included the following: nimbolide, a meliacin (Ekong 1967); meliantriol (Lavie et al. 1967); quercetin and isorhamnetin (Basak and Chakraborty 1968); β-sitosterol-β-D-glucoside, *n*-hexacosanol and β-carotene (Awasthi and Mitra 1971); a hexacyclic tetranortriterpenoid, vilasinin, a biogenetic precursor of salannin and nimbin isolated from fruits (Pachapurkar et al. 1974); quercetin glycosides, quercetin 3-*O*-L-rhamnoside and quercetin 3-*O*-B-rutinoside (rutin) (Nair and Subramaniam 1975); pentanortriterpenoids, nimbinene, 6-deacetylnimbinene, 6-*O*-acetylnimbandiol and nimbandiol (Kraus and Cramer 1981b); an isoprenylated flavanone, 8,3′-di-isoprenyl-5, 7-dihydroxy-4′-methoxyflavanone (Garg and Bhakuni 1984a); a tetranorterpenoid, 4α-6α-dihydroxy-A-homoazadiron (Bruhn et al. 1984); a tetranortriterpenoid, nimocinol (Siddiqui et al. 1984b); a limonoid, azadirachtin (Podder and Mahato 1985); 2′,3′-dehydrosalannol, a meliacin related to salannin (Garg and Bhakuni 1985); a γ-hydroxybutenolide tetranortriterpenoid named as isonimbocinolide (Siddiqui et al. 1986a); two bitter meliacins, nimocinolide and isonimocinolide (Siddiqui et al. 1986c); a triterpenoid nimbocinone and the two sterols sitosterol and stigmasterol (Siddiqui et al. 1986e); a ring C-seco-tetranortriterpenoid γ-hydroxybutenolide named as isoazadirolide, and a coumarin identified as scopoletin (Siddiqui et al. 1986g); two flavonol diglycosides (quercetin 3-*O*-β-rutinoside (rutin) and kaempferol 3-*O*-β-rutinoside) (Marco et al. 1986); cyclic trisulphide and cyclic tetrasulphide (Pant et al. 1986); nimbolide and 28-deoxonimbolide (Kigodi et al. 1989); two tetranortriterpenoids, 6-deacetylnimbinal and 28-deoxonimbolide (Bokel et al. 1990); an isoprenylated flavanone, 8-prenyl-5,7-dihydroxy-3′-(3-hydroxy-3, 3-dimethylbutyl)-4′-methoxyflavanone (Balasubramanian et al. 1993); two tetranortriterpenoids (azadirachtolide and deoxyazadirachtolide) (Ragasa et al. 1997); limonoids, nimbolide and 28-deoxonimbolide and α-linolenic acid (Nair et al. 1997), nimocinol, nimonol, 6-acetylnimonol identified as 6-acetoxyazadirone and dihydronimonol identical to isomeldenin (Suresh et al. 1997); nonterpenoidal benzenoid constituents, nimbothalin, with the structure 2-[(2,4-dicarboxy-3-methyl)-benzyl]-8,10-dimethyl-1,3,5,7,9-undeca-pentaene, and n-tridecylbenzene (Sharma et al. 1998); 14,15-epoxynimonol, a new tetranortriterpenoid (Govindachari, et al. 1999);twotriterpenoids,23-*O*-methylnimocinolide [7α-acetoxy-6α-hydroxy-23ξ-methoxy-3-oxo-24, 25,26,27-tetranorapotirucalla(apoeupha)-1, 14,20(22)-trieno-21,23-lactone] and 1, 7-*O*-deacetyl-23-*O*-methyl-7α-O-senecioylnimocinolide [6α-hydroxy-23ξ-methoxy-3-oxo-7α-senecioyloxy-24,25,26,27-tetranorapotirucalla(apoeupha)-1,14,20(22)-trieno-21,23-lactone] (Afshan et al. 1999); 6 α-*O*-acetyl-7-deacetylnimocinol, nimocinol and meliacinol (Siddiqui et al. 2000a); two triterpenoids, 22,23-dihydronimocinol (1) and desfurano-6α-hydroxyazadiradione (2), along with a known meliacin,7α-senecioyl-(7-deacetyl)-23-*O*-methylnimocinolide (Siddiqui et al. 2002); a tetranortriterpenoid, meliatetraolenone [24,25,26,27-tetranor-apotirucalla-(apoeupha)-6α-*O*-methyl, 7α-senecioyl(7-deacetyl)-11α,12α,21,23-tetrahydroxy-21,23-epoxy-2,14,20(22)-trien-1,16-dione], and odoratone (Siddiqui et al. 2003a); two tetracyclic triterpenoids, zafaral [24,25,26,27-tetranorapotirucalla-(apoeupha)-6α-methoxy-7α-acetoxy-1,14-dien-3,16-dione-21-al] and meliacinanhydride [24,25,26,27-tetranorapotirucalla-(apoeupha)-6α-hydroxy, 11α-methoxy-7α,12α-diacetoxy,1,14,20(22)-trien-3-one] along with two known constituents, nimocinol and isomeldenin (Siddiqui et al. 2004a); three tetracyclic triterpenoids of biogenetic interest, namely, melianol, desfurano-desacetylnimbin-17-one and meliatetraone (Siddiqui et al. 2001); a sulfonoglycolipid characterized as a sulfonoquinovosyldiacylglyceride (Chatterjee et al. 2010); 7 α-acetyl-15B-methoxy-29methylene 7,15-deoxonimbolide; 2-oxo-3-deacetylsalanin; 7 α-hydroxy-15β-hydroxy-7, 15-deoxonimbin (Githua et al. 2010); two flavonoids, genistein 7-*O*-glucoside (1) and (−)-epicatechin (Qudsia et al. 2011); quercetin-3-*O*-β-D-glucopyranoside (Islam et al. 2012); ferulic acid, myricetin, kaempferol, quercetin and

luteolin-7-*O*-β-d-glucoside (Sari 2012); and tripeptide from young leaves (Prabha and Ramachandramurty 2013).

Nimbolide was biosynthesized from [2-^{14}C, (4*R*)4-$^{3}H_1$]mevalonic acid lactone in the leaves of *Azadirachta indica* (Ekong and Ibiyemi 1985). A water-soluble pectic arabinogalactan with apparent molecular mass of 80 kDa and made up of (1 → 5)-/(1 → 3,5)-linked α-L-arabinosyl, (1 → 3)-/(1 → 6)-/(1 → 3,6)-linked β-D-galactosyl and terminal rhamnosyl and α-L-arabinosyl residues was isolated from *Azadirachta indica* leaves (Saha et al. 2010). Nimbolide [systematic name, (4α,5α,6α,7α,15β,17α)-7,15:21,23-diepoxy-6-hydroxy-4,8-dimethyl-1-oxo-18,24-dinor-11,12-secochola-2,13,20,22-tetraene-4,11-dicarboxylic acid gamma-lactone methyl ester] was isolated from neem leaves, and its isomer, isonimbolide [systematic name, (4α,5α,6α,7α,15α)-7,15:21,23-diepoxy-6-hydroxy-4,8-dimethyl-1-oxo-18,24-dinor-11,12-secochola-2,16,20,22-tetraene-4,11-dicarboxylic acid gamma-lactone methyl ester], was prepared from a novel rearrangement reaction of nimbolide using boron trifluoride etherate and tetrabutylammonium bromide (Solomon et al. 2005).

Conventional boiling method was an effective method to reduce tannin and phytate content in vegetables including neem leaves, but it also reduced the content of vitamin C (Somsub et al. 2008). The vitamin C contents (mg/100 g) of neem leaves were raw (71.5 mg), blanched (46.5 mg); tannin raw (723 mg), blanched (338 mg); inositol penta-phytate (IP5) raw (5 mg), blanched (1 mg); inositol hexaphosphate-phytate (IP6) raw (48 mg), blanched (35 mg); and total phytate raw (52 mg), blanched (38 mg).

Stem/Twig/Wood Phytochemicals

From the bark/stem/trunk were isolated branched chain paraffin alcohol, $C_{26}H_{54}O$, nimbosterol, sugiol and a new ketophenol, nimbiol, with molecular formula of $C_{18}H_{24}O_2$; nimbosterol was identified as β-sitosterol (Sengupta et al. 1960a); desacetylnimbin (Narayanan and Iyer 1967); two meliacins, nimbolins A and B, as well as fraxinellone and gedunin from trunk wood (Ekong et al. 1969); pentanortriterpenoids, nimbinene and 6-deacetylnimbinene (Kraus and Cramer 1981b); two isomeric diterpenoids, nimbione and nimbinone, and a new ring C-seco-tetranortriterpenoid, isonimbinolide (Ara et al. 1988); margosinone and margosinolone, two new polyacetate derivatives (Ara et al. 1989d); three tricyclic diterpenoids, margolone, margolonone and isomargolonone (Ara et al. 1989e); two diterpenoids, nimbionone and nimbionol, with structures determined as 12-hydroxy-13-methoxypodocarpa-8,11,13-trien-3,7-dione and 3,12-dihydroxy-13-methoxypodocarpa-8,11,13-trien-7-one, respectively (Siddiqui et al. 1988a); gedunin, an antimalarial agent (Khalid et al. 1989); two isomeric diterpenoids named nimbonone and nimbonolone with structures 12-ethyl-13-methoxy podocarpa-8,11,13-trien-7-one and 12-ethyl-13-methoxy podocarpa-8,11,13-trien-3-one, respectively, along with methyl grevillate (Ara et al. 1989b); gallocatechin, catechin, epigallocatechin and epicatechin (van der Nat et al. 1991b); and a limonoid, 12-hydroxyamoorastatone, along with two known limonoids, hydroxyamoorastatin-12 and 12-acetoxyam-oorastatin (Ahn et al. 1994). Two peptidoglycans, polymers NB-I and NB-II, were isolated from the crude bark extract (van der Nat et al. 1989). The carbohydrate part consisted predominantly of glucose. Arabinose, galactose and mannose were present in minor amounts (NB-II) or only as traces (NB-I). Protein was present for 5.5 % in NB-I and for 9.8 % in NB-II. From fresh green twigs the two tetranortriterpenoids γ-hydroxybutenolides desacetylnimbinolide and desacetylisonimbinolide together with desacetylnimbin were isolated (Siddiqui et al. 1986f) and two tetranortriterpenoids, isonimolide and isolimbolide (Siddiqui et al. 1987b).

Water-soluble polysaccharides, designated as GIa and GIb, were isolated from the bark (Fujiwara et al. 1982). GIa was composed of the repeating units, α-D-Glc 1 → 4α-D-Glc 1 → 4α-d-Glc 1 → 4α-D-Glc 1 → 4α-D-Glc 6 ← 1α-L-Araf, while GIb was a branched arabinofucoglucan, containing a main chain of (1 → 4)-linked α-d-glucopyranosyl units substituted in the 6th position with side chains of α-L-arabinofuranosyl units. 3-*O*-substituted fucopyranose is attached

to the α-(1→4) glucose units at the 4th position in the main chain. More water-soluble polysaccharides, designated as GIIa and GIIIa, were isolated together with GIa and GIb from the bark (Fujiwara et al. 1984). GIIa was composed of the following repeating unit: α-D-G1c1→4α-d-G1c1→3α-D-G1c1→3α-D-G1c6←1α-l-ArafGIIIa [numbrical formula], a branched arabinofucoglucan containing a main chain of 1→4-linked α-D-glucopyranosyl units substituted in the 6th position with side chains of α-l-arabinofuranose and β-L-fucopyranose. More water-soluble polysaccharides, designated as CSP-I, CSP-II and CSP-III, were isolated from neem bark (Kurokawa et al. 1988). The structure of CSP-I was composed of a β-D-(1→3)-linked galactopyranosyl backbone possessing branching points at position 0–6 to which α-l-arabinofuranose, β-D-galactopyranose and β-d-glucopyranose side chains were attached, on average to three of five galactosyl units. The component sugars of CSP-I were identified as galactose, arabinose and glucose. CSP-I contained 23 % L-arabinose, 69.2 % D-galactose and 7.6 % D-glucose, and their molar ratio was (:3:1), while CSP-II and CSP-III were found to have galactose and arabinose in the ratio of 3:1 and 2:1, respectively.

Cycloeucalenol and 24-methylenecycloartanol were identified in the wood oils (Ekong et al. 1968). 24-Methylenelophenol was identified from the heartwood (Banerji et al. 1987) and nimbolin B from the trunk wood (Ara et al. 1989c). Margosinolide and isomargosinolide, two new ring C-seco, bitter tetranortriterpenoid γ-hydroxybutenolides, were isolated from fresh, green twigs (Siddiqui et al. 1986b).

Root Phytochemicals

The following compounds were isolated: a modified diterpenoid nimbidiol (Majumder et al. 1987); a tetranortriterpenoid named as nimbolicin and nimbolin B (Ara et al. 1989c); two diterpenes, nimbilicin and nimbocidin (Ara et al. 1989a); three tricyclic diterpenoids, margocin, margocinin and margocilin with structures established as 8,11,13-abietatrien-3,7-dione, 8,11,13-abietatrien-12,16-dihydroxy-3,7-dione and 8,11,13-abietatrien-3β,12-dihydroxy-7-one (Ara et al. 1990); azadirinin (Ara et al. 1992); three limonoid antifeedants, trichilin H, 12-acetyl azedarach and 7,12-diacetyltrichilin B (Nakatani et al. 1994); four limonoids, 1-tigloyl-3,20-diacetyl-11-methoxymeliacarpinin, 3-tigloyl-1,20-diacetyl-11-methoxymeliacarpinin, 1-cinnamoyl-3-hydroxy-11-methoxy-meliacarpinin and 1-deoxy-3-methacrylyl-11-methoxy-meliacarpinin, together with known limonoid,1-cinnamoyl-3-acetyl-11-methoxymeliacarpinin (Takeya et al. 1996); and a tetranortriterpenoid nimbilin and an aromatic diterpene nimolinin (Ara et al. 1989f). It was found that neem root bark extracts contained total flavonoids in a range of 0.198–0.512 % g quercetin equivalent (Kiranmai et al. 2011). The decoction method gave the highest yield (20.2 %, w/w) of crude extract, while maceration extract gave the highest total flavonoid content (0.512 % g).

Plant (Unspecified Part) Phytochemicals and Related Derivatives

Three limonoids of the meliacin type, azadirone, azadiradione and epoxyazadiradione, and gedunin were isolated from the plant (Lavie et al. 1971). Neem gum on hydrolysis yielded L-arabinose, L-fucose, D-galactose and D-glucuronic acid (Mukherjee and Srivastava 1955). The aldobiuronic acid component of the gum obtained by graded hydrolysis was shown to be 4-*O*-(D-glucopyranosyluronic acid)-D-galactopyranose. Neem gum was found to contain D-glucosamine (Lakshmi and Pattabiraman 1967). Aldobiuronic acid, 4-*O*-(4-*O*-methyl-α-D-glucopyranosyluronic acid-d-galactose), and aldotriouronic acid were isolated from neem gum (Bajpai et al. 1970). The gum exuded by neem tree contained 35 % of proteinaceous material (Anderson and Hendrie 1971). The most abundant amino acid was aspartic acid with considerable amounts of serine and threonine and at least 2 % of amino sugars. The carbohydrate component was much more complex with galactose and arabinose, as

major components, and mannose, xylose, fucose and rhamnose. The uronic acid content (28 %) was higher, and a relatively high methoxyl content was found. The major aldobiuronic acid was 4-*O*-(4-*O*-methyl-α-D-glucopyranosyluronic acid)-D-galactose, and 4-*O*-(α-D-glucopyranosyluronic acid)-D-galactose was also present. A glycopeptide was isolated from neem gum by pronase digestion and found to contain arabinose, galactose and glucosamine in the ratio of 2.69:2.0:4.9 and amino acids asparagine, serine, threonine, arginine, proline, valine, phenylalanine and tyrosine (Nayak and Pattabiraman 1978). Acid hydrolysis of the gum exudates of neem tree, followed by acetylation and chromatographic separation, afforded the following components in the form of the corresponding acetates: diethylaspartate, 1-methyl-β-D-xylopyranoside, 3,6-di-*O*-ethyl-1-methyl-α-D-mannopyranoside, as well as its 4,6-di-*O*-ethyl isomer, the predominant component (comprising 88.7 % of the gum hydrolysates), and α-D-glucopyranose (Basaif and Abdel-Mogib 1998).

1,2,5-Trimethylnaphthalene was isolated from the dehydrogenation of a reduction product of nimbin (Sengupta et al. 1960b). The structure of deacetylazadirachtinol, an insect growth-regulating constituent of neem, had been reassigned as 3-tigloylazadirachtol (tigloyl = 2-methylcrotonoyl) (Klenk et al. 1986). Azadirachtin could be converted into three metabolites, viz.3-deacetylazadirachtin,1-detigloyl-3-deacetylazadirachtin-1-ene-3-one and 1-detigloyl-3-deacetyl-11,19-deoxa-12,19-oxa-11-oxoazadirachtin-1-ene-3-one, using *Nocardia* sp. as biocatalyst (Madyastha and Venkatakrishnan 1999).

Antioxidant Activity

Aqueous neem leaf extracts possessed free radical scavenging activity against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical (Sithisarn et al. 2006). The freeze-drying method gave the highest yield (51.50 %, w/w) of crude extract, while decoction gave the most effective DPPH scavenging activity (EC_{50}: 31.4 μg/mL). Neem leaf fractions reduced $DPPH^{\bullet}$, $ABTS^{\bullet+}$, superoxide ($O^{\bullet-}$), hydroxyl ($OH^{\bullet}$) and nitric oxide radicals to nonradical forms in a concentration-dependent manner in red blood cells (RBCs) and pBR322 DNA (Manikandan et al. 2009). Treatment with various fractions and subfractions significantly mitigated H_2O_2-induced oxidative damage to RBCs and pBR322 DNA.

Anticancer Activity

In Vitro Studies

Nimbidin from neem plant induced lethal antimitotic damage in a considerable proportion of treated meristematic cells of onion root tip cells and may hence have applications in cancer chemotherapy (Santhakumari and Stephen 1981). Limonoids, 12-hydroxyamoorastatone, hydroxyamoorastatin-12 and 12-acetoxyam-oorastatin, isolated from the roots, exhibited significant cytotoxicities against five human tumour cell lines (Ahn et al. 1994). Some limonoids from neem seed were found to be cytotoxic to N1E-115 neuroblastoma (mouse), 143B.TK^- osteosarcoma (human) and Sf9 (insect) cultured cell lines (Cohen et al. 1996). The most potent of these limonoids was nimbolide with an IC_{50} ranging from 4 to 10 μM and averaging 6 μM for the three cell lines. Other limonoids of decreasing potency and their average IC_{50} values (μM) were epoxyazadiradione 27 μM, salannin 112 μM and nimbin, deacetylnimbin and azadirachtin each >200 μM (practically nontoxic). Aqueous *Azadirachta indica* leaf extract exhibited inhibitory effects on 7,12-dimethylbenz(a)anthracene (DMBA)-induced skin carcinogenesis in BALB/c mice (Koul et al. 2006b). In the tumour-bearing mice that received neem leaf extract, a significant reduction in mean tumour burden and tumour volume was observed. Catalase activity was found to decrease significantly in the skin of mice, which received neem leaf extract treatment only. Ethanolic neem leaf extract caused cell death of prostate cancer cells (PC-3) by inducing apoptosis as evidenced by a dose-dependent increase in DNA fragmentation and a decrease in cell viability (Kumar et al. 2006). Also, neem extract showed decreased level of Bcl-2, which is

an anti-apoptotic protein and increased the level of Bax protein. A semi-purified nonterpenoid polar extract of *A. indica* seeds exhibited moderate to strong cytotoxicity on 3T6 murine fibroblasts (Di Ilio et al. 2006). PCNA (proliferating cell nuclear antigen) was significantly reduced in cells treated with that specific fraction of neem oil. Results strongly suggested a possible involvement of the mitochondrial pathway in the apoptotic cell death. Nimbolide was found to be growth inhibitory in human colon carcinoma HT-29 cells (Roy et al. 2006). Nimbolide treatment (2.5 μM) caused a 6.5-fold increase in the number of cells (55.6 %) in the G2–M phase compared with the control cells (8.8 %). At 48 h, the cell population in the G2–M phase decreased to 18 %, while that in the G0/G1 phase increased to 52.3 %. It was revealed that nimbolide-mediated G2–M arrest was accompanied by the upregulation of p21, cyclin D2 and Chk2 and downregulation of cyclin A, cyclin E, Cdk2 and Rad17. At G0/G1 cell cycle arrest, modulation in the expression of the cell cycle regulatory molecules was also observed. Nimbolide, extracted from neem flowers, exhibited moderate to very strong antiproliferative activity against U937, HL-60, THP1 and B16 cancer cell lines (Roy et al. 2007). Treatment of cells with 0.5–5.0 micron concentrations of nimbolide resulted in moderate to very strong growth inhibition in U937, HL-60, THP1 and B16 cell lines. In U937 cells, nimbolide treatment resulted in cell cycle disruption by decreasing the number of cells in G0/G1 phase, with initial increases in S and G2–M phases. Cells exposed to a higher dose of nimbolide for a longer period displayed a severely damaged DNA profile, resulting in a remarkable increase in the number of cells in the sub-G1 fraction, with a reciprocal decrease of cells in all phases. Gupta et al. (2010) found that nimbolide can sensitize tumour cells to chemotherapeutic agents through interaction with IκB kinase, leading to inhibition of nuclear factor (NF)-κB-regulated proteins.

Bose et al. (2007) found that neem leaf extract did not induce direct apoptosis of human tumour cell lines KB, MCF7 and K562; instead it stimulated human peripheral blood mononuclear cells to release cytotoxic cytokines, IFN-gamma and TNF-alpha. Pretreatment of mice with neem leaf preparation caused prophylactic growth inhibition of murine Ehrlich's carcinoma and B16 melanoma (Haque and Baral 2006). It was found that NLP-mediated activation of immune NK and NKT cells may be involved in tumour growth restriction and tumour cell cytotoxicity by enhancing the secretion of different cytotoxic cytokines.

In vitro studies showed that the HeLa tumour cell line exhibited higher sensitivity to neem oil methanolic extract than stabilized murine fibroblast line (3T6) (Ricci et al. 2008). The data strongly suggested that its toxic target was the cell membrane and that the extract contained one or more agents with antiproliferative potential. In vitro treatment of SKOV3, OVCAR4 and OVCAR8 ovarian cancer cell lines with gedunin (from neem) alone produced up to an 80 % decrease in cell proliferation, and combining gedunin with cisplatin demonstrated up to a 47 % decrease in cell proliferation compared with cisplatin treatment alone (Kamath et al. 2009). Gedunin was shown to manifest anticancer activity via inhibition of the 90 kDa heat-shock protein (Hsp90) folding machinery and to induce the degradation of Hsp90-dependent client proteins similar to other Hsp90 inhibitors (Brandt et al. 2008). Azadirone was found to possess potent cytotoxic activity against a panel of human cancer cell lines in in vitro studies (Nanduri et al. 2003). In vitro screening of a number of semisynthetic analogues of azadirone revealed that the alpha, beta-unsaturated enone moiety or its equivalent conjugated system in A-ring, C-7 acetyloxy/chloroacetyloxy or keto group in B-ring and the furan moiety were responsible for the activity of 1 and its analogues.

Sulfonoquinovosyldiacylglyceride isolated from neem leaves induced apoptosis in a dose-dependent manner with IC_{50} 8.3 μM against acute lymphoblastic leukaemia (ALL) MOLT-4 cell lines (Chatterjee et al. 2010). The compound showed significant DNA-binding properties as evidenced by the enhancement of melting temperature and perturbation of the characteristic B-form in CD evidence of calf thymus DNA.

Seven limonoid compounds (3 azadiradione type, two gedunin type and two nimbin type) exhibited cytotoxic activity against one or more cell lines (Kikuchi et al. 2011). Among these compounds, 7-deacetyl-7-benzoylepoxyazadiradione, 7-deacetyl-7-benzoylgeduin and 28-deoxonimbolide exhibited potent cytotoxic activity against HL-60 leukaemic cells with IC_{50} values in the range 2.7–3.1 μM. All 3 compounds induced early apoptosis in HL-60 cells and activated caspase-3, caspase-8 and caspase-9 in HL-60 cells. This suggested that these three compounds induced apoptotic cell death in HL-60 cells via both the mitochondrial- and the death receptor-mediated pathways.

Neem limonoids, azadirachtin and nimbolide, inhibited7,12-dimethylbenz[a]anthracene(DMBA)-induced hamster buccal pouch carcinogenesis by modulating xenobiotic-metabolizing enzymes, DNA damage, antioxidants, invasion and angiogenesis (Priyadarsini et al. 2009). Nimbolide, from neem flower and leaf, inhibited proliferation of human choriocarcinoma (BeWo) cells in a dose- and time-dependent manner with IC_{50} values of 2.01 and 1.19 μM for 7 and 24 h, respectively, accompanied by downregulation of proliferating cell nuclear antigen (Kumar et al. 2009). Examination of nuclear morphology revealed fragmentation and condensation indicating apoptosis. A decrease in Bcl-2/Bax ratio with increased expression of Apaf-1 and caspase-3 and cleavage of poly(ADP-ribose) polymerase strongly suggested that nimbolide-induced apoptosis was mediated by the mitochondrial pathway. All 32 limonoid compounds, isolated from seeds, exhibited moderate or potent inhibitory effects (IC_{50} values of 230–501 mol ratio/32 pmol TPA) against the Epstein-Barr virus early antigen (EBV-EA) activation induced by TPA (Akihisa et al. 2009). Also, azadirachtin B exhibited marked inhibitory activity on tumour-initiating activity on the two-stage carcinogenesis of mouse skin tumour induced by peroxynitrite as an initiator and TPA as a promoter. Limonoids from neem seeds, 1,3-diacetylvilasinin, 28-deoxonimbolide, ohchinin acetate, salannin, 2′,3′-dihydrosalannin, 3-deacetylsalannin and 17-defurano-17-oxosalannin, exerted moderate inhibition (IC_{50} values of 410–471 mol ratio/32 pmol TPA) of TPA-induced Epstein–Barr virus early antigen (EBV-EA) activation in Raji cells (Akihisa et al. 2011).

Both azadirachtin and nimbolide significantly suppressed the viability of human cervical cancer HeLa cells in a dose-dependent manner by inducing cell cycle arrest at G0/G1 phase accompanied by p53-dependent p21 accumulation and downregulation of the cell cycle regulatory proteins cyclin B, cyclin D1 and PCNA (proliferating cell nuclear antigen) (Priyadarsini et al. 2010). It was found that neem limonoids transduced the apoptotic signal via the mitochondrial pathway. It was concluded that antioxidants such as azadirachtin and nimbolide that could simultaneously arrest the cell cycle and target multiple molecules involved in mitochondrial apoptosis may offer immense potential as anticancer therapeutic drugs. Nimbolide effectively inhibited proliferation of WiDr colon cancer cells through inhibition of cyclin A leading to S phase arrest (Suboj et al. 2012). It also caused activation of caspase-mediated apoptosis through the inhibition of ERK1/2 and activation of p38 and JNK1/2. Further, nimbolide effectively retarded tumour cell migration and invasion through inhibition of metalloproteinase-2/9 (MMP-2/9) expression, both at the mRNA and protein level. It was also a strong inhibitor of VEGF expression, promoter activity and in vitro angiogenesis. Treatment with nimbolide resulted in dose- and time-dependent inhibition of growth of MCF-7 and MDA-MB-231 cells in vitro (Elumalai et al. 2012). It was found that nimbolide induced apoptosis by modulating modulation of apoptotic proteins (intrinsic pathway, Bax, bad, Bcl-2, Bcl-xL, Mcl-1, XIAP-1 and caspase-3 and caspase-9; extrinsic pathway, TRAIL, FasL, FADDR and caspase-8). In vitro studies by Srivastava et al. (2012) demonstrated that neem oil limonoids induced caspase-dependent and apoptosis-inducing factor-mediated apoptosis and autophagy in cancer cells.

Animal Studies

Water-soluble polysaccharides from neem bark, GIa and GIb, showed strong antitumour effect on

subcutaneously inoculated sarcoma-180 with almost complete regression of tumours when administered to mice at a daily dose of 50 mg/kg for 4 days (Fujiwara et al. 1982). GIa and GIb had no direct cytotoxic effect on sarcoma cells in vitro. Water-soluble polysaccharides, CSP-I and CSP-II, from neem bark inhibited the growth of subcutaneously inoculated sarcoma-180 in mice (Kurokawa et al. 1988). At low doses (2 mg/kg) CSP-I gave higher antitumour activity than CSP-II. Both had no direct cytocidal effect on sarcoma-190 cells in vitro. Feeding rats with diets containing 12.5 % neem flowers for 2 weeks strongly enhanced the phase II enzymes, i.e. glutathione *S*-transferase (GST) (Kusamran et al. 1998a). The results demonstrated that neem flowers contained monofunctional phase II enzyme inducers and compounds capable of repressing some monooxygenases, especially those involved in the metabolic activation of chemical carcinogens and thus may possess chemopreventive potential. Dasgupta et al. (2004) studied the anticarcinogenic potential of neem leaf extract using the protocol of benzo(a)pyrene-induced forestomach and 7,12-dimethylbenz(a)anthracene (DMBA)-induced skin papillomagenesis in Swiss albino mice . Their findings revealed its potential to induce only the phase II enzyme activity associated mainly with carcinogen detoxification in the liver of mice. The hepatic glutathione S-transferase- and DT-diaphorase-specific activities were elevated above basal level. With reference to antioxidant enzymes, the investigated doses were effective in increasing the hepatic glutathione reductase, glutathione peroxidase, superoxide dismutase and catalase activities significantly. Reduced glutathione measured as nonprotein sulphydryl was found to be significantly elevated in liver and in extrahepatic organs examined. Glutathione S-transferase and DT-diaphorase showed a dose-dependent increase in extrahepatic organs. There was a significant inhibition of tumour burden, in both the tumour model system studied. Tumour incidence was also reduced by both the doses of neem leaf extract. Administration of neem leaf extract effectively suppressed buccal pouch carcinogenesis initiated with DMBA as revealed by the reduced incidence of neoplasms in Syrian male hamsters (Balasenthil et al. 1999). Lipid peroxidation was found to be significantly decreased, whereas glutathione, glutathione peroxidase, glutathione S-transferase and gamma-glutamyl transpeptidase were elevated in the oral mucosa of tumour-bearing animals. Their data suggested that neem may exert its chemopreventive effects in the oral mucosa by modulation of lipid peroxidation, antioxidants and detoxification systems.

Tepsuwan et al. (2002) demonstrated that neem flowers contained some chemopreventive agents capable of inhibiting aflatoxin B1(AFB1)- and DMBA-induced liver and mammary gland carcinogenesis in rats. Neem flowers elicited a marked reduction in the incidence of mammary gland (about 35.2 %) and liver tumours (61.7 and 80.1 % for benign and malignant tumours, respectively). Further, the multiplicity of tumours per rats was also lower in the neem flower groups, i.e. those for mammary gland tumours and benign and malignant liver tumours were reduced to 44.0 %, 87.9 % and 88.9 %, respectively. Neem flowers were found to strongly induce the activity of GST while resulting in a significant reduction in the activities of some cytochrome P(450)-dependent monooxygenases in rat liver and to possess cancer chemopreventive potential against chemically induced mammary gland and liver carcinogenesis in rats (Sritanaudomchai et al. 2005). Nimbolide and chlorophylls were fractionated from neem flowers using a bioassay based on the induction of quinone reductase activity in mouse hepatoma Hepa 1c1c7 cultured cells and found to possess strong quinone reductase inducing activity.

Oral administration of aqueous neem leaf extract to mice with benzo(a)pyrene [B(a)P]-induced forestomach tumuorigenesis reduced aryl hydrocarbon hydroxylase (AHH) and enhanced uridinediphosphoglucuronosyltransferase (UDP-glucuronosyltransferase) activities in both the forestomach and liver, suggesting its potential in decreasing the activation and increasing the detoxification of carcinogens (Gangar and Koul 2007). Also, the lipid peroxidation levels decreased upon neem treatment in the hepatic tissue, suggesting its antioxidative and hence

anticarcinogenic effects. Administration of ethanolic neem leaf extract significantly inhibited cell proliferation and induced differentiation and apoptosis of DMBA-induced hamster buccal pouch carcinomas by inhibiting expression of PCNA, mutant p53 and Bcl-2 and overexpression of cytokeratin (Subapriya et al. 2006) and protecting against oxidative stress (Subapriya et al. 2005). Studies showed that dietary feeding of rats with neem extract at all doses (20, 100 and 250 mg/kg) significantly inhibited the induction of aberrant crypt foci, when compared to the azoxymethane-treated group (Arakaki et al. 2006). Neem extract also significantly decreased the proliferating cell nuclear antigen (PCNA) labelling indices of colon epithelium and aberrant crypt foci. Neem extract also showed antioxidative activity. The finding that dietary neem had possible chemopreventive effects in the present short-term colon carcinogenesis bioassay suggested that longer-term exposure may cause suppression of tumour development. Gangar and Koul (2008b) reported that aqueous neem leaf extract induced apoptosis in benzo(a)pyrene-induced murine forestomach tumours. Classical morphological features of apoptosis including chromatin condensation/marginalization, nuclear fragmentation and formation of apoptotic bodies were observed. DNA fragmentation and lipid peroxidation levels were observed to increase in the tumours of mice that received neem extract. They found that aqueous neem leaf extract mediated modulation of the peri-initiation phase of the process of forestomach tumourigenesis in rate induced by benzo(a)pyrene (Gangar and Koul 2008a). Neem extract reduced the activities of phase I biotransformation enzymes (cytochrome P450, cytochrome b(5) and aryl hydrocarbon hydroxylase) and enhanced the GSH contents as well as the activities of phase II biotransformation enzymes (glutathione S-transferase and UDP-glucuronosyltransferase).

Administration of hamster with neem leaf fractions reduced the incidence of DMBA-induced hamster buccal pouch carcinomas at a lower concentration compared to the crude extract (Manikandan et al. 2008b). Chemoprevention by neem leaf fractions was associated with modulation of phase I and phase II xenobiotic-metabolizing enzymes, lipid and protein oxidation, up-regulation of antioxidant defences, inhibition of cell proliferation and angiogenesis and induction of apoptosis. However, ethyl acetate fraction (EAF) was more effective than methanolic fraction (MF) in terms of antiproliferative and antiangiogenic effects and expression of CYP isoforms. The greater efficacy of EAF may be due to higher content of constituent phytochemicals as revealed by HPLC analysis and their antioxidative potential. Analysis of the free radical scavenging activities and reducing potential of crude ethanolic extract (CEE), ethyl acetate fraction (EAF) and methanolic fraction (MF) of neem leaf revealed a concentration-dependent increase in antioxidant potential that was in the order EAF>MF>CEE. Azadirachtin and nimbolide were found to mediate their antiproliferative effects by downregulating proteins involved in cell cycle progression and transduce apoptosis by both the intrinsic and extrinsic pathways in hamster buccal pouch of oral oncogenesis (Kumar et al. 2010a).

Administration of neem leaf extract (500 mg/kg) to 4T1 breast cancer BALB/c mice significantly suppressed c-Myc oncogene expression in breast cancer tissue (Othman et al. 2012). Arora et al. (2013) found that administration of neem leaf extract had a modulatory effect on cutaneous and hepatic biochemical status during promotion phase of 7,12-dimethylbenz(a)anthracene/phorbol-12-myristate-13-acetate (DMBA/TPA)-induced skin tumourigenesis in mice. Neem extract decreased DMBA/TPA-induced increase in cutaneous cytochrome P450 level and enhanced DT-diaphorase and uridine diphosphate glucuronosyltransferase activities when compared with DMBA/TPA group. In mice that received neem treatment along with DMBA/TPA, a significant increase in lipid peroxidation was observed which was associated with a decrease in cutaneous-reduced glutathione (GSH) level. Arora et al. (2013) found that administration of neem leaf extract had a modulatory effect on cutaneous and hepatic biochemical status during promotion phase of 7,12-dimethylbenz(a)anthracene/phorbol-12-myristate-13-acetate (DMBA/TPA)-induced skin tumorigenesis in mice. Neem extract decreased

DMBA/TPA-induced increase in cutaneous cytochrome P450 level and enhanced DT-diaphorase and uridine diphosphate glucuronosyltransferase activities when compared with DMBA/TPA group. In mice that received neem treatment along with DMBA/TPA, a significant increase in lipid peroxidation was observed which was associated with a decrease in cutaneous reduced glutathione (GSH) level.

Combined treatment of ethanol leaf extracts of *A. indica* and *Ocimum sanctum* improved the antioxidant status and inhibited cell proliferation and angiogenesis and induced apoptosis in N-methyl-N′-nitro-N-nitrosoguanidine (MNNG)-induced gastric carcinogenesis in male Wistar rats (Manikandan et al. 2008a). Administration of both ethyl acetate fraction (EAF) and methanolic fraction (MF) of neem leaf at a dose of 10 mg/kg bw effectively suppressed 7,12-dimethylbenz[a]anthracene (DMBA)-induced rat mammary tumour incidence (Vinothini et al. 2009). Chemoprevention by neem leaf fractions was associated with modulation of hormone and receptor status; xenobiotic-metabolizing enzymes and lipid and protein oxidation, with up-regulation of antioxidants; inhibition of oxidative DNA damage, protein modification and cell proliferation; and induction of apoptosis. However, EAF being richer in constituent phytochemicals was more effective than MF in modulating multiple molecular targets.

Antimutagenic Activity

The methanol neem leaf extract was found to contain weak antimutagen inhibiting the mutagenicities of both direct-acting mutagens, 2(2-furyl)-3(5-nitro-2-fury)acrylamide (AF-2) and sodium azide, in the Ames Salmonella mutagenicity test with *Salmonella typhimurium* TA100 as tester strain (Kusamran et al. 1998b).

Four prenylated flavanones, 5,7,4′-trihydroxy-8-prenylflavanone(1),5,4′-dihydroxy-7-methoxy-8-prenylflavanone (2), 5,7,4′-trihydroxy-3′,8-diprenylflavanone (3) and 5,7,4′-trihydroxy-3′,5′-diprenylflavanone (4), from neem flowers exhibited antimutagenic effect against heterocyclic amineTrp-P-1 (3-amino-1,4-dimethyl-5H-pyrido [4,3-b]indole) in the *Salmonella typhimurium* TA98 assay (Nakahara et al. 2003). The antimutagenic IC_{50} values of compounds 1–4 were 2.7, 3.7, 11.1 and 18.6 μM in the preincubation mixture, respectively. These compounds also similarly inhibited the mutagenicity of Trp-P-2 (3-amino-1-methyl-5H-pyrido[4,3-b]indole) and PhIP (2-amino-1-methyl-6-phenylimidazo[4,5-b] pyridine). All of the compounds 1–4 strongly inhibited ethoxyresorufin O-dealkylation activity of cytochrome P450 1A isoforms, which catalyzed N-hydroxylation of heterocyclic amines. However, compounds 1–4 did not show significant inhibition against the direct-acting mutagen NaN_3.

Antimicrobial Activity

Neem exerted antitubercular activity in sensitized guinea pigs; and nimbidin was found to inhibit the growth of *Trichophyton rubrum* in vitro (Murthy and Sirsi 1958b).

Cyclic trisulphide and cyclic tetrasulphide from neem leaves exhibited antifungal activity against *Trichophyton mentagrophytes* (Pant et al. 1986). Three tricyclic diterpenoids, margolone, margolonone and isomargolonone, isolated from neem stem bark were active against *Klebsiella, Staphylococcus* and *Serratia* species (Ara et al. 1989e). Pretreatment of *Streptococcus sanguis* with the neem stick (bark) extract at 250 μg/mL resulted in a significant inhibition of the bacterial adhesion to saliva-conditioned hydroxyapatite (Wolinsky et al. 1996). Pretreatment of saliva-conditioned hydroxyapatite with the neem stick extract prior to bacterial exposure elicited significant reductions in bacterial adhesion. The neem stick extract inhibited insoluble glucan synthesis. No inhibition of bacterial growth was observed among the streptococcal strains tested in the presence of < or = 320 μg/mL of the neem stick extract. Incubation of oral streptococci with the neem stick extract resulted in a microscopically observable bacteria aggregation. The data suggested that neem stick extract could reduce the ability of some streptococci to colonize tooth surfaces. The acetone extract of neem bark

showed marked antimicrobial activity in vitro against the cariogenic bacterium *Streptococcus sobrinus* with MIC value of 0.05 % (w/v) and bactericidal at concentrations of <1 %(w/v) (Bhuiyan et al. 1997). The aqueous extracts of chewing sticks (*Acacia arabica, Azadirachta indica, Pongamia pinnata* and *Salvadora persica*) at 5 mg phenol concentration produced 35–40 % inhibition of dextransucrase activity in *Streptococcus mutans*, a casual agent of dental caries in humans (Goyal et al. 2013). Neem oil showed antimicrobial dental plaque activity in vitro (Elavarasu et al. 2012).

Mahmoodin from neem oil showed significant antibacterial activity against various Gram-positive and Gram-negative bacteria (Siddiqui et al. 1992b). NIM-76, a spermicidal fraction from neem oil, showed stronger antimicrobial activity in vitro than the whole neem oil (Sairam et al. 2000). It inhibited growth of various pathogens tested including *Escherichia coli* and *Klebsiella pneumoniae* which were not affected by the whole neem oil. NIM-76 also exhibited antifungal activity against *Candida albicans* and antiviral activity against poliovirus replication in Vero cell lines. It also protected mice from systemic candidiasis as revealed by enhanced % survival and reduced colony-forming units of *C. albicans* in various tissues. Neem seed extract significantly distorted the growth curve of clinical isolates of dermatophytes, T*richophyton rubrum, Trichophyton mentagrophytes* and *Microsporum nanum* in vitro at MIC of 15ug/mL (Natarajan et al. 2003). The ethanol and ethyl acetate neem leaf extracts inhibited the growth of clinical isolates of dermatophytes isolated from human patients (Radhika and Michael 2013). The extracts were inhibitory to 72 isolates of *Trichophyton rubrum*, 36 isolates of *Trichophyton mentagrophytes*, 9 isolates of *Microsporum gypseum* and 9 isolates of *Trichophyton tonsurans.* The crude ethyl acetate leaf extract exhibited antimicrobial activity against Gram-positive bacteria, *Bacillus cereus, B. megaterium, B. subtilis* and *Staphylococcus aureus*; Gram negative bacteria, *Salmonella typhi* and *Vibrio mimicus*; and fungi, *Candida albicans* and *Aspergillus niger*, and weaker activity against *Escherichia coli* and *Shigella boydii* (Islam et al. 2012). The antibiotic kanamycin was far more potent against all the test microorganisms. The ethyl acetate leaf extract also showed cytotoxicity in the brine shrimp assay with LC_{50} of 0.61ug/mL.

A tetrahydrofuranyl diester isolated from petroleum ether extract of neem oil exhibited significant in vitro activities against three standard bacterial strains, including *Staphylococcus aureus*, *Escherichia coli* and *Salmonella enteritidis* (Zhang et al. 2010). Two flavonoids isolated from neem leaves exhibited antimicrobial activity in vitro (Qudsia et al. 2011). Genistein 7-*O*-glucoside was highly effective against *Lactobacillus* sp., at various concentrations reducing the bacterial growth by 52–99.8 %. (−)-Epicatechin was highly effective against *Azospirillum lipoferum* and *Bacillu*s sp., resulting in 94–100 % and 73–99 % reduction in bacterial growth, respectively.

A poly-herbal gel antiacne face wash formulation made up of the two polymers Carbopol and hydroxypropyl methylcellulose (HPMC) along with the extracts of the plants *Rauvolfia serpentina, Curcuma longa* and *Azadirachta indica* at 100 mg/mL concentration was proved to be a stable, nonirritant and effective herbal formulation for acne treatment (Rasheed et al. 2011). The efficacy when tested with a standard was almost same to that of clindamycin gel. *Azadirachta indica* had been reported to possess astringent, antiviral, discutient, stimulant and antibacterial properties and to work excellently well against acne in keeping the skin healthy.

In a 6-week clinical study of male patients (20–30 years), the use of a dental gel containing neem extract (25 mg/g) significantly reduced the plaque index and bacterial count (*Streptococcus mutans* and Lactobacilli species) compared to the control group with chlorhexidine gluconate (0.2 % w/v) mouthwash (Pai et al. 2004).

Of five endodontic irrigants formulated with neem plant parts, two neem irrigants, namely, leaf extract and a mixture of the seed–bark powder dissolved in dimethyl sulfoxide, displayed antimicrobial effect against *Candida albicans* and *Enterococcus faecalis* (Dutta and Kundabala 2013). The other neem-based irrigants, a leaf

powder dissolved in dimethyl sulfoxide, aqueous bark decoction and neem oil, did not possess any antimicrobial efficacy. Neem leaf extract was found to be effective in disrupting formation and structure of biofilm formation by *Pseudomonas aeruginosa* (Harjai et al. 2013). Levels of exopolysaccharide, alginate, hydrophobic interactions and uroepithelial cell attachment, which contributed to biofilm formation, were also affected significantly.

Antiviral Activity

Aqueous extract of neem leaves at its maximum nontoxic concentration of 1.897 mg/mL completely inhibited 100–10,000 tissue culture infective doses ($TCID_{50}$) of dengue virus type 2 as indicated by the absence of cytopathic effects (Parida et al. 2002). The in vivo protection studies with neem leaf extract at its maximum nontoxic concentrations of 120–30 mg/mL resulted in inhibition of the viral replication as confirmed by the absence of dengue-related clinical symptoms in suckling mice and absence of virus-specific 511 bp amplicon in RT-PCR. The pure neem, i.e. azadirachtin, did not reveal any inhibition on dengue virus type 2 replication in both in vitro and in vivo systems. Water-extracted polysaccharides from *Azadirachta indica* leaves showed activity against bovine herpesvirus type 1 (Saha et al. 2010). In their inhibitory concentration at 50 %, values ranging from 31.12 to 105.25 μg/mL were lower than the cytotoxicity values (>1,600–1,440 μg/mL). The antiviral effect was exerted during virus adsorption to the cell. Anionic groups in particular the sulphate groups appeared to be very important for the antiherpetic activity of these polymers. Tiwari et al. (2010) found that neem bark extract significantly blocked herpes simplex virus type 1 (HSV-1) entry into natural target cells at concentrations ranging from 50 to 100 μg/mL. Virions treated with neem bark failed to bind the cells implicating a role of the extract as an attachment step blocker. Cells treated with neem bark also inhibited HSV-1 glycoprotein-mediated cell–cell fusion and polykaryocyte formation.

Polysaccharides P1 and P2 obtained from neem leaves and their chemical sulphated derivatives (P1S and P2S) exhibited significant antiviral activity against poliovirus type 1 (PV-1) with inhibitory concentrations (IC_{50}) of 80 μg/mL, 37.5 μg/mL, 77.5 μg/mL and 12.1 μg/mL for P1, P1S, P2 and P2S, respectively, and the selectivity indices (SI) ranged from 18 to 131.9 (Faccin-Galhardi et al. 2012). A fraction of neem seed kernel alcohol extract exhibited antiviral activity against duck plague virus (DPV) in vitro with IC_{50} of 10.9 μg/mL (Xu et al. 2012).

Anti-inflammatory Activity

The inflammatory stomatitis in children was cured by neem bark extract (Lorenz 1976). Nimbidin isolated from neem seed oil significantly reduced the acute paw oedema in rats induced by kaolin and carrageenan (Pillai and Santhakumari 1981a). Nimbidin also significantly suppressed the formalin-induced arthritis of ankle joint and the fluid exudation in croton oil-induced granuloma in rats. In acute phase of inflammation, nimbidin (40 mg/kg) was found to possess significant activity as compared to phenylbutazone (100 mg/kg), a standard anti-inflammatory agent. Water-soluble polysaccharides from neem bark, GIIa and GIIIa, exhibited anti-inflammatory effect on carrageenan-induced oedema on oral administration (Fujiwara et al. 1984). The chloroform extract of neem stem bark was effective against carrageenan-induced paw oedema in rat and mouse ear inflammation (Tidjani et al. 1989).

Seven nortriterpenoids isolated from the seeds, azadiradione, epoxyazadiradione, 17-epi-17-hydroxyazadiradione,7-acetyl-16,17-dehydro-16-hydroxyneotrichilenone, 7-deacetylgedunin, nimolicinol and nimbin, on evaluation for their inhibitory effect against 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation (1 μg/ear) in mice, exhibited, except for nimbin, marked anti-inflammatory activity (ID_{50} values 0.09–0.26 mg/ear) (Akihisa et al. 2009). Eleven compounds isolated from neem seeds, 17-epiazadiradione, 17-epiazadiradione, azadiradionolide, 1,3-diacetylvilasinin,6-deacetylnimbin,6-acetylnim-

bandiol, 28-deoxonimbolide, ohchinin acetate, salannin, 2′,3′-dihydrosalannin and 3-deacetylsalannin, exhibited inhibitory activity against 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation (1.7 nmol/ear) in mice with ID_{50} values of 0.22–0.57 μmol/ear (Akihisa et al. 2011). Results of in vitro studies suggested that azadirachtin interacted with retinoic acid receptors and suppressed all *trans*-retinoic acid (ATRA) binding, inhibited falling off the receptors and activated transcription factors like CREB (cAMP-response element-binding protein), Sp1 and NF-κB (Thoh et al. 2011). The data indicated that azadirachtin exerted anti-inflammatory and antimetastatic responses by a novel pathway that would be beneficial for further anti-inflammatory and anticancer therapies. Epoxyazadiradione, a limonoid purified from neem, significantly inhibited macrophage migration inhibitory factor (MIF) (human, *Plasmodium falciparum* and *Plasmodium yoelii*)-mediated proinflammatory activities in RAW 264.7 cells (Alam et al. 2012). It prevented MIF-induced macrophage chemotactic migration, NF-κB translocation to the nucleus, up-regulation of inducible nitric oxide synthase and nitric oxide production in RAW 264.7 cells. In vivo, epoxyazadiradione prevented the release of proinflammatory cytokines such as IL-1α, IL-1β, IL-6 and TNF-α when LPS and PyMIF were co-administered to BALB/c mice. The results indicated an immense therapeutic potential of epoxyazadiradione against proinflammatory reactions induced by MIF of both malaria parasites and human.

Studies showed that animals treated with 100 mg/kg dose of carbon tetrachloride neem fruit skin extract and its isolated constituent azadiradione exhibited significant anti-inflammatory activity (Ilango et al. 2013). Anti-inflammatory activity was observed using carrageenan-induced paw oedema model. The hydroalcoholic neem leaf extract, ethyl acetate and n-butanol fractions of at 100 mg/kg body weight reduced significantly the formation of oedema induced by carrageenan in mice (Dinda et al. 2013).

Analgesic/Antinociceptive Activity

Azadirachta indica exhibited analgesic potency in experimental pain models in mice (Khanna et al. 1995). In the glacial acetic acid (GAA)-induced writhing test, neem extract (10, 30 and 100 mg/kg) dose-dependently reduced both the incidence and the number of writhes. Similarly, neem, at the dose levels tested, also enhanced tail withdrawal latencies in the tail-flick test for nociception. In the interaction studies, pretreatment with the opioid antagonist, naloxone (1 mg/kg), and the central noradrenaline depleter, DSP-4 (50 mg/kg), attenuated neem analgesia by differential degrees in both experimental models, whereas, the serotonin synthesis inhibitor, parachlorophenylalanine (300 mg/kg), potentiated the same. The results suggested that both central and peripheral mechanisms and complex neural pathways, opioid and non-opioid, may be involved in *Azadirachta indica*-induced analgesia.

Patel et al. (2005) demonstrated the antinociceptive effect of neem leaf extract in the pain model of the tail-flick test due to thermal stimulation. Mice treated with either saline or neem leaf in a dose of 3.12 mg/kg showed no significant change in tail-flick latency at intervals of 15, 30, 60, 120 and 180 min as compared to the control value at 0 min. Administration of higher doses of neem extract produced dose-dependent increase in the tail-flick latency. The combination, consisting of a low dose of neem extract (3.12 mg/kg) and a low dose of morphine (0.5 mg/kg), produced a significant increase in the tail-flick latency at all the time intervals. Naloxone pretreatment antagonized the antinociceptive effect of neem extract suggesting the involvement of endogenous opioid peptides or opioid receptors in the mediation of the antinociceptive response of neem leaf extract. Neem seed oil showed significant dose-dependent analgesic effect at doses of 1 and 2 mL/kg in the tail-flick latency test in albino rats (Kumar et al. 2012).

Recent studies showed that animals treated with 100 mg/kg dose of carbon tetrachloride neem fruit skin extract and its isolated constituent

azadiradione exhibited significant antinociceptive activity (Ilango et al. 2013). Antinociceptive screening by writhing test and hot plate technique supported both peripheral and central mechanisms, respectively. In the acetic acid-induced writhing mice model, the hydroalcoholic neem leaf extract and ethyl acetate and n-butanol fractions exerted a good analgesic effect characterized by a reduction in the number of writhes when compared to the control (Dinda et al. 2013). In tail-flick method, the extract and all the fractions at 100 mg/kg showed significant activity after 30 min.

Immunomodulatory Activity

The crude aqueous extract of *Azadirachta indica* bark was found to possess an inhibitory activity on both classical (CP) and alternative pathway (AP) activation of human complement (van der Nat et al. 1989). Two peptidoglycans, polymers NB-I and NB-II, were purified from the crude bark extract.

Ghosh et al. (2009) found that neem leaf preparation protected against apoptosis of circulating blood cells (leucocytes) induced by cisplatin and 5-fluorouracil (*cis* + 5-FU) in carcinoma-bearing mice. It also increased T lymphocyte and NK (natural killer) cell pool and augmented CD3– CD56+ natural killer (NK) and CD8 + CD56 T-cell-mediated tumour cell cytotoxicity (Bose et al. 2009). Cytotoxic T lymphocyte-mediated killing of oral cancer KB cells and NK cell-mediated killing of K562 (erythroleukaemic) cells were associated with activation of these T and NK cells by neem leaf glycoprotein. The data suggested that neem glycoprotein induced perforin-mediated tumour cell killing by T and NK cells through differential regulation of IFN-gamma signalling.

Vaccination of mice with carcinoembryonic antigen plus adjuvant assistance from neem leaf glycoprotein (NLGP) generated significantly higher antibody (IgG2a) and T-cell response than immunization protocol without NLGP (Sarkar et al. 2008). NLGP regulated the function of both B cells and macrophages by altering the expressions of various regulatory molecules, like, CD19 and CD11b. NLGP also directed carcinoembryonic antigen vaccination towards Th1 bias, by modulating cytokine secretion. This NLGP-generated anti-CEA immune response would be effective as a vaccine to lyse CEA(+) tumours in vitro and in vivo. Recent studies by Mallick et al. (2013a) found that treatment of mice bearing established sarcomas with neem leaf glycoprotein (NLP) (25 μg/mice/week subcutaneously for 4 weeks) resulted in tumour regression or dormancy. NLGP promoted the therapeutic antitumour immunity in mice by dynamically modulating the activation, expansion and recruitment of CD8(+) T cells into established tumours to induce significant tumour cell lysis and inhibit growth of mouse sarcoma.

Antidiabetic Activity

Oral administration of neem seed oil and nimbidin exerted significant hypoglycaemic effect in fasting rabbits (Pillai and Santhakumari 1981b). Neem leaf extract was found to significantly block the inhibitory effect of serotonin on insulin secretion mediated by glucose in hyperglycaemic rat pancreas (Chattopadhyay 1999). Earlier Chattopadhyay (1996) found that the reduction in peripheral utilization of glucose and glycogenolytic effect due to epinephrine action was blocked by *A. indica* leaf extract, however, almost completely in streptozotocin-induced diabetic rabbits and to a certain extent in normal ones.

In a study of patients with type 2 diabetes mellitus, administration of high dose (2 g three times per day) of *Azadirachta indica* extract for 14 days elicited significant hypoglycaemic activity (Waheed et al. 2006). In high dose, it can be successfully combined with oral hypoglycaemic agents in type 2 diabetic patients wherein diabetes was not controlled by these agents. *Azadirachta indica* was reported as one of six Indian ethnobotanically known plants with antidiabetic property (Bhat et al. 2011b). They found that *A. indica* chloroform extract exhibited a good oral glucose tolerance and significantly reduced the intestinal glucosidase activity in a diabetic murine model (Bhat et al. 2011a). Moreover, *A. indica* chloroform

extract showed significant increase in glucose-6-phosphate dehydrogenase activity and hepatic, skeletal muscle glycogen content after 21 days of treatment. In immunohistochemical analysis, they observed a regeneration of insulin-producing cells and corresponding increase in the plasma insulin and c-peptide levels with the treatment of *A. indica* chloroform extract. Oral treatment of alloxan diabetic rats with neem leaf and bark extracts were found significantly effective in reducing hyperglycaemia-induced oxidative stress (Shailey and Basir 2012).

Oral administration of combined *Abroma augusta* roots and *A. indica* leaves aqueous extract to alloxan diabetic rats once a day for 8 weeks caused significant lowering of blood sugar and serum lipids, formation of lipid peroxides and increased antioxidants (superoxide dismutase, catalase, glutathione peroxidase and glutathione transferase) in erythrocytes (Halim 2003). There was reduction in lipid peroxidation as thiobarbituric acid reactive substance (TBARS) in the heart, liver, kidney and muscles. It also prevented decrease in body weight. Combined herbal treatment gave more effective hypoglycaemic effect than given alone. An extract of Hypericum flowers (*Hypericum perforatum)* and neem oil was reported to be effective in diabetic foot wounds with exposed bone in a patient with bilateral advanced diabetic ulcers (Iabichella 2013). The use of this extract, administered by relatives at home, together with improved glycaemic control, reversed the worsening of ulcers in all treated patients, without performing any surgical intervention or hospital treatment. Ulcers fully recovered within a couple of months in all patients as well as improved diabetes control.

Gastroprotective Activity

Neem had been reported to have potent gastroprotective and antiulcer effects and to have the potential for the development of novel medicines for the therapeutic control of gastric hyperacidity and ulcer (Maity et al. 2009). Nimbidin, isolated from neem seed oil, in doses of 20–40 mg/kg (p.o.) exhibited significant protection against acetylsalicylic acid-, stress-, serotonin- and indomethacin-induced gastric lesions in rats (Pillai and Santhakumari 1984) and also in both types of chemically induced duodenal lesions in rodents. In ulcer healing tests, nimbidin significantly enhanced the healing process in acetic acid-induced chronic gastric lesions in albino rats and dogs. Nimbidin exhibited significant antisecretory activity in pylorus-ligated rats and cats (Pillai and Santhakumari 1985). In lumen-perfused rats it suppressed the basal as well as histamine- and carbachol-stimulated gastric acid output at 40 mg/kg (i.v). The antisecretory activity of nimbidin was found to be similar to that of H2 receptor antagonists, in suppressing histamine-induced gastric secretion in animals and man.

In a clinical trial of patients suffering from acid-related problems and gastroduodenal ulcers, oral administration of neem bark extract 30–60 mg twice daily for 10 weeks almost completely healed the duodenal ulcers. One case of oesophageal ulcer (gastroesophageal reflux disease) and one case of gastric ulcer were also healed completely when treated at the dose of 30 mg twice daily for 6 weeks (Bandyopadhyay et al. 2004). The volume of gastric hypersecretion and its pepsin activity were also inhibited by 63 % and 50 %, respectively. Neem leaf aqueous extract dose-dependently inhibited gastric lesions induced by restraint–cold stress, indomethacin and ethanol (Chattopadhyay et al. 2004). In stress ulcer model, it is more effective than ranitidine but less effective than omeprazole. It also dose-dependently blocks pylorus ligation and mercaptomethylimidazole-induced acid secretion. It inhibited H+–K+–ATPase activity in vitro in concentration-dependent manner to inhibit acid secretion. Oxidative membrane damage by hydroxyl radical (*OH) as measured by lipid peroxidation in stress ulcer was significantly blocked by neem leaf extract. Stress-induced apoptotic DNA fragmentation was also protected. The extract also prevented *OH-mediated mucosal DNA damage in vitro by scavenging the *OH. Aqueous neem leaf extract inhibited acid–pepsin secretion in 4 h in pylorus-ligated rats (Dorababu et al. 2006). Pretreatment with the

extract significantly reduced pentagastrin-induced acid secretion and inhibited the rat gastric mucosal proton pump activity but did not show any effect on mucin secretion. Thus, the data suggested that the ulcer-protective activity of neem leaf extract may be due to its antisecretory and proton pump inhibitory activity rather than on defensive mucin secretion. Further, acute as well as subacute toxicity studies indicated no mortality with 2.5 g/kg dose of the extract in mice and no significant alterations in body or tissue weight, food and water intake, haematological profile and various liver and kidney function tests in rats when treated for 28 days with 1 g/kg dose of neem leaf extract. Oral pretreatment of rats with neem extract (300 mg/kg) afforded protection against ethanol-induced gastric mucosal damage such as ulcerated mucosa with marked apoptotic bodies, mucosal haemorrhage and destruction of glandular elements (Ofusori et al. 2008). Their data suggested that pretreatment with neem extract may be useful in preventing prolonged ethanol-induced gastric ulcers.

Neuroprotective Activity

Administration of *A. indica* (500 mg/kg/day × 15 days) to rats with cerebral ischaemia–reperfusion injury significantly reduced hypoperfusion-induced functional disturbances (anxiety and disturbances of learning/memory) as tested by open-field paradigm and Morris water maze tests (Yanpallewar et al. 2005). Reactive changes in brain histology like gliosis, perivascular lymphocytic infiltration, recruitment of macrophages and cellular oedema following long-term hypoperfusion were also attenuated effectively by *A. indica*. Studies by Vaibhav et al. (2013) found that neem seed extract exhibited antioxidant and anti-apoptotic properties in transient middle cerebral artery occlusion rat model. It exhibited potent in-vitro reducing power (126.2 mg ascorbic acid equivalent/g extract) and free radical scavenging activities (DPPH 171.0 and NO 176.0 μg/mL) and inhibited oxidative stress and decreased the activities of caspase-3 and caspase-9, thus reducing neuronal loss in focal cerebral ischemia–reperfusion rats.

Hepatoprotective Activity

Fresh neem leaf (200 mg/kg body wt. p.o.) inhibited paracetamol (2 g/kg body wt. p.o.)-induced lipid peroxidation in albino rats and prevented depletion of sulphydryl groups in liver cells (Yanpallewar et al. 2003). Neem pretreatment restored the elevated serum levels of aspartate transaminase, alanine transaminase and alkaline phosphatase enzymes induced by paracetamol administration. Neem leaf extract has reversal effects on the adverse levels of blood and liver glutathione, Na + K(+)–ATPase activity and thiobarbituric acid reactive substances in paracetamol hepatotoxicity (Chattopadhyay 2003).

Treatment of DMBA-induced skin tumour-bearing male BALB/c mice with aqueous neem leaf extract significantly reduced hepatic damages and reversed the increased activities of hepatic tissue injury marker enzymes, namely, alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase (Koul et al. 2006a). Neem extract reduced oxidative stress by decreasing lipid peroxidation levels and enhancing the reduced glutathione contents and activities of various antioxidant enzymes. It reduced oxidative stress by decreasing lipid peroxidation levels and enhancing the reduced glutathione contents and activities of various antioxidant enzymes. Further, it caused a decrease in the activity of cytochrome P450 and cytochrome b5 and up-regulated the activity of glutathione S-transferase.

Oral administration of neem seed kernel active principle protected the male albino rat liver hepatocytes and testis seminiferous tubules from phenobarbital-induced damage (degeneration of cytoplasm and nucleus, necrosis and fragmentation of nucleus) (Raveendra et al. 2007). These deleterious changes almost returned to normal conditions in the rat liver and testis upon the oral administration of an antioxidant present in neem seed kernel extract.

Cardioprotective/Cardiovascular Activity

Studies showed that aqueous neem leaf extract (250, 500 and 1,000 mg/kg, p.o.) exerted equipotent cardioprotective activity in the experimental model of isoprenaline-induced myocardial necrosis in rats as compared to vitamin E (100 mg/kg, p.o.), a known cardioprotective antioxidant (Peer et al. 2008). Neem leaf extract and vitamin E significantly restored most of the adversely altered haemodynamic, biochemical and histopathological parameters caused by isoprenaline.

The hydroalcoholic neem leaf extract was found to reduce a dose-dependent hypotensive effect without altering the amplitude or rate of respiration (Chattopadhyay 1997). In isolated frog heart, there was no noticeable change in amplitude of contraction or rate of the heart at lower doses, but at higher doses there was temporary cardiac arrest in diastole.

Antidiarrhoeal Activity

In vitro and animal studies showed that neem leaf extract had antibacterial and antisecretory activity against *Vibrio cholerae*, a causative agent of watery diarrhoea such as cholera (Thakurta et al. 2007). Neem extract had significant antibacterial activity against multidrug-resistant *Vibrio cholerae* of serotypes O1, O139, non-O1 and non-O139 with MIC_{50} of 2.5 mg/mL, MIC_{90} of >5 g/mL and MBC of 10 mg/mL. Neem extract showed antisecretory activity on *Vibrio cholerae*-induced fluid secretion in the mouse intestine with inhibition values of 27.7, 41.1, 43.3, 57.0 and 77.9 % at doses of 100, 200, 300, 450 and 1,800 mg/kg, respectively. Oral administration of neem extract inhibited haemorrhage induced by *Vibrio cholerae* in the mouse intestine at a dose ≥300 mg/kg. The results supported the traditional use of neem in the treatment for diarrhoea and cholera.

Anxiolytic/Antidepressant Activities

A. indica exhibited anxiolytic activity in the open-field test in colchicine-lesioned animals with experimental Alzheimer's disease, which was comparable to that of diazepam (Raghavendra et al. 2013). In the elevated plus-maze test, *A. indica* significantly alleviated ibotenic acid and colchicine-induced anxiety. Ibotenic acid- and colchicine-induced depression was mitigated by *A. indica*, and the results were comparable to that of imipramine. In Morris water maze test, *A. indica* pretreatment improved reference memory, working memory and spatial learning, which were at par with the effects of donepezil. Both ibotenic acid- and colchicine-induced deficits in active avoidance learning and retention of learned behaviour were significantly reversed by *A. indica*. Also, ibotenic acid- and colchicine-induced increased lipid peroxidase activity was significantly reversed by *A. indica* (reductions in malondialdehyde level). *A. indica* stabilized rise in superoxide dismutase, and a decreasing trend in acetylcholinesterase (AChE) activity was seen with ibotenic acid and colchicine lesions. *A. indica* had no effect over the AChE activity.

Melanogenesis Inhibitory Activity

Five nortriterpenoids isolated from the seeds, nimolicinol, nimbin, 6-deacetylnimbin, α-nimolactone and desfuranoazadiradione, exhibited marked inhibitory effect on melanogenesis (74–91 % reduction of melanin content at 25 μg/mL) with no or almost no toxicity to B16 melanoma cells (Akihisa et al. 2009). Two nortriterpenoid limonoids isolated from the seeds, salannin and 3-deacetylsalannin, exhibited marked inhibitory effects (70–74 % reduction of melanin content at 25 μg/mL) on melanogenesis with only minor cytotoxicity (79–85 % of cell viability) in B16 melanoma cells (Akihisa et al. 2011).

Antipyretic Activity

Murthy and Sirsi (1958a) reported antipyretic activity in neem oil and its fraction. They found nimbidiol to have higher antipyretic activity than acetanilide experimentally. The antipyretic activity of nimbidin was reported by David (1969). Neem leaf extract was reported to have beneficial

antipyretic effect in *Escherichia coli* endotoxin-induced fever in rats (Ashorobi 1998). Administration of the same doses of neem leaf extract (125–375 mg/kg) during the early phase of fever development (during temperature rise) produced a significant fall in the rectal temperature to near normal. The maximum rise was 1.0 °C which later dropped to 0.18 °C and was sustained even beyond the experimental session.

Diuretic Activity

Sodium nimbidinate obtained from neem seed oil showed dose-dependent diuretic activity in dog when administered orally (Bhide et al. 1958). The action was primarily on the renal tubules, retarding the extraction of phenolsulphonaphthalein and reabsorption of electrolytes and water. The authors also conducted a clinical trial in nine patients with congestive cardiac failure (Sha et al. 1958). A good diuretic response was obtained in eight patients. No side effects were observed.

Insect Growth-Regulating/Larvicidal Activities

A γ-hydroxybutenolide tetranortriterpenoid named as isonimbocinolide isolated from the acidic fraction of the fresh, undried neem leaves showed insect growth-regulating properties against mosquitoes (*Aedes aegypti*) (Siddiqui et al. 1986a). Two bitter meliacins, nimocinolide and isonimocinolide, from leaves acted as insect growth regulators against houseflies (*Musca domestica*) and mosquitoes (*Aedes aegypti*) (Siddiqui et al. 1986c). Su and Mulla (1998a) found a significant antifeedancy at 5 and 10 ppm azadirachtin (AZ) for all neem formulations for larvae of *Culex tarsalis* and *Culex quinquefasciatus.* Some differences in larval susceptibility in terms of antifeedancy to the test formulations were noted between the two species. The formulated neem azadirachtin products were more persistent and effective than the technical azadirachtin in mosquito ovicidal activity (Su and Mulla 1998b). The wettable powder (WP) formulation was slightly more persistent and effective than the emulsifiable concentrate (EC).

Two triterpenoids, 23-*O*-methylnimocinolide [7α-acetoxy-6α-hydroxy-23ξ-methoxy-3-oxo-24,25,26,27-tetranorapotirucalla(apoeupha)-1,14,20(22)-trieno-21,23-lactone] and 1, 7-*O*-deacetyl-23-*O*-methyl-7α-O-senecioylnimocinolide [6α-hydroxy-23ξ-methoxy-3-oxo-7α-senecioyloxy-24,25,26,27-tetranorapotirucalla(apoeupha)-1,14,20(22)-trieno-21,23-lactone] isolated from leaves, showed insect growth-regulating effect on mosquitoes (*Aedes aegypti*) with LC_{50} 53 ppm and 2.14 ppm, respectively (Afshan et al. 1999). The senecioyloxy substituent at C-7 resulted in a significant increase of activity. Nimocinol and 6 α-*O*-acetyl-7-deacetylnimocinol isolated from neem leaf methanol extract exhibited toxicity on the fourth instar larvae of mosquitoes (*Aedes aegypti*) with LC_{50} values of 83 and 21 ppm, respectively (Siddiqui et al. 2000a). Meliacinin and azadironic acid from neem fruit coats showed toxicity against mosquito (*Anopheles stephensi*) with LC_{50} 13 and 4.5 ppm, respectively (Siddiqui et al. 2000b). Two triterpenoids, 22,23-dihydronimocinol (1) and desfurano-6α-hydroxyazadiradione (2), from neem leaves, showed mortality for the fourth instar larvae of the mosquito (*Anopheles stephensi*), with LC_{50} values of 60 and 43 ppm, respectively (Siddiqui et al. 2002). Meliatetraolenone and odoratone from neem leaves both showed mortality on the fourth instar larvae of mosquitoes (*Anopheles stephensi*) with LC_{50} values of 16 and 154 ppm, respectively (Siddiqui et al. 2003a). Twenty-seven compounds identified in nonpolar to less polar fractions of the ethanolic extract of fresh neem fruit showed pesticidal activity determined by WHO method against *Anopheles stephensi* (Siddiqui et al. 2004b). Gedunin exhibited 100 % toxic action against the fourth instar larvae of *Aedes aegypti* and *Culex quinquefasciatus* at 50 and 10 ppm (Gurulingappa et al. 2009). Epoxyazadiradione and epoxynimolicinol also showed significant toxicities (≥50 %) against larvae of both mosquito species at 50 ppm.

Oral administration of a commercial formulation NeemAzal to *Anopheles stephensi* females through artificial blood meals diminished blood intake and oviposition in a concentration-dependent manner (Lucantoni et al. 2006). Similar results were obtained on females, which had consumed NeemAzal in sucrose solution before taking a blood meal of plain blood. Neem-treated females displayed a delay in oocyte development in both the phase of vitellogenesis and the phase of choriogenesis. The ultrastructural studies on ovaries from NeemAzal treated females revealed distinct structural modifications indicative of (1) a complete block of oogenesis, (2) an impairment of vitellogenesis and vitelline envelope formation and (3) a severe degeneration of follicle cells. The results indicated that NeemAzal impaired hormone control of oogenesis and exerted a cytotoxic effect on both follicular cells and oocytes of the Asian malaria vector, *A. stephensi*. In laboratory conditions, LC_{50} and LC_{90} values for Neemarin (a neem extract) were 0.35 and 1.81 mg/L for *Anopheles stephensi*, the main local malaria vector, and 0.69 and 3.18 mg/L for *Culex quinquefasciatus* (Vatandoost and Vaziri 2004). The mortality in the pupal stage was significantly higher than the other stages. In field trials, using recommended dosages of 1 and 2 L/ha, mortality of *Anopheles* spp. larvae was also higher than *Culex* spp. Prevention of adult emerged and pupal mortality was the main activity of these compounds. The maximum time of efficacy was 7 days at the highest concentration (2 L/ha).

Neem oil exhibited good larvicidal properties against the malaria vector *Anopheles gambiae* (Okumu et al. 2007). The oil suppressed adult emergence by 50 % at a low concentration of 6 ppm. It had an LC_{50} value of 11 ppm after 8 days, which was nearly five times more toxic than the corn oil formulation. Aqueous extract of neem wood chippings inhibited all larval stages of the malarial vector *Anopheles gambiae* with IE_{50} of (<4 g/L) (Howard et al. 2009). For pupae, significant mortality occurred at 5 g/L. In addition to growth retardation, reduced reaction by larvae to visual and mechanical stimuli observed at higher neem concentrations may make them more susceptible to natural predators. Aqueous extracts of neem wood chippings could be produced locally, and their use had the potential to be a low-tech component of integrated malaria vector control schemes.

The toxicity of neem fruit fractions (KEA-1 to KEA-5) obtained from the kernels exhibited toxicity against the 3rd instar larvae of *Aedes aegypti*; toxicity of these fractions was observed to increase with the maturity of the fruits (Siddiqui et al. 2009a). The n-hexane-soluble fraction of fresh neem flowers exhibited larvicidal activity against *Anopheles stephensi*, a vector of malaria parasite (Siddiqui et al. 2009b). A field study conducted in Sanambele (Mali) in 2010 demonstrated that neem leaf slurry could be use as a sustainable dry season management strategy to control the malaria vector *Anopheles gambiae* using available tools and resources in the village (Luong et al. 2012). The 50 and 90 % lethal concentrations at 72 h were 8,825 mg/L and 15,212 mg/L, respectively, and experimental concentration ranges were 1,061–21,224 mg/L pulverized neem leaves in distilled water.

Azadirachtin was found to possess larvicidal activity similar to those of insect growth regulators against the immature stages of the horn fly, *Haematobia irritans*; the stable fly, *Stomoxys calcitrans*; and the housefly, *Musca domestica* (Miller and Chamberlain 1998). An emulsifiable concentrate had an LC_{50} for larval horn flies of 0.151 ppm and an LC_{90} of 0.268 ppm. For larval stable flies, the EC formulation had an LC_{50} of 7.7 ppm and an LC_{90} of 18.7 ppm azadirachtin in manure. Against larval houseflies, the LC_{50} and LC_{90} were 10.5 and 20.2 ppm, respectively. Laboratory tests showed that neem products containing 0.24 % azadirachtin A significantly reduced larval and pupal survival, adult emergence, pupal weight, adult wing length and fecundity on the subsequent generation, in a dose-dependent manner in housefly, *Musca domestica*, and blowfly, *Chrysomya megacephala* (Siriwattanarungsee et al. 2008). The data reinforced the efficacy of neem extract in reduced adult emergence and anti-fecundity in the subsequent generation. However, neem extract induced only low to moderate larval and pupal mortalities.

Antiparasitic Activity

Nimbolide, a constituent of *A. indica*, inhibited *Plasmodium falciparum* in vitro with EC_{50} of 0.95 μg/mL (Rochanakij et al. 1985). The EC_{50} of crude aqueous neem extract was 115 μg/mL and of crude ethanol extract was 5.0 μg/mL. However, neither the crude extracts nor nimbolide showed any activity in vivo against *Plasmodium berghei* in the mouse either through ingestion or subcutaneous injection.

Azadirachtin, from neem and selected semisynthetic derivatives, inhibited the development of the motile male malarial gamete in vitro (Jones et al. 1994). Changes in the hemiacetal group at position C-11 in the molecule resulted in a loss of activity in this assay. Udeinya et al. (2006) found two neem leaf fractions lysed 50 and 100 % of developing gametocytes of *Plasmodium falciparum*, at 10^{-3} and 1.0 μg/mL, respectively, and 50 and 100 % of mature gametocytes at 10^{-3} and 10^{2} μg/mL, respectively. The activity was superior to chloroquinone. In another subsequent study, they reported that separate 72 h cultures of both asexual parasites and mature gametocytes, treated with crude acetone–water (50/50) neem leaf extract (0.5 μg/mL), had parasite numbers of less than 50 % of the numbers in control cultures, which had 8.0 % and 8.5 % parasitaemia, respectively (Udeinya et al. 2008). In cultures containing 2.5 μ/gmL of the extract, asexual parasites and mature and immature gametocytes were reduced to 0.1 %, 0.2 % and 0 % parasitaemia, respectively. There were no parasites in the cultures containing 5.0 μg/mL of the extract. NeemAzal (R), an azadirachtin-enriched neem seed extract, completely obstructed the development of *Plasmodium berghei* in its vector *Anopheles stephensi* at an azadirachtin dose of 50 mg/kg mouse body weight (Lucantoni et al. 2010). Examination of treated mosquitoes did not reveal any oocyst, and none of the healthy mice exposed to their bites developed parasitaemia. Gedunin, azadirone and neemfruitin A from neem fruit exhibited significant antiplasmodial activity (Chianese et al. 2010).

Azadirachtin was found to have an effect on both immunity and *Trypanosoma cruzi* interaction within *Rhodnius prolixus* and other triatomines (de Azambuja and Garcia 1992). Administered through a blood meal, azadirachtin affected the immune reactivity as shown by a significant reduction in numbers of haemocytes and consequently nodule formation following challenge with *Enterobacter cloacae* beta-12, reduction in ability to produce antibacterial activities in the haemolymph when injected with bacteria and decreased ability to destroy the infection caused by inoculation of *E. cloacae* cells. A single dose of azadirachtin was able to inhibit the development of *Trypanosoma cruzi* in *Rhodnius prolixus* if given through the meal at different intervals, together with, before or after parasite infection. Similarly, these results were observed with different triatomine species and different strains of *T. cruzi*. Azadirachtin induced a permanent resistance of the vector against reinfection with *T. cruzi*. Three tetranortriterpenoids from neem leaves, 7 α-acetyl-15B-methoxy-29methylene 7,15-deoxonimbolide, 2-oxo-3-deacetylsalannin and 7 α-hydroxy-15β-hydroxy-7,15-deoxonimbin, exhibited strong antitrypanosomal activities against *Trypanosoma brucei rhodesiense* with MIC values ranging of 6.9, 15.6 and 7.8 μg/mL, respectively, and were more active than Cymelarsan (a standard drug), which had an MIC value of 187.5 μg/mL (Githua et al. 2010).

Alcohol and aqueous neem flower extracts exerted lethal contractile and paralysis effect on the microfilariae of the parasite *Setaria cervi*, with LC_{50} of 15 and 18 ng/mL, respectively (Mishra et al. 2005). A commercial shampoo based on neem seed extract was found to be more effective in vitro on head lice collected from schoolchildren than the permethrin-based product (Heukelbach et al. 2006). Three hours after neem treatment, a mortality of 94 % was obtained. NeemAzal F (neem seed oil extract) induced a significant increased in mortality rates of newly hatched larvae, unfed larvae and unfed adults reaching 100 % on the 15th, 3rd and 15th days posttreatment of the tick species *Hyalomma anatolicum excavatum*, respectively (Abdel-Shafy and Zayed 2002). The mortality rates increased with the extract concentrations. Although it had no significant effect on the moulting rates of fed

nymphs, it caused malformation or deformities in 4 % of adults moulted. It was concluded that the concentration of NeemAzal F which may be used for commercial control of this tick species was 1.6 and 3.2 %. Results of in vitro studies with engorged females of tick, *Rhipicephalus microplus,* showed that the neem seed extracts had acaricide activity inhibiting egg laying and the larval hatching rate, with the extract containing 10,000 ppm azadirachtin being the most effective (Giglioti et al. 2011).

Neem leaf and fruit extract and fractions were found to have cytotoxic and antileishmanial activity against promastigotes and amastigotes of *Leishmania amazonensis* (Carneiro et al. 2012). The ethanolic leaf extract and dichloromethane and chloroform fractions had IC_{50} values of 38, 3.9 and 1.2 µg/mL for promastigotes and 9.8, 1.1 and 0.6 µg/mL for amastigotes, respectively, at 72 h. For the ethanolic fruit integument extract and dichloromethane fraction, the IC_{50} was 2.7 and 2.1 µg/mL for promastigotes and 0.4 and 0.6 µg/mL for amastigotes.

Antifertility Activity

The number of pregnancies as well as the litter size was reduced when male mice were treated with *Azadirachta indica*, while control mice showed 100 % fertility rate (Deshpande et al. 1980). After one and half month of drug-free interval, the male mice showed a normal reproductive function as indicated by the number of pregnancies. Histological examination of testes revealed no evidence of inhibition of spermatogenesis. At subcutaneous doses up to 0.3 mL/rat, neem oil did not possess any oestrogenic, antioestrogenic or progestational activity and appeared not to interfere with the action of progesterone (Prakash et al. 1988). These findings were confirmed using the histo-architecture of the uterus of treated rats. Since the post-coital contraceptive effect of neem oil appeared to be nonhormonal, neem oil would be expected to elicit less side effects than the steroidal contraceptives. Female rats treated with neem oil remained infertile for variable periods ranging from 107 to 180 days even after repeated matings with males of proven fertility (Upadhyay et al. 1990). Neem-treated animals showed a significant leucocytic infiltration in the uterine epithelium between days 3 and 5 post coitus, i.e. during the preimplantation period. Intrauterine application of neem oil appeared to induce a preimplantation block in fertility. Subcutaneous administration of neem oil to cyclic rats caused significant damage to the luminal epithelium of the uterus and to the uterine glands, also decreased glycogen and total protein contents in the ovary and uterus and augmented the activity of acid phosphatase in these organs (Tewari et al. 1989).

Administration of neem oil to ovariectomized rats decreased protein and glycogen content and increased acid phosphatase activity in the uterus, whereas its conjoint administration with estradiol dipropionate or progesterone did not cause significant changes relative to those seen with the steroids per se. It was concluded that the histological and biochemical alterations observed were due to the toxicological potential of the neem oil rather than to hormonal properties. Oral administration of Praneem (neem seed extract) abrogated pregnancy in baboons and bonnet monkeys (Mukherjee et al. 1996). Termination of pregnancy was observed with the appearance of blood in the vaginal smears and decline in chorionic gonadotropin and progesterone. Pregnancy continued in the control animals treated with peanut oil at the same dose. Pregnancy was terminated successfully in both rodents and primates with no significant side effects by purified neem extracts (Talwar et al. 1997). Treatment caused an elevation of both immunoreactive and bioactive TNF-alpha and gamma-interferon in serum, mesenteric lymph nodes and foetoplacental tissue and an early decrease in progesterone in primates. Mukherjee et al. (1999) showed that a pure active fraction (containing six components) of neem seeds could be obtained for the purpose of early post-implantation contraception when given orally, and its mechanism of action appeared to be by activating cell-mediated immune reactions. The fraction could completely abrogate pregnancy in rodents up to a concentration of 10 %. The active fraction was identified to

be a mixture of six components, comprising saturated and mono- and diunsaturated free fatty acids and their methyl esters (Garg et al. 1998).

Volatile fraction of neem oil coded NIM-76 inhibited spermatozoal motility in a dose-dependent manner; the minimum concentration was 0.25 mg/mL for rat and 25 mg/mL for human spermatozoa (Riar et al. 1990). The activity of this fraction was not altered in the presence of vaginal or cervical mucus. Intravaginal application of NIM-76 in rabbits showed no irritation to the vaginal mucosa. NIM-76 was found to have antifertility effects in rats, rabbits and rhesus monkeys when applied before coitus but not so when applied during post-coital stages (Riar et al. 1991). Thus, it appeared to act mainly by its spermicidal effect. No alteration in the estradiol (E2) and progesterone values was observed after the application of the drug in monkeys.

Supplementation of pentoxifylline, a drug known to enhance the motility of the sperm, could not prevent the spermicidal action of NIM-76 (Sharma et al. 1996). There was damage to the cell membrane and a gradual leakage of cytosolic LDH from the sperm in the presence of NIM-76.

Neem leaf extract (200 mg/kg) induced cornified phase of oestrous cycle of adult rats which persisted till the last day of treatment (Chattopadhyay 1993). Oral administration of polar and nonpolar fractions of *A. indica* seed extract inhibited folliculogenesis in female albino rats (Roop et al. 2005). The extract reduced the number of follicles in various stages (I–VII) of follicular development. The results suggested that neem extract may have potential as an ecological safe and active control of rodent population. Aqueous neem leaf extract induced granulosa cell apoptosis through the mitochondria-mediated pathway, reduced estradiol 17β concentration and induced apoptosis in ovulated oocytes in sexually immature female rats (Tripathi et al. 2013). The results indicated that granulosa cell apoptosis mediated neem leaf extract-induced oocyte apoptosis during female fertility regulation in rat.

Studies showed that gavage administration of neem leaf methanol extract adversely affected the fertility of Wistar rats by reducing serum levels of luteinizing hormone and, subsequently, the release of ova during ovulation (Owolabi et al. 2008). Animal studies showed that both neem seed oil and azadirachtin impaired intrauterine development and altered antioxidant/oxidative status during pregnancy (Dallaqua et al. 2012). Treatment with both during pregnancy exerted no hypoglycaemic and antihyperglycaemic effects on nondiabetic and diabetic rats, respectively; affected OGTT (oral glucose tolerance test) glycaemic levels in diabetic rats; increased the proportion of foetuses classified as small for pregnancy age in all groups; and did not interfere with the lipid profile in nondiabetic dams. Neem oil reduced the rate of total cholesterol and non-esterifed fatty acids in diabetic animals. Both neem oil and azadirachtin increased lipoperoxidation, characterized by increased malondialdehyde levels in nondiabetic rats.

Toxicity Studies/Case Reports

Reported toxicity of preparations and isolated neem compounds was reported to be low, except for neem seed oil (van der Nat et al. 1991a). Margosa oil was reported to cause toxic encephalopathy particularly in infants and young children (Sinniah and Baskaran 1981; Lai et al. 1990). Usual symptoms included vomiting, drowsiness, tachypnoea and recurrent generalized seizures; leucocytosis and metabolic acidosis were also observed. Sinniah and Baskaran (1981) reported that margosa oil may be involved in the aetiology of Reye's syndrome among Indians in Malaysia. Dhongade et al. (2008) reported a case of neem oil poisoning in a 5-year-old child presented with refractory seizures and was having metabolic acidosis. Late neurological sequelae in the form of auditory and visual disturbances and ataxia were present. Bhaskar et al. (2010) reported a case of a 35-year-old female patient with ophthalmopathy, loss of bilateral vision, after suicidal consumption of neem oil for 5 days.

Technical azadirachtin administered 12 % orally to male and female rats at doses of 500, 1,000 and 1,500 mg/kg/day for 90 days did not produce any signs of toxicity and mortality and changes in tissue weight, pathology and serum

and blood parameters (Raizada et al. 2001), indicating that azadirachtin tested at the highest dose was well-tolerated by rats of both sexes. Thus, the highest dose, 1,500 mg/kg, could be used as a basal dose for the determination of the no-observed-adverse-effect level (NOAEL) of azadirachtin to calculate its safety margin. Feeding of rats with 100, 500 and 1,000 ppm technical azadirachtin through diet (equivalent to 5, 25 and 50 mg/kg body weight of rats) has not produced any adverse effects on reproductive function of rats, and data were comparable to control animals over two generations (Srivastava and Raizada 2007). There were no toxicological effects in parent rats as evidenced by clinical signs of toxicity; enzymatic parameters like AST, ALT, ALP, serum bilirubin, serum cholesterol and total protein; and histopathology of the liver, brain, kidney and testes/ovary. The litters of F(1B) and F(2B) generations were devoid of any morphological, visceral and teratological changes. Absence of any major adverse reproductive effects in adults as well as in 21-day-old pups of F(2B) generation suggested the safe use of technical azadirachtin as a biopesticide. Toxicity studies by Kupradinun et al. (2010) revealed that methanol extract of neem flowers had high LD_{50} value, greater than 12 g/kg bw which was about 800 times of human use. In subacute toxicity, the extract showed slight toxicity to rats at the dose greater than 150 mg/kg/day (10 times of human use).

Oral administration of a crude ethanol neem leaf extract to adult Swiss albino mice for 7 days at 5 mg, 10 mg or 20 mg/10 g bw/day significantly increased the incidence of structural and mitotic disruptive changes in metaphase chromosomes of bone marrow cells (Awasthy et al. 1999). They postulated that one or the other of the many constituents of the extract, along with genera free radicals, interfered with DNA to yield chromosome strand breakage or produced spindle disturbances, inducing belated genotoxic effect. Recent studies by Ashafa et al. (2012) reported that the ethanolic extract of neem stem bark at the doses of 50, 100, 200 and 300 mg/kg body weight may not be completely safe as an oral remedy and should be taken with caution as it caused adverse alterations in biochemical parameters (serum globulins, total and conjugated bilirubin, serum cholesterol, low-density lipoprotein cholesterol and computed atherogenic index) with consequential effects on the normal functioning of the organs (liver, kidney, lungs and heart) of the animals. In a 90-day subchronic toxicity study of neem oil, histopathological examinations at the 90th day showed that the 1,600 mg/kg/day dose of neem oil had varying degrees of damage on each organ except the heart, uterus and ovaries (Wang et al. 2013a). After a 30-day recovery, the degree of lesions to the tissues was lessened or even restored. The no-observed-adverse-effect level (NOAEL) of neem oil was 177 mg/kg/day for mice and the target organs of neem oil were determined to be the testicle, liver and kidneys. In another recent toxicological evaluation of neem oil, the LD_{50} values of neem oil were found to be 31.95 g/kg and the subacute treatment with neem oil failed to change body weight gain and food and water consumption (Deng et al. 2013). Serum biochemistry analysis showed no significant differences in any of the parameters examined under the dose of 1,600 mg/kg/day. Histopathological examinations showed that the target organs of neem oil were the testicle, liver and kidneys up to the dose of 1,600 mg/kg/day.

Injection of Swiss mice and Sprague–Dawley rats with neem leaf glycoprotein (NLGP) even in higher doses than effective concentration caused no behavioural changes in animals and no death (Mallick et al. 2013b). NLGP showed no adverse effect on the haematological system and caused no histological alterations in the organ microstructure of the NLGP-treated mice and rats. Histological normalcy of the liver and kidney was further confirmed by the assessment of liver enzymes like alkaline phosphatase, SGOT and SGPT and nephrological products like urea and creatinine. NLGP had no apoptotic effect on immune cells but induced proliferation of mononuclear cells collected from mice and rats. Accumulated evidence strongly suggested the nontoxic nature of NLGP. Thus, it was concluded that neem leaf glycoprotein could be recommended for human use in anticancer therapy.

Traditional Medicinal Uses

Since antiquity, neem has been extensively used in Ayurveda, Unani and homoeopathic medicine and has become a cynosure of modern medicine (Subapriya and Nagini 2005). In traditional medicine literature, preparations of neem tree are claimed to be useful in a wide spectrum of diseases especially for inflammation-related diseases (van der Nat et al. 1991a). Neem oil and the bark and leaf extracts have been therapeutically used as folk medicine to control leprosy, intestinal helminthiasis, respiratory disorders and constipation and also as a general health promoter. Its use for the treatment of rheumatism, chronic syphilitic sores, scabies and indolent ulcer has also been evident. Neem oil finds use to control various skin infections. Bark, leaf, root, flower and fruit together cure blood morbidity, biliary afflictions, itching, skin ulcers, burning sensations and phthisis. Neem finds use in skin care for acne and keeping skin elasticity.

In India, neem leaves have been employed by the indigenous people treating gastrointestinal disorder such as diarrhoea and cholera (Thakurta et al. 2007). *Azadirachta indica* has been extensively used in Ayurvedic medicine by Indian population for over 2,000 years (Faccin-Galhardi et al. 2012). It is used traditionally for the healing of various diseases. *Azadirachta indica* was found to be one of 16 traditional plant species commonly employed as malaria prophylactic by the traditional healers of three districts of Odisha, India (Nagendrappa et al. 2013).

According to Watt (1908), the root bark, bark and young fruits are tonic and antiperiodic; the oil, seeds and leaves are antiseptic, stimulant and insecticidal; the flowers are stimulant, tonic and stomachic; the gum is demulcent and tonic; the sap or 'toddy' is refrigerant, nutrient and an alterative tonic. In India, Malaysia and Indonesia, the root bark, and stem bark is prescribed as an astringent, febrifuge, malaria and fever (Burkill 1966). The young fruits are similarly used in India. The leaves are used for poulticing, for treating sores. In Indochina, tinctures of leaves and bark are taken internally for malaria and as a tonic and applied externally for sores (Crevost and Petelot 1929). In India and Sri Lanka, neem oil is employed as an anthelmintic and as antiseptic for wounds, eczema, scrofula and other skin diseases and also to kill hair lice (Burkill 1966). In Madura, neem oil is used for itch.

In Nigeria, neem chewing stick is used for oral diseases (Etkin 1981). In Niger, an infusion of pounded leaves is used to treat asthenia (Adjanohoun et al. 1980). In Togo, pounded leaves of neem and other species are used to treat malaria; a leaf decoction is used as anthelmintic for *Ascaris*; for hepatic disorders pulp is used for local application on the head (Adjanohoun et al. 1986). In south Senegal, the Diola people use a leaf decoction for diarrhoeas (Grand and Wondergem 1987). In central Nigeria (Kawar state), a leaf decoction is taken hot or cold for malaria; hot leaf extract is taken orally for catarrh or inhaled from a steam bath; stem is used as a chewing stick to clean teeth and gums, and juice is used to prevent tooth decay and gum infections (Bhat et al. 1990). In Senegal, crushed leaf extract is used to treat malaria (Van der Steur 1994). In Ivory Coast, leaf decoction is employed as malarial therapy (Ambe and Malaisse 2000). In Ghana, pounded leaves are used for enema, and neem leaves alone or mixed with other plant leaves are used in steam baths and as a drink for malaria (Asase et al. 2005; Asase and Oppong-Mensah 2009). In the Dangme West District of Ghana, various recipes of neem leaves are sued for malaria treatment: decoction of boiled neem leaves, decoction of boiled pineapple fruit peels and neem leaves, decoction of boiled neem leaves and lime fruit or leaves and decoction of sugar cane stem and neem leaves (Asase et al. 2010). In south-western Nigeria, the leaves are used as a paste for wound dressing (Adetutu et al. 2011). In Angola, a decoction of pounded leaves is taken for constipation; tea of the plant is used for malaria; tea prepared from roots is taken for asthma, root pieces in used in bath for asthenia and rickets and roots chewed for caries (Bossard 1996).

In Madagascar, bark and wood decoction is taken for diarrhoea, skin disease and itch (Rivière et al. 2005). In North Kordofan, Sudan, neem leaves are used as antipyretic, in steam bath

and as a cushion for sleeping (El-Kamali 2009). In the pastoral and agropastoral communities in Erer Valley of Babile Wereda, eastern Ethiopia, leaf concoction is given for treatment of malaria; leaf concoction, oil from seed and flower, used topically for fungal infections; and seed oil used for treating intestinal worms (Belayneh et al. 2012). In South Africa, a crushed leaf infusion is drunk twice a day for diarrhoea (de Wet et al. 2010). In Tanzania, traditional healers used infusions or decoctions of neem leaves, roots, stem barks on their own or in combination with other plant species to treat malaria and to reduce fever (Gessler et al. 1995). In villages around Kimboza forest reserve in Morogoro, Tanzania, decoctions of leaves, bark and seeds are used for treating headache, backache, malaria, fever and stomach ache and as an insecticide (Amri and Kisangau 2012). In Cameroon, leaves, bark and fruits are used for malaria treatment: leaves are boiled with sugar; solution is filtered and administered to children and adults; also, patients take a bath with warm leaf solution for malaria (Saotoing et al. 2011). In Nigeria, Ndokwa, Delta State, the Abbi people boiled the leaves, stem and bark and the decoction is taken for malaria and fever (Ogie-Odia and Oluowo 2009). The Luo mothers in the Bondo district of Kenya used decoction or infusion of neem leaves for diarrhoea and other stomach ailments; a leaf and root decoction is used as a wash for measles/chickenpox (Geissler et al. 2002). In the south coast community, Kenya, the stem and root barks and leaves are used as antimalarial remedies (Nguta et al. 2010). In the Suba district, Kenya, decoctions or steam bath of the leaves and bark is used to treat skin rashes, malaria and opportunistic infection from HIV/AIDS and leaves and bark rubbed on teeth and gums (Nagata et al. 2011). In Guinea Conakry, decoction of the leaves is used as an antiseptic against infection (Magassouba et al. 2007).

Other Uses

Neem tree has many nonedible and non-medicinal uses (Burkill 1966; Anonymous 1980; Radwanski and Wickens 1981; Lemmens et al. 1995; Stoney 1997).

In the tropics and subtropics, neem is commonly planted as shade plants around building, along roadsides, in pastures and farms as shade trees for livestock and boundary rows and as windbreaks and shelter belts to protect crops from wind damage because of its low branching and soil erosion. Being drought resistant with a well-developed root system capable of extracting nutrient and water from the lower soil levels, it is a suitable tree for dune fixation. Its twigs and leaves are relatively rich in potash and phosphates, are employed as mulch and green manure in southern India neem oil cake (residues after oil extraction from seeds) and are useful as organic manure, soil ameliorant and soil amendment. It is believed to enhance the efficiency of nitrogen fertilizers by reducing the rate of nitrification and suppressing soil pests including nematodes, fungi and insects. Uses of neem oil include the following: fuel for lamps, lubricant for machinery, insect repellent and in the production of soap, toothpaste, pharmaceuticals and cosmetics and to remove tobacco suckers. Neem oil may also have potential in the development of pesticides and fungicides. Neem oil is also used in sprays against fleas in pet animals. Studies found that neem oil and mustard oils at 20 % blend with diesel could be used as a diesel substitute (Anbumani and Singh 2010). However, mustard oil at 20 % blend with diesel gave better performance as compared to neem oil blends in terms of low smoke intensity, emission of hydrocarbon and nitric oxide.

The leaves are said to be used as fodder for livestock. In India and Pakistan, dried neem leaves are placed in cupboard to repel insect devouring clothes and also in stored grains and seeds in containers to repel insects and prevent food and seed losses. The leaves are rich in azadirachtin, a potent antifeedant and insect growth inhibitor, that disrupts insects' growth, metamorphosis and reproduction.

Neem has been cultivated in plantations in the Sudan and Sahelian zones of Africa as well as in Sierra Leone, Malawi, Zimbabwe, Tanzania, Zanzibar and the non-Sahelian areas of Guinea, Nigeria and Ghana. In Nigeria, neem is planted for fuel wood and poles for fencing. In Central America, neem is widely planted as a plantation

tree, its timber being a good substitute for *Swietenia.* Neem timber is tougher than teak, but the grain is rough and does not polish well. Nevertheless, the wood is used for light construction; to make furniture, wardrobes, bookcases and closets; for cart making; ship building; and for making packing crates, agricultural implements, and wooden idols. Neem bark contains 12–14 % tannins and compares favourably with conventional tannin chemicals.

Besides azadirachtin, many other bioactive phytochemicals from leaves, fruit, seeds and bark have been reported to have insecticidal, nematicidal, molluscicidal and fungicidal properties and have potential to be used as biopesticides.

It was observed that the molluscicidal activity of the leaf, bark, cake, neem oil and the neem-based pesticides, Achook and nimbecidine, was both time and dose dependent (Singh et al. 1996). The toxic effect of pure azadirachtin against both the snails was greater than the synthetic molluscicides.

All four neem seed compounds, azadirachtin, salannin, nimbin, and 6-desacetylnimbin, were found to inhibit, in a dose-dependent fashion, ecdysone 20-monooxygenase activity in three insect species, *Aedes aegypti, Drosophila melanogaster* and *Manduca sexta* (Mitchell et al. 1997). The concentration of these compounds required to elicit a 50 % inhibition of this steroid hydroxylase activity in the three insect species examined ranged from approximately 2×10^{-5} to 1×10^{-3}. Azadirachtin inhibited oogenesis and ovarian ecdysteroid synthesis in *Locusta migratoria migratorioides* (Rembold and Seiber 1981). All azadirachtins (A–G) were reported to be potent insect growth inhibitors with high toxicity below <10 ppm in the *Epilachna varivestis* bioassay (Rembold 1987). Isonimolicinolide and nimolicinoic acid, two triterpenoids from neem fruits, showed insect growth-regulating properties against the pulse beetle (*Callosobruchus analis*) (Siddiqui et al. 1987a). Tetranortriterpenoid lactams, salannolactam-(21) and salannolactam-(23), from neem seeds showed antifeeding activity towards the Mexican bean beetle, *Epilachna varivestis* (Kraus et al. 1987b). Deacetylazadirachtinol was found to be as potent as azadirachtin (both isolated from neem fruit) in the inhibition of insect ecdysis when fed in artificial diet to larvae of the tobacco budworm, *Heliothis virescens* (Kubo et al. 1986). The activity of 7-deacetyl-17β-hydroxyazadiradione, isolated from the seeds, as an insect growth inhibitor against *Heliothis virescens* was found to be greater than that of azadiradione and 7-deacetylazadiradione (Lee et al. 1988). The hexane neem seed kernel extract with an LC_{50} of 0.674 % exhibited a much higher activity against the mustard aphid, *Lipaphis erysimi*, than the aqueous and ethanol extracts (Singh et al. 1988). When the hexane extract was partitioned with ethanol, the ethanol-soluble fraction had an LC_{50} of 0.328 %. Among the constituents in the fraction, salannin, a salannin derivative and the nonterpenoid gave LC_{50} values of 0.055, 0.096 and 0.104 %, respectively.

Deacetylgedunin, from the methanol extract of neem oil, was the most active compound (95 % protective concentration) exhibiting antifeedant activity against *Reticulitermes speratus* (Ishida et al. 1992). This was followed by salannin, gedunin, 17-hydroxyazadiradione, nimbandiol, azadiradione, deacetylsalannin, and deacetylnimbin in descending order. Epoxyazadiradione, 17-epiazadiradione, and nimbin were not active. 6β-Hydroxygedunin, isolated from *Azadirachta indica*, exhibited growth inhibitory activity in feeding bioassays against gram pod borer, *Helicoverpa armigera*, and Asian armyworm, *Spodoptera litura*, with EC_{50} of 24.2 and 21.5 ppm, respectively (Koul et al. 2003). Its efficacy was higher in comparison to gedunin (EC_{50} = 50.8 and 40.4 ppm), salannin (EC_{50} = 74.5 and 72.0 ppm) and nimbinene (EC_{50} = 391.4 and 404.5 ppm). Azadirachtin, however, remained the most active neem allelochemical against both insect species. It was found that potentiation among non-azadirachtin limonoids having explicitly two different modes of action, such as feeding deterrence and physiological toxicity, may be playing a significant role in the potentiation effect. Neem limonoids of salannin group, namely, 3-*O*-acetyl salannol, salannol and salannin, exhibited strong antifeedant activity in tobacco armyworm *Spodoptera litura* larvae in a

choice leaf disc bioassay (Koul et al. 2004). No enhancement in activity was observed when the three compounds were co-administered.

Azadirachtin-based insecticide, NeemAzal, exhibited insecticidal effect against three stored product beetle species on rye and oats (Athanassiou et al. 2005). For *Rhyzopertha dominica*, NeemAzal was more effective on oats than on rye and peeled oats. In contrast, at rates ≥100 ppm, azadirachtin was equally effective against *Sitophilus oryzae* on whole rye and oats, where mortality was 100 % after 7 and 14 days of exposure, respectively. NeemAzal was not very effective against *Tribolium confusum* where adult mortality was low, even after 14 days of exposure at the highest rate.

Photo-oxidation of the neem limonoids nimbin and salannin with UV light in the presence of oxygen afforded two isomeric lactone products per limonoid, nimbinolide and isonimbinolide and salanninolide and isosalanninolide, respectively (Simmonds et al. 2004). When compared in insect (larvae of *Spodoptera littoralis, Spodoptera frugiperda* and *Helicoverpa armigera* and nymphs of the locusts *Schistocerca gregaria* and *Locusta migratoria*) tests with the important limonoids of neem seeds, azadirachtin, nimbin and salannin, isonimbinolide and isosalanninolide showed activity greater than that of nimbin or salannin and in some respects demonstrated activity approaching that of azadirachtin. Neem limonoids were found to affect larval duration, pupal duration, adult longevity, fecundity and mortality of the rice leaffolder *Cnaphalocrocis medinalis* (Nathan et al. 2006). Azadirachtin, salannin and deacetylgedunin showed high bioactivity at all doses, while the rest of the neem limonoids were less active and were only biologically active at high doses. Azadirachtin was most potent in all experiments and produced almost 100 % larval mortality at 1 ppm concentration.

Azadirachtins A, B and H, from neem seed oil, exhibited nematicidal and antifungal activities (Sharma et al. 2003). Azadirachtin B was the most effective against the reniform nematode *Rotylenchulus reniformis* (EC50 96.6 ppm), followed by azadirachtins A (119.1 ppm) and H (141.2 ppm). At 200 ppm concentration, the test compounds caused 50–65 % mortality of *Caenorhabditis elegans* nematode. Azadirachtin H showed the highest activity against the phytophagous fungi *Rhizoctonia solani* (EC50 63.7 ppm) and *Sclerotium rolfsii* (EC_{50} 43.9 ppm), followed by azadirachtins B and A. Application of neem seed granules at 0.2 and 0.4 % w/w and kernel granules at 0.1, 0.2 and 0.4 % w/w to soil significantly reduced the root galling due to *Meloidogyne incognita* and population density of *M. incognita* J2 in soil (Abbas et al. 2009). Application of both also improved the growth of root and shoot of the nematode-infested tomato plants.

Release of azadirachtin A from the commercial polyethylene glycol (PEG) formulation was faster than the other controlled release formulations (Kumar et al. 2010b). The study found that depending upon the polymer matrix used, the application rate of azadirachtin A can be optimized to achieve insect control at the desired level and period. Starch-coated encapsulation of neem oil nanoemulsion was found to be effective for controlled release of azadirachtin when compared to polyethylene glycol (PEG)-coated encapsulation of neem oil nanoemulsion (Jerobin et al. 2012). Further, neem oil nanoemulsion encapsulated beads coated with PEG was found to be toxic in lymphocyte cells.

Comments

Fresh neem seeds germinate readily without any pretreatment. Neem can also be propagated vegetatively by root and shoot cuttings, air layering, grafting and marcotting and from tissue culture.

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Corymbia calophylla

Scientific Name

***Corymbia calophylla* (R. Br.) K.D. Hill & L.A.S. Johnson**

Synonyms

Eucalyptus calophylla Lindl., *Eucalyptus calophylla* R. Br. nom. nud., *Eucalyptus calophylla var. maideniana* Hochr., *Eucalyptus calophylla var. multiflora* Guilfoyle nom. nud., *Eucalyptus calophylla var. parviflora* Blakely, *Eucalyptus calophylla var. rosea* Guilfoyle nom. nud., *Eucalyptus calophylla var. rubra* Guilfoyle nom. nud., *Eucalyptus calophylla var. typica* Hochr., *Eucalyptus ficifolia var. alba* Maiden ex Blakely, *Eucalyptus glaucophylla* Hoffsgg.

Family

Myrtaceae

Common/English Names

Marri, Port Gregory Gum, Red Gum

Vernacular Names

Australia: Marri (Nyoongar Aborigines)

Origin/Distribution

The species is indigenous to Western Australia, widely distributed in the south-west of Western Australia, from north of Geraldton (28°S) to Cape Riche (34°S), and inland beyond Narrogin.

Agroecology

In its native area, Marri occurs in a range of habitat flats, hills, slopes, breakaways, wetlands, fringing salt marches and beside drainage lines. It is an important component of both the Jarrah and Karri forests of Western Australia. It also occurs on the coastal plain on a range of soils. It will grow on comparatively poor soil and good soils that include clay loam, orange-brown sandy clay, gravel, grey sand over limestone, granite and laterite.

Edible Plant Parts and Uses

Blossoms called *ngumbit* soaked in water make a sweet drink; seeds can also be eaten (SERCUL undated).

Botany

Medium-sized tree up to 40 m high, 1.5 m dbh, dense and much branched, with grey-brown to red-brown brownish to dark grey, tessellated with

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Plate 1 Flowers and buds leaves

Plate 2 Flowers and leaves

reddish kino (gum) exudates. Leaves with prominent oil glands. Juvenile leaves, lanceolate to ovate, hispid with simple hairs and bristle glands, petiolate. Intermediate leaves disjunct early, lanceolate to elliptic, straight, entire, dull green, petiolate. Adult leaves disjunct, broad lanceolate to ovate, falcate or not falcate, acuminate, basally tapered or basally rounded, glossy, green, thick, concolorous (Plates 1, 2), 9–14 cm long, 25–40 mm wide with distinct lateral and intramarginal veins. Petioles narrowly flattened or channelled, 15–20 mm long. Inflorescence terminal panicles with 3–7-flowered umbellasters. Peduncles terete or narrowly flattened or angular, 15–35 mm long by 3 mm wide. Pedicels terete, 10–30 mm long. Buds clavate 7–14 mm by 7–10 mm across. Calyx calyptrate, conical, narrower than hypanthium or as wide as smooth hypanthium; persisting to anthesis. Flowers white (Plates 1 and 2), cream or pink. Fruits ovoid to urceolate, with constricted

Plate 3 Cluster of fruits

neck (Plate 3), pedicellate, 4 locular, 30–50 mm long by 25–40 mm across, thick and woody. Calyptra scar flat and disc depressed. Seeds regular and laterally compressed, cymbiform (boat-shaped), large, shallowly reticulate, dull, black.

Nutritive/Medicinal Properties

Flower Phytochemicals

Composition of Marri honey bee-collected pollens was found as protein 27.9 %, moisture 5.1 %, crude fibre 6.9 %, ash 2.3 %, lipids 1.0 %, carbohydrate 56.8 %; minerals (mg/100 g) P 386 mg, Ca 58 mg, Na 86.5 mg, K 462.7 mg, Zn 6.6 mg, Mg 88 mg, Cu 2.5 mg; and amino acids (mg/g N) isoleucine 252 mg, leucine 3245 mg, lysine 226 mg, methionine 170 mg, cysteine 123 mg, phenylalanine 260 mg, tyrosine 217 mg, threonine 240 mg, tryptophan 69 mg, valine 240 mg, aspartic acid 417 mg, arginine 367 mg, serine 233 mg, glutamic cid 383 mg, proline 399 mg, glycine 188 mg, alanine 197 mg and histidine 202 mg (Bell et al. 1983). Marri pollen was found to be relatively high in protein and to have favourable amino acid patterns; however, their relatively low digestibility will be a limiting factor in their usefulness as a food for humans and monogastric animals.

C. calophylla pollen was found to have the highest concentration of myristic and linolenic fatty acids; boron, copper, zinc, phosphorus, magnesium and sulphur minerals; crude protein; and the following amino acids: aspartic acid, methionine, threonine, glutamic acid, glycine, alanine, valine, isoleucine, tyrosine, leucine, phenylalanine, lysine and histidine compared to the pollens of *Eucalyptus accedens* powderbark, *Eucalyptus wandoo* winter wandoo, *Eucalyptus diversicolor* karri, *Eucalyptus marginata* jarrah, *Eucalyptus patens* forest blackbutt analyzed (Mannings 2001). Mannings (2001) reported the following nutrient profile in Marri pollens: amino acids (isoleucine 1.07 %, leucine 1.82 %, lysine 1.88 %, methionine 0.61 %, cysteine 0.4 %, phenylalanine 1.11 %, tyrosine 0.78 %, threonine 0.96 %, tryptophan 0.58 %, valine 1.28 %, aspartic acid 2.23 %, arginine 31.90, serine 1.17 %, glutamic cid 2.69 %, proline 3.45 %, glycine 1.27 %, alanine 1.38 % and histidine 0.85 %); total fats (0.88 %, myristic acid (C-14) 2.98 %, palmitic acid (C-16) 17.4 %, stearic acid (C-18) 4.54 %, oleic acid (C-18) 15 %, linoleic acid (C-18) 35.7 %, linolenic acid (C-18) 12.7 % and arachidic acid (C-20) 2.22 %); minerals (B 18.9 mg/kg, Cu 21.9 mg/kg, Fe 124.4 mg/kg, Mn 35.8 mg/kg, Zn 78.9 mg/kg, P 0.42 %, K 0.54 %, Na 0.01 %, Ca 0.10 %, Mg 0.09 % and S 0.3 %); and vitamin content (ascorbic acid 64.3 mg/kg, thiamin mg/100 g, riboflavin 0.62 mg/100 g, niacin 3.5 mg/100 g, pyridoxine 0.4 mg/100 g and folic acid 2 mg/100 g).

Kino (Gum) Phytochemicals

Kinos are dark cellular astringent exudations (gums) containing phenolic substances, and 12 components were resolved from *E. calophylla* kino (Hillis 1950). The kino of *E. calophylla* yielded tannin (McGookin and Heilbron 1926), aromadendrin (3,4′,5,7-tetrahydroxyflavanone) (5 %), kaempferol and ellagic acid (Hillis 1952). Pyrogallol, (+)-catechin, and a flavanol, (+)-afzelechin (3,5,7,4′-tetrahydroxy-flavan), gallocatechin and epicatechin were isolated from kino (Hillis and Carle 1960). *Eucalyptus calophylla* kino yielded besides aromadendrin and sakuranetin, levorotary leucopelargonidin (3,4,5,7,4′-pentahydroxyflavan) (Ganguly and Seshadri 1961). Reduction of aromadendrin trimethyl ether yielded two isomeric flavandiols.

Leaf Phytochemicals

The leaf volatile oil of many *Eucalyptus* species including *E. calophylla* contained α-pinene (0.2–31.1 %), β-pinene (0–12.5 %), 1,8-cineole (0.2–76.8 %), *p*-cymene (0–20.8 %), aromadendrene (0–13.6 %), bicyclogermacrene (0–43.4 %) and spathulenol (0.1–15.2 %) as principal leaf oil components; all species also contained torquatone (Bignell et al. 1996).

Root Phytochemicals

E. calophylla roots contained lignin, suberin and phenolic compounds; there were rapid increases in total soluble phenolics and lignin in roots of *E. calophylla* after infection by *Phytophthora cinnamomi* (Cahill and McComb 1992).

Antimicrobial Activity

Exceptionally high antibacterial activity was seen in hydrogen peroxide-dependent honeys derived from Marri (*C. calophylla*; median activity 25.7, maximum 29.7) and jarrah (*E. marginata*; median activity 25.1, maximum 31.4) from Western Australia (Irish et al. 2011). In most cases, the antibacterial activity was attributable to hydrogen peroxide produced by the bee-derived enzyme glucose oxidase. Honeys with hydrogen peroxide-dependent activity had been reported to be more effective than manuka honey at inhibiting dermatophyte fungi (Brady et al. 1996) and species of the yeast *Candida* (Irish et al. 2006), indicating that these honeys may be more broad spectrum and valuable as antifungal agents than manuka honey.

Traditional Medicinal Uses

Resin is used as a medicine by the local aborigines to treat upset stomach; resin mixed with water is rubbed on skin to treat eczema (SERCUL undated).

Other Uses

Marri is not suitable for most gardens or street plantings, but it is an excellent tree for paddock plantings providing shade for animals.

Marri honey-coloured timber is increasingly featured in modern household furniture.

Comments

The tree can be propagated from seed which germinates readily.

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Syzygium aromaticum

Scientific Name

***Syzygium aromaticum* (L.) Merr. & Perry**

Synonyms

Caryophyllus aromaticus L., *Caryophyllus hortensis* Noronha, *Caryophyllus silvestris* Teijsm. ex Hassk., *Eugenia aromatica* (L.) Baill. nom. illeg., *Eugenia caryophyllata* Thunb., *Eugenia caryophyllus* (Spreng.) Bullock & S. G. Harrison, *Jambosa caryophyllus* (Thunb.) Nied., *Myrtus caryophyllus* Spreng.

Family

Myrtaceae

Common/English Names

Clove, Cloves, Clove Tree, Zanzibar Redheads

Vernacular Names

Amharic: K'rinfudm
Arabic: Qaranful, Habahan, Kerounfel, Laung Ud Annawar
Brazil: Cavo-Aromático, Cravo-da-India, Cravo-Das-Molucas, Cravo-De-Doce (Portuguese)
Burmese: Lay-Hyin, Ley Nyim Bwint
Chinese: Ding Xiang, Mu Ding Xiang, Ding Heung
Czech: Hřebíčkovec kořenný, Hřebíčkovec vonný
Danish: Ægte kryddernellike, Kryddernellike, Kryddernelliketræ, Nellike
Dutch: Kruidnagel, Kruidnagelboom, Myrte soort
Estonian: Harilik nelgipuu
Finnish: Mausteneilikka
French: Clous De Girofle, Giroffle, Giroflier
German: Gewürznelke, Gewürznelkenbaum, Nägelein, Nelke, Negelken
Greek: Garifalo
Hebrew: Tziporen
Hungarian: Szegfuszeg (fa)
India: Lavanga (Bengali), Laumg, Lavamg (Hindi), Daevakusuma, Lavanga (Kannada), Grampu, Karampu, Karayampu (Malayalam), Kala Phur, Lavang (Marathi), Lawngpar (Mizoram), Bhadrasriya, Devakusuma, Devapuspa, Haricandana, Karampu, Lavanga, Lavangaka, Lavangam, Varala (Sanskrit), Kiraambu, Kirambu, Kirampu, Ilavankam (Tamil), Devakusumamu, Kaaravallu, Lavangamu, Lavangalu (Telugu), Laung, Lavang, Qaranful (Urdu)
Indonesia: Bunga Cengkeh, Bunga Cingkeh, Cingkeh
Italian: Chiodo Di Garofano
Japanese: Kuroobu, Shouji
Khmer: Khan Phluu, Khlam Puu
Laotian: Dok: Chan, Ka:nz Ph'u
Malaysia: Bunga Cengkeh, Cengkeh
Nepalese: Lwaang

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Norwegian: Kryddernellik
Persian: Mekhak
Philippines: Clovas De Comer (Spanish), Klabong Pako (Tagalog)
Polish: Gozdzik korzenny, Gozdziki
Portuguese: Cravinho, Cravo-da-India, Craveiro Da Índia, Cravina De Túnis, Cravoária, Cravo-De-Cabecinha, Rosa Da Índia
Russian: Gvozdika, Sitsigiui Gvozdichnyi
Sri Lanka: Karabu Nati (Sinhalese)
Spanish: Arbol Del Clavo, Clavero, Clavero Giroflé, Clavo, Clavo De Olor, Clavoaromatico, Dientes
Swahili: Karafuu
Swedish: Kryddnejlika, Kryddnejlikor, Nejlikor
Thai: Kaan Phlûu, Khan Plu
Tibetan: Li Si
Vietnamese: Dinh Hu'o'ng

Origin/Distribution

Cloves are native to Indonesia and occur especially in the north and central Maluka (Moluccas) and Papua Barat (Irian Jaya). It has been introduced and now widely cultivated in Brazil, Haiti, India, Kenya, Madagascar, Malaysia, Mauritius, Mexico, Seychelles, Sri Lanka and Tanzania.

Agroecology

Being strictly a tropical species, clove requires a warm humid tropical climate with an annual rainfall from 1,500 to 2,500 mm. It grows well from mean sea level up to an elevation of 1,000 m. In its native habitat it is commonly found in woodlands and rainforests. It prefers well-drained, deep loamy soils with high humus content and black loams of semi-forest regions and will also grow on loose well-drained lateritic soils.

Edible Plant Parts and Uses

The dried unopened flower buds of the tree are the cloves of commerce (Plate 6). Cloves are a versatile spice that is widely used in food, liqueur, beverage, bakery and confectionary products and for mulling wine. Cloves are commonly used in Asian, African, Middle Eastern and European cuisine. Cloves can be used in cooking either whole or in a ground form, but as they are extremely strong, they are used sparingly. In northern Indian cuisine, clove is used in almost every sauce or side dish made, mostly ground up along with other spices. In the south Indian cuisine, it finds extensive use in the *biryani* chicken dish. Ingredients and spices used for *biryani* chicken usually include ghee, peas, beans, cumin, cloves, cardamom, cinnamon, bay leaves, coriander, mint leaves, ginger, onions and garlic. Cloves are also a key ingredient in tea along with green cardamoms. Cloves are also widely used in Mexican cuisine, where it is often paired together with cumin and cinnamon. Cloves are used to spice up fish, poultry, game and meat dishes. In China, Sri Lanka, northern India, Middle East, many Arab countries, northern Africa, Indonesia and Malaysia, cloves are preferred for meat dishes. Cloves are featured in classic sauces and are used in the bakery/confectionary industry and the processed meat industry as a ground spice. Whole cloves are frequently used to flavour cooking liquids. Cloves have a traditional association with apples and are added to apple tarts, sauces, pies and puddings.

Ground cloves are a vital ingredient in many spice mixtures: Chinese *five-spice powder* (mixture typically made from fennel, cloves, Szechuan peppercorns, star anise and cinnamon); Indian c*urry powder* and *garam masala* (spicy mixture of ground roasted spices comprising green cardamom pods, cloves, black cardamom pods, mace, cinnamon, cumin seeds, coriander seeds, fennel seeds, black peppercorns and fenugreek seeds); Arabic *baharat* (a spicy blend that usually contains hot spices (such as paprika, chillies and black pepper), sweet spices (such as allspice, cloves, cinnamon, nutmeg and cardamom), warm spices (such as cumin and coriander) and herbs (such as savoury and mint); Moroccan *ras el hanout* (spicy mixture that includes cardamom, clove, cinnamon, ground chilli peppers (also known as

paprika), coriander, cumin, mace, nutmeg, peppercorn and turmeric); Tunisian *gâlat dagga* (a five-spice mixture of black peppercorn, grains of paradise, cloves, ground nutmeg and cinnamon); Ethiopian *berbere* (spice mixture of chilli peppers, ginger, cloves, coriander, allspice, rue berries and ajowan); French *quatre épices* (a four-spice mix containing ground pepper (white, black or both), cloves, nutmeg and ginger); Mexican *mole* sauces and many others. Mexican *mole* is a dark-coloured, thick gravy sauce that can have up to 50 ingredients; one recipe consists of dried chilli pasilla peppers, chopped onions, crushed garlic, shelled pumpkin seeds, whole cloves, sesame seeds, dried oregano, anise seeds, whole tomatoes, crumbled small corn tortillas, smooth peanut butter, raisins, grated chocolate, olive oil and chicken stock. The taste of the famous *Worcestershire sauce* is markedly dominated by clove aroma. The sauce is composed of several spices besides cloves—garlic, tamarind, paprika or chillies are most frequently found, along with fish extract, soy sauce, syrup, vinegar (or lemon juice) and salt. In Europe, cloves are much used for special types of sweets or sweet breads but especially for stewed fruits. In France, cloves often go into long-simmered meat stews or hearty meat broths. In England, they are most popular in pickles. In Ethiopia, coffee is often roasted together with some cloves in the so-called coffee ceremony. Clove bud oil is also used for flavouring food. In Indonesia, it is used to flavour tobacco cigarettes called *kretek* which are composed of ground cloves (about 30 %) and tobacco (70 %). Indonesia is the world largest consumer of cloves followed by India.

Clove berry has little pulp, but it can be eaten.

Plate 1 Clove tree habit

Plate 2 Young leaf flushes

Botany

A medium-sized, branched, glabrescent, evergreen tree growing to 6–15 m tall with a conical or pyramidal canopy (Plate 1) and a greyish bark. The leaves are opposite and decussate, coriaceous and shining, minutely punctuated with numerous oil glands on lower surface and borne on 4 cm long petioles. The lamina is ovate–lanceolate, 10 cm long by 5 cm wide; simple with an entire margin, acute apex and a tapering base; and pinkish-bronze when young turning to lime green with age (Plates 2 and 3). The aromatic bisexual flowers are borne in short, terminal many-flowered panicles, trichotomously divided and jointed at every division. The flower buds are pale yellowish-green turning green and then develop into a bright crimson colour when they are ready for harvesting (Plates 4 and 5). Cloves are harvested when 1.5–2 cm long, with four spreading sepals and four unopened petals which form a small ball in the centre. Flower peduncle is cylindrical and green. The flower consists of a subcylindrical, solid and glandular calyx tube, terminating in 4 concave ovate lobes, corolla

Plate 3 Close view of young and mature clove leaves

Plate 5 Cloves buds and opened flowers

Plate 4 Matured clove buds

Plate 6 Dried clove buds

with 4 round concave petals imbricated into a globe in the bud, subsequently spreading, short obtusely subulate style above the oblong, 2-loculed ovary and numerous curved, inserted stamens with small, yellow, ovate–cordate, 2-celled anthers (Plate 5). Fruit a berry purplish, elliptical and 2-seeded with sparse pulp.

Nutritive/Medicinal Properties

The food value of ground cloves per 100 g edible portion of ground cloves was reported as: water 6.86 g, energy 323 kcal (1,350 kJ), protein 5.98 g, total lipid 20.07 g, ash 5.88 g, carbohydrate 61.21 g, total dietary fibre 34.2 g, total sugars 2.38 g, sucrose 0.02 g, glucose (dextrose) 1.14 g, galactose 0.15 g; minerals—Ca 646 mg, Fe 8.68 mg, Mg 264 mg, P 105 mg, K 1,102 mg, Na 243 mg, Zn 1.09 mg, Cu 0.347 mg, Mn 30.033 mg, Se 5.9 µg; vitamins—vitamin C (total ascorbic acid) 80.8 mg, thiamin 0.115 mg, riboflavin 0.267 mg, niacin 1.458 mg, vitamin B6 0.590 mg, total folate 93 µg, total choline 37.4 mg, betaine 1.4 mg, vitamin A 530 IU, vitamin E (α-tocopherol) 8.52 mg, vitamin K (phylloquinone) 141.8 µg; total saturated fatty acids 5.438 g, 14:0 (myristic acid) 0.022 g, 16:0 (palmitic acid) 3.967 g, 18:0 (stearic acid) 0.847 g; total monounsaturated fatty acids 1.471 g, 16:1 undifferentiated (palmitoleic acid) 0.089 g, 18:1 undifferentiated (oleic acid) 1.337 g, 20:1 (gadoleic acid) 0.022 g; total polyunsaturated fatty acids 7.088 g, 18:2 undifferentiated (linoleic acid)

2.586 g, 18:3 undifferentiated (linolenic acid) 4.257 g, 20:4 undifferentiated (arachidonic acid) 0.045 g, 22:5 n-3 (docosapentaenoic acid, DPA) 0.022 g; phytosterols 256 mg; β-carotene 94 μg; and β-cryptoxanthin 468 μg (USDA 2012).

Clove powder is rich in calories, protein, total carbohydrates, minerals (Ca, Fe, Mg, P, K, Mn and Na), vitamin C, niacin, vitamin A, vitamin E and K, phytosterol and folate and also contains betaine, choline, β-carotene and β-cryptoxanthin.

Twenty-eight and 35 constituents representing 99.9 % each were identified from the clove bud oils of Indian and Madagascan origins, respectively. On the other hand leaf oil from Madagascar resulted in the identification of 22 constituents representing 99.9 % of the oil. The major constituents in bud and leaf oils were eugenol and β-caryophyllene (Srivastava et al. 2005). Another study reported 16 identified from clove leaf oil (Raina et al. 2001). The major compound was eugenol (94.4 %) followed by β-caryophyllene (2.9 %). The clove oil from Andaman was found to be comparable with the best oil produced in south India in terms of its eugenol content.

The major components of the essential oil from clove buds were eugenol (71.56 %) and eugenol acetate (8.99 %) (Nassar et al. 2007). The volatile compounds identified in the n-hexane extract of *Syzygium aromaticum* buds by using GC–MS were in descending order: eugenol 71.565, eugenyl acetate 8.99 %, caryophyllene oxide 1.67 %, nootkatin 1.05 %, phenol-4-(2,3-dihydro)-7-methoxy-3-methyl-5-(1-propenyl)-2-benzofurane 0.98 %, *p*-cymene 0.9 %, guaiol 0.90 %, thymol 0.87 %, isolongifolanone (*trans*) 0.86 %, 5-hexene-2-one 0.67 %, benzene-1-butylheptyl 0.55 %, hexadecanoic acid 0.50 %, vitamin E acetate 0.43 %, dodecatrienoic acid-3,7 0.38 %, octadecanoic acid butyl ester 0.33 %, 9,17-octadecadienal 0.24 % and 11-trimethylethyl ester. The dichloromethane extract of the buds yielded limonene and ferulic aldehyde, along with eugenol. The flavonoids tamarixetin 3-*O*-β-D-glucopyranoside, ombuin 3-*O*-β-D-glucopyranoside and quercetin were isolated from the ethanol extract. Gallic acid, caffeic acid and syringic acid were found to be present at levels of 1.58, 0.06 and 0.05 % (w/w), respectively, in *S. aromaticum* dried buds (Sutthanont et al. 2008). The average recoveries of gallic acid, caffeic acid and syringic acid using high-performance thin-layer chromatography densitometric method were 96.3, 95.7 and 92.4 %, respectively. Lee et al. (2009) isolated nine compounds in the flower bud essential oil, namely, eugenol (49 %), caryophyllene 7.5 %, 2-propanone, methylhydrazone 5.6 %, cyclopentane, methyl 4.0 %, furan, tetrahydro-3-methyl 2.5 %, a-caryophyllene 1.4 %, copaene 0.5 %, 2H-Pyran-2-one, tetrahydro-6,6-dimethyl 0.4 % and pyrrolidine, 2-buthyl-1-methyl (0.1 %).

A new polyphenolic glucoside 6′-*O*-acetylisobiflorin together with fifteen known compounds, namely, gallic acid, ellagic acid, 3,3′,4-tri-*O*-methylellagic acid, eugenol 4-*O*-(6′-*O*-galloyl)-glucoside, biflorin, isobiflorin, isorhamnetin 3-*O*-glucoside, quercetin 3-*O*-glucuronide 6″-*O*-methyl ester, 1,2,3-tri-*O*-galloylglucose, 1,2,3,6-tetra-*O*-galloylglucose, 1,2-di-*O*-galloyl-4,6-HHDP-glucose, strictinin, tellimagrandin I, tellimagrandin II and casuarictin were isolated from *S. aromaticum* flower buds (Yoshimura et al. 2011). Forty-seven compounds were identified in the hexane extract of the flower buds (Bagavan et al. 2011a). The predominant constituent was chavibetol (5-allyl-2-methoxyphenol) (58.79 %). Other major components included eugenol acetate (phenol,2-methoxy-4-(2-propenyl)-acetate) (15.09 %), caryophyllene-(I1) (2,6,10,10-tetramethylbicyclo[7.2.0]undeca-1,6-diene) (13.75 %), caryophyllene oxide (3.04 %), 2,6,6,9-tetramethyl-1,4,8-cycloundecatriene (1.67 %) and copaene (1.33 %). Other minor constituents (<1 %) included 4-allylphenol; α-cubebene; germacra-1(10),4(15),5-triene, (−)-; 1,1,7-trimethyl-4-methylenedecahydro-1H-cyclopropa[e]azulene; 1-isopropyl-7-methyl-4-methylene-1,2,3,4,4a,5,6,8a-octahydronaphthalene; 6-α-cadina-4,9-diene, (−)-; 1,5-dimethyl-8-(1-methylethylidene)-1,5-cyclodecadiene; 1-β-cadin-4-en-10-ol; 1,3,6,10-dodecatetraene, 3,7,11-trimethyl; 4-isopropyl-1,6-dimethyl-1,2,3,4,4a,7-hexahydronaphthalene; 1,1,6-trimethyl-1,2-dihydronaphthalene; (2R, 5E)-caryophyll-5-en-12-al; 1,1,6-trimethyl-1,2-dihydronaphthalene; (*Z*,*Z*)-α-farnesene; 2,5-dimethyl-3-vinyl-hexa-1,4-diene; 1,1,4,7-tetramethyldecahydro-1H-

cyclopropa[e]azulen-4-ol; humulene oxide; 3-methyl-2-(1′,1′,5′-trimethyl-5′-hexenyl)-2-cyclopropenyl methyl ketone; 1-isopropyl-4,7-dimethyl-1,3,4,5,6,8a-hexahydro-4a(2H)-naphthalenol; 4,8a-dimethyl-4a, 5,6,7,8,8a-hexahydro-2(1H)-naphthalenone; 4,4-dimethyltetracyclo[6.3.2.0E 2,5.0E1,8]tridecan-9-ol;4-isopropyl-1,6-dimethyl-1,2,3,4,4a,7,8,8a-octahydro-1-naphthalenol; 3-methyl-5-(2,6,6-trimethyl-1-cyclohexen-1-yl)-1-pentyn-3-ol; 2,2,6,7-tetramethyl bicyclo(4.3.0) nona-4,9(1)-dien-8-ol;3-methyl-5-(2,6,6-trimethyl-1-cyclohexen-1-yl)-1-pentyn-3-ol; 2′,3′,4′ trimethoxyacetophenone;1,1,4,7-tetramethyldecahydro-1H-cyclopropa[e]azulen-4-ol; 2,2-dimethyl-2-methylene-1-(3′-methyl-4′-pentenyl)-3-cyclohexen-1-ol; L-alanine, N-(4-butylbenzoyl)-, pentyl ester; N-[2-(4-tert-butyl phenoxy)ethyl]-3-(2-furyl)-2-propenamide;3-[4-(4-methylphenyl)-1,3-thiazol-2-yl]-4,5,6,7-tetrahydro-1-benzothien-2-ylamine; phenol, 4-[2,3-dihydro-7-methoxy-3-methyl-5-(1-propenyl)-2-benzofuranyl]-2-methoxy-; 1,2-Bis(4-methoxyphenyl)-N,N,N′,N′-tetramethyl-ethane-1,2-diamine; 1-(10-hydroxy-6,9,10-trimethylspiro[4.5]dec-6-en-2-yl)ethanone; phenol, 2-methoxy-4-propenyl-, (*Z*)-; N-tetracontane; and n-hexatriacontane. Kuroda et al. (2012) identified eight compounds in the ethanol flower bud extract: eugenol (1), dehydrodieugenol (2), dehydrodieugenol B (3), oleanolic acid (4), arjunolic acid (5), corosolic acid (6), Asiatic acid (7) and betulinic acid (8). Compounds 2–4 were found to have hypoglycaemic activity.

Clove leaves also contained ellagitannins and syzyginins A and B (Tanaka et al. 1996). Two new apigenin triglycosides, apigenin 6-C-[β-D-xylopyranosyl-(1′′→2′′)-β-D-galactopyranoside]-7-*O*-β-D-glucopyranoside and apigenin 6-C-[β-D-xylopyranosyl-(1′′→2′′)-β-D-galactopyranoside]-7-*O*-β-D-(6-*O*-*p*-coumaryl-glucopyranoside), were isolated from the ethanol extract of the seeds of *Syzygium aromaticum* (Nassar 2006).

Other studies reported the following constituents of clove: eugenol, acetyl eugenol, β-caryophyllene, caryophyllene oxide, α-humulene, vanillin, crategolic acid, tannins, gallotannic acid, methyl salicylate, flavonoids (eugenin, kaempferol, rhamnetin and eugenitin), triterpenoids (oleanolic acid, stigmasterol and campesterol) and several sesquiterpenes (Kramer 1985; Musenga et al. 2006).

Cloves have been reported to possess the following pharmacological properties.

Antioxidant Activity

Of 19 Thai medicinal plants, ethanol, water and hot water extract of *S. aromaticum* showed the highest antioxidant activity using DPPH assay (EC50 = 6.56, 4.73 and 5.30 μg/mL, respectively) (Makchuchit et al. 2010).

Gallic acid and eugenol were identified as the two major antioxidants in clove (Kramer 1985). The amounts of gallic acid and eugenol were determined to be 1.26 g and 3.03 g, respectively, in 100 g of clove. All extracts (ethanol, dichloromethane) and the isolated flavonoids (tamarixetin 3-*O*-β-D-glucopyranoside, ombuin 3-*O*-β-D-glucopyranoside and quercetin) showed strong antioxidant activity against 1, 2-diphenyl picrylhydrazyl (DPPH) (Nassar et al. 2007). Among the tested extracts, the ethanol extract of the clove buds showed remarkable scavenging activity, as compared with synthetic antioxidants such as butylated hydroxyl toluene (BHT). In other studies, the spices, namely, cloves (*Syzygium aromaticum*), liquorice (*Glycyrrhiza glabra*), mace (aril of *Myristica fragrans*) and greater cardamom (*Amomum subulatum*), were reported to exhibit antioxidant activities at various concentrations (Yadav and Bhatnagar 2007b). None of the spices showed pro-oxidant 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 liquorice 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 showed that spices used in the study had the 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 2007a). The spices due to higher reducing potential (in the presence of bleomycin-$FeCl_3$) showed increased DNA oxidation. Cloves showed the highest DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging activity, followed by liquorice, 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 were strong antioxidants and may have beneficial effects on human health.

The antioxidant activity of clove bud extract and its major aroma components, eugenol and eugenyl acetate, were found to be comparable to that of the natural antioxidant, α-tocopherol (vitamin E) (Lee an Shibamoto 2001). The aroma extract isolated from clove buds inhibited the oxidation of hexanal for 30 days at a level of 50 μg/mL. Clove bud extract inhibited malonaldehyde formation from cod liver oil by 93 % at 160 μg/mL level. Twenty-two compounds were identified in the extracts of clove buds by gas chromatography and gas chromatography/mass spectrometry. The major aroma constituents of clove buds were eugenol (24.371 mg/g) and eugenyl acetate (2.354 mg/g). Eugenol, eugenyl acetate and benzyl alcohol inhibited the oxidation of hexanal by 99, 99 and 82 %, respectively, for a period of 30 days at 500 μg/mL. Eugenol, eugenyl acetate and benzyl alcohol inhibited malonaldehyde formation from cod liver oil by 88, 79 and 63 %, respectively, at 160 μg/mL. The extracts of *Eugenia caryophyllata* exhibited strong total antioxidant activity (Gülçin et al. 2004). At the concentrations of 20, 40 and 60 μg/mL, water clove extract showed 93.3, 97.9 and 92.3 % inhibition on lipid peroxidation of linoleic acid emulsion, respectively. At the same concentrations, ethanol clove extract lavender exhibited 94.9 %, 98.2 % and 93.8 %, respectively. Comparably, 60 μg/mL of standard antioxidant such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and α-tocopherol exhibited 96.5, 99.2 and 61.1 % inhibition on peroxidation of linoleic acid emulsion, respectively. Clove extracts had effective reductive potential, free radical scavenging, superoxide anion radical scavenging and metal chelating activities at all tested concentrations (20, 40 and 60 μg/mL). Those various antioxidant activities were comparable to standard antioxidants such as BHA, BHT and α-tocopherol.

Treatment with *Nigella sativa* and *Syzygium aromaticum* oils of rats fed an aflatoxin-contaminated diet resulted in significant protection against aflatoxicosis (Abdel-Wahab and Aly 2005). This was attributed to the ability of these volatile oils to scavenge free radicals generated during aflatoxicosis. Moreover, *Nigella sativa* oil was found to be more effective than *Syzygium aromaticum* oil in restoring the haematological and biochemical parameters that were altered by aflatoxin in rats. The n-hexane extract of clove exhibited high oxygen radical absorbance capacity (ORAC) value of 25,975 μmol TE (Trolox equivalent)/g; its high activity was attributed to the major constituent, eugenol, which had the most potent ORAC value (39,271 μmol TE/g) (Yoshimura et al. 2011). The ethyl acetate extract containing galloylated compounds and hydrolysable tannins also exhibited high ORAC value (>9,000 μmol TE/g). The flavonol glycosides isorhamnetin 3-*O*-glucoside and quercetin 3-*O*-glucuronide 6″-*O*-methyl ester also contributed significantly to the antioxidative activity.

The electron spin resonance (ESR)-spin trapping method coupled with steady state kinetic analysis showed that all of the four extracts from *Punica granatum* (peel), *Syzygium aromaticum* (bud), *Mangifera indica* (kernel) and *Phyllanthus emblica* (fruit) directly scavenged superoxide anions and that the superoxide scavenging potential of any of the extracts was comparable to that of L-ascorbic acid (Saito et al. 2008). The four edible herbal extracts exhibited prominently potent ability to reduce the signal intensity of 5,5-dimethyl-1-pyrroline-N-oxide (DMPO)–OOH, a spin adduct formed by DMPO and superoxide anion. Furthermore, polyphenol determination indicated that the activity was at least in

part attributable to polyphenols. These extracts are allowed to be used as foodstuffs according to the Japanese legal regulation.

Anticancer/Antimutagenic Activity

The aqueous infusion of cloves exhibited protection against skin papilloma formation by 9,10-dimethyl benz(a)anthracene (DMBA) and croton oil-induced skin carcinogenesis in Swiss mice in a dose-dependent manner (Banerjee and Das 2005). It was demonstrated that oral administration of aqueous infusions of clove at a dose of 100 μL/mouse/day not only delayed the formation of papilloma but also reduced the incidence of papilloma as well as the cumulative number of papillomas per papilloma-bearing mouse. Using mice models, the incidence of hyperplasia, dysplasia and carcinoma in situ evident in the carcinogen control group on the 8th, 17th and 26th weeks, respectively, was effectively reduced after treatment with clove infusion (Banerjee et al. 2006). Significant reduction in the number of proliferating cells and an increased number of apoptotic cells were also noted in these benzo[a] pyrene-induced lung lesions following clove treatment. Western blotting analysis revealed that clove infusion up-regulates the expression of pro-apoptotic proteins p53 and Bax and downregulated the expression of anti-apoptotic protein Bcl-2 in the precancerous stages. Expression of caspase-3 and its activation by clove infusion were evident from a very early stage of carcinogenesis (eighth week). Clove infusion was also found to downregulate the expression of some growth-promoting proteins, namely, COX-2, cMyc and Hras. The observations indicated the chemopreventive potential of clove in view of its apoptogenic and antiproliferative properties.

Extracts from the leaves, stem and bark of *Syzygium aromaticum* were found to have antioxidant, antiangiogenic and cytotoxic effects (Aisha et al. 2011). The extracts were found to contain high levels of total phenolics with strong antioxidant activity. Significant inhibition of the blood vessel outgrowth was also obtained in the angiogenesis model. Cytotoxicity testing on three cell lines, namely, endothelial cells and breast and colon cancer cells, indicated high cytotoxic effects with the highest activity obtained on the oestrogen-dependent breast cancer cells. The results illustrated the importance of *Syzygium aromaticum* leaves, stems and bark as good sources of phenolic-rich extracts. Water, ethanol and oil extracts of cloves showed different patterns of cell growth inhibition activity of HeLa (cervical cancer), MCF-7 (ER-positive) and MDA-MB-231 (ER-negative) breast cancer, DU-145 prostate cancer and TE-13 oesophageal cancer cell lines with the oil extract having maximal cytotoxic activity (Dwivedi et al. 2011). Maximum cell death and apoptotic cell demise occurred in TE-13 cells within 24 h by clove oil at 300 μl/mL with 80 % cell death, whereas DU-145 cells showed minimal cell death. At the same time, no significant cytotoxicity was found in human peripheral blood mononuclear cells at the same dose.

A methanol extract from clove (*Syzygium aromaticum*) showed a suppressive effect of the SOS-inducing activity on the mutagen 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide (furylfuramide) in the *Salmonella typhimurium* TA1535/pSK1002 umu test (Miyazawa and Hisama 2001). The hexane fraction of the methanol extract also showed a suppressive effect. Suppressive compounds in the hexane fraction were identified as *trans*-isoeugenol (1) and eugenol (2). Compounds 1 and 2 suppressed the furylfuramide-induced SOS response in the umu test. Compounds 1 and 2 suppressed 42.3 and 29.9 % of the SOS-inducing activity at a concentration of 0.60 μmol/mL. When assayed with other mutagens, 4-nitroquinolin 1-oxide (4NQO) and N-methyl-N′-nitro-N-nitrosoguanidine (MNNG), aflatoxin B(1) (AfB(1)) and 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1), these compounds showed suppressive effects of the SOS-inducing activity against furylfuramide, 4NQO, AfB(1) and Trp-P-1. In subsequent studies, Miyazawa and Hisama (2003) reported that phenylpropanoids with antimutagenic activity were isolated from the buds of clove (*Syzygium aromaticum*). The isolated compounds suppressed the expression of the umu gene following the induction of SOS

response in the *Salmonella typhimurium* TA1535/pSK1002 that have been treated with various mutagens. The suppressive compounds were mainly localized in the ethyl acetate extract fraction of the processed clove which in further fractionation afforded secondary suppressive compounds identified as dehydrodieugenol (1) and *trans*-coniferyl aldehyde (2). When using 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide (furylfuramide) as the mutagen, compound 1 suppressed 58 % of the umu gene expression as compared to the controls at a concentration of 0.60 μmol/mL, with an ID_{50} (50 % inhibitory dose) value of 0.48 μmol/mL, and compound 2 suppressed 63 % of the umu gene expression as compared to the controls at a concentration of 1.20 μmol/mL, with an ID_{50} value of 0.76 μmol/mL. Additionally, compounds 1 and 2 suppressed the mutagenic activity of other well-known mutagens such as 4-nitroquinolin 1-oxide (4NQO) and N-methyl-N′-nitro-N-nitrosoguanidine (MNNG), which did not require liver-metabolizing enzymes, and aflatoxinB(1)(AfB(1))and3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1), which required liver-metabolizing enzymes and activated Trp-P-1 and UV irradiation. Finally, the antimutagenic activities of all the identified compounds against furylfuramide, Trp-P-1 and activated Trp-P-1 were also shown when assayed by the Ames test using the *S. typhimurium* TA100 strain.

Antidiabetic Activity

Clove extract was reported to act like insulin in hepatocytes and hepatoma cells by reducing phosphoenolpyruvate carboxykinase (PEPCK) and glucose 6-phosphatase (G6Pase) gene expression (Prasad et al. 2005). It increased glucose uptake into adipocytes, an insulin-like effect. A more global analysis of gene expression by DNA microarray analysis revealed that clove and insulin regulated the expression of many of the same genes in a similar manner. Insulin action was impaired in diabetic patients, which led to increased hepatic glucose production. The research demonstrated that consumption of certain plant-based diets may have beneficial effects for the treatment of diabetes and indicated a potential role for compounds derived from clove as insulin-mimetic agents. This was also confirmed in another study (Broadhurst et al. 2000), where extracts of the plants *Cinnamomum zeylanicum*, *Hamamelis virginiana* (witch hazel), *Camellia sinensis* (green and black teas), *Pimenta dioica* (allspice), *Laurus nobilis* (bay leaves), *Myristica fragrans* (nutmeg) and *Syzygium aromaticum* (cloves) showed a positive effect on insulin activity suggesting a possible role of these plants in improving glucose and insulin metabolism.

Syzygium aromaticum-derived oleanolic acid like insulin decreased blood glucose concentrations in nondiabetic and streptozotocin (STZ)-induced diabetic rats (Musabayane et al. 2010). Combined oleanolic acid and insulin treatment had even greater antihyperglycaemic response, suggestive of a synergistic effect of the two. After 5 weeks, STZ-induced diabetic rats exhibited hyperglycaemia and depleted hepatic and muscle glycogen concentrations. Oleanolic acid treatment lowered the blood glucose with concomitant restoration of glycogen concentrations to near normalcy. The results suggested that oleanolic acid may have a role in improving insulin sensitivity. The antihyperglycaemic effects of *Syzygium aromaticum*-derived oleanolic acid (OA) in streptozotocin (STZ)-induced diabetic rats had been reported to be mediated in part via increased hepatic glycogen synthesis (Ngubane et al. 2011). OA administration was found to restore the activity of key glycogenic enzymes in the liver and skeletal muscle of STZ-induced diabetic rats to enhance glycogen synthesis to improve the glycaemic status. The restoration of this principal glucose utilization pathway by OA may constitute a novel therapeutic strategy for diabetes treatment. It was found that the combination of OA and insulin did not significantly alter the activities of hexokinase and glucokinase of STZ-induced diabetic rats suggesting that glycogen synthesis could also occur from precursors such as amino acids or fructose and lactate. Studies showed that glucose transport from the mucosa to the serosa was decreased by treatment with phlorizin hypoglycaemic drug

and oleanolic acid derived from *S. aromaticum* (Khathi et al. 2013). All treatments increased the glycogen concentrations of the small intestines of fasted and non-fasted nondiabetic and STZ-induced diabetic rats after 18h. The data suggested that oleanolic acid could be a potential alternative drug therapy of postprandial hyperglycaemia via inhibition of glucose uptake across the small intestine and concomitant conversion of glucose to glycogen in the intestinal gut wall.

Clove (flower bud) ethanol extract significantly suppressed an increase in blood glucose level in type 2 diabetic KK-A(y) mice (Kuroda et al. 2012). In vitro evaluation showed the extract had human peroxisome proliferator-activated receptor (PPAR)-γ ligand-binding activity in a GAL4-PPAR-γ chimera assay. Bioassay-guided fractionation of the EtOH extract resulted in the isolation of eight compounds, of which dehydrodieugenol (2) and dehydrodieugenol B (3) had potent PPAR-γ ligand-binding activities, whereas oleanolic acid (4), a major constituent in the extract, had moderate activity. Furthermore, 2 and 3 were shown to stimulate 3 T3-L1 preadipocyte differentiation through PPAR-γ activation. The results indicated clove to have potential as a functional food ingredient for the prevention of type 2 diabetes and that compounds 2–4 mainly contribute to its hypoglycaemic effects via PPAR-γ activation.

The aqueous extracts of several tropical spices including *S. aromaticum* inhibited α-amylase (IC_{50} = 2.81–4.83 mg/mL), α-glucosidase (IC_{50} = 2.02–3.52 mg/mL), DPPH radicals (EC_{50} = 15.47–17.38 mg/mL) and sodium nitroprusside (SNP)-induced lipid peroxidation (14.17–94.38 %), with the highest α-amylase and α-glucosidase inhibitory actions and DPPH radical scavenging ability exhibited by *Xylopia aethiopica*, *Aframomum danielli* and *S. aromaticum*, respectively (Adefegha and Oboh 2012). Also, the spices possessed high total phenol (0.88–1.3 mg/mL) and flavonoid (0.24–0.52 mg/mL) contents. The results suggested that the spices may exert their antidiabetic properties through the mechanism of enzyme inhibition, free radical scavenging ability and prevention of lipid peroxidation.

Antimicrobial Activity

The oils of bay, cinnamon, clove and thyme were found to be highly inhibitory to five important food-borne pathogens, *Campylobacter jejuni, Salmonella enteritidis, Escherichia coli, Staphylococcus aureus* and *Listeria monocytogenes* (Smith-Palmer et al. 1998). These oils exhibited potent inhibition of *L. monocytogenes* and *S. enteritidis* in tryptone soya broth (TSB) and cheese and acted as natural food preservatives. In the low-fat cheese, all four oils (bay leaf, thyme, clove, cinnamon) at 1 % reduced *L. monocytogenes* to $\leq 1 \cdot 0$ $\log_{10}$cfu/mL (Smith-Palmer et al. 2001). In contrast, in the full-fat cheese, oil of clove was the only oil to achieve this reduction. In another study, five plant essential oils—bay, clove, cinnamon, nutmeg and thyme—significantly reduced the production of listeriolysin O by *Listeria monocytogenes* (Smith-Palmer et al. 2002). Clove oil was the only oil that also significantly reduced phosphatidylcholine-specific phospholipase C activity of *Listeria monocytogenes*. In other studies, clove bud oil was found to be highly active against *Escherichia coli, Listeria monocytogenes* and *Salmonella enterica* (Friedman et al. 2002). Clove was reported to have potent antimicrobial activities against *Bacillus subtilis, Escherichia coli* and *Saccharomyces cerevisiae* (De et al. 1999); yeast fungi (Arora and Kaur 1999) and common fungi causing spoilage of bakery products include *Eurotium amstelodami, Eurotium herbariorum, Eurotium repens, Eurotium rubrum, Aspergillus flavus, Aspergillus niger* and *Penicillium corylophilum* (Guynot et al. 2003).

A crude methanol extract of *Syzygium aromaticum* exhibited preferential growth-inhibitory activity against Gram-negative anaerobic periodontal oral pathogens, including *Porphyromonas gingivalis* and *Prevotella intermedia* (Cai and Wu 1996). Eight active compounds were isolated from this extract and were identified as 5,7-dihydroxy-2-methylchromone 8-C-β-D-glucopyranoside, biflorin, kaempferol, rhamnocitrin, myricetin, gallic acid, ellagic acid and oleanolic acid. The antibacterial activity of these pure compounds was determined against *Streptococcus*

mutans, Actinomyces viscosus, Porphyromonas gingivalis and Prevotella intermedia. The flavones, kaempferol and myricetin, demonstrated potent growth-inhibitory activity against the periodontal pathogens *Porphyromonas gingivalis* and *Prevotella intermedia*. The n-hexane extract of clove seeds demonstrated preferential growth-inhibitory activity against the causal cariogenic pathogens (*Streptococcus mutans*) in dental caries (Uju and Obioma 2011). The aqueous extract of several Mexican medicinal plants including *Syzygium aromaticum* exhibited high inhibitory effect against oral pathogens, *Streptococcus mutans* and *Porphyromonas gingivalis* (10.5–78.0 µg/mL) (Rosas-Piñón et al. 2012).

Essential oil of clove, dispersed (0.4 % v/v) in a concentrated sugar solution, displayed a marked germicidal effect against *Candida albicans, Staphylococcus aureus* (five strains), *Klebsiella pneumoniae, Pseudomonas aeruginosa, Clostridium perfringens* and *Escherichia coli* (Briozzo et al. 1989). Sugar was not necessary for the antimicrobial activity of clove oil, but the concentrated sugar solution provided a good vehicle for obtaining an oil dispersion that was relatively stable for certain practical applications. Clove oil also inhibited growth of *Fusarium proliferatum* in maize grains. Prasaprohyai formula, a Thai traditional medicine used for reducing fever in children, and its component, namely, *S. aromaticum*, were found to inhibit growth of *Staphylococcus aureus* and *Escherichia coli,* but other components, namely, *Lepidium sativum*, *Myristica fragrans* (seed) and *Myristica fragrans* (aril), had no antibacterial activity (Sattaponpan and Kondo 2011). Ethanol extracts of *Cinnamomum zeylanicum* and *S. aromaticum* showed the strongest in vitro antibacterial activity followed by *Cuminum cyminum* against methicillin-resistant *Staphylococcus aureus* (Mandal et al. 2011).

The antifungal activities of *S. aromaticum* oil (clove oil) against the dermatophytes (*Microsporum canis, Trichophyton mentagrophytes, Trichophyton rubrum, Epidermophyton floccosum* and *Microsporum gypseum*) tested were highest at a concentration of 0.2 mg/mL, with an effectiveness of more than 60 % (Park et al. 2007). Hyphal growth was completely inhibited in *T. mentagrophytes, T. rubrum* and *M. gypseum* by treatment with clove oil at a concentration of 0.2 mg/mL. Eugenol was the most effective antifungal constituent of clove oil against the dermatophytes *T. mentagrophytes* and *M. canis*. Morphological changes in the hyphae of *T. mentagrophytes*, such as damage to the cell wall and cell membrane and the expansion of the endoplasmic reticulum, after treatment with 0.11 mg/mL eugenol were observed by transmission electron microscopy. Another recent study showed that clove essential oil and eugenol exhibited inhibitory activity against all the tested strains (*Candida*, *Aspergillus*) and dermatophyte clinical and ATCC (American Type Culture Collection) strains (Pinto et al. 2009). Clove oil and eugenol caused also a considerable reduction of the quantity of ergosterol, a specific fungal cell membrane component. Germ tube formation by *Candida albicans* was completely or almost completely inhibited by concentrations below the MIC values, for the oil and eugenol. The study indicated that clove oil and eugenol had considerable antifungal activity against clinically relevant fungi, including fluconazole-resistant strains. The antifungal activity of essential oils and their major constituents was in the order of cinnamaldehyde > eugenol > geraniol = *Cinnamomum verum* > citral > *Syzygium aromaticum* > *Cymbopogon citratus* > *Cymbopogon martini*, both in liquid and solid media against *Aspergillus fumigatus* and *Trichophyton rubrum* (Khan and Ahmad 2011). More than 70 % reduction in elastase activity was recorded in *A. fumigatus* by the oils of *C. verum, C. martini*, eugenol, cinnamaldehyde and geraniol.

Water extract of *Syzygium aromaticum* buds was found to inhibit growth of human pathogenic bacteria, *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Salmonella enterica* serovar *Typhi* and *Pseudomonas aeruginosa* (Ali et al. 2011). *Syzygium aromaticum* (clove) showed the highest inhibitory effect of 12 plant extracts tested against *Salmonella typhimurium, Escherichia coli* O157:H7 and *Listeria monocytogenes* using a disc diffusion assay (Kim et al. 2011). Clove extract treatment significantly reduced populations of the three

tested pathogens from the surface of lettuce. Clove essential oil showed the highest inhibitory effect of food pathogen and spoilage bacteria, followed by rosemary (*Rosmarinus officinalis*) and lavender (*Lavandula angustifolia*) (Gómez-Estaca et al. 2010). When tested on an extract made of fish, clove and thyme, essential oils were the most effective as food preservative. Gelatin–chitosan-based edible films incorporated with clove essential oil exhibited antimicrobial activity when tested against six selected microorganisms: *Pseudomonas fluorescens, Shewanella putrefaciens, Photobacterium phosphoreum, Listeria innocua, Escherichia coli* and *Lactobacillus acidophilus*. Additionally, when the complex gelatin–chitosan film incorporating clove essential oil was applied to fish during chilled storage, the growth of microorganisms was drastically reduced in Gram-negative bacteria, especially enterobacteria, while lactic acid bacteria remained practically constant for much of the storage period. The effect on the microorganisms during this period was in accordance with biochemical indexes of quality, indicating the viability of these films for fish preservation. Lee et al. (2009) found that the essential oil obtained from clove flower buds exhibited antibacterial activity against *Vibrio* spp. ($n=6$), *Edwardsiella* spp. ($n=21$), *Aeromonas* spp. ($n=2$), *Escherichia coli* ($n=2$), *Flavobacterium* spp. ($n=1$), *Salmonella* spp. ($n=2$), *Streptococcus* spp. ($n=1$) and *Pseudomonas* spp. ($n=1$). *Citrobacter freundii*, *Aeromonas hydrophila*, *Pseudomonas aeruginosa*, *Streptococcus agalactiae*, *Edwardsiella tarda* and *Yersinia enterocolitica*. The MIC values ranged from 0.015 to 0.062 µg/mL.

Essential oils having new antipathogenic drug principle because of its anti-QS activity might be important in reducing virulence and pathogenicity of drug-resistant bacteria in vivo. *Syzygium aromaticum* (clove) oil showed promising anti-quorum sensing (QS) activity on both wild and mutant strains of *Chromobacterium violaceum* with zones of pigment inhibition 19 and 17 mm, respectively, followed by activity in cinnamon, lavender and peppermint oils (Khan et al. 2009b). The effect of clove oil on the extent of violacein production was estimated photometrically and found to be concentration dependent. At sub-MICs of clove oil, 78.4 % reductions in violacein production over control and up to 78 % reduction in swarming motility in *Pseudomonas aeruginosa* over control were recorded. Hexane, chloroform and methanol extracts of clove (*Syzygium aromaticum*) exhibited anti-quorum sensing activity (Krishnan et al. 2012). Hexane and methanol extracts of clove inhibited the response of *Chromobacterium violaceum* to exogenously supplied N-hexanoylhomoserine lactone, in turn preventing violacein production. Chloroform and methanol extracts of clove significantly reduced bioluminescence production by *E. coli* [pSB1075] grown in the presence of N-(3-oxododecanoyl)-L-homoserine lactone. They also demonstrated that clove extract inhibited quorum sensing-regulated phenotypes in *Pseudomonas aeruginosa* PA01, including expression of lecA::lux (by hexane extract), swarming (maximum inhibition by methanol extract) and pyocyanin (maximum inhibition by hexane extract). Their data suggested that clove extracts may be useful as the lead of anti-infective drugs.

The multidrug-resistant (MDR) strains of *Escherichia coli, Klebsiella pneumoniae* and *Candida albicans* were sensitive to the antimicrobial activity *of Acacia nilotica, Syzygium aromaticum* and *Cinnamomum zeylanicum*, whereas they exhibited strong resistance to the extracts of *Terminalia arjuna* and *Eucalyptus globulus* (Khan et al. 2009a). Community-acquired infections showed higher sensitivity than the nosocomial infections against these extracts. Taguchi et al. (2005) found that when the clove preparation was administered into the oral cavity of *Candida albicans*-infected mice, their oral symptoms were improved, and the number of viable *Candida albicans* cells in the cavity was reduced. In contrast, when the clove preparation was administered intragastrically, oral symptoms were not improved, but viable cell numbers of *Candida albicans* in the stomach and faeces were decreased. Their findings demonstrated that oral intake of a herbal food, clove, may suppress the overgrowth of *C. albicans* in the alimentary tract including the oral

cavity. *Syzygium aromaticum* and *Cymbopogon citratus* oils were more active against preformed *Candida albicans* biofilms compared to amphotericin B and fluconazole (Khan and Ahmad 2012). At 0.5× MIC, *C. citratus* followed by *S. aromaticum* were most inhibitory against biofilm formation. The results suggested exploitation of these oils as new anti-biofilm products to deal with the problem of drug resistance and recurrent infection associated with biofilm mode of growth of *Candida* spp.

Cinnamon and clove exhibited a significant inhibitory effect on histamine production and histidine decarboxylase activity of *Morganella morganii* (a potent histamine-producing bacteria in fish), whereas turmeric and cardamom had a moderate effect (Shakila et al. 1996). When applied to whole mackerel at a level of 3 %, clove and cinnamon showed a significant inhibitory effect on histamine, putrescine and tyramine formation but not on that of cadaverine. Cardamom and turmeric exhibited a moderate effect, and pepper was ineffective. Both clove and cinnamon were found to be more helpful than cardamom and turmeric in the minimization of the formation of toxic histamine in mackerel.

Antiviral Activity

Aqueous extracts of *Syzygium aromaticum* was one of eight plant extracts that exhibited active (≥90 % inhibition at 100 μg/mL) inhibition on hepatitis C virus (HCV) protease (Hussein et al. 2000).

Of 10 traditional herbal extracts, *Geum japonicum, Rhus javanica, Syzygium aromaticum* and *Terminalia chebula* showed a stronger antiherpes simplex virus type 1 (HSV-1) activity in combination with acyclovir than the other herbal extracts in vitro (Kurokawa et al. 1995). When acyclovir and/or a herbal extract was orally administered at doses corresponding to human use, each of the 4 combinations significantly limited the development of skin lesions and/or prolonged the mean survival times of infected mice compared with both acyclovir and the herbal extract alone. These combinations were not toxic to mice. They reduced virus yields in the brain and skin more strongly than acyclovir alone and exhibited stronger anti-HSV-1 activity in the brain than in the skin, in contrast to acyclovir treatment by itself. The anti-HSV action of eugeniin purified from *Geum japonicum* and *Syzygium aromaticum* was characterized. The effective concentration (5.0 μg/mL) for 50 % plaque reduction of eugeniin for wild HSV type 1 (HSV-1) on Vero cells was 13.9-fold lower than its 50 % cytotoxic concentration determined by a yield-reduction assay. Eugeniin also inhibited the growth of acyclovir-phosphonoacetic acid-resistant HSV-1, thymidine kinase-deficient HSV-1 and wild HSV type 2 (Kurokawa et al. 1998). The results showed that one of the major target sites of inhibitory action of eugeniin is viral DNA synthesis; the inhibitory action for viral DNA polymerase activity was novel compared with anti-HSV nucleoside analogues.

Geum japonicum, Syzygium aromaticum, Terminalia chebula and *Rhus javanica* were found to inhibit replication of human cytomegalovirus (HCMV) and murine cytomegalovirus (MCMV) in vitro (Yukawa et al. 1996; Shiraki et al. 1998). All four plants significantly suppressed MCMV yields in lungs of treated mice compared with water treatment. These herbs may be beneficial for the prophylaxis of CMV diseases in immune-compromised patients.

Anti-inflammatory and Analgesic Activities

In Korea, clove oil has been successfully used for asthma and various allergic disorders by oral administration. An aqueous extract of clove was found to inhibit immediate hypersensitivity by inhibition of histamine release from mast cells in vivo and in vitro (Kim et al. 1998). Using animal models, eugenol was found to significantly reduce serum histamine level (Kim et al. 1997). Eugenol was reported to prevent the anaphylactic degranulation of peritoneal mast cells. It was reported that the b-caryophyllene component in clove oil showed anti-inflammatory activity in

several experiments. Studies reported on the local anaesthetic activity of β-caryophyllene (Ghelardini et al. 2001). β-caryophyllene, but not caryophyllene oxide, was able to reduce drastically, in a dose-dependent manner, the electrically evoked contractions of the rat phrenic hemidiaphragm. In the rabbit, conjunctival reflex test treatment with a solution of β-caryophyllene (10–1,000 μg/mL) allowed a dose-dependent increase in the number of stimuli necessary to provoke the reflex.

Eugenol was reported to act on contact to depress nociceptors, the sensory receptors involved in pain perception (Brodin and Røed 1984). The findings suggested that eugenol acted as a membrane-stabilizing (local anaesthetic) drug at low concentrations. It exhibited reversible inhibition of compound-action potential (cAP) of the nerve and increased threshold, high-frequency inhibition and unresponsiveness of the resting membrane potential of the muscle to the drug. Eugenol was also found to exhibit inhibition of COX-2-catalyzed prostaglandin PGE(2) biosynthesis with an IC_{50} of 129 μM (Huss et al. 2002). In vitro studies in murine macrophages showed that clove (100 μg/well) markedly inhibited cytokine interleukin IL-1β, IL-6 and IL-10 production either before or after lipopolysaccharide (LPS) challenge (Bachiega et al. 2012). Eugenol, the principal component of clove oil, did not affect interleukin IL-1β production but inhibited IL-6 and IL-10 production.

The ethanol extracts of *Syzygium aromaticum* flower bud exhibited antinociceptive and anti-inflammatory effects in mice and Wistar rats as evaluated using acetic acid-induced abdominal contractions in mice and formalin-induced hind paw oedema in Wistar rats, respectively (Tanko et al. 2008). The extract had an LD_{50} of 565.7 mg/kg body weight intraperitoneally in mice. The extracts (50, 100 and 200 mg/kg body weight i.p.) produced significant anti-inflammatory effect at all the three doses. Similarly, the antinociceptive activity produced significant effects at all the three doses of the extract. The result supported the local use of the plant in painful and inflammatory conditions.

Hepatoprotective Activity

The ethanol extract of clove showed remarkable hepatoprotective activity against paracetamol-induced liver injury in female rats (Nassar et al. 2007).

Clove exhibited a modulatory effect on hepatic detoxification systems (Kumari 1991). Following clove administration (0.5, 1 and 2 % w/w in the diet) to Swiss albino mice for 10, 20 and 30 days, enhanced glutathione S-transferase (GST), cytochrome b5 and acid-soluble sulphhydryl (SH) levels were observed in all the treatment groups, excepting those maintained on a 0.5 % diet for 10 days which did not show significant increase in the GST and SH levels as compared to their respective controls. Significant reduction in cytochrome P-450 and malondialdehyde levels was observed in all groups at 30 days duration. While aryl hydrocarbon hydroxylase levels remained unaltered by clove administration, DT-diaphorase activity was elevated by 1 and 2 % clove diets at 30 days duration. An in vivo bone marrow micronucleus assay demonstrated that administration of 0.5 and 2 % clove diets for 10 days neither significantly induced micronuclei nor could effectively modulate the 7, 12-dimethylbenz[a] anthracene genotoxicity in mice. The results suggested whole cloves as potential chemopreventive agents.

Antiplatelet Aggregation Activity

Eugenol and acetyl eugenol in clove oil showed potent antiplatelet aggregation activity. They inhibited arachidonate-, adrenaline- and collagen-induced platelet aggregation (Srivastava and Malhotra 1991). Inhibition of aggregation appeared to be mediated through a reduced formation of thromboxane. In another study, clove oil inhibited human platelet aggregation induced by arachidonic acid (AA), platelet-activating factor (PAF) or collagen (Saeed and Gilani 1994). Clove oil was a more effective inhibitor for aggregation induced by AA and PAF (IC_{50}=4 and 6 μM, respectively) than collagen (IC_{50}: 132 μM). The in vivo experiments in rabbits

showed that clove oil (50–100 mg/kg) afforded 100 % protection against PAF (11 mg/kg, i.v.) and 70 % protection against AA (2.0 mg/kg, i.v.)-induced thrombosis and shock due to pulmonary platelet thrombosis. It also inhibited thromboxane-A2 and 12-HETE production by human platelets incubated with [C14] AA. These results indicated that clove oil was inhibitory of platelet aggregation and thromboxane synthesis and may act as antithrombotic agent.

Two antithrombotic polysaccharides with relatively high molecular weight (HMW) and low molecular weight (LMW) were isolated from the flower buds of *Syzygium aromaticum* (Lee et al. 2001). The LMW polysaccharide was mainly composed of Rha, Gal, GalA and Ara (molar % 24.1, 18.9, 18.0 and 17.9, respectively) with 10.8 % of sulphate and 18.2 % of protein. The HMW fraction consisted of Ara, Gal, Glc and Rha (molar % 26.0, 23.7, 17.5 and 12.4, respectively) with 15.4 % of sulphate and 8.0 % of protein. Both polysaccharides had the backbone of type I rhamnogalacturonan and the side chain of arabinan. Compared to the antithrombotic activity of the HMW fraction (plasma clotting time of 145 s in APTT assay), the LMW fraction displayed a slightly low activity (90 s). However, animal studies indicated that crude LMW polysaccharide did not show acute toxicity, while the acute LD50 of the HMW fraction was approximately 2-fold lower than that of heparin.

Appetite Stimulating Activity

Aydin et al. (2011) detected a ghrelin-like substance at a concentration of 4,070.75 pg/mg in the tissues of flower bud of *S. aromaticum*. Ghrelin was predominantly localized to the trachea and parenchyma cells in the flower bud of *S. aromaticum*. The concentration of ghrelin in human salivary gland tissue was 436.00 pg/mg. Ghrelin is an endogenous ligand of the growth hormone secretagogue receptor found in mammals and some plants that stimulate hunger.

Gastroprotective Activity

Clove essential oil and eugenol, its main constituent, exhibited antiulcer activities in the rat models of indomethacin- and ethanol-induced ulcer (Santin et al. 2011). The effectiveness of clove essential oil and eugenol was attributed to the ability to stimulate the synthesis of mucus, an important gastroprotective factor, and not to the activities of the nitric oxide and endogenous sulphhydryls. *Syzygium aromaticum* extract at both 50 and 100 μg/mL. was one of four plant extracts that markedly inhibited interleukin-8 secretion activity in *Helicobacter pylori*-infected gastric epithelial cells (Zaidi et al. 2012). The study revealed anti-inflammatory and cytoprotective effects of selected medicinal plants which could partially validate the traditional use of these plants in gastric intestinal disorders.

Immunomodulatory Activity

Studies established that the immunostimulatory activity found in mice treated with clove essential oil was due to improvement in humoral- and cell-mediated immune response mechanisms (Carrasco et al. 2009). Clove essential oil increased the total white blood cell (WBC) count and enhanced the delayed-type hypersensitivity (DTH) response in mice. Moreover, it restored cellular and humoral immune responses in cyclophosphamide-immunosuppressed mice in a dose-dependent manner.

Skin Whitening Activity

The methanol extract of *Syzygium aromaticum* flowering bud was found to have mushroom tyrosinase inhibitory activity (69.4 %) in a concentration-dependent manner (Adhikari et al. 2008) and to have potential to control hyperpigmentation. Eugenol and eugenol acetate were isolated as the active compounds in the methanol extract from clove bud and showed melanin inhibition of 60 and 40 % in B16 melanoma cell with less cytotoxicity at the concentration of 100 and

200 μg/mL, respectively (Arung et al. 2011). Additionally, an essential oil prepared from clove bud containing eugenol and eugenol acetate as dominant components showed melanin inhibition of 50 and 80 % in B16 melanoma cells at the concentration of 100 and 200 μg/mL, respectively.

Renal Stimulatory Activity

Studies indicate that *Syzygium aromaticum*-derived oleanolic acid enhanced renal function of streptozotocin (STZ)-induced diabetic rats as evidenced by its reversal of the previously reported inability of the kidney to excrete Na(+) in these animals (Madlala et al. 2012). They found that oleanolic acid increased Na^+ excretion of conscious male Sprague-Dawley rats from week 3 to week 5. By the end of the 5-week experimental period, oleanolic treatment significantly reduced plasma creatinine concentration of STZ-induced diabetic rats with a concomitant elevation in glomerular filtration rate. MTT assay studies demonstrated that oleanolic increased the metabolic activity of the kidney and liver cell lines.

Aphrodisiac Activity

Studies reported that a 50 % ethanolic extract of clove produced a significant and sustained increase in the sexual activity of normal male rats, without any conspicuous gastric ulceration and adverse effects (Tajuddin et al. 2004). Oral administration of the extract significantly increased mounting frequency, intromission frequency, intromission latency, erections, quick flips, long flips, as well as aggregate of penile reflexes. It caused significant reduction in the mounting latency and post-ejaculatory interval. The most appreciable effect of the extract was observed at the dose of 500 mg/kg. Thus, the resultant aphrodisiac activity of the extract supported claims for its traditional usage in sexual disorders. The results of studies by Mishra and Singh (2008) suggested the biphasic action of hexane extract of *Syzygium aromaticum* flower bud on testicular function, thereby advocating a cautious use of the flower bud as an aphrodisiac in indigenous systems of medicine in Asian countries. Oral administration of hexane extract of *Syzygium aromaticum* flower buds to Parkes strain mice did not induce systemic toxicity at the doses tested. Lower dose (15 mg) of the extract increased the activities of delta(5) 3 beta-HSD and 17 beta-HSD and serum level of testosterone. The higher doses (30 and 60 mg) of extract inhibited these parameters and induced non-uniform degenerative changes in the seminiferous tubules associated with decrease in daily sperm production and depletion of 1C (round and elongated spermatids) population.

Kumar Goswami et al. (2012) postulated that some of the Indian medicinal plants including *Syzygium aromaticum* used traditionally as aphrodisiacs and for male sexual disorder (MSD) may have rho-kinase 2 (ROCK-II) inhibitory potential and deserve further investigation. Their studies showed that plant extracts capable of inhibiting ROCK-II enzyme may be useful in management of erectile dysfunction.

Osteogenic/Antiarthritic Activity

Studies indicated that serum alkaline phosphatase (AP; 48.25 %), serum tartrate-resistant acid phosphatase (TRAP; 63.48 %), urinary calcium (14.70 %), urinary phosphate (50.30 %) and urinary creatinine (122.44 %) were significantly altered in ovariectomized female Wistar rats compared to control (Karmakar et al. 2012). All these altered responses were significantly restored (AP 27.53 %, TRAP 33.51 %, calcium 53.15 %, phosphate 27.49 %, creatinine 46.40 %) by supplementation with hydroalcoholic extract of dried clove buds. Results of bone density, bone mineral content, bone tensile strength and histological analysis also showed similar trend of results. The results suggested the hydroalcoholic extract of dried clove buds to have bone-preserving efficacy against hypogonadal osteoporosis.

Treatment with eugenol starting at the onset of arthritis (day 25) ameliorated these clinical signs of collagen-induced arthritis in mice (Grespan et al. 2012). Eugenol inhibited mononuclear cell infiltration into the knee joints of arthritic mice and also lowered the levels of cytokines (tumour necrosis factor (TNF)-α, interferon (IFN)-γ and tumour growth factor (TGF)-β) within the ankle joints and did not affect the in vitro cell viability. The authors concluded that eugenol could be useful as a beneficial supplement in treating human arthritis.

Antiparasitic Activity

Of several plant essential oils tested, clove oil was found to be the most effective in inhibiting growth of *Trypanosoma cruzi* with IC_{50} of 99.5 μg/mL for epimastigotes and 57.5 μg/mL for trypomastigotes (Santoro et al. 2007).

Clove oil was found to have anti-giardial activity (Machado et al. 2011). Clove essential oil (IC_{50} = 134 μg/mL) and eugenol (IC_{50} = 101 μg/mL) inhibited the growth of *Giardia lamblia*. Clove oil inhibited trophozoites adherence since the first hour of incubation and was able to kill almost 50 % of the parasite population in a time-dependent manner. Eugenol inhibited *G. lamblia* trophozoites adherence from the third hour and did not induce cell lyses. The main morphological alterations were modifications on the cell shape, presence of precipitates in the cytoplasm, autophagic vesicles, internalization of flagella and ventral disc, membrane blebs and intracellular and nuclear clearing. The overall findings suggested that eugenol was responsible for the anti-giardial activity of the *S. aromaticum* essential oil and the oil and eugenol had potential for use as therapeutic agents against giardiasis.

The flower bud extract of *S. aromaticum* was found to have antimalarial activity (Bagavan et al. 2011b; Bagavan and Rahuman 2011). The extract was active against the chloroquine (CQ)-sensitive (3D7) and CQ-resistant (Dd2 and INDO) strains of *Plasmodium falciparum*. The IC_{50} value for 3D7 strain was 13 μg/mL for ethyl acetate extract and 6.25 μg/mL for methanol extract.

The hexane flower bud extract of *Syzygium aromaticum* was found to be toxic to the head lice, *Pediculus humanus capitis,* an obligate ectoparasite of humans that causes pediculosis capitis (Bagavan et al. 2011a). The filter paper contact bioassay study showed pronounced pediculicidal activity in the flower bud hexane extract. The vapour phase toxicity showed a significant difference in pediculicidal activity of *S. aromaticum* extract against P. *humanus capitis* between close- and open-container methods. The mortality was higher in the closed containers than in open ones, indicating that the effect of hexane extract was largely a result of action in the vapour phase-exhibited fumigant toxicity.

Insecticidal Activity

Clove oil was reported to provide the longest duration of 100 % repellency (2–4 h) against all three species of mosquito, *Aedes aegypti, Culex quinquefasciatus* and *Anopheles dirus*, when compared with other inhibitory oils of *Cymbopogon nardus* (citronella), *Pogostemon cablin* (patchouli) and *Zanthoxylum limonella* (Thai name: makaen) (Trongtokit et al. 2004, 2005). It can be administered in the form of a gel product for possible use by low-income rural communities against various mosquito species. Eugenol, isoeugenol and methyleugenol were found to inhibit the development of stored product pests, *Sitophilus zeamais* and *Tribolium castaneum* (Huang et al. 2002).

Clove essential oil was found to be toxic against both pyrethroid-susceptible and pyrethroid-resistant *Aedes aegypti* laboratory strains at LC_{50}, LC_{95} and LC_{99} levels (Sutthanont et al. 2008). The main component of *S. aromaticum* bud oil was eugenol (77.37 %), with minor amounts of *trans*-caryophyllene (13.66 %). Flower bud extracts of *S. aromaticum* exhibited mosquito larvicidal activity: hexane extract against *Anopheles vagus* with LC_{50} value of 85.90 μg/mL, hexane extract against *Culex vishnui* with LC_{50} value of 149.56 μg/mL and

methanol extract against *Armigeres subalbatus* with LC_{50} value of 78.28 μg/mL (Bagavan and Rahuman 2011).

S. *aromaticum* essential oil was active against *Ae. aegypti* larvae (LC_{50}=62.3 and 77.0 ppm, for field-collected and Rockefeller larvae, respectively) (Barbosa et al. 2012). The larvicidal activity of eugenol, the major compound of the essential oil, was also active with LC_{50}=93.3 and 71.9 ppm for field-collected and Rockefeller larvae, respectively. The larvicidal activity of eugenol derivatives varied between 62.3 and 1,614.9 ppm. Oxidation of eugenol allylic bond to a primary alcohol and removal of the phenolic proton resulted in decreased potency. However, oxidation of the same double bond in 1-benzoate-2-methoxy-4-(2-propen-1-yl)-phenol resulted in increased potency.

Scrub typhus, a rickettsial disease transmitted by several species of *Leptotrombidium* chiggers (larvae), is endemic in many areas of Asia. Four (including clove oil) of the 13 essential oils showed promise as effective repellent against *Leptotrombidium imphalum* chiggers (Eamsobhana et al. 2009). *Syzygium aromaticum* (clove) oil exhibited 100 % repellency at 5 % concentration (dilution with absolute ethanol), whereas *Melaleuca alternifolia* (tea tree) oil exhibited 100 % repellency at 40 % concentration. Undiluted oils of *Zingiber cassumunar* (plai) and *Eucalyptus globulus* (blue gum) exhibited 100 % repellency.

Molluscicidal Activity

Bait formulations containing molluscicidal component of *Ferula asafoetida* (ferulic acid, umbelliferone), *Syzygium aromaticum* (eugenol) and *Carum carvi* (limonene) caused maximum significant reduction in free amino acid, protein, DNA and RNA levels, i.e. 41.37, 23.56, 48.36 and 14.29 % of control in the ovotestis of the snail *Lymnaea acuminata*, respectively (Kumar et al. 2011). Discontinuation of feeding after treatment of 60 % of 96 h LC50 of molluscicide containing bait for the next 72 h caused a significant recovery in free amino acid, protein, DNA and RNA levels in the ovotestis of *L. acuminata*.

Toxicity Studies

The essential oil extracted from clove (*Syzygium aromaticum*) is used as a topical application to relieve pain and promote healing in herbal medicine and also finds use in the fragrance and flavouring industries. Clove oil has two major components, eugenol and β-caryophyllene, which constitute 78 % and 13 % of the oil, respectively. Clove oil and these components are generally recognized as 'safe', but the in vitro study by Prashar et al. (2006) demonstrated cytotoxic properties of both the oil and eugenol, towards human fibroblasts and endothelial cells. Clove oil was found to be highly cytotoxic at concentrations as low as 0.03 % (v/v) with up to 73 % of this effect attributable to eugenol. β-caryophyllene did not exhibit any cytotoxic activity, indicating that other cytotoxic components may also exist within the parent oil.

Traditional Medicinal Uses

In European traditional medicine clove is considered an agreeable aromatic stimulant, antispasmodic and carminative. In Malaysia cloves are added to other substances and administered in tonics particularly after confinement. Cloves are used in poultices for headaches and may be applied to aching teeth. Powdered cloves are rubbed upon the abdomen after childbirth. They are also regarded as aphrodisiac. Cloves are used to stimulate appetite and are added to roots of *Moringa* in treating flatulence and colic.

In Ayurvedic and Tibetan folk medicine, cloves are used internally as a tea and topically as an oil for hypotonic muscles, including multiple sclerosis. The use of cloves internally is avoided in the presence of pitta (bile) inflammation such as the one found in acute flares of autoimmune diseases. In West Africa, the Yorubas use a water infusion of cloves called *Ogun Jedi-jedi* as a treatment for stomach upsets, vomiting and diarrhoea.

In traditional Chinese medicine, cloves are considered acrid, warm and aromatic, entering

the kidney, spleen and stomach meridians, and are notable in their ability to warm the middle, direct stomach *qi* downward, to treat hiccup and to fortify the kidney *yang*. It is used in herbal tea formulas for impotence to increase ejaculation or clear vaginal discharge from yang deficiency, for morning sickness together with ginseng and patchouli or for vomiting and diarrhoea due to spleen and stomach coldness.

In Western herbalism and dentistry, clove is used as an anodyne (painkiller) for dental emergencies. Cloves are used as a carminative, to treat hypochlorhydria by increasing hydrochloric acid in the stomach and to improve peristalsis. Hypochlorhydria refer to a state where the production of gastric acid in the stomach is absent or low. Cloves are also said to be a natural anthelmintic.

Clove oil is aromatic, stimulant and irritant. In traditional folk medicine, it is used to allay vomiting and stomach sickness, to stimulate the digestive functions, to improve labour or operation and to prevent a tendency to their producing sickness or griping. The essential oil is used in aromatherapy when stimulation and warming is needed, especially for digestive problems. Topical application over the stomach or abdomen will warm the digestive tract. Clove oil is applied externally for toothache, headache, cold, arthritis and rheumatism. The oil is also useful for ulcers, bruises, burns, bronchitis, asthma, minor infections and colic. Use of clove oil should be avoided during pregnancy or if with sensitive skin.

Other Uses

Clove bud oil is used for flavouring food and in perfumery. Clove stem oil is obtained from steam distillation of dried peduncles and stem of clove buds. The eugenol content of the oil ranges from 90 to 95 %. The oil is a coarser and woodier odour than bud oil. Clove leaf oil is obtained from distillation of the leaves. It is a dark brown liquid with a harsh woody odour. When rectified, it turns pale yellow and smells sweeter with a eugenol content of 80–85 %.

Clove oleoresin may be prepared by cold or hot extraction of crushed spices using organic solvents like acetone. The oleoresin is primarily used in perfumery, and when used for flavouring it is dispersed on salt and flour. Cloves are also an important incense material in Chinese and Japanese culture. Jews smell cloves in the service that closes the Sabbath (Havdalah). Clove trees can be intercropped with coconut or planted as an ornamental shade tree.

Comments

Cloves are usually propagated by seeds or by cuttings. They can also be propagated by approach grafting or cleft grafting.

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Bougainvillea glabra

Scientific Name

***Bougainvillea glabra* Choisy**

Synonyms

Bougainvillea brachycarpa Heimerl, *Bougainvillea glabra* var. *acutibracteata* Heimerl, *Bougainvillea glabra* var. *alba* Mendes & Viégas, *Bougain-villea glabra* var. *brachycarpa* (Heimerl) Heimerl, *Bougainvillea glabra* var. *graciliflora* Heimerl, *Bougainvillea glabra* var. *obtusibracteata* Heimerl, *Bougainvillea glabra* var. *sanderiana* Boss-chere, *Bougainvillea rubicunda* Schott ex Rohrb., *Bougainvillea spectabilis* var. *glabra* (Choisy) Hook.

Family

Nyctaginaceae

Common/English Names

Bougainvillea, Glory of the Garden, Lesser Bougainvillea, Paper Flower

Vernacular Names

Brazil: Buganvilea, Cansarina, Ceboleiro, Flor-De-Papel, Juvu, Pataguinha, Primavera, Rios Do Prado, Roseiro, Roseta, Snata-Rira, Sempre-Lustrosa, Tres-Marias (Portuguese)
Burmese: Sekku-Pan
Catalan: Buguenvíl.Lea, Buguenvíl.Lea Comuna
Chinese: Guang Yi Zi Hua
French: Bougainvillée, Bougainvillier
German: Bougainvillie, Drillingsblume
India: Baganbilas (Bengali), Booganbel (Hindi), Bouganvila (Konkani), Booganvel (Marathi), Cherei (Manipuri), Kagithala Puvvu (Telugu)
Indonesia: Kembang Kertas
Italian: Buganvillea
Malaysia: Bunga Kertas, Buganvil, Buginvila
Mexico: Bugambilia, Shpupu-Kutshanat
Philippines: Bogambilya, Bongabilya (Tagalog)
Spanish: Bogambilia, Boganvilla, Bugambilia Morada, Bugambilia Roja, Buganvilla, Buganvillea Lisa, Buganvilia, Bugenvil, Dania, Enredadera De Papel, Flor De Papel, Flor De Varano, Santa Rita, Trinitaria, Veranilla
Swedish: Blank Trillingblomma
Thai: Fueangfa
Vietnamese: Hoa Giấy Nhẵn

Origin/Distribution

Bougainvillea species including *B. glabra* are native to South America from Brazil to Peru and to Southern Argentina (Chubut Province). It has been introduced pantropically and is a popular ornamental plant in the warm areas of Asia, Southeast Asia, Australia, the Pacific Islands, the Mediterranean region, the Caribbean, Mexico,

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South Africa and the United States in Arizona, California, Florida, Hawaii and Southern Texas.

Agroecology

All *Bougainvillea* species do well in warm to hot climates and are frost sensitive. Bougainvilleas perform best in a well-drained, fertile, light soil in a sunny position. Although drought tolerant, they need plenty of moisture during the flowering season.

Edible Plant Parts and Uses

In Thailand, flower bracts are used in salad and frying (Kaisoon et al. 2011, 2012).

Botany

Vigorous, evergreen rambling shrub or woody liane, 1–7 m high with thick, glabrous to sparsely pubescent stem and pendent branches with curved axillary spines, 5–15 mm long. Leaves on 1 cm long petioles, alternate, finely pubescent abaxially, glabrous adaxially, ovate, ovate–lanceolate to elliptical, 5–13×3–6 cm, chartaceous, dark green. Flowers insignificant, bisexual, occurs in 3-flowered cymose units subtended by showy colourful chartaceous, foliaceous bracts. Bracts ovate to deltoid–ovate, 2–5 cm long, 1.54 cm wide, with acuminate or acutely pointed tips and cordate bases, usually purple or magenta, but also red, pink, orange or white (Plates 1 and 2). Flowers with 1–2.5 cm long perianth tube which is dilated basally, distinctly angled, sparsely pubescent, ribbed, apex 5-lobed white to creamy white, curved away from pedicel. From the base of the tube arises a single carpel, and encircling the ovary is a cup-shaped nectar, from its rim arises 6–8 stamens. Fruit small, dry, one-seeded and ribbed achene.

Nutritive/Medicinal Properties

The following phenolic acids were detected in the ethanol extract of *Bougainvillea glabra* flowers (mg/100 g DW): gallic acid 9.77 mg, protocatechuic acid 5.27 mg, *p*-hydroxy benzoic acid 19.96 mg, chlorogenic acid 9.72 mg, vanillic acid 12.17 mg, caffeic acid 7.24 mg, syringic acid 6.03 mg, *p*-coumaric acid 65.15 mg, ferulic acid 14.50 mg and sinapic acid 78.49 mg, total 228.29 mg (Kaisoon et al. 2012). Flavonoid compounds found in the lyophilized hydrophilic extracts of *Bougainvillea glabra* flowers (mg/100 g DW): rutin 1.3 mg, myricetin 61.52 mg, quercetin 14.17 mg, apigenin 8.89 mg and kaempferol 87.18 mg, and total 173.06 mg. Alkaloids, flavonoids, phenolic compounds and tannins were detected in the flowers and floral bracts of *B. glabra* (Sahu and Saxena 2012).

Betacyanins were isolated from the bracts of *Bougainvillea glabra* and characterized as gomphrenin I (betanidin 6-*O*-β-glucoside) and various derivatives of bougainvillein-v (betanidin 6-*O*-β-sophoroside), i.e. mono- and diglucosyl-sophorosides, acylated with 4-coumaric and caffeic acid (monoesters and diesters) (Heuer et al. 1994). Besides the betacyanins, *B. glabra* bracts accumulated large amounts of flavonols (kaempferol and quercetin conjugates) reaching ratios of flavonol to betacyanin of 1:1.

Plate 1 *Bougainvillea glabra* cv. Easter Parade

Plate 2 Purplish-red Bougainvillea flowers

The natural pigment composition of purple bracts of *Bougainvillea glabra* was found to consist of a highly complex mixture of betacyanins solely differing by the substitution with a variety of acyl-oligoglycoside units (Wybraniec et al. 2010; Jerz et al. 2010). Six principal acyl-oligosaccharide linked betacyanins were found. The detected molecular weights of the pigments ranged up to maximum values of 1,653 and 1,683 Da for the largest molecules due to oligosaccharide linkage and multiple acyl substitutions. A total sum of 146 different betacyanin pigments were detected in the CCC (countercurrent chromatography) fractions of reduced complexity.

Three glycosides were isolated from *Bougainvillea glabra* and their structures elucidated as momordin IIc (quinoside D) [β-D-glucopyranosyl 3-*O*-[β-D-xylopyranosyl-(1 → 3)-*O*-(β-D-glucopyranosyluronic acid)] oleanolate]; second compound was quercetin 3-*O*-α-L-(rhamnopyranosyl)(1 → 6)-[α-L-rhamnopyranosyl(1 → 2)]-β-D-galactopyranoside and the third compound was its derivative quercetin 3-*O*-α-L-(4-caffeoyl-rhamnopyranosyl)(1 → 6)-[α-L-rhamnopyranosyl (1 → 2)]-β-D-galactopyranoside (Simon et al. 2006).

Antioxidant Activity

Of four edible flowers, the phenolics (mg GAE (gallic acid equivalent)/g DW) of the flowers were determined as follows: *Tagetes erecta* (212.9) > *Antigonon leptopus* (177.2) > *Bougainvillea glabra* (138.2) > *Cosmos sulphureus* (102.5) (Kaisoon et al. 2012). Total reducing capacity (FRAP) (μmol Fe^{2+}/g DW) was ranked as *Tagetes erecta* (329.4) > *Bougainvillea glabra* (307.1) > *Antigonon leptopus* (281.9) > *Cosmos sulphureus* (99.9). The ORAC (oxygen radical absorbance capacity) (μmol T Eq (trolox equivalent)/g DW) ranks were *Antigonon leptopus* (491.9) > *Tagetes erecta* (394.2) > *Bougainvillea glabra* (276) > *Cosmos sulphureus* (214.8). Cellular antioxidant activity (CAA) (μM QE (quercetin equivalent)/g DW) ranks were *Tagetes erecta* (413, most effective) > *Bougainvillea glabra* (859.6) > *Cosmos sulphureus* (966.1) > *Antigonon leptopus* (967.4).

Antiproliferative Activity

Bougainvillea glabra flower extract exhibited antiproliferative activity among four edible flowers tested against several cancer cell lines (Kaisoon et al. 2012). Antiproliferative activity (IC_{50} mg/mL) of polyphenolic extract against HC-29 (colorectal adenocarcinoma) cells was *Tagetes erecta* > (1.5) > *Bougainvillea glabra* (1.7) > *Antigonon leptopus* (2.4) > *Cosmos sulphureus* (5.2). Antiproliferative activity (IC_{50} mg/mL) of polyphenolic extract against AGS (gastric adenocarcinoma) cells was *Antigonon leptopus* (0.2) > *Bougainvillea glabra* (2.1) > *Tagetes erecta* (2.2) > *Cosmos sulphureus* (44.8). Antiproliferative activity (IC_{50} mg/mL) of polyphenolic extract against Bl-13 (bladder cancer) cells was *Antigonon leptopus* (0.9) > *Bougainvillea glabra* (2.3) > *Tagetes erecta* (3.0) > *Cosmos sulphureus* (56.5).

Antidiabetic Activity

The aqueous leaf extract of *Bougainvillea glabra* at a dose level of 150 mg/kg showed significant antihyperglycaemic activity (Edwin et al. 2006). Studies showed that the aqueous leaf extract of *B. glabra* significantly reduced hyperglycaemia in alloxan-induced diabetic rats (from 12 mmol/L in untreated control to 4.04 mmol/L in treated) (Adebayo et al. 2009). Likewise, the extract significantly reduced the total cholesterol (TC), triglyceride (TG) and low-density lipoprotein cholesterol (LDL cholesterol), while increasing the high-density lipoprotein cholesterol (HDL-C). The results supported the use of the plant by traditional medicine practitioners for the treatment of diabetes mellitus.

Inhibitory activity of lyophilized hydrophilic extracts obtained from four edible Thai flowers against α-glucosidase enzyme was found as *Tagetes erecta* (98.51 % inhibition, IC_{50} 0.06 mg/mL) > *Antigonon leptopus* (58.24 % inhibition, IC_{50} 3.26 mg/mL) > *Bougainvillea glabra* (37.30 % inhibition, IC_{50} 5.21 mg/mL) > *Cosmos sulphureus* (32.32 % inhibition, IC_{50} 5.62 mg/mL) (Kaisoon et al. 2012).

Hypolipidemic Activity

Inhibitory activity of lyophilized hydrophilic extracts obtained from four edible Thai flowers against lipase activity was determined as *Cosmos sulphureus* (43.39 % inhibition, IC_{50} 4.60 mg/mL) > *Tagetes erecta* (41.61 % inhibition, IC_{50} 4.82 mg/mL) > *Bougainvillea glabra* (40.05 % inhibition, IC_{50} 5.14 mg/mL) > *Antigonon leptopus* (26.70 % inhibition, IC_{50} 7.87 mg/mL) (Kaisoon et al. 2012).

Antidiarrhoeal Activity

The acetone, ethanolic and aqueous of *B. glabra* leaves exhibited antidiarrhoeal activity (castor oil-induced diarrhoea) in rats, and comparatively, acetone extract was found to be the most effective followed by the aqueous extract (Edwin et al. 2007).

Antipyretic Activity

The methanolic extract of *Bougainvillea glabra* leaves exhibited significant antipyretic activity in Brewer's yeast-induced pyrexia in rats (Elumalai et al. 2012).

Analgesic Activity

Using the tail immersion method in mice, the methanolic extract of *Bougainvillea glabra* leaves exhibited significant analgesic activity (Elumalai et al. 2012). At 300 mg/kg dose, the extract recorded 79.88 % inhibition compared to 81.21 % inhibition with pentazocaine 30 mg/kg.

Anti-inflammatory Activity

The petroleum-ether fraction of the methanol leaf extract of *B. glabra* leaves showed significant anti-inflammatory action in carrageenan-induced rat paw oedema when given intraperitoneally at a dose of 100 mg/kg (Giri et al. 1988). The anti-inflammatory activity was due to the presence of steroidal component in the leaves. In another study, the methanolic extract of *B. glabra* leaves exhibited dose-dependent inhibition of carrageenan-induced rat paw oedema and was comparable to indomethacin (Elumalai et al. 2012).

Antiulcer Activity

The acetone, ethanolic and aqueous of *B. glabra* leaves exhibited antiulcer activity (ethanol-induced ulcers) in rats (Edwin et al. 2007). The acetone extract showed marked antiulcer (70 and 83.4 % protection at 200 and 400 mg/kg doses, respectively) which was comparable to standard drug (omeprazole) used, followed by aqueous and ethanolic extract.

Antimicrobial Activity

The acetone leaf extract exhibit good antimicrobial activity in vitro against all the microorganisms tested, namely, *Escherichia coli, Bacillus subtilis, Klebsiella Pneumoniae, Staphylococcus aureus* and *Proteus vulgaris* (Edwin et al. 2007). Hydroalcoholic extract of *B. glabra* leaves was found to be inhibitory in vitro against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Salmonella typhi, Klebsiella pneumoniae* and *Vibrio cholera* (Gupta et al. 2009).

Wound Healing Activity

Studies by Rupesh et al. (2011) found that after 10 days of topical application of albino Wistar rats with the ointment of aqueous extract of *Bougainvillea glabra* leaves or oral administration of aqueous Bougainvillea leaf extract (200 mg/kg) in the dead space and incision wound models, significantly increased wound contraction, wound breaking strength, granulation tissue weight as compared to the control groups. The results suggested a beneficial role of *Bougainvillea glabra* leaf aqueous extract in healing of wounds in experimental rats.

Acetylcholinesterase Inhibitory Activity

The extract of the stem and branch of *B. glabra* was found to have acetylcholinesterase (AChE) inhibitory activity (Gupta and Gupta 1997).

Antileishmanial Activity

Schlein et al. (2001) found that one night on branches of *Solanum jasminoides, Ricinus communis* or *Bougainvillea glabra* drastically shortened the life span of the sand fly *Phlebotomus papatasi* which transmits *Leishmania major*, the causal agent of cutaneous leishmaniasis, in vast regions of the Old World. Flowering *B. glabra* attracted *P. papatasi* in the field. Nevertheless, in the region endemic for *L. major* in yards abounding with vector sand flies, the number of *P. papatasi* trapped near hedges of *B. glabra* was eight times less (62 vs. 502 flies trapped) than in the control sites. The results implied that *B. glabra* afforded local protection against sand fly bites and decreased the risk of leishmaniasis.

Anthelmintic Activity

The methanol leaf extract of *B. glabra* exhibited anthelmintic activity against the earthworm, *Pheretima posthuma*, in a dose-dependent manner (Eswaraiah et al. 2012).

Traditional Medicinal Uses

In India, *Bougainvillea glabra* (mainly leaves) have been used by traditional practitioners of Mandsaur for variety of disorders like diarrhoea, excessive stomach acidity, cough and sore throat; decoction of dried flowers for blood vessels and leucorrhoea; and decoction of the stem for hepatitis (Gupta et al. 2009). The plant has been reported to be used by traditional medicine practitioners for the treatment of diabetes mellitus (Adebayo et al. 2009).

Other Uses

B. glabra is popularly cultivated as ornamental landscape features, garden, potted and indoor plants and can also be used for bonsai.

The juice obtained from flowers of *Bougainvillea glabra* could be used to differentiate solutions in pH range of 7–10 because it showed different colours at each pH from 7 to 10 (Gaurav et al. 2010). It afforded similar results as obtained by phenolphthalein and could be used as an acid-base indicator.

Hernandez-Martinez et al. (2011) compared the performance of new dye-sensitized solar cell (DSSC) based in a natural dye extracted from the *Bougainvillea spectabilis*' bracts and *B. glabra* and their mixtures. In all cases the pigments were betalains, obtained from reddish-purple extract. The obtained solar energy conversion efficiency was of 0.48 % with a current density J(SC) of 2.29 mA/cm^2 using an irradiation of 100 mW/cm^2 at 25 °C.

Comments

The genus *Bougainvillea* comprises about 33 species but only 18 are accepted species name. Of these 18 species only three species, *B. glabra, B. spectabilis* and *B. peruviana*, are involved in the origin of modern-day cultivars of *Bougainvillea*. Three major hybrid groups have been recognized *Bougainvillea* × *buttiana* (*B. glabra* × *B. peruviana*), *Bougainvillea spectro-glabra* (*B. glabra* × *B. spectabilis*) and *Bougainvillea spectoperuviana* (*B. spectabilis* × *B. peruviana*). Double floral-bracted cultivars have been evolved from the cultivars of *B.* × *buttiana*. Variegated bud sports have occurred in many of the hybrid cultivars.

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Bougainvillea spectabilis

Scientific Name

***Bougainvillea spectabilis* Willd.**

Synonyms

Bougainvillea bracteata Pers., *Bougainvillea brasiliensis* Raeusch., *Bougainvillea brasiliensis* Lund ex Choisy [Invalid], *Bougainvillea peruviana* Nees & Mart. [Illegitimate], *Bougainvillea speciosa* Schnizl., *Bougainvillea spectabilis* var. *hirsutissima* J.A. Schmidt, *Bougainvillea spectabilis* var. *parviflora* Mart. ex J.A. Schmidt, *Bougainvillea spectabilis* var. *virescens* (Choisy) J.A. Schmidt, *Bougainvillea virescens* Choisy

Family

Nyctaginaceae

Common/English Names

Bougainvillea, Great Bougainvillea, Paper Flower, Purple Bougainvillea

Vernacular Names

Brazil: Buganvilia, Espinho-De-Santa-Rita, Primavera, Três-Marias
Burmese: Sekku-Pan
Catalan: Bungavillea, Buguenvíl.Lea Vermella
Chamorro: Putitainubyu
Chinese: Ye Zi Hua
Chuukese: Irátong
Cook Islands: ʻĪtāria, Tāria, Tiare Taratara (Maori)
French: Bougainvillée, Bougainvillier
Galápagos Islands: Buganvilla, Veranera (Spanish)
German: Bougainvillie, Drillingsblume
India: Kagithampoolu (Andhra Pradesh), Baganbilas (Bengali), Booganbel (Hindi), Bouganvila (Konkani), Booganvel (Marathi), Cherei (Manipuri), Kagithala Puvvu (Telugu)
Indonesia: Bougenvil, Bunga Kerta, Kembang Kertas
Italian: Buganvillea
Japanese: Bugenbirea, Ikadakazura
Kiribati: Te Akanta
Majorcan: Bungavilia
Malaysia: Bunga Kertas, Buganvil, Buginvila
Marshallese: Ikdeele, Kõtõmãnlimpo, K Limpok, L
Mexico: Bugambilia, Shpupu-Kutshanat
Naruan: Tsita, Tsitta
Niuean: Felila, Malila
Philippines: Bogambilya, Bongabilya (Tagalog)
Samoan: Felila
Spanish: Bongavilia, Bougainvillea, Bugambilia, Buganvilla
Swedish: Stor Trillingblomma
Tahitian: Tiare Vareau
Thai: Fueang Fa
Vietnamese: Hoa Giấy Nhẵn

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Origin/Distribution

B. spectabilis is native to South America from Brazil to Peru and to Southern Argentina (Chubut Province). It has been introduced pantropically and is a popular ornamental plant in the warm areas of Asia, Southeast Asia, Australia, the Pacific Islands, the Mediterranean region, the Caribbean, Mexico, South Africa and the United States in Arizona, California, Florida, Hawaii and Southern Texas.

Agroecology

All *Bougainvillea* species do well in warm to hot climates and are frost sensitive. It does best in areas with night temperature of 18–20 °C and day temperatures of 24–32 °C. It can tolerate temperatures above 37 °C and will grow in areas with more than 600 mm rainfall per annum. Bougainvilleas perform best in a well-drained, fertile, light, acidic soil with pH 5.5–6.in a sunny position. It abhors water-logged conditions. Although drought tolerant, they need plenty of moisture during the flowering season.

Edible Plant Parts and Uses

Floral bracts are edible and used in salad and drinks (Kaisoon et al. 2011; King 2007).

Botany

A woody, evergreen rambling vine; stems and branches pubescent with stout, recurved spines. Leaves alternate, petiolate, simple, ovate or elliptic, to 10 cm long, margin entire, pubescent (Plates 2, 3 and 4). Flowers in axillary cymose inflorescence of three small, trumped flowers subtended by showy bracts of various colours: dark red or light purple-red, pink, orange or white; elliptic–ovate, 2.5–6.5 × 1.5–4 cm, base rotund to cordate, tips obtuse to broadly subacute, single-bracted or double-bracted (Plates 1, 2, 3 and 4). Flowers with a narrowly tubular, rounded, 1.6–2.4 cm, densely pubescent, perianth tube concolorous with the bracts, with five spreading creamy or white lobes at the apex. From the base of the tube arises a single carpel, and encircling the ovary is a cup-shaped nectar, from its rim arises usually 8 stamens. Fruit small, dry, elongate, one-seeded ribbed achene.

Plate 1 Red single-bracted cultivar

Plate 2 Close view of red single-bracted cultivar

Plate 3 Purplish-pink single-bracted cultivar

Plate 4 Pink double-bracted cultivar

Varieties with multi-whorled bracts do not develop any sexual organs, i.e. perianth, pistil (ovary, style, stigma) and stamens.

Nutritive/Medicinal Properties

Srivastava and Krishnan (1962) found the presence of a plastid-bound oxalic acid oxidase in the leaves of *Bougainvillea spectabilis*. Phytoferritin was found in the cambial zone of *B. spectabilis* plant and represented the nontoxic storage form of iron as iron-protein complex which could later be used to elaborate materials required for photosynthetic and other activities (Nwankiti 1982).

Antioxidant Activity

In radical scavenging activity (RSA) studies, it was found that stem aqueous extracts from *Bougainvillea spectabilis* produced more DPPH absorbance reduction (95.66 %), with an IC_{50} and AP (reciprocal of IC_{50}) values of 0.03 μg/mL and 33.33, respectively, than *Bauhinia divaricata* stem aqueous extracts (Chaires-Martinez et al. 2009). The results were superior to common synthetic antioxidants used in the food industry like butylated hydroxyl toluene (BHT, $IC_{50}=62$ μg/mL) and can be useful for further applications of these plants or its constituents in pharmaceutical and alimentary preparations.

Studies found that the methanolic leaf extract of *B. spectabilis* showed greater amount of phytochemicals and higher antioxidant activity than aqueous leaf extract (Venkatachalam et al. 2012). The amount of phytochemical constituents and antioxidant activity exhibited significant linear relationship. The methanolic leaf extract had 3.17 mg/g total phenol content, 5.40 mg/g total flavonoids, 2.26 mg/g sugar and 1.48 mg/g tannin, while the aqueous leaf extract had 2.85 mg/g total phenol content, 4.03 mg/g total flavonoids, 1.81 mg/g sugar and 1.33 mg/g tannin. The leaves contained 0.017 g/L of total chlorophyll made up of 0.006 g/L chlorophyll a and 0.011 g/L chlorophyll b and also had 0.419 g/L carotenes. Both aqueous and alcoholic leaf extracts produced DPPH anion scavenging power, but the methanolic extract (226.66 mg/g) showed a far higher scavenging property than the aqueous leaf extract (79.16 mg/g). The NO scavenging activity in bougainvillea leaves was estimated to be 77.16 mg ascorbic acid equivalent in methanolic extract and 58.66 mg ascorbic acid equivalent in aqueous extract indicating a significant difference between both extracts of bougainvillea leaves. DPPH and NO scavenging activity of the extracts could be correlated to the presence of flavonoids. The FRAP in bougainvillea leaves was estimated to be 27.83 mg ascorbic acid equivalent in methanolic extract and 43.5 mg ascorbic acid equivalent in aqueous extract. This shows a significant difference between both extracts indicating a high FRAP of bougainvillea leaves. The FRAP activity was correlated to catechin, ferulic acid and total phenols which were present in bougainvillea. The reducing power in 30 g bougainvillea leaves was found to be higher in methanolic extract (1.48 mg/g ascorbic acid equivalent) than in aqueous extract (1.33 mg/g). The SO scavenging activity in bougainvillea leaves was estimated to be 299.16 mg ascorbic acid equivalent in methanolic extract and 321.6 mg ascorbic acid equivalent in aqueous extracts of bougainvillea leaves. The H_2O_2 scavenging activity in 1 g bougainvillea leaves was estimated to be 11.2 mg ascorbic acid equivalent in methanolic extract and 7.9 mg ascorbic acid equivalent in aqueous extract indicating a significant scavenging activity in bougainvillea leaves. In the linoleic assay, the antioxidation activity was estimated to be 44 mg ascorbic acid

equivalent in methanolic extract and 39.6 mg ascorbic acid equivalent in aqueous extract indicating better activity in the methanolic extract.

Antidiabetic Activity

The alcoholic leaf extract of *B. spectabilis* administered to diabetic mice elicited significant hypoglycaemic activity (Narayanan et al. 1984). The use of *B. spectabilis* leaves as an antidiabetic led to the isolation of its hypoglycaemic principle, pinitol, from the leaves (Narayanan et al. 1987). Pinitol was determined to be a methyl ester of chiro-inositol and elucidated as 3-*O*-methyl-1,2,4-*cis*-3,5,6-*trans*-hexahydroxycyclohexanol. Pinitol had been reported to be metabolized to chiro-inositol in humans (Phillips et al. 1982).

Studies confirmed that D-pinitol (3-*O*-methyl-chiro-inositol), an active principle of *B. spectabilis*, could exert an insulin-like effect to improve glycaemic control in hypoinsulinaemic STZ-diabetic mice (Bates et al. 2000). In streptozotocin (STZ)-diabetic mice, D-pinitol (100 mg/kg p.o.) acutely decreased the hyperglycaemia (by 22 % at 6 h). A similar decrease in plasma glucose (by 21 %) was observed after 100 mg/kg i.p. D-pinitol. Insulin concentrations and the rate of insulin-induced glucose disappearance were not altered by 100 mg/kg p.o. D-pinitol. Chronic administration of D-pinitol (100 mg/kg i.p. twice daily for 11 days) to STZ-diabetic mice maintained a reduction in plasma glucose concentrations from about 14 to 10 mmol/L. In normal non-diabetic and severely insulin-resistant ob/ob mice, 100 mg/kg p.o. D-pinitol did not significantly affect plasma glucose or insulin during acute studies. The study showed that D-pinitol may act via a post-receptor pathway of insulin action affecting glucose uptake. In separate studies, oral administration of D-pinitol (3-*O*-methyl-chiro-inositol), an active principle of *B. spectabilis*, to streptozotocin (STZ)-induced diabetic Wistar rats elicited significant decrease in the elevated levels of blood glucose and total cholesterol, triglycerides, free fatty acids and phospholipids in serum, liver, kidney, heart and brain (Geethan and Prince 2008). D-pinitol also lowered significantly LDL and VLDL cholesterol levels and increased significantly HDL cholesterol levels in the serum of diabetic rats. Results clearly indicated the anti-hyperlipidemic effect of D-pinitol in STZ-induced type II diabetic rats.

In a randomized placebo, 7-week study of 15 old people (age 66 ± 8 y), pinitol supplementation was found not to influence whole-body insulin-mediated glucose metabolism and muscle insulin receptor content and phosphorylation in non-diabetic, older people (Campbell et al. 2004). Pinitol did not affect indices of hepatic and whole-body insulin sensitivity from the oral glucose tolerance test and indices of insulin sensitivity, acute insulin response to glucose and glucose effectiveness from the intravenous glucose tolerance test, estimated using minimal modelling. Pinitol did not differentially affect total insulin receptor content and insulin receptor phosphotyrosine 1158 and insulin receptor phosphotyrosine 1162/1163 activation in vastus lateralis samples taken during an oral glucose-induced hyperglycaemic and hyperinsulinemic states.

The chloroform extract of *B. spectabilis* leaves was found to have significant α-amylase inhibitory activity and could be useful in managing postprandial hyperglycaemia, a complication of diabetes (Bhat et al. 2011b). In vivo studies using a diabetic murine model showed that *B. spectabilis* aqueous and methanolic extracts showed a good oral glucose tolerance and significantly reduced the intestinal glucosidase activity (Bhat et al. 2011a). Also, *B. spectabilis* aqueous extracts showed significant increase in glucose-6-phosphate dehydrogenase activity and hepatic, skeletal muscle glycogen content after 21 days of treatment. They observed a regeneration of insulin-producing cells and corresponding increase in the plasma insulin and c-peptide levels with the treatment of *B. spectabilis* aqueous and methanolic extracts. The results suggested *B. spectabilis* aqueous extracts to be potential d candidates for developing new nutraceuticals treatment for diabetes.

Jawla et al. (2011) found that permanent hyperglycaemia in alloxan-induced diabetic rats was reversed when treated up to a week with ethanol extract of *B. spectabilis* root bark. Highest hypoglycaemic activity was observed with root

bark extract at 100 mg/kg/day after 7 days. It was found to be 12.5 % more potent than standard oral hypoglycaemic drug, glibenclamide 0.2 mg/ kg.

Anti-inflammatory Activity

Ethanolic leaf extract of *B. spectabilis* produced significant anti-inflammatory activity when compared with the standard indomethacin and untreated control (Manivannan et al. 2012). The extract (300 mg/kg, p.o.) inhibited carrageenan-induced left hind paw oedema in Wistar rats. It also reduced granuloma weight in the cotton pellet granuloma model.

Antiviral/Antitumour Activities

A single-chain (type 1) ribosome-inactivating protein (RIP) was isolated from the leaves of *Bougainvillea spectabilis* Willd. (Bolognesi et al. 1997). The RIP inhibited protein synthesis both in a cell-free system and in various cell lines. The protein had toxicity to mice with an $LD_{50} > 32$ mg/g and did not cross-react with any antiserum tested. The protein inhibited infection of *Nicotiana benthamiana* by artichoke mottled crinkle virus (AMCV). An antiviral protein, Bougainvillea antiviral protein I (BAP I), active against mechanical transmission of tomato spotted wilt virus was identified in the root tissues of *Bougainvillea spectabilis* and purified (Balasaraswathi et al. 1998). The N-terminal sequence of BAP I showed homology with other plant antiviral proteins. Preliminary tests suggested that purified BAP I was capable of interfering with in vitro protein synthesis.

Bouganin, a ribosome-inactivating protein isolated from *Bougainvillea spectabilis,* was synthesized as a pro-peptide consisting of 305 amino acids (den Hartog et al. 2002). The mature protein consists of 250 amino acids and had similar activity in a cell-free protein synthesis assay and had comparable toxicity on living cells as compared to the isolated native bouganin. VB6-845, an anti-EpCAM immunotoxin containing a T-cell epitope-depleted variant of the plant toxin bouganin, a type I ribosome inactivating protein isolated from the leaf of *Bougainvillea spectabilis*, was constructed by genetically linking the T-cell epitope-depleted variant of bouganin to an anti-epithelial cell adhesion molecule (EpCAM) Fab moiety via a peptidic linker containing a furin proteolytic site (Cizeau et al. 2009). An in vitro assessment of the biological activity of VB6-845 showed that it bound and selectively killed EpCAM-positive cell lines with a greater potency than many commonly used chemotherapeutic agents. In vivo efficacy was demonstrated using an EpCAM-positive human tumour xenograft model in SCID mice with the majority of the mice treated being tumour free at the end of the study.

Antibacterial Activity

The ethanolic, methanolic, chloroform and ethyl acetate extracts of *Bougainvillea spectabilis* leaves showed maximum in vitro inhibitory effect on all tested Gram-positive and Gram-negative bacteria, namely, *Staphylococcus aureus, Bacillus subtilis, Streptococcus faecalis, Micrococcus luteus, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Klebsiella pneumoniae, Proteus vulgaris, Serratia marcescens, Shigella flexneri* except *Vibrio cholerae* (Umamaheswari et al. 2008).

Antihypercholesterolemic Activity

Administration of the ethanol extract of *Bougainvillea spectabilis* leaves to rats was found to significantly reduce packed cell volume, haemoglobin concentration and red blood cell count at the dose of 200 mg/kg body weight when compared with controls, while other doses administered had no significant effect on these parameters (Adebayo et al. 2005). The extract also significantly reduced white blood cell count at all doses administered when compared with control. Additionally, the extract significantly reduced total cholesterol concentration in the serum while it had no significant effect on serum HDL cholesterol concentration at all doses administered when compared with controls.

However, the extract significantly increased serum triacylglycerol concentration at the dose of 50 mg/kg body weight, while other doses administered had no significant effect on serum triacylglycerol concentration. The results suggested that the extract may have beneficial effect on serum cholesterol concentration reduction, although it possibly possesses the potential of adversely affecting haematological indices.

Antihyperlipidemic Activity

The alcoholic leaf extract of *Bougainvillea spectabilis* elicited a significant reduction in total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL) levels and significant increase in high density lipoproteins (HDL) in hypercholesteromic rats; the extract at 200 mg/kg/day was more effective than that at 100 mg/kg/day (Saikia and Lama 2011). There was also significant improvement in atherogenic index in extract treated animals. The results indicted the *B. spectabilis* leaf extract to have excellent lipid lowering potential.

Antifertility Activity

Oral administration of the aqueous leaf extract (800 mg/kg body weight) to male Swiss albino mice for 30 days caused a decrease testis weight, sperm count and reduction in size of seminiferous tubules along with thickness of germinal cells, though some epithelial cells and interstitial cells of Leydig showed hypertrophy (Mishra et al. 2009). Also the lumen of tubules was found to be devoid of sperms. In female Swiss albino mice, there was a slight disruption of estrous cycle with prolonged metaestrous phase which was increased by 145.28 %. Testosterone and oestrogen levels were decreased significantly.

Effect on Liver/Kidney Function

Studies showed that administration of the ethanol leaf extract of *B. spectabilis* leaves to rats for 7 days significantly reduced serum albumin and calcium ion concentrations while it significantly increased serum phosphate ion, urea and creatinine concentrations compared with control (Malomo et al. 2007). The extract did not have any significant effect on the serum sodium ion concentration while it reduced serum potassium ion concentration significantly at the dose of 200 mg/kg body weight compared with controls. Generally, activities of liver ALP, AST, ALT and Ca^{2+}–Mg^{2+} ATPase were not significantly affected.

Miscellaneous Pharmacological Activities

Ali et al. (2005) found that the methanolic extract of white *B. spectabilis* flowers was the most biologically active among all tested extracts. The extracts of white, orange and shocking pink flowers inhibited, while the extracts of red and violet flowers promoted the growth of *Lemna* plants. The extract of white flowers also exhibited toxicity against shrimp larvae with a LD_{50} value of 33.5627 µg/mL. However, none of the tested samples gave positive responses against any tested fungi.

Traditional Medicinal Uses

The Yanadi tribe in the Chittoor district in Andhra Pradesh, India, used the leaves for diabetes (Vedavathy et al. 1997).

Other Uses

B. spectabilis is popularly cultivated as ornamental landscape features, garden, potted and indoor plants and can also be used for bonsai.

Comments

Bougainvillea may be readily propagated from root and branch cuttings.

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Mirabilis jalapa

Scientific Name

***Mirabilis jalapa* L.**

Synonyms

Jalapa congesta Moench, *Jalapa officinalis* Garsault (Inval.), *Mirabilis ambigua* Trautv., *Mirabilis pedunculata* Stokes, *Mirabilis planiflora* Trautv., *Mirabilis pubescens* Zipp. ex Span., *Mirabilis suaveolens* Billb. ex Beurl., *Mirabilis xalapa* Noronha, *Nyctago hortensis* Juss. ex Roem. & Schult., *Nyctago jalapae* (L.) DC., *Nyctago versicolor* Salisb. (Illeg.)

Family

Nyctaginaceae

Common/English Names

Beauty of the Night, Common Four O'Clock, False Jalap, Four O'Clock, Four O'Clock Flower, Four O'Clock Plant, Garden Jalap, Jalap Plant, Japanese Wonder Flower, Low Red Shrub, Marvel of Peru, Marvel of the World, Pearl of Egypt, Prairie Four O'Clock, Pretty-by-Night

Vernacular Names

Afrikaans: Vieruurtjie
Arabic: Zahr-Ul-Ajl
Benin: Azehonzo (Fon), Azehonzo (Goun)
Brazil: Boa-Noite, Bonina, Clavillia, Maravilha
Burundi: Karifomo (Kirundi)
Chamorro: Maravilla
Chinese: Xǐzǎo Huā, Zhǔfàn Huā, Yan Zhi Hua, Fen Dou Hua, Ye Fan Hua, Zhuang Yuan Hua, Ding Xiang Ye, Ku Ding Xiang, Zi Mo Li
Chuukese: Apetin Woun, Kulok Elu, Pilooris, Pilores
Cook Islands: Tiare Moe, 'Ura'Ura (Maori)
Czech: Nocenka Jalapovitá, Nocenka Zahradní
Danish: Vidunderblomst
Democratic Republic Of Congo: Kalofomo (Kivu, Swahili)
Estonian: Lõhnatu Imelill
Esperanto: Niktago
Fijian: Lalawavu, Lali Vau, Laweivou, Ronggolali, Vakarau Ni Lali
Finnish: Ihmekukka
French: Belle-De-Nuit
German: Wunderblume
Hawaiian: Nani Ahiahi, Pua Ahiahi, Puahiahi
I-Kiribati: Marvel Of Te Aoaua, Te Aoaaua, Te Aoaua, Te Aoua, Te Auaua, Te Awaaua, Te Awaava, Te Awaawa

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India: 'Godhuli Gopal (Assamese), Sandhyamaloti, Sandhya Malati (Bengali), Gulabans, Gulabash, Gulabbas, Gule-Aabbas, Guleaabbas (Hindi), Chandra Mallige, Chandra-Mallige, Chandramallige, Gulabaasa, Gulamaji, Gullumunchi, Kalluli, Madhyaana Mallige, Madhyahna Mallige, Madhyanha Malligay, Madhyanhamallige, Naalku Gante Hoo, Naalku Gante Hoovu, Naalku Ghante Hoo, Sanja-Mallige, Sanjamallige, Sanje Amllige, Sanjimallige, Vibhoothi Gida (Kannada), Akashmuri, Meremdi (Konkani), Sanjhaa Phool (Maithili), Andi-Malleri, Anthimalari, Anti-Malari, Anti-Mantaram, Antimalari, Antimantaram, Naalumani Poovu (Malayalam), Emdraks, Gulabakshi, Gulbaashi, Gulbas, Meremdi, Saayankaali (Marathi), Rangami (Oriya), Krishnakeli, Krisnakeli, Sandhya-Raga, Sandhyakali (Sanskrit), Ammukkili, Andimalli, Andimalligai, Andimandarai, Annmalarntan, Anthi-Mallikai, Anthi Mandhaarai, Anti, Antimalakikacceti, Antimalarakikam, Antimalarantan, Antimalari, Antimallai, Antimalli, Antimallikai, Antimantarai, Antimantaram, Antinarulu, Antippu, Arukolacceti, Arukolam, Bhathrakshi, Cannata Vali, Cannatavali, Cantira Mallikai, Cantiramallikai, Civappuantimalli, Kanankacikam, Kenta, Malai Antimalli, Malaiantimalligaicceti, Malaiyantimalli, Malaiyantimallikaicceti, Paruvaikkantam, Paruvatikantam, Patrashi, Pattarachi, Pattaracu, Pattarashu, Pattiraksi, Pattiratcam, Pattiratci, Ripuncakacceti, Ripuncakaceti, Ripuncakam, Taimilamuli, Taittilamuli, Taittilamulicceti, Tivacattiyacceti, Tivacattiyam, Tivacttiyaceti, Tumpara Mallikai, Tumparamallikai (Tamil), Badrakshi, Batharachi, Bhadraakshi, Bhadrakshi, Bhandrakanta, Chandra-Kanta, Chandra-Kantha, Chandra-Mali, Chandrakaantha, Chandrakanta, Chandramalle, Chandramalli (Telugu)

Indonesia: Kupa Oras (Ambon), Noja (Bali), Kederat, Segerat, Segerat Tegerat (Java), Kembang Pagi Sore, Kembang Pukul Empat, Bunga Waktu Kechil (Malay), Bunga-Bunga Paranggi (Makasar), Pukul Ampa (Minahasa), Bungga Ledonosko (Roti), Cako Rana (Ternate), Loro Laka (Timor)

Italian: Bella Di Notte, Bella-Di-Notte Comune

Japanese: Oshiroi-Bana

Korean: Punkkot

Madagascar: Belakariva (Betsileo), Folera, Voampolera (Merina), Belakariva (Sakalawa)

Malaysia: Bunga Pukul Empat, Bunga Pecah Empat, Bunga Wakyu Kecil, Kembang Dzohor, Kembang Lohor, Kembang Pukul Empat, Seroja

Marshallese: Eman Aur, Eman Awa, Emân Awa, Emãn-Awa, Emen Auö, Emen Aur

Mokilese: Pohk Kiloak

Nauruan: Teoua, Teowa

Nepal: Maritidhs, Nakajali (Gurung), Lankaphul, Lankasoni, Malati (Nepali), Labujana, Langasani (Tamang), Barka Gurubands (Tharu)

Pakistan: Gul Abas (Urdu)

Persian: Gule-Aabbas, Guli-Aabbas

Peru: Jalapa, Maravilla

Philippines: A Las Cuatro, Maravillas, Oracion, Suspiros (Spanish–Filipino), Talang (Sulu), Gilala (Tagalog)

Pingelapan: Pesikulck

Pohnpeian: Pwohrkuloak

Polish: Dziwaczek Jalapa, Dziwaczek Pospolity

Popular Republic Of Congo: Bende (Mbaamba)

Portuguese: Jalapa Verdadeira

Rakahanga-Manihiki: Tiare Nūmero

Samoan: Peteli

Satawalese: Flores

Slovaščina: Navadna Nočna Lepotica, Sorta

Spanish: Arrebolera, Clavellina, Buenas Tardes, Dondiego, Dondiego De Noche, Hoja De Xalapa, Jalapa Falsa, Maravilla, Maravilla Del Perú, Mechoacán Negro, Pasana, Pericón, San Pedro

Swedish: Underblomma

Sri Lanka: Hendirikka, Sendirika

Thai: Baan Yen, Dtôn Baan Yen, Dtôn Jan Yam, Dtôn Jam Yam, Dtôn Dtaam Yam, Dtôn-Dtee-Dtâa-Châo

Tongan: Matala Po'Uli

Tuamotuan: Numera

Turkish: Akşam Sefası

Tuvaluan: Petel, Peteli

Ulithian: Gaelun

Vietnamese: Hoa Phấn, Bông Phấn, Sâm Ớt

Origin/Distribution

M. jalapa is native to tropical south America but has become naturalized throughout tropical and warm temperate regions. In cooler temperate areas, it will die back with the first frosts, resprouting in the following spring from the tuberous roots.

Agroecology

The plant thrives in moderately fertile, moist but well-drained, sandy, loamy or chalky soil in full sun. It benefits from shelter from cold, drying winds and a good mulch. Top growth is killed by frost but the plant will resprout from the tubers with the advent of spring.

Edible Plant Parts and Uses

Tender young leaves are cooked as a vegetable (Tanaka 1976; Facciola 1990; Manandhar and Manandhar 2002). An edible crimson dye is obtained from the flowers (Uphof 1968; Usher 1974; Tanaka 1976; Kunkel 1984) and is used for colouring cakes and jellies (Facciola 1990). The seed is crushed and used as a pepper substitute (Tanaka 1976; Kunkel 1984; Facciola 1990).

Botany

An erect, bushy, branched, glabrous or slightly pubescent, perennial often grown as an annual 0.5–1 m high and wide, with blackish brown tuberous roots and fragrant flowers opening in the late afternoon and closing in the morning. Leaves are opposite, ovate or ovate–deltoid, 3–15 by 2–9 cm, base truncate or cordate, margin entire, apex acuminate and borne on 1–4 cm petioles (Plates 1 and 2). Flowers regular, bisexual and sweetly fragrant, usually several (3–5) clustered at apex of branches and on 1–2 mm pedicels. Involucre campanulate, about 1 cm, 5-lobed, lobes triangular–ovate, acuminate, glabrous, persistent. Perianth purple, red, pink, yellow, white or variegated (Plates 1 and 2); five-lobed, fused into a tube 2–6 cm long, constricted above ovary; limb 2.5–3 cm in diameter, spreading and deciduous. Stamens 5, filaments slender, exserted and united at the base, anthers globose. Ovary superior, unilocular with a single ovule, and surrounded by a nectariferous disc; style filiform with capitate stigma. Fruit a leathery ribbed, plicate, black, globose or ovoid achene (Plate 2), 5–9 mm across with white mealy endosperm.

Plate 1 Flowers, buds and leaves

Plate 2 Flowers, leaves and fruit (black)

Nutritive/Medicinal Properties

Flower Phytochemicals

Eight betaxanthins were isolated from *Mirabilis jalapa* flowers: indicaxanthin, vulgaxanthin-I,

miraxanthin-I, miraxanthin-II, miraxanthin-III, miraxanthin-IV, miraxanthin-V and miraxanthin-VI (Piattelli et al. 1965). From *Mirabilis jalapa* flowers, an aliphatic monocarboxylic acid (mirabalisoic acid) and a monocyclic homoditerpene (mirabalisol) were isolated and their structures were established as n-tetracos-5-one-8-o1-24-oic acid and 10-(12, 16, 16-trimethyl cyclohexanyl)-4, 8-dimethyl decan-8-ol-10-one (Ali et al. 2001). A family of expansin transcripts that include seven α-expansins (MjExp1 through MjExp7) and three β-expansins (MjExpB1 through MjExpB3) were identified from *Mirabilis jalapa* flowers that showed dramatic changes in transcript abundance during the rapid expansion and subsequent senescence of the ephemeral flowers (Gookin et al. 2003). Amino acid, carbohydrate, lactone, organic acid, phenol and volatile oil were found in the water extracts of *M. jalapa* flowers (Li and Tuerxunayi 2009). Phenol, coumarin, cardiac glycoside and flavonoid were obtained from the ethanol extracts of flowers and lactone found in the petroleum flower extracts.

Betaxanthins were detected in *Mirabilis jalapa* flowers by HPLC using a fluorescence detector (Gandía-Herrero et al. 2005). Another pathway involving UDP-glucose/cyclo-DOPA 5-*O*-glucosyltransferase activity was proposed by Sasaki et al. (2004) besides the postulated pathway for betacyanin biosynthesis in *M. jalapa* flowers in which the glucose moiety of betanin was conjugated to the aglycone, betanidin, as the glucosyltransferase activity that produced betanin had been reported and its cDNA isolated. In this other pathway, betanin was proposed to be formed by glucosyltransferase acting at the 5,6-dihydroxyindoline-2-carboxylic acid (cyclo-DOPA) step, followed by condensation of the product with betalamic acid and not at the betanidin aglycone step.

The floral scent of *M. jalapa* was found to consist primarily of the monoterpene (*E*)-β-ocimene with additional compounds such as α-farnesene, (*Z*)-3-hexenyl acetate and myrcene (Heath and Manukian 1994; Levin et al. 2001; Effmert et al. 2005). Heath and Manukian (1994) also reported the presence of indole and benzaldehyde, while Levin et al. (2001) detected 14 other scent compounds as follows: monoterpenoids (myrcene 0.58 %, *cis*-β-ocimene 1.31 %, *trans*-β-ocimene 38.10 %, allo-ocimene trace, unknown 3.12 %), sesquiterpenoids (4,8-dimethyl-nona-1,3,7-triene 0.81 %, α-farnesene 57.03 %, nerolidol 0.21 %, unknown 0.7 %), aliphatic compounds (*cis*-3-hexenyl acetate 3.44 %, *cis*-3-hexen-1-ol 0.79 %, *cis*-3-hexenyl-2-methyl butanoate 0.43 %, *cis*-jasmone 1.32 %) and benzenoids (methyl benzoate 0.44 %, benzyl acetate 5.31 %, methyl salicylate 0.57 %, benzyl butanoate 0.27 %, benzyl alcohol 1.67 %, *cis*-3-hexenyl benzoate 0.27 % and benzyl benzoate 3.63 %). Effmert et al. (2005) found β-myrcene, (*Z*)-3-hexenyl acetate, (*Z*)-ocimene, (4) (*E*)-β-ocimene, (5) (*E*)-epoxy-ocimene, benzyl benzoate and traces of methyl salicylate in the floral volatiles.

Aerial Parts/Leaf Phytochemicals

The plant was reported to contain galactose and arabinose (Wehmer 1911). The alkaloid trigonelline, with purgative action, was detected in the leaves and stems (Yoshimura and Trier 1912; Zhou et al. 2013). The methanolic extract of the aerial parts yielded β-sitosterol, stigmasterol, ursolic acid, oleanolic acid and brassicasterol (Siddiqui et al. 1990). From the aerial plant parts, the steroids brassicasterol, β-sitosterol, β-sitosterol acetate and stigmasterol; triterpenes oleanoic acid, ursolic acid and 3-oxo-urs-12-en-28-oic acid methyl ester; and diterpene *trans*-phytol were found (Siddiqui et al. 1994).

An active polyphenolic amide: N-t*rans*-feruloyl 4′-*O*-methyldopamine was isolated from *M. jalapa* methanol extract (Michalet et al. 2007). The methanol plant extract of *M. jalapa* was found to contain the ether compound 3,3′-methylenebis(4-hydroxycoumarin) (17.07 %), *N*-D-α-phenylglycine (38.76 %), laminaribiitol (7.75 %), 3-(4-(dimethylamino)cinnamoyl)-4-hydroxycoumarin (16.89 %) and two unknown compounds (5.28 % and 10.26 %) (Mahalingam et al. 2012).

Light petroleum extract of *M. jalapa* leaves was found to contain hydrocarbon (17.8 %),

ketones (18 %), alcohols (12.1 %), sterols (21.2 %), acids (7 %) and an unidentified residue (23.9 %) (Behari et al. 1976). The compounds detected included campesterol, β-sitosterol, stigmasterol, n-dotriacontane, n-hentriacontane, n-triacontane, n-tricosane, tricosane-12-one, n-tritriacontane, n-tetracosane, n-tetratriacontane, n-pentacosane, n-pentatriacontane, n-hexacosane n-heptacosane, n-octacosane, n-nonasane, hexacosan-1-ol and lignoceric acid. Presence of valine, tryptophan, leucine, alanine, glycine, tartaric acid and citric acid was also detected in the aqueous–ethanolic leaf extract. Amino acid, organic acid and phenol were found in the water extracts of leaves (Li and Tuerxunayi 2009). Flavonoid, phenol, coumarin, and anthraquinone were obtained from the ethanol extracts of leaves and steroid and terpenoid detected in the petroleum leaf extracts. The presence of alkaloids, flavanoids, phenols, glycosides, tannins, saponins and lignins was detected in the methanol leaf extract of *M. jalapa* (Kumar et al. 2010). The following compounds were identified in the bioactive fraction of the leaves: 4-phenyl-tetrahydro-pyran-4-nyl-piperidinyl methanone; threonine; isoquinoline-1-(3-benzyloxy 5-hydroxy benzyl)-*N*-formyl-1,2,3,4; 4-benzyloxy-3-methoxy-2-nitro benzoic acid; oleic acid; 2,6,10 trimethyl dodecane; and 3,8 dimethyl decane (Eneji et al. 2011). Aqueous and alcoholic leaf extracts were found to contain glycosides, tannins, phenolic compounds, resins, alkaloids and proteins, while saponins and flavonoids were not found (Mohammed 2013). The leaves of *M. jalapa* were also found to contain in μg/mL K 161.2, Ca 12, Na 19, Zn 14.2, Fe 18.7, Cd 0.8, Cu 0.3 and Pb 0.1 μg/mL.

Seed Phytochemicals

The cotyledon of the seed of *Mirabilis jalapa* was found to contain a D-glucan (Ghosh and Rao 1981). Both α- and β-D-glucosidic linkages were present in the polysaccharide, the former preponderating. Starch was isolated from *Mirabilis jalapa* seed (Chang et al. 1983). The nearly spherical starch granules were approximately 1.5–3.0 μm in diameter and had a pasting temperature of 72.5 °C and an iodine affinity of 3.6 %. The Bra-bender viscoamylogram and the swelling pattern indicated the starch underwent restricted swelling. The starch contained only trace amounts of phosphate. The properties of this isolated small-granule starch differed from other such starches reported in the literature. *M. jalapa* seeds yielded only 3.0 % of oil, of 0.70 g/mL density, 26.10 dynes/cm surface tension and 169.5 millipoise viscosity at 20.5 °C (Uma Devi et al. 1983). The determined iodine value was 80 and saponification value 172. It was found to have a high oleic content. A fatty acid, 8-hydroxyoctadeca-*cis*-11,14-dienoic acid, was found as a minor component in the seed oil of *Mirabilis jalapa* (Ahmad et al. 1984). In a separate study, *Mirabilis jalapa* seeds yielded 4–5 % of fatty oil, comprising 18.3 % C16:0, 55.3 % C18:1, 11.5 % C18:2 and 14.9 % C18:3 (Patel and Patel 1985). β-Amyrin and β-amyrin 3-*O*-α-l-rhamnosyl-*O*-β-D-glucoside were found in the seeds (Saxena and Gupta 1986).

Two antimicrobial peptides, designated Mj-AMP1 and Mj-AMP2, were isolated from *M. jalapa* seeds (Cammue et al. 1992). These peptides were highly basic and consist of 37 and 36 residues for Mj-AMP1 and Mj-AMP2, respectively, and contained three disulphide bridges and differ from one another only by 4 amino acids. The peptides associated into dimers in their native form. A genomic gene for MAP, a ribosome-inactivating protein from *Mirabilis jalapa*, was found to contain an intron (Kataoka et al. 1993). The cDNAs encoding the seed antimicrobial peptides (AMPs) from *Mirabilis jalapa* (Mj-AMP2) had previously been characterized, and it was found that Mj-AMP2 was processed from a precursor preprotein (De Bolle et al. 1995). The Mj-AMP1- and Mj-AMP2-encoding genes were interrupted in their coding sequences by a single intron (380 bp and 900 bp for Mj-AMP1 and Mj-AMP2 genes, respectively). The processing, sorting and biological activity of Mj-AMP2 wild-type gene construct and Mj-AMP2 mutant gene construct in transgenic tobacco were studied (De Bolle et al. 1996). The in vitro antifungal activity of the AMPs purified

from transgenic tobacco expressing any of the two different precursor proteins was similar to that of the authentic proteins. However, none of the transgenic plants showed enhanced resistance against infection with either *Botrytis cinerea* or *Alternaria longipes*.

Proteins isolated from the ripe seeds of *Mirabilis jalapa* showed both antifungal and antibacterial activities (Leelamanit et al. 2002). SDS-PAGE analysis showed three major bands of molecular weight of approximately 31, 24.5 and 13 kDa that were proved to be glycoproteins.

Mirabilis jalapa trypsin inhibitors, MJTI I and II, were isolated from the seeds (Kowalska et al. 2007). Their primary structures differed from those of known trypsin inhibitors but showed significant similarity to the antimicrobial peptides isolated from the seeds of *M. jalapa* (Mj-AMP1, Mj-AMP2), *Mesembryanthemum crystallinum* (AMP1) and *Phytolacca americana* (AMP-2 and PAFP-S) and from the haemolymph of *Acrocinus longimanus* (Alo-1, 2 and 3).

Root/Tuber Phytochemicals

The roots were reported to the alkaloid trigonelline (Yoshimura and Trier 1912) and oxymethylanthraquinone (Maurin 1925; Jayaweera 1982). A neutral polysaccharide was isolated from the roots (Ray et al. 1988). The following sterols were found in the roots: stigmasterol, β-sitosterol (Stanic et al. 1988) and triterpenes: α-amyrin and α-amyrin acetate (Begum et al. 1994).

Four new rotenoids named mirabijalones A–D, together with 9-*O*-methyl-4-hydroxyboeravinone B, boeravinone C, boeravinone F and 1,2,3,4-tetrahydro-1-methylisoquinoline-7,8-diol, were isolated from *Mirabilis jalapa* roots (Wang et al. 2002). The rotenoids boeravinone B, boeravinone E and mirabijalone B were isolated from the roots (Xu et al. 2010). Four compounds, 2,5-dioxoimidazolidin-4-yl-urea, glycerin monoeicosate, boeravinone and β-sitosterol, were isolated from 75 % ethanol extract of the roots (Wei et al. 2003). The following compounds were isolated from the roots: chrysophanol, physcion, stigmasterol, mirabijalone A, boeravinone C, aurantiamide acetate, glycerin monoeicosate, β-sitosterol and 4-hydroxy-3-methoxybenzoic acid (Zou 2007). Eleven compounds were isolated from the roots and identified as astragaloside II; astragaloside III; astragaloside IV; astragaloside VI; flazin; 4′-hydroxy-2,3-dihydroflavone 7-β-D-glucopyranoside; gingerglycolipid A; 3,4-dihydroxybenzaldehyde; *p*-hydroxybenzaldehyde; β-sitosterol; and daucosterol (Lai et al. 2008). GC/MS analysis of *M. jalapa* tubers dichloromethane and methanol extracts showed that oleic acid and β-sitosterol were, respectively, the major compounds (Hajji et al. 2010). LC/MS analysis of the aqueous extract showed a high content of flavanol and flavonol compounds. Phenolic acids such as ferulic and caffeic acid were also detected. The total phenolic and flavonoid contents varied from 21.45 to 364.6 mg gallic acid equivalent (GAE)/g dried extract and 5.2–71.6 mg quercetin/g dried extract, respectively.

The protein MAP, which is active against mechanical transmission of plant viruses, was purified to homogeneity from *M. jalapa* roots (Takanami et al. 1990). MAP was found to be a lysine-rich, basic simple protein having an isoelectric point of 9.8 and containing no sugar moiety and made up of a polypeptide chain of approx. 24–200 MW. Mirabilis antiviral protein (MAP) was also purified from root tubers of *M. jalapa* by Wong et al. (1992) and crystal of MAP obtained by Miyano et al. (1992).

Callus/Culture Phytochemicals

Mirabilis anti-plant viral protein (MAP) was found in *M. jalapa* suspension-cultured cells (Ikeda et al. 1987). The MAP content of cultured cells reached the highest level (0.6 mg/g dry weight) on the 9th day after inoculation, which was less than one-third of the content of the roots but three times larger than that of the leaves. The MAP content of the *Mirabilis jalapa* cell strain H9-52 obtained in the 9th selection was 6.3 mg/g dry weight which was about 3 times that of the root and was about 20 times that of the original cells (Ikeda et al. 1988a, b). MAP was also isolated from the strain H8-50, and its anti-plant

viral activity was the same level as that of the root. The MAP productivity of strain H8-50 was maintained during 14 successive subculturings.

Callus, suspension and immobilized cell cultures of *M. jalapa* on Murashige–Skoog medium synthesized both extracellular and intracellular protease (Tamer and Mavituna 1997). When compared with the leaves of the original plant, the proteolytic enzyme activity was 54- and 36-fold higher in the cell suspension and the callus cultures, respectively. Some of the sucrose was converted to glucose and fructose by the cultures, and all three sugars were consumed simultaneously. Suspension and immobilized cultures also produced ethanol during batch cultivation. Three phenolic compounds, the isoflavone 2′-*O*-methyl abronisoflavone and dehydrorotenoid 9-*O*-methyl-4-hydroxyboeravinone B and rotenoid 6-methoxy boeravinone C, were isolated from *M. jalapa* plant cell culture (Yang et al. 2001).

Antioxidant Activity

Water extract of *Mirabilis jalapa* tubers was the most potent antioxidant in all assays used, followed by methanol extract (Hajji et al. 2010). The total phenolic and flavonoid contents varied from 21.45 to 364.6 mg gallic acid equivalent (GAE)/g dried extract and 5.2–71.6 mg quercetin/g dried extract, respectively. The aerial parts (stem bark and leaves) and the root methanol extracts of *Mirabilis jalapa* exhibited antioxidant activity in the $ABTS^{+}$ (2,2′-azino-bis(3-ethyl benzothiazoline-6-sulphonic acid) and DPPH (1,1-diphenyl-2-picrylhydrazyl) free radical scavenging assays (Zachariah et al. 2011). The extracts showed the presence of alkaloids, tannins, phytosterols, triterpenoids and flavonoids in significantly detectable amounts. *M. jalapa* plant exhibited significant antioxidant properties in various in vitro models like hydrogen peroxide scavenging method and reducing power assay and could serve as a free radical inhibitor or scavenger (Zachariah et al. 2012b). Preliminary phytochemical screening revealed the presence of alkaloids, flavonoids and polyphenols like phenolic compounds and tannins. The total flavonoid content of the extract was found to be 4.41 mg/g. *M. jalapa* ethanol leaf extract showed high activity in reducing iron chloride solution, and it also exhibited high antioxidant activity in 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging test with IC_{50} value of 0.84 mg/mL (Oladunmoye 2012).

The total phenolic content (TPC), total flavonoid content (TFC), ferric reducing/antioxidant power (FRAP) and scavenging activities of different solvent extract of *M. jalapa* seed against DPPH and OH radical were in the following order: ethyl acetate > ethanol > methanol > water (Wang and Dai 2012). The TPC of ethyl acetate extract was 4.24 mg GAE/g of dry power weight (DPW) and TFC 0.39 mg RE/g DPW. Ethyl acetate extract exhibited high free radical scavenging rate; IC_{50} of DPPH and OH assay were 6.62 mg DPW/mL and 3.49 mg DPW/mL, respectively. The TPC values and IC_{50} obtained from DPPH assay and FRAP assay were highly correlated with correlation of determination ($R^2 = 0.9878$, $R^2 = 0.9419$).

Antidiabetic/Hypoglycaemic and Hypolipidaemic Activities

Repeated administrations to mice pre- and post-streptozotocin induction with 4 and 8 g/kg ethanolic root extract of *Mirabilis jalapa* continually lowered blood glucose level, decreased serum insulin level and improved insulin sensitivity index, and lowered serum total cholesterol, triglyceride levels and triglyceride content in liver and skeletal muscle and increased glycogen content in these tissues; but repeated administration had no influence on those indexes of normal mice (Zhou et al. 2012b). The results suggested that ethanolic root extract of *M. jalapa* possessed potential insulin sensitivity, hypoglycaemic and hypolipidaemic effects on diabetes. In a separate study, fasting blood glucose level in normoglycaemic, streptozotocin-induced hyperglycaemic rats and in oral glucose tolerance test showed a significant decrease at defined time points after administration of the hydroalcoholic extract of aerial parts

of *Mirabilis jalapa*, while the observed biochemical and physical parameters showed a good agreement with antihyperglycaemic property of the extract (Prakash et al. 2012). Treatment with trigonelline, a compound from *M. jalapa*, significantly decreased blood glucose, total cholesterol and triglyceride levels of diabetic rats induced by streptozotocin and a high-carbohydrate/high-fat diet (Zhou et al. 2013). Pancreas-to-body weight ratio, insulin level, insulin sensitivity index, insulin content in pancreas, malonaldehyde and nitric oxide contents and superoxide dismutase, catalase, glutathione and inducible nitric oxide synthase activities were altered in diabetic rats and were near control levels when treated with trigonelline. The findings suggested that trigonelline had beneficial effect for diabetes through decreasing blood glucose and lipid levels, increasing insulin sensitivity index and insulin content, up-regulating antioxidant enzyme activity and decreasing lipid peroxidation. Studies by Ghule et al. (2012) found that trigonelline ameliorated diabetic hypertensive nephropathy by suppression of oxidative stress in kidney and reduction in renal cell apoptosis and fibrosis in streptozotocin-induced neonatal diabetic rats.

Spasmolytic/Spasmodic Activity

Of eight medicinal plant extracts, *M. jalapa* and *Satureja macrostema* extracts exhibited highest inhibitory activity on jejunum muscular contractility with concentrations (IC_{50}) of 18 and 73 μg/mL, respectively (Arroyo et al. 2004). Flowers (petals, calices and buds) of *M. jalapa* were the most active part of the plant. A semi-purified sample of the flowers was found to be about five times more active than the crude extract. Furthermore, β-sitosterol, a compound reported as constitutive of *M. jalapa*, showed no effect on jejunum contractility.

The flower extract of *Mirabilis jalapa* (1–1,000 μg/mL) exhibited an inhibitory effect (IC_{50} = 18 μg/mL) on gut smooth muscle contractility, whereas it stimulated the contraction of rabbit aortic muscle (EC_{50} = 11.60 μg/mL) in a concentration-dependent manner (Aoki et al. 2008). These effects were not due to either acetylcholine or histamine receptor blockage, inositol 1,4,5-trisphosphate (IP3), cyclic nucleotides cAMP and cGMP, $Ca2^{+}$ release from intracellular storage or protein kinase-mediated contraction–relaxation mechanisms. The effects elicited by the *Mirabilis jalapa* extract may involve a serotoninergic mechanism, which, in turn, interacted with other adrenergic systems.

Central Nervous System/ Antinociceptive Activity

The crude hydroethanolic extract from *M. jalapa* leaves (CrdL) was more potent than the crude extract from stems (CrdS) to inhibit abdominal constrictions induced by acetic acid, with ID_{50} values of 5.5 (2.3–13.1) and 18.0 (11.3–28.5) mg/kg, respectively (Walker et al. 2008). Among the fractions tested, the ethanol fraction from leaves (Eta) was more effective (maximal inhibition of 83 %) and potent (ID_{50} of 1.1 (0.6–2.1) mg/kg) to induce antinociception. Eta and CrdL also possessed an antinociceptive effect in the tail-flick test. Pre-treatment with naloxone did not modify the antinociceptive effect of Eta, but co-administration with atropine completely prevented it. This suggests that the antinociceptive effect might depend on the cholinergic system. Eta did not alter locomotor activity, body temperature, gastrointestinal transit and did not produce gastric lesions. The study suggested that *Mirabilis jalapa* possessed antinociceptive activity in mice, which supported its folkloric use as an analgesic.

Trigonelline, an alkaloid found in *M. jalapa* and fenugreek, had been reported to have beneficial effects in the treatment of diabetes and central nervous system disease (Zhou et al. 2012a). Trigonelline had been reported to possess hypoglycaemic, hypolipidaemic, neuroprotective, antimigraine, sedative, memory-improving, antibacterial, antiviral and antitumour activities.

Anti-inflammatory/Anti-allergic/ Antiasthmatic/Antiarthritic Activities

The aqueous leaf extract of *M. jalapa* was found to possess significant anti-inflammatory potential (Singh et al. 2010). The aqueous extract showed significant inhibition of paw oedema, 37.5 % and 54.0 % on the 4th hour at the doses of 200 and 400 mg/kg, respectively, in the carrageenan-induced paw model in Wistar albino rats. Similar pattern of paw oedema inhibition 32.9 % and 43.0 % on the 4th day at the doses of 200 and 400 mg/kg, respectively, was seen in formalin-induced paw oedema model.

The effect of an ethanol to acetone (1:1) extract of *M. jalapa* roots (0.5 mL of 100 mg/mL) inhibited histamine-induced guinea pig tracheal chain contractions noncompetitively (Maxia et al. 2010). The extract (100 or 200 mg/kg i.p.) inhibited milk-induced eosinophilia, albumin-induced paw oedema and protected mast cells against clonidine-induced granulation in mice. The results supported the folkloric use of *M. jalapa* in the treatment of allergic diseases and asthma.

The alcoholic leaf extract at the dose of 300 mg/kg p.o. and successive petroleum ether fraction at the dose of 200 mg/kg exhibited significant anti-inflammatory activity in carrageenan-induced paw oedema model (Nath et al. 2010). Hydroethanolic flower extract of *Mirabilis jalapa* significantly suppressed the paw oedema in both formaldehyde-induced and complete Freund's adjuvant (CFA)-induced arthritic models in Wistar rats (Augustine et al. 2013). Body weight and haematological and antioxidant changes in the CFA arthritic rats were restored to normal.

Anticancer/Cytotoxicity Activity

Mirabilis antiviral protein (MAP) was demonstrated to possess inhibitory effect on cell-free protein synthesis and antiproliferative effect on tumour cells (Wong et al. 1992). Proteins isolated from the ripe seeds of *Mirabilis jalapa* exhibited potent anticancer activity to permanent cell lines L929 (mouse fibroblasts) (Leelamanit et al. 2002). The ribosome-inactivating protein (RIP) from *M. jalapa* leaves was shown to be more cytotoxic to HeLa cell line (LC_{50} = 0.65 mg/mL) than to Raji cell line (1.815 mg/mL) after 48 h incubation (Ikawati et al. 2003). It was demonstrated that the death of HeLa cells caused by RIP was due to induction of apoptosis, while death of Raji cell line was not due to apoptosis, presumably via necrosis. The 30 kDa protein fraction with properties of ribosome-inactivating protein (RIP) was isolated from *Mirabilis jalapa* leaves and named MJ-30 (Ikawati et al. 2006). MJ-30 exhibited cytotoxicity against breast cancer T47D cell and cervical cancer SiHa cell lines, and the LC_{50} values were 0.36 µg/mL and 5.6 µg/mL, respectively. In normal cells, represented by human mononuclear cells, MJ-30 was considerably less toxic, with an LC_{50} of 21.04 µg/mL.

The petroleum ether extract of *M. jalapa* bark showed significant cytotoxic activity with the LC_{50} value 8.12 µg/mL compared to vincristine sulphate (LC_{50} 0.33 µg/mL) in the brine shrimp lethality bioassay (Rumzhum et al. 2008). On the other hand, the methanol crude extract of the bark showed mild antioxidant activity with the IC_{50} value 598.02 µg/mL compared to ascorbic acid (IC_{50} 70.985 µg/mL) in the 1,1-diphenyl-2-picrylhydrazyl-hydrate (DPPH) free radical scavenging assay.

The rotenoids boeravinone B, boeravinone E and mirabijalone B isolated from the roots exhibited cytotoxic activity against tumour cell lines tested (Xu et al. 2010).

Antimicrobial Activity

The ethanol extract of the plant (Oskay and Sari 2007) and extract of the seed powder had been reported to have antibacterial activity (Kusamba et al. 1991). The antimicrobial peptides Mj-AMPs isolated from *M. jalapa* seeds exhibited a broad spectrum of antifungal activity since they are active against all 13 tested plant pathogenic fungi (Cammue et al. 1992). Concentrations required for 50 % inhibition of fungal growth vary from 6 to 300 µg/mL for Mj-AMP1 and from 0.5 to 20 µg/mL for Mj-AMP2. These peptides were also active on two tested Gram-positive bacteria

but were apparently nontoxic for Gram-negative bacteria and cultured human cells. Although the Mj-AMPs showed sequence similarity to muagatoxins, a class of insecticidal neurotoxic peptides isolated from the venom of spiders, they did not affect pulse transmission in insect nerves. Mj-AMPs, antimicrobial peptides from *Mirabilis jalapa* seeds, showed significant sequence similarities with PAFP-S, antifungal peptides from *Phytolacca americana* seeds, and were found to belong to the knottin-type antimicrobial peptide (Shao et al. 1999). Proteins isolated from the ripe seeds of *Mirabilis jalapa* showed both antifungal and antibacterial activities (Leelamanit et al. 2002). The antibacterial activity of crude proteins was tested against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Salmonella typhimurium* and was only active against *B. subtilis* at protein concentration of 0.37 mg/disc.

Three phenolic compounds, the isoflavone 2′-*O*-methyl abronisoflavone, dehydrorotenoid 9-*O*-methyl-4-hydroxyboeravinone B and rotenoid 6-methoxy boeravinone C, were identified as the principal antifungal principles from this plant cell culture with IC_{50}'s of 25 and 48 μg/mL, respectively, against the test organism, *Candida albicans* (Yang et al. 2001). The rotenoid was inactive at 200 μg/mL in this assay.

An active polyphenolic amide, *N-trans*-feruloyl 4′-*O*-methyldopamine, isolated from *M. jalapa* methanol extract exhibited moderate activity as an efflux pump inhibitor (EPI) against multidrug-resistant (MDR) *Staphylococcus aureus* overexpressing the multidrug efflux transporter NorA, causing an eightfold reduction of norfloxacin MIC at 292 μM (100 μg/mL) (Michalet et al. 2007). Aqueous extracts of *Mirabilis jalapa* (white-, cream-, yellow- and pink-flowered plants) did not display any inhibition to *Staphylococcus aureus* (Naveed et al. 2010, 2011). However, the ethanolic extract of only white-flowered plant showed good antibacterial activity (54 %) against *S. aureus*, while that of the other three colours, i.e. cream, yellow and pink, did not show any inhibitory activity. The methanol leaf extract of *M. jalapa* inhibited in vitro growth of *Staphylococcus aureus* (MIC 39 μg/mL) and *Aspergillus flavus* (MIC 45 μg/mL) (Kumar et al. 2010). Water extract of *M. jalapa* tubers was the most effective with minimum inhibitory concentration <200 μg/mL against *Staphylococcus aureus*, *Micrococcus luteus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Bacillus cereus* and *Enterococcus faecalis* (Hajji et al. 2010). Only water extract showed antifungal activity against *Aspergillus niger*, *Fusarium solani*, *Fusarium oxysporum* and *Fusarium granularium*.

Leaf extracts of *Mirabilis jalapa* exhibited antimicrobial effect in vitro against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*, Gram-negative *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* and against the fungus *Candida albicans* (Muthumani et al. 2009). The ethanolic leaf extract of *Mirabilis jalapa* was found to be inhibitory in vitro to the disease-causing enteric pathogens *Salmonella typhi* and *Bacillus cereus* (Eneji et al. 2011). The ethanol leaf extract showed highest antimicrobial effect in vitro against some of the tested pathogenic bacteria, *Pseudomonas aeruginosa*, *Proteus mirabilis* and *Salmonella typhi*, in descending order, followed by the methanol extract (Akintobi et al. 2011). *Staphylococcus aureus*, *Escherichia coli* and *Klebsiella pneumoniae* were resistant to the ethanol extract. The ethanol leaf extract exhibited antimicrobial activity in vitro against *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Clostridium botulinum*, *Bacillus cereus*, *Staphylococcus aureus* and fungi *Aspergillus flavus*, *Aspergillus niger* and *Candida* sp. (Oladunmoye 2012). Generally bacteria were found to be more susceptible to the extract than fungi.

Ethanol extract of *M. jalapa* leaves exhibited antimicrobial activity against all tested biofilm-producing uropathogenic *Escherichia coli* (UPEC) strains, whereas it inhibited only the extended spectrum beta lactamase (ESBL)-producing UPEC strains 42 and 96 (Poovendran et al. 2011). Similarly, the acetone extract of *M. jalapa* leaves inhibited the growth of biofilm-producing UPEC strains 1, 17 and 82, whereas it inhibited only the ESBL-producing UPEC strains 42 and 96. *Mirabilis jalapa* was found to possess antibacterial potential (Zachariah et al. 2012b). Its methanol plant extract displayed a wide

spectrum of inhibition against Gram-positive and Gram-negative bacteria in vitro, in particular against *Pseudomonas* sp. The aqueous and alcoholic leaf extracts of *M. jalapa* were found to be inhibitory to growth of *Staphylococcus aureus*, *E. coli* and *Proteus mirabilis* (Mohammed 2013).

Antiviral Activity

Mirabilis anti-plant viral protein (MAP) was highly effective in preventing viral infection caused by contact-transmitted virus and that cultured cells of *M. jalapa* also produced MAP (Ikeda et al. 1987, 1988a, b). Mirabilis antiviral protein (MAP) was purified from root tubers of *M. jalapa* (Wong et al. 1992). MAP was found to be a type I ribosome-inactivating protein. Among the rotenoids isolated from the roots, 1,2,3,4-tetrahydro-1-methylisoquinoline-7,8-diol showed a 48 % inhibition against HIV-1 reverse transcriptase at 210 μg/mL (Wang et al. 2002).

Protein Synthesis Inhibitory/ Ribosome-Inactivating Activity

Mirabilis antiviral protein (MAP), a ribosome-inactivating protein, exhibits inhibitory effects on both eukaryotic and prokaryotic protein synthesis in vitro (Habuka et al. 1990). MAP was found to inhibit plant virus infection, the in vitro protein synthesis of rabbit reticulocyte and wheat germ. It further showed an IC_{50} concentration of approximately 200 nM in an *Escherichia coli* in vitro translation system in contrast to ricin A chain, a well-known ribosome-inactivating protein. *Escherichia coli* ribosome was found to be inactivated by Mirabilis antiviral protein (MAP) which cleaved the N-glycosidic bond at A2660 of 23S ribosomal RNA (Habuka et al. 1991). Mirabilis antiviral protein (MAP) inactivated both eukaryotic and prokaryotic ribosomes by means of site-specific RNA N-glycosidase activity (Habuka et al. 1992). When the in vitro protein synthesis of rabbit reticulocyte was treated with MAP variants secreted into culture media of *Escherichia coli* transformants, the inhibitory effect of R26L and R48L (R26L designates MAP variant with Arg-26 changed to Leu) was found to be similar to that of native MAP. Both purified Y72F and Y118F had the same effect as native MAP, and E168D had a slightly weaker effect. In contrast, on the protein synthesis of *E. coli*, Y118F had one-tenth the effect of native MAP, and Y72F and E168D approximately one-hundredth the effect. These three variant proteins also exhibited reduced RNA N-glycosidase activity on substrate *E. coli* ribosomes. These results suggested that Tyr-72 and Glu-168 were involved in RNA N-glycosidase activity. Kataoka et al. (1991) cloned a cDNA for Mirabilis antiviral protein (MAP), a ribosome-inactivating protein (RIP), that inhibited the mechanical transmission of plant virus and the in vitro protein synthesis of both prokaryotes and eukaryotes. The cDNA consisted of 1,066 nucleotides and could encode 278 amino acids. The major part of the amino acid sequence (from Ala29 to Ser278) was identical with the sequence of native MAP as determined by protein sequencing. MAP precursor also appeared to inhibit the protein synthesis of *E. coli* just as native MAP had been observed to do.

Activities of ribosome-inactivating proteins (RIPs), currently classified as rRNA N-glycosylases, were highest in seed; intermediate in flower bud, immature seed, sepal+gynoecium, leaf and root; and very low in all other tissues of *M. jalapa* (Bolognesi et al. 2002). MAP depurinated not only rRNA in intact ribosomes, thus inhibiting protein synthesis, but also other polynucleotides such as poly(A), DNA and tobacco mosaic virus RNA. Autologous DNA was depurinated more extensively than other polynucleotides. Therefore, the enzymatic activity of this protein may be better described as adenine polynucleotide glycosylase activity rather than rRNA N-glycosylase activity. Further, MAP did not cross-react immunologically with other commonly utilized RIPs.

Wound Healing Activity

In the excision wound and dead space wound models, significant wound healing was observed in Wistar albino rats treated with *M. jalapa* tuberous root extract as compared to control (Gogoi et al. 2013). A significant

increase in rate of wound contraction, a decrease in colony-forming unit (CFU) count and a decrease in epithelialization period were observed in 5 and 10 % of treated groups as compared to control. A significant increase in hydroxyproline content and up-regulated expression of collagen type III were observed in treated groups as compared to control which was supported by histological evidences. The results validated its traditional use in wounds and inflammation.

Blood Clotting Activity

Studies found that the seed extract of *M. jalapa* elicited a decrease in prothrombin time, a decrease in activated partial thromboplastin time, a decrease in bleeding time and prolonged blood clotting time in rabbits (Alam et al. 2012). The bleeding time in the high-dose-treated rabbits was 79.1 s compared to 95.6 s in the control group. The clotting time was 103.9 s in control group compared to 121.7 in the low-dose group and 115 s in the high-dose group. Prothrombin time was 9.0 s in the control group versus 8.7 in the high-dose group. Activated partial thromboplastin time was 25.2 s in control group and 23.4 s in the high-dose groups.

Haemolytic Activity

M. jalapa ethanol leaf extract was found to lyse blood cells in the haemolytic assay (Oladunmoye 2012). The observed haemolytic ability of the extract could be associated with the presence of constituents like saponins, tannins and cardioglycosides.

Abortifacient Activity

Besides its antiviral property, Mirabilis antiviral protein (MAP) was demonstrated to possess abortifacient activity in pregnant mice (Wong et al. 1992).

Anthelmintic Activity

The methanolic extracts of *M. jalapa* aerial parts at 80 % w/v concentration were found to be potent as anthelmintic giving shortest time of paralysis and death of the test worm *Pheretima posthuma* in a dose-dependent manner (Zachariah et al. 2012a). This was postulated to be due to the presence of flavonoids, glycosides and tannins in the extracts. The methanolic extract caused paralysis in 12.6 min and death in 13.5 min. The reference drug albendazole showed the same at 2.3 and 3.24 min.

Traditional Medicinal Uses

The root is aphrodisiac, diuretic and purgative and used in the treatment of dropsy (Uphof 1968; Usher 1974; Duke and Ayensu 1985; Chopra et al. 1986). The tuberous root is a mild purgative and the fresh juice of the leaves is applied to the body to allay heat and itching (urticaria) arising from dyspepsia (Jayaweera 1982). In Nepal, a paste of the root is applied as a poultice to treat scabies and muscular swellings; root juice is used in the treatment of diarrhoea, indigestion and fevers, and powdered root, baked with corn flour, is employed for the treatment of menstrual disorders (Manandhar and Manandhar 2002). The leaves are deemed diuretic (Manandhar and Manandhar 2002); an infusion of the leaves is prescribed as a diuretic for dropsy (Jayaweera 1982) and used to reduce inflammation (Chopra et al. 1986). Bruised leaves are used for poulticing boils and abscesses (Jayaweera 1982), and leaf decoction is used to treat abscesses and leaf juice is used to treat wounds (Duke and Ayensu 1985).

According to Burkill (1966), crushed leaves are used in India and Java for poulticing boils and abscesses and juice used for uterine discharges. Leaf juice is prescribed internally in a mixture for gonorrhoea in the Medical Book of Malayan Medicine. The tubers are employed as a purgative in Europe, and in western India, the dried root is given with milk as a strengthening medicine. Pounded seeds are used in Peninsular Malaysia

and elsewhere by Chinese and Japanese women for making cosmetic powder and are believed to remove acne, hence their appellation of 'ubat jerawat'. Citing Rumpf, Burkill (1966) reported that powdered root is employed with rice powder and sandalwood for the same purpose by Spanish women in Ternate and the juice of white flowers applied on the face when going out in the sun. The Malays use the plant to treat influenza, fever and inflammation, and the Chinese used it for diabetes (Herbal Medicine Research Center 2002). In Thailand, seed powder is used to treat infections (Stuart 2012).

The indigenous people of Mexico use *Mirabilis jalapa* to cure many infirmities including dysentery, diarrhoea, muscular pain and abdominal colic (Aoki et al. 2008). *Mirabilis jalapa* leaf infusions or decoctions are used as traditional folk medicine in the south of Brazil to treat inflammatory and painful diseases (Walker et al. 2008; Singh et al. 2010). *Mirabilis jalapa* is extensively used for treatment of dysentery and vaginal discharge and as a laxative (purgative) by Mexican people (Encarnacion et al. 1998; Marquez et al. 1999) and for treatment of diarrhoea, muscular pain and abdominal colic by people in the Easter Island, Guatemala and Brazil (Holdsworth 1992; Comerford 1996; Moreira 1996). In Brazil, Kayapo Indians inhale the powdered dried flowers as a snuff for headaches; the Assurani Indians grate the tuberous seeds and drink it for intestinal parasites. Indigenous Peruvian people use a root decoction as a diuretic; the Shipibo–Conibo Indians put the flowers in baths to treat colds and flu (Oladunmoye 2012). In the United States, the plant is used for mumps and bone fractures and as a uterine stimulant to hasten childbirth (Simpson and Orgazaly 1986).

The roots of *Mirabilis jalapa* are used traditionally in allergic skin disorders and asthma (Maxia et al. 2010). *M. jalapa* was one of many plants used for the treatment of gonorrhoea in Guatemala (Cáceres et al. 1995). In Kivu, Democratic Republic of Congo, powder of the seeds is employed for conjunctivitis, and juice of the flower and scrapings of banana stem is used for cataracts in animals (Balagizi et al. 2005). In Madagascar, washed root or root powder decoction is used with sugar in chicken soup as a purgative (Boiteau and Allorge-Boiteau 1993). Root pulp diluted in palm oil is used as local topical application for local application swellings in Popular Republic of Congo (Bouquet 1969). In Burundi, the whole ripe fruit is dried, powdered and used locally for wounds (Baerts and Lehmann 1989). In Benin, powdered dried roots are used to treat female sterility, and leaves are used as a magical charm in a sauce with belly of beef, fruits of *Piper guineense* and palm oil (Adjanohoun et al. 1989).

Other Uses

This species is used as a medicinal herb and as an ornamental in pots or in the ground.

A protein designated as MAP (Mirabilis antiviral protein) was highly active against mechanical transmission of tobacco mosaic tobamovirus (TMV), cucumber green mottle mosaic tobamovirus, potato Y potyvirus, turnip mosaic potyvirus and cucumber mosaic cucumovirus (Kubo et al. 1990). Almost complete inhibition was achieved when MAP at 0.8 μg/mL was applied to the upper surface of Xanthi nc tobacco leaves 24 h before TMV inoculation and 50 % inhibition with MAP at 10 μg/mL on the undersurface. The content of MAP was much higher in the root than in other plant parts and that of a yellow flower variant *of M. jalapa* reached 1.1 mg/g fresh wt. *M. jalapa* appeared to be a promising source of antiviral substances for practical use. In another study, root extracts of *M. jalapa* containing Mirabilis antiviral protein (MAP) sprayed on potato plants 24 h before virus or viroid inoculation inhibited infection by almost 100 %, as corroborated by infectivity assays and the nucleic acid spot hybridization test (Vivanco et al. 1999). Antiviral activity of MAP extracts was observed against mechanically transmitted viruses but not against aphid-transmitted viruses. Purified MAP showed the same antiviral effect as the crude extracts.

Mirabilis jalapa flower extract was found to have use as a natural indicator in different types of acid–base titrations (Shishir et al. 2008). This

natural indicator was found to be very useful, economical, simple and accurate.

Results of a study by Zhou et al. (2012c) suggested the feasibility of *M. jalapa* applied to phytoremediation of nitrobenzene-contaminated soils. Although the absorption of nitrobenzene in shoots and roots of *M. jalapa* was weak, plant-promoted biodegradation of nitrobenzene and the dominant contribution in the removal of nitrobenzene from contaminated soils were considerable.

Comments

The flowers are pollinated by long-tongued moths of the Sphingidae family, such as the sphinx moths or hawk moths, and other nocturnal pollinators attracted by the sweet-smelling fragrance. The plant is readily propagated from seeds and from division of tubers.

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Nymphaea lotus

Scientific Name

***Nymphaea lotus* L.**

Synonyms

Castalia edulis Salisb., *Castalia lotus* Tratt., *Castalia mystica* Salisb., *Castalia pubescens* Wood, *Castalia sacra* Salisb., *Leuconymphaea lotus* Kuntze, *Nymphaea dentata* Schumach. & Thonn., *Nymphaea liberiensis A.* Chev.

Family

Nymphaeaceae

Common/English Names

Egyptian Lotus, Egyptian White Water Lily, Tiger Lotus White Egyptian Lotus, White Lotus, White Water Lily

Vernacular Names

Angola: Mbandu (*Kimbundu*)
Arabic: Bashneen Abiad
Benin: Sotodyame (Peul)
Brazzaville: Itookopeli (Akwa), Biloolonga (Laadi)
Burkina Faso: Béli
Burmese: Kra
Catalan: Lotus Egipci
Czech: Leknín Posvátný
Democratic Republic of Congo: Mitoko-Toko, Kilonga-Longa (Kikongo)
French: Lotier d'Egypte, Lotus Tigré, Nénuphar Blanc
German: Ägyptische Lotosblume, Weiße Ägyptische Seerose, Weißer Ägyptischer Lotus Tigerlotus
Ghana: Kùlchí (Dagomba)
India: Kumud (Hindi), Aambal, Alli (Tamil)
Japanese: Nettai Suiren
Korean: Sulyeon
Madagascar: Agoagga, Retsimilana, Voahirana
Niger: Bödo (Beriberi), Nénuphar (Local French), Bâdo (Hausa), Baloli (Peuhl), Tikindint (Tamacheck), Dundu (Zarma)
Nigeria: Ira, Osibata (Yoruba)
Norwegian: Bokmål
Polish: Grzybienie Egipskie
Portuguese: Golfão-Vermelho
Senegal: Agname (Niominka), Bakoyo (Socé)
Serbian: Egyptowska Lotoska
Slovencina: Lekno Egyptské
Spanish: Lirio De Agua Egipcio. Loto
Sri Lanka: Olu (Sinhala), Ambal (Tamil)
Sudan: Suteib
Swedish: Egyptisk Vitlotus
Thai: Bua Kin Saai
Uganda: Lora
Vietnamese: Súng

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Origin/Distribution

N. lotus is native to Egypt, central and west Africa and Madagascar.

Agroecology

It is found in slow-moving rivers, streams, marshes, lakes and fresh and stagnant ponds in its native range.

Edible Plant Parts and Uses

The flower stalks (Plate 3) are edible, raw or cooked (Hedrick 1972; Tanaka 1976; Pongpangan and Poobrasert 1985; Facciola 1990). In Thailand, the flower stalks eaten raw with chilli sauce or added to 'kaeng som' (sweet and sour curry), cooked with mackerel in curry or fried with pork, prawns or shrimp (JIRCAS 2010). Fishing communities in the Kanji Lake basin, Nigeria, use leaves, petioles, roots and seeds in preparation of concoctions for consumption and medicine (Mohamad et al. 2008). Rhizome is used as food in Angola (Bossard 1996). Seed is used as famine food or eaten by children in Ghana (Blench 2012). Seeds are pickled, put into curries, roasted in sand or ground and mixed with flour to make cakes; unripe fruits are eaten raw in salads and tubers consumed raw or roasted (Hedrick 1972; Tanaka 1976; Facciola 1990). White lotus is a wholly edible species and is cultivated widely for its crisp rhizome and seeds, though the flowers and leaves are also eaten in some parts. Petals of the lotus flowers are used as garnish, while the stems are dried and used as a fragrant herbal tea. Rhizomes are used in soups or stir-fried and eaten (Anonymous 2013).

Botany

Annual or perennial aquatic herb with rhizome submerged in mud. Leaves ovate to suborbicular, deeply cordate with a notch at the petiole, coarsely dentate, 15–20 (–40 cm) cm in diameter,

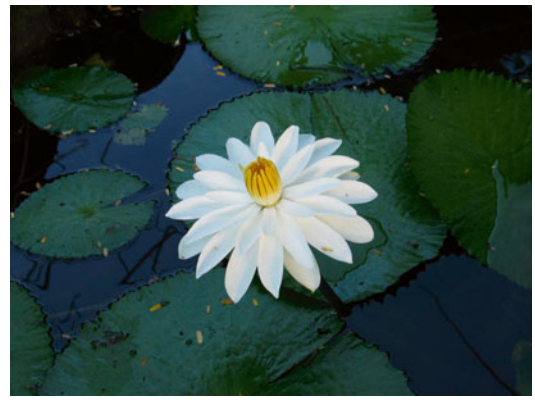

Plate 1 Leaves and flower

Plate 2 Close view of flower

green, floating (Plates 1 and 2); petiole cylindrical, glabrous, long. Submerged leaves are reddish brown. Flowers solitary, large, 5–8 cm across, with 4 outer green oblong, caducous sepals; petals 12–14 (–30), elliptic–oblong, obtuse, white (occasionally pink); stamens with yellow anthers (Plates 1 and 2); carpels united into single ovary, stigma 12–15 (–20) rays. Fruit globose, compressed, 3.5–5 cm., fleshy, ripening under the water. Seeds subglobose, 1–2 mm, numerous.

Nutritive/Medicinal Properties

Proximate nutrient composition (% dry weight) of *Nymphaea lotus* was determined as follows:
Leaves: 6.40 % moisture, ash 14.48 %, crude fat 4.83 %, crude protein 19.54 %, crude fibre 15.53 %, nitrogen (N) free extract 44.78 %

Plate 3 Flower peduncles sold as vegetables in a local Thai market

Petiole: 6.17 % moisture, ash 27.36 %, crude fat 2.27 %, crude protein 9.04 %, crude fibre 15.10 %, N free extract 34.74 %

Root: 4.85 % moisture, ash 22.55 %, crude fat 2.98 %, crude protein 19,545.03 %, crude fibre 1,512.53 %, N free extract 42.71 %

Rhizome: 20.40 % moisture, ash 9.68 %, crude fat 2.82 %, crude protein 11.74 %, crude fibre 13.24 %, N free extract 31.21 %

Seeds: 4.18 % moisture, ash 2.81 %, crude fat 9.95 %, crude protein 3.27 %, crude fibre 1.60 %, N free extract 78.15 % (Mohamad et al. 2013)

Nine known amino acids (alanine, tyrosine, phenyl alanine, valine, threonine, arginine, leucine, D- and L-isoleucine and aspartic acid), 2 alkanoic acids in the form of butanoic acids and its α-hydroxyl isomer, a dipeptide (serine–arginine) as well as a rare compound named 2-amino-7-methyl octanoic acid, were isolated from *Nymphaea lotus* plant (Sowemimo et al. 2007b).

Three novel flavonols, myricetin-3′-*O*-(6″-*p*-coumaroyl)glucoside and two epimeric macrocyclic derivatives nymphalid A and B, as well as the known myricetin-3-*O*-rhamnoside (myricitrin) and 1,2,3,4,6-pentagalloyl glucose, were isolated from the wild water lily *Nymphaea lotus* (Elegami et al. 2003).

Glucose, fructose and sucrose were identified in the cold water extract of *N. lotus* roots and mannitol, galacturonic acid and raffinose in the 80 % ethanolic extract (Hujjatullah et al. 1967). The polysaccharide fraction on complete hydrolysis with 90 % formic acid was shown to contain only glucose; and ten amino acids were found in the protein fraction.

A number of alkaloids had been recorded from *Nymphaea* spp. including *N. lotus*, namely, nymphaeine, nymphaline, nupharine and α- and β-nupharidine (Hegnauer 1962–1968; Chopra et al. 1986; Schmelzer 2001). These chemicals had been reported to be respiratory excitants; an overdose may cause death by respiratory poisoning, as had been seen in frogs, mice rats, guinea pigs and pigeons (Delphaut and Balansard 1943; Chopra et al. 1986).

Antioxidant Activity

The IC_{50} results indicated that the extracts of *Nymphaea lotus* flowers, *Acacia nilotica* beans, *Terminalia bellirica* fruits and *Terminalia chebula* (fruits, brown) were stronger antioxidants than alpha-tocopherol, exhibiting 85 % inhibition of lipid peroxidation in vitro (Saleem et al. 2001). Total phenolic concentration (hydroxycinnamic acid derivatives, flavonol aglycones and their glycosides), expressed as gallic acid equivalents, showed close correlation with the antioxidant activity.

Antibacterial Activity

In vitro studies showed that both methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Staphylococcus aureus* (VRSA) were susceptible to *Nymphaea lotus* leaf ethanol extracts at various concentrations (5, 10, 20, 40, 80 mg/mL) (Akinjogunla et al. 2010).

Anticancer Activity

The ethanol extract of *N. lotus* plant was found to have potential as an anticancer agent when evaluated by the brine shrimp lethality test, standard telomerase elongation assay (STEA) as well as the observed induced chromosomal aberrations

in rat lymphocytes (Sowemimo et al. 2007a). The results supported the use of the plant in the traditional management of cancer in south-west Nigeria.

Antiviral Activity

In the single-cycle vector-based antiviral screening assays, the dichloromethane extract of *N. lotus* plant was also the most active against HIV, with an IC_{50} of 42.5 μg/mL and a selectivity index of 3.62 among all the extracts tested (Esimone et al. 2006). This extract also ranked second in activity after *Jatropha tanjorensis* dichloromethane extract among all the tested extracts. The other extracts from *N. lotus* that exhibited anti-HIV activity were in the order: hexanol > ethyl acetate > water > butanol.

Traditional Medicinal Uses

In Africa, the plant is used in traditional medicine for treatment of fever, skin diseases, cancer, gonorrhoea and bronchitis (Burkill 1998). In Senegal, the fruit is employed as a vermifuge, for nausea, anxiety and nervous disorder (Kerharo and Adam 1964). In Brazzaville, leaf juice is prescribed for tachycardia and anxiety and nervous disorders (Bouquet 1969). In Niger, powdered ripe fruit is used to treat urogenital infections (Adjanohoun et al. 1980). A decoction of leaf and bark from a selection of plants such as *N. lotus, Noronhia linocerioides, Vepris ampody, Zanthoxylum tsihanimposa* and *Peddia involucrata*, is used to relieve malarial symptoms, tiredness, muscular aches and pains and poisoning in eastern Madagascar (Randrianarivelojosia et al. 2003). In western Sudan, cataplasm of roots of *Nymphaea lotus* is used as a treatment for hangnail (Doka and Yagi 2009). In south-western Nigeria, a leaf decoction of *N. lotus* is used topically for cancer (Ashidi et al. 2010); Poultice of the leaves is applied to wounds and burns (Adetutu et al. 2011). The fresh leaves are ground and then applied to boils in Ghana (Blench 2012).

Other Uses

Nymphaea lotus is often used as an aquarium plant or in water gardens. It is also cultivated in ponds and lakes in parks and gardens. Sometimes it is grown for its flowers, while other aquarists prefer to trim the lily pads and just have the underwater foliage.

Comments

The Egyptian lotus is the national flower of Egypt. It is depicted on many of the seals of the different provinces in Thailand. It is also an element of the Coptic flag.

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The Plant List (2013) *Nymphaea lotus* L. http://www.theplantlist.org

Nymphaea nouchali

Scientific Name

***Nymphaea nouchali* Burm.f.**

Synonyms

Castalia caerulea Tratt., *Castalia scutifolia* Salisb., *Castalia stellaris* Salisb. [Illeg.], *Castalia stellata* (Willd.) Blume, *Leuconymphaea stellata* (Willd.) Kuntze, *Nymphaea bernierana* Planch., *Nymphaea cyanea* Roxb. ex G. Don, *Nymphaea emirnensis* Planch., *Nymphaea madagascariensis* DC., *Nymphaea stellata* Willd., *Nymphaea stellata* var. *cyanea* (Roxb. ex G. Don) Hook.f. & Thomson, *Nymphaea stellata* var. *parviflora* Hook.f. & Thomson.

Family

Nymphaeaceae

Common/English Names

Blue Star Water Lily, Blue Water Lily, Indian Blue Water Lily, Lotus Lily, Red Water Lily, Star Lotus

Vernacular Names

Bangladesh: Shapla
Brazil: Loto, Ninféia
Burmese: Kra-Ño
Chinese: Yan Yao Shui Lian
Danish: Indiens Blå Lotusblomst
German: Stern-Seerose
India: Boga Bhet, Seluk (Assamese), Kumud, Sundi (Bengali), Poyanu (Gujarati), Bhenght, Kamal, Kanval, Koi, Koka, Kokka, Kumudini, Neel Kamal (Hindi), Bilenaydilie, Biletavare, Neela Naidile, Neela Thaavare, Neela Thavare, Neeltare (Kannada), Ambal Poovu, Ampal, Cit-Ambel (Malayalam), Kamoda, Krishnakamal, Neel Kamal (Marathi), Kamalini, Neel Kamal (Punjabi), Indeevaram, Indivar, Kamala, Kumuda, Kumudam, Nilakamal, Nilotpala, Padma, Raktotpala, Utpala (Sanskrit), Alli, Allittamarai, Ambal, Karuneythal, Nilotpalam, Vellampal (Tamil), Alli Kaada, Allikada, Indeevaramu, Indivara, Kalava Puvvu, Kaluvva Poovu, Nalla Kalava, Nallani Padmamu, Neeti Tamara, Tellakaluva (Telugu), Neelofar (Urdu)
Indonesia: Tunjung
Kampuchea: Rum-Chang
Laos: Bwa Khiiz Beez, Bau-Na Neai
Malaysia: Ati-Ati Paya, Kelipok, Seroja Biru, Telepok, Teratai Kecil, Tunjong Biri
Nepali: Nilo Kamal
Philippines: Talailo, Tunas (Bisaya), Labas, Lauas, Pulau, Tunas (Tagalog)
Spanish: Nenúfar De Sri Lanka, Rojo Azul
Sri Lanka: Nil Mahanel, Nil Mānel
Swedish: Stjärnlotus
Thai: Bua-Phuan, Bua-Khap, Bua-Phan, Bua-Sai
Vietnamese: Súng, Súng Lam

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Origin/Distribution

The native range of this aquatic plant extends from the Indian subcontinent to Papua New Guinea and Australia.

Agroecology

In its native range, this aquatic plant occurs in full sun, in ponds, in shallow lakes and in waterways.

Edible Plant Parts and Uses

The rhizomes are eaten raw or roasted, seeds are parched and eaten and flowers are also eaten (Uphof 1968; Hedrick 1972; Tanaka 1976; Facciola 1990). The rhizomes are rich in starch and eaten as food (Schmelzer 2001). The tender young leaves and flower peduncles are also valued as food (Irvine and Trickett 1953).

Botany

A clump forming perennial with underwater, thick, black, spongy, unbranched tuberous rhizomes anchored in the mud by spreading roots. Leaf blade large, flat, elliptic–orbicular to orbicular (Plate 1), 7–15(−40) cm in diameter papery, abaxially glabrous, green and waxy, abaxially darker and pubescent, peltate a few mm from base of sinus, base cordate, basal lobes parallel to spreading, margin subentire to crenate. Leaves floating on the water surface, on long petiole, and may spread 1.4–1.5 m from where the rhizome is rooted. Flower slightly emergent above water, 4–15 cm across, bisexual, stellate and regular (actinomorphic), solitary, on 1–1.5 m long peduncle, with 4 lanceolate to oblong–lanceolate sepals, 2.5–6 cm, slightly veined, persistent, green on the outside and white to blue on the inside, adnate to base of receptacle; receptacle with cup-shaped apex; petals numerous 10–35, multiseriate, linear–oblong to lanceolate, 4.5–5.5 cm, purple, blue (Plates 1, 2 and 3), or purple-red, or white tinged with purple, weakly fragrant; stamens numerous, outer with broad petaloid yellow filaments, and anthers yellow with apically appendaged connective; carpels 10–16 partially connate with triangular tapering appendages, multiloculed;

Plate 1 Lotus lily flower and leaf

Plate 2 Close view of flower on long erect stalk

Plate 3 Close-up of lotus lily flower

stigma radiate with 8–10 or more rays. Fruit oblate, 3–5 cm diameter, spongy containing numerous ellipsoid–globose, 1–1.7 mm long seeds striated with longitudinal rows of hairs.

Nutritive/Medicinal Properties

The following phenolics were isolated from the hot methanol flower extract: 3-*O*-methyl kaempferol, kaempferol, 3-*O*-methyl quercetin, quercetin, methyl gallate, gallic acid and equilibrated mixture of methyl m- galloylgallate and *p*-galloylgallate, corilagin, astragalin, 3-*O*-methyl quercetin 3′-*O*-β-D-xylopyranoside, quercetin 3′-*O*-β-D-xylopyranoside and 2,3,4,6-tetra-*O*-galloyl D-glucose (Kizu and Tomimori 2003). Gallic acid in hydroalcoholic extract of dried flowers was quantified (Rakesh et al. 2009). The average recovery of gallic acid was found to be 98.33 %. 1,2,3,4,6-Penta-*O*-galloyl-β-D-glucose was identified together with two phenolic compounds of gallic acid and corilagin from the flowers (Huang et al. 2010). Nymphayol (25,26-dinorcholest-5-en-3beta-ol), a steroid, was isolated from the flowers (Subash-Babu et al. 2009; Raja et al. 2010). The flowers were found to contain flavonoids, gallic acid, astragalin, quercetin and kaempferol and nymphayol (Das et al. 2012). A steroid was isolated from methanolic fraction of ethanol extract of seeds of *Nymphaea stellata* and was characterized as 24-methyl-cholesta-5-ene-3-ol-(23,24,29)-cyclopropane (1) and designated as nymphasterol (Verma et al. 2012). Phytochemical analysis revealed the presence of phenols, flavones, tannins, protein, reducing sugars, glycosides, saponins, alkaloids and steroids in *N. nouchali* seeds (Parimala and Shoba 2013). The total tannin content of hydroalcoholic seed extract was high (195.84 GE/g), followed by phenolics (179.56 GE/g) and flavonoids (23.55 QE/g); total carbohydrate content was 13.92 %, total protein 17.47 % and total content lipid 0.1 %. The total antioxidant capacity was high with 577.73 mg vitamin E/g of the extract, and the seed extract showed a moderately high vitamin C content of 197.22 mg/g. The flowers were reported to contain alkali-soluble polysaccharides (Hoque and Hannan 1997).

β-sitosterol and coclaurine were identified in aerial parts of *N. stellata* (Mukherjee et al. 1986). Three steroids, namely, 24-ethyl-5α-cholestan-3-one, 5α-stigmast-22-en-3-one and stigmast-5, 22-dien-3-one, were isolated from *N. stellata* stem (Chowdhury et al. 2013).

A lectin (termed NNTL) with molecular mass 27 kDa was purified from *Nymphaea nouchali* tuber extracts (Kabir et al. 2011). NNTL was glycoprotein containing 8 % neutral sugar and rich in leucine, methionine and glycine residues. NNTL was an *o*-nitrophenyl β-D-galactopyranoside sugar-specific lectin that agglutinated rat, chicken and different groups of human blood cells and exhibited high agglutination activity over the pH range 5–9 and temperatures of 30–60 °C. It had a requirement of Ca(2+) for the stability.

Proximate composition of *N. nouchali* (red-flowered) and *N. stellata* (blue-flowered) plants were reported respectively as dry matter 8.4, 7.0 %, crude protein 16.8, 16.7 %, ash 18.7, 14.1 %, crude fat 2.8, 2.6 %, crude fibre 24, 19.1 %, nitrogen free extract 35.4, 42.6 %, Na 1.19, 0.93 %, K 2.23, 1.30 %, Ca 0.52, 0.95 % and P 0.32, 0.21 % (Banerjee and Matai 1990). The plants also contained anti-nutritive factors such as nitrates 2.0, 0.9 %; total polyphenols 8.7, 10.2 %; free polyphenols 5.9, 9.3 %; bound polyphenols 2.8, 0.9 %; and alkaloids. All parts of the plant except the seeds were reported to contain the alkaloid nymphaeine (Schmelzer 2001).

Antioxidant Activity

N. nouchali leaf extracts exhibited good antioxidant activity in the DPPH (1,1-diphenyl-2-picrylhydrazyl) assay (Noor et al. 2013). The IC_{50} value of the ethanol extract was 10.02 µg/mL and chloroform extract 13.11 µg/mL compared to ascorbic acid with an IC_{50} value of 19.89 µg/mL. The content of phenolic compounds in the extracts correlated with the antioxidant activity, being higher in ethanol leaf extract (6.53 mg/g GAE) and lower in chloroform leaf extract (5.55 mg/g GAE). Flavonoid contents were 4.58 mg/g quercetin

equivalent for chloroform extract and 5.99 mg/g quercetin equivalent for the ethanol extract. Both extracts contained almost similar amount of total antioxidant capacity 2.75 mg/g ascorbic acid equivalent (AAE) for the ethanol extract and 2.69 mg/g AAE for the chloroform extract.

The ethanolic and aqueous extracts of *Nymphaea stellata* flower exhibited high antiradical activity against DPPH, nitric oxide and hydroxyl radicals (Somasundaram et al. 2012). The ethanolic extract showed more scavenging activity than the aqueous extract. The antioxidant activity of the extract was comparable with that of the standard. In the DPPH, peroxynitrate ($ONOO^-$) and total ROS scavenging assays, the methanolic flower extract showed good antioxidant activity with IC_{50} values of 10.33, 20.16 and 31.72 μg/mL, respectively (Jahan et al. 2012).

The activities of the seed extract against DPPH, nitric oxide and lipid peroxidation were concentration dependent with IC_{50} values of 42.82, 23.58 and 54.65 μg/mL, respectively (Parimala and Shoba 2013).

Antidiabetic Activity

Oral administration of *Nymphaea stellata* leaf ethanol extract to alloxan diabetic rats at dose of 100 and 200 mg/kg/day for 7 days reduced significantly the elevated plasma glucose level induced by intraperitoneal injection of 120 mg/day of alloxan by 31.6 and 42.6 % respectively (Dhanabal et al. 2007). Further, the treatment significantly lowered the plasma level of cholesterol and triglyceride.

Results of animal studies suggested that *N. stellata* flower hydroethanol extract exhibited antihyperglycaemic as well as antihyperlipidaemic effects on alloxan-induced diabetic rats (Rajagopal and Sasikala 2008a, b). The flower extract exerted a significant reduction in levels of fasting blood glucose, water intake, food intake, urine sugar, blood urea, total lipids, total cholesterol, triglycerides, phospholipids, free fatty acids, low density lipoproteins, very low density lipoproteins and atherogenic index. It also elicited a significant increase in body weight, plasma insulin, protein, haemoglobin and high-density lipoprotein levels. Treatment with the flower extract in alloxan-induced diabetic rats increased the hexokinase and LDH activities and decrease glucose-6-phosphate. The results indicated that *N. stellata* flowers possessed promising antidiabetic activity. Oral administration for 45 days of nymphayol (25,26-dinorcholest-5-en-3beta-ol) (isolated from the flowers) significantly lowered the blood glucose level, and more importantly it effectively increased the insulin content in diabetic rats (Subash-Babu et al. 2009). Further, nymphayol increased the number of beta cell mass enormously. Islet-like cell clusters in the islets of Langerhans were clearly observed.

Studies showed that *Nymphaea stellata* flower extract exhibited significant intestinal α-glucosidase inhibitory activity, without showing any acute toxicity or genotoxicity, which may be useful in suppressing postprandial hyperglycaemia in diabetics (Huang et al. 2010). The main α-glucosidase inhibitor, 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose, was identified in the flower extract. Nymphayol, a steroid isolated from the flowers, had been scientifically proven to be responsible for the traditionally claimed antidiabetic activity; it reverted the damaged endocrine tissue and stimulated secretion of insulin in the B cells (Raja et al. 2010).

Antitumour Activity

N. nouchali was found to be moderately active in inhibiting tumour promoter 12-*O*-hexadecanoylphorbol-13-acetate (HPA)-induced Epstein–Barr virus activation in Raji cells (Murakami et al. 2000).

A lectin (termed NNTL) from *N. nouchali* tuber, exhibited antiproliferative activity against EAC (Ehrlich ascites carcinoma) cells with 56 and 76 % inhibition in vivo in mice at 1.5 and 3 mg/kg/day, respectively (Kabir et al. 2011). The crude extract and the fractions of *N. stellata* showed significant cytotoxic effect when subjected to brine shrimp lethality bioassay (Chowdhury et al. 2013).

Hepatoprotective Activity

Oral administration of varying dosage of extract of *Nymphaea stellata* flower extract to albino rats for 10 days afforded good hepatoprotection against carbon tetrachloride-induced elevation in serum marker enzymes and serum bilirubin, liver lipid peroxidation and reduction in liver glutathione, liver glutathione peroxidase, glycogen, superoxide dismutase and catalase activities (Bhandarkar and Khan 2004). Recently, *Nymphaea stellata* flowers had been reported to have hepatoprotective activity against CCl_4-induced hepatic damage (Das et al. 2012).

Aphrodisiac Activity

Administration of the ethanol leaf extract to male rats produced an overall increase in sexual behaviour as evidenced by an increase in mounting frequency, intromission frequency and ejaculatory latency and a decrease in mounting latency, intromission latency and post-ejaculatory interval (Raja et al. 2012). Increase in orientational activities, weight of primary and accessory sex organs, libido and potency were also observed. The results indicated that *N. stellata* leaf extract had aphrodisiac activity particularly at the dose level 500 mg/kg and supported its traditional claim.

Anti-inflammatory Activity (Membrane Stabilizing Activity)

Methanolic flower extract at the dose of 100 and 200 mg/kg caused significant inhibition of carrageenan-induced paw oedema after 4 h in a dose-dependent manner (Jahan et al. 2012). The methanol extract and fractions of *N. nouchali* petals at a concentration of 1.0 mg/mL significantly protected the lysis of mice erythrocyte membrane induced by hypotonic solution and heat, as compared to the standard acetyl salicylic acid (0.10 mg/mL) (Sikder et al. 2012). In hypotonic solution-induced haemolysis, the aqueous-soluble fraction (AQSF) inhibited 66.55 % haemolysis of RBC as compared to 71.9 % produced by acetyl salicylic acid. The chloroform and petroleum ether-soluble extractives also revealed significant inhibition of haemolysis of RBCs.

Analgesic Activity

Methanolic flower extract at the dose of 100 and 200 mg/kg produced a significant increase in pain threshold in hot plate method whereas significantly reduced the writhing caused by acetic acid and the number of licks induced by formalin in a dose-dependent manner (Jahan et al. 2012).

Antimicrobial Activity

A lectin (termed NNTL) from *N. nouchali* tuber showed toxicity against brine shrimp nauplii with an LC_{50} value of 120 µg/mL and exerted strong agglutination activity against four pathogenic bacteria (*Bacillus subtilis, Sarcina lutea, Shigella shiga* and *Shigella sonne*i) (Kabir et al. 2011). Both the aqueous-soluble and chloroform-soluble fractions of *N. nouchali* petals exhibited the significant growth inhibition of in vitro *Bacillus megaterium, Bacillus subtilis, Staphylococcus aureus, Sarcina lutea, Escherichia coli, Pseudomonas aeruginosa, Shigella boydii, Shigella dysenteriae, Vibrio parahaemolyticus* and also *Saccharomyces cerevisiae* (Sikder et al. 2012) The carbon tetrachloride-soluble fraction showed highest growth inhibitory activity against *Vibrio parahaemolyticus*. The crude methanol extract exhibited mild antimicrobial activity against most of the test organisms, while the petroleum ether-soluble fraction revealed moderate inhibition against *Shigella boydii.*

Methanol flower extract of *N. nouchali* was found to possess better antibacterial activity in vitro against two pathogenic bacteria, *Bacillus subtilis* and *Sarcina lutea*, than the commercial antibiotic nalidixic acid (Dash et al. 2013). The acetone flower extract showed moderate sensitivity and *Xanthomonas campestris*

showed resistance to ethyl acetate and petroleum spirit extracts.

Traditional Medicinal Uses

Nymphaea stellata is an important and well-known medicinal plant, widely used in the Ayurveda and Siddha systems of medicines for the treatment of diabetes, inflammation, liver disorders, urinary disorders, menorrhagia, blennorrhagia and menstruation problem, as an aphrodisiac and as a bitter tonic (Raja et al. 2010). In India, the leaves, roots and flowers are used as cardiotonic, emollient, diuretic, antidiabetic, and aphrodisiac and used for inflammatory diseases of brain, for removing impurities from blood and treating urinary tract infections (Kirtikar and Basu 1989).

In Bangladesh, powdered rhizomes are deemed to be demulcent and diuretic and used in piles, dysentery and dyspepsia (Yusuf et al. 2009). Flowers are astringent, cardiotonic and refrigerant used to alleviate cough, bile, vomiting, giddiness, worms and burning of the skin. Filaments are astringent and cooling and deemed useful in burning of the body, bleeding piles and menorrhagia. Seeds are used as a cooling medicine in cutaneous diseases; *Nymphaea stellata* flowers are used as a traditional medicine in India and Nepal to treat diabetic disease (Huang et al. 2010). Especially the rhizomes, but also the other parts of *Nymphaea nouchali*, are considered astringent and tonic in Southeast Asia, and a decoction is given for diarrhoea (Schmelzer 2001). In Vietnam, the rhizomes are also used as remedy back ache and stomach ache and in Cambodia as a therapy for colic. An infusion of the fresh rhizomes is deemed emollient and diuretic and employed for blennorrhagia and infections of the urinary tract. In the Philippines, the slightly bitter juice of the leaves and petioles is administered for gonorrhoea. Leaf juice possesses mildly narcotic properties and is rubbed on the forehead and temples to produce sleep. In Cambodia, leaf juice or the macerated leaves are used as an ingredient of a lotion applied to the skin for fever. The flowers are astringent and taken as a cardiotonic in India and Thailand.

Other Uses

N. nouchali is highly valued as a garden ornamental flower in Thailand and Myanmar to decorate ponds and gardens. It is also popularly grown for its flowers, and dwarf varieties are used as an aquarium plant for its underwater foliage.

Although the plant has been reported to be used for animal forage, studies revealed that on the basis of overall nutrient compositions, *N. nouchali* (red-flowered) and *N. stellata* (blue-flowered) plants do not contain sufficient quantities of nutrients but are safe enough to be considered as potential livestock feed (Banerjee and Matai 1990).

Comments

Nymphaea nouchali (white-flowered form) is the national flower of Bangladesh while the blue-flowered form is the national flower of Sri Lanka.

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Forsythia × *intermedia*

Scientific Name

***Forsythia* × *intermedia* Zabel**

Synonyms

Forsythia × *densiflora* (Koehne) Koehne, *Forsythia* × *intermedia* var. *densiflora* Koehne, *Forsythia* × *intermedia* var. *divaricata* Koehne, *Forsythia* × *intermedia* var. *primulina* Rehder, *Forsythia* × *intermedia* var. *spectabilis* (Koehne) Spath, *Forsythia* × *intermedia* var. *vitellina* Koehne, *Forsythia* × *spectabilis* Koehne, *Forsythia* × *vitellina* (Koehne) Koehne

Family

Oleaceae

Common/English Names

Border Forsythia, Forsythia, Golden Bells, Showy Forsythia, Yellow Bells

Vernacular Names

French: Fosrsythia
German: Garten-Forsythie; Hybrid-Forsythie
Italian: Forsizia

Origin/Distribution

The hybrid is considered to be a cross between *Forsythia viridissima* and *F. suspensa* var. *fortune*, both native of East Asia. A plant of seedling origin was discovered growing in the Göttingen Botanic Gardens in Germany by the director of the municipal gardens in Münden, H. Zabel, in 1878 who formally described and named the hybrid in *Gartenflora* in 1885. Repeated crosses of its two parents have made reiterations of *F.* × *intermedia* quite variable (Plate 1).

Agroecology

A cool climate plant; thrives in full sun or partial shade, in moist, well-drained acid, neutral or alkaline soils including sand, loam, clay and chalk.

Edible Plant Parts and Uses

The blossoms are spicy, minty and slightly bitter (Derby 1997; Deane 2007–2012; Anonymous 2012). They add a cheery garnish to salads. These beautiful flowers can be steamed and dried, used in decoctions and infusions or processed into teas and Forsythia syrup (Local Kitchen 2009).

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Plate 1 Flowers and leaves

Botany

A deciduous branched, erect shrub 1–2.5 m high. Stem grey brown, quadrangular and prominently lenticellate. Leaves opposite, petiolate, medium to dark green above, pale green below, simple, narrowly ovate to lanceolate, 7.5–13.5 cm long by 1.5–2.5 cm wide, sometimes tri-parted to trifoliate, with entire or serrated margins and acute tips. Flowers relatively large, bright yellow, borne profusely before the leaves in Spring. Calyx deeply 4-lobed. Corolla campanulate with 4 spreading lobes longer than tube, imbricate in bud. Stamen 2 inserted at base of corolla tube. Style slender with bifid stigma. Fruit a dry, loculicidal capsule containing several winged seeds.

Nutritive/Medicinal Properties

Four lignans [phillygenin, (+)-epipinoresinol, arctigenin and matairesinol], four lignan glucosides [phillyrin, (+)-epipinoresinol-4″-β-D-glucoside, arctiin and matairesinoside], two phenylpropanoids [forsythiaside and acteoside] and one flavonoid [rutin] were isolated from the leaves of *Forsythia* × *intermedia* Zabel, a hybrid, derived from parents *F. suspensa* Vahl and *F. viridissima* Lindley (Nishibe et al. 1988). All the major compounds in both of the parents occurred additively in the hybrid as major compounds.

Leaf and stem material of *Forsythia intermedia* were found to contain four main lignans and their *O*-glucosides, identified as the dibenzylbutyrolactone derivatives (−)-arctigenin, arctiin [(−)-arctigenin 4′-*O*-glucoside], matairesinol and (−)-matairesinol 4′-*O*-glucoside, together with the furofuran lignans (+)-phillygenin, phillyrin [(+)-phillygenin 4-*O*-glucoside], (+)-epipinoresinol and (+)-epipinoresinol 4′-*O*-glucoside (Rahman et al. 1990b). The lignan contents varied according to tissue type and season. Feeding experiments with young shoots of *Forsythia intermedia* showed phenylalanine and ferulic acid to be good precursors of the dibenzylbutyrolactone lignan arctigenin and the furofuran lignans phillygenin and epipinoresinol (Rahman et al. 1990a). Although matairesinol was incorporated into arctigenin, and epipinoresinol into phillygenin, in accord with late methylation steps in the biosynthetic pathway, some incorporation of label from one lignan class into the other was observed, particularly from epipinoresinol into arctigenin. It was found that the lignans arose by oxidative coupling of two coniferyl alcohol units, rather than from two ferulic acid or coniferaldehyde units. The observed increase in isotopic ratio probably resulted from a primary isotope effect in the reversible oxidation–reduction reactions interrelating cinnamic acids and cinnamyl alcohols. Callus and cell suspension cultures of *Forsythia intermedia* exhibited the capacity to produce lignans which was markedly dependent on the culture medium used and not on the source of the original explants (Rahman et al. 1990c). Cell lines were established which synthesized either matairesinol 4′-*O*-glucoside or epipinoresinol 4′-*O*-glucoside as the major lignans.

Studies by Ozawa et al. (1993) found that post-coupling methylation did not proceed via regiospecific methylation of matairesinol to give arctigenin directly in *Forsythia intermedia* cell-free extracts. Instead, regiospecific glucosylation first occurred to produce matairesinoside; subsequent methylation afforded arctiin, which was then converted into arctigenin via action of a β-glucosidase. Further, the cell-free extracts also catalyzed the synthesis of (+)- and (−)-isoarctigenins, with (−)-matairesinol again the preferred substrate. A crude cell-free extract from *Forsythia intermedia* catalyzed the formation of (−)secoisolariciresinol, and not its (+) enantiomer, when

incubated with coniferyl alcohol in the presence of NAD(P)H and H_2O_2 (Umezawa et al. 1990). Umezawa et al. (1991) found that in *Forsythia intermedia* plant tissue, the lignans, (−)-secoisolariciresinol and (−)-matairesinol, were derived from two coniferyl alcohol molecules. Administration of (+−)-[Ar-3H]secoisolariciresinols to excised shoots of *F. intermedia* resulted in a significant conversion into (−)-matairesinol. Experiments using cell-free extracts of *F. intermedia* confirmed and extended these findings. In the presence of NAD(P)H and H_2O_2, the cell-free extracts catalyzed the formation of (−)-secoisolariciresinol, with either labelled [8–14C]- or [9,9-2H2,OC2H3]coniferyl alcohols as substrates. Katayama et al. (1992) found that soluble cell-free preparations from *Forsythia intermedia* catalyzed the formation of the enantiomerically pure lignan, (−)-secoisolariciresinol, when incubated with coniferyl alcohol in the presence of NAD(P)H and H_2O_2. Surprisingly, (−)-pinoresinol also accumulates in this soluble cell-free assay mixture in >96 % enantiomeric excess, even though it is not the naturally occurring antipode present in *Forsythia* sp.

F. suspensa, one of its parents, is considered one of the 50 fundamental herbs in Chinese herbology.

Other Uses

A popular ornamental plant in informal gardens and also planted as hedging, screens, on slopes and banks. The flowers are also used as cut flowers.

Comments

The plant is readily propagated by using semi-hardwood cuttings.

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Jasminum sambac

Scientific Name

***Jasminum sambac* (L.) Sol.**

Family

Oleaceae

Synonyms

Jasminum bicorollatum Noronha, *Jasminum blancoi* Hassk., *Jasminum fragrans* Salisb. [Illeg.], *Jasminum heyneanum* Wall. ex G. Don, *Jasminum odoratum* Noronha, *Jasminum pubescens* Buch.-Ham. ex Wall. [Inval.], *Jasminum quadrifolium* Buch.-Ham. ex Wall. [Inval.], *Jasminum quinqueflorum* B. Heyne ex G. Don, *Jasminum quinqueflorum* var. *pubescens* G. Don, *Jasminum sambac* var. *duplex* Voigt, *Jasminum sambac* var. *gimea* (Zuccagni) DC., *Jasminum sambac* var. *goaense* (Zuccagni) DC., *Jasminum sambac* var. *heyneanum* (Wall. ex G. Don) C.B. Clarke, *Jasminum sambac* var. *kerianum* Kuntze, *Jasminum sambac* var. *nemocalyx* Kuntze, *Jasminum sambac* var. *plenum* Stokes, *Jasminum sambac* var. *syringifolium* Wall. ex Kuntze, *Jasminum sambac* var. *trifoliatum* Vahl, *Jasminum sambac* var. *trifoliatum* (L.) Sims, *Jasminum sambac* var. *undulatum* (L.) Kuntze, *Jasminum sambac* var. *verum* DC., *Jasminum sanjurium* Buch.-Ham. ex DC. [Inval.], *Jasminum undulatum* (L.) Willd., *Jasminum sambac* Roxb., *Mogorium gimea* Zuccagni, *Mogorium goaense* Zuccagni, *Mogorium sambac* (L.) Lam., *Mogorium undulatum* (L.) Lam., *Nyctanthes goa* Steud., *Nyctanthes sambac* L., *Nyctanthes undulata* L.

Common Names

Arabian Jasmine, Asian Jasmine, Asiatic Jasmine, Indian Jasmine, Jasmin, Maid of Orleans, Sacred Jasmine, Sambac Jasmine, Tuscan Jasmine

Vernacular Names

Arabic: Full
Bangladesh: Bel, Beli
Chamorro: Sampagita
Chinese: Mo Li Hua, Mo Li
Chuukese: Ulo
Cook Islands: Pitate, Pītate Papa'Ā (Maori)
Cuba: Diamela
Czech: Jasmín Arabský
Danish: Tempeljasmin
Dutch: Arabische Jasmijn, Malati
Estonian: Valgeõieline Jasmiin
Finnish: Arabianjasmiini
French: Jasmin D'arabie
German: Arabischer Jasmin
Hawaiian: Pikake, Pīkake
I-Kiribati: Te Bitati
India: Beli, Ban Mallika (Bengali), Banmallika, Bel, Chamba, Bel Mogra, Mogra, Mogre-Ke-Phul, Motia, Mugra (Hindi), Chandumallige, Dundumallige, Elusuttinamallige, Gundumallige,

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Iravantige, Kadurumallige, Kolumallige, Mallige, Mallige-Huvvu (Kannada), Moghra (Marathi), Juhi Mahli (Oriya), Asphota, Mallika, Navamalika, Vanamallika, Varshiki (Sanskrit), Anaimalli, Anangam, Atittacenam, Cakurtti, Calparani, Caturtti, Ciriparani, Cumati, Curanaci, Curanuva, Iruvachi, Iruvadi, Kalici, Karumugai, Kenta, Koguttam, Kudamalligai, Kuvaku, Madurai, Makakocari, Maladi, Malli, Malligai, Malligaip-Pu, Malligam, Mallikaipu, Mallip-Pu, Mukuram, Peramalli, Peramallikai, Pitari, Tiraciravam, Tirikartta, Tirikattaceti, Tirikattam, Tunkamalli, Tunkamallicceti, Visamaccuranacani (Tamil), Boddumalle, Bondumalle, Gundemalle, Malle, Malle-Puvvulu, Mallelu, Manmathabanamu, Virajadi, Virajaji (Telugu)

Indonesia: Melati, Melati Putih, Menur
Italian: Gesimino D'arabia, Mugherine
Japanese: Jyasumin No Hana, Matsuri
Khmer: Molih
Malaysia: Melati, Bunga Melor
Marquesan: Pitate;
Nauruan: Rimone
Pakistan: Kaliyan
Philippines: Manul (Bisaya), Lumabi, Malul (Maguindanao), Kulatai, Kampupot, Pongso (Pampangan), Hubar, Malur (Sulu), Sampagita, Kampupot (Tagalog)
Polish: Jaśmin Wielkolistny
Portuguese: Bogarim, Jasmim
Samoan: Pua Samoa, Pua Sosola, Pua Sosolo
Spanish: Jazmín De Arabia, Jazmín De Duque, Sampaguita
Swedish: Arabisk Jasmin
Tahitian: Pitate, Pitate Maohi
Thailand: Mali, Maliwan, Khao Taek, Tiamuun, Mali Son
Turkish: Arap Yasemini, Yasemini
Tuvaluan: Pitasi
Vietnamese: Lai, Lai Hoa Nhai

Origin/Distribution

The species probably originated from India, Bengal to Sri Lanka and Myanmar, Yunnan and adjacent mountains of Guizhou and Guangxi in China. It was introduced into Malaysia and Java, now cultivated widely in the Malesian region and the Pacific Islands.

Agroecology

In its native habitat, it is found from near sea level to 800 m altitude. Jasmine grows on almost any soil type with soil pH of 4.9–8.3 and ample water supply and in full sun in areas with temperatures from 11 to 28 °C and annual precipitation of 300–2,800 mm.

Edible Plant Parts and Uses

Jasmine flowers are edible, primarily used in teas and flavouring; the flowers are also a source of an essential oil employed as flavouring (Grieve 1971; Morton 1976; Tanaka 1976; Facciola 1990; Barash 1997; Creasey 1999; Roberts 2000; Hu 2005; Wetwitayaklung et al. 2008; Mittal et al. 2011). Flowers are also added to dry food stuff (tea, rice) for fragrance.

In China, the flower is processed and used as the main ingredient in jasmine tea. It is similarly used in Java to flavour tea to prepare jasmine tea. The flowers are also used for flavouring in other herbal and black teas and used in dessert, e.g. jasmine and strawberry dessert (Roberts 2000). The flowers can be used to infuse simple syrups, and the syrups are used as a base for sorbets or ice cream or it can be poured over melons, figs and peaches (Creasey 1999).

Botany

Scandent or erect, evergreen shrub growing to 2 m tall with pubescent, terete, angular twigs. Leaves are opposite or in whorls of three, entire, elliptic or broad elliptic to suborbicular, obtuse at both ends, very variable in size, up to 9 cm long and 6 cm broad, glabrous, shining green above (Plates 1 and 2); nerves 4–6 on each side of midrib prominent beneath; petiole short, pubescent. Flowers very fragrant, in 2–5-flowered terminal cymes, pedicels up to 6 mm; bracts linear, subulate

Plate 1 Jasmine flowers, buds and leaves

Plate 2 Close view of jasmine flowers

Plate 3 Jasmine flower garland

up to 6 mm long. Calyx lobe 5–9, linear, 1 cm long, V-shaped, pubescent. Corolla white, simple or double, tube 0.7–1.5 cm long, lobes 5–9, oblong, acute or obtuse (Plates 1, 2 and 3). Stamens, 2, included, ovary, 2-loculed. Berry simple or didymous, globose, 10 mm across, purplish-black when ripe.

Nutritive/Medicinal Properties

Flower Phytochemicals

A secoiridoid glucoside 8,9-dihydrojasminin (4), 4,9-deoxy-jasminigenin (1), jasminin (2) and unidentified compound (3) were isolated from the flowers (Ross and Abdel-Hafiz 1985). Twenty -eight volatile compounds were identified in the fragrance distillate *of J. sambac* (Sun et al. 1985). The major components were linalool, benzyl acetate, *cis*-caryophyllene, *cis*-3-benzyl benzoate, methyl anthranilate and indole. Other components included 1-methylethyl-benzene; Δ-3-carene; styrene; 1,7-octadien-3-one, -2-methyl-6-methylene; 3-hexene-1-yl-acetate, *cis*-3-hexene-1-ol; *cis*-3-hexenyl-*N*-butyrate, linalool oxide; α-copaene, β-elemene; *trans*-caryophyllene; methyl benzoate; γ-muurolene; farnesol, γ-cadinene; benzyl alcohol; torreyol, *cis*-3-hexenyl benzoate; *trans*-3-hexenyl benzoate, *trans*-β-farnesene, 11-tricosane, tetracosane and benzyl benzoate. Besides a known trimeric iridoidal glycoside, sambacoside A, five new oligomeric iridoidal glycosides, molihuasides, A–E were isolated from *Jasminum sambac* flowers (Zhang et al. 1995). Among them, molihuasides A and C–E represented new dimeric iridoidal glycosides and molihuaside B a new trimeric iridoidal glycoside.

Linalyl β-D-glucopyranoside 1 and its 6′-*O*-malonate 2 were isolated as aroma precursors of linalool from flower buds of *Jasminum sambac* (Moon et al. 1994). Benzyl 6-*O*-β-D-xylopyranosyl-β-D-glucopyranoside (β-primeveroside) (1), 2-phenylethyl β-primeveroside (2) and 2-phenylethyl

6-*O*-α-L-rhamnopyranosyl-β-D-glucopyranoside (β-rutinoside) (3) were isolated as aroma precursors of benzyl alcohol and 2-phenylethanol from flower buds of *Jasminum sambac* (Inagaki et al. 1995). The potent odorants found in Jasmine flowers included linalool (floral), methyl anthranilate (grapelike), 4-hexanolide (sweet), 4-nonanolide (sweet), (E)-2-hexenyl hexanoate (green) and 4-hydroxy-2,5-dimethyl-3(2H)-furanone (sweet) (Ito et al. 2002). Secondary metabolites, namely, caryophyllene oxide (1), a mixture of benzyl benzoate (2) and farnesyl acetate (3), methyl isoeugenol (4), squalene (5) and sitosterol (6) were isolated from *J. sambac* flowers (Ragasa et al. 2003). The scent of the flowers was attributed to compounds 2–4. Nine known compounds were isolated from the flowers of *Jasminum sambac* and elucidated as benzyl-*O*-β-D-glucopyranoside (1), benzyl-*O*-β-D-xylopyranosyl (1 → 6)-β-D-glucopyranoside (2), tertraol (3), molihuaoside D (4), sambacoside A (5), sambacoside E (6), rutin (7), kaempferol-3-*O*-(2, 6-di-*O*-α-L-rhamnopyranosyl)-β-D-galactopyranoside (8) and quercetin-3-*O*-(2, 6-di-*O*-α-L-rhamnopyranosyl)- β-D-galactopyranoside (9) (Liu et al. 2004).

Methyl anthranilate and (R)-(−)-linalool were found to be the key odorants of the jasmine tea flavour. The analytes identified in the volatile organic compounds from *J. sambac* flowers included alcohols, esters, phenolic compounds and terpenoids (Pragadheesh et al. 2011). The main constituents identified in the flower aroma of *Jasminum sambac* using different solid-phase microextraction fibres were *cis*-3-hexenyl acetate, (*E*)-β-ocimene, linalool, benzyl acetate and (*E*,*E*)-α-farnesene in a high proportion. Among other constituents identified, *cis*-3-hexenyl acetate, linalool and benzyl acetate were major aroma contributors in plucked and living flowers extracts. PDMS/DVB fibres recorded the highest emission for benzyl acetate while the (*E*)-β-ocimene proportion was highest in DVB/Carboxen/PDMS fibres when compared with the rest. The highest linalool content, with increasing proportion from morning to noon, was found using mixed coating fibres. The ethanolic Jasmine flower extract was found to contain mixtures of coumarins, cardiac glycosides, essential oils, flavonoids, phenolics, saponins and steroids, while alkaloids, anthraquinones and tannins were not detected (Kunhachan et al. 2012).

Thirty-seven constituents were identified in the headspace of *J. sambac* flowers (Zhu et al. 1984). They are ethyl acetate (0.22 %), 3-methyl cyclopentene (0.13 %), 2-methyl hexane (0.09 %), 2,2,3,4-tetramethyl pentane (0.07 %), n-heptane (0.03 %), phenyl- 2-propanone (0.05 %), 2-methyl butate (0.03 %), 3-methyl heptane (0.02 %), butyl acetate (0.12 %), 2-methyl propen-2-1y acetate (0.04 %), *n*-hexen-l-ol (1.06 %), 6-methyl-2-hepta none (0.18 %), 6-methyl 5-hepten-2-one (0.12 %), carbamyl benzoate (0.42 %), β-pinene (0.53 %), 3-hexenyl acetate (13.80 %), limonene (0.12 %), benzaldehyde (1.13 %), ocimene (0.06 %), methyl benzoate (6.27 %), linalool (25.01 %), *trans*-linalool oxide (0.32 %), benzyl acetate (23.71 %), 3-hexenyl butate (1.72 %), methyl salicylate (2.55 %), cyclohexyl formate (0.10 %), indole (1.83 %), 2, 6-dimethyl 5-heptenal (0.05 %), methyl anthranilate (1.56 %), 2,6-dimethyl heptenal (0.53 %), β-caryophyllene (0.32 %), β-farnesene (0.10 %), humulene (0.21 %), γ-cadinene (0.62 %), *cis*-caryophyllene (13.67 %), *trans*, *trans*-farnesol (0.35 %) and cyclohexyl benzoate (3.37 %). The main volatile constituents of the concrete headspace and absolute of *J. sambac* flowers, respectively, were benzyl acetate (23.7 and 14.2 %), indole (13.1 and 13.4 %), *E*-*E*-α-farnesene (15.9 and 13.1 %), *Z*-3-hexenyl benzoate (4.9 and 9.4 %), benzyl alcohol (7.7 and 8.4 %), linalool (10.6 and 6.3 %) and methyl anthranilate (5.0 and 4.7 %) (Edris et al. 2008). The major volatile constituents of Egyptian *J. sambac* absolute were almost qualitatively similar but quantitatively different from those grown in other geographical regions.

Four alkylated pyridines (1–4), viz., 3-ethylpyridine (1), 3-vinylpyridine (2) 3-ethyl-4-methylpyridine (3) and 4-methyl-3-vinylpyridine (4), and ten alkyl-substituted nicotinates (8–17), viz., methylnicotinate (8), ethyl nicotinate (9), methyl 4-methylnicotinate (10), methyl 5-ethylnicotinate (11), 5-ethylnicotinic acid (12), methyl 5-vinylnicotinate (13), 5-vinylnicotinic acid (14), methyl 5-ethyl-4-methylnicotinate (15), methyl

4-methyl-5-vinylnicotinate (16) and ethyl 5-ethyl-4-methylnicotinate (17), were newly identified in jasmine absolutes with 3 known anthranilates, viz., methyl anthranilate (5), methyl N-methyl anthranilate (6) and methyl N-acetyl anthranilate (7) (Toyoda et al. 1978). The major basic component (29 %) of the Chinese jasmine absolute based on *J. sambac* was methyl 5-ethyl-4-methylnicotinate, while that (86, 72 %) of the other jasmine absolutes, e.g. Egyptian, Moroccan, based on *J. grandiflorum*, was methyl anthranilate.

Fifty components of *J. sambac* absolute were identified by GC–MS on capillary column OV 101 and GC–MS on capillary column PEG-20 M (Wu et al. 1987). Several important components were 2,6-dimethyl heptanal; methyl n-methyl anthranilate; bergamotene; torreyol; *cis*-3-hexenyl butyrate; *cis*-linalool oxide; 2H-pyran-3-ol, 6-ethenyl tetrahydro-2,2,6-trimethyl and a few sesquiterpenes. The chemical components of *J. sambac* absolute by GC–MS on capillary column OV 101 identified included methyl n-methyl anthranilate 0.08 %, bergamotene 0.44 %, torreyol 0.34 %, *cis*-3-hexenyl butyrate 0.27 %, 2H-pyran-3-ol, 6-ethenyl tetrahydro-2,2,6-trimethyl 0.40 %, *cis*-3-hexenol 1.24 %, 3-hexen-1-yl acetate 1.15 %, benzyl alcohol 6.75 %, methyl benzoate 0.45 %, linalool 8.35 %, benzyl acetate 7.53 %, methyl salicylate 3.41 %, indole 2.44 %, 2,6-dimethyl hept-5-en-al 0.57 %, methyl anthranilate 1.15 %, β-elemene 0.38 %, *trans*-caryophyllene trace, humulene trace, γ-cadinene 0.40 %, *cis*-caryophyllene 9.52 %, β-bisabolene 0.20 %, β-cadinene 0.32 %, *cis*-3-hexenyl benzoate 15.58 %, benzyl benzoate 2.12 %, methyl palmitate 0.61 %, 9,11,octadeca-9,12,15-trien-1ol 3.02 %, methyl 16-methyl heptadecanoate 0.25 %, dicosane 0.59 %, 11-tricosane 7.08 % and tricosane 0.31 %. Chemical components of *J. sambac* absolute identified by GC–MS on capillary column PEG-20 M included *cis* 3-hexen-1-yl acetate 0.32 %, 6-methyl-hep-5-en-2-one 0.15 %, *cis*-3-hexenol-1-ol 0.41 %, cyclohexanol 0.11 %, *cis*-3-hexenyl butyrate 0.15 %, *cis*-linalool oxide 0.56 %, benzaldehyde 0.03 %, linalool 8.46 %, β-elemene 0.19 %, *trans*-caryophyllene 0.17 %, methyl benzoate 0.60 %, ethyl benzoate 0.05 %, benzyl formate 0.13 %, γ-cadinene 0.85 %, benzyl acetate 8.09 %, *cis*-caryophyllene 9.98 %, methyl salicylate 0.81 %, farnesol 0.13 %, benzyl alcohol 4.06 %, dendrolasin 0.27 %, torreyol 5.41 %, β-bisabolene 0.21 %, nor-hexenyl benzoate 0.30 %, *trans*-3-hexenyl benzoate 0.35 %, *cis*-3-hexenyl benzoate 17.07 %, methyl anthranilate 4.34 %, 11-tricosane 9.11 %, methyl-9-*cis*, 12-*cis*, 15-*cis* octadecatrienoate 4.03 % and benzyl benzoate 2.25 %.

Major compounds identified in *J. sambac* flower essential oil were citronellol, phenyl ethyl alcohol, geraniol, eugenol, farnesol, geranyl acetate, citrinyl acetate, 2-phenyl ethyl acetate, citral (mixture of *cis* and *trans*), linalool, nerol, neryl acetate and benzaldehyde (Younis et al. 2011). Both harvesting stages, i.e. closed bud and open flower stages, yielded oil with differences in the percentage composition of each component, but flowers harvested at the open stage had higher yield and more components than those from the closed bud stage. Thirty-nine compounds were determined from flower bud essential oils of *J. sambac* cv. Unifoliatum and 38 compounds from the flower buds of cv. Bifoliatum and cv. Trifoliatum, comprising 27 terpenoid, 9 esters, 1 alkane, 1 alcohol and 1 indole compound (Guo et al. 2011). The most abundant compounds were *p*-menth-3-en-1-ol,(−)-isoledene and α-longipinene. Other major compounds included (*Z*)-3-hexenyl pentenoate; acetic acid phenylmethyl ester; benzoic acid ethyl ester; butanoic acid; 4-hexen-1-yl ester; benzoic acid 2-hydroxy-ethyl ester; 1H-indole; γ-elemene; *trans*-caryophyllene; *cis*-α-bisabolene; valencene 2,3-hexen-1-ol benzoate; and γ-gurjunene. Twenty different sesquiterpenoids were found; cv. Unifoliatum had 63.13 %, cv. Bifoliatum had 22.71 % and cv. Trifoliatum 19.68 %. In terms of scent richness, the ranking of the cultivars was cv. Unifoliatum, cv. Bifoliatum and cv. Trifoliatum.

Leaf Phytochemicals

Ross et al. (1982) isolated a new iridoid glycoside, sambacin, quercetin, isoquercetin, rutin, quercetin-3-dirhamnoglycoside, kaempferol-3-rhamnoglycoside, mannitol, α-amyrin and β-sitosterol from the leaves. A lignan-secoiridoid

glucoside named sambocolignoside and an oligomeric iridoid glycoside oleoside 11-methyl ester were isolated from the leaves (Tanahashi et al. 1987). Three tetrameric iridoid glucosides, sambacosides A, E and F, were isolated from the leaves (Tanahashi and Nagakura 1988). Leaves of *Jasminum sambac* were reported to contain the secoiridoid glycosides, jasminin, quercetin, isoquercetin, rutin, quercetin 3-dirhamnoglycoside, kaempferol 3-rhamnoglycoside, mannitol, alpha amyrin, beta sitosterol and an iridoid glycoside, sambacin (Khare 2004). *J. sambac* leaves were found to contain 14 total ash, 8.5 % acid-insoluble ash, 7 % water-soluble ash, 32 % ethanol-soluble extractive, 12.8 % water-soluble extractive and 15 % crude fibre (Sabharwal et al. 2011). The leaves also contained fats, glycosides, carbohydrates, flavonoids, steroids, saponins, proteins and amino acids, tannins and phenolic compounds.

Root Phytochemicals

Dotriacontanoic acid, dotriacontanol, oleanolic acid, daucosterol and hesperidin were isolated from the roots (Zhang et al. 2004).

Antioxidant Activity

The percent yield of extract and the amount of total polyphenols in g/100 g calculated as gallic acid on dried flowers and crude methanolic extracts basis for *J. sambac* were reported as 21.70 (% yield), 0.59 g total polyphenols (g/100 g dried flower) and 2.71 g total polyphenols (g/100 g crude extract) (Wetwitayaklung et al. 2008). Antioxidant capacity for *J. sambac* flowers expressed in TEAC (trolox equivalent antioxidant capacity) = 0.02 and IC_{50} = 571.97 μg/50 μL. There was good linear relationship between antioxidant activity and flower extract concentrations with R^2 = 0.9925.

J. sambac was found to have antioxidant activity. Research demonstrated that using several in vitro models, namely, DPPH radical scavenging activity, nitric oxide radical scavenging activity, hydroxyl radical scavenging activity, β-carotene bleaching assay and reducing power, aqueous extracts of Jasmine leaves exhibited the most potent antioxidant activities over ethyl acetate and n-butanol extracts (Tenpe et al. 2008). This activity was attributed to the presence of polar phenolic compound flavonoid, tannin and other chemicals. In the DPPH free radical scavenging assay, the IC_{50} value of *Jasminum sambac* essential oil and methanol extract were 7.43 and 2.30 μg/mL, respectively (Fatouma et al. 2010). In the β-carotene-linoleic acid assay, oxidation was effectively inhibited by *Jasminum sambac*; the reducing antioxidant activity values of the essential oil and methanol extract were 96.6 and 93.9 %, respectively. When compared to BHT (butylated hydroxytoluene), the essential oil and methanol extract had nearly the same activities.

The methanolic extract of *Jasminum sambac* flower exhibited strong in vitro antioxidant scavenging activity when evaluated using DPPH, ABTS+, hydroxyl radical, hydrogen peroxide, superoxide anion, nitric oxide radical, reducing power, FRAP and total antioxidant capacity assays (Kalaiselvi et al. 2011b). The extract showed maximum inhibition activity at 2.5 mg/mL concentration when compared to the standard antioxidants BHT, vitamin-C, vitamin-E and rutin. The percentage of inhibition increased in a dose-dependent manner. Administration of hydrogen peroxide induced a significant decline in the levels of antioxidant enzymes in goat liver homogenate (Kalaiselvi et al. 2011a). Pretreatment with *J. sambac* methanol extract significantly prevented the decline and maintained them within the normal range. Also the extract normalized the lipid peroxidation which evidently showed that the methanolic extract of *J. sambac* had a potent antilipid peroxidative effect.

Anticancer Activity

Jasminum sambac was one of the 16 plants tested, whose extracts showed significant antiproliferative activity against Hep-2, MCF-7 and Vero cell lines (Talib and Mahasneh 2010). The

crude ethanolic leaf extract produced prominent cytotoxic activity against brine shrimp *Artemia salina* (LC_{50} = 50 μg/mL and LC_{90} = 100 μg/mL) (Rahman et al. 2011). The methanolic extract of *J. sambac* flower was found to possess significant anticancer properties against Dalton's ascites lymphoma-induced Swiss albino mice in in-vitro and in-vivo model (Kalaiselvi et al. 2012). The methanolic flower extract elicited dose-dependent tumour cell proliferation inhibitory activity in both HeLa and mouse fibroblast cells. At concentrations 25–400 μg/mL, the percentage of cell inhibition concentration of normal and cancer cells was found to be 123.3 and 93.8 μg/mL, respectively. The methanolic extract at oral dose of 100 mg/kg body weight exhibited a significant change in the levels of haematological profiles, aspartate transaminase, alanine transaminase, acid phosphatase and lactate dehydrogenase and cancer marker enzymes such as 5′nucleotidase, β-D-glucuronidase and γ-glutamyl transferase as compared to Dalton's ascites lymphoma-induced Swiss albino mice control group.

Antiviral Activity

The water flower extract was found to have varying antiviral potency against herpes simplex viruses (HSV-1 and HSV-2) and adenoviruses including ADV-11 (Chiang et al. 2003).

Central Nervous System Activity

Jasmine sambac is very useful as an antidepressant giving optimism and confidence, producing a feeling of euphoria and helps overcome apathy and listlessness. Jasmine tea has a calming and sedative effect on the nervous system and is especially beneficial in conditions caused by psychological stress and imbalance. Studies found Jasmine tea to cause significant decrease in heart rate and significant increases in spectral integrated values at high-frequency component in comparison with the control (Kuroda et al. 2005). The odour produced calm and vigorous mood states. (R)-(−)-linalool, one of its components, elicited a significant decrease in heart rate and an increase in high-frequency component in comparison with the controls and produced calm and vigorous mood states. The results showed low intensity of jasmine tea odour had sedative effects on both autonomic nerve activity and mood states, and (R)-(−)-linalool, one of its components, could mimic these effects. The researchers also reported that the low-intensity odour produced by diluting 20-fold the jasmine tea used for the high-intensity odour test elicited an increase in parasympathetic nervous activity in both the predilection and antipathy volunteer groups (Inoue et al. 2003). The high-intensity odour produced an increase in parasympathetic nervous activity in the predilection group, and also an increase in sympathetic nervous activity in the antipathy group. The odour of Chinese green tea, a basic ingredient of jasmine tea, produced no effects similar to those of the jasmine tea odour. Their results suggested that the jasmine tea odour activated the parasympathetic nerve, whereas the higher-intensity odour activated the sympathetic nerve in those subjects who disliked the odour.

Vasodilatation Effect

Compared with the control group, the 95 % ethanolic jasmine flower extract in 0.05 % DMSO clearly reduced tonus of isolated rat endothelium thoracic aortic rings preconstricted with phenylephrine (10^{-6} M) in a dose-dependent manner (Kunhachan et al. 2012). This pharmacological effect disappeared after the preincubation of the rings with atropine (10^{-6} M) or with N(ω)-nitro-l-arginine (10^{-4} M). The effects were postulated to the actions of the active components on the vessel muscarinic receptors or by causing the release of nitric oxide.

Antimicrobial Activity

Secondary metabolites, caryophyllene oxide (1), benzyl benzoate (2), farnesyl acetate (3) and methyl isoeugenol (4), isolated from *J. sambac*

flowers exhibited moderate activities against *Pseudomonas aeruginosa* and *Aspergillus niger* and slight activity against *Escherichia coli, Bacillus subtilis, Candida albicans* and *Trichophyton mentagrophytes* (Ragasa et al. 2003). Methyl isoeugenol had slight activity against *Staphylococcus aureus*. Jasmine essential oil and six major components exhibit bactericidal activity against *Escherichia coli* with MIC values of 1.9–31.25 µL/mL (Rath et al. 2008). *J. sambac* essential oil and methanol extract showed higher activities against bacterial species than yeast (Fatouma et al. 2010).

Jasminum sambac plant extract also has antimicrobial properties. Studies showed that the plant callus extracts containing alkaloids, glycoside, flavonoids, terpenes, tannin, resin and salicylic acid exhibited highest antimicrobial activity against all the tested skin pathogenic strains: *Staphylococcus albus, Staphylococcus aureus, Proteus mirabilis* and *Salmonella typhi* at concentrations of 500, 250 mg/mL (Joy and Raja 2008). It scored highest with *Salmonella typhi* and lowest against *Staphylococcus aureus*. The studies supported its use in traditional medicine in India for skin disorders. The dried leaves soaked in water and made into poultice are used in indolent ulcers. The young leaves and flowers are used to make a putty, which was mixed and eaten with rice to dry scabies and other skin eruptions. *J. sambac* (flowers and leaves) extracts were very active (>15 mm inhibition zone) against Gram-positive methicillin-resistant *S. aureus* and *B. subtilis*, as well as against Gram-negative *E. coli*, *S. typhimurium* and *K. pneumoniae* and fungi, including the filamentous *A. niger* and *A. fumigatus* and the yeasts *Candida albicans* and *Candida glabrata* (Al-Hussaini and Mahasneh 2009). However, weak anti-quorum sensing activities were observed with extracts of *Jasminum sambac* (flowers and leaves).

Jasminum sambac and *J. grandiflorum* leaf extracts were found to be highly inhibitory in vitro against *Alternaria* sp., one of the fungal pathogens of foot infections in cancer patients (Mishra et al. 2010). It inhibited hyphal growth and sporulation of the fungus.

Puerperal Lactation Suppression Activity

Jasmine flowers seem to be an effective and inexpensive method of suppressing puerperal lactation and can be used as an alternative in situations where cost and non-availability restrict the use of bromocriptine. Studies reported that both bromocriptine and jasmine flowers brought about a significant reduction in serum prolactin; the decrease was significantly greater with bromocriptine (Shrivastav et al. 1988). However, clinical parameters such as breast engorgement, milk production and analgesic intake showed the two modes of therapy to be equally effective.

Hypotensive Activity

J. sambac was one of the 22 Indian medicinal plants surveyed that was found to have angiotensin converting enzyme inhibitory activity (Somanadhan et al. 1999).

Analgesic Activity

Studies showed that ethanol leaf extract of *J. sambac* produced significant writhing inhibition in acetic acid-induced writhing in mice at the oral dose of 250 and 500 mg/kg of body weight comparable to the standard drug diclofenac sodium at the dose of 25 mg/kg of body weight (Rahman et al. 2011). The petroleum ether extract leaf extract of *Jasminum sambac* at 200 and 400 mg/kg showed significant decrease in acetic acid-induced writhings in mice with a maximum of 67.49 % at 400 mg/kg (Bhangale et al. 2012). In tail immersion and hot plate method, treatment with the extract (200 and 400 mg/kg) showed significant pain latencies as compared to vehicle-treated group of animals.

Anti-inflammatory Activity

The aqueous and ethanol leaf extracts exhibited anti-inflammatory activity against

carrageenan-induced paw oedema in albino rats at a dose of 300 mg/kg (Bhagat et al. 2007). The aqueous extract was more effective than the ethyl acetate extract. Bhangale et al. (2012) reported that the petroleum ether leaf extract of *Jasminum sambac* at 200 and 400 mg/kg significantly inhibited carrageenan-induced paw oedema in mice. The anti-inflammatory effects observed with the extract were comparable to that of the standard.

Antidepressant Activity

In a study of 40 healthy volunteers, topical application of jasmine oil to the abdomen skin caused significant increases of breathing rate, blood oxygen saturation and systolic and diastolic blood pressure, which indicated an increase of autonomic arousal (Hongratanaworakit 2010). At the emotional level, subjects in the jasmine oil group rated themselves as more alert, more vigorous and less relaxed than subjects in the control group. The finding suggested an increase of subjective behavioural arousal. The results demonstrated the stimulating/activating effect of jasmine oil and provided evidence for its use in aromatherapy for the relief of depression and uplifting mood in humans.

Gastroprotective Activity

Studies showed that rats with acidified ethanol-induced gastric ulcers exhibited significantly severe mucosal injury as compared to similarly ulcerated rats treated with omeprazole or *J. sambac* ethanol leaf extract (Alrashdi et al. 2012). The latter treatments elicited significant reduction of ulcer area and a marked reduction of oedema and leucocytes infiltration of submucosal layer. Immunohistochemistry showed overexpression of Hsp70 protein and down-expression of Bax protein in rats pretreated with jasmine leaf extract. Significant increases in pH, mucus of gastric content and high levels of PGE(2), SOD and reduced amount of MDA were observed.

Wound Healing Activity

J. sambac elicited significant increase in wound contraction, hydroxyproline content and decreased epithelization period in excision wound model in albino mice as compared to ethanol extract (Sabharwal et al. 2012). The enhanced wound healing activity of aqueous extract was postulated to be due to free radical scavenging action and antibacterial property of the phytoconstituents (viz., tannins, phenolic acids, flavonoids) present in it.

Toxicity Studies

By intravenous injection at a single dose of 0.5 mL/mouse (15 mg) of the ethanol flower extract, no systemic biological toxicity was demonstrated in ICR mice (Kunhachan et al. 2012). In Wistar rats, the LD_{50} of the extract was higher than 5,000 mg/kg BW by oral administration.

Traditional Medicinal Uses

All parts of the plant have been used in traditional folk medicine in Asia (Burkill 1966; Duke and Ayensu 1985; Chopra et al. 1986; Zhang et al. 1995; Khare 2004; Lu 2005; Joy and Raja 2008; Rath et al. 2008; Fatouma et al. 2010; Mittal et al. 2011; Stuart 2012). *Jasminum sambac* possesses many beneficial medicinal properties such as thermogenic, aphrodisiac, antiseptic, emollient, anthelmintic and tonic and is commonly used for stomatitis, ulcers and skin diseases. The action of jasmine is deemed warming, opening and relieving of spasm and recommended where there is cold, listlessness, spasm, depression, catarrh or other discharge. In India, *Jasmine sambac* has a long history of use as a major therapy for male and female reproductive conditions; it is said to help prevent postnatal depression and infertility and is ranked among the 'aphrodisiac' herbs and is considered calmative. In India, Jasmine (*Jasminum sambac*) is extensively used in manufacturing high-grade aromatherapy oils. In aromatherapy, jasmine oil is recommended for any

kind of physical pain. Jasmine oil is also beneficial in treating many health problems. It is regarded to be a powerful antiseptic, sedative and tonic recommended for breathing difficulties, coughing and nervous debility.

In traditional Chinese medicine, jasmine flowers are used to regulate energy in the body and balance the internal region and are deemed good for abdominal pains, diarrhoea, dermatitis and conjunctivitis. The flowers act as lactifuge and are said to arrest the secretion of milk in puerperal states in case of threatened abscess. In India flowers are applied to the breast. In Malaysia, an infusion of flowers is used as a facial wash because of its fragrance, cleansing and soothing properties. Flowers are used in ben oil or coconut oil for hair, facial or body use or as a perfume oil or perfume base. The flowers are also digested with vegetable oil to make oil tinctures or liniments. The flowers are used by Malays in Malaysia in a paste compounded with Gardenia flowers and the root of *Acacia myriophylla* and applied to the head for congestive headache. Eye lotions are also made with jasmine flowers and the juice from *Conocephalus* or the rhizome of *Kaempferia*. The flowers have also been used to cure sapraemia. Flowers are also reported to be antipyretic and decongestant.

Leaves are also reported to be antipyretic and decongestant. In Malaysia, a leaf decoction is employed for fever and used for poulticing skin complaints and wounds. Leaves are more effective as lactifuge and are so used in Indonesia and with success in India. Juices from the leaves of *J. sambac* are applied to treat ulcers, to remove corns and are used in expelling worms, regulating menstrual flow and cleaning kidney waste and treating inflamed and bloodshot eyes. The leaves are chewed and used in the treatment of ulcerations of the mouth. The leaves and roots of the plant are used for treating diarrhoea and fever and as an anaesthetic and an analgesic, respectively. The root is considered purgative, analgesic, expectorant and anthelmintic—active against ringworm and tapeworm—and is used to treat headache, paralysis and rheumatism. The root is given fresh for venereal diseases in Malaysia and used with leaves to make an eye lotion. In Indonesia the root is taken for fever.

Other Uses

Jasmine is also a popular ornamental plant. Jasmine flower oil is important in high-grade perfumes and cosmetics, such as creams, oils, soaps and shampoos. Jasmine flowers afford a yellow dye which is used as a substitute for saffron.

Jasmine is the national flower of the Philippines. In South India, jasmines are strung into thick strands and worn as a hair adornment or as neck garlands for honoured guests. The flowers of one of the double varieties ('Belle of India') are held sacred to Vishnu and are used as votive offerings in Hindu religious ceremonies. In Hawaii, jasmine flowers—single (pikake lahilahi) or double forms (pikake pupupu)—are used to make fragrant leis.

Comments

Jasmine essential oil is one of the most expensive oils used in cosmetics, the pharmaceutical industry, perfumery and aromatherapy (Younis et al. 2011).

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Syringa vulgaris

Scientific Name

***Syringa vulgaris* L.**

Synonyms

Lilac caerulea (Jonst.) Lunell, *Lilac cordatifolia* Gilib. (Inval.), *Lilac suaveolens* Gilib. (Inval.), *Lilac vulgaris* (L.) Lam., *Lilac vulgaris* var. *alba* (Weston) Jacques & Hérincq, *Lilac vulgaris* var. *purpurea* (Weston) Jacques & Hérincq, *Lilac vulgaris* var. *violacea* (Sol.) Jacques & Hérincq, *Liliacum album* (Weston) Renault, *Liliacum vulgare* (L.) Renault, *Syringa alba* (Weston) A.Dietr. ex Dippel, *Syringa albiflora* Opiz, *Syringa amoena* K.Koch, *Syringa bicolor* K.Koch, *Syringa caerulea* Jonst., *Syringa carlsruhensis* K.Koch, *Syringa cordifolia* Stokes, *Syringa cordifolia* var. *alba* Stokes, *Syringa cordifolia* var. *caerulescens* Stokes, *Syringa cordifolia* var. *purpurascens* Stokes, *Syringa latifolia* Salisb., *Syringa lilac* Garsault (Inval.), *Syringa marliensis* K.Koch, *Syringa nigricans* K.Koch, *Syringa notgeri* K.Koch, *Syringa philemon* K.Koch, *Syringa rhodopea* Velen., *Syringa versaliensis* K.Koch, *Syringa virginalis* K.Koch, *Syringa vulgaris* var. *alba* Sol., *Syringa vulgaris* var. *alba* Weston, *Syringa vulgaris* f. *albipleniflora* S.D.Zhao, *Syringa vulgaris* var. *caerulea* Weston, *Syringa vulgaris* var. *lilacina* Sweet, *Syringa vulgaris* var. *macrantha* Borbás, *Syringa vulgaris* var. *pulchella* Velen., *Syringa vulgaris* var. *purpurea* Weston, *Syringa vulgaris* var. *rubra* Loudon, *Syringa vulgaris* var. *transsilvanica* Schur, *Syringa vulgaris* var. *violacea* Sol.

Family

Oleaceae

Common/English Names

Common Lilac, French Lilac, Lilac, Syringa

Vernacular Names

Bulgarian: Ljuljak
Danish: Almindelig Siren, Syren
Dutch: Gewone Sering
Czech: Šeoík Obecný, Šeřík Obecný
Estonian: Harilik Sirel
Esperanto: Siringo
Finnish: Pihasyreeni, Yleinen Sireenipuu
French: Bois De Lilas, Lilas, Lilas Commun, Lilas Vulgaire
German: Flieder, Garten-Flieder, Gemeiner Flieder, Gewöhnlicher Flieder, Gewöhnlicher Flieder Lilac, Lila, Lilak, Nagelblume, Nägelchenbaum, Nägelein, Pfeifenstrauch, Spanischer Flieder, Türkischer Holunder
Hungarian: Orgona, Orgona Növény
Icelandic: Dísarunni, Garðasýrena

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Italian: Lilacco Commune, Lilla, Lilla Commune, Lillatro, Serenella, Siringa, Sirings Lilla
Norwegian: Syrin
Polish: Lilak, Lilak Pospolity
Portuguese: Lilás, Lilazeiro
Slovaščina: Lipovka, Španski Bezeg
Slovencina: Orgován Obyčajný
Spanish: Lila, Lilo
Swedish: Syren
Turkish: Leylak

Plate 1 Lilac inflorescences and leaves

Plate 2 Close view of flower and leaf

Origin/Distribution

S. vulgaris is indigenous native to the Balkan Peninsula in Southeastern Europe.

Agroecology

In its native range, it is found in woodlands and scrub on rocky hills. Lilac prefers neutral to slightly alkaline soils rich in organic matter. It thrives best in well-drained soils in full sun.

Edible Plant Parts and Uses

Flowers can be eaten raw and in yoghurt or folded into batter and fried to make fritters (MacNicol 1967; Facciola 1990; Barash 1997). The flowers can be crystallized by beating in egg white and rolling in granulated sugar.

Botany

A large deciduous shrub or small, multi-stemmed tree growing to 6 m high. Bark grey-brown, smooth on young stems and flaky and furrowed on older stems. Leaves simple, entire, pale green to glaucous, cordate to subcordate with acuminate to mucronate apex, 5–10 cm long by 3–8 cm wide on 2 cm long petioles (Plates 1 and 2). Flowers sweetly fragrant, lilac, deep purple or white, sometimes doubled in large panicles, 8–18 cm long, arising from lateral buds with leaves at the base (Plates 1 and 2). Flowers with 4-toothed, 2 mm long calyx; corolla tube narrowly cylindrical, 6–10 mm long with an open, 4 oval, lobed apex 5–8 mm across. Anthers yellow included. Fruit a dry, smooth, shining brown capsule, 1–2 cm long, dehiscing into two to release two-winged, compressed seeds.

Nutritive/Medicinal Properties

Phytochemicals from Flowers

Aceteoside (previously named verbascoside) and salidroside were extracted from violet flowers (Birkofer et al. 1968).

Using modern headspace techniques, the sweet and beautiful fragrance of lilac flowers was found to be attributed to characteristic components such as (*E*)-ocimene as the predominant component, furanoid terpene aldehyde ‘lilac

aldehyde' and the corresponding alcohols (four diastereoisomers each), benzyl methyl ether, 1,4-dimethoxybenzene (hydroquinone dimethyl ether) and indole (Mookherjee et al. 1990; Surburg and Güntert 1991; Kreck and Mosandl 2003; Saveer et al. 2012). Minor constituents of the lilac headspace were anisaldehyde, 8-oxolinalool, cinnamic alcohol and elemicin. The so-called syringaldehyde or syringic aldehyde (= 4-hydroxy-3, 5-dimethoxybenzaldehyde), derived from the glucoside syringin, was first isolated from lilac bark and appeared to be of little importance in the headspace of lilacs.

Headspace constituents of living dark purple, purple and French purple lilac flowers included benzyl methyl ether 7.0, 6.5, 1.5 %; *trans* β-ocimene 26.0, 38.0, 52 %; lilac aldehydes 9.3, 11.0, 1.5 %; lilac alcohols 8.0, 4.3, 1.0 %; 1,4′-dimethoxy benzene 3.0, 7.0, 5.0; indole-, 0.2, 0.2 %, respectively (Mookherjee et al. 1990). Constituents from white lilac flowers were benzyl methyl ether 2.6 %, *trans* β-ocimene 31.5 %, 1, 4′-dimethoxy benzene 21.4 %, lilac alcohols 1.0 % and indole 0.8 %. Acteoside, a phenylpropanoid, was isolated from the violet flowers of *Syringa vulgaris* (Ahmad et al. 1995).

The structure and olfactometric analysis of lilac alcohols stereoisomers were elucidated by Kreck and Mosandl (2003) as:

(2R,2′S,5′S)-Lilac alcohol = (2R)-2-[(2S,5S)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl]propenol imparting green, grassy, fresh note with odour threshold of 4 ng

(2S,2′R,5′R)-Lilac alcohol = (2S)-2-[(2R,5R)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl]propenol—sweet, odour threshold = 80 ng

(2S,2′S,5′S)-Lilac alcohol = (2S)-2-[(2S,5S)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl]propenol—flowery, odour threshold = 2 ng; (2R,2′R,5′R)-lilac alcohol = (2R)-2-[(2R,5R)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propenol—odourless at >100 ng by GC sniffing, odour threshold = >100 ng

(2R,2′R,5′S)-Lilac alcohol = (2R)-2-[(2R,5S)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propenol—flowery, sweet, body, odour threshold = 4 ng

(2S,2′S,5′R)-Lilac alcohol = (2S)-2-[(2S,5R)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl]propenol—herbaceous, slightly flowery, odour threshold = 74 ng

(2S,2′R,5′S)-Lilac alcohol = (2S)-2-[(2R,5S)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propenol—sweet, flowery, odour threshold = 2 ng and (2R,2′S,5′R)-lilac alcohol = (2R)-2-[(2S,5R)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl]propenol—sweet, odour threshold = 22 ng

The structure and olfactometric analysis of lilac aldehydes stereoisomers were elucidated by Kreck and Mosandl (2003) as:

(2S,2′S,5′S)-Lilac aldehyde = (2S)-2-[(2S,5S)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propanal—fresh, flowery note, odour threshold = 0.2 ng

(2R,2′R,5′R)-Lilac aldehyde = (2R)-2-[(2R,5R)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propanal—flowery, odour threshold = 22 ng

(2R,2′S,5′S)-Lilac aldehyde = (2R)-2-[(2S,5S)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propanal—pleasant, flowery, fresh, odour threshold = 0.3 ng

(2S,2′R,5′R)-Lilac aldehyde = (2S)-2-[(2R,5R)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propanal—flowery, odour threshold = 20 ng

(2S,2′R,5′S)-Lilac aldehyde = (2S)-2-[(2R,5S)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propanal—sweet, flowery, odour threshold = 0.3 ng

(2R,2′S,5′R)-Lilac aldehyde = (2R)-2-[(2S,5R)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propanal—flowery, fresh, odour threshold = 18 ng

(2R,2′R,5′S)-Lilac aldehyde = (2R)-2-[(2R,5S)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propanal—sweet, flowery, odour threshold = 0.4 ng

(2S,2′S,5′R)-Lilac aldehyde = (2S)-2-[(2S,5R)-2,5-dimethyl-5-vinyltetrahydrofuran-2-yl] propanal—flowery, fresh, odour threshold = 4 ng

Studies showed that deuterium-labelled precursors were bioconverted into lilac aldehydes and lilac alcohols via the mevalonate-independent 1-deoxy-D-xylose 5-phosphate/2C-methyl-D-erythritol 4-phosphate pathway in lilac flowers

(Kreck et al. 2003; Burkhardt and Mosandl 2003). Incubation of petals with an aqueous solution of deuterated d(5)-(R/S)-linalool 3 indicated an autonomic terpene biosynthesis of lilac flavour compounds in the flower petals of lilac.

Volatile odour compounds (ng/minute) emitted from lilac flower included lilac benzaldehyde 13.4 ng, benzyl methyl ether 13.3 ng, 4-methylanisole 1.1 ng, (*Z*)-β-ocimene 11.4 ng, (*E*)-β-ocimene 114.2 ng, acetophenone 4.0 ng, unknown 3 ng, unknown 5.5 ng, (*S*)-(+)-linalool 5.8 ng, lilac aldehyde a 17.4 ng, lilac aldehyde B 3.6 ng, 1,4-dimethoxybenzene 80.9 ng, unknown 1.2 ng, estragole 3.5 ng and lilac alcohols 9.1 ng (Saveer et al. 2012). Also phenylacetadehyde 0.6 ng and benzyl alcohol 2.4 ng were detected from DB wax column.

Damtoft et al. (1995a) characterized secoiridoids, fliederoside and lilacoside from *S. vulgaris*. Using deuterium-labelled precursors, they showed that the biosynthesis of oleoside-type secoiridoids (e.g. oleuropein) proceeded via iridodial, iridotrial, deoxy-loganic acid aglycone and deoxy-loganic acid. Hydroxylation of the 7α-position followed by oxidation and methylation of C-11 afforded 7-ketologanin, the last carbocyclic iridoid precursor of the oleosides. 8-Epi-kingisidic acid and 8-epi-kingiside could be formed from 8-ketologanic acid (and its methyl ester). Further Damtoft et al. (1995b) found that oleoside 11-methyl ester was an efficient precursor for the oleosides in *S. vulgaris*, and the major pathway to the oleosides appeared to proceed via a direct ring fission of ketologanin to oleoside 11-methyl ester.

Phytochemicals from Leaves

D-mannite, quercetin, rutin, kaempferol-3-rutinoside, isoquercetin and astragalin were isolated from the leaves, and rutin was found to be predominating (Kurkin et al. 1980). Two new secoiridoid glucosides, named syringa lactone A and syringa lactone B, were isolated from *S. vulgaris* leaves (Sticher et al. 1982). The leaves were found to be a rich source of the iridoid glucoside, syringopicroside (Asaka et al. 1970; Liu et al. 2010).

In the leaves, most of the chlorophyll was found in the palisade parenchyma, the chlorophyll a/b ratio being the highest in the upper layer (Pilarski 1999). The highest concentration of chlorophyll in the leaves was 1.2 mg/dm^2, and the highest value of the chlorophyll a/b ratio in the leaves varied from 4.5 to 3.8.

Phytochemicals from Bark

Ten phenolic compounds isolated from the bark included derivatives of phenethyl alcohol (tyrosol (4-hydroxyphenylethanol), 3,4-dihydroxyphenylethanol, salidroside and *O*-(3,4-dihydroxyphenethyl) β-D-glucopyranoside), phenylpropanoids (cinnamylglycosides syrigin and coniferin, the acylglycosides acetoside and forsythiaside), a coumarin esculatin and a flavonoid astragalin (Kurkin et al. 1989). Iridoids isolated from common lilac bark included oleuropein, ligustroside, nuzhenide and demethyloleuropein (Kurkin et al. 1990). On saponification with 2 % NaOH, oleuropein, demethyl oleuropein yielded 3,4-dihydroxy-β-phenylethanol (3-hydroxytyrosol), ligustroside gave 4-hydroxy-β-phenylethanol (tyrosol) and nuzhenide gave the tyrosol glycoside salidroside (4-hydroxy-β-phenylethyl 8-day-glucopoyranoside). Two lignans isolated from the bark of *Syringa vulgaris* were identified as (+)-lariciresinol 4-β-D-glucopyranoside (I) and -olivil 4-β-D-glucopyranoside (Kurkin et al. 1991). The bark was found to contain syrigin (Kurkin et al. 1992; Ahmad and Aftab 1995). Fourteen components were identified in the bark extract: phenylethanol derivatives (tyrosol, hydroxytyrosol and their glycosides salidroside and hydroxysalidroside); phenylpropanoids (the acylglycosides acteoside and forsythiaside, the cinnamylglycosides syringing and coniferin, lignan glucosides lariciresinol 4-glucoside and o1ivil 4-glucoside); and also iridoids in the form of conjugates with tyrosol and hydroxytyrosol (oleuropein, noroleuropein, ligustroside and nuzhenide) (Kurkin et al. 1992).

Chlorophyll and carotenoids were present through the whole thickness of the bark, except the

cork (Pilarski 1999). It was found that chlorophylls a and b and carotenoids were present mainly in the outer layer of the bark, immediately under the cork, to a depth of 400 μm. The highest concentration of chlorophyll in the bark is 0.44 mg/dm^2, and the highest value of the chlorophyll a/b ratio in the bark is 3.8 and the lowest 0.5.

Some of the pharmacological properties of lilac plant parts are elaborated below.

Hypotensive Activity

Intravenous administration of syrigin, isolated from the bark, caused a dose-dependent decline in systolic, diastolic and mean arterial blood pressure in anaesthetized Wistar rats, whereas heart rate also decreased at a slightly higher dose (Ahmad and Aftab 1995). Syringin had no effect on the pressor effect induced by norepinephrine or carotid occlusion. Acteoside, a phenylpropanoid, was isolated from the violet flowers of *Syringa vulgaris* and exhibited a dose-dependent decrease in systolic, diastolic and mean arterial blood pressure in normotensive pentothal anaesthetized rats (Ahmad et al. 1995). The median effective dose was 10 mg/kg and lasted for 2–3 min, while heart rate also decreased.

Anti-inflammatory Activity

Studies showed that extract containing verbascoside and teupolioside (produced from *S. vulgaris* cell cultures) significantly accelerated wound healing and exhibited remarkable anti-inflammatory action in the excision wound model (Korkina et al. 2007). These effects correlated with the inhibition of reactive oxygen species released from the whole blood leucocytes and with the ferrous ion chelating capacity but not with free radical scavenging or with the inhibition of lipid peroxidation in the cell-free systems. Additionally, both extracts were extremely effective inhibitors of chemokine and growth factor expression by cultured human keratinocytes treated with proinflammatory cytokines, TNF-alpha and interferon-gamma.

Daily verbascoside (from *S. vulgaris*) treatment for 4 days of rats with colitis induced by intracolonic instillation of 2,4 dinitrobenzene sulphonic acid significantly reduced macroscopic damage score, loss of body weight, myeloperoxidase activity and thiobarbituric acid-reactant substances (Mazzon et al. 2009). Further, the intensity of the positive staining for tumour necrosis factor-alpha, interleukin-1beta, intercellular adhesion molecule-1, *P*-selectin, inducible nitric oxide synthase and poly(ADP-ribose) was also significantly reduced by verbascoside treatment. Verbascoside treatment significantly reduced the degree of nuclear factor-kappa B p65 and activation of the proactive form metalloproteinase (MMP)-2 and pro-MMP-9 activity. The results suggested that administration of verbascoside may be beneficial for the treatment of inflammatory bowel disease. Verbascoside from *Syringa vulgaris* was shown to exert an anti-inflammatory role in a rat model of ligature-induced periodontitis and was able to ameliorate the tissue damage associated with ligature-induced periodontitis (Paola et al. 2011). Oral administration of verbascoside (2 mg/kg daily for 8 days) significantly decreased all of the parameters of inflammation: (1) myeloperoxidase activity, (2) thiobarbituric acid-reactant substance measurements, (3) NF-κB expression, (4) iNOS expression, (5) nitration of tyrosine residues, (6) activation of the nuclear enzyme poly(ADP-ribose) polymerase, (7) Bax and Bcl-2 expression and (8) a degree of gingivomucosal tissue injury.

Neuroprotective Activity

Studies showed mice with induced spinal cord injury exhibited severe trauma characterized by oedema, tissue damage, a marked increase on expression for nitrotyrosine, inducible nitric oxide synthase, poly(ADP-ribose) and apoptosis events (increase of Bax and Bcl-2 expression) in the spinal cord tissue (Genovese et al. 2010). Additionally, these inflammatory events were associated with the cytokines expression (TNF-α and IL-1β), neutrophil infiltration (myeloperoxidase) and activation of NF-κB. At 1 and 6 h after

injury, administration of verbascoside from culture cells of *S. vulgaris* ameliorated all these parameters of inflammation and tissue injury events associated with spinal cord trauma. In vitro studies showed that verbascoside protected activated C6 glioma cells via modulation of transcription factors and consequent altered gene expression, resulting in downregulation of inflammation and may provide a promising approach for the treatment of oxidative stress-related neurodegenerative diseases (Esposito et al. 2010). Treatment with bacterial endotoxin/cytokine lipopolysaccharide (LPS)/interferon (IFN)-gamma for 24 h elicited the induction of inducible nitric oxide synthase (iNOS) activity. Preincubation with verbascoside (10–100 µg/mL) dose-dependently abrogated the mixed cytokine-mediated induction of iNOS indicating an inhibitory effect of verbascoside on neuronal nitric oxide synthase expression. Verbascoside was found to reduce the expression of proinflammatory enzymes in LPS/IFN-gamma through the inhibition of the activation of nuclear factor-kappa B and mitogen-activated protein kinase signalling pathway.

Neurostimulant Activity

Syringin from *S. vulgaris* bark was found to have neurostimulant (spontaneous motor activity and antihypnotic) properties like other glycosides of cinnamyl alcohol (Sokolov et al. 1990).

Photoprotective Activity

The glycosylated phenylpropanoid verbascoside isolated from *S. vulgaris* cultured cells had been characterized as an effective scavenger of biologically active free radicals such as hydroxyl, superoxide and nitric oxide, as a chelator of redox active transition metal ions (Fe^{2+}, Fe^{3+}, Cu^{2+} and Ni^{2+}) and an inhibitor of lipid peroxidation (Kostyuk et al. 2008). In subsequent studies they showed that verbascoside and the glycosylated flavonoid rutin and its aglycone quercetin afforded effective protection against UVC-induced necrosis and did not prevent UVC-induced apoptosis in both normal human keratinocytes (HaCaT) cells and breast cancer cells (MCF 7). They found that UVC protection strongly depended on the lipid peroxidation inhibiting and Fe (2+) chelating properties of the polyphenols, suggesting the potential of these plant polyphenols in photoprotection of human skin.

Hypothermic Activity

The leaf extract of *S. vulgaris* was reported to have antipyretic activity, when orally or intraperitoneally administered to rats (Bálint et al. 1965).

Traditional Medicinal Uses

The decoction of leaves is used as astringent and antipyretic, and macerated flower in oil is used to soothe the skin in Italy. In Bulgaria, the bark, fruits and leaves are crushed and boiled in water and used as appetizer and antipyretic (Leporatti and Ivancheva 2003).

Other Uses

Planted worldwide in temperate areas as ornamental for the showy and sweet-scented flowers. In Ukraine special selections are cultivated for the essential oil from the flowers.

Comments

Lilac can be easily and successfully established by using root sprouts, which is faster than seeds.

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Fuchsia × hybrida

Scientific Name

***Fuchsia* × *hybrida* Voss**

Synonyms

No synonyms recorded for this name

Family

Onagraceae

Common/English Names

Fuchsia, Hybrid Fuchsia

Vernacular Names

Brazil: Brinco-De-Princesa
Czech: Fuchsie
Danish: Fuchsia
Dutch: Bellenplant
French: Fuchsia
German: Fuchsie
Italian: Fucsia
Polish: Fuksja, Fuksja Ułanka
Spanish: Arete, Aretillo

Origin/Distribution

Fuchsias are native to Central and South America from Northern Argentina to Colombia and Venezuela, and. several species are found in Hispaniola in the Caribbean (two species), in New Zealand (3 species) and in Tahiti (one species).

Agroecology

Fuchsia thrives in a warm–cool subtropical climate regime. It grows well in fertile, moist but well-drained soil, with shelter from cold, drying winds in the ground or containers. Fuchsias prefer shade for the hottest part of the day. Fuchsia is intolerant of drought or water-logged conditions.

Edible Plant Parts and Uses

Fuchsia petals are edible (Roberts 2000; Rop et al. 2012) and used in salads or as garnish but have no distinctive flavour. According to Wilson (2013) Fuchsia flowers are not delicious—they have a slightly acidic flavour—but if used sparingly, they make for a wonderfully colourful garnish. Some recipes of fuchsia flowers include fuchsia and potato mash, cold chicken and fuchsia salad (Roberts 2000). The fruit of all species and cultivars of fuchsia are edible, but the quality

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is variable: some are tasteless, others have an unpleasant aftertaste. The fairly large fruit of *Fuchsia splendens* are reputedly the most worthwhile, having a citrusy, peppery tang. They are best used for jam.

Botany

Most fuchsias including hybrid fuchsia are shrubs from 0.2 to 4 m, deciduous or evergreen. Fuchsia leaves are opposite or in whorls of 3–5, simple lanceolate and usually have serrated margins or entire margins in some species, 1–25 cm long. The flowers are very decorative pendulous 'ear-drop' shape, borne in profusion. The flower is borne on a thin pedicel which swells out to form the inferior ovary. Above the ovary is a tube formed by four slender sepals; the nectary is found at the top of the tube. When the flower is only a bud, the sepals are closed. As the flower bursts open, the sepals part and curl upward. Above the sepals are the brightly coloured petals (usually 4), from which the stamens (8) and single style and stigma protrude. The sepals are bright red and the petals purple, but the colours can vary from white to dark red, pink, purple-blue and orange (Plates 1, 2 and 3). A few have yellowish tones, and recent hybrids have added the colour white in various combinations. The fruit is a small, 0.5–2.5 cm, dark reddish green, deep red or deep purple, edible epigynous berry containing numerous very small seeds. There are now over 7,000 Fuchsia varieties.

Plate 1 Fuchsia 'Blue Lagoon' (red sepal double purple petal)

Nutritive/Medicinal Properties

Rop et al. (2012) reported that edible flowers of *Fuchsia* × *hybrida* had a dry matter content (%w/w) of 8.37 %, crude protein of 2.41 g/kg and the following elements (mg/kg fresh mass (FM)): P 215.46 mg, K 1,967.30 mg, Ca 239.10 mg, Mg 170.71 mg, Na 125.58 mg, Fe 8.12 mg, Mn 4.17 mg, Cu 2.70 mg, Zn 11.45 mg and Mo 0.71 mg. The flowers had total antioxidant capacity of 5.20 g ascorbic acid equivalents/kg FM,

Plate 2 Fuchsia variety with white pink sepal, purple single petal

Plate 3 Fuchsia variety with pink sepal single red petal

total phenolic content of 3.45 g gallic acid/kg FM and total flavonoid content of 1.66 g rutin/kg FM.

In two cultivars of *Fuchsia*, malvidin 3,5-diglucoside appeared to be the dominant pigment, with peonidin 3,5-diglucoside as a minor component (Nozzolillo 1970). There appeared to be no change in the pigments themselves with age, although the colour ranged from blue in young flowers to magenta in old flowers. This colour change was correlated with a decline in pH from about 5.5 in young blue flowers to about 4.0 in old flowers, a reduction which appeared to occur abruptly about the time of pollen release. The operation of a co-pigmentation effect was confirmed, and the presence of a co-pigment in addition to quercetin glucosides was suggested. Co-pigmentation was found to be effected in violet petals by pale yellow substance soluble in isoamyl alcohol glycosides of quercetin, identified as spiraesoside (4″-glucoside), isoquercetin (3-glucoside) and quercetin (3-rhamnoside) (Yazaki and Hayashi 1967). The anthocyanin malvin was found to be the sole component in violet petals, while peonin and cyanin were present in nearly equal amounts in the red calyces malvin, and the 3 quercetin glycosides played a primary role in the manifestation of the violet colour in Fuchsia petals.

Pure malvin was isolated from Fuchsia petals and characterized as the malvin anhydro-base (Yazaki 1976). The colour change from blue-violet in young Fuchsia petals to purple-red in old ones was caused by co-pigmentation and the pH change from 4.8 to 4.2. The decrease of pH in the old petals was due to the increase of organic acids such as aspartic, malic and tartaric. 3-Glucosides and 3,5-diglucosides of pelargonidin, cyanidin, peonidin, delphinidin, petunidin and malvidin have been identified as flower pigments in *Fuchsia* species (Crowden et al. 1977). These pigments in varying admixture appear to be solely responsible for different flower colours in this genus.

A comprehensive survey of 225 populations of 80 taxa of *Fuchsia* showed flavonol monoglycosides, especially quercetin and kaempferol 3-0-glucosides, to be ubiquitous in all species examined (Averett et al. 1986). Flavonol diglycosides were unusual and occurred in just eight species in five of the nine sections of the genus. Flavone glycosides were found in only nine species belonging to five sections and were associated with primitive taxa. Thirteen anthocyanidin 3,5-diglucosides (six), 3-monoglycosides (five) and 3-(2″-galloylglucosides) (two), were identified in flowers of *Fuchsia arborescens, F. boliviana, F. fulgens* var. 'Variegata', *F. magellanica* and 29 *F. magellanica* cultivars (Jordheim et al. 2011). Peonidin 3-*O*-(2″-*O*-galloyl-β-glucopyranoside), which has not been reported before, was found in *F. magellanica* and *F. fulgens* var. 'Variegata'. The various corollas with purple nuances were correlated with a relatively high content of malvidin 3,5-diglucoside.

Flavonols were found to be abundant in the leaves of all *Fuchsia* taxa except *F. procumbens* (Williams et al. 1983). Flavone glycosides were found in only three species: luteolin 7-glucoside in *F. splendens* and luteolin and apigenin 7-glucuronides and 7-glucuronidesulphates, tricin 7-glucuronidesulphate and diosmetin 7-glucuronide from one or both of the New Zealand species. Luteolin 7- glucuronidesulphate was reported for the first time. Other less common phenolics identified include the flavanone, eriodictyol 7-glucoside from *F. excorticata*, a galloylglucose from *F. triphylla* and a galloylglucosesulphate present in all taxa. Eight of the flavonoid glycosides proved useful as marker substances for particular *Fuchsia* species: quercetin 3-rhamnoside, 3-glucuronide and 3-rutinoside for *F. fulgens*; quercetin and kaempferol 3-galactosides for *F. boliviana* var. *luxurians*; diosmetin 7-glucuronide for F. excorticata; and apigenin 7-glucuronide and 7-glucuronidesulphate for *F. procumbens*. Among approximately 100 species of Fuchsia, Averett and Raven (1984) identified 12 flavonoid glycosides, including four flavones and eight flavonols. The flavones include two sulphates. The flavonols include six 3-*O*-glycosides based on kaempferol, quercetin, or myricetin and two methyl ethers. Flavonol glycosides were found in each of the species examined.

Other Uses

Fuchsias are excellent in summer-bedding schemes, hanging containers, pots or in the ground. Fuchsias can also be trained as hoops or standards. Some fuchsias are hard enough to be used as hedges and in permanent plantings.

Comments

Fuchsias can be propagated by softwood, semi-matured and hardwood cuttings.

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Oenothera speciosa

Scientific Name

***Oenothera speciosa* Nutt.**

Synonyms

Hartmannia speciosa (Nutt.) Small, *Xylopleurum drummondi* Spach, *Xylopleurum nuttallii* Spach, *Xylopleurum obtusifolium* Spach, *Xylopleurum speciosum* (Nutt.) Raim.

Family

Onagraceae

Common/English Names

Mexican Evening Primrose, Pink Evening Primrose, Pink Ladies, Showy Evening Primrose, Snowy Evening Primrose, White Evening Primrose

Vernacular Names

Spanish: Amapola del Campo
Swedish: Silvernattljus

Origin/Distribution

White evening primrose comes from the South-Central United States. It is native to the rocky prairies and savannas of the lower Midwest but occurs commonly along slopes and roadsides and in disturbed areas over a much broader region.

Agroecology

White evening primrose is adaptable to all kinds of soil and will grow on poor, rocky soil in full sun. Soil should be well drained and loose as the plant is susceptible to root rot in wet soils. This plant can spread aggressively at dry, sunny locations as it is drought resistant and can become invasive.

Edible Plant Parts and Uses

The flowers have a similar taste to lettuce, so it will make a fine addition to any green salad while also adding some colour (Anonymous 2012).

Botany

A herbaceous perennial, 20–60 cm high, with a spread of 38–40 cm, rosetted when young, forming large patches from weakly ascending to erect,

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Plate 1 White evening primrose flowers and leaves

Plate 2 Close-up of flower

terete, minutely pubescent stems and woody rhizomes. Leaves alternate, pubescent, sessile to subsessile, 10 cm long by 4 cm wide, linear to oblanceolate, with toothed (Plate 1) or wavy, undulating margins. Flowers (4–5 cm) emerge from distal axils on nodding pedicels, hypanthium 10–23 mm, sepals 15–30 mm, petals 4 each 25–40 mm, white fading to rosy-pink stamens 8 with yellowish anthers, stigma yellowish white, long and 4-cleft (Plates 1 and 2). Fruit 8-ribbed, cylindric capsule, 10–25 mm. Seeds obliquely oblanceolate, finely granular-papillate.

Nutritive/Medicinal Properties

The following flavonoids were found in *O. speciosa*: kaempferol 3-*O*-glucoside; quercetin 3-*O*-glucoside; quercetin 3-*O*-arabinoside; quercetin 3-*O*-rhamnoside; quercetin 3-*O*-glucuronide; quercetin 3, 7-*O*-diglucuronide; quercetin 3-*O*-sulphate; myricetin-3-*O*-galactoside; myricetin-3-*O*-arabinoside; myricetin-3-*O*-rhamnoside; myricetin 3,7-*O*-diglucuronide; and myricetin 3 methyl ether, 3′*O*-glucoside (Averett et al. 1987, 1988). Myricetin 3-*O*-methyl ether 3′-*O*-β-D-glucoside was found to be the major flavonoid of *Oenothera speciosa* (Howard and Mabry 1970).

Two new flavonol glycosides, myricetin 4′-*O*-α-L-rhamnopyranoside and quercetin 3′-*O*-α-L-rhamnopyranoside, together with a novel biflavonol compound, speciin (3), as well as 11 phenolic metabolites, namely, myricitrin, europetin 3-*O*-α-L-$^{1}C_{4}$-rhamnopyranoside, quercetin, hyperin, rhamnetin 3-*O*-β-galactopyranoside, caffeic acid, caffeic acid methyl ester, chlorogenic acid, chlorogenic acid methyl ester, gallic acid and gallic acid methyl ester, were identified from the 80 % methanol extract of the aerial parts (leaves and stems) of *Oenothera speciosa* (Marzouk et al. 2009). In addition, myricetin, quercetin and ellagic acid were identified from the chloroform extract. It was found that 80 % aqueous methanol extract of *O. speciosa* was nontoxic to mice up to 5 g/kg body weight. The investigated extract exhibited significant antihyperglycaemic and anti-inflammatory activities in a dose-dependant manner. Also, the 80 % methanol extract, myricitrin and hyperin showed potent

antioxidant activity in vitro using 1,1-diphenyl 2-picryl hydrazyl (DPPH) radical assay.

Other Uses

White evening primrose is an excellent wildflower for roadside beautification. It will readily form showy colonies on rocky highway and gravelly driveway edges. The flowers also attract bees, moths and hummingbirds.

Comments

White evening primroses are easy to grow from seeds.

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Dendrobium bigibbum

Scientific Name

***Dendrobium bigibbum* Lindl.**

Synonyms

Callista bigibba (Lindl.) Kuntze, *Callista phalaenopsis* (Fitzg.) Kuntze, *Callista sumneri* (F.Muell.) Kuntze, *Dendrobium bigibbum* var. *albomarginatum* F.M.Bailey, *Dendrobium bigibbum* var. *albopurpuratum* auct., *Dendrobium bigibbum* var. *album* F.M.Bailey, *Dendrobium bigibbum* var. *candidum* Rchb.f., *Dendrobium bigibbum* var. *compactum* C.T.White, *Dendrobium bigibbum* var. *macranthum* F.M.Bailey, *Dendrobium bigibbum* var. *phalaenopsis* (Fitzg.) F.M.Bailey, *Dendrobium bigibbum* f. *phalaenopsis* (Fitzg.) St.Cloud, *Dendrobium bigibbum* var. *sumneri* (F.Muell.) F.M.Bailey, *Dendrobium bigibbum* f. *superbium* G.Piper, *Dendrobium bigibbum* var. *superbum* Rchb.f., *Dendrobium bigibbum* f. *venosum* F.M.Bailey, *Dendrobium lithocola* D.L.Jones & M.A.Clem., *Dendrobium phalaenopsis* Fitzg., *Dendrobium phalaenopsis* var. *albopurpureum* auct., *Dendrobium phalaenopsis* var. *album* B.S.Williams, *Dendrobium phalaenopsis* var. *album* auct., *Dendrobium phalaenopsis* var. *chamberlainianum* auct., *Dendrobium phalaenopsis* var. *compactum* C.T.White, *Dendrobium phalaenopsis* var. *dellense* B.S.Williams, *Dendrobium phalaenopsis* var. *highburyense* auct., *Dendrobium phalaenopsis* var. *hololeuca* auct., *Dendrobium phalaenopsis* var. *lindeniae* auct., *Dendrobium phalaenopsis* var. *rothschildianum* Kraenzl., *Dendrobium phalaenopsis* var. *rubescens* Nash, *Dendrobium phalaenopsis* var. *schroderianum* Rolfe, *Dendrobium phalaenopsis* var. *splendens* auct., *Dendrobium phalaenopsis* var. *statterianum* auct., *Dendrobium phalaenopsis* var. *thundersleyense* auct., *Dendrobium sumneri* F.Muell., *Vappodes bigibba* (Lindl.) M.A.Clem. & D.L.Jones, *Vappodes lithocola* (D.L.Jones & M.A.Clem.) M.A.Clem. & D.L.Jones, *Vappodes phalaenopsis* (Fitzg.) M.A.Clem. & D.L.Jones

Family

Orchidaceae

Common/English Names

Cooktown Orchid, Den-Phal, Mauve Butterfly Orchid, The Two-Humped Dendrobium

Vernacular Names

None

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Origin/Distribution

D. bigibbum is found naturally in a restricted area from the Endeavour River Valley, west of Cooktown, south to the Font Hills, west of Mount Molloy, in far northern Queensland in Australia.

Agroecology

This orchid adapts to a humid tropical or subtropical environment growing as an epiphyte on the trunks and branches of trees or as a lithophyte on exposed rocks in dappled shade in its natural habitat. The species prefers a growing regime of 50–75 % relative humidity, day temperature of 24–28 °C, night temperatures of 16–20 °C and away from full sun. Cultivated plants have much larger flowers than those in the wild. This orchid requires infrequent watering, 2–3 time weekly and grows well in well-drained orchid potting mix containing sphagnum moss or fir-bark.

Edible Plant Parts and Uses

The blossoms are used in salads and as a garnish (Deane 2007–2012). Dendrobiums are being stir-fried in many Asian countries and also being used for making sauces in Singapore and Thailand (Sotirov 2012). In Thailand, Dendrobium flowers are dipped in batter and deep fried, while many European cooks garnish desserts and cakes with them. In Hawaii, locals use orchids to prepare salads and sugar-coated candies and in main dishes with scallops.

Botany

An epiphytic or lithophytic, sympodial orchid with cylindrical fleshy pseudobulbs, swollen at the centre, tapering more towards the base and top; 30–60 cm long and bearing in the upper section of the stem a variable number of alternate, distichous leaves, coriaceous, ovate to lanceolate, 5–15 cm by 1–3.5 cm. Inflorescence terminal, 2–4 appearing from the upper nodes are curved or

Plate 1 Dendrobium inflorescence with (>10 flowers)

Plate 2 Close-view of dendrobium flowers

arching racemes, 10–40 cm long carrying 6–20 flowers of 4–9 cm diameter in two rows along the stem (Plate 1). Flowers are pinkish-mauve or lavender or purple or (occasionally) (Plates 1 and 2) white with a darker labellum base and long-lasting. Sepals oblong with acute apex, 2–3 cm long, the lateral sepals fused together at the base of the column forming a spur (mentum) bilobed 1–2 cm long. Petals 3–3.5 cm long 2–2.5 cm broad, flat, the labellum is trilobed with central lobe oblong pubescent and darker at the base, lateral ones obovate with attenuate bases, surrounding the column. The stigma is located near the column foot above the inferior ovary, the stamens containing pollinia is located near the top of the column.

Nutritive/Medicinal Properties

A new acylated anthocyanin with the structure cyanidin-3-*O*-(malonyl)-(β-D-glucopyranoside) 7,3′-di-*O*-(6-*O*-(4-*O*-(β-D-glucopyranosyl)

oxybenzoyl)-β-D-glucopyranoside) was isolated from the red-purple flowers of *Dendrobium* 'Pramot' (phalaenopsis type cultivar) as a major anthocyanin (Saito et al. 1994). The colours of three blue genotypes, *Dendrobium gouldii* K280-6, *D. bigibbum* 'blue' and *D. kultana* 'blue', were light violet to purple by RHS standards and contained anthocyanins based on cyanidin (Kuehnle et al. 1997). Cyanidin appeared as 86 % (*D. bigibbum* 'blue') and 92 % (*D. gouldii* K280-6, *D.* Kultana 'blue') of the total anthocyanins present, with peonidin and pelargonidin comprising the remainder. Predominant co-pigments were flavonol glycosides based on kaempferol, quercetin, myricetin and methylated derivatives. Flavonol aglycones and glycosylation sites differed little among two colour forms of *D. gouldii* and two *Dendrobium* Jaquelyn Thomas hybrids. Accumulation of quercetin, myricetin and cyanidin indicated flavonoid 3′ and 3′,5′ hydroxylation activities in several *Dendrobium* varieties. Additional accumulation of isorhamnetin, syringetin and peonidin indicated active flavonoid 3′- and 3′,5′- *O*-methyltransferase enzymes. *Dendrobium* Jaquelyn Thomas is a primary hybrid of *D. gouldii* × *D. phalaenopsis*, registered by Thomas in 1949.

Two rare anthocyanins, cyanidin 3-(6-malonylglucoside)-7,3′-di(6-sinapylglucoside) and the demalonyl derivative, were characterized as the purple floral pigments of *Dendrobium* cv. 'Pompadour' (Williams et al. 2002). *Dendrobium* × Mme. '*Pompadour*' is historically an old cross of the hybrid *Dendrobium* × Louis Bleriot (*Dendrobium* phalaenopsis 'Schroederianum'). Nine known flavonol glycosides were also identified, including the 3-rutinoside-7-glucosides of kaempferol and quercetin. One new glycoside was detected: the ferulyl ester of quercetin 7-rutinoside-7-glucoside.

Orchid flowers in the genus *Dendrobium* section Phalaenanthe were found to contain acylated anthocyanins: cyanidin 3-glucosyl-7, 3′-di-(glucosyl-*p*-hydroxybenzoylglucoside); 2, cyanidin 3-malonylglucosyl-7,3′-di-(glucosyl-*p*-hydroxybenzoylglucoside); 3, cyanidin 3-glucosyl-7, 3′-di-(sinapoylglucoside); 4, cyanidin 3-malonylglucosyl-7,3′-di-(sinapoylglucoside) (Tatsuzawa et al. 2005). *Dendrobium* section Phalaenanthe (Orchidaceae) includes species *Dendrobium affine, D. bigibbum (D. phalaenopsis), D. compactum, D. dicuphum, D. superbiens, D. williamsianum* and their hybrids. Two new acylated anthocyanins were isolated from the purple flowers of *Dendrobium* × *superbiens* (belonging to *Dendrobium* section Phalaenanthe), along with four known pigments (Tatsuzawa et al. 2006). These pigments were all based on cyanidin 3,7,3′-triglucoside and acylated variously with malonic, sinapic and *p*-hydroxybenzoic acids. One of the anthocyanins was elucidated as cyanidin3-*O*-[6-*O*-(malonyl)-β-D-glucopyranoside]-7-*O*-[6-*O*-(*p*-hydroxybenzoyl)-β-D-glucopyranoside]-3′-*O*-[6-*O*-(4-(β-D-glucopyranosyl)-*p*-hydroxybenzoyl)-β-D-glucopyranoside] and the other cyanidin 3-malonylglucoside-7-glucosyl-*p*-hydroxybenzoylglucoside-3′-*p*-hydroxybenzoylglucoside. Recently Li et al. (2013) found astaxanthin glucoside (both acylated cyanidin -3,7,3′- three glucoside) and flavonol glycosides (aglycone with quercetin, kaempferol and isorhamnetin—three kinds) in Phalaenopsis type *Dendrobium* flowers.

No nutritive or medicinal value or medicinal uses have been recorded for this species.

Other Uses

This orchid is popularly cultivated as ornamental house plants, and many of its hybrids are cultivated commercially for its cut flowers.

Comments

Cooktown Orchid, *Dendrobium bigibbum* var. *phalaenopsis*, was proclaimed as the floral emblem of Queensland in November 1959 (Boden 1995).

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Paeonia lactiflora

Scientific Name

***Paeonia lactiflora* Pallas**

Family

Paeoniaceae also in Ranunculaceae

Synonyms

Paeonia albiflora Pall., *Paeonia albiflora* var. *edulis* (Salisb.) Pursh, *Paeonia albiflora* var. *fragrans* Sabine, *Paeonia albiflora* var. *humei* Sabine, *Paeonia albiflora* f. *nuda* Nakai, *Paeonia albiflora* f. *pilifera* Schipcz., *Paeonia albiflora* f. *pilosella* Nakai, *Paeonia albiflora* var. *purpurea* Korsh., *Paeonia albiflora* var. *spontanea* Makino, *Paeonia albiflora* var. *trichocarpa* Bunge, *Paeonia albiflora* var. *whitleyi* Sabine, *Paeonia chinensis* L. Vilmorin, *Paeonia edulis* Salisb., *Paeonia edulis* var. *reevesiana* Paxton, *Paeonia edulis* var. *sinensis* Sims, *Paeonia fragrans* (Sabine) Redouté, *Paeonia humei* (Sabine) Bailly, *Paeonia lactea* Pall. (Invalid), *Paeonia lactiflora* f. *nuda* (Nakai) Kitag., *Paeonia lactiflora* f. *pilosella* (Nakai) Kitag., *Paeonia lactiflora* var. *trichocarpa* (Bunge) Stern, *Paeonia lactiflora* var. *villosa* M.S.Yan & K.Sun, *Paeonia lobata* Pall. (Invalid), *Paeonia makoya* Marnock, *Paeonia officinalis* Thunb., *Paeonia reevesiana* (Paxton) Loudon, *Paeonia sinensis* Steud. (Invalid), *Paeonia whitleyi* (Sabine) auct., *Paeonia yui* W.P.Fang

Common/English Names

Chinese Peony, Common Garden Peony, Common Peony, Coral Peony, Fragrant Peony, White Peony

Vernacular Names

Chinese: Bái Shá, Jiu Chao Bai Shao, Moutan, Mu Dan Pi, Sháo, Shao Yao
Czech: Pivoňka Bělokorá
Danish: Silkepæon
Estonian: Valgeõieline Pojeng
Finnish: Jalopioni
German: Garten-Pfingstrose, Weisse Pfingstrose
Japanese: Shaku-Yaku
Korean: Cham-Jag-Yak, Hambagggot, Ho-Jak-Yag, Jag-Yag, Min-Cham-Jag-Yak
Polish: Piwonia Chinska
Slovenian: Potonika
Swedish: Luktpion
Vietnamese: Thuốc Ruoc, Mẫu Đơn; Bạch Thược

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Origin/Distribution

Chinese peony is native to temperate Asia—Japan, Korea, China, Mongolia and Russia—and eastern Siberia.

Agroecology

A cold climate species found in woods and grasslands from 400 to 2,300 m elevations in its native range. The plant is hardy to about −25 °C, but there are many named cultivars which are hardy to about −50 °C. It is tolerant of a wide range of soil conditions, but is intolerant of too dry or water-logged soil. The plant and thrives best in a deep rich, well-drained and moist soil, preferably neutral or slightly alkaline in full sun or partial shade. It is lime tolerant. Plants grown on sandy soils are reported to produce more foliage and less flowers, while those growing on clayey soils take longer to become established but produce better blooms.

Edible Plant Parts and Uses

Petals are edible and used in salad or floated in punches and lemonade (Deane 2007–2012). Another option is to parboil the petals, add a little sugar and use them as a sweet treat. In China, the fallen petals are parboiled and sweetened as a tea-time delicacy. Peony water was used for drinking in the middle ages. Steenbergs Dried Peony Flowers are beautiful rose pink-coloured, natural flower that look great in salads or used in home baking or added as a flourish over fruit salads (Steenbergs Organic 2012).

In China, slices of dried roots with bark removed are used for preparing health food—an important ingredient in the common bupin mixture called the 'Four Precious Tonifying Soup' comprising roots of *Paeonia lactiflora* 'bai-shao', *Rehmannia glutinosa, Ligusticum wallichii* and *Angelica sinensis* and onions (Chevallier 1996; Hu 2005).

Roots are also cooked and eaten in a broth (Uphof 1968; Hedrick 1972; Grieve 1971; Facciola 1990) and stems eaten cooked (Kunkel 1984). Seeds are powdered and mixed with tea (Grieve 1971; Facciola 1990).

Botany

Stout perennial, erect herb, 40–80 cm tall, with thickened (1.3 cm diameter), tuberous root and glabrous branched stems. Leaves (Plate 1) alternate, basal leaves biternate; all leaflets decurrent at base, terminal leaflets 2 or 3 segmented, leaflets and segments up to 15, oblong–elliptic, oblique–ovate to lanceolate, 4.5–16 by 1.5–4.8 cm, pilose beneath, margins rough–scabrous. Flowers 1–3 per shoot, both terminal and axillary, single or double, 7–10 cm across, fragrant (Plates 1, 2). Bracts 4 or 5, lanceolate, unequal. Sepals 3 or 4, broadly ovate or suborbicular, 1–1.5 by 1–1.7 cm. Petals 9–13, white, red or pink (in wild plants), or varying in colour (in cultivated plants), obovate, 3.56 by 1.5–4.5 cm. Stamens numerous, with yellow filaments and anthers. Disc yellow, annular. Carpels 4–5, green or purple, apocar-

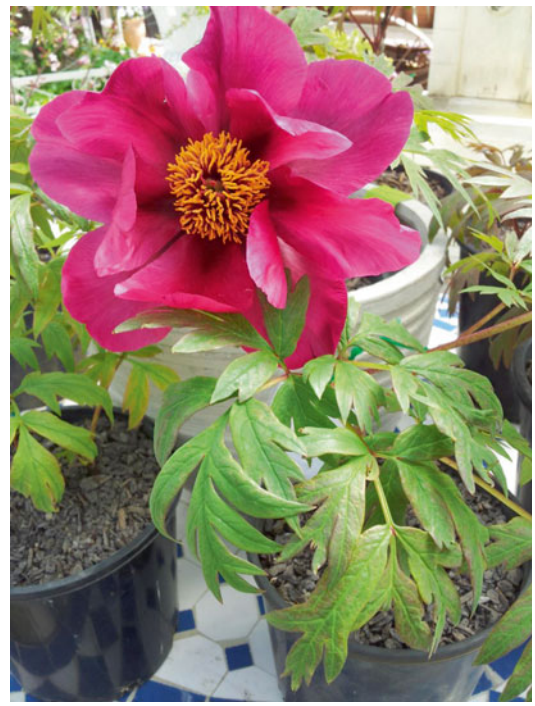

Plate 1 Chinese peony flower and leaves

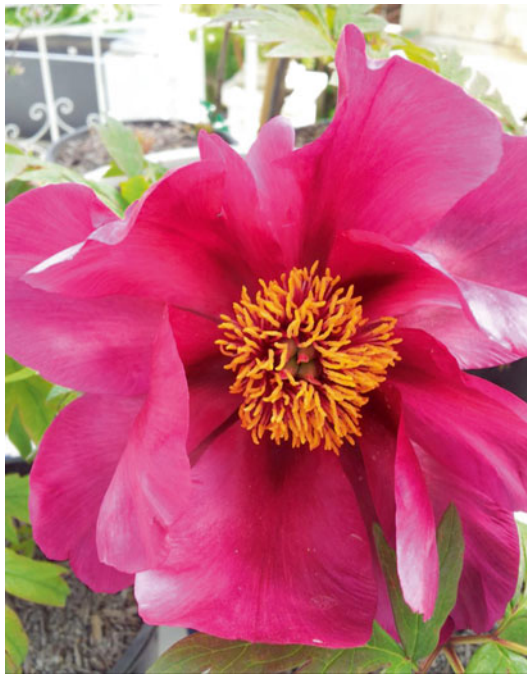

Plate 2 Close-up of flower

pous, glabrous. Follicles oblong–ellipsoid, 2.53 by 1.21.5 cm in horizontal spreading clusters.

Nutritive/Medicinal Properties

Flower Phytochemicals

Two kaempferol glycosides, astragalin (kaempferol-3-glucoside) and kaempferol-3,7-diglucoside (paeoniside), were isolated from double white flowers of *Paeonia albiflora* (Egger 1961). From the light petroleum extract of dried petals of peony, pyrethrin and gallotannin were isolated (Chimielewska and Kasprzyk 1962). Fragrant components of fresh peony flower included oxygenated mono- and sesquiterpenes, aliphatic and aromatic aldehydes and esters and alcohols; 3-oxo-1,8-cineole was found as a new compound (Kumar and Motto 1986). Kazuhiko et al. (2000) found that linalool, citronellol, citronellyl acetate, geraniol, geranyl acetate, nerol, benzaldehyde, 1,3,5-trimethoxybenzene, etc., identified in the headspace gases significantly contributed to the flower odour in seven varieties of Chinese peony, three of Japanese, three of French or American peonies. Eight genes encoding phenylalanine ammonia lyase (PAL), chalcone synthase (CHS), chalcone isomerase (CHI), flavanone 3-hydroxylase (F3H), flavonoid 3′-hydroxylase (F3′H), dihydroflavonol 4-reductase (DFR), anthocyanidin synthase (ANS) and UDP-glucose: flavonoid 3–*O*–glucosyltransferase (UF3GT) were isolated from *Paeonia lactiflora* (Zhao et al. 2012). Moreover, the expression patterns of these eight genes and UF5GT in the flowers were investigated in three cultivars, namely, 'Hongyanzhenghui', 'Yulouhongxing' and 'Huangjinlun' with purplish-red, white and yellow flower, respectively. Additionally, anthoxanthins and anthocyanins were detected in 'Hongyanzhenghui' and 'Yulouhongxing', chalcones and anthoxanthins were found in 'Huangjinlun'.

Fruit Phytochemicals

Four dimeric ellagitannins, paeonianins A–D, were isolated from *Paeonia lactiflora* fruit, together with an ellagitannin monomer, paeonianin E. Paeonianins A–D were found to be positional isomers formed by condensation of pentagalloyl-β-D-glucose with 5-desgalloylstachyurin or casuariin. Paeonianin E was found to be a C-glycosidic ellagitannin with a gallic acid methyl ester moiety at the glucose C-1 position.

Seed Phytochemicals

Seven stilbenes, a new *cis*-ε-viniferin and the six known stilbenes, *trans*-resveratrol, *trans*-resveratrol-4′–*O*-β-D-glucopyranoside, *trans*-ε-viniferin, gnetin H and suffruticosols A and B, were isolated from the seeds (Kim et al. 2002a, b, c). Six compounds, luteolin, resveratrol, *trans*-ε-viniferin, gnetin H, suffruticosol A and suffruticosol B, were isolated from the seeds (Choi et al. 2009). The following resveratrol oligomers were isolated from the seeds: (−)-7a,8a-*cis*-ε-viniferin, *trans*-ε-viniferin, *cis*-ε-viniferin, *trans*-resveratrol, vitisinol C, vitisinol E, gnetin H, suffruticosol A and suffruticosol B (Choi et al. 2011).

Aerial Part/Plant Phytochemicals

Two flavonoids, astragalin and peonosides, were isolated from the aerial parts (Kamiya et al. 1997). Five compounds, paeoniflorin, benzoylpaeoniflorin, galloylpaeoniflorin, 1,2,3,4,6 galloyl glucose and daucosterol, were found in *P. lactiflora* (Zhang et al. 2001). Nine compounds, paeoniflorin, oxypaeoniflorin, benzoylpaeoniflorin, lactiflorin, 4-ethyl-paeoniflorin, 1,2,3-trihydroxybenzene, dihydroapigenin, benzoic acid and β-sitosterol, were isolated from *P. lactiflora* (Wang et al. 2006b). Ten compounds, evofolin B, (1S,2S,4R)-*trans*-2-hydroxy-1,8-cineole-β-D-glucopyranoside, (2R,3R)-4-methoxyl-distylin, 1,2,3,4,6-penta-galloyl-glucose, catechin, benzoic acid, gallic acid, vanillic acid, methyl gallate and progallin A, were isolated from the plant (Duan et al. 2009a).

A homogeneous polysaccharide–protein complex PAII of average molecular weight 5.25×10^4, comprising 85.0 % carbohydrate and 13.2 % protein content, was isolated; the saccharide and protein were linked by non-*O*-glycosidic band (Yu et al. 2008). PAII was consisted mainly of D-glucose; the molar ratio of glucose, arabinose, mannose, rhamnose and xylose was 153 : 2.6 : 1.25 : 1 : 1

The amounts of paeoniflorin and albiflorin found in the raw peony herb were 33.2 and 1.8 mg/g, respectively; and in the dried aqueous extract, the amounts were 34.8 and 15.7 mg/g, respectively (Lee et al. 2009). The limits of detection for paeoniflorin and albiflorin were 0.37 and 1.39 mg/g, respectively, for the raw peony herb and 0.25 and 0.06 mg/g, respectively, for the dried aqueous extract. The contents of catechin and paeoniflorin in *Paeonia lactiflora* in different plant parts collected in autumn were the highest, and the contents of benzoic acid were lower than that of those collected at other times (Jian et al. 2010). The older the plant of *Paeonia lactiflora*, the higher were the contents of catechin and paeoniflorin. The contents of catechin and paeoniflorin in the root of *Paeonia lactiflora* were higher than those in other parts of the plant. Paeoniflorin was also found in the leaves. It was deduced that paeoniflorin was synthesized in the leaf and then transported to the root. Catechin was not synthesized in the leaf, but mainly in the root. The leaves and stem were found to be rich in oleanoic and ursolic acids, reaching maximum levels in August–September (Zhou et al. 2011a).

Root Phytochemicals

Radix Paeoniae was found to be rich in minerals K, Ca, Na, Mg, Zn and Fe (Xu et al. 2008). From the roots were isolated paeoniflorin, albiflorin, oxypaeoniflorin, benzoylpaeoniflorin and alliflorin (Shibata and Nakara 1963; Shibata et al. 1963; Aimi et al. 1969; Kaneda et al. 1972); 1,2,3,4,6-penta-*O*-galloyl glucose, (+)-catechin and gallic acid (Shibutani et al. 1981); paeoniflorigenone, benzoic acid and *p*-hydroxybenzoic acid (Shimizu et al. 1981, 1983); lactiflorin (Lang et al. 1983); monoterpene glycoside (*Z*)-(1*S*,5*R*)-β-pinen-10-yl β-vicianoside (Lang et al. 1984); paeonilactones A, B and C monoterpenoids (Hayashi et al. 1985); daucosterol (β-sitosterol-D-glucoside) (Xu 1986); monoterpene glycoside lactiflorin (Yu et al. 1990); acylated monoterpene glucoside and galloylpaeoniflorin (Kang et al. 1991); palbinone and a known compound, paeonilactone-B (Kadota et al. 1993); paeoniflorin and tannin (Yamashita et al. 1994); paeoniflorin and 8-debenzoylpaeoniflorin (Hsu et al. 1997); and paeoniflorin, albiflorin and pentagalloylglucose; other compounds included gallic acid, oxypaeoniflorin, benzoic acid, paeonol and benzoylalbiflorin from commercial root samples (Chuang et al. 1996); 6–*O*-(β-D-glucopyranosyl) lactinolide; lactinolide; 1–*O*- (β-D-glucopyranosyl) paeonisuffrone; oxybenzoyl-paeoniflorin; paeonilactinone; 8 known constituents, 10-hydroxyverbenone, (+)-1-*p*-menthane-7.8-diol, paeoniflorin, lactiflorin, benzoyloxypaeoniflorin, benzoylpaeoniflorin, albiflorin and oxypaeoniflorin (Murakami et al. 1996); seven triterpenoids, oleanoic acid, betulinic acid, 23-hydroxybetulinic acid, hederagenin, norhederagenin, 3β-hydroxyolean-12-en-28-al and 11α, 11α, 12α-epoxy-3β, 23-dihydroxy-30-norolean-20(29)-en-28,13 β-olide (Kamiya et al. 1997); albiflorin R1, a monoterpene glycoside

(Zhang et al. 2002); monoterpene glycoside, galloylalbiflorin together with nine known ones, mudanpioside J, 3-*O*-methylpaeoniflorin, paeoniflorin, benzoylpaeoniflorin, oxypaeoniflorin, benzoyloxypaeoniflorin, oxybenzoylpaeoniflorin, albiflorin and lactiflorin (Wang et al. 2006a); 2-methoxy-5-(*E*)-propenyl-phenol-β-vicianoside (Guo et al. 2006); 6′-*O*-β-D-glucopyranosylalbiflorin, albiflorin, 6′-*O*-benzoylalbiflorin, paeoniflorin and benzoyl paeoniflorin (Pham et al. 2007); monoterpene glycoside, 6′-*O*-β-D-glucopyranosylalbiflorin; albiflorin; 1-*O*-β-D-glucopyranosyl-8-*O*-benzoylpaeonisuffrone, 1-*O*-β-D-glucopyranosyl paeonisuffrone and paeonidanin (Kim et al. 2008; ten monoterpene glucosides were isolated and identified as lactiflorin (1), benzoylpaeoniflorin (2), mudanpioside C (3), 1-*O*-β-D-glucosylpaeonisuffrone (4), paeonidanin (5), 1-*O*-β-D-glucosyl-8-*O*-benzoylpaeonisuffrone (6), paeoniflorin (7), albiflorin (8), oxypaeoniflorin (9) and mudanpioside E (10) (Yean et al. 2008); 4-*O*-methyl-paeoniflorin, isopaeoniflorin and isobenzoylpaeoniflorin and paeoniflorin and benzoylpaeoniflorin (Braca et al. 2008); four 'cage-like' monoterpene glucosides (Wang et al. 2009); 4′-*O*-benzoylpaeoniflorin and 4-*O*-galloylalbiflorin (Ren et al. 2009); monoterpene glycoside, 3′-*O*-galloylpaeoniflorin (1); four known compounds, 6′-*O*-galloylalbiflorin (2), pentagalloylglucose (3), 6′-*O*-benzoylpaeoniflorin (4) and 6′-*O*-galloylpaeoniflorin (5) (Washida et al. 2009a); two galloylated monoterpene glycosides, 4-*O*-galloylalbiflorin and 4′-*O*-galloylpaeoniflorin (Washida et al. 2009b); eleven monoterpenes, paeonidangenin (1), paeonidanin A (2), paeonidanin B (3), paeonidanin C (4), paeonidanin D (5), paeonidanin E (6), paeoniflorone (7), 4-*O*-methylbenzoylpaeoniflorin (8), 4-*O*-methylgalloylpaeoniflorin (9), 4-*O*-methyldebenzoylpaeoniflorin (10) and 4-*O*-methylalbiflorin (11) (Duan et al. 2009c); seven monoterpenes, paeonilactone-B, paeonilactone-C, paeoniflorigenone, benzoylpaeoniflorin, paeoniflorin, oxypaeoniflorin and albiflorin (Kim et al. 2009); 1,2,3,4,6-penta-*O*-galloyl-D-glucopyranose (Baumgartner et al. 2010); paeoniflorin; albiflorin; 4-*O*-galloylalbiflorin; galloypaeonbiflorin; alloylalbiflorin; 6-*O*-galloyl-β-D-glucopyraneose; pyrogallol; gallic acid; methyl gallate; ethyl gallate; catechin; 1,2,3,4,6-pentagalloylglucose; di-(2-ethylhexyl) phthalate; sucrose; β-sitosterol (Tan et al. 2010); and three new monoterpene glycosides, 2′-*O*-benzoylpaeoniflorin, albiflorin R_2 and albiflorin R_3 (Fu et al. 2013).

Together with 1,2,3,6-tetra-*O*-galloyl-β-D-glucose and 1,2,3,4,6-penta-*O*-galloyl-β-D-glucoses, homologous series of hexa- and heptagalloylglucoses were isolated from the tannin fraction of *P. lactiflora* roots (Nishizawa et al. 1983a, b). The hexagalloylglucose fraction comprised three components: 2-*O*-di-galloyl-1,3,4,6-tetra-*O*-galloyl-β-D-glucose, 3-*O*-di-galloyl-1,3,4,6-tetra-*O*-galloyl-β-D-glucose and 6-*O*-di-galloyl-1,3,4,6-tetra-*O*-galloyl-β-D-glucose. The heptagalloylglucose fraction yielded five components: 2,3-bis-*O*-digalloyl-1,4,6-tri-*O*-galloyl-β-D-glucose, 3-*O*-trigalloyl-1,2,4,6-tetra-*O*-galloyl-β-D-glucose, 4,6- bis-*O*-digalloyl-1,2,3-tri-*O*-galloyl-β-D-glucose, 3,6,-bis-*O*-1,2,4-tri-*O*-galloyl- β-D-glucose and 2,6,-bis-*O*-1,2,4-tri-*O*-galloyl-β-D-glucose. Octa-, nona- and decagalloylglucose fractions comprised more than five components with a 1,2,3,4,6-pentagalloylglucose core, and octagalloylglucose comprised a compound 2,3,6-tris-*O*-galloyl-1,4-di-*O*-galloyl-β-D-glucose and more than five components.

From the roots of *P. lactiflora*, seven new monoterpene glycoside esters related to paeoniflorin were isolated from Radix Paeoniae, together with polymeric proanthocyanidins, polygalloylglucoses and 48 known compounds (a benzoyl sucrose, seven aromatic acids, adenosine, nine monoterpene glycosides, eight flavan-3-ols, a catechin dimer formed by oxidation, seven proanthocyanidins, three galloylsucroses, five galloylglucoses and six ellagitannins) (Tanaka et al. 2000). The seven new monoterpene glycoside esters were 8-*O*-galloyl desbenzoylpaeoniflorin, 8-*O*-isovaleryl desbenzoylpaeoniflorin, 6′-*O*-galloyl desbenzoylpaeoniflorin, 6′-*O*-vanillypaeoniflorin, 3′,6′-di-*O*-galloylpaeoniflorin, 6′-*O*-α-glucopyranosylpaeoniflorin named isomaltopaeoniflorin and 6′-*O*-galloyl desbenzoylalbiflorin and 1′*O*-benzoylsucrose, isolated for

the first time from natural source. The remaining compounds were identified as seven aromatic carboxylic acids [gallic acid, benzoic acid, vanillic acid, syringic acid, *p*-hydroxybenzoic acid, 4,5-dihydroxy-3-methoxybenzoic acid and an equilibrium mixture of *m*-digallate and *p*-digallate]; adenosine; nine monoterpene glycosides [paeoniflorin, oxypaeoniflorin, benzoylpaeoniflorin, benzoyloxypaeoniflorin, galloylpaeoniflorin, galloyloxypaeoniflorin, mudanpioside E, mudanpioside F and desbenzoylpaeoniflorin]; three galloylsucroses [6-*O*-galloylsucrose, 1′-*O*-galloylsucrose, 6′-*O*-galloylsucrose]; eight flavan-3-ols [(+)-catechin, catechin 5-*O*-glucoside, catechin 7-*O*-glucoside, catechin 3′-*O*-glucoside, catechin 4′-*O*-glucoside, catechin 7-*O*-gallate, catechin 3′(4′)-*O*-gallate (an equilibrium mixture), epicatechin 3-*O*-gallate]; catechin dimer formed by oxidation; seven proanthocyanidins [procyanidin B-3, procyanidin B-1, procyanidin B-1 3-*O*-gallate, procyanidin B-2 3′-*O*-gallate, procyanidin B-7, procyanidin AC-trimer and procyanidin arecatannin A-1]; five galloylglucoses [1,2,3-tri-*O*-galloyl-β-D-glucose,1,2,6-tri-*O*-galloyl-β-D-glucose, 1,2,3,4-tetra-*O*-galloyl-β-D-glucose, 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose, 2,3,4,6-tetra-*O*-galloyl-D-glucose}; and six ellagitannins [2,3-(*S*)-hexahydroxydiphenoyl-D-glucose, eugeniin, pterocaryanin B, casuariin, pedunculagin and 1(β)-*O*-galloylpedunculagin]. Seventeen compounds were obtained from peony roots and their structures were identified as 1,2,6-benzenetriol-1-*O*-α-D-glucoside (1), paeoniflorin (2), 4-methylpaeoniflorin (3), albiflorin (4), paeonidanin (5), benzoylpaeoniflorin (6),4-methylbenzoylpaeoniflorin (7), benzoylalbiflorin (8), paeonidanin A (9), galloylalbiflorin (10), desbenzoylalbiflorin (11), 4′,5-dihydroxyflavanone-7-*O*-β-D-glucoside (12), 5,7-dihydroxy flavanone-4′-*O*-β-D-glucoside (13),(+)-catechin (14), gallic acid (15), vanillic acid (16) and 1,2,3-benzenetriol (17) (He et al. 2011).

Five phenolic compounds, (+)-taxifolin-3-*O*-β-D-glucopyranoside (0.23–0.52 %), benzoic acid (0.2–0.3 %), gallic acid (0.26–0.28 %), (−)-epicatechin (0.09–0.12 %) and (+)-catechin (0.34–0.63 %), were isolated from *P. lactiflora* roots (Choung et al. 2000). Four compounds named (3R,4S)-3-methyl-3,4-dihydro-5,6,7-trihydroxy-4-(3′-methoxy-4′-hydroxyphenyl)-1H-[2]-benzopyran-1-one (1), 5-hydroxy-6-methyl-1H-indole-3-carbaldehyde (2), *trans*-5-hydroxy-2-methoxy-6-methyl-2,3-dihydrobenzofuran-3-yl methyl benzoate (3) and *cis*-5-hydroxy-2-methoxy-6-methyl-2,3-dihydrobenzofuran-3-yl methyl benzoate (4) and two known ones, (7S,8S)-3-methoxy-3′,7-epoxy-8,4′-oxyneligna-4,9,9′-triol (5) and (7S,8R)-dihydrodehydrodiconifery alcohol (6), were isolated from the roots (Duan et al. 2009b).

Six gallotannins (pentagalloylglucose, hexagalloylglucose, heptagalloylglucose, octagalloylglucose, nonagalloylglucose, decagalloylglucose) were isolated from the roots (Nishizawa et al. 1980). The structure of pentagalloylglucose was elucidated as 1,2,3,4,6-pentakistri-*O*-methylgalloyl-β-D-glucose and hexagalloylglucose as 6-*m*-digalloyl-1,2,3,4-tetragalloyl-β-D-glucose. An acidic polysaccharide, called peonan PA, with molecular mass of 6.0×10^4,was isolated from *Paeonia lactiflora* roots (Tomoda et al. 1994). It was composed of L-arabinose: D-galactose:D-galacturonic acid in the molar ratio of 2:1:10, in addition to small amounts of *O*-acetyl groups and peptide moieties. About 40 % of the hexuronic acid residues in peonan PA existed as methyl esters. Its main structural features was found to involve both alpha-1,5-linked L-arabino-β-3,6-branched D-galactan-type and α-1,4-linked D-galacturonan-type structural units.

Benzoic acid (0.6635 %) was found mostly distributed in peony root cortex (Wang et al. 2008). Paeoniflorin, sucrose, glucose and fructose in traditional Chinese medicine, Radix Paeoniae Alba, were separated and determined using capillary electrophoresis (Chen et al. 2005). Peony roots were found to contain paeoniflorin, 1,2,3,4,6-penta-*O*-galloyl-glucoside, albiflorin, methyl gallate and other compounds (Yang et al. 2007). Monoterpene glycosides such as paeoniflorin, albiflorin, oxypaeoniflorin, benzoylpaeoniflorin and benzoyloxypaeoniflorin and other compounds such as (+)-catechin) and β-sitosterol were found to be common to both Radix

Paeoniae Alba (Bai-shao in Chinese) and Radix Paeoniae Rubra (Chi-shao in Chinese), categories of *Paeonia lactiflora* root (Yang et al. 2009). Furthermore, the two roots also contained some galloyl glucoses, flavonoids and lipophilic components such as monoterpene aglycones, triterpenes and acetophenones. However, the fingerprint of Bai-shao displayed more bands than that of Chi-shao, and the ratios of peak-to-peak intensities were also rather different between the two roots. Wild peony root (Radix Paeoniae Rubra, Chi-shao) extract had markedly higher content of paeoniflorin and catechin than cultivated peony root (Radix Paeoniae Alba, Bai-shao) extract, whereas Bai-shao possessed higher content of albiflorin than Chi-shao (Wang et al. 2012b). Drying after boiling, drying after decorticating and boiling and drying after boiling and decorticating methods reduced the content of benzoic acid and paeonol to trace in both root extract types.

The main volatile chemical components of Radix Paeoniae Rubra (*P. lactiflora*) were (*Z*,*Z*)-9,12-octadecadienoic acid (30.11 %), *n*-hexadecanoic acid (20.18 %), 2-hydroxybenzaldehyde (17.10 %), 1-(2-hydroxy-4-methoxyphenyl)-ethanone (5.99 %), 6,6-dimethylbicyclo[3.1.1] heptane-2-methanol (3.39 %), 4,7-dimethyl-benzofuran (2.41 %), phenylmethyl ester 2-hydroxy-benzoic acid (1.86 %), 4-(1-methylethenyl)-1-cyclohexene-1-carboxaldehyde (1.55 %) and cyclohexadecane (1.46 %) (Li et al. 2007b). Other components included as follows: (1,4-dimethyl-3-cyclohexen-1-yl)-ethanone (0.98 %), (*E*)-2-methoxy-4(1-propenyl)-phenol (0.85 %), 6,6-dimethylbicyclo[3.1.1]heptane-2-carboxaldehyd (0.85 %), 1-methyl-4-(1-methylethyl) 1,4-cyclohexadiene (0.66 %), benzyl benzoate (0.57 %), 6,6-dimethylbicyclo[3.1.1]hept-2-ene-2-carboxaldehyde (0.56 %), 3-hexyl-cyclopetene (0.13 %), tridecanol (0.04 %), 6-methyl-spiro[4.5] and decan-6-ol (0.03 %). Eighteen compounds were isolated from the roots: seven simple phenolic or flavonoid compounds [benzoic acid, *p*-hydroxybenzoic acid, gallic acid, methyl gallate, paeonol, paeonoside and (+)-catechin], six monoterpenoids [paeoniflorigenone, paeoniflorin, oxypaeoniflorin, benzoylpaeoniflorin, benzoyloxypaeoniflorin and galloylpaeoniflorin] and five steroids and triterpenoids [betulinic acid, β-sitosterol, daucosterol, hederagenin and oleanolic acid] (Koo et al. 2010).

The compositions of the essential oil of *P. lactiflora* roots with and without bark were, respectively, determined as follows: benzoic acid (44.38, 37.23 %), paeonol (13.25, 12.29 %), benzyl alcohol (5.20, 6.65 %), butyl alcohol (0.02, 0.03 %), furfural (0.95, 1.25 %), 3-hydroxypyridine (tr (trace), tr), 2-furyl methyl ketone (tr, tr), benzaldehyde (0.99, 1.4 %), 5-methyl-2-furfural (1.25, 2.06 %), methyl benzoate (0.56, 0.79 %), phenyl acetaldehyde (0.5, 0.3 %), acetophenone (0.75, 0.85 %), furfuryl alcohol (0.03, 0.05 %), 4,7-dimethyl benzofuran (1.35, 1.38 %), α,α-dimethyl benzyl alcohol (0.53, 0.65 %), methyl salicylate (1.35, 1.87 %), *o*-hydroxyacetophenone (tr, tr), ethyl salicylate (0.05, 0.06 %), 2-methoxyphenol (tr, tr), β-phenylethyl alcohol (1.98, 2.25 %), 2,6-di-*tert*-butyl-4-methyl phenol (tr, tr), 2-acetyl pyrrole (tr, tr), phenol (2.05, 2.34 %), *p*-cresol (tr, tr), *m*-cresol (tr, tr), *m*-*tert*-butyl (tr, tr), *p*-methoxyacetophenone (0.62, 0.53 %), thymol (tr, tr), carvacrol (tr, tr) and 4-hydroxy-3-methoxy acetophenone (tr, tr) (Miyazawa et al. 1984).

Callus Tissue Phytochemicals

Four triterpenoids isolated from the callus tissues of *Paeonia japonica, P. lactiflora* and *P. suffruticosa* included the following: 11α,12α-epoxy-3β,23-dihydroxyolean-28,13β-olide; 3β-hydroxy-11-oxo-olean-12-en-28-oic acid, 3β-hydroxy-oleana-11,13(18)-dien-28-oic acid and 3β,23-dihydroxy-oleana-11,13(18)-dien-28-oic acid (Ikuta et al. 1995).

Antioxidative Activity

Ethanol root extract of *Paeonia lactiflora* and its constituents, gallic acid and methyl gallate, exhibited protective free radical scavenging effect, against 1,1-diphenyl-2-picrylhydrazine (DPPH),

and lipid peroxidation (Lee et al. 2005). Among seven stilbenes isolated from the seeds, *trans*-ε-viniferin and gnetin H significantly inhibited 2-deoxyribose degradation and lipid peroxidation in rat liver microsomes (Kim et al. 2002a). In addition, *cis*-ε-viniferin and suffruticosols A and B also exhibited moderate antioxidative activity. The results suggested that resveratrol dimers and trimers, together with resveratrol from seeds of *Paeonia lactiflora*, may be useful as potential sources of natural antioxidants. The total polyphenol content of peony root methanol extract was 73.45 mg/g, and the content of the ethyl acetate fraction was 514.50 mg/g as the highest content of fractions (Im and Lee 2011). In DPPH radical scavenging ability, SC_{50} value of the ethyl acetate was 3.86 μg/mL as a result of greater activity in the positive control (ascorbic acid).

Paeoniflorin, from peony root, exhibited a protective effect against H_2O_2 oxidative damage in human umbilical vein endothelial cells (HUVECs) (Chen et al. 2011b). It markedly attenuated H_2O_2-induced apoptosis and intracellular reactive oxygen species production and also displayed a dose-dependent reduction of lactate dehydrogenase leakage, malondialdehyde formation and caspase-3 proteolytic activities in H_2O_2-treated cells, which was accompanied by a restoration of the activities of endogenous antioxidants, including total superoxide dismutase and glutathione peroxidase. Paeoniflorin also reversed H_2O_2 up-regulated phosphorylation of extracellular signal-regulated kinase 1/2 in HUVECs.

Anticancer Activity

In vitro studies showed that the aqueous peony root extract inhibited the growth of both HepG2 and Hep3B hepatoma cell lines via apoptosis (Lee et al. 2002). The gene expression of BNIP3 was up-regulated, while ZK1, RAD23B and HSPD1 were downregulated during early apoptosis of the hepatoma cell mediated by peony extract. Six stilbenes, *trans*-resveratrol, *cis*-ε-viniferin, *trans*-ε-viniferin, gnetin H and suffruticosols A and B isolated from the seeds, showed cytotoxic activity in a dose-dependent manner and especially potent cytotoxic activity against C6 (mouse glioma) cancer cell with IC_{50} values ranging from 8.2 to 20.5 μg/mL (Kim et al. 2002a). *trans*-Resveratrol showed significant cytotoxic activity against HepG2 (liver hepatoma) and HT-29 (colon) human cancer cell lines with IC_{50} values of 11.8 and 25.2 g/mL, respectively. In contrast, *trans*-epsilon-viniferin, *cis*-ε-viniferin and gnetin H exhibited marked cytotoxic activity against Hela (cervix) and MCF-7 (breast) human cancer cell lines with IC_{50} values of 20.4, 21.5 and 12.9 μg/mL, respectively. However, suffruticosols A and B had less cytotoxic effect against all cancer cells except C6. All resveratrol and its derivatives viniferin, gnetin H and suffruticosol B reduced viability of human promyelocytic leukaemia HL-60 cells in a dose-dependent manner with their IC_{50} values of 20–90 μM (Kang et al. 2003). Ascending orders of IC_{50} values were suffruticosol B, gnetin H, viniferin and resveratrol, respectively. HL-60 cells treated with the four stilbenes exhibited the distinct morphological change characteristics of cell apoptosis such as chromatin condensation, apoptotic bodies and DNA fragmentations. Cells treated with 25 μ of resveratrol, viniferin, gnetin H and suffruticosol B for 24 h resulted in increment of sub-G1 population by 51, 5, 11 and 59 %, respectively. Treatment of cells with 0–20 μ resveratrol for 5 h produced a concentration-dependent decrease in cytochrome P450 (CYP) 1B1 mRNA levels. Suffruticosol B also suppressed CYP1B1 gene expression. The results demonstrated that resveratrol oligomers also strongly suppressed HL-60 cell proliferation and induced DNA damage. Further, CYP1B1 gene suppression may suggest an involvement in the resveratrol-induced apoptosis in HL-60 cells. Kwon et al. (2006) found that Radix Paeoniae Alba extract induced apoptotic changes in HL-60 leukaemic cells in a dose-dependent manner. The results suggested that peony root-induced apoptosis was stimulated by the release of cytochrome C to the cytosol, by procaspase-9 processing and via a caspase-3-dependent mechanism.

The compound 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG) from *P. lactiflora* roots was found to have antiangiogenic activity; it inhibited

the binding of vascular endothelial growth factor (VEGF) to tyrosine kinase KDR/Flk-1 (Lee et al. 2004). PGG also efficiently blocked VEGF-induced human umbilical vein endothelial cell proliferation and the growth of immortalized human microvascular endothelial cells, but did not affect the growth of HT1080 human fibrosarcoma and DU-145 human prostate carcinoma cells. PGG also blocked VEGF-induced capillary-like tube formation of endothelial cell on Matrigel. Tsuboi et al. (2004) found that paeoniflorin induced apoptosis in both murine T-lineage cells and human T-cell leukaemic Jurkat cells. This apoptosis was mediated through the reduction of mitochondrial membrane potential, activation of caspase and fragmentation of DNA. Additionally, paeoniflorin induced the phosphorylation of three mitogen-activated protein (MAP) family kinases, extracellular signal-regulated kinase, c-Jun amino-terminal kinase (JNK) and p38 MAP kinase.

TPG (total peony glucosides) (12.5, 62.5 and 312.5 μg/mL) resulted in a dose-dependent reduction in the proliferation of human vascular endothelial cells (Deng et al. 2010). Fluorescence-activated cell sorting analysis data showed an accumulation of cells in the G0/G1 phase of the cell cycle, which exhibited apoptotic features indicative of cell death. The migration properties and tube-forming abilities of endothelial cells were dramatically inhibited by the TPG extract. The results indicated that TPG could inhibit angiogenesis in vitro and in vivo.

Peony root extract inhibited the growth of urinary bladder TSGH-8301 cancer cells via induction of apoptosis and cell cycle arrest (Ou et al. 2011). Treatment of TSGH-8301 cells with peony extract resulted in G2–M phase arrest that was associated with a marked decline in protein levels of cdc2, cyclin B1, cell division cycle 25B (Cdc25B) and Cdc25C. Further, in a rat model of bladder cancer induced by N-butyl-N-(4-hydroxybutyl) nitrosamine (OH-BBN), tumours from peony-treated rats showed significant decrease in the expression of Bcl2, cyclin D1 and PCNA and increase in the expression of *p*-Chk2 (Thr-68), Bax and Cip1/p21. The data suggested that peony extract could modulate apoptosis in models of bladder cancer.

Antimutagenic Activity

Six stilbenes, *trans*-resveratrol, *cis*-ε-viniferin, *trans*-ε-viniferin, gnetin H and suffruticosols A and B, isolated from the seeds exerted antimutagenic activity in a dose-dependent fashion (Kim et al. 2002a). Among them, *trans*-resveratrol exhibited the strongest antimutagenic effect against N-methyl-N′-nitro-N-nitrosoguanidine (MNNG) in *Salmonella typhimurium* TA100 with IC_{50} value of 27.0 μg/plate, while other five resveratrol oligomers also did moderate antimutagenic activity with IC_{50} values ranging from 31.7 to 35.2 μg/plate.

Antiviral Activity

The ethyl acetate fraction of *P. lactiflora* root showed anti-hepatitis B virus (HBV) activity (IC_{50}, 8.1 μg/mL) (Lee et al. 2006). The active anti-HBV principle was isolated and identified as 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG). In the extracellular medium of HepG2.2.15 cells after an 8-day treatment, PGG decreased the level of extracellular HBV (IC_{50}, 1.0 μg/mL) in a dose-dependent manner. PGG also reduced the HBsAg level by 25 % at a concentration of 4 μg/mL. In vitro studies showed that *P. lactiflora* was time-dependently and dose-dependently effective against human respiratory syncytial virus (HRSV) in both human upper (human larynx epidermoid carcinoma cell line, HEp-2) and lower (human lung carcinoma cell line, A549) respiratory tract cells (Lin et al. 2013). *P. lactiflora* had a comparable anti-HRSV activity to 10 μg/mL ribavirin, a broad-spectrum antiviral agent. *P. lactiflora* was dose-dependently effective against viral attachment, with a better effect on A549 cells, and was effective against viral penetration particularly if supplemented before viral inoculation. Moreover, *P. lactiflora* stimulated IFN-β secretion without any effect on TNF-α secretion. *P. lactiflora* could be beneficial at preventing HRSV infection by inhibiting viral attachment and internalization and stimulating IFN secretion.

The aqueous ethanol seed extract of *Paeonia lactiflora* exhibited potent neuraminidase inhibition

(Yuk et al. 2013). Purification of the extract yielded four chiral neuraminidase inhibitory polyphenols, suffruticosol A (1), suffruticosol B (2), *trans*-ε-viniferin (3) and *trans*-gnetin H (4). Mechanistic analysis of 1-4′s inhibition showed that they were all reversible, non-competitive inhibitors.

Antidiabetic Activity

Paeoniflorin and 8-debenzoylpaeoniflorin, isolated from roots, exerted significant blood sugar lowering effect in streptozotocin-treated rats and had a maximum effect at 25 min after treatment (Hsu et al. 1997). This hypoglycaemic action was also observed in normoglycaemic rats only at 1 mg/kg. The antihyperglycaemic activity of 8-debenzoylpaeoniflorin appeared lower than that of paeoniflorin. Plasma insulin was not changed in paeoniflorin-treated normoglycaemic rats indicating an insulin-independent action. Also, this glucoside reduced the elevation of blood sugar in glucose-challenged rats. Results of in vitro studies suggested that paeoniflorin stimulated the release of adenosine from isolated rat white adipocytes and the released adenosine may activate the adenosine A1 receptor to enhance glucose uptake (Tang et al. 2003).

Among the tested extracts, *P. lactiflora* seed extract demonstrated a significant degree of inhibition on α-glucosidase (Choi et al. 2009). Of six bioactive components isolated from the extract, luteolin (1), resveratrol (2), *trans-e*-viniferin (ε), gnetin H (4), suffruticosol A (5) and suffruticosol B (6), compounds 3–6 exhibited relatively strong inhibition of α-glucosidase, and their IC_{50} values were calculated as 0.92 mM (2), 3.15 mM (3), 1.15 mM (4), 2.53 mM (5) and 3.15 mM (6). In contrast, the (IC_{50}) value of the reference drug, acarbose, was estimated as 8.28 mM in vitro.

Animal studies found that total glucosides of peony may protect liver function and modulate serum lipid for the fatty liver rats caused by insulin resistance, and its action mechanism may be concerned with enhancing insulin sensitivity and antioxidative ability, decreasing serum lipid (Zheng et al. 2008). Paeonol was found to protect the endothelial cells of streptozotocin-induced diabetic rat (Min et al. 2009). Expressions of intercellular adhesion molecule (ICAM)-1, vascular cell adhesion molecular VCAM-1, C-reactive protein (CRP), endothelin-1 (ET-1) and thromboxane (TXA2) were decreased and prostaglandin PGI increased.

In another study, total glucosides of peony (TGP) treatment (50, 100, 200 mg/kg), once daily for 8 weeks, significantly lowered 24-h urinary albumin excretion rate in diabetic rats and attenuated glomerular volume (Su et al. 2010a). TGP treatment with 100 and 200 mg/kg significantly reduced indices for tubulointerstitial injury in diabetic rats. The level of malonaldehyde was significantly increased in the kidney of diabetic rats and attenuated by TGP treatment at the dose of 200 mg/kg. TGP treatment in a dose-dependent manner decreased the level of 3-NT protein of the kidney which increased under diabetes. Total antioxidant capacity was significantly reduced in diabetic rat kidney and remarkably increased by TGP treatment at the dose of 100 and 200 mg/kg. Activity of antioxidant enzyme such as superoxide dismutase and catalase was markedly elevated by TGP treatment with 200 mg/kg. *P*-p38 MAPK and NF-kappaB p65 protein expression increased in diabetic rat kidney, but were significantly decreased by TGP treatment.

The ethanol peony root extract dose- and time-dependently suppressed diabetic hyperglycaemia and phosphoenolpyruvate carboxykinase (PEPCK) transcription in streptozotocin-induced diabetic and db/db mice (Juan et al. 2010) Paeonol and paeoniflorin, two well-known constituents in peony root, did not suppress PEPCK expression at testing concentration. It was clearly demonstrated that transcriptional inhibition of gluconeogenesis was one of the important antidiabetic actions of Radix Paeoniae. The compound 1,2,3,4,6-penta-*O*-galloyl-D-glucopyranose isolated from the *P. lactiflora* roots was found to be an inhibitor of protein tyrosine phosphatase 1B, with an IC_{50} value of 4.8 μM and with antidiabetic activity (Baumgartner et al. 2010). Further, the compound was shown to act as an

insulin sensitizer in human hepatoma cells (HCC-1.2) at a concentration of 10 μM. Peony root extract lacking the insulin mimetic compound, 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG), and termed the non-PGG fraction (NPF), consisting of tannin polymers, suppressed phosphoenolpyruvate carboxykinase (PEPCK) gene expression in the presence of an insulin receptor antagonist (HNMPA-AM(3)), suggesting the action of this fraction was independent of the insulin receptor (Juan et al. 2011). NPF also prevented Dex-stimulated GR nuclear localization and transactivation and inhibited 8-bromo-cAMP-stimulated element-binding protein (CREB) serine phosphorylation and DNA binding in H4IIE cells. The results suggested that the potent suppressive activity on PEPCK gene transcription observed with Radix Paeoniae Rubra extract could be attributed to at least two distinct components, namely, PGG and NPF. Hence, NPF antagonized both signalling pathways that induce PEPCK gene transcription.

Cardiovascular Protective/ Antihyperlipidaemic/ Atheroprotective Activities

Oral administration of cholesterol-fed rabbits with nifedipine (15 mg/kg/day) and *Paeonia lactiflora* (0.5 g/kg per day) with 2 % cholesterol diet for 15 weeks caused 60.75 and 74.24 % reduction in the lesion area of the aorta, respectively (Zhang and Yan 1990). The levels of plasma lipid peroxide, thromboxane B2, cholesterol, phospholipid and calcium of the intima–media of the aorta in the treated groups were significantly lower than those in the control group, but the level of 6-keto-PGF1 alpha (a stable hydrolysis product of prostacyclin (PG12)) in the treated groups was significantly higher. It was demonstrated that calcium metabolism played an important role in thromboxane, prostaglandin and plasma lipid peroxide synthesis. It was concluded that the inhibition of lipid peroxide production and the regulation of TXA2 (thromboxane A2)–PGI2 balance may be one of the mechanisms of antiatherogenesis of calcium antagonists and *Paeonia lactiflora*. Oral administration of nifedipine (15 mg/kg/day), diltiazem (30 mg/kg/day) and *Paeonia lactiflora* (5 g/kg/day) to rabbits caused 60.8, 45.2 and 74.2 % reduction in the area of atherosclerosis in the aorta, respectively (Zhang 1991). The levels of plasma lipid peroxides and thromboxane TXB2 and the contents of cholesterol, phospholipid and calcium in the intima–media of the aorta in the treated groups were significantly lower than those in the cholesterol group, but the level of plasma 6-keto-PGF1 alpha in the treated groups was significantly higher. It was concluded that the inhibition of plasma lipid peroxide production and regulation of thromboxane A2 (TXA2) and prostacyclin (PGI2) balance may be one of the main mechanisms of the antiatherogenic effects of calcium antagonists and *Paeonia lactiflora*.

Paeoniflorin isolated from the methanol extract of *Paeonia lactiflora* exhibited a significantly lowering effect of total cholesterol, LDL and triglyceride levels in the experimentally induced hyperlipidaemic rats compared to the control group at the dose of 200 and 400 mg/kg, p.o. once a day for 4 weeks (Yang et al. 2004).

Studies using the mammalian one-hybrid and transient transfection reporter assays showed that paeoniflorin transactivated GAL4, rat cholesterol 7 α-hydroxylase, phospholipid transfer protein and ATP-binding cassette A1 gene promoters in dose-dependent manner (Lin 2013). The results showed that paeoniflorin acted as a liver X receptor agonist.

Paeonol, from *P. lactiflora*, concentration-dependently inhibited the production of intercellular adhesion molecule-1 (ICAM-1) in tumour necrosis factor-alpha (TNF-alpha)-activated human umbilical vein endothelial cells (HUVECs) (Nizamutdinova et al. 2007). They found that the inhibitory effect of paeonol on ICAM-1 production might be mediated by inhibiting the TNF-alpha-induced phosphorylation of p38 and extracellular signal-regulated kinase (ERK) and nuclear factor-kappaB (NF-kappaB) p65 signalling pathways, which were involved in TNF-alpha-induced ICAM-1 production. Thus, paeonol may be beneficial in the treatment of cardiovascular disorders such as atherosclerosis.

Studies demonstrated that administration of 10 mg/kg of paeoniflorin or paeonol, active compounds of *P. albiflora*, 1 h prior to myocardial ischaemia and reperfusion (I/R)-induced injury in Sprague–Dawley rats significantly reduced infract size and improved haemodynamic parameters (Nizamutdinova et al. 2008). Further, both PF and PN decreased the caspase-3 and Bax expressions but up-regulated Bcl-2 in the left ventricles. The results showed that both paeoniflorin and paeonol reduced myocardial damage in rat through protection from apoptosis, suggesting that *P. albiflora* might be useful in treating myocardial infarction.

Compared to controls, total peony glucoside (TPG) significantly lowered the serum level of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), apolipoprotein ApoB, tumour necrosis factor-alpha (TNF-alpha), IL-6 and C-reactive protein (CRP); increased the ratios of high-density lipoprotein cholesterol (HDL-C)/LDL-C and ApoA1/ApoB; decreased the intima–media thickness of abdominal aortal wall; and improved the morphological change of the aorta of rats with atherosclerosis induced by excessive administration of vitamin D and cholesterol (Li et al. 2011a). The attenuation of atherosclerotic disease in rats by TPG was associated with its lowering of blood lipids and its inhibition of the expression of inflammatory cytokines. The results of animal studies suggested that total peony glycosides (TPG) significantly ameliorate isoprenaline-induced myocardial ischaemia in rats, and their action might be through reducing oxidative stress in ischaemic myocardium. Compared with model rats, TPG treatment, TPG therapy and the positive control treatment exhibited significantly reduced activities of glutamic oxaloacetic transaminase (GOT), creatine kinase (CK), lactate dehydrogenase (LDH) and antioxidant enzyme superoxide dismutase (SOD) and lower levels of malondialdehyde (MDA) (Long et al. 2012). Also the protective effect of TPG treatment was even better than that of propranolol.

In vitro studies indicated that paeoniflorin elicited effective protection against cobalt chloride hypoxia-induced apoptosis of endothelial cells by preventing cobalt chloride-induced hypoxia-induced factor-1α (HIF-1α) accumulation and downregulating the expressions of p53 and Bcl-2/adenovirus E1B 19 kDa interacting protein 3 (BNIP3) (Ji et al. 2012). Hypoxia had been reported to have a profound impact on endothelial cell properties during cardiovascular disease processes and to be involved in the initiation and development of atherosclerotic lesion.

Steroid Hormone Inhibitory Activity

NADPH-linked 3 alpha-hydroxysteroid dehydrogenase reduces ketosteroids and therefore plays an important role in the metabolism of steroid hormones. Palbinone, isolated from the roots, showed a strong inhibitory activity on the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH)-linked 3 alpha-hydroxysteroid dehydrogenase (3 alpha-HSD) of rat liver cytosol (Kadota et al. 1992, 1993).

Anti-allergic Activity

The compound 1-*O*-β-D-glucopyranosyl-paeonisuffrone isolated from the roots was found to inhibit histamine release from rat peritoneal exudate cells induced by antigen–antibody reaction (Murakami et al. 1996). *P. lactiflora* roots, paeoniflorin and paeonol, isolated from the roots, potently inhibited passive cutaneous anaphylaxis (PCA) reaction induced by IgE–antigen complex and scratching behaviours induced by compound 48/80 in mice (Lee et al. 2008a). Paeoniflorin exhibited the most potent inhibition against scratching behaviours and the acetic acid-induced writhing syndrome in mice. Paeonol most potently inhibited PCA reaction and mast cell degranulation.

Anti-inflammatory Activity

In Vitro Studies

Of the four compounds examined, namely, 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG) from

peony root, (-)-epigallocatechin gallate (EGCG), gallic acid and gallacetophenone, PGG was found to be the most potent in inhibiting both iNOS (IC_{50} approximately 18 μg/mL) and COX-2 activity (prostaglandin E2 (PGE2) IC_{50} approximately 8 μg/mL and prostaglandin D2 (PGD2), IC_{50} approximately 12 μg/mL), respectively, in LPS-activated RAW 264.7 cells (Lee et al. 2003). Their results suggested that PGG might be a candidate for developing anti-inflammatory and cancer chemopreventive agents. In vitro studies in human nasal mucosal fibroblasts showed that peony root extract significantly decreased the secretion of monocyte chemotactic proteins MCP-1 and MCP-3 potent chemokines mediating allergic nasal inflammation (Leem et al. 2004). Total glucosides of peony exhibited inhibitory effect on hyperfunctional synoviocytes from rats with collagen-induced arthritis, and its mechanism of action may be related to its suppression of inhibition of abnormal excessive proliferation and overproduction of IL-1, TNF-alpha and PGE2 in the synoviocytes (Zhu et al. 2006).

The ethyl acetate fraction of peony root methanol extract showed strong nitric oxide (NO) production inhibitory effect in lipopolysaccharide (LPS)-stimulated RAW 264.7 cell (Im and Lee 2012). However, in NO scavenging ability, the chloroform fraction was higher than the other fractions and the extract. In the lactate dehydrogenase (LDH) assay against RAW 264.7 cell, the extract and fractions exhibited normal LDH release level as nontoxic result without the ethyl acetate fraction of 100 μg/mL. Total peony glucosides (TPG) inhibited lipopolysaccharide-induced NF-kappaB activation in rat peritoneal macrophages through arresting IKBalpha protein degradation, NF-kappaB p65 protein nuclear translocation and DNA-binding activity of NF-kappaB complex (Chen et al. 2008).

Ear inflammation of ovalbumin-immunized mice was inhibited by TPG (total peony glucosides) (150 mg/kg, i.p.×11 days); the antigen presenting capacity of dendritic cells derived from TPG-treated mice was arrested and ovalbumin-specific T-cell proliferation inhibited (Zhou et al. 2012). Further, the maturation of dendritic cells was decreased by TPG treatment. Inhibitory effect on dendritic cell maturation had been reported to alter immune-mediated inflammatory reaction in vivo. The results demonstrated that TPG inhibited dendritic cell maturation and function by selectively blocking TLR4/5 activation in vivo, which in turn led to reduced immune-mediated inflammation in vivo, indicating therapeutic target of TPG for inflammatory and autoimmune disease treatment.

The results of in vitro studies indicated that a chronic inflammatory process in collagen-induced arthritis induced up-regulation of G-protein-coupled receptor kinase 2 (GRK2) in fibroblast-like synoviocytes, and paeoniflorin could reverse this change, which might be one of the important mechanisms for paeoniflorin regulating G-protein-coupled receptor (GPCRs) signalling and suppressing the proliferation of fibroblast-like synoviocytes in collagen-induced arthritis (Chen et al. 2012a). Paeoniflorin significantly ameliorated the immune complex-induced inflammatory vascular damage, leucocyte infiltrates and adhesion molecule expression in a mouse model of cutaneous Arthus reaction and cultured human dermal microvascular endothelial cells (HDMECs) (Chen et al. 2013a). Further, paeoniflorin markedly blocked tumour necrosis factor-α (TNF-α)-induced E-selectin and intercellular adhesion molecule-1 (ICAM-1) expression in HDMECs at both mRNA and protein levels and also suppressed TNF-α-induced adhesion of polymorphonuclear leucocytes (PMNs) to HDMECs. The data suggested that paeoniflorin, as an anti-inflammatory agent, could down-regulate adhesion molecule expression and may be a candidate medicine for the treatment of immune complex-induced inflammatory response. Paeoniflorin, the main active ingredient of *Paeonia lactiflora*, attenuated lipopolysaccharide (LPS)-induced permeability of endothelial cells (Xu et al. 2013). Paeoniflorin (10, 30 and 100 μM) inhibited dextran extravasation and leucocyte migration through human umbilical vein endothelial cells (HUVECs) induced by LPS in a concentration-dependent manner. Further, paeoniflorin suppressed phosphorylations of PI3K/Akt, PKC and cofilin, as well as F-actin reorganization, in HUVECs induced by LPS.

Animal Studies

Paeoniflorin from peony root exhibited anti-inflammatory effect significantly inhibiting the rat paw oedema induced by carrageenan and showing a tendency to inhibit dextran- or α-chymotrypsin-induced oedema and exudation of dye into the abdominal cavity of the mouse (Takagi and Harada 1969b). It also prevented stress ulcer in the rat. The paeoniflorin and liquorice component FM100 exhibited synergistic inhibitory effect on gastric and anti-inflammatory effect by intraperitoneal administration.

Studies found that total peony glucosides (TPG) exerted a suppressive effect on joint destruction in rat with collagen-induced arthritis (Zhu et al. 2005). The therapeutic effect of TPG could be associated with its ability to ameliorate the secretion and metabolism of synoviocytes and to inhibit the abnormal proliferation and production of vascular epidermal growth factor, basic fibroblast growth factor, matrix metalloproteinase 1 (MMP-1) and MMP-3 by fibroblast-like synoviocytes. Zheng and Wei (2005) found that the administration of total glucosides of peony (TGP) (50 and 100 mg/kg, i.g. days 14–21) in adjuvant arthritic rats significantly decreased the production of IL-1, PGE2 and TNF-alpha by macrophage-like synoviocytes (MLS). Further, the increased phosphorylation of mitogen-activated protein kinases, cell proliferation and matrix metalloproteinase expression in fibroblast-like synoviocytes stimulated by supernatants of MLS in AA rats could also be inhibited by TGP. The results suggested that TGP exhibited anti-inflammatory effects by modulating the proinflammatory mediator production from macrophage-like synoviocytes and phosphorylation of mitogen-activated protein kinases from fibroblast-like synoviocytes. Results of another animal study suggested that the inhibitory effect of total peony glucosides (TPG) on anti-inflammation may be related to decreasing the expression of NF-κB/p65 protein and suppressing the production of TNF-α and IL-1β in type II collagen-induced arthritic rats (Liu et al. 2010).

In another study, intragastric administration of paeoniflorin (10, 20 mg/kg/day, 14–20 days) inhibited the inflammatory response and restored the weight of immune organs of complete Freund's adjuvant-induced adjuvant arthritic rats (Zheng et al. 2007). Paeoniflorin significantly reduced the elevated synoviocyte proliferation and the elevated levels of IL-1, PGE2, IL-6, VEGF and GM-CSF in synovial homogenates of adjuvant arthritic rats. The results suggested that paeoniflorin suppressed adjuvant arthritis at least partly by inhibiting abnormal proliferation of synoviocytes and the production of IL-1, prostaglandin E(2) (PGE2), IL-6, VEGF and GM-CSF by synoviocytes and reducing Gi and COX-2 expression in synovium. Separate studies by Xu et al. (2007) showed that total glucosides of peony (TGP) significantly inhibited the progression of complete Freund's adjuvant arthritis in male Sprague–Dawley rats, and the inhibitory effects might be associated with its ability to mediate the level of cyclic adenosine monophosphate (cAMP) and inhibit the production of IL-1, TNF-alpha, IL-6 and PGE(2) from activated synoviocytes. Another study showed that TGP significantly inhibited the proliferation of synoviocytes; decreased the production of IL-1, tumour necrosis factor-alpha and prostaglandin E(2); and elevated the levels of cAMP (Chang et al. 2009, 2011). Also, TGP could up-regulate the expression of *E*-prostanoids (2) and (4). The results indicated that TGP might exert its anti-inflammatory effects through inhibiting the production of proinflammatory mediators in synoviocytes of collagen-induced arthritic Sprague–Dawley rats, which might be associated with its ability to regulate cAMP-dependent EP(2)/EP(4)-mediated pathway. Similar results were found for paeoniflorin (Chang et al. 2011). Paeoniflorin inhibited function of synoviocytes pretreated by rIL-1α and regulated EP4 receptor expression. Bai-shao (peony root) extract at low concentration significantly inhibited cAMP-phosphodiesterase (PDE) activity, exerted dose-dependent restraint on neutrophil respiratory burst, but at high concentration promoted elastase release and suppressed local inflammation in an animal model (Jiang et al. 2011). The Bai-shao extract was found to have five components identified as gallic acid, paeoniflorin sulphonate, albiflorin, paeoniflorin and benzoic

acid, among which gallic acid had the largest inhibition on cAMP-PDE activity.

The extract prepared from the roots of *Paeonia lactiflora* and *Astragalus membranaceus* (PAE) demonstrated higher hepatoprotective activity than the single herbs used individually (Sun et al. 2007). The results suggested that PAE significantly inhibited the progression of hepatic fibrosis induced by CCl_4 in male Sprague–Dawley rats, and the inhibitory effect of PAE on hepatic fibrosis was suggested to be associated with its ability to scavenge free radicals, to decrease the level of TGF-beta1 and to inhibit collagen synthesis and proliferation in hepatic stellate cells. In further studies, Sun et al. (2008) found that after administration of *P. lactiflora* and *Astragalus membranaceus* (60, 120 and 240 mg/kg, intragastrically) daily for 10 days, the degree of liver damage in bacillus Calmette–Guérin and lipopolysaccharide (BCG/LPS)-induced liver injury, as well as the elevation of serum transaminase activities and level of nitric oxide in live injured mice, was significantly reduced. The protective effect of *P. lactiflora* and *A. membranaceus* on BCG/LPS-induced liver-injured mice may be associated with the antioxidant properties, ability to reduce nitric oxide production and suppression of Kupffer cell activity and proinflammatory mediator and cytokine production. Qi-Shao-Shuang-Gan, a combination of *Astragalus membranaceus* saponins with *Paeonia lactiflora* glycosides, was found to ameliorate polymicrobial sepsis induced by cecal ligation and puncture in mice by inhibiting systemic inflammatory response and up-regulating protein C pathway (Gao et al. 2011). Synergistic effects between the two herbs were observed.

Studies showed that paeoniflorin (50, 100 mg/kg) from peony roots could alleviate lipopolysaccharide (LPS)-induced acute lung injury in mice, as evidenced by reduced pulmonary oedema, improved histological changes and attenuated inflammatory cell accumulation in the interstitium and alveolar space as well as microvascular permeability (Zhou et al. 2011b). It also markedly downregulated the expressions of proinflammatory cytokines interleukin (IL)-1β and tumour necrosis factor (TNF)-α at both transcription and protein levels. Additionally, PF inhibited the phosphorylations of p38 MAP kinase (p38) and c-Jun NH2-terminal kinase (JNK) but not extracellular signal-regulated kinase (ERK) and prevented the activation of nuclear factor-kappaB (NF-κB) in the lung tissues. Results from animal studies showed that paeoniflorin had an anti-inflammatory ability against TNF-α-induced chemokine (including CCL2, CCL5, CCL20, CXCL8, CXCL16 and CX3CL1) production and leucocyte migration, which may be at least partly related to the inhibition of nuclear factor-κB and ERK pathway (Chen et al. 2011a). Paeoniflorin may be a candidate medicine for the treatment of inflammatory skin diseases.

Preclinical/Clinical Studies

In a clinical study of 61 rheumatoid arthritic patients, combined treatment of methotrexate and total peony glucosides (TPG) was found to be more clinically efficacious and suitable because of its quick action, few side effects and high compliance (Du and Dong 2005). In a random-controlled trial of 80 patients with rheumatoid arthritis, combined application of total peony glucosides (TPG) and leflunomide was found to be superior to using leflunomide alone in treating rheumatoid arthritis, owing to its quicker initiating action and less adverse reaction (Zhao and Liu 2006). Similar results were obtained in a study of 260 patients with rheumatoid arthritis, wherein total peony glucoside (TPG) combined with methotrexate treatment exerted a favourable effect (Wang and Xing 2007). A clinical study of 67 patients with ankylosing spondylitis showed that total peony glucosides (TPG) and sulfasalazine exerted a favourable effect on ankylosing spondylitis with less and milder adverse reaction (Wang et al. 2007). Changes of clinical efficacy-related indices were observed including lumbar pain index, morning stiffness time, peripheral joint pain index, thoracic expansion, Schober test, Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), the levels of erythrocyte sedimentation and C-reactive protein and x-ray of sacroiliac joint.

Preclinical studies showed that water/ethanol extract of Radix Paeoniae known as total glycosides of peony (TGP)/paeoniflorin was able to diminish pain, joint swelling, synovial hypertrophy and the severity of bone erosion and cartilage degradation in experimental arthritis (Zhang and Dai 2012). TGP/paeoniflorin was found to suppress inflammatory process by reducing the production of prostaglandin E2, leukotriene B4, nitric oxide, reactive oxygen species, proinflammatory cytokines and chemokines. TGP/paeoniflorin was also found to inhibit the proliferation of lymphocytes and fibroblast-like synoviocytes, the formation of new blood vessels and the production of matrix metalloproteinases. Clinical data showed TGP to be effective in ameliorating the symptoms and signs of rheumatoid arthritis without significant adverse effects.

Immunomodulatory Activity

Wu et al. (2007) demonstrated that administration of paeoniflorin (50, 100 mg/kg, days 17–24) significantly diminished the secondary hind paw swelling and arthritis scores in adjuvant arthritic (AA) rats, reversed the decrease of anti-inflammatory cytokines interleukin (IL)-4 and transforming growth factor-beta 1 (TGF-beta1) and further decreased the lowered proliferation of mesenteric lymph node lymphocytes. In vitro, paeoniflorin restored the earlier increased level of cAMP of mesenteric lymph node lymphocytes (MLN) at the concentrations of 12.5, 62.5 and 312.5 mg/L. Concurrently, paeoniflorin increased protein expressions of beta-2-AR and GRK2 and decreased that of beta-arrestin 1, 2 of MLN lymphocytes in AA rats. The results suggested that paeoniflorin might induce the Th1 cell immune tolerance, which then shift to Th2, Th3 cells mediated activities producing the anti-inflammatory and immunoregulatory effects.

The polysaccharide peonan PA isolated from roots exhibited remarkable reticuloendothelial system-potentiating activity in a carbon clearance test and considerable anti-complementary activity (Tomoda et al. 1994). Paeoniflorin had therapeutic effects on rats with collagen-induced arthritis (Li et al. 2012). Paeoniflorin decreased arthritis score; relieved ankle and paw swelling; improved spleen histopathology in CIA rats; decreased the levels of IgA, IgM, IgG and anti-CII antibody; and significantly decreased the expressions of PI3K/Akt/mTOR signalling mediated by BAFF/BAFF-R in antibody production.

Autoimmune Protective Activity

Clinical studies found that long-term total peony glucoside (TPG) treatment of patients with systemic lupus erythematosus had marked therapeutic efficacy (Zhang et al. 2011). TPG could reduce the average daily dose of prednisone and the total cyclophosphamide dose, lowering the recurrent cases and episodes of infection, especially for the medication of more than 5 years. No adverse reaction correlated to TPG.

In a 2-year retrospective study conducted on 27 patients with nonsystemic involved Sjögren syndrome (an autoimmune disease), treatment with total peony glucosides (TPG) was found to be equally efficacious as that of hydroxychloroquine sulphate but with higher safety, and the effect initiating time was about 6–12 months (Zhang et al. 2007). TPG demonstrated similar effectiveness as hydroxychloroquine in delaying the onset of Sjögren syndrome-like disease in nonobese diabetic mice (Li et al. 2013). Saliva flow rate (SFR), ratio of regulatory T cells and histological changes in submandibular gland index were significantly higher, and the level of anti-SSA/anti-SSB antibodies and lymphocytic foci were significantly lower compared to the normal saline group.

Vasodilatory/Muscle Relaxation Activity

Paeoniflorin exhibited hypotensive effect on the guinea pig, an effect suggested to be associated to peripheral vasodilation (Takagi and Harada 1969c). Paeoniflorin produced vasodilation of

coronary vessel and hind limb of the dog. Relaxation and inhibition of movement and tonus of smooth muscle organs such as rat stomach or rat uterus were also found. Paeoniflorin was found to decompose into desbenzoylpaeoniflorin and benzoic acid, but both compounds scarcely showed such pharmacological effects. Peony root extract (Radix Paeoniae) was found to relax prostaglandin F2a-precontracted aortic ring preparations of isolated rat aorta that contained endothelium but not aorta without endothelium (Goto et al. 1996). Paeoniflorin and paeonol, the main active components of Radix Paeoniae, lacked a vasodilator effect, but its gallotannin components pentagalloylglucose, hexagalloylglucose, heptagalloylglucose and octagalloylglucose relaxed aortic rings with endothelium, but failed to relax aortic rings without endothelium. Administration of *P. lactiflora* root extract to rats increased the endothelium-dependent relaxation, and the activities of superoxide dismutase of erythrocytes significantly compared with the high-cholesterol diet group (Goto et al. 1999). Hypercholesterolaemia induced an increase of endothelial superoxide anion and endothelial dysfunction. Radix Paeoniae was suggested to have a protective effect on endothelial cells and their function.

Paeonia lactiflora ethanol extract induced relaxation of the phenylephrine-precontracted aortic rings in a concentration-dependent manner (Jin et al. 2012). The data suggested that the extract relaxed vascular smooth muscle via endothelium-dependent and Akt (protein kinase B)- and SOCE–eNOS–cGMP (store-operated Ca^{2+} entry–endothelial nitric oxide synthase–cyclic guanosine monophosphate)-mediated pathways through activation of both K(Ca) and K(ATP) channels and inhibition of L-type Ca^{2+} channels.

Antigenotoxic Activity

Oral administration of 50 % peony ethanol root extract and its active constituents, gallic acid and methyl gallate, potently inhibited the formation of micronucleated reticulocytes in the mouse peripheral blood induced by a potassium bromate treatment in vivo (Lee et al. 2005). The extract and both its active constituents exhibited a significant free radical scavenging effect against 1,1-diphenyl-2-picryl hydrazine (DPPH) radical generation and had an inhibitory effect on lipid peroxidation, as measured by the level of malondialdehyde (MDA) formation, and had no pro-oxidant effect (Lee et al. 2005). They strongly inhibited the hydrogen peroxide-induced DNA damage from NIH/3T3 fibroblasts. Therefore, peony root extract containing gallic acid and methyl gallate may be a useful antigenotoxic antioxidant by scavenging free radicals, inhibiting lipid peroxidation and protecting against oxidative DNA damage without exhibiting any pro-oxidant effect.

Neuroprotective Activity

In Vitro Studies

In vitro studies showed that paeoniflorin, a glycoside from peony root, could block L-type Ca^{2+} channels in rat glioma hybrid NG108-15 neuronal cells in a mechanism unlinked to the binding of adenosine receptors (Tsai et al. 2005). The effects of paeoniflorin on ion currents may partly, if not entirely, contribute to the underlying mechanisms through which it affected neuronal or neuroendocrine function. Peony root extract showed a clear inhibitory effect on the iberiotoxin-sensitive calcium-activated potassium current which also exerted distinct inhibitory effects on spontaneous bursting activity and conductance calcium-activated potassium (BKCa) current in the cerebral cortical neurons of the EL mouse, a hereditary epilepsy animal model (Sugaya et al. 2006). The results revealed the protective effect against neuronal damage and indicated peony root extract to be a promising herbal drug for inhibition of convulsions.

P. lactiflora extract 10–100 μg/mL prevented H_2O_2-induced reduction in PC12 cell survival and also suppressed apoptosis of H_2O_2-stressed PC12 neuronal cells (Lee et al. 2008b). The neuroprotective effect of the extract was attributed to its antioxidant property. Total phenolic content of PLE was 89.65 mg of gallic acid equivalent

per gram of PLE. IC_{50} values for reducing power, hydrogen peroxide scavenging activity and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity were 297.57, 3.33 and 32.74 μg, respectively. The results suggested that *P. lactiflora* extract could be a potential candidate as an antioxidant against neuronal diseases. Among seven compounds isolated from the roots, paeonilactone-C and benzoylpaeoniflorin significantly protected primary cultures of rat cortical cells against H_2O_2-induced neurotoxicity (Kim et al. 2009). Total peony glucoside (TPG) treatment at increasing doses (1–10 mg/L) protected PC12 cells against corticosterone-induced neurotoxicity in a dose-dependent manner (Mao et al. 2009c). The cytoprotection afforded by TGP treatment was associated with the inhibition of caspase-3 activity and the up-regulation of bcl-2/Bax mRNA ratio. The anti-apoptotic effect of TGP was mediated by the suppression of the mitochondrial pathway leading to apoptosis. Results of in vitro studies suggested that paeonol downregulated H_2O_2-induced NF-κB activity, as well as NF-κB-associated amyloid precursor protein expression in human neuroblastoma SH-SY5Y cells (Su et al. 2010b). Additionally, the gene expression profile accompanying the suppression of NF-κB by paeonol was identified.

Amiloride (100 μM), positive control drug, and paeoniflorin (50 μM) both protected murine neuronal PC12 cells against methyl-4-phenylpyridinium (MPP^+)- or acid-induced injury as assessed by MTT assay, lactate dehydrogenase release and apoptosis rate (Cao et al. 2010). The concentrations of cytosolic-free Ca^{2+} augmented after exposure to MPP^+ or acidosis were reduced. The mechanisms of neuroprotective effects of amiloride and paeoniflorin were found to be closely associated with the up-regulation of LC3-II protein, which was specifically associated with autophagic vacuole membranes. Also, amiloride and paeoniflorin suppressed the MPP^+- or acid-induced overexpression of LAMP2a which was associated with the activity of the chaperone-mediated autophagy pathway. The results suggested that paeoniflorin modulated autophagy in models of neuron injury and also established a relationship between autophagy–lysosome pathway and acid-sensing ion channels.

The neuroprotective mechanisms of paeoniflorin were listed by Zhu et al. (2010) as follows: activating adenosine A1 receptor, ameliorating the function of cholinergic nerve, regulating ion channel homeostasis, retarding oxidative stress and apoptosis of the neurocytes, promoting nerve growth, having an influence on astrocytes and being able to penetrate though the blood–brain barrier. In vitro studies showed that paeoniflorin and albiflorin, major constituents of peony roots, exhibited protective effects against glutamate-induced toxicity damage of PC12 neuronal cells (Wang et al. 2013a). They ameliorated glutamate-induced reduction of cell viability, nuclear and mitochondrial apoptotic alteration, reactive oxygen species accumulation and B-cell lymphoma 2 (Bcl-2)/Bax ratio. The two isomers also enhanced phosphorylation of AKT and its downstream element glycogen synthase kinase-3β paeoniflorin. Further, paeoniflorin displayed remarkable effects in preventing intracellular Ca2+ overload and suppressing overexpression of calcium/calmodulin protein kinase II.

Aqueous extract of *P. lactiflora* and its active compound paeoniflorin significantly suppressed aggregation of intranuclear and cytoplasmic misfolded polyQ proteins in 293 ATXN3/Q75-GFP neuronal cells (Chang et al. 2013). *P. lactiflora* and paeoniflorin up-regulated HSF1 and HSP70 chaperones in the same cell models. The results suggested that *P. lactiflora* and paeoniflorin could have potential in the treatment of spinocerebellar ataxia type 3 and other polyQ diseases. In organotypic hippocampal slice cultures, paeoniflorin significantly blocked lipopolysaccharide (LPS)-induced hippocampal cell death and productions of nitric oxide (NO) and interleukin (IL)-1β (Nam et al. 2013). Paeoniflorin also inhibited the LPS-stimulated productions of NO, tumour necrosis factor-α and IL-1β from primary microglial cells. The results suggested that paeoniflorin possessed neuroprotective activity by reducing the production of proinflammatory factors from

activated microglial cells. The results of in vitro studies in PC12 cells exposed to methyl-4-phenylpyridine ion (MPP+), a neurotoxin, showed that pretreatment with paeoniflorin significantly improved cell viability (Wang et al. 2013b) The neuroprotective effects of paeoniflorin were related to its modulation of multiple anti-apoptotic and pro-apoptotic pathways, including blockade of intracellular calcium overload, prevention of mitochondrial membrane integrity, inhibition of pro-apoptotic molecules and up-regulation of anti-apoptotic proteins associated with cell survival and proliferation. The study indicated paeoniflorin as a potential therapeutic agent for the treatment of neurodegenerative diseases and neural injury.

All isolated resveratrol oligomers, (-)-7a,8a-*cis*-ε-viniferin, *trans*-ε-viniferin, *cis*-ε-viniferin, *trans*-resveratrol, vitisinol C, vitisinol E, gnetin H, suffruticosol A and suffruticosol B, exhibited significant inhibition on baculovirus-expressed beta-site APP-cleaving enzyme 1 (BACE1) in a dose-dependent manner in vitro (Choi et al. 2011). BACE1 had been found to be a key enzyme that selectively cleaved the amyloid precursor protein (APP) to generate the toxic amyloid-B (AB) in the brain, and inhibition of this key enzyme is the target for therapeutic intervention of Alzheimer's disease.

Animal Studies

Compared with control model group, total peony glycoside (TPG) at the doses of 200 and 400 mg/kg could significantly relieve brain oedema, enhance superoxide dismutase activity and lower malonaldehyde concentration in the gerbils (Ma et al. 2005). Pathological examination showed that the gerbils with TPG treatment had milder injury of the cells in the hippocampal CA1 region. The results indicated the protective effect of TPG against global cerebral ischaemia–reperfusion injury.

One day (10 mg/kg, twice, s.c.) or 7-day (2.5–10 mg/kg, twice a day, s.c.) injection of paeoniflorin isolated from roots significantly reduced the infarct volume and ameliorated the deficits in neurological symptoms caused by transient cerebral ischaemia induced by middle cerebral artery occlusion (MCAO) at the chronic stage in rats (Xiao et al. 2005). Transient MCAO also induced impairments in tongue protrusion and performance in the water maze. Treatment with paeoniflorin was able to reverse or alleviate these impairments. The results suggested that paeoniflorin may be effective for treatment of stroke. Animal studies showed that paeonol reduced cerebral infarct and neuro-deficit in male Sprague–Dawley rat, suggesting paeonol might play a similar role in reducing cerebral infarction in humans (Hsieh et al. 2006). Also, paeonol suppressed and scavenged superoxide anion and inhibited microglial activation and IL-1beta in ischaemia–reperfusion injured rats. Studies found that administration of peony root extract to mouse prior to cobalt application prevented neuronal death (Kajiwara et al. 2008). Its protective effect involved the up-regulation of transthyretin and phosphoglycerate mutase in the cobalt-treated mouse cerebrum in association with up-regulation of neurogranin/RC3, a target of the transcriptional activation by thyroid hormones and retinoids.

Tang et al. (2010) showed that both pretreatment and posttreatment with paeoniflorin reduced cerebral infarct and neurological deficit in ischaemia–reperfusion injured rats, suggesting that paeoniflorin may have a similar effect in humans and might be a suitable treatment for stroke. Paeoniflorin reduced cerebral infarct, at least in part, involving the anti-inflammatory properties. *Paeonia lactiflora* extract and paeoniflorin significantly attenuated cerebral infarction in ischaemia–reperfusion injured rats and the severity of intimal hyperplasia in mice where the carotid artery was ligated (Chen et al. 2013b). The extract and paeoniflorin reduced PDGF-stimulated vascular smooth muscle cell proliferation and migration in a dose-dependent manner. Paeoniflorin significantly reduced protein levels of Ras, MEK, *p*-MEK and *p*-ERK, but not MMP-2 and MMP-9. In summary, Paeonia lactiflora reduced cerebral ischaemia and arterial intimal hyperplasia which were mainly attributed to paeoniflorin via modulation of the Ras/MEK/ERK signalling pathway.

Lung Protective Activity

Radix Paeoniae Rubra exhibited a protective effect on endotoxin-induced acute lung injury in rats (Zhan et al. 2006). The expression of induced nitric oxide synthase (iNOS) was significantly lower, while the expression of HO-1 was higher than that in lipopolysaccharide (LPS) group. Parameters of lung injury were significantly lower in peony-treated rats than in the LPS group.

Antiosteoporotic Activity

The monoterpene glycoside, 6′-*O*-β-D-glucopyranosylalbiflorin, isolated from the roots, significantly increased the alkaline phosphatase activity and nodule mineralization of osteoblastic MC3T3-E1 cells compared to those of the control (Pham et al. 2007). The results suggested that this monoterpene glycoside had a direct stimulatory effect on bone formation in vitro and may contribute to the prevention for osteoporosis. Studies by Tsai et al. (2008) suggested that paeonol (2′-hydroxy-4′-methoxyacetophenone), a main active compound from *P. lactiflora*, inhibited osteoclastogenesis from bone marrow stromal cells and macrophage cells via attenuation of receptor activator of nuclear factor-kappaB ligand (RANKL)-induced extracellular signal-regulated kinases (ERK), p38 and NF-kappaB activation, which in turn protected bone loss from ovariectomy.

Albiflorin isolated from the root exhibited protective effects against antimycin A-induced osteoblast toxicity in osteoblast-like MC3T3-E1 cell line (Suh et al. 2013). Pretreatment with albiflorin reversed the loss of cell viability, decreased apoptosis and lactate dehydrogenase release, decreased ROS/RNS levels and increased mitochondrial function compared to antimycin A-treated cultures. Additionally, albiflorin increased the mineralization reduced by antimycin A. Albiflorin reduced antimycin A-induced mitochondrial cytochrome *c* loss and cardiolipin peroxidation, conferring protection against ROS. The results confirmed the crucial role of cytochrome *c* and cardiolipin in the underlying mechanistic action of albiflorin and suggested that albiflorin enhanced mitochondrial function to suppress antimycin A-induced oxidative damage via the preservation of cytochrome *c* and cardiolipin. All of these data indicated that albiflorin may reduce or prevent osteoblast degeneration in osteoporosis.

Paeoniflorin decreased osteoblastic MC3T3-E1 cell death induced by antimycin A, an inhibitor of mitochondrial complex III (Choi and lee 2013). Paeoniflorin restored antimycin A-induced inactivation of phosphoinositide 3-kinase (PI3K) and thioredoxin reductase, suggesting that PI3K and thioredoxin reductase may be involved in paeoniflorin-induced cytoprotective responses. Further, paeoniflorin inhibited mitochondrial membrane potential dissipation, ATP loss, inactivation of complexes I and IV, cytochrome c release and cardiolipin oxidation induced by antimycin A and prevented antimycin A-induced ROS release and nitrotyrosine increase. The results implied that paeoniflorin protected osteoblasts from antimycin A-induced cell death via improved mitochondrial function.

Antityrosinase Activity

Among the stilbenes isolated from the seeds, the resveratrol trimer, gnetin H, exhibited the most potent inhibitory activities against tyrosinase and soybean lipoxygenase (Kim et al. 2002c). Additionally, the resveratrol dimers, *trans*-ε-viniferin and *cis*-ε-viniferin, exhibited significant inhibitory activity against the two oxidative enzymes. Meanwhile, three other stilbene derivatives, such as *trans*-resveratrol, suffruticosol A and suffruticosol B, had also weak inhibition activity. The least inhibitory activity was observed in *trans*-resveratrol-4-*O*-β-D-glucoside. The results suggested that resveratrol dimers and trimer in the seeds of *Paeonia lactiflora* may be potentially useful therapeutic agents against pathological disorders such as hyperpigmentation and inflammation. The ethyl acetate fraction

of peony root methanol extract showed higher tyrosinase activity than arbutin used as a positive control (Im and Lee 2011). In the cytotoxicity measurement by MTT assay, the extract and fractions exhibited cell viabilities of 76.96–157.26 % against RAW 264.7 and B16F10 cell in concentration of 10–100 μg/mL. In nontoxic concentration range, the ethyl acetate fraction showed strong melanin production inhibitory effect in α-melanocyte-stimulating hormone (α-MSH)-stimulated B16F10 cell. As a result, the ethyl acetate fraction of the methanol root extract could be used as functional materials for skin whitening agents. In another study, the ethyl acetate root fraction of *P. lactiflora* showed the highest activity among the four plant fractions, namely, *Smilax china* (rhizome), *P. lactiflora*, *Polyporus umbellatus* (sclerotium) and butanol fraction of *Evodia officinalis* (fruit), in the inhibition assay of intracellular tyrosinase activity and melanogenesis in B16 melanoma cell line (Son and Heo 2013). *P. lactiflora* fraction also had low toxicity.

Antiplatelet Aggregation Activity

In vitro studies showed that *Paeonia lactiflora* extract prolonged the prothrombin time and partial thromboplastin time, significantly inhibiting thrombin and reducing urokinase activity (Wang and Ma 1990). The extract possessed stimulatory effect on plasminogen. The inhibitory effect of *P. lactiflora* on thrombin and effective effect on plasminogen might be an important mechanism of its action of promoting blood circulation and removing blood stasis. Paeonol, paeoniflorin, benzoylpaeoniflorin and benzoyloxypaeoniflorin were found to be the major common active root constituents that collectively contributed to improving blood circulation through their inhibitory effects on both platelet aggregation and blood coagulation (Koo et al. 2010). Additionally, methyl gallate, (+)-catechin, paeoniflorigenone, galloylpaeoniflorin and daucosterol may also be involved in improving blood circulation by inhibiting either platelet aggregation or blood coagulation.

Androgen Receptor-Binding Activity

Compounds 6′-*O*-galloylalbiforin (2) and pentagalloylglucose (3), isolated from the roots, showed strong androgen receptor-binding activity (IC_{50} values of 33.7 and 4.1 μg/mL, respectively, while 3′-*O*-galloylpaeoniflorin (1), 6′-*O*-benzoylpaeoniflorin (4) and 6′-*O*-galloylpaeoniflorin (5) showed weak activity of 20, 31, 12 %, respectively (Washida et al. 2009a). The structure of paeoniflorin and albiflorin (IC_{50} values >120 μg/mL), having structures related to compounds 1, 2, 4 and 5, showed no activity. In addition compounds 1–5 inhibited growth of an androgen-dependent LNCaP-FGC (prostate cancer cell line) with IC_{50} values of >120, 58, 22, 84 and 141 μg/mL, respectively. These were indicated to be androgen activity antagonists. Paeoniflorin and albiflorin had no activity with IC_{50} values >200 μg/mL. Two new galloylated monoterpene glycosides, 4-*O*-galloylalbiflorin and 4′-*O*-galloylpaeoniflorin, isolated from the roots, showed androgen receptor-binding activity (Washida et al. 2009b).

Hepatoprotective Activity

Administration of *P. lactiflora* to rats with acute liver damage induced by D-galactosamine augmented plasma fibronectin levels and improved reticuloendothelial system function and plasma opsonic activity (Qi 1991). Aggregation of microaggregated albumin, collagen fragment and immune complexes was markedly reduced. Liver immune damage and microcirculation disorder were avoided. It was concluded that *P. lactiflora* had a protective role in hepatocyte. In vitro studies showed that *P. lactiflora* root extract and its active components, paeonol and 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG), inhibited platelet-derived growth factor (PDGF)-BB-induced hepatic stellate cell migration and α-smooth muscle actin (α-SMA) and collagen expressions in a concentration-dependent manner (Kuo et al. 2012). The inhibitory effects were associated with downregulation of PDGF

receptor-α, ERK, p38 and JNK activation. Both paeonol and PGG participated in hepatic stellate cell migration, but via differential mechanisms.

Total peony glucoside (TPG) was found to have beneficial effects on hepatic fibrosis in rats by inhibition of collagen synthesis and decreasing oxidative stress (Wang et al. 2005). TPG improved the human albumin-induced alterations in the liver structure, alleviated lobular necrosis and significantly lowered collagen content. This was evidenced by decreased serum content of serum procollagen type III (PC III) and laminin in TPG-treated group. TPG also reduced the hydroxyproline content in liver homogenates, but had no effect on the level of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and the ratio of A/G. Further, TPG significantly blocked the increase in malondialdehyde and NO, associated with a partial elevation in liver total antioxidant capacity including superoxide dismutase (SOD) and glutathione peroxidase.

Studies showed that paeoniflorin, from peony root, could significantly protect against immunological liver injury induced by bacillus Calmette–Guérin plus lipopolysaccharide in mice by attenuating the area and extent of necrosis and reducing the immigration of inflammatory cells (Liu et al. 2006). The protective mechanism of paeoniflorin might be partially related to modulation of TNF-alpha, IL-6, LBP (lipopolysaccharide binding protein) and CD14 mRNA expressions in mouse liver.

The extract prepared from the roots of *Paeonia lactiflora* and *Astragalus membranaceus* (PAE) demonstrated hepatoprotective activity against liver fibrosis induced by intraperitoneal injection of porcine serum in rats (Sun et al. 2012). After a 16-week treatment, PAE-treated rats showed significantly reduced liver damage and symptoms of liver fibrosis. Administration of PAE significantly decreased serum hyaluronic acid, procollagen type III levels and content of hydroxyproline in the liver tissue of fibrotic rats. It also restored the decrease in SOD and GSH-Px activities and inhibited the formation of lipid peroxidative products during porcine serum treatment. In vitro, PAE also significantly decreased [3H]-thymidine incorporation in hepatic stellate cells stimulated with platelet-derived growth factor-B subunit homodimer (PDGF-BB). Further, PAE significantly decreased the expression of PDGF receptor beta (PDGFR-β) and *p*-ERK1/2, p-p38 and *p*-JNK. The results showed that PAE exhibited antifibrotic effects in rats induced by porcine serum, probably via its ability to scavenge free radicals, decreasing the expression of PDGFR-β, inhibition of hematopoietic stem cell proliferation and mitogen-activated protein kinases activation.

A 24-week, open-label, randomized, multicenter clinical trial of 204 patients with active rheumatoid arthritis found with significantly less frequent hepatotoxicity was observed in patients with total glucosides of peony (TGP) than those without (Chen et al. 2013c). The proportion of patients whose alanine aminotransferase or aspartate aminotransferase levels were >1.5 to ≤2 times and >2 to ≤3 times the upper limits of normal were lower in TGP group than the control. The study also demonstrated the hepatoprotective and additive role of TGP in combination with methotrexate and leflunomide in the treatment of active rheumatoid arthritis.

Renoprotective Activity

Intraperitoneal administration of peony root decreased blood urea nitrogen (BUN) concentration in rat serum (Shibutani et al. 1981). The acetone and ethyl acetate fractions also decreased BUN concentration. Purification of the ethyl acetate fraction yielded 1,2,3,4,6-penta-*O*-galloyl glucose, (+)-catechin and gallic acid. (+)-Catechin and gallic acid showed no activity, only 1,2,3,4,6-penta-*O*-galloyl glucose; gallotannin was active. After intraperitoneal administration all the galloylglucoses from Radix Paeoniae caused marked decrease of blood urea nitrogen (BUN) in rat serum, and the results of the hexa-deca-galloylglucoses were higher than that reported for the 1,2,3,4,6-pentagalloylglucoses (Nishizawa et al. 1983a, b). Treatment of streptozotocin-induced diabetic rats with total glucosides of peony (TGP) at 50, 100 and

200 mg/kg significantly lowered 24-h urinary albumin excretion rate and markedly attenuated glomerular volume (Wu et al. 2009). At 100 and 200 mg/kg, TGP markedly reduced indices for tubulointerstitial injury in diabetic rats. The expressions of 1α (IV) collagen, intercellular adhesion molecule (ICAM)-1, interleukin (IL)-1, tumour necrosis factor (TNF)-α, NF-κB p65, transforming growth factor (TGF)-β1 protein and 3-nitrotyrosine (3-NT) protein were increased in the kidneys of diabetic rats; the increases in these proteins were all dose-dependently and significantly inhibited by TGP treatment. The expression of nephrin protein was significantly reduced in the kidneys from diabetic rats and markedly increased by TGP treatment. The data suggested that TGP treatment ameliorated early renal injury via the inhibition of expression of ICAM-1, IL-1, TNF-α and 3-NT in the kidneys of diabetic rats.

Zhang et al. (2009b) found that total peony glucosides (TPG) could decrease urinary albumin excretion rate in streptozotocin-induced diabetic rat and that its mechanism may be at least partly correlated with up-regulation of the expression of nephrin in the kidney (Zhang et al. 2009b). TPG also significantly inhibited the expressions of TNF-alpha, NF-kappaB p65 and 3-NT protein in the kidneys of diabetic rats. In another study, treatment of streptozotocin-induced diabetic rats with total peony glucosides (TPG) significantly inhibited diabetic nephropathy progression (Wang et al. 2012a). The elevated 24-h urinary albumin excretion rate was markedly attenuated by treatment with 50, 100 and 200 mg/kg TPG. The renoprotective effect of TPG was associated with its ability to inhibit the JAK2/STAT3 pathway and macrophage proliferation in diabetic kidneys and action.

Oral administration of paeoniflorin for 7 days suppressed epithelial–mesenchymal transition (EMT) by downregulating TGF-β1 expression and maintaining bone morphogenetic protein-7 (BMP-7) mRNA expression and inhibited Smad 2/3 activation in fibrotic kidneys induced by unilateral ureteral obstruction in mice (Zeng et al. 2013). The data suggested that paeoniflorin could effectively prevent renal interstitial fibrosis, and the underlying mechanisms were, partially, through blocking EMT via BMP-7 recovery and TGF-β/Smad signalling inhibition.

Antihypotensive Activity

Intravenous injection of paeoniflorin, purified from peony root, could reverse guanethidine-induced hypotension via activation of adenosine A1 receptors in the brain of Wistar rats.

Antihypertensive Activity

Treatment of 32 patients suffering decompensative chronic cor pulmonale (CCP) (noninvasive method group, NMG) with *P. lactiflora* intravenous injection significantly improved clinical features of blood stasis (Jia and Tang 1991). In ten patients with CCP and pulmonary hypertension (invasive method group, IMG), PAP (pulmonary artery pressure) was reduced by 0.71 kPa; PaO_2 (arterial oxygen tension) was augmented significantly in NMG. The results of impedance cardiogram and pheopneumogram (such as Q-B, B-Y interval and Q-B/B-Y ratio, cardiac output), the haemorheologic parameters (such as blood viscosity, plasma viscosity, haematocrit and erythrocyte electrophoresis) and oxygen consumption of myocardium were improved significantly in both NMG and IMG. All of these changes were statistically significant. There was no statistical significance about the change of $PaCO_2$ (arterial carbon dioxide tension), SaO_2 (arterial saturation of haemoglobin), blood pH and BP (blood pressure). Radix Paeoniae Rubra administration to rats had a therapeutic effect on noxious heat blood stasis syndrome (Xie et al. 2005). This effect could be associated with regulation of serum proteins xPr 1, 2, 3, 4, 9 and 16.

In hyperlipidaemic rabbits, the level of platelet cytosolic-free calcium in the group administered with *P. lactiflora* (276.25 nmol/L) was significantly lower than that in the cholesterol group (390.88 nmol/L); the basal and calmodulin-stimulated activities of erythrocyte membrane

Ca^{2+}–Mg^{2+}–ATPase in *P. lactiflora* group were higher than that in the cholesterol group (Zheng et al. 1996).

Sedative/Analgesic/Antipyretic Activity

Paeoniflorin, from peony root, exhibited sedative effect in mice and had low acute toxicity (Takagi and Harada 1969a). Sleeping duration induced by hexobarbital was prolonged. Writhing symptom induced by intraperitoneal administration of AcOH was inhibited. Loss of righting reflex was obtained in the rat by intraventricular administration. Weak hypothermia and weak anticonvulsive effect to pentylenetetrazol were found. Analgesia was found in both writhing test and tail-pressure test. Marked hypothermic and antipyretic effects and weak anticonvulsive effect to pentylenetetrazol were found by intraperitoneal administration. The combined effects of paeoniflorin with liquorice component FM100 were found to be synergistic in almost all experiments. Compared with saline control, systemic pre- and posttreatment with paeoniflorin resulted in an apparent antinociception against both persistent spontaneous nociception and primary heat hypersensitivity in the bee venom model in rats, while for the primary mechanical hypersensitivity, only pretreatment was effective (Yu et al. 2007). Moreover, pre- and early posttreatment with paeoniflorin (5 min after bee venom (BV) injection) could successfully suppress the occurrence and maintenance of the mirror-image heat hypersensitivity, whereas late posttreatment (3 h after BV) did not exert any significant impact. In the rotarod treadmill test, paeoniflorin administration did not affect the motor coordinating performance of rats. Furthermore, systemic paeoniflorin application produced no significant influence upon BV-induced paw oedema and swelling. Finally, the paeoniflorin-produced antinociception was likely to be mediated by endogenous opioid receptors because of its naloxone reversibility. The results suggested that besides its well-established neuroprotective actions in the CNS, paeoniflorin was also able to produce analgesia against various 'phenotypes' of nociception and hypersensitivity via opioid receptor mediation.

Zhang et al. (2008a) demonstrated that paeoniflorin exerted an analgesic effect on pain in visceral hyperalgesic rats with neonatal maternal separation and that this effect may be mediated by kappa-opioid receptors and alpha(2)-adrenoceptors in the central nervous system. The results suggest that paeoniflorin might be potentially useful in clinical therapy for irritable bowel syndrome as a pharmacological agent in alleviating visceral pain. Separate studies showed that paeoniflorin, a chief active ingredient in peony root, was effective in relieving colorectal distention (CRD)-induced visceral pain in rats with visceral hyperalgesia induced by neonatal maternal separation (Zhang et al. 2009a). The results suggested that paeoniflorin's analgesic effect was possibly mediated by adenosine A(1) receptor by inhibiting colorectal distention-evoked glutamate release and the NMDA (N-methyl-D-aspartate) receptor-dependent ERK (extracellular signal-regulated protein kinase) signalling.

Antidepressant Activity

Peony extract demonstrated antidepressant effect in various animal models of depression (Mao et al. 2008a). Intragastric administration of the extract at the doses of 250 and 500 mg/kg for 7 days significantly reduced the duration of immobility in both forced swim test and tail suspension test. The extract at the dose of 500 mg/kg was as effective as the positive control (chlorimipramine, 20 mg/kg) in these tests. However, these treatments did not affect the number of crossing and rearing in the open-field test. Treating mice with the extract at the doses of 250 and 500 mg/kg significantly antagonized reserpine-induced ptosis and hypothermia. The results suggested that the action of *Paeonia lactiflora* may be mediated via the central monoaminergic neurotransmitter system. Mao et al. (2008b) also found that intragastric administration of total glycosides of peony (TGP) at 80 and 160 mg/kg for 7 days in mice caused a significant reduction of immobility time in both forced

swim and tail suspension tests, yet TGP did not stimulate locomotor activity in the open-field test. In addition, TGP treatment antagonized reserpine-induced ptosis and inhibited the activities of monoamine oxidases in the mouse cerebrum. In a subsequent study, daily intragastric administration of TGP (80 or 160 mg/kg/day) during the 6 weeks of chronic unpredictable mild stress (CUMS)-induced depression significantly suppressed behavioural and biochemical changes induced by CUMS in mice (Mao et al. 2009b). The results suggested that the antidepressant-like action of TPG was likely mediated by modulating the function of hypothalamic–pituitary–adrenal axis and increasing the expression of brain-derived neurotrophic factor in brain tissues. Further, they found that the antidepressant-like activity of TGP in depression induced by chronic unpredictable stress was probably mediated by inhibition of monoamine oxidases and the attenuation of oxidative stress in the mouse brain (Mao et al. 2009a). In another study Mao et al. (2010) found that daily intragastric administration of TPG (80 or 160 mg/kg/day) during the 5 weeks of chronic unpredictable mild stress (CUMS) significantly suppressed behavioural and biochemical changes induced by CUMS (Mao et al. 2010). Treating non-stressed animals with TPG (160 mg/kg) for 5 weeks also significantly increased brain-derived neurotrophic factor contents in the hippocampus and frontal cortex and nerve growth factor contents in the frontal cortex. The results suggested that the antidepressant-like action of TPG was mediated, at least in part, by increasing the expression of brain-derived neurotrophic factor and nerve growth factor in selective brain tissues.

Mao et al. (2012) in their mini-review reported peony extract to be active in the mouse forced swim test and tail suspension test and to elicit antidepressant effects in chronic unpredictable mild stress-induced depression model in mice and rats. The antidepressant mechanisms of peony were reported to be likely mediated by the inhibition of monoamine oxidase activity, neuroprotection, modulation of the function of hypothalamic–pituitary–adrenal axis, inhibition of oxidative stress and the up-regulation of neurotrophins.

Cognitive Impairment Ameliorative Activity

Animal studies showed that intraperitoneal injections of paeoniflorin and the adenosine A1 receptor antagonist 1,3-dipropyl-8-cyclopentylxanthine (DPCPX) significantly attenuated the deficit in retention performance caused by pre-training administration of the selective adenosine A1 receptor agonist N6-cyclopentyladenosine (CPA) (Tabata et al. 2001). The results suggested that paeoniflorin ameliorated memory disruption mediated by adenosine A1 receptor and that modulation of adenosine-mediated inhibition of long-term potentiation in the hippocampus was implicated in its beneficial effect on learning and memory impairment in rodents.

Studies showed that paeonol extracted from peony or moutan root significantly improved the learning and memory ability in Morris water maze test and step-down passive avoidance test in D-galactose-treated ICR mice (Zhong et al. 2009). The effect of paeonol on improvement of cognitive deficit was related to its ability to inhibit the biochemical changes in the brains of D-galactose-treated mice. Paeonol increased acetylcholine and glutathione levels and restored superoxide dismutase and Na^+, K^+–adenosine triphosphatase (Na^+, K^+–ATPase) activities, but decreased cholinesterase acetylcholine activity and malondialdehyde level in D-galactose-treated mice. Furthermore, paeonol ameliorated neuronal damage in both the hippocampus and temporal cortex in D-galactose-treated mice. The results suggested that paeonol possessed anti-aging efficacy and may have potential in the treatment of neurodegenerative diseases.

Antiulcerogenic Activity

Animal studies showed that paeoniflorin treatment effectively alleviated the symptoms of oxazolone-induced colitis in mice by attenuating lesion in the colonic mucosa via regulating the expression of human β-defensin 2 (HBD-2), IL-6 and IL-10 (Zhou et al. 2010). Intraperitoneal administration of paeoniflorin distinctly induced

heat-shock protein Hsp70 in mouse stomach, and paeoniflorin exerted a protective effect on the HCl- and ethanol-triggered gastric mucosal injury (Asai et al. 2011). Hsp70 was also induced in the liver, heart and brain by paeoniflorin. No apparent systemic side effect of paeoniflorin has been observed thus far. From the results, it was suggested that paeoniflorin and paeoniflorin-containing herbal medicines might be used clinically as HSP inducers for the prevention and treatment of diseases associated with protein conformation and of various other pathological states, such as stress ulcers and irritant- or ischaemia-induced injuries.

Antimicrobial Activity

Methanol root extracts of *Paeonia lactiflora* exerted antibacterial activity against *Bacillus subtilis* (Boo et al. 2011). These extracts generated superoxide radicals in the *B. subtilis* lysate. Superoxide radicals were important in the antibacterial actions of the extracts. Of the constituents found in peony roots, benzoic acid and paeonol showed strong bactericidal effect against *Helicobacter pylori* at pH 4, while methyl gallate and 1,2,3,4,6-penta-*O*-galloyl-β-D-glucopyranose (PGG) were effective at pH 7 (Ngan et al. 2012b). These constituents exhibited strong growth-inhibiting and bactericidal activity towards the five strains resistant to amoxicillin (minimal inhibitory concentration (MIC) 12.5 mg/L), clarithromycin (64 mg/L), metronidazole (64 mg/L) or tetracycline (15 mg/L), indicating that these constituents and the antibiotics do not share a common mode of action. *H. pylori* urease inhibitory activity of PGG was comparable to that of acetohydroxamic acid, while methyl gallate was less potent at inhibiting urease than thiourea. These constituents showed no significant cytotoxicity.

The ethyl acetate fraction of peony root methanol extract showed stronger antibacterial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* than other fractions and the extract (Im and Lee 2012).

Antiviral Activity

Methanol root extracts of *Paeonia lactiflora* exerted a pivotal inhibition role in trafficking of viral glycoprotein in virus infected baby hamster kidney (BHK) cells (Boo et al. 2011). The methanol extract effectively inhibited syncytium formation in a concentration-dependent manner, and it did not affect glycoprotein synthesis. The results suggested that oxygen radical affected the transport process of viral glycoprotein without its synthesis.

Wound Healing Activity

Studies found that aqueous peony root extract accelerated the wound healing process in Wistar rats by decreasing the surface area of the wound and increasing the tensile strength (Malviya and Jain 2009). The histological examination of the granulation tissue of peony-treated group showed increased cross-linking of collagen fibres and absence of monocytes.

Detoxifying Activity

Co-administration of paeoniflorin was found to significantly reduce acute toxicity of aconitine in rats by alterations of the pharmacokinetic behaviour of aconitine in the animals (Fan et al. 2012). Animals co-treated with paeoniflorin (240 mg/kg) and aconitine (1.8 mg/kg) revealed a significant decreased death rate than those that received aconitine treatment alone (15 % vs. 50 %).

Anti-pancreatitis Activity

In a randomized controlled trial on the comparative efficacy of red peony root and rhubarb on 96 patients with severe acute pancreatitis, red peony root decoction was found to be more effective than rhubarb (Zhang et al. 2008b). The durations of abdominal tenderness, fever and abdominal distension in peony treatment group were less than those in the rhubarb group and the time

length for antibiotic (including antibacterial drug and antifungal agent) use, nasojejunal feeding start, nasojejunal feeding, gastrointestinal decompression, fasting diet, hospital stays and hospitalization costs were decreased in peony treatment group.

Ocular Disease Protective Activity

Animal studies showed that paeoniflorin could protect against optic nerve crush (Li et al. 2007a). Survival rate of ganglion cells in the left eye after optic crush increased from 40.22 to 64.53 % in paeoniflorin-treated rats. In vitro studies showed that paeoniflorin could protect human retinal pigment epithelium ARPE-19 cells from the cellular apoptosis induced by H_2O_2 oxidative stress (Xie et al. 2011). Pretreatment with paeoniflorin attenuated H_2O_2-induced p38MAPK and extracellular signal-regulated kinase (ERK) phosphorylation in human RPE cells. The results suggested the potential of paeoniflorin in treatment of ocular diseases, such as age-related macular degeneration (AMD).

Mitochondrial Respiration Inhibitory Effect

Gallotannins from *P. lactiflora* roots were found to have an inhibitory effect on the respiration of rat liver mitochondria (Nishizawa et al. 1983b).

Drug/Drug Potentiating Activity

Paeoniflorin, derived from peony root and sinomenine from *Sinomenium acutum* stem, have been, and are currently, widely used for treatment of rheumatic and arthritic diseases in China and Japan (Chan et al. 2006). Earlier studies demonstrated that sinomenine could significantly improve the bioavailability of paeoniflorin in rats. In vitro studies using an everted rat gut sac model showed that sinomenine significantly enhance the intestinal absorption of paeoniflorin, subsequently improving the bioavailability of paeoniflorin. They proposed that sinomenine could decrease the efflux transport of paeoniflorin by *P*-glycoprotein, thereby enhancing the bioavailability of paeoniflorin.

Pharmacokinetic Studies

Paeoniflorin, oxypaeoniflorin and benzoylpaeoniflorin were isolated from the roots; paeoniflorin was converted to three metabolites (paeonimetabolines I, II and III) by intestinal bacteria (Hattori et al. 1985). All the tested bacterial strains metabolized 42–100 % of paeoniflorin within 24 h; among these *Clostridium butyricum, Bacteroides fragilis, Lactobacillus fermentum* and *Lactobacillus plantarum* completely decomposed paeoniflorin, but no metabolites were detected from the culture broth of the two *Lactobacillus* strains. Only *Peptostreptococcus anaerobius* showed potent ability to transform paeoniflorin to paeonimetaboline I in relatively high yield, though *Clostridium butyricum* and *Bacteroides fragilis* exhibited weak activity. In vitro studies showed that *Bacteroides fragilis* or *Lactobacillus brevis* isolated from human intestinal flora converted paeoniflorin into the 7S and 7R isomers of paeonimetaboline I as major metabolites, along with the 7R and 7S isomers of paeonimetaboline II as minor metabolites in the case of the former strain (Shu et al. 1987).

Studies showed that paeoniflorin was metabolized in the liver and other organs after intravenous and oral administration in rats (Takeda et al. 1995). Paeoniflorin absorbed was excreted mainly in urine; it had a low bioavailability and its metabolites may be involved in the pharmacological action of peony root. Animal studies showed that paeoniflorin was transformed by intestinal bacteria to its metabolite paeonimetaboline which was rapidly absorbed from the gastrointestinal tract, and a significantly high concentration of paeonimetaboline, rather than paeoniflorin, was present in the plasma after oral administration of paeoniflorin (Heikal et al. 1997). Studies found that after oral administration to rats with peony root decoction, paeoniflorin was not

absorbed per se, whereas its deglucosylated metabolite aglycone paeoniflorgenin was absorbable and circulated in the bloodstream (Hsiu et al. 2003). Paeoniflorin was found to be hydrolyzed into paeoniflorgenin through incubation with faeces of rabbit, rat, pig or human. The kinetic process of paeoniflorin in plasma showed two-compartment model after oral administration of Radix Paeoniae Alba extract at doses of 0.2, 0.4 and 0.8 g/kg to rats (Bao et al. 2010).

Studies showed that sulphur fumigation had an effect on the pharmacokinetics of the main monoterpene glucoside components in white peony root by improving their bioavailability and delaying their absorption in mice (Cheng et al. 2010). It was found that C(max) and AUC of sodium paeoniflorin sulphonate and benzoylpaeoniflorin sulphonate were increased, and the T(max) and t(1/2) were prolonged by comparison with that of paeoniflorin. Similar results were also observed for the pharmacokinetic parameters of sodium paeoniflorin sulphonate in sulphur-fumigated white peony root extract and paeoniflorin in white peony root extract. However, benzoylpaeoniflorin was not detected in plasma collected at certain intervals after orally administered to mice.

Studies on the quantification of paeoniflorin showed that ischaemia–reperfusion in rats significantly increased the plasma concentration–time (AUC) values, decreased clearance values and prolonged the terminal half-life of paeoniflorin compared to normal rats (He et al. 2004). The findings suggested that the injuries of ischaemia–reperfusion could play an important role in pharmacokinetic process of paeoniflorin. The pharmacokinetics of paeoniflorin in rat plasma was found to be significantly affected when administered with Radix Angelicae Sinensis (Wu et al. 2008). After oral administration of peony root and Danggui-Shaoyao-San herbal extracts to rats, albiflorin reached maximum concentrations of 4,637 ng/mL (0.40 h) and 226 ng/mL (0.35 h) and paeoniflorin reached maximum concentrations of 2,132 ng/mL (0.40 h) and 143 ng/mL (0.45 h), respectively (Li et al. 2011b). The C(max), AUC and K(el) of albiflorin and paeoniflorin were markedly increased during oral administration of peony root extract in comparison to that of albiflorin extract. In a recent study using the rat intestinal perfusion model, *P. lactiflora* extract showed significant increase in permeability coefficient compared with the paeoniflorin monomer, indicating that other ingredients in the extract could improve the absorption of paeoniflorin (Chen et al. 2012b). However, due to the poor absorption of paeoniflorin, this effect failed to increase the concentration of paeoniflorin in the bile and plasma.

A total of 13 new absorbed constituents and 90 new metabolites of dried roots of *Paeonia lactiflora* decoction were detected in rats (Liang et al. 2013). Among these metabolites were 22 new metabolites of paeoniflorin, 10 new metabolites of gallic acid-related compounds, 1 new metabolite of (epi)catechin-related compounds and 2 new metabolites of other compounds. The results also indicated that (epi)catechin-related compounds, gallic acid-related compounds and paeoniflorin were the main precursors of these metabolites. Phase I reactions (dehydroxylation, decarboxylation, dehydrogenation) and phase II reactions (sulphation, glucuronidation and methylation) were observed as the main metabolic pathways of *P. lactiflora* root extract.

Traditional Medicinal Uses

The roots of *P. suffruticosa, P. albiflora, P. lactiflora* and *P. obovata* are the most important crude drugs in traditional Chinese medicine and have been used for over 1,500 years in Chinese medicine (Wu et al. 2010). Dry roots of *Paeonia lactiflora* and dry root bark of *P. suffruticosa* are used under the traditional names of Radix Paeoniae and moutan cortex, respectively, traditional medicines in Korea, China and Japan (Koo et al. 2010). Both Radix Paeoniae and moutan cortex have been used as remedies for cardiovascular diseases, for improving blood circulation or for other uses. The roots of *P. suffruticosa,*

P. albiflora, P. lactiflora and *P. obovata* have been used as analgesic, sedative and anti-inflammatory agents and as remedies for cardiovascular, extravasated blood, stagnated blood and female genital disease (Wu et al. 2010).

The root of *P. lactiflora* is deemed as alterative, analgesic, anodyne, antibacterial, anti-inflammatory, antipyretic, antiseptic, antispasmodic, astringent, carminative, diuretic, emmenagogue, antidiabetic, expectorant, febrifuge, hypotensive, nervine, sedative and tonic (Yeung 1985; Duke and Ayensu 1985; Bown 1995; Chevallier 1996; Page 1997; Lee et al. 2008a; Wu et al. 2010; Juan et al. 2011). *Paeonia lactiflora* root is categorized into Radix Paeoniae Alba (Bai-shao in Chinese) and Radix Paeoniae Rubra (Chi-shao in Chinese) in the Chinese pharmacopoeia and are popularly used in traditional Chinese medicine (Yang et al. 2009). In terms of the herbal source, the only difference consists in the processing method and growth conditions of the two herbal roots: Bai-shao is the steamed and dried root of cultivated *P. lactiflora*, while Chi-shao is the dried root of wild *P. lactiflora*. According to traditional Chinese medicine theory, Radix Paeoniae Alba is usually used for the remedy of female disorders as an analgesic and anti-inflammatory agent, while Radix Paeoniae Rubra is often employed to remove heat from blood, eliminate blood stasis and relieve pain (Yang et al. 2009).

P. lactiflora is known most widely as one of the herbs used to make 'Four Things Soup', a woman's tonic, and it is also a remedy for gynaecological problems and for cramp, pain and giddiness (Chevallier 1996). The other species used are *Rehmannia glutinosa, Ligusticum wallichii* and *Angelica sinensis*. The roots of *Paeonia lactiflora* (Radix Paeoniae, shakuyaku in Japanese) are one of the most important crude drugs in Japan and China, being used in many traditional 'Kampo' formulas (Washida et al. 2009b). In particular, they are frequently used in 'Kampo' formulas, such as Tokishakuyakusan, Shimotsuto and Keishibukuryogan, for women's hormone-related problems such as menopausal symptoms and menstrual problem (Kumagai et al. 2005; Watanabe et al. 2006). Radix Paeoniae (the roots of *Paeonia lactiflora*) is a crude drug that is used in Asia and Europe to improve blood flow (Goto et al. 1996). *Paeonia lactiflora* root has been used frequently as an antipyretic and anti-inflammatory agent in traditional medicines of Korea, China and Japan (Lee et al. 2008a). *Paeonia lactiflora* is a common ingredient of Sheng-Ma-Ge-Gen-Tang (SMGGT; Shoma-kakkon-to) and Ge-Gen-Tang (GGT; kakkon-to). Both SMGGT and GGT are different prescriptions of traditional Chinese medicine with different ingredients designed for airway symptoms (Lin et al. 2013). Radix Paeoniae Rubra (root of *Paeonia lactiflora*) has been frequently employed in traditional Chinese medicine (TCM) as an antidiabetic therapy to enhance blood circulation and dissipate stasis (Juan et al. 2011). In China, Korea and Japan, a decoction of the dried peony root without bark has been used in the treatment of rheumatoid arthritis, systemic lupus erythematosus, hepatitis, dysmenorrhoea, muscle cramping and spasms and fever for more than 1,200 years (He and Dai 2011). Chinese peony is used clinically to treat depression-like symptoms in Chinese medicine (Mao et al. 2012).

Paeoniflorin, the active ingredient of the root, is taken internally in the treatment of menstrual disorders, injuries, high blood pressure, premenstrual tension and liver disorders (Bown 1995). It should only be used under the supervision of a qualified practitioner and should not be prescribed for pregnant women. Paeoniflorin, isolated from peony root, has been used as a herbal medicine for more than 1,200 years in China, Korea and Japan for its anti-allergic, anti-inflammatory and immunoregulatory effects (Tsuboi et al. 2004). Paeoniflorin is the principal bioactive component of Radix Paeoniae Alba, which is widely used in TCM for the treatment of neurodegenerative disorders such as Parkinson's disease (Cao et al. 2010).

A tea made from the dried crushed petals of various peony species including *P. lactiflora* has been used as a cough remedy and as a treatment for haemorrhoids and varicose veins (Page 1997).

Other Uses

Peony is widely grown as an ornamental plant in gardens in the temperate areas, with several hundred selected cultivars; many of the cultivars have double flowers.

Daucosterol (β-sitosterol-D-glucoside) was isolated from the roots and was found to be a phytosterol, exhibiting both auxin and kinetin activities (Xu 1986). Bioassays showed that daucosterol increased fresh weight of cumber cotyledons, promoted elongation of wheat coleoptiles and delayed destruction of chlorophyll.

Comments

Refer also to notes under *Paeonia* × *suffruticosa*.

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Paeonia × suffruticosa

Scientific Name

***Paeonia* × *suffruticosa* Andrews**

Synonyms

Paeonia × *arborea* C.C.Gmel., *Paeonia* × *chinensis* Oken, *Paeonia* × *fruticosa* Dum. Cours., *Paeonia* × *moutan* Sims, *Paeonia* × *moutan* var. *anneslei* Sabine, *Paeonia* × *moutan* var. *papaveracea* (Andrews) DC., *Paeonia* × *papaveracea* Andrews, *Paeonia* × *suffruticosa* f. *anneslei* (Sabine) Rehder, *Paeonia* × *suffruticosa* f. *maculata* Hong C.Zheng, *Paeonia* × *suffruticosa* var. *papaveracea* (Andrews) Kern., *Paeonia* × *suffruticosa* var. *purpurea* Andrews, *Paeonia* × *suffruticosa* f. *rubida* Hong C.Zheng, *Paeonia* × *yunnanensis* W.P.Fang

Family

Paeoniaceae

Common/English Names

Mountain Peony, Moutan, Moutan Cortex, Moutan Peony, Tree Peony

Vernacular Names

Chinese: Mudan, Mudan Pi
Czech: Pivoňka Keoovitá, Pivoňka Křovitá
Danish: Almindelig Træpæon, Træpæon
Dutch: Boompioen, Gewone Boompioen
Estonian: Põõsaspojeng
French: Pivoine En Arbre
German: Baumartige Pfingstrose, Rote Baump fingstrose, Strauch-Pfingstrose, Strauchpäonie
Icelandic: Trjábóndarós
Japanese: Botan, Botanpi
Polish: Piwonia Drzewiasta
Slovaščina: Grmasta Potonika
Slovencina: Pivonka Polokrovitá
Turkish: Şakayığı
Vietnamese: Bạch Thược Cao, Mẫu Đơn Bụi

Origin/Distribution

Tree peony is native to China, in central Anhui and western Henan. It is widely cultivated in China and elsewhere in cool climatic regimes.

Agroecology

Tree peony is robust and thrives best in partial shade in an uncrowded situation. It prefers a fertile yet reasonably well-drained soil, pH 6 to

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slightly alkaline. Clay, chalk and sand are all fine, as long as they do not become too wet in the winter.

Edible Plant Parts and Uses

Tree peony flowers are edible and used as traditional Chinese medicine materials (Li et al. 2009a). Since ancient times, the flowers of tree peony have been used to prepare traditional food such as casseroles, cakes, herbal tea and drinks (Voon et al. 2013). The presence of significant amount of crude fibre, carbohydrate, proteins, essential amino acids, fatty acids and essential minerals provides a strong base to use tree peony flower buds as a potential source of nutraceutical for the development of new functional foods (Voon et al. 2013). The petals are also reported to be parboiled and sweetened for teatime delicacy or cooked in various dishes (Uphof 1968; Usher 1974; Tanaka 1976; Kunkel 1984; Facciola 1990).

Botany

Moutan peony is a shrub growing to 1.5 m high with grey-brown glabrous stems. Proximal leaves biternate with ovate, glabrous leaflets 4.5–8 by 2.5–7 cm; terminal leaflets deeply 3-lobed, lobes shallowly subdivided again; some lateral leaflets 2- or 3-lobed, others entire; all lobes acute at apex (Plates 1 and 2). Flowers solitary, terminal, single or double (Plates 1 and 2) in cultivated plants, 10–17 cm across. Bracts 5, long elliptic. Sepals 5, green, broadly ovate, unequal. Petals (in single flowers) 5–11, white, pink, red or red-purple, obovate, 5–8 × 4.2–6 cm, apex irregularly incised. Filaments pink or purple, white distally, 1.3 cm; anthers ellipsoid, 4 mm long. Disc completely enveloping carpels at anthesis, purple-red, apex dentate or lobed. Carpels 5, rarely more, densely tomentose. Stigmas red. Follicles oblong, densely brown-yellow and tomentose.

Plate 1 Flowering moutan peony plant

Plate 2 Moutan flowers (double petals)

Nutritive/Medicinal Properties

Flower Nutrients and Phytochemicals

The proximate nutrient composition of tree peony flower buds was reported as follows: moisture 5.68 %; crude protein 15.73 %; crude fibre 13.11 %; crude fat 2.74 %; total ash 4.89 %; total crude carbohydrate 57.84 %; energy 1,332.03 KJ/100 g; essential amino acid, histidine 2.45 %, isoleucine 4.36 %, leucine 6.66 %, lysine 4.94 %, methionine 0.23 %, phenylalanine 4.29 %, threonine 4.38 % and valine 5.35 %; non-essential amino acid, alanine 6.02 %, arginine 6.56 %, aspartic acid 16.40 %, cysteine 0.55 %,

glutamic acid 17.28 %, glycine 4.38 %, proline 7.82 %, serine 4.91 % and tyrosine 3.43 %; sulphur-containing amino acid (methionine, cysteine) 0.79 %; aromatic amino acid (phenylalanine, tyrosine) 7.72 %; saturated fatty acids, caprylic acid C8:0 36.18 %, lauric acid C12:0 0.19 %, tridecylic acid C13:0 0.3 %, myristic acid C14:0 4.11 %, pentadecylic acid C15:0 0.19 %, palmitic acid C16:0 17.02 %, stearic acid C18:0 4.00 % and arachidic acid C20:0 0.88 %; unsaturated fatty acids, myristoleic acid C14:1 0.27 %, *cis*-10-pentadecanoic acid C15:1 0.07 %, palmitoleic acid C16:1n7 4.14 %, hexadecatrienoic acid C16:3n4 2.63 %, oleic acid C18:1n9 3.61 %, vaccenic acid C18:1n7 1.45 %, linoleic acid C18:2n6 14.37 %, gamma-linolenic acid C18:3n6 6.74 % and alpha-linolenic acid C18:3n3 5.66 %; and minerals(mg/100 g), K 1,540.37 mg, Ca 462.46 mg, Mg 241.51 mg, P 420 mg, Na 12.75 mg, Se <0.25 mg, Cr <0.25 mg, Cu 1.73 mg, Fe 2.29 mg, Mn 2.29 mg, Zn 4.09 mg, Al 1.86 mg, B <0.10 mg, Cd <0.05 mg, Ni <0.05 mg, Hg,0.05 mg, PB <0.5 mg and As <0.05 mg (Voon et al. 2013). The presence of significant amount of crude fibre, carbohydrate, proteins, essential amino acids, fatty acids and essential minerals provides a strong base to use tree peony flower buds as a potential source of ingredient for food and pharmaceutical applications.

Four flavonoids, apigenin-7-*O*-neohesperi doside, luteolin-7-*O*-glucoside, apigenin-7-*O*-glucoside and kaempferol-7-*O*-glucoside, were isolated from *Paeonia suffruticosa* flowers (Wang et al. 2005b). Twenty-six flavonoids were identified in yellow flowers of tree peony; glycosides of kaempferol, luteolin and apigenin as well as isosalipurposide were the main flavonoids found (Li et al. 2009a).

2-Phenylethanol (38.20 %) and 2,7-dimethyl-2, 6-octadi-4-ol (13.40 %) were the main essential oil floral compounds of Zhao Fen cultivar of *P. suffruticosa*, and the key components with floral fragrance properties were as follows: *E, E*-10, 12-hexadeca-dien-1-ol (10.76 %), 3,7-dimethyl-6-octen-1-ol (cephrol, 7.78 %) and 2-[(*3S,5R,8S*)-3,8-dimethyl-1,2,3,4,5,6,7,8-octahydroazulen-5-yl] propan-2-ol (guaiol, 2.35 %) (Yin et al. 2012). Other components were 3,7-dimethyl-1,6-octadien-3-ol (0.83 %), 2-(1-methylethylidene)-cyclohexanone (0.43 %), 2,7-dimethyl-2,6-octadi-enen (0.56 %), *E*, 2-(1,1-dimethylethyl)-clohexanol (0.38 %), *cis-4-tert*-butylcyclohexyl acetate (0.70 %), (6E)-2,6-dimethyl-2,6-octadiene (0.4 %), 3,7-dimethyl-6-octenal (1.59 %), methyl-4-methyl-(*E*)-pentenoate (0.81 %), unknown (2.11 %), 1,2-benzenedicarboxylic acid, mono(2-ethylhexyl) ester (0.41 %), 1-(2-hydrooxy-6-methoxyphenyl)-ethenone (2.81 %), 1,1,4,7-tetramethyl-1a,2,3,5,6,7,7a,7b, namicaldehyde-octahydro-1H-cycloprop [e]azulene (Lilial) (0.42 %), α,α-4-trimethyl-3-cyclohexen-1-ol (2.34 %), 2-phenylethyl-cyclopropane-1-carboxylate (0.81 %), 2-(4-methoxyphenoxy)ethan-1-ol (1.22 %), but-3-yn-2-yl 3-methylbenzoate (0.19 %), *p-t*-butyl-α-methylhydrocin-enen-1-ol (0.31 %), 2-butyl-2-methyl-1,3-benzo-dioxole (2.76 %), 5,6,-dipropyldecane (0.91 %), 3-oxo-2-pentyl-methylester (*1R-trans*)-cyclopentaneacetic acid (0.40 %), (*Z*)-13-octadecene-L-ol (0.94 %), *cis,cis*-7,10,-hexadecadiene (0. 34 %), *E,E*-10,12-hexadecadien-1-ol acetate (10.76 %) and 2,3,6,7,8,8a-hexahydro-1,4,9,9-tetramethyl-(1α,3α,7α,8a,β-)-1H-3a,7-methanoazulene (0.36 %). 2-Phenylethanol (26.20 %) and 2,7-dimethyl-2,6-octadi-en-1-ol (3.56 %) were the main essential oil floral compounds of Rou Fu Rong cultivar of *P. suffruticosa*, and 2-hydroxy-4,4,6,6-tetramethyl-2-cyclohexen-1-one (21.31 %), tetrahydro-2,2-dimethyl-5-(1-methylpropenyl)furan(3.86%),2-butyl-2-methyl-1,3-benzo-dioxole (2.71 %), eugenol (3.69 %) and *trans*-linaloloxide (5.65 %) were the key components of aromatic odour of this variety. Other components were pentacosane (3.22 %), β-cubebene (2.36 %), tridecane (1.11 %), heptadecane (1.36 %), heneicosane (1.35 %), tricosane (0.18 %), 9-butyl-9-butyldocosane (0.68 %), 2-ethyl-1-hexanol(1.82%),5-(3,3-dimethyloxiran-2-yl)-3-methylpent-1-en-3-ol (*cis*-linaloloxide) (2.86 %), α-farnesene, octan-2-yl-benzoate (2.28 %), nonadecane (0.29 %), 1,7,7-trimethylbicyclo-[2. 2.1]-hept-5-en-2-ol (1.17 %), β-citronellol (1.95 %), 4-oxo-2-[(tetradecyloxy)-2,2-dimethylpropanoate] (1.71 %), 2,6,6-trimethyl,

1-cyclohexene-1-ethanol (0.39 %), pinanediol (2.35 %), 5,6-dipropyldecane (1.43 %), 2-methyl-4-[1-methyl]-2-cyclohexan-one (0.59 %), 2-octylbenzoate (0.71 %), butylated hydroxytoluene (0.30 %), 1-heptyl-2-methyl, cyclopropane (0.40 %) and β-citronellyl acetate (0.66 %).

Seed Phytochemicals

Three novel resveratrol trimers (suffruticosol A, suffruticosol B and suffruticosol C), together with *cis*-resveratrol and paeoniflorin, were isolated from *Paeonia suffruticosa* seeds (Sarker et al. 1999). Three oligostilbenes, *trans-suffruticosol* D, *cis*-suffruticosol D and *cis*-gnetin H, were isolated along with the eight known stilbenes, *trans*-resveratrol, *trans*-ε-viniferin, *cis*-ε-viniferin, gnetin H, suffruticosol A, suffruticosol B, suffruticosol C and *cis*-ampelopsin E, from *Paeonia suffruticosa* seeds (He et al. 2010a). Thirteen compounds were isolated from *P. suffruticosa* seeds and identified as follows: paeoniflorin, oxy paeoniflorin, 6′-*O*-β-D-glucopyranosylalbiflorin, 8-debenzoylpaeoniflorin, 8-debenzoylpaeonidanin, 1-*O*-β-D-glucopyranosylpaeonisuf-frone, 1-*O*-β-D-ethyl-mannopyranoside, sucrose, luteolin, apigenin, benzoic acid and 1-*O*-β-D-(4-hydroxy benzoyl) glucose (He et al. 2010b).

Root Phytochemicals

Seven constituents, paeoniflorin, benzoylpaeoniflorin, oxypaeoniflorin, paeonol, paeonoside, apiopaeonoside and paeonolide, were found in *P. suffruticosa* root (Yu and Xiao 1985). Higher amounts of the compounds were determined in early and late spring or in autumn. Monoterpene glucosides such as paeoniflorin, oxypaeoniflorin, benzoylpaeoniflorin and benzoyloxypaeoniflorin were found to exist mainly in moutan periderm and its adjacent tissues in the root and to a lesser extent in xylem (Tani et al. 1980b). Paeonol was found to accumulate mainly in the periderm, cambium and adjacent tissues of the root and to a smaller extent also in the xylem (Tani et al. 1980a). Apiopaeonoside was isolated from *Paeonia suffruticosa* root, and its structure was elucidated as paeonol-[D-apio-β-D-furanosyl] (1 → 6)-β-D-glucopyranoside (Yu et al. 1986). Five other compounds isolated were paeoniflorin, benzoylpaeoniflorin, paeonol, paeonoside and paeonolide. Five new antioxidative glycosides named galloyloxypaeoniflorin and suffruticosides A, B, C and D and a new paeonol glycoside named suffruticoside E were isolated from Chinese Moutan Cortex, the root cortex of *Paeonia suffruticosa*, together with antioxidative galloylpaeoniflorin (Yoshikawa et al. 1992). Six monoterpene glycosides, namely, mudanpiosides A–F, were isolated as minor components from an ethanol extract of *Paeonia suffruticosa* root cortex together with five known glycosides, paeoniflorin, oxypaeoniflorin, benzoylpaeoniflorin, benzoyloxypaeoniflorin and apiopaeonoside (Lin et al. 1996). A new hexacyclic triterpenoid, mudanpinoic acid A, and a new gallic acid glycoside, mudanoside B, along with nine known compounds, benzoic acid, resacetophenone, paeoniflorigenone, β-sitosterol, betulinic acid, oleanolic acid, quercetin, β-sitosterol-β-D-glucoside and *trans*-caffeic acid stearyl ester, were isolated from the dried root cortex of *Paeonia suffruticosa* (Lin et al. 1998). Four glycosides, namely, mudanpioside G, mudanpioside H, mudanpioside I and mudanoside A, together with three known compounds, gallic acid, adenosine and *p*-hydroxybenzoic acid, were isolated from the root bark (Ding et al. 1999). Two monoterpenes paeonisuffrone and paeonisuffral were isolated from the ethyl acetate-soluble fraction of Moutan Cortex methanol extract (Yoshikawa et al. 2000). Five paeonol glycosides, suffruticosides A, B, C, D and E, and a monoterpene glucoside, galloyloxypaeoniflorin, were isolated from the glycosidic fraction of Chinese Moutan Cortex together with paeonolide, apiopaeonoside, galloylpaeoniflorin, oxypaeoniflorin and paeoniflorin (Matsuda et al. 2001). Paeonol, 2,5-dihydroxy-4-methoxyacetophenone, acetovanillone, paeonoside, paeoniflorin, oxypaeoniflorin, apiopaeo noside and methyl 3-hydroxy-4-methoxybenzoate were isolated from the root cortex (Li et al. 2004). A paeoniflorin derivative identified as

paeoniflorin-4-ethyl ether was isolated from the root bark as an artefact produced during extraction (Wang et al. 2005c).

Three bioactive constituents (paeonol, benzoyloxypaeoniflorin and oxypaeoniflorin) in traditional Chinese medicine, Moutan Cortex (*Paeonia suffruticosa* root cortex), were separated and determined by capillary electrophoresis (Chen et al. 2005). Chen et al. (2006) isolated paeoniflorin, paeonoside, sucrose, glucose and fructose in Moutan Cortex. The chloroform–methanol (1:1) extract of *Paeonia suffruticosa* root bark furnished three monoterpene glycosides, 6-*O*-vanillyoxypaeoniflorin, mudanpioside H and galloyloxypaeoniflorin (An et al. 2006). α-Benzoyloxypaeoniflorin, a new antioxidant monoterpene α-glycoside anomer, was isolated from *Paeonia suffruticosa* root along with known compounds, β-benzoyloxypaeoniflorin, paeonolide, paeoniflorin and mudanpioside H (Ryu et al. 2001). Thirty-eight components such as monoterpene glucosides, galloyl glucoses and acetophenones were isolated from Moutan Cortex extract (Xu et al. 2006a). Among them, over 30 compounds were identified, including paeonol, paeoniflorin, oxypaeoniflorin, benzoylpaeoniflorin, benzoyloxypaeoniflorin, galloylpaeoniflorin, galloyloxypaeoniflorin and mudan piosides A, C, D, E and H. A total of 50 compounds were observed in the 50 % (v/v) methanolic extracts of root cortices of *P. suffruticosa*, *P. delavayi* and *P. decomposita*, including 17 monoterpenes, 14 galloyl glucoses, 10 acetophenones, 5 phenolic acids, 3 flavonoids and 1 triterpene (Xu et al. 2006b). Paeonol was the predominant constituent of *P. suffruticosa* and *P. decomposita*. Six compounds were isolated from *P. suffruticosa* bark and identified as (+)-catechin, paeonidanin, paeoniflorigenone, 2, 5-dihydroxy-4-methoxy acetophenone, paeonol and gallic acid (Hu et al. 2006). A new pyrrole derivative, 2-methyl-5-(2′-*O*-α-D-glucopyranosyl-1′-oxygen)-propylpyrrole, named paesuffrioside, was isolated from the water-soluble extract of *P. suffruticosa* root cortex together with 11 known compounds (Xiao et al. 2008). From the roots, Wu and Gu (2009) isolated paeoniflorin, mudanpioside H, galloylpaeoniflorin, benzoylpaeoniflorin, benzoyloxypaeoniflorin, paeonol, mudanoside B and 1,2,3,4,6-pentagalloylglucose; Ding et al. (2009) isolated kaempferol, quercetin, mudanpioside B, benzoyloxypaeoniflorin, mudanpioside H and pentagalloyl-β-(D)-glucose. Three new compounds, 5-hydroxy-3**S**-hydroxymethyl-6-methyl-2,3-dihydrobenzofuran, 8-*O*-benzoylpaeoniflorin and 4-*O*-butylpaeoniflorin (Ha et al. 2009a), and 13 known compounds, paeonol, paeonoside, apiopaeonoside, paeonolide, paeoniflorigenone, 6-methoxypaeonigenone, paeoniflorin, benzoylpaeoniflorin, galloylpaeoniflorin, oxypaeoniflorin, mudanpioside H, α-benzoylpaeoniflorin and β-benzoylpaeoniflorin, were isolated from Moutan Cortex (Ha et al. 2010). Three new paeonidanin-type monoterpene glycosides, named suffrupaeonidanins A–C, were isolated as minor components from the root cortex of *Paeonia suffruticosa* (Yang et al. 2010). Two new monoterpene diglycosides, suffruyabiosides A and B, and seven known compounds, paeoniflorin, salicylpaeoniflorin, oxypaeoniflorin, mudanpioside, mudanpioside D, galloylpaeoniflorin and mudanpioside I, were isolated from Moutan Cortex (Furuya et al. 2012). From the roots, a novel phenylesteric compound, oxo-acetic acid 2-ethoxy-4-(3-hydroxy-2-oxopropyl) phenyl ester, was isolated (Choi et al. 2012b). Wang et al. (2013) isolated paeonol, the flavan-3-ols catechin and epicatechin-3-*O*-gallate, the dimeric proanthocyanidin epicatechin-(4β → 8)-catechin, a mixture of trigalloyl-glucoses and 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG) from Moutan Cortex.

The essential oil constituents of Moutan Cortex radicis (*P. suffruticosa*) comprised predominantly paeonol (93.15–97.80 %) (Miyazawa et al. 1983). Other constituents included 4-benzoic acid (1.38–3.01 %), phenol (0.15–1.02 %) and compounds (traces to <0.71 %) furfural, 3-hydroxypyridine, 2-furyl methyl ketone, benzaldehyde, 5-methyl-2-furfural, methyl benzoate, β-phenylacetaldehyde, acetophenone, furfuryl alcohol, 4,7,dimethylbenzofuran, methyl salicylate, perilla alcohol, ethyl salicylate, *o*-hydroxyacetophenone, 2-methoxyphenol, benzyl alcohol, β-phenylethyl alcohol, 2,6-di-*tert-butyl*-4-methyl phenol, 2-acetylpyrrole,

o-cresol, *p*-cresol, *m*-cresol, *m-tert*-butylphenol, *p*-methoxyacetophenone, thymol, carvacrol and hydroxy-3-methoxy acetophenone.

In vitro studies found that hydroxymethyl glutaryl-CoA synthase and phosphomevalonate kinase in the mevalonate pathway and 3-dehydroquinate dehydratase/shikimate dehydrogenase in shikimate biosynthesis were potentially closely related to the accumulation of paeoniflorin and benzoylpaeoniflorin in *Paeonia lactiflora* (Bai Shao, Chi Shao) and *P. suffruticosa* (Dan Pi) (Yuan et al. 2013). Paeoniflorin and its derived aromatic amino acids were found to be predominant in the bark.

The paeonol content in roasted Moutan Cortex was increased about three times (454.3 μg/mg ethanol extract) after roasting at 190 °C for 30 min compared to that of untreated one (Jeon et al. 2004). Roasting processing did not affect the DPPH radical scavenging activity of moutan extracts. The contents of paeonol in Chinese moutan cultivars remained nearly constant at different root harvesting times, but the paeoniflorin contents changed significantly during the harvesting time (Choi et al. 2005). These showed increasing tendency in May, July and September. Total extraction rates of *P. suffruticosa* by ethanol circumfluence, distillation–decoction, CO_2-SFE (supercritical fluid extraction with CO_2) and traditional decoction were 12.66 %, 13.51 %, 7.28 % and 7.56 %, respectively, and extraction rates of paeonol were, respectively, 2.45 %, 2.26 %, 0.31 % and 1.15 % (Wang et al. 2005a). Phenolic glycosides could be extracted by ethanol circumfluence, distillation–decoction and traditional decoction, but not by CO_2-SFE. Distillation–decoction was found to be the most optimal for proper extraction technology of *P. suffruticosa.* The average recoveries of gallic acid and paeonol from *P. suffruticosa* root bark methanol extract by reversed-phase HPLC system were 98.6 % and 98.2 %, respectively (Tian et al. 2005).

Besides the root cortex of *P. suffruticosa*, the root core also possessed pharmacological properties. Comparative studies by Li et al. (1997) found no marked difference between the cortex and core in reducing inflammation, promoting thrombocyte coagulation, inhibiting convulsion, depressing blood pressure and strengthening antiseptic activity. The toxicity of the core was 38.5 % of the cortex.

Antioxidant Activity

The methanol plant extract of *Paeonia suffruticosa* was one of the 14 plants found to have potential as antioxidant source activity evaluated using Fenton's reagent/ethyl linoleate system and for free radical scavenging activity using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical generating system (Kim et al. 1997). Aqueous *P. suffruticosa* extract exhibited high potency in inhibiting rat erythrocyte hemolysis and lipid peroxidation in rat kidney and brain homogenates (Liu and Ng 2000). It also demonstrated strong superoxide and hydroxyl radical scavenging activity, but exerted only a slight pro-oxidant effect. *Paeonia suffruticosa* methanol extract strongly enhanced viability against hydrogen peroxide-induced oxidative damage in Chinese hamster lung fibroblast (V79-4) cells and had relatively high levels of DPPH radical scavenging activity ($IC_{50} < 6.0$ μg/mL) (Lee et al. 2003).

The methanolic extract and the ethyl acetate-soluble and methanol-eluted fractions from Chinese Moutan Cortex were found to exhibit scavenging effect on DPPH radical and superoxide anion radical generated by the xanthine–xanthine oxidase system (Yoshikawa et al. 2000). Two monoterpenes paeonisuffrone and paeonisuffral were isolated from the ethyl acetate-soluble fraction. Both Moutan Cortex (root cortex of *Paeonia suffruticosa*) and Radix Paeoniae (root of *Paeonia lactiflora*) drugs suppressed the cleavage of pUC18 DNA induced by phenylhydroquinone and scavenged the superoxide and hydroxy radical generated by the chemical (Okubo et al. 2000). They also inhibited the oxidative DNA cleavage by tert-butylhydroquinone (TBHQ), one of the major metabolites of butylated hydroxyanisole. Among their constituents, galloylpaeoniflorin and 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG) were found to be the most potent inhibitors of the DNA cleavage. These constituents also had oxygen radical scavenging activity.

Paeonol also attenuated the DNA cleavage, while paeoniflorin and albiflorin had relatively small inhibitory effects on DNA cleavage. However, catechin enhanced the phenylhydro quinone-induced DNA cleavage.

Galloyloxypaeoniflorin, galloylpaeoniflorin and suffruticosides A, B, C and D isolated from the root cortex showed more potent radical scavenging and antioxidative effects than α-tocopherol (Yoshikawa et al. 1992). Monoterpene glycosides suffruticosides A, B, C and D; galloyloxypaeoniflorin; and galloylpaeoniflorin from moutan root cortex exhibited more potent radical scavenging effects than α-tocopherol (Matsuda et al. 2001). Of the compounds isolated from Moutan Cortex, galloylpaeoniflorin and salicylpaeoniflorin exhibited a more pronounced radical scavenging effect than α-tocopherol (positive control) in the SOD (superoxide dismutase) assay (Furuya et al. 2012). Increase in the number of phenolic hydroxyl groups in the compounds produced a more effective radical scavenging effect (galloylpaeoniflorin > mudanpioside E > oxypaeoniflorin). Comparing the effect of salicylpaeoniflorin with oxypaeoniflorin showed that *o*-substitution with a phenolic hydroxyl group was more effective than *p*-substitution. Moreover, mudanpioside I was more effective than paeoniflorin (**3**), indicating that a benzoyl group connected to a C-6 of the α-glucose by the ester linkage was more effective for radical scavenging than a benzoyl group attached to the C-8 monoterpene pinane-type skeleton.

Tree peony petal extracts showed high antioxidant activity as evaluated by the DPPH$^{\bullet}$, ABTS$^{\bullet+}$ and OH$^{\bullet}$ scavenging assays and ferric reducing/antioxidant power assay (Li et al. 2009a). There were significant correlations between antioxidant activity and both the total polyphenol content (determined by Folin–Ciocalteu method) and the total content of quercetin, kaempferol and luteolin glycosides.

α-Benzoyloxypaeoniflorin, from *Paeonia suffruticosa* root, exhibited moderately potent radical scavenging activity on DPPH radical (Ryu et al. 2001). Several compounds including monoterpene glycosides isolated from the n-butanol-soluble fraction of ethanol extract of *Paeonia suffruticosa* exhibited strong inhibitory activity on nitric oxide (NO production) with IC_{50} values of 6.87–41.94 μM in lipopolysaccharide (LPS)-induced RAW 264.7 cells (Ding et al. 2012c) and in LPS-activated macrophages (Ding et al. 2012a).

Danzhixiaoyao Wan, a common Chinese herbal formulation, and some of its herbal constituents were found to have inhibitory effect on nitric oxide (NO) production by lipopolysaccharide (LPS)-activated RAW 264.7 macrophages and antioxidant activity based on the oxygen radical absorbance capacity (ORAC) assay (Liao et al. 2007). The ORAC value of the herbal formulation was 450 μmol TE/g. The order of antioxidant (ORAC) activity of the herbal constituents was *Mentha haplocalyx* (1,352 μmol TE/g), *Glycyrrhiza uralensis* (1,184 μmol TE/g), *Gardenia jasminoides* (1,129 μmol TE/g) and *Paeonia suffruticosa* (465 μmol TE/g), with the contributions being additive rather than synergistic.

Anticancer Activity

1,2,3,4,6-Penta-*O*-galloyl-β-D-glucose (PGG), a major component of *P. suffruticosa* root, was found to exhibit in vitro growth-inhibiting effect on human hepatocellular carcinoma cell line, SK-HEP-1 cells, via G(0)/G(1) phase arrest and suppression of nuclear factor-kappa B activity (Oh et al. 2001). Oh et al. (2004) also reported that gallotannin penta-*O*-galloyl-β-D-glucose (PGG), a major constituent of *Paeonia suffruticosa* root cortex, inhibited IL-8 gene expression in human monocytic U937 cells stimulated with phorbol myristate acetate (PMA), a tumour promoter, and U937 cells stimulated with tumour necrosis factor-alpha by a mechanism involving its inhibition of NF-kappa B activation, which was dependent on IkappaBalpha degradation.

In an in vitro study, paeoniflorin exhibited antiproliferative activity against human lung adenocarcinoma epithelial A549 cells by arresting cell cycle progression in the G0/G1 phase and inducing apoptosis (Hung et al. 2008). It was found that induction of p21/wild-type p53-activated fragment 1 (WAF1) and the activity of the Fas/Fas ligand apoptotic system may participate

in the antiproliferative activity of paeoniflorin in A549 cells. In another study, paeonol and crude total glycosides (CTG) extracted from Moutan Cortex significantly reduced DLD-1 human colon cancer cell viability in a dose- and time-dependent manner (Xing et al. 2010). The induction of apoptosis in DLD-1 cells was characterized by morphological changes and an increased percentage of hypodiploid cells. After treatment for 48 h with paeonol (400 μg/mL) or CTG (200 μg/mL), the ratio of apoptotic cells reached 34.79 and 48.12 %, respectively. In vitro study demonstrated that treating human gastric cancer AGS cells with the *Paeonia suffruticosa* root bark (Moutan Cortex) extract significantly inhibited cell proliferation and induced cytotoxicity in a dose- and time-dependent manner (Choi et al. 2012a). The extract also induced apoptosis via the extrinsic Fas-mediated apoptosis pathway, which was concurrent with the activation of caspases, including caspase-8 and caspase-3, and cleavage of PARP and also involved the MDM2-p53 pathway. Wang et al. (2012) found that the aqueous extract of *Paeonia suffruticosa* (PS-A) exerted strong inhibitory effects on renal carcinoma cancer cell migration, mobility and invasion by decreasing expression of VEGF receptor-3 (VEGFR-3), phosphorylation of FAK and activation of Rac-1 to disrupt actin filament polymerization. Mouse xenograft experiments showed that the treatment of PS-A significantly suppressed tumour growth and pulmonary metastasis. In vitro studies showed that co-pretreatment with tunicamycin and paeonol significantly increased apoptosis induced by doxorubicin in hepatocellular carcinoma cells undergoing endoplasmic reticulum stress by decreasing expression of COX-2 levels and activation of Akt and increasing the levels of pro-apoptotic transcription factor CHOP (Fan et al. 2013).

Of the compounds isolated from Moutan Cortex assay for cytotoxicity activity against human lung adenocarcinoma epithelial A549 cells, salicylpaeoniflorin and paeoniflorin exhibited moderate cytotoxicities (viabilities, 31 % and 52 %, respectively), while other compounds including suffruyabiosides A and B showed very weak activities (viabilities, 63–100 %) (Furuya et al. 2012).

Antimicrobial Activity

Three monoterpene glycosides, 6-*O*-vanillyoxy paeoniflorin, mudanpioside H and galloyloxy-paeoniflorin isolated from *Paeonia suffruticosa* root bark, showed broad, but moderate, antibacterial activity with minimum inhibitory concentration (MIC) values in the range of 100–500 μg/mL against 18 pathogenic microorganisms of concern for public health or zoonosis (An et al. 2006). Total glycosides of *P. suffruticosa* exhibited antibacterial activity in vitro, with the strongest activity against *Pseudomonas aeruginosa* and the weakest activity against *Klebsiella pneumoniae* (Du et al. 2008). Paeonol also displayed antibacterial activity, but MIC of paeonol was higher than total glycosides; polysaccharides of *P. suffruticosa* also had antibacterial activity against *Pseudomonas aeruginosa* and *Enterococcus faecalis*. The antibacterial activity of the combination of paeonol and total glycosides was better than paeonol or total glycosides, especially on *Enterococcus faecalis*.

Antiviral Activity

Paeonia suffruticosa was found to be a rich source of anti-HIV compounds (Au et al. 2001). After removal of polyphenolic compounds, the methanol extract of *P. suffruticosa* still exerted potent inhibition of HIV-1 integrase ($EC_{50} = 15$ μg/mL). Studies showed that methanolic extract of *Paeonia suffruticosa* had anti-herpes simplex virus (HSV) activity (Hsiang et al. 2001). The methanol extract prevented the process of virus attachment and penetration. Aqueous extract of *P. suffruticosa* also inhibited virus attachment to cell surface.

Anti-inflammatory and Analgesic Activities

Intragastric administration of a hot water extract of Radix Paeoniae to rats inhibited inflammation in adjuvant-induced arthritis (Cho et al. 1982) and carrageenan-induced paw oedema (Arichi et al. 1979). Methanol extract of Moutan Cortex significantly inhibited phorbol myristate acetate

(PMA)-induced secretions of IL-8 and macrophage chemoattractant protein (MCP)-1 in a dose-dependent manner in human monocytic U937 cells (Oh et al. 2003). The inhibition of these chemokines by the extract was due to its suppression of IL-8 and MCP-1 genes. Furthermore, 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose, one of major constituents isolated from moutan methanol, inhibited PMA-induced secretions of IL-8 and MCP-1 by its suppression of IL-8 and MCP-1 genes. Pre- and posttreatment of rats with paeonol (30, 50 or 100 mg/kg, i.p.) dose-dependently inhibited the carrageenan-evoked thermal hyperalgesia (Chou 2003). Treatment with paeonol dose-dependently inhibited tumour necrosis factor-alpha (TNF-alpha) and interleukin-lbeta formation, but enhanced IL-10 production in the rat paw exudates both at the early (1.5 h) and late phase (4 h) after carrageenan injection; however, inhibition of IL-6 formation by paeonol was only observed at the late phase. Paeonol also dose-dependently decreased the formation of prostaglandin E(2) in rat paw exudates with a greater inhibition at the late phase and reduced the carrageenan-induced elevated myeloperoxidase activity. Their results suggested that the mechanisms by which paeonol exerted its anti-inflammatory and analgesic effects in this inflammatory model may be associated with decreased production of pro-inflammatory cytokines, NO and PGE(2), and increased production of IL-10, an anti-inflammatory cytokine, in carrageenan-injected rat paws. Further, attenuation of the elevated iNOS and COX-2 protein expression as well as neutrophil infiltration in carrageenan-injected paws may also be involved in the beneficial effects of paeonol. In RAW macrophage cells paeonol regulated the production of TNF-α and IL-1β, IL-6 and IL-10 via inactivation of IκBα, ERK1/2, JNK and p38 MAPK (Chen et al. 2013). In the mouse model of lipopolysaccharide-induced endotoxemia, pro- and anti-inflammatory cytokines were significantly regulated, and the survival rates of lipopolysaccharide-challenged mice were enhanced by paeonol (150, 200 or 250 mg/kg).

Paeonol, the main component of Moutan Cortex, was suggested to be largely responsible for its anti-inflammatory, analgesic and antispasmodic activities (Haraka et al. 1972). Paeonol prevented stress-induced gastric erosion in mice and inhibited gastric juice secretion in rats. It also had a weak anticholinesterase action and antihistamine action on the isolated mouse ileum and guinea pig ileum, respectively, and weak anti-oxytocic action on the isolated rat uterus. Further, paeonol exerted inhibitory effect on the spontaneous movement of the rat uterus in situ, suggesting the action of paeonol was musculotropic. Paeonol also showed a weak transient hypotensive effect and synchronous depression of respiration and heart rate.

Among compounds isolated from the root cortex, acetovanillone afforded the highest protection against sepsis in mice (Li et al. 2004). It gave the highest survival rate (100 % with a dose of 30 mg/kg versus 17 % for the control experiment) and reduced alanine aminotransferase level to be half of the control value in the mouse sepsis model induced by lipopolysaccharide/D-galactosamine.

Chun et al. (2007) reported on the anti-inflammatory activity of the methanol extract of Moutan Cortex in RAW264.7 cells after treatment with lipopolysaccharide (LPS) and suggested that the anti-inflammatory effects were induced through the inhibition of iNOS and COX-2 expression by suppressing the phosphorylation of IκBα and the activation of NF-κB. Pan and Dai (2009) found that paeonol inhibited TNF-alpha-induced vascular cell adhesion molecule-1 (VCAM-1) expression in a concentration-dependent manner in rat aortic endothelial cells by the attenuation of p38 and ERK1/2 signal transduction pathways. They concluded that paeonol had the potential therapeutic development for use in anti-inflammatory and vascular disorders. Pretreatment of rats with Moutan Cortex prior to lipopolysaccharide (LPS) administration ameliorated symptoms of LPS-induced acute lung injury through anti-inflammatory process (Fu et al. 2012). The number of total cells and neutrophils and the concentration of protein exudation in bronchoalveolar lavage fluid (BALF) were significantly decreased in the Moutan Cortex-LPS group. Cytokine levels, including levels of interleukin (IL)-1β, macrophage-inflammatory peptide (MIP)-2, IL-6 and IL-10,

in BALF and myeloperoxidase activity in lung tissue were also significantly inhibited at 16 h after LPS administration in the Moutan Cortex-LPS group. In concentrations of 5–20 μM, penta-*O*-galloyl-β-D-glucose (PGG) exerted statistically significant inhibition of reactive oxygen species (ROS generation), IL-8 secretion and β_2 integrin expression in stimulated neutrophils (Kiss et al. 2013). The inhibition of L-selectin expression by PGG resulted in prevention in neutrophils' endothelial attachment. The results elucidate the anti-inflammatory activity of PGG. Studies showed that Moutan Cortex radicis extract could inhibit a wide variety of activations of inflammation-related genes in cultured human gingival fibroblasts stimulated with lipopolysaccharide, and this effect may be attributable to paeonol and paeoniflorin (Yun et al. 2013). The result suggested that Moutan Cortex may be employed to alleviate the inflammation of periodontal diseases.

Of the 16 compounds, isolated from Moutan Cortex evaluated on glucose metabolism in HepG2 cells under high glucose conditions, compounds paeonoside, apiopaeonoside and 6-methoxypaeonigenone displayed highly potent effects on the stimulation of glucose uptake and glycogen synthesis in human HepG2 cells (Ha et al. 2010). All three compounds phosphorylated AMPK (AMP-activated protein kinase), resulting in increased phosphorylation of GSK-3β and suppression of lipogenic expression (ACC and FAS) in a dose-dependent manner. The compounds also demonstrated strong eNOS phosphorylation in human umbilical vein endothelial cells (HUVECs). Compounds paeonol, paeonolide, paeoniflorigenone, 6-methoxy paeonigenone, paeoniflorin, benzoylpaeoniflorin, galloylpaeoniflorin, 5-hydroxy-3*S*-hydroxymethyl-6-methyl-2,3-dihydrobenzofuran, 8-*O*-benzoylpaeoniflorin and 4-*O*-butylpaeoni florin and mudanpioside H also exhibited considerable effects on hepatic glucose production, AMPK activation and phosphorylation of GSK-3β gene in HepG2 cells under high glucose conditions. These effects indicated that the activation of AMPK by bioactive compounds from Moutan Cortex had considerable potential for reversing the metabolic abnormalities associated with type 2 diabetes. In an in vitro assay with RAW 264.7 cells, oxo-acetic acid 2-ethoxy-4-(3-hydroxy-2-oxopropyl) phenyl ester isolated from the roots was shown to be an inhibitor of IL-1β with an IC_{50} value of 56 μM (Choi et al. 2012b). The compound was shown to inhibit the production of proinflammatory cytokines and may have potential for the treatment of rheumatoid arthritis.

In vitro studies found that *cis*-ampelopsin E, isolated from *Paeonia suffruticosa* seeds, dose-dependently reduced the nitric oxide (NO) production from lipopolysaccharide (LPS)-stimulated RAW 264.7 cells (Cai and Cai 2011). By inhibiting LPS-induced inhibitor kinase (IKKα/β) phosphorylation, *cis*-ampelopsin E significantly decreased LPS-induced IκBα phosphorylation, prevented IκBα degradation and subsequently reduced the translocation of transcription factor p65 into the nucleus; thus, LPS-induced up-regulation of NF-κB transcriptional activity was efficiently inhibited. In addition, *cis*-ampelopsin E inhibited LPS-induced cyclooxygenase-2 (COX-2) expression, cPLA2 activation and prostaglandin E2 (PGE2) production. The results suggested that *cis*-ampelopsin E might exert potential anti-inflammatory effects via obstruction of the NF-κB signalling pathway.

JCICM-6, an antiarthritic herbal extract, composed *of Sinomenium acutum*, *Aconitum carmichaelii*, *Curcuma longa*, *Paeonia lactiflora* and *Paeonia suffruticosa* medicinal herbs, was found to be effective in reducing experimentally induced inflammation and nociception using nine animal models (Zhou et al. 2006). JCICM-6 orally administered in a range of dosages from 0.438 to 1.75 g/kg significantly and dose-dependently suppressed the paw oedema of rats induced by carrageenan or various proinflammatory mediators including histamine, serotonin, bradykinin and prostaglandin E(2) (PGE(2)) and the ear oedema of mice induced by arachidonic acid or 12-*O*-tetradecanoylphorbol 13-acetate. JCICM-6 also significantly prolonged the reaction time of rats to radiant heat stimulation and reduced the numbers of writhing episodes of

mice. The results indicated that JCICM-6 possessed significant anti-inflammatory and analgesic effects and could be a potential candidate for further investigation as a new antiarthritic botanical drug for humans. Wu and Gu (2009) found that Moutan Cortex exhibited anti-inflammatory activity as evidenced by its decrease of IL-6 production in IL-1β-stimulated synoviocytes. Its active constituents paeonol, paeoniflorin, glycosides and pentagalloylglucose were found to contribute to its anti-inflammatory effect.

Animal studies showed that administration of guizhi-fuling capsules (GZFLC), a traditional Chinese medical (Kampo) formulation composed of five medicinal plants, *Cinnamomum cassia* (cinnamomi cortex), *Paeonia lactiflora* (peony radix), *Paeonia suffruticosa* (Moutan Cortex), *Prunus persica* (persicae semen) and *Poria cocos* (Hoelen), after focal cerebral ischaemia significantly decreased brain infarction and water contents in rats subjected to 2-h ischaemia followed by 24-h reperfusion (Li et al. 2007). Further GZFLC treatment significantly downregulated expressions of proinflammatory cytokines including interleukin (IL)-1beta and tissue necrosis factor-alpha and markedly up-regulated expressions of anti-inflammatory cytokines IL-10 and IL-10R both in mRNA and protein levels. The serum levels of these inflammatory cytokines were also similarly regulated.

Antianaphylactic Activity

Results of studies suggested that paeonol from moutan root cortex exhibited antianaphylactic activity by regulating histamine and TNF-alpha (Kim et al. 2004b). Paeonol significantly inhibited histamine release from the rat peritoneal mast cells treated with compound 48/80, a mast cell degranulator, and also inhibited IgE production in B cells activated by anti-CD40 mAb, recombinant interleukin-4 (rIL-4) and recombinant histamine-releasing factor (rHRF). Paeonol effectively downregulated the expression of IL-4 in the activated B cells by reverse transcription polymerase chain reaction. Further, paeonol effectively inhibited anaphylactic shock in mice by 90 % at a dose of 0.5 mg/mouse 2 h after the i.p. injection of compound 48/80.

Anti-osteoporotic Activity

The Korean herbal medicine Yukmi-jihang-tang (YJ), composed of seven herbs such as *Rehmannia glutinosa*, *Dioscorea japonica*, *Cornus officinalis*, *Smilax glabra*, *Paeonia suffruticosa*, *Alisma plantago-aquatica* var. *orientale* and *Hominis placenta*, was found to have antibone resorption properties (Jin et al. 2006). The herbal medicine (100 μg/mL), transforming growth factor beta (TGF-β) and their combinations reduced cyclooxygenase-2 (COX-2) mRNA level, prostaglandin E2 (PGE2) biosynthesis and bone resorption induced by IL-1beta, IL-6 tumour necrosis factor-alpha (TNF-alpha) or their combination. The herbal mixture also inhibited in vitro and in vivo bone resorption by inhibition of phosphorylation of peptide substrates. The parathyroid hormone-induced bone resorption in mouse fetal long bone cultures was inhibited with an IC_{50} of 16 μg/mL. The herbal mixture dose-dependently reduced the hypercalcaemia induced in mice by IL-1beta and partly prevented bone loss and microarchitectural changes in young ovariectomized rats, showing that the protective effect on bone was exerted via the inhibition of bone resorption. The results indicate the herbal mixture as a possible Src family kinase inhibitor which may be useful for the treatment of diseases associated with elevated bone loss.

Antidiabetic Activity

Moutan radicis cortex was found to have hypoglycaemic effect in α-glucoamylase-suppressing actions in 3T3-L1 adipocytes (Park et al. 2004).

After 4 weeks oral administration of herb extracts, *Rhus verniciflua*, *Agrimonia pilosa*, *Sophora japonica* and *Paeonia suffruticosa*, lowered blood glucose levels and thiobarbituric acid-reactive substances (TBARS) in streptozotocin-induced diabetic rats (Jung et al. 2006). *Sophora japonica* and *Paeonia suffruticosa* extracts

significantly reduced TBARS levels versus diabetic controls. Moutan Cortex (root bark of *Paeonia suffruticosa*) showed significant in vitro antidiabetic effects by inhibiting glucose uptake of intestinal brush border membrane vesicles (BBMV) and enhancing glucose uptake into human skin fibroblast cell line Hs68 and mouse adipocyte 3T3-L1 cells (Lau et al. 2007). Paeonol was confirmed to be one of the active constituents for inhibiting BBMV glucose uptake. With neonatal streptozotocin diabetic rats, paeonol (200 and 400 mg/kg body wt.) was found to improve oral glucose tolerance in vivo.

Triterpenes, namely, palbinone, ursolic acid, betulinic acid, β-sitosterol, daucosterol, oleanolic acid and 30-norhederagenin, isolated from Moutan Cortex, remarkably stimulated AMP-activated protein kinase (AMPK), GSK-3beta and acetyl-CoA carboxylase *(*ACC*)* phosphorylation in HepG2 cells under high glucose conditions (Ha et al. 2009b). The compounds also increased glucose uptake and enhanced glycogen synthesis. Among these, palbinone displayed the greatest potential antidiabetic activity through the AMPK activation pathway. Palbinone significantly increased the levels of phospho-AMPK, phospho-ACC and phospho-GSK-3beta and stimulated glucose uptake and glycogen synthesis in a dose-dependent fashion. Their results suggested that these compounds, especially palbinone, may have beneficial roles in glucose metabolism via the AMPK pathway. Of the compounds isolated from the methanol extract of Moutan Cortex, two triterpenes showed the most potent inhibitory activity against rat lens aldose reductase, with IC_{50} values of 11.4 and 28.8 μM, respectively; compound 4-*O*-butylpaeoniflorin had an IC_{50} value of 36.2 μM, and the positive control, 3,3-tetramethyleneglutamic acid, had an IC_{50} value of 31.8 μM (Ha et al. 2009a). Compound 4-*O*-butylpaeoniflorin inhibited advanced glycation end product formation with an IC_{50} value of 10.8 μM, and 5-hydroxy-3S-hydroxymethyl-6-methyl-2,3-dihydrobenzofuran had an IC_{50} value of 177.0 μM, whereas the positive control, aminoguanidine, had an IC_{50} value of 1,026.8 μM.

Of the 16 compounds, isolated from Moutan Cortex evaluated on glucose metabolism in HepG2 cells under high glucose conditions, compounds paeonoside, apiopaeonoside 2,3 and 6-methoxypaeonigenone displayed highly potent effects on the stimulation of glucose uptake and glycogen synthesis in human HepG2 cells (Ha et al. 2010). All three compounds phosphorylated AMPK (AMP-activated protein kinase), resulting in increased phosphorylation of GSK-3 and suppression of lipogenic expression (ACC and FAS) in a dose-dependent manner. The compounds also demonstrated strong eNOS phosphorylation in human umbilical vein endothelial cells (HUVECs). Compounds paeonol, paeonolide, paeoniflorigenone, 6-methoxypaeonigenone, paeoniflorin, benzoylpaeoniflorin, galloylpaeoniflorin, 5-hydroxy-3S-hydroxymethyl-6-methyl-2,3-dihydrobenzofuran, 8-*O*-benzoylpaeoniflorin and 4-*O*-butylpaeoniflorin and mudanpioside H also exhibited considerable effects on hepatic glucose production, AMPK activation and phosphorylation of GSK-3 gene in HepG2 cells under high glucose conditions. These effects indicated that the activation of AMPK by bioactive compounds from Moutan Cortex had considerable potential for reversing the metabolic abnormalities associated with type 2 diabetes.

Antiatherosclerotic Activity

Paeonol, from *P. lactiflora*, concentration dependently inhibited the production of intercellular adhesion molecule-1 (ICAM-1) in tumour necrosis factor-alpha (TNF-alpha)-activated human umbilical vein endothelial cells (HUVECs) (Nizamutdinova et al. 2007). They found that the inhibitory effect of paeonol on ICAM-1 production might be mediated by inhibiting the TNF-alpha-induced phosphorylation of p38 and extracellular signal-regulated kinase (ERK) and nuclear factor-kappa B (NF-kappa B) p65 signalling pathways, which were involved in TNF-alpha-induced ICAM-1 production. Thus, paeonol may be beneficial in the treatment of cardiovascular disorders such as atherosclerosis. Paeonol, active constituent of Moutan Cortex, attenuated high-fat-induced atherosclerosis in rabbits by its anti-inflammatory

activity (Li et al. 2009b). Histological analysis showed significant improvement in atherosclerosis plaque in the paeonol-treated rabbits. Further, the blood levels of TNF-alpha, IL-1beta and CRP and the translocation of NF-kappa B to the nucleus were significantly suppressed in paeonol groups, as was the inhibition of lipid peroxidation.

Anticataract Activity

Hachimi-jio-gan, a herbal medicine containing 8 herbs including Moutan Cortex, exhibited strong inhibitory activity on aldose reductase activity (Shimizu et al. 1993). Fractionation of Hachimi-jio-gan led to the isolation of 5-(hydroxymethyl)-2-furfuraldehyde and ellagic acid which had been reported to be a strong aldose reductase inhibitor. Studies showed that polysaccharides-2b from mudan cortex extract exhibited protective effect on diabetic cataract in rats induced by streptozotocin and Freund's complete adjuvant (Zhao et al. 2007). The extract significantly delayed the occurrence and alleviated the opacity degree of the lens. Also, treatment with the extract reduced the elevated malondialdehyde level and increased the levels of superoxide dismutase, glutathione peroxidase and catalase in serum and lens and promoted Na^+–K^+ -ATPase activity.

Neuroprotective Activity

Studies showed that exposure of Neuro-2A cells to 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG), a major component of *P. suffruticosa* root (10–50 μM), resulted in a concentration- and time-dependent induction of neuronal heme oxygenase-1 mRNA and protein expressions and heme oxygenase activity (Choi et al. 2002). Also, pretreatment of the neuronal cells with PGG resulted in enhanced cellular resistance to hydrogen peroxide. Results suggested that PGG could protect neuronal cells from oxidative stress via the induction of heme oxygenase-1 gene expression. Studies showed that paeonol 15 and 20 mg/kg pretreatment and 20 mg posttreatment reduced the cerebral infarction area; paeonol 15 and 20 mg/kg pretreatment reduced the neuro-deficit score in rats with cerebral infarct (Hsieh et al. 2006). Additionally, paeonol 20 mg/kg pretreatment reduced the lucigenin CL counts at 2 h period of reperfusion. Paeonol suppressed and scavenged superoxide anion and inhibited microglial activation and IL-1beta in ischaemia–reperfusion injured rats. In vitro studies showed that paeonol protect against oxidative-related injury in human neuroblastoma SH-SY5Y cells by downregulating H_2O_2-induced NF-κB activity, as well as NF-κB-associated amyloid precursor protein expression (Su et al. 2010). Further, they found that paeonol protected rats from memory loss after ischaemic stroke by reducing levels of amyloid precursor protein (APP)- and beta-site APP cleaving enzyme (BACE; β-secretase)-immunoreactive cells and terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labelling (TUNEL)-positive cells and via apoptosis (Su et al. 2012).

Studies showed that paeonol significantly improved the learning and memory ability in Morris water maze test and step-down passive avoidance test in D-galactose-treated ICR mice (Zhong et al. 2009). Paeonol increased acetylcholine and glutathione levels, restored superoxide dismutase and Na^+, K^+-adenosine triphos phatase ((Na^+, K^+)ATPase) activities but decreased cholinesterase activity and malondialdehyde level in D-galactose-treated mice. Also, paeonol ameliorated neuronal damage in both hippocampus and temporal cortex in D-galactose-treated mice. The results suggested that paeonol possessed anti-aging efficacy and may have potential in treatment of neurodegenerative diseases. Chronic supplementation of paeonol combined with danshensu was found to improve vascular reactivity in the cerebral basilar artery of diabetic rats (Hu et al. 2012). The combination of paeonol and danshensu elicited significant protective effects against diabetes-induced vascular damage through the reduction of oxidative stress and through intracellular Ca^{2+} regulatory mechanisms.

Studies showed that paeonol, active compound from *P. suffruticosa* root bark, ameliorated pathological damage of diabetic encephalopathy streptozotocin-induced diabetic rats via modulation of serum advanced glycation end products (AGEs), receptor for advanced glycation end products (RAGE) and nuclear factor-kappa B (NF-κB) pathways in hippocampus and cerebral cortical neurons (Liu et al. 2013). The results suggested that paeonol might be a promising candidate for the prevention and treatment of diabetic encephalopathy.

Central Nervous System Activity

Both intraperitoneal and oral administration of paeonol to mice afforded the following results (Harada and Yamashita 1969): acute toxicity was low. Sedation (decrease of spontaneous motor activity and caffeine-induced hyperactivity) and hypnosis (loss of righting reflex) were observed, the latter in higher intraperitoneal doses. Hexobarbital-induced anaesthesia was prolonged. Analgesic activity was found in both the inhibition of writhing symptom induced with intraperitoneal administration of acetic acid and mouse tail pain by pressing. Hypothermia and antipyretic activity in typhoid–paratyphoid vaccine-febrile mouse were found. Anticonvulsive effect on maximal electroshock was obtained and the same effect was also obtained on pentetrazol- and nicotine-induced convulsions. Thus, it was found that paeonol exhibited many central depressive effects and may be associated with some parts of the therapeutic effects of peony bark cortex in oriental medicine.

Results of studies suggested that both *Paeonia suffruticosa* and its active constituent PGG exerted potent inhibitory effects on the formation of Abeta fibrils in vitro and in vivo (Fujiwara et al. 2009). *P. suffruticosa* not only inhibited fibril formation of both Abeta(1–40) and Abeta(1–42), but it also destabilized preformed Abeta fibrils in a concentration-dependent manner and improved long-term memory impairment in the transgenic mice and inhibited the accumulation of Abeta in the brain. Thus, PGG may be a promising lead compound in the development of disease-modifying drugs to prevent and/or cure Alzheimer's disease. In another study, paeonol treatment of Alzheimer's diseased Sprague-Dawley rats induced by intrahippocampal injection of amyloid peptide Aβ1-42 increased levels of cortical cytochrome oxidase and vascular actin, reduced number of lesions and apoptotic cells in the walls of the cerebral vascular elements and improved behavioural indices of learning (Zhou et al. 2011). Treatment with paeonol was found to protect against many of the morphological, biochemical and behavioural alterations resulting from administration of Aβ1-42 in a rat model of AD. The results suggested that paeonol may be a possible therapeutic measure in slowing down the pathogenic processes associated with AD.

Nephroprotective Activity

Seven herbal plant extracts evaluated including *Paeonia suffruticosa* root cortex had a strong recovery effect on cisplatin-induced nephrotoxic damage in HEK 293 cells (Sohn et al. 2009b). It was found that 1 μg/mL *P. suffruticosa* treatment showed greater than 20 % recovery of 14 μM cisplatin-induced 50 % loss of cell proliferation (IC_{50}) as determined by mitochondrial activity MTS assay in HEK 293 cells. Further studies using the microarray analysis and real-time RT-PCR revealed that DNA repair- and cell proliferation-related genes were up-regulated in *Paeonia* root extract-treated HEK 293 cells (Sohn et al. 2009a). The mechanism responsible was closely associated with the regulation of DNA repair and cell proliferation. The results suggested that *P. suffruticosa* possessed novel therapeutic potential that could be used for the prevention or treatment of cisplatin-induced nephrotoxicity. Animal studies showed that mice pretreated with paeonol 4 days before intraperitoneal administration of cisplatin showed marked attenuation of serum creatine and blood urea nitrogen levels as well as reduced levels of proinflammatory cytokines

and nitric oxide when compared to the control group (Lee et al. 2013). Further, the paeonol-treated group showed prolonged survival and marked attenuation of renal tissue injury. The results demonstrated that paeonol could prevent the renal toxic effects of cisplatin.

Two major compounds in *P. suffruticosa*, paeoniflorin and oxypaeoniflora, exhibited protective effect on advanced glycation end product (AGE)-induced oxidative stress and inflammation in mesangial cells HBZY-1 (Zhang et al. 2013). The IC_{50} values of paeoniflorin and oxypaeoniflora for inhibiting 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid) formation were 4.197×10^{-4} M and 1.002×10^{-4} M, respectively. The pretreatment with paeoniflorin and oxypaeoniflora significantly increased advanced glycation end product-induced glutathione peroxidase and catalase activities. In the coculture system of HBZY-1 and macrophages, paeoniflorin and oxypaeoniflora could inhibit remarkably the migration of macrophages. Additionally, paeoniflorin and oxypaeoniflora attenuated markedly advanced glycation end product-induced inflammation cytokines interleukin-6 and monocyte chemoattractant protein-1 levels in a dose-dependent manner. The results indicated that paeoniflorin and oxypaeoniflora were able to attenuate advanced glycation end product-induced oxidative damage and inflammation in mesangial cells and might therefore have a beneficial effect in the treatment of diabetic nephropathy.

Hepatoprotective Activity

Moutan Cortex extract exhibited dose-dependent protective effect acetaminophen-induced cytotoxicity in human Chang liver cells (Shon and Nam 2002). Moutan Cortex exerted dose-dependent increases in MTT metabolism, glutathione and ATP and DNA levels in acetamino phen-treated cells and counteracted the inhibition of mitochondrial function caused by acetaminophen. Pretreatment of ICR mice with Moutan Cortex prior to acetaminophen administration prevented liver injury as indicated by the decrease of serum alanine aminotransferase level (Shon and Nam 2004). Moutan Cortex also protected acetaminophen-induced hepatic glutathione depletion. Cytochrome P450 2E1-dependent aniline and *p*-nitrophenol hydroxylase activities in microsomal incubations were significantly inhibited by Moutan Cortex.

Animal studies showed that administration of Moutan Cortex radicis had a protective effect on acute liver injury induced by carbon tetrachloride, D-galactosamine and α-naphthylisothio cyanate (Park et al. 2011). Enhanced aminotransferase, multiple and extensive areas of portal inflammation, hepatocellular necrosis and an increase in inflammatory cell infiltration were all attenuated by Moutan Cortex. The increase in serum total bilirubin concentration and the significant decrease in bile flow 48 h after α-naphthylisothiocyanate treatment, were also rectified by Moutan Cortex.

Studies by Ha et al. (2014) found that palbinone from *Paeonia suffruticosa* protected hepatic cells by up-regulation of heme oxygenase-1 via activation of Nrf2 and may involve PI3K/Akt and ERK1/2 pathways.

Antiplatelet Aggregating Activity

Extracts of the xylem of moutan root containing such monoterpene glucosides such as paeoniflorin, oxypaeoniflorin, benzoylpaeoniflorin and benzoyloxypaeoniflorin were found to possess inhibitory effects on blood platelet aggregation, plasminogen and plasmin activities like Moutan Cortex extracts (Tani et al. 1980b). One-week oral administration of water extract of Moutan Cortex (3 g/day) significantly reduced platelet aggregation and thromboxane B2 (TXB2) formation induced by collagen, epinephrine and ADP (Hirai et al. 1983). Paeonol, its major constituent, dose-dependently inhibited ADP and collagen-induced platelet aggregation in vitro. Moutan Cortex and paeonol dose-dependently inhibited the conversion of exogenous [14C] arachidonic acid to [14C]heptadecatetraenoic acid and [14C] thromboxane B2 by washed human platelets,

while both of them increased its conversion to [14C]12-hydroxyeicosatetraenoic acid. The results suggested that a reduction in platelet aggregation by the oral administration of Moutan Cortex might be ascribed to a decrease in thromboxane synthesis and that paeonol might play an important role in the antiaggregatory effect of Moutan Cortex because of its potent inhibitory effect on platelet aggregation and thromboxane formation.

Paeonol was found to regulate blood rheology like aspirin by its antiaggregating activity and to improve blood flow in rats (Li et al. 2000). Of the 18 compounds, isolated from the dry roots of *Paeonia lactiflora* (Radix Paeoniae) and dry root bark of *P. suffruticosa* (Moutan Cortex), paeonol, paeoniflorin, benzoylpaeoniflorin and benzoyloxypaeoniflorin were found to be the major common active constituents that would collectively contribute to improving blood circulation through their inhibitory effects on both platelet aggregation and blood coagulation (Koo et al. 2010). Additionally, methyl gallate, (+)-catechin, paeoniflorigenone, galloylpaeoniflorin and daucosterol may also take part in improving blood circulation by inhibiting either platelet aggregation or blood coagulation.

Antityrosinase/Skin Whitening Activity

Six mushroom tyrosinase inhibitors isolated from *Paeonia suffruticosa* root were identified as kaempferol, quercetin, mudanpioside B, benzoyloxypaeoniflorin, mudanpioside H and pentagalloyl-β-(D)-glucose with IC_{50} values of 0.120, 0.108, 0.368, 0.453, 0.324 and 0.063 mM, respectively (Ding et al. 2009). *Paeonia suffruticosa* pretreatment suppressed sunburn cell formation in the three-dimensional skin model and erythema formation and pigmentation in volunteers exposed to UVB irradiation (Kurata et al. 2010). Up-regulation of CXCR3 and its ligands, CXCL9/monokine induced by interferon (IFN)-γ (MIG), CXCL10/10-kDa IFN-γ-induced protein (IP-10) and CXCL11/inducible T-cell α-chemoattractant (I-TAC) after UVB irradiation was partially suppressed by *P. suffruticosa* pretreatment. Melanin biosynthesis increased upon stimulation of CXCR3 ligands (MIG, IP-10 or I-TAC) and decreased following CXCR3 downregulation by shRNA knockdown. *P. suffruticosa* pretreatment showed a lightening effect partly by attenuating CXCR3-mediated signalling at the transcriptional level.

The antioxidant EC_{50} values of eight *Paeonia suffruticosa* extracts Ps-1–8 were 10.0, 9.8, 63.6, >100, 3.8, 85.1, 6.9 and 0.7 μg/mL for (DPPH·) radical scavenging efficiency and 22.9, 11.4, 53.1, >100, 7.5, 97.6, 43.7 and 4.2 μg/mL for 2,2′-azinobis(3-ethylbenzothiazoline-6-sulphonic acid) diammonium salt (ABTS·(+)) radical scavenging capacity, respectively (Ding et al. 2011). The high free radical scavenging capacity, ion chelating ability, reducing power and inhibition of lipid peroxidation exhibited by Ps-8 may be attributable to its abundant phenolic and flavonoid content. In human skin fibroblast Hs68 and mice melanoma B16 cells treated with 100 μg/mL Ps-1, Ps-3, Ps-4 and Ps-6, expressions of toxic activities were lower than those in cells treated with arbutin and ascorbic acid. The antimelanogenesis properties were also tested in B16 cells. Extract Ps-1, and particularly extract Ps-6, considerably inhibited cellular tyrosinase and 3,4-dihydroxyphenylalanine (DOPA) oxidase activity and also reduced melanin content in B16 cells by down-expression of melanocortin-1 receptor (MC1R), microphthalmia-associated transcription factor (MITF), tyrosinase and tyrosinase-related protein-1 (TRP-1). The results suggested *P. suffruticosa* extracts had antioxidant and antimelanogenesis activities with potential applications in cosmetic materials or food additives.

trans-Caffeic acid stearyl ester (TCASE), from *Paeonia suffruticosa* roots, markedly and dose-dependently inhibited melanin synthesis and reduced intracellular cyclic adenosine monophosphate (cAMP) levels, tyrosinase activity and L-3-(3,4-dihydroxyphenyl)-alanine (DOPA) oxidase activity in the presence of α-melanocyte-stimulating hormone (α-MSH) in murine melanoma B16 cells, and the inhibition

efficiency of TCASE exceeds that of ascorbic acid and arbutin (Liang et al. 2012). TCASE reduced melanocortin-1 receptor (MC1R), microphthalmia transcription factor (MITF), tyrosinase, tyrosinase-related protein-2 (TRP-2) and TRP-1 mRNA and protein levels in murine melanoma B16 cells. In the cell viability assay, TCASE did not show a cytotoxic effect at a dose of 65 μM for 48 h in murine B16, human premalignant keratinocytic, HaCaT and human skin fibroblast, Hs68 cells.

Vasodilatory Activity

PGG (1,2,3,4,6-penta-*O*-galloyl-β-D-glucose) isolated from root bark induced a concentration-dependent relaxation of the phenylephrine-precontracted rat aorta (Kang et al. 2005). It was found that PGG dilated vascular smooth muscle and suppressed the vascular inflammatory process via endothelium-dependent nitric oxide (NO)/cGMP signalling. Recent studies showed that paeonol from *P. suffruticosa* root bark relaxed isolated rat aorta rings by 95.6 %, and the EC_{50} of vasodilatation by paeonol was 2.9×10^{-4} M (Li et al. 2010). Although paeonol exerted endothelium-independent relaxation, L-NAME (NG-nitro-L-arginine methyl ester) treatment inhibited paeonol-induced vasodilation of endothelium intact rings, while indomethacin did not. Both L-NAME and ODQ (1H-[1,2,4] oxadiazolo[4,3-a]quinoxalin-1-one) did not affect paeonol relaxation in the rings without endothelium. Paeonol markedly blocked vasoconstriction induced by angiotensin II, prostaglandin F2 alpha *(*PGF2 alpha), 5-hydroxytryp tamine, dopamine, vasopressin, endothelin-1 and pre-eclampsia in pretreated aortic rings (without endothelium). In addition, paeonol markedly elevated NO generation in cultured endothelial cells. The study also found that voltage-dependent and receptor-operated Ca^{2+} channel and intracellular Ca^{2+} release were all inhibited by paeonol, thus indicating intracellular Ca^{2+} regulatory mechanism may be responsible for the potent vasodilatory effect of paeonol.

Diuretic Activity

Paeonol at the doses of 62.5–250 mg/kg p.o. produced dose-dependent increases in urinary water, sodium and chloride and osmolality in bicarbonate saline-loaded rats (Kawashima et al. 1985). Urinary potassium was unchanged at the lower doses and decreased at the highest dose. The lowest effective dose of paeonol in diuretic action was 62.5 mg/kg. The highest dose of paeonol produced the same degree of increase in urine as hydrochlorothiazide (HTZ) (10 mg/kg), while the increases in electrolyte excretion by HTZ were significantly greater than by paeonol. The data demonstrated that paeonol has a diuretic action.

Anti-allergic Activity

Moutan Cortex radicis treatment suppressed eotaxin secretion from A549 epithelial cells via the inhibition of NF-kappa B activation, indicating that it may have therapeutic value in treating asthma (Kim et al. 2007). Eotaxin is a potent eosinophil-specific chemokine that is released in the respiratory epithelium after allergic stimulation. PentaHerbs formula (PHF) containing Moutan Cortex, and four other herbs, and its herbal components, i.e. Moutan Cortex and *Mentha haplocalyx*, significantly attenuated histamine release and prostaglandin D(2) synthesis from rat peritoneal mast cells (RPMCs) activated by anti-IgE and compound 48/80 (Chan et al. 2008). Also, with the exception of Moutan Cortex, PHF and the other four component herbs failed to affect cytokine production in HMC-1. PHF was reported to be useful in the management of atopic eczema.

The ethanol Moutan Cortex extract (200 mg/kg) significantly inhibited the passive cutaneous anaphylactic reaction in vivo and suppressed the release of histamine from rat peritoneal mast cells induced by compound 48/80 (Hong et al. 2010). The anti-allergic inflammation of Moutan Cortex extract was found to be associated with its inhibition of the NF-kappa B/IkappaBalpha signalling pathway and the phosphorylation of

extracellular signal-regulated kinase (ERK). Moutan Cortex extract also decreased the expressions of TNF-alpha and IL-6 in PMA- and A23187-stimulated human mast HMC-1 cells.

Antiobesity Activity

Results of animal studies indicated that tree peony could protect against obesity, especially in male (SLN×C3H/He) F1 obese mice, at least partly by a decrease in food intake and index of obesity and an increase in glucose metabolism (Nagasawa et al. 1991). *Paeonia suffruticosa* was one of several plants successfully identified for the treatment of obesity (Vasudeva et al. 2012).

Wound Healing Activity

Moutan Cortex extract significantly increased cell viability of human HaCaT keratinocyte and human primary dermal fibroblasts (pNHDF) in a dose-dependent way (Wang et al. 2013). Its proanthocyanidin-containing fractions as well as 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (PGG)-containing fractions contributed substantially to the skin cell-stimulating effects. PGG-containing fractions enhanced cell viability and cellular proliferation of HaCaT keratinocytes at a concentration of 100 nM.

Xerostomia Protective Activity

Herbal extracts from the root barks of *Juncus effusus* and *Paeonia suffruticosa* were found to have therapeutic effects on xerostomia (dry mouth), a serious side effect caused by *cis*-platinum (II) diammine dichloride (CDDP), a platinum-based anticancer agent (Mukudai et al. 2013). Both extracts exhibited protective effect in human salivary gland acinar NS-SV-AC cells from the cytotoxicity and apoptosis caused by CDDP. The effect was dependent on the p53 pathway, protein kinase B/Akt 1 and mitochondrial apoptosis-related proteins (i.e. Bcl-2 and Bax).

Pharmacokinetic Studies

Paeonol showed greater permeation from artificial gastric juice into artificial plasma when it was applied as a decoction or freeze-dried extract of Moutan Cortex than when applied as purified paeonol alone in in-vitro studies using an absorption simulator (Tani et al. 1987).

Six metabolites were isolated from human urine after oral administration of paeonol, and their structures were elucidated as resacetophenone,resacetophenone-2-*O*-sulphate,2-hydroxy-4-methoxyacetophenone-5-*O*-sulphate, 2-hydroxy-4-methoxyacetophenone-5-*O*-glucopyranuronoside, 2-hydroxyacetophenone-4-*O*-glucopyranuronoside and 2,5-dihydroxy-4-meth oxyacetophenone (Ding et al. 2012b). In addition, three more metabolites, 2,4-dihydroxyacetophenone-5-*O*-sulphate, paeonol-2-*O*-gluco pyranuronoside and paeonol-2-O-sulphate, were also identified in human urine.

Herb–Drug Interaction Studies

Mu Dan Pi (*Paeonia suffruticosa*) was found to have remarkable inhibiting effects on the metabolism of CYP3A4 in metabolism-based herb–drug interactions in human liver microsomes and in rats (Pao et al. 2012). In rats, Mu Dan Pi greatly increased the C(max) and AUC of midazolam indicating herb–drug interactions.

Acaricidal Activity

Paeonia suffruticosa var. *papaveracea* was found to have 2′-hydroxy-4′-methoxyacetophenone (paeonol) as an insecticidal ingredient in the root (Xu et al. 2003). Paeonia root bark-derived materials, particularly paeonol and benzoic acid, exhibited acaricidal activity against adults of house dust mites, *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* (Kim et al. 2004a). On the basis of 24 h LD_{50} values, the acaricidal activities of paeonol (7.82 μg/cm^3) and benzoic acid (6.58 μg/cm^3) against adult

D. farinae were comparable to that of benzyl benzoate (7.72 μg/cm^3) but higher than those of DEET (36.34 μg/cm^3) and dibutyl phthalate (33.92 μg/cm^3). Against adult *D. pteronyssinus*, the acaricidal activities of paeonol (7.08 μg/cm^3) and benzyl benzoate (7.22 μg/cm^3) were comparable to that of benzyl benzoate (7.14 μg/cm^3). Paeonol and benzoic acid were much more effective in closed containers than open ones, indicating that the effect of these compounds was largely a result of action in the vapour phase. Neither benzyl benzoate, DEET nor dibutyl phthalate exhibited fumigant toxicity.

The acaricidal activities of paeonol (2′-hydroxy-4′-methoxyacetophenone) and benzoic acid from tree peony exhibited acaricidal activity against copra mite, *Tyrophagus putrescentiae* adults (Tak et al. 2006). Based on LD_{50} values in fabric-piece contact toxicity bioassays, the acaricidal activities of benzoic acid (4.80 μg/cm^{-2}) and paeonol (5.29 μg/cm^{-2}) were comparable to that of benzyl benzoate (4.46 μg/cm^{-2}) but more pronounced than those of DEET (N,N-diethyl-m-toluamide) (30.03 μg/cm^{-2}) and dibutyl phthalate (25.23 μg/cm^{-2}). In vapour-phase toxicity bioassays, paeonol and benzoic acid were much more effective in closed containers than in open ones, indicating that the effects of these compounds were largely due to action in the vapour phase. Potent fumigant toxicity was also observed.

Reproductive Hormonal Activity

Long-term (14 days) daily oral administration of 300 mg/kg of Keishi-bukuryo-gan (KBG), a traditional Chinese herbal remedy containing five components including root bark of *P. suffruticosa*, to immature rats was found to decrease plasma levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH) and estradiol (E2), by 94 %, 67 % and 50 %, respectively, compared to controls. Uterine wet weight and thymidine kinase activity were reduced to 65 % and 64 % that of controls, respectively (Sakamoto et al. 1988). Short-term simultaneous administration of KBG (three consecutive doses, every 12 h) with E2 reduced E2-induced increases in uterine wet weight and thymidine kinase activity by 29 % and 39 %, respectively. Treatment with KBG also enhanced luteinizing hormone-releasing hormone-induced increases in plasma LH and FSH levels 1.2- and 2.5-fold, respectively, as compared with controls. The results obtained in the study indicated that TJ-25 may act as a luteinizing hormone-releasing hormone antagonist and/or as a weak antioestrogen. In a subsequent study of 110 premenopausal patients with uterine myomas, clinical symptoms of hypermenorrhoea and dysmenorrhoea were improved in more than 90 % of the cases with shrinking of uterine myomas in roughly 60 % of the cases (Sakamoto et al. 1992).

Resveratrol and its oligomers from *P. suffruticosa* seeds were found to be active as ecdysteroid antagonists (ED_{50} values = 10 to 50 μM *vs.* 5×10^{-8} M 20-hydroxyecdysone) in the *Drosophila melanogaster* B_{II} bioassay (Sarker et al. 1999).

Antimutagenic Activity

Only the ether extract of Moutan Cortex (*P. suffruticosa*) showed a bio-antimutagenic effect by suppression of 4NQO (4-nitroquinoline 1-oxide)-induced mutation in *Escherichia coli* WP2s, but no decrease in 4NQO- or MNNG (N-methyl-N′-nitro-N-nitrosoguanidine)-induced mutation in *E. coli* WP2 was observed upon addition of the extract (Fukuhara and Yoshida 1987). Paeonol was found to be the bioactive component.

Mutagenic Activity

Paeonia suffruticosa extract was one of several plant extracts found to be mutagenic in the micronucleus and chromosomal aberration assays in mice (Yin et al. 1991).

Traditional Medicinal Uses

Since ancient times, *P. suffruticosa* root cortex (Moutan Cortex or ‘Mu Dan Pi’ or ‘Botanpi’) has been employed as an important crude drug in

Chinese medicine; its flowers have also been used medicinally. Moutan Cortex has been used in prescriptions for chronic inflammatory disease, which is considered to produce a state of stagnation of disordered blood, or 'ynxie', as expressed in Chinese medicine (Kubo et al. 1979; Miyazawa et al. 1983). Examples of such prescriptions are 'guizhi-fuling-wan and wen-jing-tang' for chronic female genital diseases; 'ba-wei-tang' for diseases of the aged, e.g., diabetes and arteriosclerosis; and dahuang-mudan-tang for appendicitis and carbuncles (Kubo et al. 1979). Moutan Cortex has been employed as an analgesic, sedative, anti-inflammatory and antipyretic agent and as a remedy for cardiovascular, extravasated blood, stagnated blood and female genital diseases (Chang and But 1986; Yoshikawa et al. 1992; Ding et al. 1999; Xu et al. 2006b; Fu et al. 2012), and one of the common herbs found in antidiabetic traditional Chinese medicine formulas (Lau et al. 2007) and employed for vitalizing blood circulation and alleviating liver and inflammatory diseases (Ha et al. 2014). Traditionally, Chinese used flowers and roots of tree peony for herbal medicine preparations as a remedy for women to cure irregular menstruation and dysmenorrhoea (Wang et al. 2005a; Li et al. 2009b). Additionally, flower extracts have been used as an ingredient in skincare products to enhance skin flexibility, reduce pigment accumulation and prevent fleck formation (Voon et al. 2013).

In traditional Chinese medicine, 'mudan' has been used mainly as pills or in combination with 'guipi', i.e. bark of *Cinnamomum* species (Kubo et al. 1979). Keishi-bukuryo-gan (TJ-25, KBG) is a traditional Chinese herbal remedy containing five components: bark of *Cinnamomum cassia*, root of *Paeonia lactiflora*, seed of *Prunus persica* or *P. persiba* var. *davidiana*, carpophores of *Poria cocos* and root bark of *Paeonia suffruticosa* (Sakamoto et al. 1988). KBG is used in the treatment of gynaecological disorders such as hypermenorrhoea, dysmenorrhoea and infertility. Moutan Cortex (Botanpi) is one of the eight herbal constituents of Kampo medicine (Hachimi-jio-gan), an important Chinese medical prescription for senile cataracts and diabetic complications and diabetes (Shimizu et al. 1993). Danzhixiaoyao Wan, a common Chinese herbal formulation (comprising 10 herbs, 10 including *P. suffruticosa*), has been employed to regulate several clinical conditions affecting women (Liao et al. 2007).

Other Uses

P. suffruticosa is popularly planted as an ornamental and also as a medicinal plant.

Paeonol from *P. suffruticosa* exhibited inhibitory effects on phytopathogens *Xanthomonas oryzae* pv. *oryzicola*, *Pseudomonas solanacearum*, *Phyllosticta mali* and *Rhizoctonia solani* (Wu et al. 2003). Paeonol and sodium paeonol sulphonate had antibiotic effect on maize sheath blight.

Comments

Two subspecies have been recognized:

1. *P. suffruticosa* subsp. *suffruticosa* with double flowers, petals variously coloured, white, pink, red or red-purple
2. *P. suffruticosa* subsp. *yinpingmudan* with single flowers, petals white or pale red-purple

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Eschscholzia californica

Scientific Name

***Eschscholzia californica* Cham.**

Synonyms

Eschscholzia californica var. *douglasii* (Hook. & Arn. ex Torr. & A. Gray) Jeps., *Eschscholzia californica* var. *luxurians* Fedde, *Eschscholzia californica* var. *maritima* (Greene) Jeps., *Eschscholzia californica* var. *peninsularis* (Greene) Munz, *Eschscholzia californica* var. *stricta* (Greene) Jeps., *Eschscholzia calosperma* Greene, *Eschscholzia chartacea* Fedde, *Eschscholzia clevelandi* Greene, *Eschscholzia cognata* Greene, *Eschscholzia columbiana* Greene, *Eschscholzia compacta* (Lindl.) Walp., *Eschscholzia confinis* Greene, *Eschscholzia crocea* Benth., *Eschscholzia crocea* var. *apiifolia* Greene, *Eschscholzia crocea* var. *longissima* Greene, *Eschscholzia crocea* var. *sanctarum* (Greene) Fedde, *Eschscholzia cucullata* Greene, *Eschscholzia cyathifera* Greene, *Eschscholzia debilis* Greene, *Eschscholzia diversiloba* Greene, *Eschscholzia douglasii* (Hook. & Arn. ex Torr. & A. Gray) Walp., *Eschscholzia douglasii* Benth. (illeg.), *Eschscholzia douglasii* Hook. & Arn., *Eschscholzia eastwoodiae* Greene, *Eschscholzia floribunda* Greene, *Eschscholzia floribunda* var. *gorgonica* Greene, *Eschscholzia floribunda* var. *gracillima* Fedde, *Eschscholzia foeniculacea* Greene, *Eschscholzia glauca* Greene, *Eschscholzia granulata* Greene, *Eschscholzia granulata* var. *minuscula* Fedde, *Eschscholzia helleriana* Greene, *Eschscholzia helleriana* var. *tilingii* Fedde, *Eschscholzia inflata* Greene, *Eschscholzia isostigma* Greene, *Eschscholzia juncea* Greene, *Eschscholzia lacera* Greene, *Eschscholzia leptandra* Greene, *Eschscholzia leptomitra* Greene, *Eschscholzia leucosticta* Greene, *Eschscholzia marcida* Greene, *Eschscholzia marcida* var. *monticola* Greene, *Eschscholzia maritima* Greene, *Eschscholzia menziesiana* Greene, *Eschscholzia menziesiana* var. *anemophila* Greene, *Eschscholzia menziesiana* var. *coarctata* Fedde, *Eschscholzia menziesiana* var. *nesiaca* Fedde, *Eschscholzia menziesiana* var. *recedens* Greene, *Eschscholzia microloba* Greene, *Eschscholzia nitrophila* Greene, *Eschscholzia oregana* Greene, *Eschscholzia peninsularis* Greene, *Eschscholzia physodes* Greene, *Eschscholzia picta* Greene, *Eschscholzia pseudoinflata* Fedde, *Eschscholzia recta* Greene, *Eschscholzia revoluta* Greene, *Eschscholzia revoluta* var. *caudatocalyx* Fedde, *Eschscholzia rigida* Greene, *Eschscholzia robusta* Greene, *Eschscholzia rosea* auct., *Eschscholzia sanctarum* Greene, *Eschscholzia scariosa* Greene, *Eschscholzia scariosa* var. *dichasiophora* Fedde, *Eschscholzia setchellii* Fedde, *Eschscholzia shastensis* Greene, *Eschscholzia straminea* Greene, *Eschscholzia stricta* Greene, *Eschscholzia tenuisecta* Greene, *Eschscholzia thermophila* Greene, *Eschscholzia tristis* Fedde, *Eschscholzia vernalis* Greene, *Eschscholzia xylorrhiza* Greene, *Eschscholzia yainacensis*

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Greene, *Eschscholzia yainacensis* var. *modocensis* Fedde, *Omonoia californica* Raf.

Common/English Names

California Golden Poppy, California Poppy, California Sunlight, Cup Of Gold, Golden Poppy, Gold Poppy, Golden Cup, Mexican Gold, Mexican Gold Poppy, Western Poppy

Vernacular Names

Chile: Dedal De Oro, Hierba Del Ferrocarril
Chinese: Hua Ling Cao
Czech: Sluncovka Kalifornská
Danish: Californisk Guldvalmue, Guld-Valmue, Kalifornisk Guldvalmue, Kalifornisk Valmue
Dutch: Knipmutsje, Slaapmutsje
Estonian: Kalifornia Läänemagun
Finnish: Kaliforniantuliunikko, Tuliunikko
French: Eschscholzie De Californie, Globe Du Soleil, Pavot De Californie, Pavot Jaune De Californie
German: Eschscholzie, Goldmohn, Kalifornischer Goldmohn, Kalifornischer Kappenmohn, Kalifornischer Mohn, Schlafmützchen
Hungarian: Kakukkmák, Kaliforniai Mák
India: Videshiposta
Norwegian: Californiavalmue, Kaliforniavalmue
Polish: Eszolcja, Maczek Kalifornijski, Pozłotka, Pozłotka Kalifornijska
Portuguese: Papoila-Da-Califórnia
Slovaščina: Zlati Kalifornijski Mak
Spanish: Amapola Amarilla, Amapolla, Amapola De California, Amapola De Los Indios, Copa De Oro
Swedish: Sömntuta

Origin/Distribution

The species is native to the United States (i.e. Oregon, Washington, New Mexico, Texas, Arizona, California, Nevada and Utah) and northern Mexico.

Agroecology

Californian poppy survives mild winters in its native range, dying completely in colder climates. It thrives best in full sun and in sandy, well-drained, poor soil but will grow in any ordinary garden soil. It is drought tolerant, self-seeding and easy to grow in gardens. It is best grown as an annual.

Edible Plant Parts and Uses

Flowers are used in teas, in salads and in stir-fries with aubergine (Roberts 2000). Its leaves are edible if cooked (Yanovsky 1936; Uphof 1968; Usher 1974).

Botany

An herbaceous annual or short-lived branched, glabrous, perennial with a prominent taproot and erect or spreading stem, 30–60. Leaves alternate, glaucous (bluish green), 10–30 cm, petiolate, lamina blade tripinnatipartite variously lobed acutely linear, acutely oblong or obtusely spatulate-oblong, with 3 terminal lobes (Plates 1 and 2), upper leaves progressively smaller and shortly petiolate. Flowers solitary, terminal on 5–15 cm pedicels (Plates 1 and 2). Receptacles concave, funnelform, 3–4 mm in diam., cupular after flowering, margin undulately reflexed. Sepals 2 fused, ovoid, 1 cm, apically shortly conical. Petals 4 (except double flowers), yellow to orange (Plate 3) (white, cream or pink), deltoid-flabellate, 2.5–3 cm. Stamens 12 to (>40); filaments filiform, basally inflated, 3 mm; anthers orange, linear, 5–6 mm. Ovary long, narrow; styles short; stigmas 4, subulate-linear, unequally long. Capsule narrowly cylindric, 5–8 cm, dehiscent from base. Seeds many, spherical, 1–1.5 mm across, net ridged, bur like or pitted, tan, brown and distinctly tessellate.

Plate 1 Flowers and leaves

Plate 2 Close view of flower and leaves

Plate 3 Close-up of flower

Nutritive/Medicinal Properties

Alkaloids (All Plant Parts)

The following alkaloids were identified in *Eschscholzia californica*: eschscholtzine, protopine, allocryptopine, cryptopine, chelerythrine and lauroscholtzine, a new name for *N*-methyllaurotetanine (Manske and Shin 1965). Eschscholtzine was shown to be the bismethylenedioxy analogue of *N*-methylpavine (argemonine) (Manske et al. 1965). Chemical fragmentation of the alkaloids also afforded compounds of the eschscholtzine series, eschscholtzinemethine, eschscholtzinemethine hydrochloride, dihydroeschscholtzinemethine hydrochloride, cyclooctatriene; 2,3,8,9-bismethylenedioxydibenzo[*a,e*]cyclooctadiene, 2,3,8,9-tetramethoxydibenzo[*a,e*]cyclooctadiene and 2,3,8,9-bismethylenedioxydibenzo[*a,e*]cyclooctatriene, and compounds of the *N*-methylpavine series: *N*-methylpavinemethine, *N*-methylpavinemethine hydrochloride, dihydro-*N*-methylpavinemethine hydrochloride, tetramethoxydibenzo[*a,e*]cyclooctatriene and dibenzocyclooctadiene.

Eschscholzia californica was found to contain the aporphine, pavine and a number of protopines (protopine, californine or eschscholtzine, escholinine, eschscholtzidine and the isomers cryptopine and allocryptopine), protoberberine, benzophenanthridine and simple isoquinoline alkaloids (Prieninger 1986; Paul and Maurer 2003). The alkaloids eschscholtzine and eschscholtzine-*N*-oxide were isolated from the petals (Urzúa and Mendoza 1986). The main alkaloids of *Eschscholzia californica* were, namely, allocryptopine, californidine, chelerythrine, eschscholtzine, *N*-methyllaurotetanine, protopine and sanguinarine (Guédon et al. 1990). Allocryptopine was the major constituent in roots, while californidine was the main alkaloid

in all aerial organs except flowers where the major compound was eschscholtzine.

Seven compounds were detected in different populations of *Eschscholzia californica*: *O*-methylcaryachine, protopine, α-allocryptopine, eschscholtzine, californidine, sanguinarine and chelerythrine (Tome et al. 1999). In all samples the major components were the pavine alkaloids eschscholtzine and californidine, although their content varied to a large extent (from 1- to 10-fold). The commercial drug contained a significantly lower concentration of alkaloids.

A 70 % ethanol extract of Californian poppy yielded the known alkaloids californidine, escholtzine, *N*-methyllaurotetanine, caryachine and *O*-methylcaryachine, along with a new pavine alkaloid, 6*S*,12*S*-neocaryachine-7-*O*-methyl ether *N*-metho salt (Gafner et al. 2006). The isoquinoline alkaloids hunnemanine and norsanguinarine were isolated from methanolic plant extract of *Eschscholzia californica* (Singh et al. 2009). Fourteen isoquinoline alkaloids including 1-(3-hydroxy-4-methoxybenzyl)-2-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline and reticuline were isolated from the plant (Cahlíková et al. 2010). A total of 23 alkaloids of six structural types (pavinane, protopine, benzylisoquinoline, benzophenanthridine, aporphine and protoberberine) were identified in *Argemone* and *Eschscholzia* (Cahlíková et al. 2012).

Alkaloids (Cell Suspension Cultures)

Rueffer et al. (1990) partially purified the enzyme (S)-tetrahydroprotoberberine-*cis*-*N*-methyltransferase from *Eschscholzia californica* cell suspension cultures that specifically *N*-methylated certain (*S*)-tetrahydroprotoberberine alkaloids such as (*S*)-canadine and (*S*)-stylopine at the expense of *S*-adenosyl-L-methionine. From cell cultures of *Eschscholzia californica*, three benzo[c]phenanthridine alkaloids, namely, 10-hydroxysanguinarine, 12-hydroxychelirubine and 10-hydroxychelerythrine, and two dihydrobenzo[c]phenanthridine alkaloids, 10-hydroxydihydrosanguinarine and 12-hydroxydihydrochelirubine, together with the known constituents sanguinarine, chelirubine, macarpine, dihydrosanguinarine, dihydrochelirubine and dihydromacarpine, were isolated and characterized (Tanahashi and Zenk 1990). Byun et al. (1990) found that elicitation in combination with two-phase culture of *Eschscholzia californica* increased tenfold the production of benzophenanthridine alkaloids sanguinarine, chelerythrine, chelirubine and macarpine. Large increases in sanguinarine production were observed in two-phase suspension cultured *Eschscholzia californica* cells treated with elicitors prepared from yeast extract, *Colletotrichum lindemuthianum* and *Verticillium dahliae* (Byun et al. 1992). A significant amount of benzophenanthridine alkaloids sanguinarine and chelerythrine was released into the medium, reaching maximum levels a few hours after yeast elicitation of suspension cultures of *Eschscholzia californica* (Collinge and Brodelius 1989). Thereafter, their levels declined and the amount of macarpine increased. Chelerythrine and sanguinarine, two benzophenanthridine alkaloids, have been isolated from a crude methanolic extract of *Eschscholzia californica* cell suspension cultures (Granger et al. 1992). Villegas et al. (2000) found cell suspension cultures of *Eschscholzia californica* produced relatively large amounts of benzophenanthridine alkaloids upon elicitation into the growth medium (up to 50 % of total alkaloids) when yeast was used as elicitor, whereas small amounts of alkaloids were released into the growth medium when sodium orthovanadate was used as abiotic elicitor. The biosynthesis of benzophenanthridine alkaloids, phytoalexins of *Eschscholzia californica*, in cultured cells could be induced by a glycoprotein preparation from yeast, methyl jasmonate, artificial acidification with permeant acids or mild osmotic stress (Färber et al. 2003). The following benzophenanthridine alkaloids, namely, sanguinarine, chelirubine, macarpine, chelerythrine and chelilutine, were produced by cell cultures of *Eschscholzia californica* (Klvana et al. 2006). Production of the benzophenanthridine alkaloids in *Eschscholzia californica* suspension cell cultures was optimized by adding 0.5 mg methyl jasmonate (MJ) and 0.02 mg salicylic acid (SA)/g fresh culture weight after 7 days cultivation (Cho et al. 2007). Sanguinarine reached 24 mg/g DCW by such treatment, 10 times higher than in control cell cultures. MJ and SA induced expression of

berberine bridge enzyme and 3′-hydroxy-(S)-*N*-methylcoclaurine-4′–*O*-methyltransferase, respectively. MJ and yeast had different effects on protein expression and benzophenanthridine alkaloid accumulation in *E. californica* suspension cell cultures (Cho et al. 2008). Using 7-day-old cultures, MJ induced the earlier metabolite (dihydrosanguinarine), whereas yeast promoted conversion to the subsequent metabolite (sanguinarine) in the benzophenanthridine alkaloid biosynthetic pathway. Alkaloids of elicitor-treated cell cultures of *E. californica* identified by ESI-MS/MS (electrospray ionization with tandem mass spectrometry) and ESI-FTICR-MS electrospray ionization (ESI-Fourier transform ion cyclotron resonance mass spectrometer) included the following: *N*-methylnorcoclaurine, magnocurarine (*N,N*-dimethylcoclaurine), 3′*O*-methylreticuline (codamine), reticuline, magnoflorine, romneine, *N*-methylscoulerine (cyclanoline), sinactine, escholidine, *N*-methyltetrahydrothalifendine, *N*-methylcheilanthifoline, chelidonine, chelirubine, chelirubine isomer, dihydrochelirubine, allocryptopine, dihydromacarpine, macarpine, protopine, 10-hydroxydihydrosanguinarine isomer, *N*-methylcanadine, *N*-methylstylopine and columbamine (Liscombe et al. 2009).

In root-derived cell cultures of *Eschscholzia californica*, the overproduction of cytotoxic benzophenanthridine alkaloids could be triggered by a minimum of pathogen pressure that does not evoke hypersensitive reactions (Angelova et al. 2010). The four proteins showing the highest overexpression were identical between cells that received low- or high-elicitor treatment and overlapped with the three proteins up-regulated by artificial pH shifts. They comprised one biosynthetic enzyme (norcoclaurine, SAM 4′ *O*-methyl-transferase) plus a unique combination of stress-protective proteins: a heat-shock protein (HSP70), a peptidyl-prolyl-*cis*/*trans* isomerase (cyclophilin) and a glyceraldehyde-3-phosphate dehydrogenase. They found that overproduction of the benzophenanthridine phytoalexins required the up-regulation of a rate-limiting biosynthetic enzyme plus the coordinated expression of a specific set of protective enzymes and thus was managed like an oxidative stress. Alkaloid profile of transgenic California poppy cells with *CjTHBO* gene (DNA of tetrahydroberberine oxidase (THBO) from cultured *Coptis japonica* cells) comprised protopine, allocryptopine, sanguinarine, 10-hydroxychelerythrine, chelerythrine, chelirubine, dehydrocheilanthifoline and coptisine (Matsushima et al. 2012).

Alkaloid Biosynthesis

Park et al. (2002) working on benzophenanthridine alkaloid biosynthesis in transgenic cell cultures of California poppy found that all benzylisoquinoline alkaloids shared a common biosynthetic origin beginning with a lattice of decarboxylations, *ortho*-hydroxylations and deaminations that convert L-tyrosine into both dopamine and 4-hydroxyphenylacetaldehyde. Stadler et al. (1987, 1989) found that dopamine and 4-hydroxyphenylacetaldehyde condensed to form the trihydroxylated alkaloid (*S*)-norcoclaurine, the central precursor to all benzylisoquinoline alkaloids produced in plants. Stadler et al. (1989) demonstrated that (*S*)-norcoclaurine was specifically incorporated into protoberberine, aporphine and benzophenanthridine alkaloids in cell suspension cultures, as well as into pavine and benzophenanthridine alkaloids in whole plants. (*S*)-Norcoclaurine was found to be converted to (*S*)-reticuline by a 6-*O*-methyltransferase (Morishige et al. 2000), an *N*-methyltransferase (Choi et al. 2001), a P450 hydroxylase (Pauli and Kutchan 1998) and a 4′-*O*-methyltransferase (Morishige et al. 2000). Studies by Pauli and Kutchan (1998) established that a P450-dependent monooxygenase (CYP80B1) isolated from California poppy converted (*S*)-*N*-methylcoclaurine to (*S*)-3′-hydroxy-*N*-methylcoclaurine and not by a phenolase as suggested by Loeffler and Zenk (1990) to be involved in the two separate reactions in the formation of reticuline, namely, the hydroxylation of tyrosine (tyramine) to DOPA (dopamine) and the 3′-hydroxylation of *N*-methylcoclaurine to

3′-hydroxy-*N*-methylcoclaurine, the penultimate intermediate to reticuline.

Paul et al. (2004) found the cytochrome *P*450 (CYP) isoenzyme dependence of the main metabolic steps of the *Eschscholzia californica* alkaloids californine and protopine using rat liver microsomes. Californine *N*-demethylation was mainly catalysed by CYP3A2 and to a minor extent by CYP1A2 and CYP2D1, but not by CYP2C11. CYP2D1 and CYP2C11 were shown to be mainly involved in demethylenation of both californine and protopine, while CYP1A2 and CYP3A2 showed only minor contribution. Two cytochrome P450 cDNA enzymes, CYP719A2 and CYP719A3, involved in stylopine biosynthesis were isolated from cultured *Eschscholzia californica* cells (Ikezawa et al. 2007). Both CYP719A2 and CYP719A3 had stylopine synthase activity to catalyse methylenedioxy bridge formation from cheilanthifoline to stylopine, but not cheilanthifoline synthase activity to convert scoulerine to cheilanthifoline. CYP719A2 was found to have high substrate affinity only towards (*R*,*S*)-cheilanthifoline, whereas CYP719A3 had high affinity towards three similar substrates (*R*,*S*)-cheilanthifoline, (*S*)-scoulerine and (*S*)-tetrahydrocolumbamine. An expression analysis in *E. californica* plant tissues showed that CYP719A2 and CYP719A3 exhibited expression patterns similar to those of three stylopine biosynthetic genes (CYP80B1, berberine bridge enzyme and *S*-adenosyl-L-methionine: 3′-hydroxy-*N*-methylcoclaurine 4′-*O*-methyltransferase), whereas the specific expression of CYP719A3 in root was notable. Treatment of *E. californica* seedlings with methyl jasmonate resulted in the coordinated induction of CYP719A2 and CYP719A3 genes. Four kinds of cytochrome P450 CYP719A genes from *E. californica* were isolated and their functions characterized (Ikezawa et al. 2009). These four cDNA-encoded amino acid sequences that were highly homologous to *Coptis japonica* CYP719A1 and *E. californica* CYP719A2 and CYP719A3 may be involved in isoquinoline alkaloid biosynthesis in *E. californica.* Expression analysis of these genes showed that two genes (CYP719A9 and CYP719A11) were preferentially expressed in plant leaf, where pavine-type alkaloids accumulated, whereas the other two showed higher expression in root than in other tissues. CYP719A5 was found to have cheilanthifoline synthase activity. In addition, enzyme assay analysis of recombinant CYP719A9 suggested that it has methylenedioxy bridge-forming activity towards (*R,S*)-reticuline. CYP719A9 might be involved in the biosynthesis of pavine-type and/or simple benzylisoquinoline-type alkaloids, possessed a methylenedioxy bridge in an isoquinoline ring, in *E. californica* leaf.

Four cytochrome P450s involved in the biosynthesis of benzylisoquinoline alkaloid sanguinarine from reticuline, i.e. cheilanthifoline synthase, stylopine synthase, *N*-methylstylopine hydroxylase and protopine 6-hydroxylase, were isolated from *Eschscholzia californica* (Takemura et al. 2013). Recombinant CYP82N2v2 was produced in *Saccharomyces cerevisiae* and showed protopine conversion to produce dihydrosanguinarine and allocryptopine conversion to produce dihydrochelerythrine.

Two enzymes involved in benzophenanthridine alkaloid biosynthesis, dihydrosanguinarine-10-hydroxylase and 10-hydroxydihydrosanguinarine-10-*O*-methyltransferase, were found in cell-free extracts derived from *Eschscholzia californica* cell suspension cultures (De-Eknamkul et al. 1992). The hydroxylase was found to be a microsome-associated, cytochrome P450-dependent monooxygenase acting specifically at C-10 of dihydrosanguinarine. The methyltransferase was found to methylate only the hydroxyl moiety at C-10 to form dihydrochelirubine. Both enzymes were found to be highly substrate specific. Novel gene targets found in *E. californica* included reticuline 3′-*O*-methyltransferase and cheilanthifoline *O*-methyltransferase. Eight benzophenanthridine alkaloids, sanguinarine, 10-hydro-sanguinarine, chelerythrine, chelirubine, macarpine, dihydrochelerythrine, dihydrochelirubine and dihydrosanguinarine, were identified from yeast-elicited *Eschscholzia californica* cell cultures (Gathungu et al. 2012).

Flavonoids and Other Phytochemicals

A *retro*-carotenoid was isolated from the petals of the Californian yellow poppy, *Eschscholzia californica*, and determined as (all-*E*)-(3*S*,5*R*,3′*S*)-4′,5-*retro*-β,β-carotene-3,5,3′-triol (Maoka et al. 2000). From the petals were isolated rutin (5 %), yielding on acid hydrolysis quercetin and penta-acteylquercetin (Sando and Bartlett 1920). The following carotenoids were found in the pollen and petals: neoxanthin, antheraxanthin, crocetin, eschscholtzxanthin and β-cryptoxanthin (Wakelin et al. 2003). The absolute configuration of eschscholtzxanthin was determined as all-*trans* (3*S*,3′*S*)-4′,5′-didehydro-4,5′-*retro*-β,βcarotene-3,3′-diol (Andrewes et al. 1979). Other intermediate carotenoids found in the petals included phytofluene, ζ-carotene, β-carotene and zeaxanthin, besides the end products such as *retro*-carotene-triol and eschscholtzxanthin.

Two new isoflavones, together with quercitrin, were isolated from whole plants of *Eschscholzia californica* (Jain et al. 1996). The structures of the new isoflavones were determined as 2′-methoxyformononetin and 7-methoxy-2′,4′-dihydroxyisoflavone. The aqueous ethanol extract of aerial parts of *Eschscholzia californica* yielded six flavonol 3-*O*-glycosides including two new compounds, quercetin 3-*O*-[α-rhamnopyranosyl-(1–4)-α-rhamnopyranosyl-(1–6)-β-glucopyranoside] and isorhamnetin 3-*O*-[α-rhamnopyranosyl-(1–4)-α-rhamnopyranosyl-(1–6)-β-glucopyranoside], and β-D-glycoside, α-L-rhamno (1 → 6)- β-D-glycoside, α-L-rhamno(1 → 4)-a-l-rhamno(1 → 6)- β-D-glycoside and β-D-glycoside-a-L-rhamnoside (Beck and Haberlein 1999a, b). The plant also contained rutin, quercetin and isorhamnetin (Duke 1992).

Carbohydrates and organic acids, namely, lactic acid, glycolic acid, benzoic acid, succinic acid, malic acid, threonic acid, citric acid and large amounts of glyceric acid, were separated from the herbal dry extracts of *Eschscholzia californica* (Schiller et al. 2002). Glyceric acid together with sugars, namely, glucose, fructose and glucose, detected may be responsible for the increased hygroscopicity and the poor processing behaviour of the extracts.

Anxiolytic/Sedative/Analgesic: Neuromodulatory Activity

California poppy was found to have a sedating effect on the central nervous system and a relaxing effect on the smooth musculature of the ileum (Vincieri et al. 1988). In animal studies, an aqueous extract of *Eschscholzia californica* exhibited sedative and anxiolytic properties in mice challenged with a variety of behavioural tests (Rolland et al. 1991). Doses of more than 25 mg/kg exerted anxiolytic effects, whereas higher dosages of up to 200 mg/kg promoted sedation. The extract was found to be nontoxic with intraperitoneal injection. In the medicinal herb *Eschscholzia californica*, californine and protopine were found to be mainly responsible for the sedative and spasmolytic effects (Rey et al. 1991). Kleber et al. (1995) demonstrated that an aqueous–alcoholic extract of *Eschscholzia californica* inhibited the enzymatic degradation of catecholamines, including dopamine β-hydroxylase and monoamine oxidase (MAO-B), as well as the synthesis of adrenaline. The extract preserved high catecholamine levels thus explaining its sedative, antidepressive and hypnotic activities. The herbal drug Phytonoxon N (abbreviated as PN) composed of alcoholic extracts of *Corydalis cava* (20 %) and *Eschscholzia californica* (80 %) had been prescribed for nervousness-induced insomnia, agitation and/or anxiety (Schäfer et al. 1995). Both plants had been reported to be rich in isoquinoline alkaloids derived from tyrosine metabolism. Recent research showed that they may influence neurotransmitter metabolism. Researchers found that the peroxidase-catalysed dimerization via the tyrosine residues is especially inhibited by Phytonoxon N (Reimeier et al. 1995). The tyrosinase-catalysed reaction yielded five different products A–E. Phytonoxon N stimulated the formation of the minor products A, B

and E, whereas the formation of the major products C and D was inhibited. Only products C and D exhibited properties similar to the peroxidase-derived dimer. Product A was likely to be identical to DOPA-enkephalin. Enkephalin had been reported to bind to opioid receptors of the nociceptive system thus provoking analgesic responses. In a later study an aqueous alcohol extract of *Eschscholzia californica* was found to possess sedative and anxiolytic effect in mice (Rolland et al. 2001). The plant extract did not protect mice against the convulsant effects of pentylenetetrazol and did not cause muscle relaxant effects but appeared to have an affinity for the benzodiazepine receptor, demonstrated by concurrent administration of flumazenil, a benzodiazepine antagonist, which suppressed the sedative and anxiolytic effects of the extract. The aqueous alcohol extract of *Eschscholzia californica* induced peripheral analgesic effects in mice but did not possess antidepressant, neuroleptic or antihistaminic effects. Of the known alkaloids isolated from *E. californica*, *N*-methyllaurotetanine showed the highest inhibition of [(3)H]8-hydroxy-2-(di-*N*-propylamino) tetralin ([(3)H]8-OH-DPAT) binding to 5-HT1A receptors in vitro with an EC_{50} value of 155 nM and a K(i) of 85 nM (Gafner et al. 2006).

In a double-blind, randomized, placebo-controlled trial involving a total of 264 patients (81 % females; mean age, 44.6 years) with generalized anxiety (DSM-III-R) of mild-to-moderate intensity (total Hamilton Anxiety Rating Scale score between 16 and 28), administration of the preparation containing fixed quantities of *Crataegus oxyacantha, Eschscholzia californica* and magnesium (two tablets twice daily for 3 months) proved safe and more effective than placebo in treating mild-to-moderate anxiety disorders (Hanus et al. 2004). In a review of plant-based medicines for anxiety disorders, preclinical evidence of anxiolytic activity (without human clinical trials) was found for many plants including *Eschscholzia californica* (Sarris et al. 2013). Common mechanisms of action for the majority of botanicals reviewed primarily involve GABA, either via direct receptor binding or ionic channel or cell membrane modulation; GABA transaminase or glutamic acid decarboxylase inhibition; a range of monoaminergic effects; and potential cannabinoid receptor modulation.

Acetylcholinesterase and Butyrylcholinesterase Inhibitory Activity

Two benzylisoquinoline alkaloids, reticuline and 1-(3-hydroxy-4-methoxybenzyl)-2-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline, showed promising inhibitory activity against human plasma butyrylcholinesterase (Cahlíková et al. 2010). None of the benzylisoquinoline alkaloids isolated significantly inhibited both human blood acetylcholinesterases.

Antibacterial Activity

Sanguinarine has been in use in the United States and on the continent in mouthwashes and toothpastes as it had been reported to curb bacterial supragingival plaque (Grenby 1995).

Antidiuretic Hormonal Activity

Chelerythrine and sanguinarine, two benzophenanthridine alkaloids from *E. californica*, exhibited affinity for rat liver vasopressin V1 receptors and were competitive inhibitors of [3H]-vasopressin binding within the micromolar range (Ki) (Granger et al. 1992). Chelerythrine and sanguinarine represented two non-peptidic molecules providing original chemical leads for the design of synthetic vasopressin compounds.

Inotropic Activity

Sanguinarine exerted a concentration-dependent positive inotropic effect in isometrically contracting left guinea pig atria and inhibited cardiac Na^+, K^+–ATPase isolated from guinea pig myocardium (Seifen et al. 1979).

Traditional Medicinal Uses

Californian poppy is often prescribed both as a phytotherapeutic preparation and as a pharmaceutical medicine for sleep disturbances in children (Vincieri et al. 1988), insomnia and neuralgia (Cheney 1963). Californian poppy is a bitter sedative herb that acts as a diuretic, analgesic, spasmolytic and diaphoretic (Bown 1995; Chevallier 1996). The whole plant is harvested when in flower and dried for use in tinctures and infusions. It is taken internally in the treatment of nervous tension, anxiety, insomnia, incontinence and bed-wetting (especially in children) (Bown 1995; Chevallier 1996). The watery sap is mildly narcotic and has been used to relieve toothache (Bown 1995). An extract of the root is used as a wash on the breasts to suppress the flow of milk in lactating females (Moerman 1998).

Other Uses

The species is widely cultivated in temperate and Mediterranean-type gardens and widely introduced as courtyard ornamentals in China.

Californian poppy contains alkaloids, some of which have fungicidal activity.

Californian poppy alkaloid, hunnemanine, exhibited 100 % inhibition of spore germination of *Alternaria brassicae, Helminthosporium pennisetti* and *Fusarium lini* at 1,000 ppm, whereas norsanguinarine exhibited 100 % inhibition of *Alternaria brassicicola* and *Curvularia maculans* at this concentration (Singh et al. 2009).

Comments

California poppy is the official state flower of California. The species is sometimes regarded as an environmental weed in Western Australia, New South Wales and Victoria and an invasive species in Central Chile (Véliz et al. 2012).

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Antirrhinum majus

Scientific Name

***Antirrhinum majus* L.**

Synonyms

Antirrhinum grandiflorum Stokes, *Antirrhinum hispanorum* Bordère ex Rothm., *Antirrhinum latifolium* var. *pseudomajus* Rouy, *Antirrhinum latifolium* var. *purpurascens* Benth., *Antirrhinum majus* var. *longipedunculatum* Regel, *Antirrhinum majus* var. *peloria* Migout, *Antirrhinum majus* var. *pseudomajus* (Rouy) Rouy, *Antirrhinum murale* Salisb., *Antirrhinum vulgare* Bubani, *Orontium majus* Pers., *Termontis racemosa* Raf.

Family

Plantaginaceae

Common/English Names

Common Snapdragon, Garden Snapdragon, Dragon Flower, Snapdragon

Vernacular Names

Brazil: Boca-De-Leão
Czech: Hledík Větší
Dutch: Grote Leeuwebek
Estonian: Suur Lõvilõug
Esperanto: Antirino Granda, Antirino Maja, Leonfaŭko Granda
Finnish: Iso Jalopeuran Kita, Leijonankita
French: Grand Muflier, Gueule-De-Lion, Gueule-De-Loup, Muflier, Muflier Des Jardins
Gaelic: Srubh Lao
German: Garten-Löwenmaul, Garten-Löwenmäulchen, Grosses Löwenmaul, Grosses Löwenmäulchen, Löwenmaul
Italian: Bocca Di Leone, Bocca Di Leone Commune
Norwegian: Prydløvemunn
Polish: Lwia Paszcza, Wyżlin Większy, Wyżlin Większy
Slovašcina: Odolin Veliki, Veliki Odolin, Zajčki
Slovencina: Papuľka Väčšia
Spanish: Boca De Dragon, Boca De Sapo, Conejitos, Dragón, Dragoncillo, Hierba Becerra, Morros De Lobo, Perritos
Swedish: Lejongap
Turkish: Aslanağzı

Origin/Distribution

Garden snapdragon is indigenous to the Mediterranean region, from Morocco and Portugal north to southern France, and east to Turkey and Syria.

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Agroecology

In its native range it is found in disturbed areas, woodlands, scrublands and on hard rock outcrops.

Snapdragon thrives best in well-drained, moist, organic-rich, slightly acid soil in full sun. They are intolerant of subzero freezing temperatures and overwatering.

Edible Plant Parts and Uses

Flowers have been reported to be used in a moderate way in salads or crystallized (Roberts 2000; Anonymous 2004; Stradley 2010; Rop et al. 2012). An oil that is inferior to olive oil is said to be obtained from the seeds (Grieve 1971).

Botany

It is a herbaceous perennial chamaephyte with erect, slender green stems, 50–90 (−150) cm high, glabrous proximal to the inflorescence. Leaves opposite basally and alternate distally, simple, entire, and broadly lanceolate, 1–7 cm long by 2–2.5 cm wide with subacute apex and tapering towards the base (Plates 1, 4, 5, 6). Flowers zygomorphic, bisexual, produced in erect, 10–20 flowered terminal racemes, violet, red, pink, yellow, or white, 3.5–4.5 cm long with ovate bracts and on 2–5 mm pedicels (Plates 1–6). Each flower has a calyx of five equal pubescent lobes; corolla sympetalous, bilabiate, upper lip of two dorsal broad recurved petals and lower lip comprises two lateral lobes and raised swollen ventral lobe, closing the corolla throat. The five petals are united for part of their length forming a short corolla tube which ends in a sharp border with the petal lobes. Androecium comprises four didynamous stamens adnate to the corolla tube. Gynoecium consists of a single compound pistil of two carpels, a single style, an inconspicuous stigma and a superior, sometimes asymmetric ovary with two sometimes unequal locules with numerous axial ovules. The fruit is an ovoid capsule, 10–14 mm diameter, containing numerous small, 0.8–1.1 mm, oblong–ovoid, reticulate and black seeds.

Plate 1 Flowers, buds and leaves of garden snapdragon

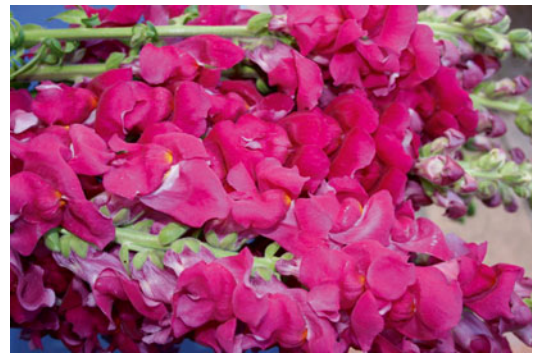

Plate 2 Maroon snapdragon flowers

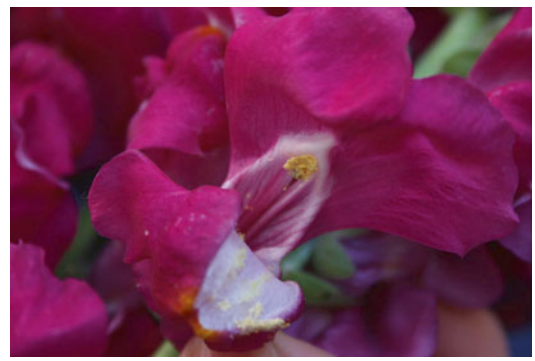

Plate 3 Lower lip of flower separated to show the pollens

Plate 4 Leaves, buds and white flowers

Plate 5 Leaves, bud and orange flowers

Plate 6 Leaves, buds and yellow flowers

Nutritive/Medicinal Properties

Rop et al. (2012) reported that edible flowers of *Antirrhinum majus* had a dry matter content (%w/w) of 12.61 %, crude protein of 4.85 g/kg and the following elements (mg/kg fresh mass (FM): P 417.62 mg, K 2861.83 mg, Ca 357.20 mg, Mg 172.02 mg, Na 87.74 mg, Fe 4.38 mg, Mn 5.73 mg, Cu 1.62 mg, Zn 8.89 mg and Mo 0.84 mg. The flowers had total antioxidant capacity of 5.06 g ascorbic acid equivalents/kg FM, total phenolic content of 3.49 g gallic acid/kg FM and total flavonoid content of 1.78 g rutin/kg FM.

Whedale (1913), Wheldale and Bassett (1913, 1914) in their study of Mendelian factors controlling flower colour in *Antirrhinum majus*, isolated apigenin, 5, 7, 4′-trihydroxyflavone, and luteolin, 5,7, 3′, 4′-tetrahydroxyfiavone. Crossing white with yellow or ivory varieties produced plants bearing red or magenta flowers. This led them to hypothesize that an anthocyanin was formed from a flavone by the action of some factors contained in the white flower. They further suggested that the anthocyanin was either an oxidation or condensation product of a flavone or both. Scott-Moncrieff (1930) isolated the magenta anthocyanin pigment, antirrhinin from crimson flowers, and elucidated the structure as 3-rhamnoglucoside of cyanidin. Subsequently

Geissman and his co-workers conducted more thorough investigations (Geissman et al. 1954; Geissman and Harborne 1955a; Jorgensen and Geissman 1955a, b; Harborne and Corner 1961; Geissman 1962; Harborne 1963). A biogenetic relationship was found between certain of the flavonoids present and different flower colour genotypes. Flower pigmentation in *A. majus* was found to be controlled by three colour factors P, M and Y (Geissman et al. 1954). The P factor controlled oxidation of the C_3 fragment that joins the two 6-carbon rings; when P was dominant, anthocyanidins and flavonols were present. The M factor controlled the oxidation state of the C_6(B) ring in the flavones, flavonols and anthocyanidins; thus quercetin, apigenin, luteolin and cyanidin were formed in the presence of M while kaempferol, apigenin and pelargonidin in its absence. The Y factor appeared to operate at an early stage in the synthesis, in its dominant form permitting the formation of small amounts of aurone pigment and in its recessive form permitting large quantities of aurone to be produced. Aurone pigment was produced in the flower petals only; the other pigments were found in flowers, stems and leaves. A naringenin glycoside was found to occur in the plant. Geissman and Harborne (1955b) showed that the albino (yy) genotypes did not contain any detectable amounts of flavonoid pigments but that it contained 4-hydroxycinnamic acid (*p*-coumaric acid) and 3′:4′-dihydroxycinnamic acid (caffeic acid) as a number of aliphatic esters. Increased numbers of recessive factors result in decreased anthocyanin production. They found that genotypes containing pelargonidin glycoside had a significantly lower concentration of anthocyanin than genotypes containing cyanidin glycoside. Highest concentration of aurone was associated with genotypes—yy—and increased numbers of dominant factors resulted in decreased aurone production. Also, high anthocyanin concentration was related to low aurone concentration and, conversely, low anthocyanin concentration was related to high aurone concentration.

Anthochlor pigment of yellow *A. majus* flowers was isolated in the form of its heptaacetate and shown to be a glucoside of 3′,4′,4, 6-tetrahydroxybenzalcourmaranone (Seikel and Geissman 1950). The pigment was designated aureusin and its aglucone aureusidin. In addition, a flavanone glycoside in the form of its hexaacetate was shown to be a hexoside of naringenin (4′,5, 7-trihydroxyflavanone). Geissman and Harborne (1955a) showed aureusin to be the 6-glucoside of 3′,4′, 4,6-tetrahydroxybenzalacoumaranone. Sherratt (1958) confirmed the presence of cyanidin, pelargonidin, apigenin, luteolin and kaempferol and aureusidin in the flowers. Further, it was found that most genotypes except the recessive yy contain aureusidin and apigenin. The gene R was found necessary for the formation of anthocyanin; in the presence of gene b, pelargonidin was formed, but in the presence of gene B cyanidin only was formed. *Antirrhinum majus* flowers were found to have cinnamic esters (Harborne and Corner 1961); flavones, namely, apigenin 7,4′-diglucuronide, luteolin 7-glucuronide, chrysoeriol 7-glucuronide, kaempferol 3-glucoside and kaempferol 3,7-diglucoside; and an aurone, bracteatin 6-glucoside (Harborne 1963). *A. majus* was found to contain the following anthocyanins, cyanidin-3-glucoside, cyanidin-3-rutinoside (Gilbert 1971) and pelargonidin-3-glucoside (Gilbert 1972b). Three chalcones were found in yellow flowers of *A. majus*, two of which were identified as chalcononaringenin 4′-glucoside and 3,4,2′,4′,6′-pentahydroxychalcone 4′-glucoside (Gilbert 1972a).

The yellow colouration of *Antirrhinum majus* flowers was reported to be mainly conferred by aurone flavonoids such as 6-glucosides of aureusidin and bracteatin (Sato et al. 2001). Studies showed that aureusidin could be from of 2′,4′,6′,4-tetrahydroxychalcone (THC) or 2′,4′,6′,3,4-pentahydroxychalcone (PHC) whereas bracteatin was not produced through the 5′-hydroxylation of aureusidin but arose solely from PHC. They identified aureusidin synthase (AmAS1) as the key enzyme that catalyzed aurone biosynthesis from chalcones in *A. majus* (Ono et al. 2006). They also found that that chalcone 4′–*O*-glucosyltransferase (4′CGT) was essential for aurone biosynthesis and yellow colouration in vivo. In separate studies, Davies et al. (2006) reported that the petals of *Antirrhinum*

majus produced aurones, bright yellow flavonoids (Davies et al. 2006). The biosynthesis of aurones was suggested to occur by the action of aureusidin synthase (AUS) and possibly aureusidin 7-*O*-glucosyltransferase (A7GT). A number of conserved potential regulatory regions were identified, in particular a consensus site for the MYB (myoblastoma)-type transcription factors. Further, they (Shang et al. 2011) found pigment stripes associated with veins (venation) to be a common flower colour pattern. The venation pattern was found to be determined by *Venosa* (encoding an R2R3MYB transcription factor). Recent studies by Shakya et al. (2012) found altered leaf colour to be associated with increased superoxide scavenging activity in aureusidin-producing transgenic plants. Their studies suggested that the nutritional qualities of leafy vegetables can be enhanced through the introduction of aurone biosynthetic pathways.

Deuterium-labelled studies by Breinholt et al. (1992) found a higher incorporation of 8-e*pi*-iridotrial than of 8-*epi*-iridotrial glucoside in the biosynthesis of the iridoid, antirrhinoside in *Antirrhinum majus* indicating the former to be an intermediate in the biosynthesis of antirrhinoside. Further, they found that the last steps in the biosynthesis of antirrhinoside in *Antirrhinum majus* involved an initial hydroxylation of the 6-position of 6,10-dideoxyaucubin to give linaride (10-deoxyaucubin), followed by epoxidation to give 10-deoxycatalpol (5-deoxyantirrhinoside) and finally hydroxylation of the 5-position to give antirrhinoside (Damtoft et al. 1995). The content of the four iridoids, namely, antirrhinoside, antirrhide, 5-glucosyl-antirrhinoside and linarioside, found in cultivars of *Antirrhinum majus*, exhibited seasonal variations (Høgedal and Mølgaard 2000). The seasonal variation in total iridoid content showed a marked bimodal distribution with high total values (around 100 mg/g dry matter) early and late in the season and a very low content of all iridoids coinciding with the onset of flowering at the beginning of August. The relative contribution of antirrhinoside was significantly higher before flowering than after bud break. The relative decrease in antirrhinoside was counteracted by an increase of antirrhide, which was significantly higher after the onset of flowering than before.

Normal (*n*-) alkanes were found to be the major wax class in petals (29.0–34.3 %) from flower opening to senescence (12 days) (Goodwin et al. 2003). Besides *n*-alkanes, snapdragon petals possessed significant amounts of methyl branched alkanes (23.6–27.8 %) and hydroxy esters (12.0–14.0 %). Changes in amount of methyl benzoate (the major snapdragon floral scent compound) inside the petals followed closely with levels of methyl benzoate emission, suggesting that snapdragon petal cuticle may provide little diffusive resistance to volatile emissions.

The volatile ester methyl benzoate was found to be the most abundant scent compound in snapdragon flowers (Dudareva et al. 2000). The compound was synthesized by and emitted from only the upper and lower lobes of petals, where pollinators (bumblebees) come in contact with the flower. A novel *S*-adenosyl-L-methionine/benzoic acid carboxyl methyl transferase (BAMT), the final enzyme in the biosynthesis of methyl benzoate and its corresponding cDNA were isolated and characterized. Snapdragon flowers were found to emit two monoterpene olefins, myrcene and (*E*)-β-ocimene, derived from geranyl diphosphate, in addition to a major phenylpropanoid floral scent component, methyl benzoate (Dudareva et al. 2003). Emission of these monoterpenes was regulated developmentally and followed diurnal rhythms controlled by a circadian clock. The two myrcene synthases and (*E*)-β-ocimene synthase were isolated. (*E*)-β-ocimene synthase was highly similar to snapdragon myrcene synthases (92 % amino acid identity) producing predominantly (*E*)-β-ocimene (97 % of total monoterpene olefin product) with small amounts of (*Z*)-β-ocimene and myrcene. These newly isolated snapdragon monoterpene synthases, together with Arabidopsis AtTPS14 (At1g61680), defined a new subfamily of the terpene synthase (TPS) family designated the *Tps-g* group.

Two subspecies of *A. majus* had significantly different flora scent mainly attributable to differences in benzenoids and the percentage occurrence and emission rates of other volatile organic chemicals (VOC) (Suchet et al. 2010). Twenty

fatty acid derivatives, including green leaf volatiles, one nitrogen containing compound (syn-3-methyl-butyl-aldoxime), 11 monoterpenes (cyclic, α-pinene, β-pinene, *p*-cymene, limonene, γ-terpene; non-cyclic, β-myrcene, (*Z*)-β-ocimene, (*E*)-β-ocimene,3,4-dimethyl-2,4,6-octatriene,(*E*,*E*)-2,6-dimethyl-1,3,5,7-octatetraene; and irregulars, 6-methyl-5-hepten-2-one) and five benzenoids were detected; the other VOCs were found in both subspecies but differed in percentage occurrence and emission rates. Three benzenoids (acetophenone, benzaldehyde, and methyl benzoate) were only emitted by *A. majus pseudomajus* and were totally absent in *A. majus striatum*; two benezenoids, viz. hemimelitene and mesitylene, were common to both subspecies. The 20 fatty acid derivatives comprised aldehydes, 2-methyl-propanal, 3-methyl-butanal, pentanal, *Z*-3-hexenal, heptanal, octanal, nonanal, decanal; alcohol, 1-pentanol; alkenes, 1,3,5-cycloheptatriene and 1-octene; alkanes, 1,1-diethoxy-ethane, nonane, decane, dodecane; esters, ethyl acetate, hexyl acetate; ketone- 2-butanone; and an ether, eucalyptol.

Traditional Medicinal Uses

Snapdragon leaves and flowers are anti-inflammatory, bitter, resolvent and stimulant (Grieve 1971; Chiej 1984). They have been used in poultices on tumours and ulcers and to treat different types of inflammations and haemorrhoids.

Other Uses

Snapdragon is popularly planted as garden ornamentals for mass display, borders, bedding, containers, pots and cut flowers.

Comments

Antirrhinum used to subsumed under the family Scrophulariaceae, but studies of DNA sequences have led to its inclusion in a vastly enlarged family Plantaginaceae (Oyama and Baum 2004; Albach et al. 2005; Tank et al. 2006). Although the taxonomy of this genus is still unresolved many modern botanists have adopted the sensu lato circumscription proposed by Thompson (1988) who placed 36 species in the genus. In contrast, the USDA Plant Database recognises only the Old World species of sect. *Antirrhinum* in the genus, listing only *Antirrhinum majus* (the only species in the section naturalized in North America).

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Saccharum spontaneum var. *edulis*

Scientific Name

***Saccharum spontaneum* var. *edulis* (Hassk.) K. Shum.**

Synonyms

Saccharum spontaneum L. var. *edulis* (Hassk.) K. Schum. & Lauterb., *Saccharum* × *edule* Hassk.

Family

Poaceae

Common/English Names

Cane Inflorescence, Coastal Pitpit, Cultivated Sugarcane, Duruka, Fiji Asparagus, Pitpit, Vegetable Cane

Vernacular Names

Fiji: Duruka
Indonesia: Trubus, Tebu Telur, Tebu Bertelor
Papua New Guinea: Bwêy, Pit, Pitpit
Vanuatu: Naviso

Origin/Distribution

The species is indigenous to New Guinea. It is cultivated in Java and Kalimantan, New Guinea, Melanesia, New Hebrides and Fiji.

Agroecology

Duruka can tolerate a wide range of climatic and soil conditions. It thrives on deep- and fine-textured soils of lowland plains subject to brief seasonal inundation and on footslopes, drainage lines and seepage areas of hilly and undulating terrain and alluvial fans from sea level to 600 m altitude. A fertile soil and adequate rainfall ensure good quality yields.

Edible Plant Parts and Uses

Edible unopened inflorescences, which are relished as a vegetable either raw or cooked, steamed or roasted in various dishes. They are used in soups or curries or added to many dishes, roasted over fire or baked in lovo and eaten. In Fiji, Duruka is normally cooked in coconut cream and served as a vegetable, often with fish. Fiji is exporting canned Duruka in brine to Australia, New Zealand and the United States. Apart from canning, Duruka can be vacuum-packed to extend its availability in the market.

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Plate 1 (**a**, **b**) Duruka on sale in a local market in Papua New Guinea and Fiji

Botany

A tough perennial tillering herb that spreads by stolons or rhizomes, growing to 1.5–4 m high. Culms are green or yellowish green and are large and cylindrical (2–10 m high, 2–3 cm diameter). The upper leaves of the culm have hirsute leaf sheaths. The leaf blade is oblong-lanceolate, 1–2 m by 2.5–6 cm and hairy on both sides. The inflorescence is abnormally swollen and consists of a mass of creamy, underdeveloped and aborted floral primordial, 10–20 cm long, and remains enclosed within leaf sheaths (Plates 1 and 2).

Plate 2 Sheath removed showing the abnormally swollen inflorescence

Nutritive/Medicinal Properties

Per 100 g edible portion, Pitpit was reported to contain water, 90 g; energy, 168 kJ (40 kcal); protein, 4.1 g; total fat, 0.2 g; available carbohydrates, 6 g; dietary fibre, 1.2 g; Na, 3 mg; K, 601 mg; Ca, 12 mg; Fe, 0.9 mg; total vitamin A equivalent, 5μg; β-carotene equivalent, 30 μg; thiamin, 0.18 mg; riboflavin, 0.2 mg; niacin, 1 mg; and vitamin C, 33 mg (Dignan et al. 1994). The nutrient composition of raw Duruka (per 100 g edible portion) analysed by Fiji National Food and Nutrition Committee was reported as water, 89.3 g; energy, 142 kJ (34 kcal); protein, 4.2 g; fat, 1.0 g; sugars, 1.1 g; starch, 0.6 g; ash, 1.4 g; dietary fibre, 3.6 g; β-carotene, <5 μg; thiamin, 0.04 mg; riboflavin, 0.06 mg; niacin, 1.3 mg; vitamin C, 14 mg; Na, 18 mg; K, 636 mg; Ca, 4 mg; Fe, 1.1 mg; Mg, 48 mg; Zn, 1.1 mg; Cu, 0.3 mg; and Mn, 0.5 mg (Mudaliar 2007).

Methanol root extract of *S. spontaneum* was found to have antioxidant activity (Khalid et al. 2011). It exhibited DPPH-scavenging activity of 91.23 at 1.50 mg/mL and nitric oxide inhibition activity of 90.17 %. It also exhibited thiocyanate reduction potential with maximum absorbance of 0.314 nm obtained at 120 mg/mL concentration of the extract. The total phenolic content was found to be 351.25 µg/mL and the flavonoid content was 48.60 µg/mL.

Traditional Medicinal Uses

The roots of *S. spontaneum* are a traditional herb used in the treatment of gynaecological troubles and respiratory diseases and are used as galactagogue and diuretic in the Ayurveda system (Khalid et al. 2011). The roots are also used as astringent, emollient, refrigerant, diuretic, purgative, tonic and aphrodisiac and are useful in the treatment of dyspepsia, burning sensation, piles and sexual weakness.

Other Uses

Its leaves have been used for thatching.

Comments

Saccharum edule is morphologically similar to *S. robustum* except that the flower spike or inflorescence is compacted. It is believed to be derived from the introgression of *S. robustum* with *Miscanthus floridulus*.

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Antigonon leptopus

Scientific Name

***Antigonon leptopus* Hook. & Arnott**

Synonyms

Antigonon cinerascens M. Martens & Galeotti, *Antigonon cordatum* M. Martens & Galeotti, *Antigonon platypus* Hook. & Arn., *Corculum leptopum* (Hook. & Arn.) Stuntz, *Corculum leptopus* (Hook. & Arn.) Stuntz

Family

Polygonaceae

Common/English Names

Bride's Tears, Chain-of-Love, Chinese Love Vine, Confederate Vine, Confederate-Vine, Coral Bells, Coral Creeper, Coral Vine, Coralita, Corallita, Coral Vine, Hearts on a Chain, Honolulu Creeper, Love Chain, Love-Vine, Mexican Coral Vine, Mexican Creeper, Mexican-Creeper, Mexican Love Vine, Mountain Rose, Mountain-Rose Coralvine, Mountain-Rose Coralvine, Pink Vine, Queen's Jewels, Queen's Wreath, San Miguelito Vine, Sandwich Island Creeper

Vernacular Names

Chamorro: Cadena De Amor, Flores Kádena
French: Rosa-De-Montana, Antigone
India: Anantalata (Bengali), Kodi Rose (Tamil), Picchibatani (Telugu)
Indonesia: Bunga Air Mata Pengantin
Jamaica: Coralila, Coralita
Malaysia: Honolulu Creeper, Bunga Bonet, Bunga Berteh
Mexico: Kadena De Amor
Northern Marianas Islands: Flores Ka-dena
Palauan: Dilngau
Papiamento: Beyisima
Philippines: Cadena-De-Amor (Tagalog), Cadena-De-Amor (Spanish), Flores De Singapore
Pohnpei: Rohsapoak
Portuguese: Amor Em Penca, Amor Entrelacado, Amor-Agarradinho, Coralia, Coralita, Entrada De Baile, Georgina, Mimo Do Ceu, Rosa De Sao Miguelito, Rosalia
Spanish: Bellísima, Corazon Bello, Corona, Coronilla, Kadena De Amor, Rosa De Montana
Thai: Puang Chom-Poo
Vietnamese: Dây Ti Gôn; Hiếu Nữ; Hoa Tigôn, Nho Hoa

Origin/Distribution

The species is native to Mexico, now common in warm tropical countries globally.

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Agroecology

A. leptopus grows well in full sun in disturbed areas especially limestone areas in dry to moist lowland areas but is well adapted to dry conditions. It occurs as a smothering vine that invades disturbed areas and forest edges. The plant prefers near-neutral to alkaline soils with pH of 6.1–7.8, moderately fertile sandy or light soils with moderate moisture level. It is drought tolerant; once established it needs occasional water.

Edible Plant Parts and Uses

Leaves and pink flowers are often eaten as cooked vegetables in Thailand (Pongpangan and Poobrasert 1985; Facciola 1990; Wessapan et al. 2007; Wetwitayaklung et al. 2008; Vanisree et al. 2008; Wongwattanasathien et al. 2010) In Thailand, the leaves and flowers are dipped in flour, fried and served with vermicelli. The flowers are also mixed into omelettes. Herbal teas are made from the leaves and blossoms. The small tubers are edible and are valued in its native area for the nutlike flavour.

Botany

A climbing, somewhat woody, robust vine up to 10 m long, with cordate–ovate, hastate–ovate or triangular (2.5–9 cm) leaves. The leaves are borne on short often winged, glabrate petioles and have reticulate venation, cordate base, ciliate margins and acute to acuminate tips (Plates 1 and 2). Inflorescence 4–20 cm long panicle with clusters of white or pink flowers along the rachis which has a tendrilate tip (Plates 1 and 2). Flower with ovate to elliptic tepals with entire margins and acute apex on 3–10 mm glabrous or pubescent pedicels. Fruit a conical and 3-angled achene 8–12 mm by 4–7 mm, shining, loosely surrounded by the persistent tepals of the flower.

Plate 1 Flowers and leaves

Plate 2 Close view of flowers

Nutritive/Medicinal Properties

The % yield of extract and the amount of total polyphenols in g/100 g calculated as gallic acid on dried flowers and crude methanolic extract basis for *A. leptopus* were reported as 33.04 (% yield), 6.35 g total polyphenols (g/100 g dried flower) and 19.23 g total polyphenols (g/100 g crude extract) (Wetwitayaklung et al. 2008). Antioxidant capacity for *A. leptopus* flowers expressed in TEAC (trolox equivalent antioxidant capacity) = 0.19 and IC_{50} = 48.81 µg/50 µL. There was a good linear relationship between antioxidant activity and flower extract concentrations with R^2 = 0.9657. Phenols, saponins, amino acids, steroids, phytosterols, triterpenoids, sapogenins, tannins, xanthoprotein, carboxylic acid and coumarins were detected in the methanolic extracts of *A. leptopus* flowers (Marimuthu et al. 2012).

Phenolic acids detected in the ethanol extract of *Antigonon leptopus* flowers (mg/100 g DW): gallic acid 8.41 mg, protocatechuic acid 24.33 mg, *p*-hydroxy benzoic acid 33.04 mg, chlorogenic acid 37.60 mg, vanillic acid 3.25 mg, caffeic acid 10.32 mg, syringic acid 17.14 mg, *p*-coumaric acid 5.37 mg, ferulic acid 33.36 mg and sinapic acid 100.08 mg, total 272.879 mg (Kaisoon et al. 2012). Flavonoid compounds found in the lyophilized hydrophilic extracts of *Antigonon leptopus* flowers (mg/100 g DW): rutin 21.95 mg, myricetin 47.54 mg, quercetin 11.08 mg, apigenin 0.83 mg and kaempferol 75.86 mg, total 157.26 mg.

Flavonoidal compounds, viz. quercetin, rhamnetin, quercetin-3-*O*-β-D-glucopyranoside and a new anthraquinone glycoside 1, 5-dihydroxy-3-ethyl anthraquinone-8-*O*-(4-*O*-α-L-arabino furanosyl)-β-D-glucopyranoside (Tiwari and Minocha 1980a) and quercetin-3-*O*-rhamnosyl rhamnoside (Valsakumari and Sulochana 1992), and two anthocyanins, viz. pelargonin and malvin (Tiwari and Minocha 1980b), were isolated from the acidic (1 % HCl) methanolic extract of fresh flowers. A new anthraquinoid pigment 1, 6, 8-trimethoxy-3-propanoyl anthraquinone was isolated from the methanolic extract of flowers (Minocha and Masood 1981).

Leaves were found to contain flavonoidal glycosides, viz. quercetin-3-rhamnoside and quercetine-3-*O*-glucoronide (Kawasaki et al. 1986).

Antioxidant Activity

Four edible flower extracts including *A. leptopus* elicited antioxidant activity in ABTS assay with the trolox equivalent antioxidant capacity (TEAC) of 0.15–0.70 (Wessapan et al. 2007). Vanisree et al. (2008) reported that *A. leptopus* plant exhibited ability to scavenge reactive oxygen species and reduce oxidative stress in vitro and in vivo. The soluble phenol acids (per g dry weight) identified in *Antigonon leptopus* flower extract were as follows: gallic acid 25.3 μg, protocatechuic acid 7.2 μg, *p*-hydroxy benzoic acid 7.5 μg, vanillic acid 3.3 μg, chlorogenic acid 14.8 μg, caffeic acid 8.2 μg, syringic acid 5.7 μg, *p*-coumaric acid 4.6 μg, ferulic acid 13.7 μg, sinapic acid 26.3 μg and total phenolic acid 116.6 μg (Kaisoon et al. 2011). The flowers contained 183.9 μg total bound phenolic acid made up of gallic acid 34.8 μg, protocatechuic acid 66.2 μg, *p*-hydroxy benzoic acid 25.5 μg, *p*-coumaric acid 15.8 μg, ferulic acid 16.3 μg and sinapic acid 25.3 μg. The flowers contained 307.4 μg total soluble flavonoid made up of rutin 5.7 μg, myricetin 4.50 μg, quercetin 294.1 μg and kaempferol 3.06 μg and bound flavonoid 130.4 μg made up of quercetin 56.1 μg and apigenin 18.2 μg. The DPPH radical scavenging activity (% inhibition) of soluble and bound phenolic fraction of the flower was 89.36 % and 34.14 %, respectively. Bound phenolics exhibited lower antioxidant activity than soluble ones. The reducing potential of the soluble and bound phenolic fraction of the flower as evaluated by FRAP (ferric reducing antioxidant power) assay (mmol $FeSO_4$/100 g dry weight) was 61.97 mmol and 91.5 mmol, respectively.

In a subsequent comparative study of four edible flowers, the phenolics (mg GAE (gallic acid equivalent)/g DW) of the flowers were determined as follows: *Tagetes erecta* (212.9) > *Antigonon leptopus* (177.2) > *Bougainvillea glabra* (138.2) > *Cosmos sulphureus* (102.5) (Kaisoon et al. 2012). Total reducing capacity (FRAP) (μmol Fe^{2+}/g DW) was ranked as *Tagetes erecta* (329.4) > *Bougainvillea glabra* (307.1) > *Antigonon leptopus* (281.9) > *Cosmos sulphureus* (99.9). The ORAC (oxygen radical absorbance capacity) (μmol T Eq (trolox equivalent)/g DW) rank was *Antigonon leptopus* (491.9) > *Tagetes erecta* (394.2) > *Bougainvillea glabra* (276) > *Cosmos sulphureus (214.8).* Cellular antioxidant activity (CAA) (μM QE (quercetin equivalent)/g DW) rank was *Tagetes erecta* (413, most effective) > *Bougainvillea glabra* (859.6) > *Cosmos sulphureus* (966.1) > *Antigonon leptopus* (967.4).

Anti-inflammatory and Antioxidant Activity

Antigonon leptopus was found to contain compounds that displayed lipid peroxidation (LPO)

and cyclooxygenase enzyme (COX) inhibitory activities (Vanisree et al. 2008). Methanol extract of the aerial parts of *A. leptopus* inhibited lipid peroxidation (LPO) by 89 % and cyclooxygenase enzymes, COX-1 and COX-2, by 50.4 % and 72.5 %, respectively, at 250 μg/mL. Purification of the methanolic extract yielded n-hentriacontane (1), ferulic acid (2), 4-hydroxycinnamic acid (3), quercetin-3-rhamnoside (4) and kaempherol-3-glucoside (5) along with β-sitosterol, β-sitosterol-glucoside and D-mannitol. Compounds 3, 4 and 5 inhibited LPO by 19.5 %, 41.0 % and 60.5 %, respectively, at 5 μg/mL. Similarly, compounds 3, 4 and 5 inhibited COX-1 enzyme by 64.7 %, 16.9 % and 38.5 % and COX-2 enzyme by 87.4 %, 88.8 % and 90.2 %, respectively, at 25 μg/mL. Compounds 3, 4 and 5 showed 50 % inhibition (IC_{50}) at 17.4 %, 68.9 % and 36.3 μg/mL, against COX-1 and 8.57 %, 7.86 % and 6.78 μg/mL for COX-2, respectively.

Recent studies reported that *Antigonon leptopus* tea as a dried extract inhibited lipid peroxidation (LPO) and cyclooxygenase, COX-1 and COX-2 enzymes, by 78 %, 38 % and 89 %, respectively, at 100 μg/mL (Mulabagal et al. 2011). Tea prepared from the aerial parts of *Antigonon leptopus* is used as a remedy for cold and pain relief in many countries. Bioassay-guided fractionation of the extract yielded a selective COX-2 enzyme inhibitory phenolic aldehyde, 2,3,4-trihydroxy benzaldehyde (compound 1). Also, it showed LPO inhibitory activity by 68.3 % at 6.25 μg/mL. Among its other hydroxy benzaldehydes and their methoxy analogues, compound 1 gave the highest COX-2 enzyme inhibitory activity as indicated by a 50 % inhibitory concentration (IC(50)) at 9.7 μg/mL. The analogues showed only marginal LPO activity at 6.25 μg/mL. The hydroxy analogues 6, 7 and 9 showed 55, 61 and 43 % of COX-2 inhibition at 100 μg/mL. However, hydroxy benzaldehydes 3 and 12 showed selective COX-1 inhibition, while compounds 4 and 10 gave little or no COX-2 enzyme inhibition at 100 μg/mL. At the same concentration, compounds 14, 21 and 22 inhibited COX-1 by 83, 85 and 70 %, respectively. Similarly, compounds 18, 19 and 23 inhibited COX-2 by 68, 72 and 70 %, at 100 μg/mL.

Antithrombin Activity

Methylene chloride and methanol extracts of *Antigonon leptopus* demonstrated antithrombin (anticoagulant) activity of 80 % or higher in the chromogenic bioassay system (Chistokhodova et al. 2002).

Analgesic and Anti-inflammatory Activities

Antigonon leptopus roots were found to possess significant analgesic and anti-inflammatory properties (Mamidipalli et al. 2008). Methanolic extract inhibited paw oedema in a dose-dependent manner. A dose-dependent analgesic action was obtained against chemical (writhing test), and thermic (hotplate test) stimuli indicating antinociceptive activity may involve inhibition of pain by peripheral and central mechanisms.

Antidiabetic Activity

Oral administration of toluene, ethyl acetate and butanone fractions of *A. leptopus* leaf methanol extract at 50 and 100 mg/kg b.w. significantly reduced the fasting blood glucose level in streptozotocin-induced diabetic rats (Swaroopa Rani et al. 2010). Among these fractions, the ethyl acetate fraction was found to be more effective. The results substantiated the traditional medicinal use of the leaves of *A. leptopus* in the treatment of diabetes. Sujatha et al. (2012) found that administration of methanol extract of *A. leptopus* flowers reduced blood glucose level in alloxan-induced diabetic rats. The antihyperglycaemic effect of the extract at 200 mg/kg b.w. was supported by the reversal of changes that occurred in other parameters such as body weight, serum insulin, aspartate transaminase (AST), alanine transaminase (ALT), serum triglycerides, serum cholesterol and serum total proteins. They found that the hypoglycaemic and antidiabetic effects of the flower extract were well comparable with glibenclamide (10 mg/kg, b.w, p.o.), a reference drug used in type 2 diabetes therapy.

Inhibitory activity of lyophilized hydrophilic extracts obtained from four edible Thai flowers against α-glucosidase enzyme was found as follows: *Tagetes erecta* (98.51 % inhibition, IC_{50} 0.06 mg/mL) > *Antigonon leptopus* (58.24 % inhibition, IC_{50} 3.26 mg/mL) > *Bougainvillea glabra* (37.30 % inhibition, IC_{50} 5.21 mg/mL) > *Cosmos sulphureus* (32.32 % inhibition, IC_{50} 5.62 mg/mL) (Kaisoon et al. 2012).

Hypolipidaemic Activity

Inhibitory activity of lyophilized hydrophilic extracts obtained from four edible Thai flowers against lipase activity was determined as follows: *Cosmos sulphureus* (43.39 % inhibition, IC_{50} 4.60 mg/mL) > *Tagetes erecta* (41.61 % inhibition, IC_{50} 4.82 mg/mL) > *Bougainvillea glabra* (40.05 % inhibition, IC_{50} 5.14 mg/mL) > *Antigonon leptopus* (26.70 % inhibition, IC_{50} 7.87 mg/mL) (Kaisoon et al. 2012).

Hepatoprotective Activity

The methanolic extract of the roots and rhizomes of *Antigonon leptopus* significantly lowered levels of serum glutamyl oxalacetic acid transaminase (SGOT), serum glutamyl pyruvate transaminase (SGPT), alkaline phosphatase (ALKP) and serum bilirubin (SBLN) levels in carbon tetrachloride-treated rats (Rao et al 2009) suggesting its high hepatoprotective activity. Similar results were obtained by Raju and Rao (2010) with ethyl acetate and methanolic extracts of *A. leptopus* root/rhizomes that protected the liver against the injury induced by CCl_4 in Wistar albino rats (Raju and Rao 2010). This was evident from significant reduction in serum enzyme, SGOT (serum glutamic oxaloacetic transaminase), SGPT (serum glutamic pyruvate transaminase), ALP (alkaline phosphatase) and total bilirubin (TB). Various pathological changes like centribular necrosis and vacuolization observed in CCl_4-treated rats were significantly protected in groups treated with *Antigonon* extract and silymarin. Administration of methanolic extract of aerial parts of *Antigonon leptopus* at doses of 200 and 400 mg/kg also inhibited CCl_4-induced liver toxicity in Wistar albino rats as assessed by the biochemical changes and histopathological studies (Angothu et al. 2010).

Antimicrobial Activity

Methanol flower extracts of five edible flowers including *Antigonon leptopus* exhibited antibacterial effect in vitro against *Staphylococcus aureus* with MIC at 50–800 µg/mL (Wessapan et al. 2007). The ethanol and chloroform extracts of *A. leptopus* flowers significantly and dose dependently inhibited growth of *Bacillus subtilis, B. pertolis* and *Salmonella typhi* (Bolla and Bhogavalli 2010). The ethanol extract and chloroform extracts of *Antigonon leptopus* flowers exhibited significant inhibition against microbial strains causing dental carries, namely, *Micrococcus albus, Staphylococcus aureus, Proteus vulgaris* and *Pseudomonas aeruginosa* (Gupta et al. 2011). All the extracts showed concentration-dependent activity comparable with the reference drug streptomycin.

Antiproliferative Activity

Antigonon leptopus flower extract had highest antiproliferative activity among the four edible flowers tested against two cancer cell lines (Kaisoon et al. 2012). The antiproliferative activity (IC_{50} mg/mL) of polyphenolic extract against HC-29 (colorectal adenocarcinoma) cells was *Tagetes erecta* > (1.5) > *Bougainvillea glabra* (1.7) > *Antigonon leptopus* (2.4) > *Cosmos sulphureus* (5.2). The antiproliferative activity (IC_{50} mg/mL) of polyphenolic extract against AGS (gastric adenocarcinoma) cells was *Antigonon leptopus* (0.2) > *Bougainvillea glabra* (2.1) > *Tagetes erecta* (2.2) > *Cosmos sulphureus* (44.8). Antiproliferative activity (IC_{50} mg/mL) of polyphenolic extract against Bl-13 (bladder cancer) cells was *Antigonon leptopus* (0.9) >

Bougainvillea glabra (2.3) > *Tagetes erecta* (3.0) > *Cosmos sulphureus* (56.5).

Antimutagenic Activity

The dichloromethane, methanol and water extract of *Antigonon leptopus* flowers were found not to be mutagenic for *Salmonella typhimurium* strains TA 98 and TA 100 without metabolic activation (Wongwattanasathien et al. 2010). Additionally, the methanol flower extract was antimutagenic on strain TA100. The results indicated that the flowers were safe to be consumed.

Anthelmintic Activity

The ethyl acetate and methanol extracts of *Antigonon leptopus* roots in doses (10, 20, 40 and 80 mg/mL) significantly paralysed earthworms (*Pheretima posthuma*) and also caused death of worms especially at higher concentration of 80 mg/mL as compared to standard drug (Raju and Rao 2011). The methanolic extract was more active than the ethyl acetate extract.

Juvenoid Activity

Antigonon leptopus was one of five most active plants exhibiting juvenoid activity against filarial mosquito *Culex quinquefasciatus* with LC_{50} value of 17 ppm (Neraliya and Gaur 2004).

Traditional Medicinal Uses

The leaves are used in Caribbean folk medicine as poultices for boils and swellings. In Trinidad and Tobago, *Antigonon leptopus* has been used in traditional medicine for diabetes and low blood pressure and as a heart tonic (Lans 2006). Tea from the leaves is used for hypertension, diabetes, flu and menstrual pains. In the West Indies, hot tea prepared from the aerial parts of *A. leptopus* is used traditionally for the prevention and treatment of cough, sore throat and flu-related pain (Mitchell and Ahmad 2006). In Sumatra it is used as a poultice and locally called 'riang-riang' (Burkill 1966). In the Philippines, an isolated report stated it is used by Ifugao migrants in the foothills of the Sierra Madre for wound closure (Stuart 2013). In Nigeria, the root extract has been employed to treat asthma, liver and spleen disorders (Idu and Onyibe 2007).

Other Uses

A. leptopus is a very good ornamental plant with amenity value. The flower inflorescence is used for floral arrangement. Its flowers provide a very good source of nectar and pollen, extensively visited by honey bees (*Apis mellifera, A. cerana, A. dorsata* and *A. florea*), also visited by a variety of solitary bee species, such as carpenter bees (*Xylocopa fenestrata*). It also provides a light brown-coloured honey which has a pleasant aroma and flavour.

Comments

The plant is deemed a weed in Fiji and completely smothers native plants in the wet season, outcompeting vines and understorey plants.

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Primula × *polyantha*

Scientific Name

***Primula* × *polyantha* Mill. (Pro. Sp.)**

Synonyms

Primula veris × *vulgaris*, *Primula* × *variabilis* non Bast. Goupil

Family

Primulaceae

Common/English Names

Elatior Hybrid Primroses, False Oxlip, Florist Primrose Polyanthus, Polyanthus Primrose, Polyanthus Primula

Vernacular Names

Dutch: Sleutelblom
French: primevère multiflore, primevère des jardins
German: die Polyanthus-Hybride, gartenprimel
Irish: Baisleach Bréige
Swedish: Trädgårdsviva
Welsh: Briallen Groesryw, Briallu Croesryw, Briallu Tal Ffug

Origin/Distribution

Polyanthus (*Primula* × *polyantha*) is a popular horticultural hybrid of *Primula polyanthus* and is a horticultural hybrid probably derived from cowslip (*P. veris*) and the common primrose (*Primula vulgaris*) (Scott-Moncrieff 1930) or a complex hybrid of primrose (*Primula vulgaris*), cowslip (*P. veris*) and oxlip (*P. elatior*) (Mabberley 1997). All the parents are native to temperate Europe and Asia. However, the true oxslip is a much rarer plant.

Agroecology

Primroses including polyanthus are cool climate plants. They grow best in areas with daytime temperatures below 26 °C and night temperatures of 10–15 °C although tolerant of subzero temperatures. They appreciate full sun in spring but prefer partial shade as the temperature warms up. They thrive in humus-rich slightly acidic soil of pH 6–6.5 that is well drained. They require regular but light watering.

Edible Plant Parts and Uses

The flowers and leaves of primroses, cowslips and polyanthus are edible (Macnicol 1967; Grieve 1971; Facciola 1990; Anonymous 2012). Fresh polyanthus blossoms can be sprinkled onto

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salad, used as garnish or used in conserves, custards tarts or confections; flowers can be crystallized and used as decorations, making them ideal for special cakes and desserts, for example, on Mothering Sunday or at Easter (Anonymous 2012). Flowers can also be used to make a tea and a wine. Leaves of primrose and cowslip can be used to prepare tea. Primrose leaves are added to salad, eaten as potherb or mixed with other herbs as stuffing for meat and poultry. Leaves of cowslip are also eaten in salad.

Botany

A herbaceous, low-growing, clumping perennial, 7–15 cm (–20 cm) high, with a basal stemless or shortly stemmed rosette of green leaves. Leaves are linear or obovate (tongue-shaped), 8–15 cm long by 3–6 cm wide with an irregularly crenate margin, textured and crinkled surface (Plates 1, 2, 3, 4, 5, 6, 7, 8 and 9). Short flower stalks arise from the centre of the rosette, each bearing a cluster of 2.5–5 cm flowers in a wide array of colours magenta, yellow, white, crimson, orange, pink and brick-red. The flowers are hermaphrodite

Plate 1 Primula flowers and leaves

Plate 2 Thrum-eyed yellow flowers

Plate 3 Pink thrum-eyed Primula flowers

Plate 4 Primula 'Crescendo Golden' (thrum-eyed yellow flowers)

Plate 5 Primula 'Crescendo Pink and Rose Shades' (thrum-eyed flowers)

Plate 6 Primula 'Crescendo Bright Red' (thrum-eyed flowers)

Plate 7 Primula 'Crescendo Blue Shades' (pin-eyed flowers)

Plate 8 Primula yellow pin-eyed flowers

Plate 9 Primula white, pin-eyed flowers

but heterostylous; individual plants bear either 'pin' flowers (longuistylous flower: with the capita of the style prominent and short stamens) or 'thrum' flowers (brevistylous flower: with short style and the stamens prominent) (Plates 1, 2, 3, 4, 5, 6, 7, 8 and 9). Fertilization can only take place between pin and thrum flowers. Calyx of five sepals, joined halfway, usually slightly inflated, generally pale green. Corolla of five lobes, prominently notched and tubular at the base. Stamens five. Ovary superior forming a capsule after fertilization which opens by valves to release the small black seeds.

Nutritive/Medicinal Properties

The magenta and dark red flowers of *P. polyanthus* were found to contain an anthocyanin pigment named primulin, which consisted of 3-monoglucosidylmalvidin chloride together with traces of a lower methylated compound (Scott-Moncrieff 1930).

The anthocyanin rosinidin was found in *P. rosea* and *P. polyanthus* (Harborne 1958). The structure of quercetin 3-glucosyl(1→2)gentiobioside, isolated from the violet blue flowers of *Primula polyantha*, was determined to be quercetin 3-*O*-(β-D-glucopyranosyl(1→2)-*O*-β-D-glucopyranosyl (1→6))-β-D-glucopyranoside (Saito et al. 1990).

Volemitol (D-glycero-D-manno-heptitol, α-sedoheptitol), an unusual seven-carbon sugar alcohol was the major nonstructural carbohydrate in leaves of horticultural hybrid polyanthus (*Primula* × *polyantha*) at all stages of development, with concentrations of up to 50 mg/g fresh weight in source leaves (about 25 % of the dry weight), followed by sedoheptulose (D-*altro*-2-heptulose, 36 mg/g fresh weight) and sucrose (4 mg/g fresh weight) (Haefliger et al. 1999). Volemitol was found to be a prominent phloem-mobile carbohydrate. It accounted for about 24 % (mol/mol) of the phloem sap carbohydrates, surpassed only by sucrose (63 %). They found a novel NADPH-dependent ketose reductase called sedoheptulose reductase to be responsible for the biosynthesis of volemitol. Sedoheptulose reductase was shown to have a pH optimum between 7.0 and 8.0, a very high substrate specificity, and displayed saturable concentration dependence for both sedoheptulose (apparent $K_m = 21$ mm) and NADPH (apparent $K_m = 0.4$ mm). Their results suggested volemitol to be important in certain *Primula* species as a photosynthetic product, phloem translocate and storage carbohydrate.

The carotenoid composition in the yellow petals of *Primula* × *polyantha* and *P. helodoxa* was (9*Z*)-violaxanthin, (all-*E*)-violaxanthin, lutein and antheraxanthin (Yamamizo et al. 2011). The carotenoid composition in the pale green petals of *P.* × *polyantha* was completely different from that in the yellow petals; the former accumulated predominantly lutein and β-carotene. Carotenoids in the yellow petals were present in the esterified form, while those in the pale green petals were in the free form. The mature petals of the yellow-flowered *P.* × *polyantha* and *P. helodoxa* contained high levels of carotenoids (>270 μg/g FW), while those of the pale green-flowered *P.* × *polyantha* contained only small amounts (<7 μg/g FW). The petals of the yellow-flowered *P.* × *polyantha* and *P. helodoxa* showed similar carotenoid profiles, predominantly accumulating (9*Z*)-violaxanthin. The levels of (all-*E*)-violaxanthin, lutein and antheraxanthin were also high.

Traditional Medicinal Uses

Polyanthus has not been reported to have traditional medicinal uses unlike its parents *P. vulgaris* (common primrose) and *P. veris* (cowslip). Both parent plants have a very long history of medicinal use and have been particularly employed in treating conditions involving spasms, cramps, paralysis and rheumatic pains, but primrose is considered to be less effective than the related cowslip (Bown 1995). Both species contain saponins, which have an expectorant effect, and salicylates which are the main ingredient of aspirin and have anodyne, anti-inflammatory and febrifuge effects (Bown 1995). The roots of flowering primrose herb are anodyne, antispasmodic, astringent, emetic, sedative and vermifuge, and an infusion is used as remedy for nervous headaches (Grieve 1971). An ointment made from the plant has been used for treating skin wounds (Phillips and Foy 1992). The yellow corolla of cowslip flower is antispasmodic and sedative (Grieve1971) and has been prescribed for treating overactivity and sleeplessness, especially in children (Chevallier 1996). They are potentially valuable in the treatment of asthma and other allergic conditions. Cowslip roots contain 5–10 % triterpenoid saponins which are strongly expectorant, stimulating a more liquid mucous and so easing the clearance of phlegm (Chevallier 1996); the root is also mildly diuretic and antirheumatic and slows the clotting of blood

(Launert 1981; Chevallier 1996). It is used in the treatment of chronic coughs (especially those associated with chronic bronchitis and catarrhal congestion), flu and other febrile conditions (Launert 1981).

Other Uses

It is a popular garden ornamental suitable for beds, containers and shady rock gardens. They combine well with spring-flowering bulbs.

Comments

According to The Plant List (2013), *Primula polyantha* Miller is an unresolved name.

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Banksia grandis

Scientific Name

***Banksia grandis* Willd.**

Synonyms

Sirmuellera grandis (Willd.) Kuntze

Family

Proteaceae

Common/English Names

Bull Banksia, Giant Banksia, Mangite

Vernacular Names

Australia: Bulgalla, Poolgarla ('Aborigines')

Origin/Distribution

The species is indigenous to south-west Western Australia.

Agroecology

The plant is adapted to a Mediterranean climate. In its native range, it occurs in sand on the coastal plain, in woodland and in heath. It is also common in laterite soil in the Jarrah forest of the Darling Plateau near Perth. Bull Banksia grows in well-drained, sandy soils and in full sun to partial shade; it is drought tolerant and moderately frost resistant to −4 °C.

Edible Plant Parts and Uses

The flower spikes can be used to make a drink of honey-sweet mead known as mangite or mungitch (SERCUL undated). The nectar can also be sucked directly from the flowers. Grubs which burrow into the flower spikes can be gathered and eaten.

Botany

Bull Banksia is a small- to medium-sized tree, grows to 4–10 m high sometimes to 15 m. It is also found in the form of a stunted, spreading shrub, near the south coast, and whenever it occurs among granite rocks. Its trunks are short, stout and often crooked and bark rough and grey.

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Plate 1 Pale yellow cylindrical flower spikes and distinctive foliage

Plate 2 Close-up of cylindrical flower spikes and triangular-lobed leaves

The leaves are most distinctive; very large, 45 cm long by 10 cm wide, and consist of a series of triangular lobes that go right back to the prominent midrib (Plates 1 and 2). The lobes are glossy green above with a soft white tomentum underneath. The cylindrical flower spikes are very large to 40 cm long by 8–10 cm across, pale yellow, made up of hundreds of flowers densely packed in a spiral woody axis (Plates 1 and 2). Flowering occurs from spring through to midsummer. The flowers are followed by very large fruiting cones.

Nutritive/Medicinal Properties

The amino acid pool of *Banksia grandis* and *Hakea prostrata* foliage were dominated by seven amino acids (aspartic acid, glutamic acid, asparagine, glutamine, serine, proline and arginine) (Warren and Adams 2000). Of these, asparagine and glutamine dominated at low N-supply, whereas at high N-supply, the concentration of arginine increased and dominated amino-N. Plants grown with nitrate had a greater concentration of proline relative to plants with ammonium. In *Banksia* the concentration of amides was greatest and arginine least with a nitrate N-source, whereas in *Hakea* amides were least and arginine greatest with nitrate N-source. The concentration of sugars was greater in *Banksia* than *Hakea* and in both species at greater N-supply. Ammonium N-application had a greater impact on leaf total nitrogen, amino acid and soluble sugar levels than nitrate N-application at the same dose of application (8 mM). Total nitrogen content (mg/g) in the leaves was 16.9 mg/g, total amino acids 63.2 μM/g and total soluble sugars 143.4 μM/g with ammonium N-application. In contrast, total nitrogen content in the leaves was 9.6 mg/g, total amino acids 39.3 μm/g and total soluble sugars 79.2 μM/g with nitrate N-application.

Banksia grandis grown on Fe-phosphate or Al-phosphate formed 'proteoid' or 'cluster' roots exuded significant amounts of carboxylates (Lambers et al. 2002). Tri- and dicarboxylates (citrate, 60 %; malate, 25 %; *trans*-aconitate, 14 %) were the major carboxylates in root exudates when phosphorus was supplied as Al-phosphate. The same tri- and dicarboxylates were also exuded when P was supplied as Fe-phosphate (31, 14 and 12 %, respectively). In addition, these plants exuded monocarboxylates (lactate, 30 %; acetate, 12 %). Cluster roots of *Banksia grandis*, *Banksia prionotes*, *Banksia occidentalis* exuded malate, malonate, lactate, acetate, maleate, citrate, fumarate and *cis*- and *trans*-aconitate (Roelofs et al. 2001). The relative contributions of each of these carboxylates differed between species. Malate, malonate, lactate, citrate and *trans*-aconitate, however, were invariably present in large proportions of total carboxylate exudation.

Bull Banksia has not been reported to have medicinal value.

Other Uses

The old fruiting cones are used by wood turners for vases, or cut and varnished to be used in decorative woodwork. When alight, the dried flower cones smoulder like a torch and are used by local Nyungar natives to transport fire from one

campsite to the next. The Nyungar people also kept the lighted cones under their cloaks to keep themselves warm in cold weather.

Comments

Propagation from seed is reliable without pretreatment, and cuttings may be successful but may be slow to strike with a success rate maybe well below 100 %. Its seeds take 22–42 days to germinate. This species develops a lignotuber and can regenerate by vegetative means from the lignotuber if the upper parts of the plant are destroyed by fire. It can also regenerate from seed.

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Banksia integrifolia

Scientific Name

***Banksia integrifolia* L. f.**

Synonyms

Banksia asplenifolia Salisb., *Banksia glauca* Cav., *Banksia integrifolia* var. *dentata* Meisn., *Banksia integrifolia* var. *major* R.Br. ex Meisn., *Banksia integrifolia* var. *minor* R.Br. ex Meisn., *Banksia oleifolia* Cav. [Illeg.], *Banksia reticulata* H. Wendl. ex Hoffmanns., *Banksia spicata* Gaertn., *Hakea pubescens* Schult. & Schult.f., *Isostylis integrifolia* Britten, *Sirmuellera integrifolia* Kuntze

Family

Proteaceae

Common/English Names

Coast Banksia, Coastal Banksia, Honeysuckle, Honeysuckle Oak, White Banksia, White Bottlebrush, White Honeysuckle

Vernacular Names

Australia: Birrna ('Gunai Aborigines'), War Rak ('Wurundjeri Abrogines')

Origin/Distribution

The species is indigenous to East and Southeast Australia, occurring in a coastal strip from Central Queensland through New South Wales to Victoria (Doran and Turnbull 1997; Boland et al. 1992). There was an isolated population on Long Island, Tasmania, in 1999, and an 1876 record allegedly from King Island (George 1999).

Agroecology

Banksia integrifolia spans a broader geographical, climatic, latitudinal, altitudinal and ecological range than any other *Banksia* species (George 1981; Thiele and Ladiges 1994). The latitudinal range is 20–40°S and the altitudinal range is from sea level to 1,700 m. It occurs in a broad range of habitats, from coastal dunes to mountains. It grows near coastal cliffs and headlands, alongside river estuaries and even on stabilized sand dunes. The temperature range for this area is around 0–30 °C, in warm subhumid and humid climatic zones with almost no frosts (Taylor and Hopper 1988; Boland et al. 1992). *B. integrifolia* is found up to 200 km inland, with *B. integrifolia* subsp. *monticola* occurring in the Blue Mountains at altitudes up to 1,500 m with 65 frosts a year. Mean annual rainfall is 850–1,200 mm with a strong summer maximum in northern areas and a spring maximum in Victoria. This species is found on a wide variety of soil types, but best development is on acidic or neutral, well-drained,

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poor quality sandy soils derived from sandstone or loamy soils and alluvia derived from granite and basalt. It grows as a component of eucalypt open forest, woodland, low woodland, shrub-land and sometimes in mixed rainforest communities.

Edible Plant Parts and Uses

Indigenous Australians obtained nectar from *B. integrifolia* by stroking the flower spikes then licking their hands or by sucking the flower spikes or by steeping flower spikes in a coolamon overnight to obtain a sweet drink (Anonymous 2006).

Botany

A perennial tree that can grow to 6–25 m tall and 3 m wide but may attain height of 35 m in sheltered position. It has a single stout trunk, often twisted and gnarled, with the rough tessellated or fissured, grey bark and striate branchlets which are pubescent when young. Leaves are dark green with a white tomentose underside (Plate 1), growing in whorls of 3–5 on 4–10 mm long petioles. Leaves are narrow-obovate to narrow-elliptic, 4–20 cm long and 6–35 mm wide, apex obtuse or acute, base cuneate to attenuate, margins shallowly dentate when young becoming entire. Flowers occur in cylindrical spikes, 10–12 cm high by 5 cm wide, consisting of several hundred flowers densely packed in a spiral around the main axis (Plate 1). Flowers are greenish or pinkish in bud and yellow when mature. Each individual flower is 22–25 mm long, consists of a tubular perianth made up of four united tepals and one long curved or straight style. Fruit cone consists of a woody axis embedded with numerous small follicles (8–15 mm long) opening when mature (Plate 2), each follicle containing 1–2 feathery black seeds, 6–10–20 mm long.

Nutritive/Medicinal Properties

No nutritive or medicinal properties have been published.

Early settlers used Coast Banksia nectar as syrup for sore throats and colds (Anonymous 2006).

Other Uses

A hardy and versatile garden plant, *B. integrifolia* is widely planted in gardens, parks and streetscapes and has been used for bush revegetation, for stabilization of dunes and as windbreaks. Its hardiness has prompted research into its suitability for use as a rootstock in the cut flower trade. Its reddish timber is sometimes used for cabinet panelling, specialty furniture, ornamental turnery and bullock yokes, and its natural bends were once sought after for making boat knees (Sedgley 1996; Cribb and Cribb 1981). It also provides a useful, quality fuelwood. More recently, it has been used in the art of bonsai (Bowie 2002). Its flowers produce nectar for honey production, pollen has value for apiculture or foliage and fruits have potential for floriculture.

Plate 1 Flowering spikes and leaves

Plate 2 Dried cone with many open follicles

Indigenous Australians also used the flower spikes as hairbrushes, and bushmen would impregnate barren 'cones' with fat to make a slow-burning candle (Sedgley 1996).

Comments

Three subspecies have been recognized (Thiel and Ladiges 1994):

- *Banksia integrifolia* subsp. *integrifolia* which extends from Southern Queensland to Victoria, occurring near coastal cliffs and headlands, river estuaries and sand dunes
- *Banksia integrifolia* subsp. *compar* is endemic to similar sites along the coast of central Queensland as far north as Proserpine; the two subspecies are distinguishable by their leaves, which are larger and glossy with wavy margins on *B. integrifolia* subsp. *compar*
- *Banksia integrifolia* subsp. *monicolia* commonly known as White Mountain Banksia, a montane species, occurring at higher altitudes in the ranges of central to northern New South Wales. It is similar in form to *B. integrifolia* subsp. *integrifolia* but differs in having longer, narrower leaves and follicles that are more deeply embedded in the old flower spike

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Telopea speciosissima

Scientific Name

***Telopea speciosissima* (Sm.) R.Br.**

Synonyms

Embothrium speciosissimum, Smith; *Embothrium spathulatum,* Cav.; *Embothrium speciosissimum* Salisb. (nom. illeg.); *Hylogyna speciosa* (Salisb.) Salisb. ex Knight (nom. illeg., nom.rej.)

Family

Proteaceae

Common/English Names

New South Wales waratah, Warath, Native Tulip

Vernacular Names

Australia: Mooloone (Dharawal Aborigines), Mewah (Aborigines)

Origin/Distribution

Waratah is endemic to New South Wales in Australia from the Watagan Mountains southward to Ulladulla, with a relatively widespread distribution in the Central Coast region (Crisp and Weston 1995).

Agroecology

Telopea speciosissima usually occurs as an understory shrub in open forest on sandy soils in areas with moderately high rainfall, receiving mean annual rainfall of 1,200 mm (Crisp and Weston 1995; Nixon 1997). Although they grow naturally on deep sandy soils, the species has been found adaptable to other deep, well-drained soils, especially where natural slopes assist drainage. Despite their natural occurrence in woodland, waratahs flowers are best in full sun, although they tolerate the dappled shade of Eucalypts dry sclerophyll forests and sandstone soils (Wrigley and Fagg 1991). Waratah is a pyrogenic-flowering species, relying on postfire flowering followed by production and dispersal of nondormant seeds to exploit favourable growing conditions in the altered environment following a fire (Denham and Auld 2002).

Waratahs are usually grown as field crops in a relatively open environment, with windbreaks for protection in some commercial plantations (Tranter 1998). However, information describing the optimal light requirements for waratah flower initiation and flower quality is contradictory. Worrall (1997) suggested that waratahs 'grow and flower best in the full sun', with shaded plants displaying less vigour, producing fewer inflorescences and flowering 2–4 weeks later

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than those in full sun. Martyn et al. (2007a) found that shading (50 % shade cloth) significantly reduced bract browning in potted and commercially grown waratahs of cultivars 'Fire and Brimstone', 'Olympic Flame' and 'Wirrimbirra White'. Shade cloth (50 %) significantly reduced the light intensity experienced by waratah plants throughout the day, as well as reduced the daily maximum temperature and minimum relative humidity. They found that bract browning in waratah was not a localized calcium-deficiency disorder (Martyn et al. 2007b). The inconsistent response of waratahs to calcium applied as a spray or to the potting media, and the lack of reduction in bract browning, suggested that factors other than calcium nutrition have a greater impact on the development and control of bract browning.

Edible Plant Parts and Uses

Waratah flowers produce copious amounts of nectar that can be sipped directly or used to make a sweet beverage (Cribb and Cribb 1987; Low 1989; Facciola 1990).

Botany

A large woody, multi-stemmed, stout shrub, growing to 3–4 m high with a spread of 2 m. Several stems arise from a distinctive woody base known as a lignotuber; the stems are sparsely branched. Leaves alternate, large 12–25 cm long, oblanceolate to narrowly obovate, dark green, irregularly and coarsely toothed, with 1–3 teeth below middle of either margin, glabrous or rarely moderately ferruginous hairy beneath (Plate 1). Conflorescence terminal, capitate, ovoid or subglobular flower heads, 5–10 cm in diameter containing up to 250 individual flowers, with red to pink ovate–lanceolate involucres bracts, the inner ones being 5–8 cm long (Plate 1). Flowers strongly incurved in bud, red, crimson, scarlet or pink, rarely white or yellow; floral orientation diagonal. Flower head retains a compact shape—before they

Plate 1 Waratah flower and leaves

mature and split open, revealing the stigma, style and anther. Perianth (4) coherent in a split tube after anthesis. Anther 4, sessile, lacking a filament and lies next to the stigma at the end of the style. Each of these sessile anthers, in the bud, is in close contact with the rather conical-shaped pollen presenter, which is placed laterally towards the end of the style. Ovary superior, unicarpellate containing numerous ovules at the base of the style atop the gynophore and crescent-shaped nectary lies at the base of the gynophore. Follicle woody, brown and woody, 8–13 cm long, splayed nearly flat after dehiscence revealing numerous winged seeds.

Nutritive/Medicinal Properties

No medicinal uses have been reported and no nutritive properties have been published for waratah.

Other Uses

Waratahs are commercially grown for its unusual, decorative and attractive three-dimensional blooms which are popularly used as cut flowers. The blooms are borne on strong, 0.3–1 m long stalks and a vase life of more than 13 days (Offord 1996). The plants are also popularly planted as ornamental and landscape features in gardens and parks. The stems are also used in basket making (Cribb and Cribb 1982).

Comments

Waratahs are particularly popular in New South Wales, where it is the state floral emblem.

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Aquilegia caerulea

Scientific Name

***Aquilegia caerulea* E. James**

Synonyms

Aquilegia advena Regel, *Aquilegia caerulea* var. *albiflora* A. Gray [Illeg.], *Aquilegia caerulea* subsp. *albiflora* (A. Gray) A. Gray ex Payson, *Aquilegia caerulea* var. *alpina* A. Nelson, *Aquilegia caerulea* subsp. *alpina* (A. Nelson) Payson, *Aquilegia caerulea* var. *daileyae* Eastw., *Aquilegia caerulea* subsp. *daileyae* (Eastw.) Payson, *Aquilegia caerulea* f. *glandulosa* Cockerell, *Aquilegia caerulea* var. *leptocera* (Nutt.) A. Nelson, *Aquilegia caerulea* var. *macrantha* Hook. ex Brühl, *Aquilegia caerulea* var. *macrantha* (Hook. & Arn.) Rapaics, *Aquilegia caerulea* var. *ochroleuca* Hook., *Aquilegia caerulea* f. *pallidiflora* Cockerell, *Aquilegia caerulea* subsp. *pinetorum* (Tidestr.) Payson, *Aquilegia caerulea* var. *pinetorum* (Tidestr.) Payson ex Kearney & Peebles, *Aquilegia canadensis* subsp. *caerulea* (E. James) Brühl, *Aquilegia formosa* var. *macrantha* (Hook. & Arn.) Brühl, *Aquilegia macrantha* Hook. & Arn., *Aquilegia oreophila* Rydb., *Aquilegia piersoniana* L.O. Williams, *Aquilegia pinetorum* Tidestr.

Family

Ranunculaceae

Common/English Names

Colorado Blue Columbine, Columbine, Rocky Mountain Columbine

Vernacular Names

Czech: Orlíček modrý
Danish: Colorado-Akeleje
Estonian: Sinine kurekell
German: Garten-Akelei, Rocky-Mountains-Akelei
Icelandic: Indíánavatnberi
Norwegian: Praktakeleie
Polish: Orlik niebieski
Spanish: Colombina del Colorado azul
Swedish: Coloradoakleja

Origin/Distribution

Rocky Mountain columbine occurs in the southern and central Rocky Mountains of North America at high elevations from Montana south to New Mexico.

Agroecology

Aquilegia caerulea is a cold-hardy, temperate perennial herbaceous species, occupying a variety of montane and subalpine habitats at elevations of 2,100–3,700 m. It is adapted to silt, sand, loam, clay loam, silt loam, sandy loam, loamy

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sand, silty clay loam and sandy clay loam soils. It prefers medium fertility, slightly acid (pH of 5.5–6.2), well-drained, moist soil in a sunny position. It also tolerates dappled shade. It is intolerant of heavy clays or waterlogged condition and is drought intolerant.

Edible Plant Parts and Uses

Aquilegia caerulea flowers are edible (Schofield 2003; Deane 2007–2012a, b). The nectar-heavy flowers are eaten as a snack or tossed into salads. They also make a good jelly.

Botany

A herbaceous, bushy clumping perennial, 20–80 cm high with slender stems. Leaves alternate, basal leaves 2–3 x-ternately compound, 9–37 cm, leaflets green adaxially, to 13–42(–61) mm, not viscid, notched and/or lobed with 2 or 3 segments on glabrous to pilose petiolules. Flowers large, upward-facing, bicoloured, erect; sepals 5, petaloid, perpendicular to floral axis, white, blue or pink, elliptic-ovate to lanceolate–ovate, 26–51 × 8–23 mm, apex obtuse to acute or acuminate; petals 5, with backward-extending, straight and slender blue, white or pink nectar-producing spurs, straight or parallel or divergent, 28–72 mm, slender, evenly tapered from base, petal blades white with basal pink or blue blotches, oblong or spatulate, 13–28 × 5–14 mm; stamens numerous, 13–24 mm with white filaments and yellow anthers (Plates 1, 2, 3, 4, 5, 6, 7 and 8). Follicles 20–30 mm; beak 8–12 mm.

Aquilegia caerulea exhibited considerable geographic variation in flower colour and in size of different floral organs, reflecting adaptation to different pollinators in different parts of its range (Miller 1981). Three major varieties were recognized on the basis of differences in flower colour and length of the floral spurs: *A. caerulea* var. *caerulea* with blue flowers and spurs of 4.0–5.0 cm, common in Colorado and northern New Mexico; *A. caerulea* var. *ochroleuca* with white flowers and spurs of 4.0–5.0 cm, occurring in central and northern Utah, Idaho and Western Wyoming; and *A. caerulea* var. *pinetorum* with pale blue or white flowers and spurs of 5.0–7.0 cm, in southern Utah and northern Arizona. Earlier, based on

Plate 1 *Aquilegia caerulea* Crimson Star

Plate 2 Flowers and leaves

Plate 3 Close-up of flower

Plate 4 *Aquilegia caerulea* Songbird hybrid

flower colour and spur length, Munz (1946) recognized five varieties.

Nutritive/Medicinal Properties

Bylka (2001) found that flowers of *Aquilegia* including *A. caerulea* contained kaempferol 3,7-*O*-diglucoside as the predominant flavonoid and also kaempferol 3,7,4′-*O*-triglucoside, kaempferol 3-*O*-glucoside, kaempferol 7-*O*-glucoside and kaempferol 7,4′-*O*-diglucoside.

Plate 5 Close-up of flowers

Plate 6 *Aquilegia caerulea* with white flowers

Plate 7 *Aquilegia caerulea* with pink flowers

Plate 8 *Aquilegia caerulea* with pale yellow flowers

The content of 4′-methoxyapigenin 6-C-glucoside (isocytisoside) was the main component determined in the methanol extracts of leaves and stem of *Aquilegia* species including *A. caerulea* (Bylka 2001). The flavonoid fraction comprised also isocytisoside 7-*O*-glucoside, isooreintin, orientin, apigenin, apigenin 7-*O*-glucoside, apigenin 7-*O*-rutinoside and isovitexin 3′*O*-glucoside.

The Gosiute tribe used the plant for heart pain, chewed the seeds of *Aquilegia caerulea* or used an infusion made from the roots to treat abdominal pains or as a panacea (Moerman 2009).

Other Uses

The plant is widely planted as ornamental in borders, cottage gardens, open shade gardens, native plant gardens or naturalized areas.

Comments

Most authors have spelled the epithet ‘caerulea’; ‘coerulea’ is the original spelling. Columbine (as *Aquilegia caerulea*) is the state flower of Colorado.

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Rosa × hybrida

Scientific Name

Rosa* × *hybrida (see origin)

Synonyms

None

Family

Rosaceae

Common/English Names

Rose, Common Rose, English, Hybrid Tea Rose, Floribunda Rose, Hybrid Musk Rose, Hybrid Perpetual Rose (see plates)

Vernacular Names

Arabic: Zaira
Bosnian: Ruža
Brazil: Roseira
Breton: Roz
Catalan: Rosa
Chinese: Xiang Shui Yue Ji
Croatian: Ruža
Czech: Růže
Danish: Rose
Dutch: Roos, Roze
Estonian: Roos, Roosa, Roosipõõsas
Esperanto: Rozo
Finnish: Ruusut
French: Rose, Rosier
German: Rose, Tea Rose
Hungarian: Rózsa, Rózsaszín
India: Gulab (Hindi), Gulab (Manipuri), Gulap (Marathi), Jappa, Jawaa (Sanskrit), Roja (Tamil)
Indonesian: Bunga Mawar
Italian: Rosa
Japanese: Bara
Korean: Jangmi
Lithuanian: Rožinė, Rožė
Malaysian: Bunga Ros, Bunga Mawar
Maltese: Roża, Sġajra, Warda
Norwegian: Rosa, Rose, Roseslekta
Polish: Róża, Różowy
Portuguese: Rosa
Romanian: Trandafir, Trandafiriu
Russian: Роза
Slovenian: Vrtnica
Spanish: Rosa, Rosado
Swedish: Ros
Thai: KuħLāb
Turkish: Gül
Vietnamese: Hoa Hồng
Welsh: Brail, Breila, Breilylwyn, Rhôs, Rhoswydd, Rhosyn

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Origin/Distribution

The species *Rosa* × *hybrida* is an artificial category that encompasses modern roses and is not an accepted species in the botanical sense but a complex artificial species category that is used to described non-species roses and modern rose cultivars (Gudin 2000, 2003). *Rosa hybrida* is a heterozygous tetraploid species that arose from complex interspecific crosses involving only ten wild species among the >100 belonging to the genus *Rosa*. According to Wylie (1954) modern cultivated roses were developed through crosses among only eight diploid species which are all classified into septet A. Hurst (1925, 1928) considered the basic rose chromosome number 'septet' ($n=7$) as a unit and classified diploid rose species into five categories, septet A to E, and the double septets in differential diploid species as AA, BB, CC, DD and EE based on morphological, physiological and ecological characteristics; mitotic and meiotic chromosome configurations; and genetical tests. The polyploid species of *Rosa*, so far known, are triploid, tetraploid, pentaploid, hexaploid or octaploid in their septets of chromosomes. Modern roses that possess the recurrent flowering character originated from early hybrids developed from crossing of *R. chinensis* Jacq. and *R. chinensis gigantean* Coll. (section Indicae) cultivars with the recessive gene for 'recurrent flowering' introduced into Europe around 1800 AD with cultivars of short flowering season, including *R. damascena* Mill. (section Gallicanae) and *R. moschata* Herrm. and *R. multiflora* Thunb. (section Synstylae) (Yokoya et al. 2000). Modern roses are grouped into horticultural classes that include polyanthas ($2n=2x$), hybrid teas ($2n=3x,4x$), floribundas ($2n=3x,4x$) and miniatures ($2n=2x,3x,4x$), the genomic origins of which have been partially obscured by intercrossing. Hybrid teas and floribundas (derived from hybrid teas) make up the largest and most popular classes of modern roses (Phillips and Rix 1988; Cairns 2003; Zlesak 2006).

Agroecology

Garden rose grows and flowers well in cool subtropical to temperate climatic regimes. Temperature and light have been found to be the primary factors influencing rose crop growth and development and flowering. Light intensity affects mainly the photosynthetic rate (Pasian and Lieth 1989), while temperature affects both photosynthesis of leaves and development of shoots (Moe and Kristofferson 1969; Moe 1972, 1988; Zieslin et al. 1987; Lieth and Pasian 1990). Low temperatures <15 °C produce malformed flowers, blind shoots and poor flower colour (Moe 1988), and frost is detrimental. High temperatures above 25 °C produce smaller flowers, more leafy growth and paler flower colour (Moe 1988; Moe and Kristofferson 1969). At 18 °C, 3–3.5 times more flowers per plant were harvested, compared with a constant temperature of 12 °C, due to lower blind shoot formation at this high temperature (Moe 1988). With fluctuating day and night temperatures, an average temperature of 18 °C produced approximately the same yield as a constant temperature of 18 °C. Night temperatures in the range of 14–18 °C were found to be optimal (Moe 1972; Zieslin et al. 1987). Rose grows and flowers best under full sun. Low light intensities exacerbated blind shoots (Moe 1988; Moe and Kristofferson 1969). Day extension lighting with incandescent lamps (low R:FR ratio) inhibited lateral bud growth and induced blind shoot formation, while lighting with fluorescent lamps (high R:FR ratio) had the opposite effect, indicating blind shoot formation to be controlled by the phytochrome. Blom and Tsujita (2003) found optimal production achieved with a light sum of 12–15 mol/m^2/day plants grown undercover required supplemental lighting.

Roses grow best under full sun, in well-drained, fertile loamy soils rich in organic matter. Roses are quite drought and salinity tolerant. Roses require a deep, twice weekly watering; a feeding with an organic fertilizer two or three times a year; and a good mulch of compost during

the winter. Pruning is essential in midwinter and deadheading should never be neglected to ensure masses of blooms.

Edible Plant Parts and Uses

All roses are edible (Barash 1993; Lauderdale and Evans 1999; Roberts 2000; Newman and O'Connor 2009; Rop et al. 2012) with the flavour being more pronounced in the darker varieties. The petals can garnish ice cream and desserts or scattered in desserts or salads. Petals can be used in herbal teas, syrups, jellies, perfumed butters, sweet spreads and sauces or crystallized. Frozen petals in ice cubes can be floated in punches. According to Wilson (2013) all rose petals are edible, but the bitter white base has to be removed first; the perfumed petals are often added to summer cocktails, floating decoratively on the surface of your drink, but they also make a great garnish for light desserts. The darker the petal, the richer the flavour. Crushed rose petals and rose powder are used for flavouring cakes, jellies, jams, wines and sweetmeats. Alcoholic extracts or aqueous distillates ('rose water', obtained as a by-product when distilling oil of rose petals) are also used in the kitchen. Rose hips are used for tisanes, jams, jellies, syrups, rose hip soup, beverages, pies, breads, wines and marmalades. They can also be eaten raw, like a berry, if care is used to avoid the hairs inside the fruit. Rose hips can be used to make 'palinka', a traditional Hungarian alcoholic beverage. Some recipes listed by Roberts (2000) include rose hip syrup, rose petal cream jelly and rose punch. Rose petal syrup and rose petal tea (Plate 11).

The reddish brown, tender shoots of any roses including the old roses are eaten raw or steamed in lablab and eaten with rice in Indonesia (Ochse and Bakhuizen van den Brink 1980).

Plate 1 Hybrid tea 'Lincoln'

Plate 2 Hybrid tea 'Iceberg'

Plate 3 Hybrid tea 'Double Delight'

Botany

R. × *hybrida*—thorny semi-evergreen to evergreen shrubs up to 1.5 m high or higher when grown as standards (Plates 1, 2, 3, 4, 5, 6, 7 and 8). Stem and branches are robust, glabrous with curved thorns. Leaves imparipinnate with leafy stipules adnate to the 5–10 cm long petioles; leaflets 5–9, elliptic, ovate, or oblong-ovate, 2–7 × 1.5–3 cm, leathery, light to dark-green, both surfaces glabrous, apex acute or acuminate, base

Plate 4 Floribunda bush 'Gold Bunny'

Plate 5 Floribunda rose cv. Cathedral City

Plate 6 Floribunda rose 'Bonica'

Plate 7 Dublin Bay climbing rose

cuneate or sub-obtuse, margin appressed-serrate (Plates 1, 2, 3, 4, 5, 6, 7 and 8). Flowers solitary, or 2 or 3 and fasciculate, very fragrant, 3–12 cm across; pedicel 2–3 cm on long stem; bracts 1–3 linear with attenuate tips; hypanthium oblate containing several inferior carpels; sepals 5 abaxially glabrous, adaxially densely villous, margin entire, apex long acuminate, after anthesis reflexed, deciduous; petals numerous (20–50), imbricate, semi-double or double, obovate, base cuneate, apex emarginate white, red, pink, yellow, orange, purple, fragrant (Plates 1, 2, 3, 4, 5, 6, 7 and 8); ovary inferior; styles free, exserted, nearly equaling stamens. Stamens numerous radiating with concolorous anther. Hip—an aggregate fruit of several fruitlets, oblate, orangey red to red when ripe, comprising outer fleshy hypanthium containing numerous seeds embedded in a mass of stiff hairs (Plates 9 and 10).

Nutritive/Medicinal Properties

Flower Nutrients and Phytochemicals

Rop et al. (2012) reported that edible flowers of *Rosa odorata* had a dry matter content (%w/w) of 10.09 %, crude protein of 2.66 g/kg, and the

Plate 8 Multiflora climbing rose 'Cottage pink'

Plate 9 *R. hybrida* rose hip

Plate 10 X-section of rose hip

Plate 11 Rose petal tea

following elements (mg/kg fresh mass (FM)): P 225.17 mg, K 1,969.11 mg, Ca 275.15 mg, Mg 141.83 mg, Na 76.61 mg, Fe 3.55 mg, Mn 3.44 mg, Cu 2.28 mg, Zn 4.55 mg and Mo 0.64 mg. The flowers had total antioxidant capacity of 6.85 g ascorbic acid equivalents/kg FM, total phenolic content of 5.02 g gallic acid/kg FM and total flavonoid content of 2.04 g rutin/kg FM.

In a survey of pigments found in the flowers and fruits of old and modern varieties of roses, Eugster et al. (1991) reported that yellow colours were produced by carotenoids, the reds by anthocyanins and the modern oranges by a mixture of the two. They found the old yellow roses, which arose from crosses with Chinese varieties, mainly contained carotenoids from early stages in the biosynthesis, while in the modern yellow roses, which were descended from Central Asian *foetida* types, hydroxylations, epoxidations and epoxide transformations readily occurred. They presented a carotenoid degradation sequence as follows: $C_{40} \rightarrow C_{13} + C_{27} \rightarrow C_{13} + C_{14}$. The C_{13} compounds were reported to be odoriferous substances that contributed to the scent of roses and that copigmentation with flavonol glycosides was crucial for stabilization of the anthocyanin chromophores. Many roses, including the 'apothecary's rose', which was once used medicinally, were found to contain large amounts of strongly astringent ellagitannins, monosaccharide esters of gallic acid.

In a survey of flower flavonoids in 120 taxa from 10 sections of subgenus *Rosa*, 19 flavonols and six anthocyanins were detected as follows: six

kaempferol glycosides 3-glucoside (in 99 % taxa), 3-rutinoside (63 %), 3-sophoroside (60 %), 3-rhamnoside (70 %), 7-glucoside (94 %) and 4′-glucoside (4 %); six quercetin glycosides 3-glucoside (91 %), 3-glucuronide (62 %), 3-rutinoside (63 %), 3-sophoroside (69 %), 7-glucoside (90 %) and 4′-glucoside (4 %); seven unidentified flavonols; two cyanidin glycosides 3,5-diglucoside (68 %) and 3-glucoside (16 %); two peonidin glycosides 3,5-diglucoside (41 %) and 3-glucoside (4 %); and two unidentified anthocyanins (Mikanagi et al. 1995). *Rosa* plants contained large amounts of kaempferol and quercetin 3-sophorosides and anthocyanins in their petals, but they did not contain 4′-glucosides. Anthocyanins—3-glucosides and 3,5-diglucosides of cyanidin, pelargonidin and peonidin, 3-rutinosides and 3-*ρ*-coumaroylglucoside-5-glucosides of cyanidin and peonidin and cyanidin 3-sophoroside—were isolated from the flowers of 44 taxa of 3 sections (*Cinnamomeae* (=*Rosa*) 26, *Chinenses* 8 and *Gallicanae* 10) and eight modern garden roses in the genus *Rosa* (Mikanagi et al. 2000). Four anthocyanins—cyanidin 3-rutinoside, peonidin 3-rutinoside, peonidin 3-*ρ*-coumaroylglucoside-5-glucoside and cyanidin 3-sophoroside—were found in *Rosa* flowers.

Anthocyanin had been reported to be the principal pigment in rose flowers, conferring intense red to blue cyanic colours on petals and helping to attract pollinators, and its biosynthesis involved glycosylation steps mediated by a single enzyme glucosyltransferase (Ogata et al. 2005). *Rosa hybrida* petals were found to contain anthocyanidin 5,3-glucosyltransferase (A53GT) that catalysed 5-glucosylation of anthocyanidins and then 3-glucosylation to accumulate anthocyanidin 3,5-diglucoside, the dominant anthocyanin in *Rosa hybrid* petals. Fukuchi-Mizutani et al. (2011) reported rose petals to contain 3-glucosylated anthocyanidins and flavonols, and they isolated three flavonoid 3-glucosyltransferase (UF3GT) homologue genes (RhUF3GT1, RhUF3GT2 and RhUF3GT3) from *Rosa* × *hybrida*. Their findings suggested that RhUF3GT2 catalysed flavonol 3-glucosylation in rose petals and that it also contributed to accumulation of anthocyanidin 3-glucoside in the petals.

Rosa hybrida was reported to lack violet to blue flower varieties due to the absence of delphinidin-based anthocyanins, usually the major constituents of violet and blue flowers, because roses do not possess flavonoid 3′,5′-hydoxylase (F3′5′H), a key enzyme for delphinidin biosynthesis (Katsumoto et al. 2007). The downregulation of the endogenous dihydroflavonol 4-reductase (DFR) gene and overexpression of the *Iris* × *hollandica* DFR gene in addition to the viola F3′5′H gene in a rose cultivar successfully generated blue-hued rose flowers by accumulating delphinidin. Thus these transgenic *Rosa* × *hybrida* petals accumulated delphinidin 3-glucoside as well as delphinidin 3,5-diglucoside. Changes in petal colour from yellow to red in *Rosa* × *hybrid* ‘Charleston’ were due to accumulation of cyanidin 3-glucoside after flower opening (Hennayake et al. 2006b). These results indicated that rose petals should have a pathway leading to anthocyanidin 3-glucoside in addition to the pathway catalysed by A53GT. Mature petals of ‘Charleston’ and ‘Ehigasa’ were found to accumulate cyanidin 3-glucoside and cyanidin 3,5-diglucoside (Hennayake et al. 2006a). Culture cells derived from rose leaves treated with UVB radiation and media stress produced cyanidin 3-glucoside (Hennayake et al. 2006b). Earlier, Helsper et al. (2003) found that supplemental UVA radiation induced small increases in levels of chlorophylls a and b, the carotenoids antheraxanthin and lutein and β-carotene and high increases in the flavonols quercetin and kaempferol in the leaves but not petals of *Rosa hybrida* cv. Honesty. UVA induced increases in concentrations of these antioxidant species and did not lead to significant increases in antioxidant capacity of tissues, but light absorption at 355 nm of leaf extracts was significantly increased upon UVA exposure. Their results suggested that the major protection towards UVA exposure, in particular in rose leaves, would originate from absorption of irradiation and not from scavenging reactive oxygen species.

Two novel pigments were found to coexist with anthocyanins in the mauve rose *Rosa hybrida* ‘M’me. Violet’ (Fukui et al. 2000). The major blue pigment, rosacyanin A, and the minor red one, rosacyanin B, possessed molecular

formula of $C_{56}H_{37}O_{31}$ and $C_{22}H_{11}O_9$, respectively. Rosacyanin B had structure where the C-1-position of gallic acid was bound to the C-4-position of cyanidin by C–C bond formation (Fukui et al. 2000, 2002). Rosacyanin A had a structure where the 3-position of flavylium in rosacyanin B was linked by an ether bond to the hexahydroxydiphenoyl part of tellimagrandin II (Fukui et al. 2000). Another two novel blue pigments, rosacyanins A1 and A2, were isolated from the petals of *Rosa hybrida* cv. 'M'me. Violet' with molecular formulas of $C_{56}H_{37}O_{31}$ and $C_{63}H_{41}O_{35}$, respectively (Fukui et al. 2006). The structures of rosacyanins A1 and A2 consisted of a common chromophore containing cyanidin with a galloyl group link between positions 4 and 5 of the hydroxyl group of the flavylium nucleus and tellimagrandins.

Total anthocyanin in the 60 mg/g dry wt consisting of various mixtures of cyanidin 3,5-diglucoside and pelargonidin 3,5-diglucoside was observed, while only pure cyanidin 3,5-diglucoside was found to accumulate in amounts above 60 mg/g dry wt petals of more than 100 cyanic cultivars of *Rosa* × *hybrida* (Biolley et al. 1994b). Only a small amount of the related 3-monoglucosides was detected, and peonidin 3,5-diglucoside was rarely present. Cultivars producing almost exclusively kaempferol, as well as those dominated by quercetin, exhibited chemotypes based mainly on 3-glucosides, 4′-glucosides and 3-rhamnosides. Native glycosides of cyanidin, pelargonidin, quercetin and kaempferol were precisely quantified in four modern rose varieties (*Rosa* × *hybrida*) (Biolley et al. 1994a). Mutations strongly enhanced flavonol glycoside (quercetin or kaempferol), as well as anthocyanin concentrations. The increase of the total flavonol concentrations, without changes in the balance between kaempferol and quercetin, also led to new distributions between the different flavonol glycosides. Anthocyanins found in the red petals of Korean edible rose (*Rosa hybrida* cv. Noblered) were characterized as cyanidin 3,5-di-*O*-glucoside and pelargonidin 3,5-di-*O*-glucoside (Lee et al. 2011b). Cyanidin 3,5-di-*O*-glucoside was the predominant constituent (375 mg/100 g), representing about 85 % of the total content.

The content of major anthocyanins in rose petals, cyanidin-3,5-di-glucoside, pelargonidin-3,5-di-glucoside, cyanidin-3-glucoside, pelargonidin-3-glucoside and peonidin-3-glucoside, was drastically reduced after Regalis® (prohexadione-calcium) application in both orange-red cultivar 'KORcrisett' and a dark-red cultivar 'KORikis' (Schmitzer et al. 2012). Also, the content of quercetin and kaempferol compounds generally decreased to the point of detection; however, newly formed eriodictyol was identified in the petals of the treated 'KORikis' flowers 15 days after application and in the petals of 'KORcrisett' flowers 9 and 15 days after application. A significant visual change in red petal coloration was observed and recorded as a decline of the colour parameter a^* after the application of Regalis® on day 9 and particularly on day 15. Similarly, lightness (L^*) increased and chroma (C) decreased in both analysed cultivars as expected in paler petals. Foliar application of ProCa thus altered visual properties of red roseflowers, which had been directly correlated to the content of anthocyanins, and also induced the formation of 3-deoxyflavonoids, normally not present in roses under natural conditions.

The β-D-glucosides of geraniol, nerol and citronellol were isolated hybrid tea rose 'Lady Seton' flowers (Francis and Allcock 1969). Accumulation of both free monoterpenes and monoterpene β-D-glucosides occurred when the flower opened. Both forms were present at maximum levels of 100–200 μg/g wet weight monoterpene although the maximum levels of monoterpene β-D-glucosides occurred at an earlier stage of flower maturity than do those of the free monoterpenes. Volatile components emitted in the headspace of rose flowers included monoterpenols geraniol, nerol and citronellol; oxidized monoterpenols *E*-citral, *Z*-citral and methylgeranylate; sesquiterpenes and dihydro-β-ionone *trans*-caryophyllene, β-cubebene and dihydro-β-ionone; and aliphatic and aromatic compounds 2-phenylethanol, 2-phenylethyl acetate, 3,5-dimethoxytoluene and hexyl acetate (Helsper et al. 1998). A total of 41 compounds comprising alcohols, aldehydes, alkanes, monoterpenes, sesquiterpenes, esters, ethers and ketones were

identified in the floral fragrances of *Rosa hybrida* (Kim et al. 2000). Citral, *n*-nonane, *n*-butyl acetate, *n*-decane, β-phenylethyl acetate and hexadecanol were major components. It was also found that floral fragrance of *Rosa hybrida* contained 2-ethyl hexanol, hexadecanol, *cis*-3-hexen-1-ol, pentadecanol, tetradecanol, benzaldehyde, hexadecane, tetradecane, benzyl acetate, methyl benzoate, methyl salicylate, cineole, 2-cyclohexen-1-one and isophorone which were not reported earlier. Floral fragrances differed between rose species and sample to sample within a single species. The cultivar 'Cardinal' contained sesquiterpene caryophyllene, hexadecanol, hexanol and nonane as the major components. Citral and β-myrcene were abundantly present in 'Silva' species cv.; and 'Sandra' cultivar contained significantly higher amounts of β-myrcene, limonene and caryophyllene. Small amounts of geranyl acetate, neryl acetate and undecanone were found in 'Cardinal' and 'Silva'. Pentadecanol was found only in 'Cardinal', whereas methyl eugenol and β-citronellol were observed only in 'Silva'. Also, endocrine disruptors such as bis(2-ethylhexyl) phthalate was detected.

The aroma of roses (*Rosa hybrida*) was found due to more than 400 volatile compounds including terpenes, esters and phenolic derivatives (Shalit et al. 2003). 2-Phenylethyl acetate, *cis*-3-hexenyl acetate, geranyl acetate and citronellyl acetate were identified as the main volatile esters emitted by the flowers of the scented rose var. 'Fragrant Cloud'. They found a cDNA (RhAAT1) gene encoding a protein with acetyl-coenzyme A/geraniol acetyltransferase enzymatic activity was expressed exclusively in floral tissue with maximum transcript levels occurring at stage 4 of flower development, where scent emission was at its peak. Earlier studies by Helsper et al. (1998) had shown diurnal oscillation of scent emission in rose flowers with a peak during the day. A similar daily fluctuation was found in the endogenous level of geranyl acetate and in the expression of its biosynthetic gene, alcohol acetyl transferase (RhAAT) in *Rosa hybrida* cv. Fragrant Cloud (Hendel-Rahmanim et al. 2007). Geranyl acetate production was found to be limited by the level of its substrate geraniol, which was suppressed under continuous light conditions.

The methoxylated phenolic derivative 3,5-dimethoxytoluene (orcinol dimethyl ether) was found to be one of the most prominent compounds in the floral volatiles of many rose (*Rosa hybrida*) varieties (Lavid et al. 2002). Cell-free extracts derived from developing rose petals displayed *O*-methyltransferase (OMT) activities towards several phenolic substrates, including 3,5-dihydroxytoluene (orcinol), 3-methoxy,5-hydroxytoluene (orcinol monomethyl ether), 1-methoxy, 2-hydroxybenzene (guaiacol) and eugenol. The activity was most prominent in rose cv. Golden Gate, a variety known to produce relatively high levels of orcinol dimethyl ether, as compared with rose cv. Fragrant Cloud, an otherwise scented variety but which emitted almost no orcinol dimethyl ether. The authors found enzymes, designated orcinol OMTs (OOMT1 and OOMT2), were closely related to other plant methyltransferases whose substrates range from isoflavones to phenylpropenes. The peak in the levels of OOMT1 and OOMT2 transcripts in the flowers coincided with peak OMT activity and with the emission of orcinol dimethyl ether. In separate studies Scalliet et al. (2002) found two methylated phenolic derivatives, 3,5-dimethoxytoluene and 1,3,5-trimethoxybenzene, to be major scent components in Chinese rose species and in many modern varieties. They showed that cell-free extracts of rose petals orcinol *O*-methyltransferases catalysed the biosynthesis of 3,5-dimethoxytoluene (DMT) and 1,3,5-trimethoxybenzene from un-methylated precursors. The phenolic methyl ether 3,5-dimethoxytoluene (DMT) was reported to be a major scent compound of many modern rose varieties, and its fragrance afforded the characteristic 'tea scent' that gave their name to tea and hybrid tea roses (Scalliet et al. 2006, 2008). The last steps of the biosynthetic pathways leading to DMT involved two methylation reactions catalysed by the highly similar orcinol *O*-methyltransferases (OOMTs) 1 and 2. OOMTs were shown to be localized specifically in the petal, predominantly in the adaxial epidermal

cells, making petals the major source of scent in *Rosa* × *hybrida*. They found that in heavily scented cultivars, the spectrum and amount of volatiles emitted by the flower broadly correlated with the spectrum and contents of volatiles contained within the petal, throughout petal development (Bergougnoux et al. 2007). Analysis of rose cultivars that lacked a detectable scent indicated that the absence of fragrance was due to a reduction in both the biosynthesis and emission of scent volatiles. The upper epidermal layer of cells and the epicuticular wax surface of Lady Seton rose petals were found to be sites of biosynthesis and accumulation, respectively, of terpinyl fatty acyl esters (Dunphy 2006). These esters represented 14–64 % of the total monoterpenes present in the petals. The lipophilic nature of these non-volatile esters of the monoterpene alcohols contrasted with that of the lipophilic volatile parent alcohols themselves and with the hydrophilic, non-volatile, glucoside derivative of the other principal petal fragrant compounds, the phenylpropanoids, β-phenyl ethanol and benzyl alcohol. These latter compounds were also synthesized and are resident in the petal.

Volatile components emitted in the headspace of rose flowers were geraniol, nerol, citronellol, *E*-citral, *Z*-citral, methylgeranylate, *trans*-caryophyllene, β-cubebene, dihydro-β-ionone, 2-phenylethanol, 2-phenylethyl acetate, 3,5-dimethoxytoluene and hexyl acetate (Helsper et al. 1998). When exposed to a 12 h photoperiod, these components showed maximum emission during the light period and a rhythmicity which differed for the individual compounds. Rhythmicity in emission was not observed when flowers were kept in darkness before flower bud opening, but started immediately upon exposure to a 12 h photoperiod. A total of 46 compounds were identified in Korean *Rosa hybrida* cv. Mi-hyang (Cho et al. 2006). The identified compounds comprised 17 alcohols, 14 carbonyls, 7 aliphatic hydrocarbons, 2 terpene hydrocarbons, 4 benzenes, 1 ester and 1 miscellaneous compound. Quantitatively, carbonyls (12.96–21.79 % in essential oils of SDE (steam distillation and solvent extraction) and 2.89–8.44 % in SPME (solid phase micro extraction) headspace) and alcohols (7.98–11.73 % in essential oils of SDE and 3.39–17.35 % in SPME headspace) were dominant in Mi-hyang's volatiles. In SDE extracts, 3,5-dimethyoxy toluene (10.93 %), tricosane (9.90 %), β-ionone (9.15 %), eicosane (6.70 %), dihydro-β-ionone (6.39 %), dihydro-β-ionol (6.94 %) and *trans*-2-hexenal (6.04 %) on DB-5MS column and 2,7-dihydroxy-4-m ethylcyclohepta-2,4,6-trien-1-on (6.22 %), heneicosane (5.33 %), β-ionone (4.43 %) and dihydro-β-ionol (2.29 %) on Innowax column were the major compounds, quantitatively. In the SPME headspace 3,5-dimethyoxytoluene (9.66 %), β-ionone (3.18 %) and 2,4-diisocyanto-1-methyl-1-benzene (2.59 %) on DB-5MS column and 1,2-butanediol (13.78 %), 3,5-dimethyoxy toluene (5.31 %) and diphenyl methanone (1.56 %) on Innowax column were the major compounds. Several compounds with rose odour and other floral notes detected included dihydro-β-ionone (woody), β-ionone (fruity), linalool (1.42 %) (floral), α-terpineol (0.34 %) (sweety), *trans*-2-hexenal (leafy), geranyl acetate (0.20 %) (rose lavender), benzyl alcohol (0.68 %) (burning note), methyl eugenol (0.79 %), eugenol (0.84) (clove-like), dihydro-β-ionol (6.94 %) (woody flowery), hexanal (0.55 %) (fruity), nerolidol (0.44 %) (rose-like), 2,4-hexadienal (0.01 %) (fresh floral), benzaldehyde (0.03 %) (bitter almond), theaspirane (4.06 %) (sweet fruity), β-caryophyllene (0.19 %) (clove-like), nonanal (0.06 %) (citrus-like), furfural (0.52 %) (penetrating), 2-pentenal (0.2 %) (green), *cis*-3-hexenol (1.05 %) (green), 1-penten-3-ol (0.04 %) (mild green) and linalool oxide (0.06 %) (sweety wood). Other minor compounds found in small amounts were ethyl alcohol, 2-penten-1-ol, 1-hexenol, 1,3-butanediol, phenyl ethyl alcohol, 2,6-bis[1,1-dimethylethyl]-4-methyl phenol, geranyl linalool isomer, (*E,E*)-2,4-heptadienal, dihydro-2[3H]-furanone, benzeneacetaldehyde, 2,7-dihydroxy-4-ethylcyclohepta-2, 3,6-trien-1-one, heptadecane, nonadecane, heneicosane, docosane, tetracosane, methyl-benzene (toluene), 2,4-disiocyanto-1-methyl-benzene and 1,3,5-trimethoxy benzene. Rose oil was found to contain nine compounds identified as myrcene,

benzyl alcohol, 2-phenethyl alcohol, citronellol, geraniol, citronellyl acetate, eugenol, geranyl acetate and methyl eugenol (Umezu et al. 2002).

Headspace solid phase microextraction combined to capillary gas chromatography (HS–PME–GC) was applied for the determination of changes in the volatile profile of rose petals (*Rosa hybrida*, cvs. David Austin) following processing (heat treatment and addition as an ingredient to a food product, e.g. yoghurt) (Bianchi et al. 2007). Polydimethylsiloxane–divinylbenzene (PDMS–DVB) fibre at the sampling temperature of 60 °C was the most suitable to sample the rose alcohols phenyl ethanol, citronellol, nerol, geraniol and eugenol.

Leaf Phytochemicals

Phenolic and flavonoid compounds detected in aqueous 80 % methanol leaf extract of rose (*R. hybrid*a) included unknown phenolic acid, 3-*O*-caffeoylquinic acid (neochlorogenic acid), 5-*O*-caffeoylquinic acid (chlorogenic acid), quercetin-3-*O*-gentiobioside, quercetin diglycoside, quercetin derivative, quercetin pentoside, quercetin-3-*O*-galactoside (hyperoside), quercetin-3-*O*-rutinoside (rutin), quercetin-3-*O*-glucoside (isoquercitrin), quercetin-3-*O*-arbinoside (avicularin), quercetin-3-*O*-rhamnoside (quercitrin), kaempferol-3-*O*-pentoside and kaempferol-3-*O*-rhamnoside (afzelin) (Shetty et al. 2011).

Antioxidant Activity

Rose petal teas from different cultivars exhibited scavenging capacity towards 2,2′-azino-bis-(3-ethylbenzothiazoline)-6-sulfonate cation radical (ABTS+) ranging between 712.7 and 1,770.7 μM trolox equivalents (TE) per gram of dry petals, as compared with 1,227.6 μM TE/g dry weight in green tea (Vinokur et al. 2006). The range of total phenols content in rose teas was 50.7–119.5 mg gallic acid equivalents (GAE)/g dry matter, as compared with 62.1 mg GAE/g dry weight in green tea. The rose teas were rich in free gallic acid. The highest values of antioxidant activity, total phenols and gallic acid contents were found in the cultivars San Francisco, Katharina Zeimet and Mercedes and in the essential-oil-bearing rose *Rosa damascena*. The correlation coefficients between antioxidant activity, the contents of total phenols and of gallic acid in various rose cultivars, on the other hand, were 0.79 and 0.81, respectively. Four essential oils including rose oil inhibited hexanal oxidation by over 95 % after 40 days at 500 μg/ml in the aldehyde/carboxylic assay and exhibited DPPH scavenging abilities from 39 % for angelica seed oil to 90 % for jasmine oil at 200 μg/ml (Wei and Shibamoto 2007). Rose oil also inhibited (46 %) malonaldehyde formation from squalene. The main compound of rose oil showing high antioxidant activity was citronellol (34.2 %). Cyanidin 3,5-di-*O*-glucoside, isolated from *Rosa hybrida* cv. Noblered petals, exhibited good scavenging activity against DPPH radical with IC_{50} value of 55.2 μg/ml (Lee et al. 2011b).

Anticancer Activity

Pelargonidin 3,5-di-*O*-glucoside, isolated from *Rosa hybrida* cv. Noblered petals, showed potent anticancer effects against LNCap (human prostate cell line), ACHN (human renal cell line) and MOLT-4 F (human leukaemia cell line) cell cultures, with IC_{50} values of 6.43, 18.3 and 6.78 μg/ml, respectively (Lee et al. 2011b). Anti-allergic activities were only moderate.

Anti-inflammatory Activity

Oral administration (200 mg/kg) of *Piper cubeba* (fruit), *Physalis angulata* (flower) and *Rosa hybrida* (flower) extracts exhibited inhibitory effects against acute and subacute inflammation as determined by carrageenan-induced paw oedema and arachidonic acid-induced ear oedema (Choi and Hwang 2003). Also, administration (200 mg/kg, p.o.) of the plant extracts for 1 week significantly inhibited type IV allergic reaction in mice induced by formaldehyde. Lee et al. (2011a) found the hexane fraction obtained from

white *Rosa hybrida* flowers possessed excellent anti-inflammatory potency by reducing inflammatory repertoires, such as inducible nitric oxide synthase, interleukin-1β and cyclooxygenase-2 in RAW264.7 cells when stimulated with lipopolysaccharide (LPS), a proinflammatory mediator. The fraction effectively inhibited LPS-mediated nuclear factor-κB (NF-κB) p65 subunit translocation into the nucleus and extracellular signal-regulated kinase (ERK)1/2 phosphorylation, suggesting that rose hexane fraction anti-inflammatory activity may be based on inhibition of the NF-κB and MAPK pathways.

Analgesic Activity

Rosa hybrida showed an analgesic effect against hotplate-induced thermal stimulation at a dose of 200 mg/kg (Choi and Hwang 2003).

Anxiolytic Activity

Of the 9 compounds found in rose oil, geraniol and eugenol decreased the response rate during the safe period of the Geller and Vogel conflict tests in ICR mice, but did not affect the response rate during the alarm period (Umezu et al. 2002). In contrast, 2-phenethyl alcohol and citronellol, like rose oil, produced an increasing effect on the response rate during the alarm period in the Geller conflict test. Further, both chemicals increased the number of electric shocks mice received in the Vogel conflict test in a manner similar to that of rose oil. Given that 2-phenethyl alcohol and citronellol produced the same anti-conflict effects in both tests as rose oil, the authors concluded that they were the pharmacologically active constituents of antianxiety-like effect of rose oil.

Adaptogenic Activity

Studies showed that in rats subjected to acute restraint stress, rose essential oil inhalation significantly inhibited the increase in plasma corticosterone and reduced the increases in the number of c-Fos-positive cells in hypothalamic paraventricular nucleus (Fukada et al. 2012). Inhalation of rose essential oil significantly inhibited the following effects of chronic stress: (1) the elevation of transepidermal water loss (TEWL); an index of the disruption of skin-barrier function, in both rats and humans; and (2) the increase in the salivary concentration of cortisol in humans. The results suggested that in rats and humans, chronic stress-induced disruption of the skin barrier could be limited or prevented by rose essential oil inhalation, possibly through its inhibitory effect on the hypothalamic–pituitary–adrenocortical axis.

Skin Permeation Enhancement Activity

The percutaneous permeation of monoterpenes and phenylpropanoids applied in pure native rose oil was much higher than in their neat form suggesting synergistic interaction between essential oil components (Schmitt et al. 2010). For substances applied in rose oil, a clear relationship between their lipophilic character, chemical structure and skin permeation could be confirmed. Regarding the permeation values the substances were ranked in the following order: monoterpene hydrocarbons < monoterpene alcohols < monoterpene ketones < phenylpropanoids. In contrast, for neat single substances there were no relationships between their lipophilic characters, structures and skin permeation.

Traditional Medicinal Uses

Rose petal tea has a calming, tranquillizing effect (Roberts 2000). The Arab physician Avicenna prescribed rose water for skin ailments, and rose water mixed with honey was used as a cough syrup. Rose water may be splashed on the outside of the eyes in cases of conjunctivitis. It has an antiseptic and soothing quality and can be used even on sensitive skins. Rose hips can be used in cough mixtures. Its high vitamin C content,

as well as fruit acids, and betacarotene, pectin and tannin content boost the body's immune system and make an excellent tonic that will give energy and vitality and strengthen the artery walls, thus aiding circulation (Roberts 2000).

Red rose petals are official in many pharmacopoeias (Grieve 1971). Red rose petal acid infusion, prepared with dilute sulphuric acid and sugar, is used for treatment of night sweats resulting from depression. A nonacid infusion is used as lotion for ophthalmia and conjunctivitis. Syrup of rose is used to impart agreeable flavour and odour to other syrups and mixtures. Honey of rose made from clarified honey and rose fluid extract was commonly used in the olden days for sore throat and mouth ulcers. Rose vinegar prepared by steeping rose petals in distilled vinegar is employed for headache by applying rags soaked in it on the forehead. Ointment of rose water commonly known as cold cream is popular as a soothing, cooling application for chapping of the hands and face, abrasion and other superficial skin lesions. Rose hips are also official in many pharmacopoeia as refrigerant and astringent. Its astringency is considered useful for strengthening the stomach and useful in diarrhoea, dysentery, allaying thirst and as pectoral for coughs and spitting of blood.

Other Uses

Hybrid tea and floribunda roses are favoured in small gardens and parks in formal situations, and hybrid teas are cultivated in commercial farms for the cut flower industry. Another popular group of modern roses is the grandiflora, developed from crosses between hybrid teas and floribundas; they are taller (up to 2 m) and have clustered flowers like the floribundas but larger and with the long stems of hybrid teas.

Comments

Scientific papers published have largely used this artificial binomial nomenclature of *Rosa* × *hybrida*.

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Rosa × rugosa

Scientific Name

***Rosa × rugosa* Thunb.**

Synonyms

Rosa ferox Lawrance, *Rosa pubescens* Baker

Family

Rosaceae

Common/English Names

Beach Plum, Beach Rose, Beach Tomato, Japanese Rose, Ramanas Ros, Rugosa Rose, Saltspray Rose, Turkestan Rose, Sea Tomato, Wrinkled Rose

Vernacular Names

Chinese: Mei Gui, Mei Gui Hua
Czech: Růže Svraskalá, Růže Svrasklá
Danish: Hyben, Hybenrose, Rynket Rose
Dutch: Bottelroos, Rimpelroos
Estonian: Kurdlehine Kibuvits
Esperanto: Tordrozo
Finnish: Aekaeruusu, Jaapanin Ruusu, Kurttulehtiruusu, Kurtturuusu
French: Rosier Du Japon, Rosier Rugueux
Gaelic: Rós Rúsacach, Rós Rúscach
German: Hecjenrose, Japanische Apfelrose, Kamtschatkarose, Kartoffel-Rose, Runzelrose
Hungarian: Japán Rózsa, Ráncoslevelű Rózsa
Icelandic: Garðarós, Ígul-Rós, Skráp-Rós
Japanese: Hamanasu, Hamanashi
Korean: Hae-Dang-Hwa
Latvian: Rievainā Roze
Lithuanian: Raukšlėtalapis Erškėtis
Norwegian: Rukkerose, Rynkeros, Rynkerose
Polish: Róża Pomarszczona
Russian: Morshchinistaya Rosa, Roza Kamčatskaja
Slovaščina: Japonski Šipek
Slovencina: Ruža Vráskavá
Swedish: Vresros
Turkish: Türkistan Gülü
Welsh: Rhosyn Japan

Origin/Distribution

This rose species is native to colder climes of north-eastern Asia that include North-eastern China, Japan, Korea and south-eastern Siberia and the subarctic zone of Kamchatka and Okhotsk.

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It has been cultivated in both Japan and China for thousands of years. It has been introduced to numerous areas of Europe, North America, Australia and elsewhere.

Agroecology

R. rugosa is a cold climate species. It grows on sandy or gravely beaches as well as in sandy dune grassland communities in its native range. It can form dense thickets. It is tolerant of poor soil conditions and to high-salt conditions of seasides and road edges.

Edible Plant Parts and Uses

Fragrant *Rosa rugosa* flowers are edible raw or cooked and are used in jellies and preserves (Facciola 1990). Its petals are used for production of teas, jams, wines and juices (Nowak et al. 2013). In northern China, *R. rugosa* cv. Plena is widely grown for essential oil and the flowers are also used medicinally and as food (Wu et al. 1985). Flower petals are gathered in the morning, mixed with sugar and used in pastry; fruits are used fresh or dried (Hu 2005).

The fruit is also edible raw or cooked (Hedrick 1972; Elias and Dykeman 2009). *R. rugosa* is the standard rose for edible hip production. A pleasant-tasting fruity-flavoured tea is made from the fruit; it is rich in vitamin C (Lust 1974). The seed is a good source of vitamin E; it can be ground into a powder and mixed with flour or added to other foods as a supplement (Facciola 1990). Young tender shoots are cooked and used as a potherb (Facciola 1990). A tea is also made from the leaves (Duke and Ayensu 1985).

Botany

An erect, deciduous, suckering shrub, 1–1.5 m tall with robust stem and tomentose branchlets covered with numerous short, straight prickles, 3–10 mm long, mixed with glandular bristles (Plates 3 and 4). Leaves are imparipinnately compound (Plate 1, 2 and 3), borne on 5–13 cm petioles with adnate stipule and with 5(−7)–9 elliptic or elliptic–obovate leaflets, 1.5–4.5 cm long by 1–2.5 cm wide, abaxially tomentose, reticulate, adaxially glabrous, shiny, rugose due to concave veins, base rounded or broadly cuneate,

Plate 1 *Rosa rugosa* Roseraie De L'hay flowers and leaves

Plate 2 *Rosa rugosa* Frau Dagmar Hastrup flowers and leaves

Plate 3 *Rosa rugosa* Ann Endt flowers and leaves

Plate 4 Prickly stem of *R. rugosa scabrosa*

Plate 5 *R. rugosa* fruits

apex acute or rounded–obtuse, margin acutely serrate. Flowers fragrant, solitary, or several and fasciculate, axillary, 4–6.5 cm cross borne on 5–25 mm pedicels with ovate, tomentose bracts. Hypanthium subglobose and glabrous. Sepals 5, ovate–lanceolate, often leaflike, pubescent. Petals 5, double or semi-double; purple-red, dark pink or white; obovate; base cuneate; apex emarginate (Plates 1, 2 and 3). Styles free, slightly exserted, much shorter than stamens. Hip red, depressed–globose, 2–2.5 cm across, smooth, with persistent, erect sepals (Plate 5).

Nutritive/Medicinal Properties

Plant Phytochemicals

The secondary metabolites of *Rosa rugosa* could be grouped according to structural classes and include hydrolysable tannins (contained in the leaves and petals), catechin derivatives (roots), flavonoids (leaves), 2-phenoxychromones (leaves), monoterpenes (floral parts, leaves), sesquiterpenes (leaves, especially from glandular trichomes) and triterpenes (leaves and roots) (Hashidoko 1996).

Olech et al. (2012) found the flower, leaf and root ethanolic extracts of *R. rugosa* to have the highest phenolic content, ranging from 12.75 to 13.9 mg/ml. Appreciable amounts were found in hip tincture (11.88 mg/mL), whereas the lowest content was in nut (seed) ethanolic extract (2.88 mg/mL). Teas contained lower amounts per millilitre ranging from 0.14 to 1.52 mg of phenols for nut and flower tea, respectively. The highest concentrations of flavonoids were found in flower and leaf tinctures (1.14 and 1.25 mg/mL, respectively). The root ethanolic extract also contained considerable amounts (0.82 mg/mL), and the content of flavonoids in hip tincture amounted to 0.39 mg/mL. The lowest quantity was found in the nut extracts (0.12 mg/mL). For the *o*-dihydroxyphenols content, the highest amounts were present in the root, leaf and flower tinctures (4.07, 2.61 and 2.15 mg/mL, respectively). The lowest content was found in tea made from the nuts (seeds)—0.02 mg/mL. The amount of tannins in the plant parts ranged from 0.001 to 0.225 mg/mL; the content found in root tea was high compared to the other teas. They also reported that the content of β-carotene ranged from 0 to 9.6 μg/mL and there was also large variation among tea and tincture galenic preparations. The best sources of carotenoids were hip extracts (240 and 275 μg per serving for tincture and tea, respectively) and flower tincture with 131.75 μg per serving.

Fruit Nutrients and Phytochemicals

The proximate nutrient composition per 100 g edible portion of wild rose hip had been reported by USDA (2013) as follows: water 58.66 g, energy 162 kcal (679 kJ), protein 1.60 g, total lipid 0.34 g, ash 1.18 g, carbohydrate 38.22 g, total dietary fibre 24.1 g, total sugars 2.58 g, sucrose 0.07 g, glucose 1.34 g, fructose 1.16 g, Fe 1.06 mg, Mg 69 mg, P 61 mg, K 429 mg, Na 4 mg,

Zn 0.25 mg, Cu 0.113 mg, Mn 1.020 mg, vitamin C 426 mg, thiamine 0.016 mg, riboflavin 0.166 mg, niacin 1.3 mg, pantothenic acid 0.8 mg, vitamin B-6 0.076 mg, total choline 12 mg, total folate 3 μg, betaine 2.9 mg, vitamin A RAE 217 μg, vitamin A 4,345 IU, β-carotene 2,350 μg, α-carotene 31 μg, β-cryptoxanthin 483 μg, lycopene 6,800 μg, lutein + zeaxanthin 2,001 μg, vitamin E (α-tocopherol) 5.84 mg, β-tocopherol 0.05 mg, γ-tocopherol 1.34 mg, δ-tocopherol 0.14 mg and vitamin K (phylloquinone) 25.9 μg.

Nine carotenoids were determined in the fruits of two *Rosa* species (*Rosa canina* and *Rosa rugosa*) and of chokeberry (*Aronia melanocarpa*): three carotenes (lycopene, ζ-carotene, β-carotene) and six xanthophylls (neoxanthin, *trans*-violaxanthin, *cis*-violaxan-thin, 5,6-epoxylutein, lutein, β-cryptoxanthin) (Razungles et al. 1989). Rosa hips contained the highest concentrations of total carotenoids, which were mainly comprised of lycopene and β-carotene. Conversely, total xanthophylls were low.

Eleven major phenolic acids (gallic, protocatechuic, gentisic, *p*-hydroxybenzoic, vanillic, caffeic, syringic, *p*-coumaric, ferulic, *p*-hydroxyphenylacetic, salicylic) were quantitatively investigated in the fruit of 14 *Rosa* species (Nowak 2006). The amount of individual compounds ranged from 0.2 to 303.2 mg/g of dry material. Conjugated forms of phenolic acids were predominant in the fruits and were hydrolyzed mainly to gallic acid (93–303 mg/g in dry plant material). The total amount of phenolic acid after hydrolyses was from 186.4 mg/g (*R. inodora*) to 466 mg/g (*R. rugosa*) of dry weight of plant material. All volatile hip oil samples of nine Rosa species were dominated by the following components: vitispirane (isomer) (1.8–17.38 %), α-*E*-acaridial (0–13.55 %), hexadecanoic acid (2.45–14.26 %), β-ionone (0.11–10.97 %), dodecanoic acid (0.62–11.98 %), 6-methyl-5-hepten-2-one (0–14.49 %), myristic acid (0.52–4.05 %), linoleic acid (0–21.95 %) and docosane (C22) (0–13.29 %) (Nowak 2005). There appeared to be a correlation between the essential oil patterns and the classification within *Rosa* L. Cluster analysis of the composition of main components clearly showed two groups, one constituted by *R. rugosa* from the Cinnamomea section and the other constituted by the remaining taxa from the Caninae section. The chemical composition of *R. rugosa* hip (pseudofruit) essential oil comprised 3-methyl-3-hexen-2-ol (0.8 %), *cis*-3-hexenal (27.50 %), 5-methyl-3- hexanone and 2-heptanone(0.52 %), styrene (0.35 %), 5-methylhexanal (2.32 %), 4,4′-dimethyl-hexanal (0.25 %) hydrocarbon (0.65 %), methyl caproate (0.17 %), benzaldehyde and α-pinene (0.31 %), 2-heptenol (0.61 %), *β*-methoxy-2- furanethanol (0.39 %), *n*-amyl propionate or isoamyl propionate and 1,5-octadiene derivative (0.19 %), 2-hexenoic acid methyl ester (0.12 %), 6-methyl-5-hepten-2-one (14.49 %), β-pinene (0.30 %), 2,4-heptadienal and 2-pentylfuran (0.14 %), octanal (0.29 %), β-myrcene (0.07 %), 2-carene (tr), benzene acetaldehyde (0.685), salicylaldehyde (0.87 %), *p*-cymene (0.92 %), 2,2′-bifuran (0.50 %), 1,8-cineole (tr), limonene (0.15 %), 2-octenal (isomer) and methylbenzaldehyde (0.55 %), 2-octenal (isomer) and β-*E*-ocimene (0.24 %), butyric acid isopentyl ester (0.10 %), γ-terpinene (0.05 %), 2,2′-methylenedifuran (0.42 %), terpinolene and guaiacol (0.05 %), nonanal (2.51 %), linalool (0.95 %), perylene (0.05 %), caprylic acid methyl ester (0.05 %), 7-methyl-3-octen-2-one (0.31 %), *n*-amyl isovalerate and acetic acid benzyl ester and *trans*-2-undecenal (0.25 %), safranol (0.40 %), methyl salicylate (0.31 %), eucarvone (tr), bicyclo-[3.3.1]-nonan-2-one and decanal (0.64 %), β-cyclocitral (0.17 %), unknown (1.16 %), neral and benzyl methyl ketone (0.92 %), geraniol (0.67 %), geranial (1.01 %), α-*E*-acaridial (0.75 %), vitispirane (isomer) (5.845), undecanal and phenylacetic acid propyl ester or butanoic acid phenylmethyl ester (0.27 %), (*E*,*E*)-2,4-decadienal (0.76 %), edulan (0.22 %), methyl caproate (0.22 %), α-damascenone (0.17 %), decanoic acid (1.99 %), asterica-3(15)-6-diene (0.51 %), unknown (0.55 %), *trans*-geranyl-acetone (1.96 %), 2,3-dehydro-4-oxo-β-ionol (0.14 %), α-cadinene (0.14 %), β-ionone (0,80 %), α-farnesene (0.23 %), *cis*-ψ-ionone (9.16 %) and lauric acid methyl ester (0.45 %).

Grabowska and Janeczko (2012) reported on the fatty acid (FA) composition of the monogalactosyldiacylglycerol (MGDG) fraction obtained from *R. canina* and *R. rugosa* pericarps and seeds. The fatty acid composition of MGDG found in pericarps was similar for both rose species. They found unsaturated fatty acids to be dominant in the pericarps of both species (93.745–94.856 %). The major unsaturated FA of MGDG from the pericarps of *Rosa canina* and *Rosa rugosa* were those with chain length of 18C (93.886 % and 92.795 %, respectively), while the content of unsaturated FA with chain length of 16 and 17C was less than 1 %. The dominant FA of MGDG from the pericarps of both species was linolenic acid (18:3 n-3), and the percentage of the compound was 74.486 % of MGDG FA from *R. canina* and 86.057 % of MGDG FA from *R. rugosa*. They also found high amounts of 18:2 n-6 fatty acid. In contrast to MGDG from the pericarps, the content of the saturated FA of MGDG from the seeds of both species was 6–8 times higher (25.856–40.554 %). The saturated FA composition of MGDG found in the seeds consisted of the following FA: 12:0, 14:0, 16:0, 18:0 and 24:0. In the MGDG composition from the seeds of both species, we have also observed high amounts of unsaturated FA. The dominant unsaturated FA was linolenic acid, and its percentage was 27.545 % in the seeds of *R. canina* and 37.510 % in *R. rugosa* seeds. They also found high amounts of 18:2 n-6 and 18:1 n-9 FA. The content of 18:1 n-9 was much higher in the seeds than in the pericarps.

Flower Phytochemicals

Thirty components were identified in *R. rugosa* cv. Plena, violet-red-flowered essential oil; the major compounds were β-citronellol, geraniol, geraniol acetate, citronellyl acetate, methyl eugenol and linalool (Wu et al. 1985). In a survey of flower flavonoids in 120 taxa from 10 sections of subgenus *Rosa*, 19 flavonols and six anthocyanins were detected: six kaempferol glycosides, 3-glucoside (in 99 % taxa), 3-rutinoside (63 %), 3-sophoroside (60 %), 3-rhamnoside (70 %), 7-glucoside (94 %) and 4′-glucoside (4 %); six quercetin glycosides, 3-glucoside (91 %), 3-glucuronide (62 %), 3-rutinoside (63 %), 3-sophoroside (69 %), 7-glucoside (90 %) and 4′-glucoside (4 %); and seven unidentified flavonols and two cyanidin glycosides, 3,5-diglucoside (68 %) and 3-glucoside (16 %); two peonidin glycosides, 3,5-diglucoside (41 %) and 3-glucoside (4 %); and two unidentified anthocyanins (Mikanagi et al. 1995). The major flavonoids in *R. rugosa* petals were kaempferol 3-sophoroside, quercetin 3-sophoroside, kaempferol 7-glucoside, quercetin 3-glucoside and anthocyanins cyanidin 3,5-diglucoside, peonidin 3,5-diglucoside and peonidin 3-glucoside (Mikanagi et al. 1994). These flavonols were present in the petals of all intersectional hybrids with sect. *Synstylae* and sect. *Pimpinellifoliae*. Eleven compounds including kaempferol and quercetin flavonoids and a phenylethylglycoside were found in the alcohol extract of *R. rugosa* flowers: kaempferol, quercetin, juglanin, avicularin, astragalin, hyperoside, kaempferol-3-*O*-(2″-*O*-β-D-glucopyranosyl)-β-D-glucopyranoside, quercetin-3-*O*-(2″-*O*-β-D-glucopyranosyl)-β-D-galactopyranoside, 2-phenylethyl-*O*-β-D-glucopyranoside, protocatechuic acid and gallic acid (Xiao et al. 2006).

Mikanagi et al. (2000) found the following anthocyanins in the flowers of *R. rugosa* and its variety and cultivars: *R. rugosa:* cyanidin 3,5-diglucoside, cyanidin 3-sophoroside, cyanidin 3 rutinoside, cyanidin 3-glucoside, *cis*- and *trans*-cyanidin 3-*p*-coumaroylglucoside-5-glucoside, peonidin 3,5-diglucoside, peonidin 3-rutinoside, peonidin 3-glucoside, *cis*- and *trans*-peonidin 3-*p*-coumaroylglucoside-5-glucoside, peonidin 3,5-diglucoside. *R. rugosa* var. *plena*: as with *R. rugosa* but not cyanidin 3-rutinoside. *R. rugosa* cv. Roseraie del'Hay: as with *R. rugosa* but not cyanidin 3-sophoroside and cyanidin 3-glucoside. *R. rugosa* cv. Maikwai: as with *R. rugosa* but not cyanidin 3-rutinoside. *R. rugosa* cv. Salmon Pink: cyanidin 3,5-diglucoside, cyanidin 3-sophoroside, cyanidin 3 rutinoside, cyanidin 3-glucoside, peonidin 3-rutinoside, peonidin 3-glucoside. *R. rugosa* cv. Scabrosa: cyanidin 3,5-diglucoside,

cyanidin 3-sophoroside, *cis*- and *trans*-cyanidin 3-*p*-coumaroylglucoside-5-glucoside, peonidin 3-rutinoside, *cis*- and *trans*-peonidin 3-*p*-coumaroylglucoside-5-glucoside. *R. rugosa* cv. Scarlett: as with cv. Scabrosa except for *trans*-peonidin 3-*p*-coumaroylglucoside-5-glucoside. Flowers of *R. rugosa* was found to contain cyanidin-3,5-diglucoside (Wang et al. 2009); avivularin, juglanin, astragalin, quercetin, ellagic acid and gallic acid (Zhong et al. 2009); and kaempferol and quercetin flavonoids (Xiao et al. 2006).

The petals of *R. rugosa* were found to contain abundant hydrolysable tannins, which have galloyl, hexahydroxydiphenoyl (HHDP) and valoneoyl groups attached to a glucose core (Hashidoko 1996). The following hydrolyzable tannins were isolated from the petals of *R. rugosa* flowers: rugosins A, B and C (Okuda et al. 1982; Hatano et al. 1990b); rugosins D, E, F and G (Hatano et al. 1990a); tellimagrandin I together with eugeniin and casuarictin (Tamura et al. 2010); five hydrolyzable tannins, tellimagrandin I (10.4–41.6 mg/g), tellimagrandin II (1.5–35.3 mg/g), rugosin A (<10 mg/g), rugosin D (8.2–48.1 mg/g) and casuarictin (<10 mg); and related compounds gallic acid, ellagic acid, 1,2,3-tri-*O*-galloyl-b-D-glucose, strictinin, isostrictinin and 3-*O*-galloyl-4,6-*O*-HHDP-D-glucose were isolated from the dried petals (Ochir et al. 2010). Total phenolic, flavonoid, phenolic acid, tannin, carotenoid and polysaccharide contents in *R. rugosa* petals were determined; five phenolic acids and six flavonoids previously not reported in the plant material were identified (Nowak et al. 2013).

Each flower part of *R. rugosa* showed a distinctive volatile fragrance profile (Dobson et al. 1990). Petal volatiles, dominated by terpenoid and benzenoid alcohols, contributed most to the whole-flower fragrance. Sepal odours contained mainly sesquiterpenes, together with several compounds found in the petals. The major volatiles in the androecium were more diverse and were generally different from those in the perianth. Empty anthers shared a high proportion of their volatile profile with pollen. Pollen odour appeared to be self-contained, showing only minor adsorption of volatiles from sepals and petals. Compounds typical of the androecium were present as significant components (though in small amounts) of the whole-flower fragrance, where they may well function as signals to pollen-seeking insects. Some of the components included citronellol, 2-phenylethanol, citronellyl acetate, *E,E*-α-farnesene, eugenol, geranial, geraniol, geranyl acetate, geranyl acetone, heptan-2-ol, methyl eugenol, neral, nerol, neryl acetate, phenylethyl acetate, phenyl methanol and sulcatone.

Forty-three constituents of fragrance volatiles from fresh *R. rugosa* flowers were separated and 26 components identified (Li et al. 1988). The major components were phenyl ethanol (18.31 %), β-citronellol (35.44 %), citronellyl acetate (11.33 %), geraniol (17.21 %) and geranyl acetate (7.38 %). Other minor components included 1-hexanol, myrcene, γ-terpinene, sabinene hydrate, thymol, *cis*-rose oxide, *trans*-rose oxide, linalool, 3-cyclohexene-1-methanol α,α,4-trimethyl-, nerol, 2-undecanone, geranial, geranyl formate, tridecane,2,5-dimethyl-, aromadendrene, eugenol, caryophyllene and 2-tridecanone.

Up to 33 volatile floral compounds were identified from the 23 Chinese *Rosa rugosa* germplasms, including nine alcohols, five esters, three alkanes, ten terpenes, three aldehydes, two ketones and one ether (Feng et al. 2010). The main floral components identified were 2-phenylethanol, β-citronellol, ethanol and *n*-hexane. The cultivars 'Xizi', 'Miaofengshan', 'Xiangciguo' and 'Tangbai' contained the highest amounts of 2-phenylethanol (84.66 μg/g), β-citronellol (70.98 μg/g), ethanol (83.87 μg/g) and n-hexane (18.23 μg/g), respectively. Other minor components detected included 3-methylpentane, 3-methylcyclopentene, 2-heptanone, methylcyclopentane, isopentyl alcohol, *cis*-3-hexen-1-ol, *n*-hexanol, 5-methyl-2-hexanol, α-pinene, β-pinene, β-myrcene, 4-hexen-1-ol acetate, *n*-hexyl acetate, benzyl alcohol, *D*-limonene, 3-carene, ocimene, *trans*-β-ocimene, 2-ethylidene-6-methyl-3,5-heptadienal, *trans*-rose oxide, β-citronellal, β-phenylethyl acetate, α-citral, *cis*-geraniol, 2-undecanone, citronellol acetate, nerol acetate, aromadendrene and α-farnesene.

Forty-two volatile aroma compounds were identified in petals of *R. rugosa* cultivars 'Ritausma', 'Sniedze', 'Zaiga', 'Liga', 'Frau Dagmar Hastrup', *R. rugosa* and *R. rugosa* 'Plena'(Sparinska and Rostoks 2012). The volatiles found in the largest amounts were phenylethyl alcohol (28.6–79.9 % depending on cultivar), β-citronellol (10–57.2 % depending on cultivar), but the amount of benzyl alcohol was only 0.9–2.6 % and the composition of compounds varied among cultivars. Other significant compounds were nerol (up to 39 % of the total amount of volatiles, but absent in 'Ritausma' and 'Liga'), geraniol (up to 8 %, not found in 'Ritausma') and methyl eugenol (up to 10 %, not found in 'Ritausma'). Other minor volatiles found included undecane,5,7dimethyl; α-phellandrene; dodecane,2,6,11trimethyl; decane,2,3,5,8 tetramethyl; heptadecane,2,6,10,15 tetramethyl; acetic acid hexylester; 2-heptanol; 3-hexen-1-ol, acetate; pentafluoro-propionic acid, hexyl ester; 1-hexanol; rose oxide; 3-hexen-1-ol; 2-hexen-1-ol; furan, 3-(4-methyl-3-penthyl); acetic acid; copaene; 2-octen-3-ol-3,7 dimethyl; 2-octen-3-ol-3,7 dimethyl acetate, α-cubenene; α-farnesene; 2-tridecanone; 9-nonadecene; methyl eugenol and eugenol.

Fifty-two constituents were separated from the essential oil of fresh *R. rugosa* flowers and 35 identified (Li et al. 1988). Major components were phenyl ethanol (34.23 %), β-citronellol (29.96 %) and geraniol (12.96 %). Minor components were citronellyl acetate; methyl eugenol; eugenol; tricosane; *cis*-rose oxide; *trans*-rose oxide; linalool; 3-cyclohexene-1-methanol, α,α,4-trimethyl-; nerol; 2-undecanone; geranial; geranyl formate; tridecane; 2,5-dimethyl-; benzyl alcohol; aromadendrene; caryophyllene; 2-tridecanone; nerolidol; farnesol; nootkatone; 9-undecen-2-one; calamine; elemol; heneicosane; docosane; tricosane; tetracosane; pentacosane; 1,2-benzene; dicarboxylic acid; diisobutyl ester; benzene 1,2,3-trimethoxyl-*E*-(2-propenyl)-2(SH)-napthalenone,4,4α5,6,7; 8-hexahydro-4,4α-dimethyl-6(1-methylethenyl)-; and 1H-3α,7-methanoazulen-6-ol, octahydro-3,6,8,8-tetramethyl-. A total of 108 compounds were identified in the volatile flower oil of *Rosa rugosa* var. *plena* growing in China (Ueyama et al. 1990). This rose essential oil was high in citronellol (60.0 %), geraniol (8.6 %), nerol (2.8 %), citronellyl acetate (2.7 %), *E, E*-farnesol (2.4 %) and tridecan-2-one (2.3 %), accounting for 78.8 % of oil.

Bee pollen polysaccharides from *Rosa rugosa* were purified and fractionated to neutral (WRPP-N) and acidic polysaccharides (WRPP-1, WRPP-2) (Wang et al. 2013). WRPP-N was mainly composed of glucose, mannose, arabinose and galactose, indicating the existence of glucan, arabinogalactan and mannoglucan. WRPP-1 mainly consisted of rhamnose (3.0 %), galacturonic acid (12.4 %), galactose (24.7 %) and arabinose (53.9 %) and contained a large proportion of arabinogalactans. WRPP-2 consisted of rhamnose (7.8 %), galacturonic acid (23.0 %), galactose (15 %) and arabinose (48.7 %), while WRPP-2 contained more galacturonic acid compared to WRPP-1. WRPP-1 and WRPP-2 were composed by type I rhamnogalacturonan, homogalacturonan and arabinogalactan fragments, while WRPP-2 contained more homogalacturonan and type I rhamnogalacturonan.

Leaf Phytochemicals

An antimicrobial sesquiterpene isolated from diffusates of damaged *R. rugosa* leaves was found to be a novel carotane with an α,β-unsaturated aldehyde group, an *endo*-peroxide bridge and an allyl alcohol partial structure (Hashidoko et al. 1989b). A sesquiterpene, (7*R*,10*R*)-carota-1,4-dienaldehyde, was identified in *Rosa rugosa* leaves (Hashidoko et al. 1990). The new compound was markedly unstable under air exposure to give several oxidized derivatives, in which rugosal A was found as the main product due to the 1,4-diene structure. The corresponding carboxylic acid, carota-1,4-dienoic acid, was found in the leaves. The corresponding carboxylic acid was found in intact leaves of *R. rugosa*, but the compound was non-fungitoxic. Rugosal A, an antifungal sesquiterpene, was found to have a carotane skeleton oxidized at C-14 to an aldehyde group (Hashidoko et al. 1989a).

Bisaborosaol A, a novel sesquiterpene belonging to the bisabolane class, was isolated from *Rosa rugosa* leaves (Hashidoko et al. 1991g). Bisaborosaol A and its corresponding carboxylic acid may be biogenetically related to the carotenoids which constitute the major sesquiterpenes of *R. rugosa* leaves. Five novel bisabolane sesquiterpenes possessing a tetrahydrofuran ring or a hydroperoxy group were isolated from *Rosa rugosa* leaves (Hashidoko et al. 1991c). These highly oxidized sesquiterpenes were structurally related to bisaborosaol A, the major bisabolanoid of the plant.

In the investigation of minor sesquiterpenoids in *Rosa rugosa* leaves, 11 novel sesquiterpenes comprising eight carotane aldehydes (daucenaldehyde, epoxydaucenaldehyde A, epoxydaucenaldehyde B, isodaucenaldehyde, hydroxycarotaldehyde, dehydrodaucenaldehyde, hydroxyisodaucenaldehyde and isotrienecatoanal epoxide), two carotane acids (dehydrodaucenoic acid and isodaucenoic acid) and an acoranoid, rosacoranone, were isolated and their structures elucidated (Hashidoko et al. 1991d). The present study showed *R. rugosa* to be a major source of C-14-oxygenated carotenoids. Two phenoxychromones, 6-demethoxy-4′-*O*-methylcapillarisin and 6-demethoxycapillarisin, were identified in *Rosa rugosa* leaves (Hashidoko et al. 1991b). Apigenin was also found in the leaves. Four carotenoids rugosic acid D, rugosic acid C, rugosic acid B and rugosic acid A methyl ester were isolated as metabolites of rugosic acid A in *R. rugosa* leaves (Hashidoko et al. 1991f). Carota-1, 4-dienaldehyde (3) increased in the leaves during the budding and flowering stages of *R. rugosa*, but drastically decreased after flowering (Hashidoko et al. 1991a). Rugosal A (1) followed after compound 3 increased and was at a high level over flowering and ripening stages, and their concentrations were sufficient to suppress many fungi. Rugosic acid A (2) accumulated through leaf maturation and diminished in coloured or falling leaves. Further, leaf detaching or injury caused a rapid oxidation of 3 into 2 via 1. Compound 1 which was actively released from the tissues when the leaves were mechanically damaged and soaked in water appeared to originate mostly from compound 3 in tissues. In the autoxidation of (7*R*,10*R*)-carota-1,4-dien-14-al (1), a precursor of an antifungal compound rugosal A (2) in *Rosa rugosa* leaves, an intermediate possessing a 1,5-endoperox-2-hydroperoxy system (4) was isolated as a major product (Hashidoko et al. 1991e). The structures of compound (4) and other by-products including rugosal A and rugosic acid A were determined.

Two long chain alkyl esters of cinnamic acid, 4′-hydroxy-*cis*-cinnamic acid docosyl ester and 4′-hydroxy-2,3-dihydrocinnamic acid pentacosyl ester, in association with known 4′-hydroxy-c*is*-cinnamic acid hexacosyl ester and octacosyl ester, were isolated from *Rosa rugosa* leaves (Hashidoko et al. 1992a). Eight novel sesquiterpenes rugosal D, epirugosal D, secocarotanal, isodaucenol, rosacorenol, bisaborosaol F, bisaborosaol E1 and bisaborosaol E2 were isolated from leaves of *Rosa rugosa* and their structures elucidated (Hashidoko et al. 1993). The glandular trichome exudate of *R. rugosa* leaves was thus found to contain several minor carotane, secocarotane, bisabolane and acorane sesquiterpenes. In investigations of the less polar fraction of the glandular trichome exudate, some sesquiterpene hydrocarbons were found and three major sesquiterpene hydrocarbons (acora-3(4),7(15)-diene, carota-4(5),11(12)-diene (isodaucene) and carota-1,4-diene) and two minor ones (daucene and acora-3(4),7(8)-diene) were identified (Hashidoko et al. 1992c). 4-epi-a-bisabol, 7-nor-a-bisabol and 10-hydroxyisodaucene were isolated from the glandular trichome exudate together with linalool, nerol and carota-1,4-dien-14-ol as major constituents and some unknowns (Hashidoko and Tahara 1995).

In the course of an investigation of the leaf fragrance of *Rosa rugosa*, three sesquiterpene alcohols (4-epi-α-bisabolol [(4R:8S)-bisabola-1(7),12(13)-dien-8-ol], norbisabolol [7-norbisabola-1(2),12(13)-dien-8-ol] and 10-hydroxyisodaucene [carota-4(5),11(12)-dien-10-ol]) and two sesquiterpene peroxides (1,5-epidioxy-4-hydroperoxycarot-2-ene and 1,5-epidioxy-2-hydroxycarot-3-ene) were isolated from the glandular trichome exudates of the leaves (Hashidoko et al. 1994).

5-Hydroxycarota-1,3-dien-14-oic acid ethyl ester, regarded as an artefact, was also isolated and its structure elucidated. The glandular trichome exudate of *Rosa rugosa* leaves was found to be mainly composed of two major carotane sesquiterpenes, rugosal A and rugosic acid A, and carota-1, 4-dienaldehyde was also present (Hashidoko et al. 1992b). The occurrence of rugosal A in the exudate suggested a possible defensive role of the glandular trichome against pest organisms, as it exhibited antifeedant activity against tobacco cutworm larvae. The glandular trichomes were found to be a potential source of enzymes associated with the biosynthesis and/or bioconversion of sesquiterpenes of *R. rugosa* (Hashidoko and Urashima 1995). *Rosa rugosa* leaves were found to exude a large amount of syrup-like droplets (10–20 mg/g fresh leaves) from multicellular tips of the leaf glandular trichomes in which carotane and bisabolane sesquiterpenoids are contained as predominant constituents (Hashidoko et al. 1992b). In these exudates, carotane sesquiterpenes were found to mainly accumulate as epidioxy derivatives (rugosal A and rugosic acid A), the oxidized form of carota-l,4- dienaldehyde (Hashidoko et al. 1990), while the bisabolane-class sesquiterpene, bisaborosaol A, was another major constituent (Hashidoko 1996).

Wild-type *Rosa rugosa*, its varieties and hybrids were found to contain bisaborosaol A (1) and carota-1,4-dienaldehyde (2) as the major representative sesquiterpenes of the bisabolane and carotane classes, respectively, in the leaves (Hashidoko et al. 2001). The concentrations of bisaborosaol A and carota-1,4-dienaldehyde were positively correlated with the density of the glandular trichomes. Furthermore, an approximately regular correlation was observed between the concentrations of 1 and 2 in most of the sesquiterpene-producing hybrid rugosas, regardless of their productivity. They found the following leaf volatile components: acora-3(4),7(15)-diene; carota-1,4-diene; isodaucene; daucenal; rosacorenone; 4-epi-a-bisabolol; carota-1,4-dienaldehyde; carota-1,4-dien-14-ol; isodaucenal; bisaborosaol B 1; bisaborosaol B2; bisaborosaol A; and (+)-phytol. Other compounds were n-alkanes with odd numbers of carbons (C2S, C27, C29, C31 and C33), *n*-alk(en)yl alcohols with even numbers of carbons (C22, C24, C26 and C2S) and steroids (β-stigmasterol and an ursen-3-ol). The leaves of several *Rosa rugosa* hybrids (hybrid rugosas), Martin Frobisher and Vanguard, were found to accumulate a large amount of (+)-4-epi-alphabisabolol (1) as a single constituent (Hashidoko et al. 2000). Although glandular trichomes of Martin Frobisher on the leaves were dense, this *R. rugosa* hybrid produced none of the carota-1,4dienaldehyde (2) and bisaborosaol A (3) that were both found as representative sesquiterpenes of the carotane and bisabolane classes, respectively, in a glandular trichome exudate of wild-type *R. rugosa*. Compound 1 was also apparent as a nearly single constituent detectable by GC in the leaf constituents of Vanguard which possessed sparse glandular trichomes on the leaf. Martin Frobisher and Vanguard had likely lost their capability to form carotane-type sesquiterpenes and had also lost their activity to oxygenate the C-7 allyl methyl carbon of compound 1 to convert 3. The presence of (+)-4-epi-alphabisabolol-accumulating *R. rugosa* hybrids was significant when considering the sesquiterpene biogenesis of *Rosa rugosa*.

Root Phytochemicals

(+)-Catechin was isolated from the ethyl acetate-soluble fraction of the methanol extract of the underground part (Young et al. 1987a). From the underground parts of *Rosa rugosa*, triterpenoid glycosides, euscaphic acid (2α, 3α, 19α-trihydroxy-urs-12-en-28-oic acid), kaji-ichigoside F1 (28-β-D-glucopyranosyl euscaphic acid), tormentic acid (2α, 3β, 19α-trihydroxy-urs-12-en-28-oic acid), rosamultin (28-β-D-glucopyranosyl tormentic acid), arjunic acid (2α, 3μ, 19α-trihydroxy olean-12-en-28-oic acid) and arjunetin (28-β-D-glucopyranosyl arjunic acid), were isolated (Young et al. 1987b). 19α-hydroxyursane-type triterpenoids, namely, (kaji-ichigoside F1(euscaphic acid 28-*O*-glucoside)), euscaphic acid and tormentic acid were isolated from the roots of *Rosa rugosa* (Jung et al. 2005; An et al. 2011; Kim et al. 2012).

Antioxidant Activity

In a study of antioxidative activity of 12 medicinal plants, Cho et al. (2003b) found that compounds with the strongest activities were 3,4-dihydroxylbenzoic acid, quercetin, the quercetin glycosides quercetin-3-*O*-β-D-galactoside, quercetin-3-*O*-α-L-rhamnoside, quercetin-3-*O*-β-D-glucoside and quercetin-3-*O*-rutinose, catechin, gallic acid, methyl gallate and rosamultin isolated from *Zanthoxylum piperitum, Houttuynia cordata, Rosa rugosa* and *Cedrela sinensis*. The quercetin glycosides exhibited stronger activity than quercetin, suggesting that glycosylation increased the antioxidative activity of quercetin. Among the Rosaceae, *Rosa rugosa* and *Rosa davurica* showed strong DPPH radical scavenging activity (Cho et al. 2003a). Fractions of flower extracts containing hydrolysable tannins were found to have antioxidant activity (Lee et al. 2004). All its partitioned fractions including crude extract showed potent scavenging effect against DPPH radical, peroxynitrite and lipid peroxidation. *n*-Butanol fraction, in particular, was found to be the most effective in DPPH radical scavenging ability as well as inhibition against lipid peroxidation. The 15 % aqueous methanol fraction also showed a strong potency which was slightly lower than n-butanol fraction. A gallic acid derivative isolated from the aqueous extract of *R. rugosa* flowers was found to exhibit high antioxidative potency (Ng et al. 2004). Two polysaccharide–peptide complex components showed less potent antioxidant activity.

Studies by Park et al. (2009) found that the hexane fraction of white *Rosa rugosa* flowers, which contained a significant amount of polyphenols and volatile components, had excellent antioxidant potency and could scavenge free radicals of 2,2-diphenyl-1-picrylhydrazyl hydrate (DPPH) and 2,2′-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS). The hexane fraction inhibited lipid peroxidation to almost the same degree as a chemical antioxidant. In the nitric oxide (NO) assay, the hexane fraction effectively scavenged free radicals at all dose ranges. The hexane fraction effectively prevented oxidative damage, induced by Cu2+/H_2O_2, to target proteins at lower concentrations (>1 μg/mL). The DNA fragmentation and the cell-level assays suggested that the hexane fraction may play a crucial role in inhibiting peroxynitrite and H_2O_2 attack. The findings suggested the hexane fraction to have promise for use as a novel pharmaceutical antioxidant. It was found that the activities of Cu, Zn-SOD (superoxide dismutase) and catalase in mouse erythrocytes were markedly increased after incubation for 3 h with *Rosa rugosa* flower fractions containing two antioxidant components (polysaccharopeptide complex P(1-a) and condensed tannin P(1-b)) at the concentration of 500 μg/mL (Jiang et al. 2009). Similar changes were also observed in the erythrocyte gene expression of SOD and catalase. These results showed P(1-a) and P(1-b) to be effective antioxidants that could increase the activity and the gene expression of SOD and catalase in mouse erythrocytes.

In all *R. rugosa* cultivars, 'Ritausma', 'Sniedze', 'Zaiga', 'Liga', 'Frau Dagmar Hastrup', and 'Plena', DPPH scavenging activities were rather high compared with widely used herbs (Sparinska and Rostoks 2012). The free radical DPPH scavenging activity of rose petal extracts at fully open stage ranged from 80 to 91 %. The lowest scavenging activity of only 80 % was exhibited by rugosa hybrid 'Frau Dagmar Hastrup'. *R. rugosa* had the strongest scavenging activity—91 %. Rugosa hybrid 'Sniedze' had approximately the same scavenging capacity. Other hybrids also scavenged nearly 90 % of DPPH. The cultivar 'Sniedze' scavenged ~90 % of free radicals, which was the best result for rugosa hybrids. Leaf extracts had less scavenging activity, although all hybrids had activity of more than 80 %.

Animal studies showed that the activities of catalase (CAT) and glutathione peroxidase (GPx) in 9-month-old senescence-accelerated mice (SAM mice) treated with *R. rugosa* flower extract showed a marked increase in whole blood and liver (Ng et al. 2005). At the same time, the gene expression level of CAT and GPx was upregulated in the liver, while malondialdehyde content in liver and brain decreased. Male SAM mice were more sensitive than female SAM mice. The mean and the longest life span of SAM mice

were longer after treatment with the rose flower extract. Another in-vivo studies showed that rats fed with a standard diet enriched with 6 % dried *Rosa rugosa* fruit powder for 3 months had significantly lower liver peroxide, protein oxidation, glutathione levels and plasma alanine transaminase (ALT) and aspartate transaminase (AST) activities compared with the rats in the CCl_4-treated control group (Altiner and Kiliçgün 2008). These findings suggested *Rosa rugosa* to possess antioxidant activity. Olech and Nowak (2012) found that in order to obtain extracts from *Rosa rugosa* petals with the highest antioxidant activity and phenolic content, the use of mixture of polar organic solvents (acetone, in particular) with water was recommended. *R. rugosa* petals exhibited antiradical properties with IC_{50} value of 1.33–0.08 mg/mg $DPPH^{\bullet}$ (Nowak et al. 2013).

All the extracts of *R. rugosa* plant parts demonstrated high free radical (DPPH) scavenging activity (Olech et al. 2012). *R. rugosa* flower extracts were the most potent radical scavengers. Leaves and roots had almost equal effects, neutralizing all free radicals within 15 min, while the slowest for DPPH inhibition were the preparations obtained from nuts (seeds) and hip tinctures. Both types of galenic preparations (tea and tinctures) obtained from roots, leaves and flowers showed the highest antiradical activity. Hips and nuts had lower activities. The antiradical potential of teas increased in the order nuts < hips < flowers < roots < leaves, whereas the activity of tinctures increased as follows: hips < nuts < flowers < leaves < roots. They found that free radical scavenging effects of root and leaf (IC_{50} 0.19–0.22) preparations were comparable to those of trolox (IC_{50} 0.185).

Anti-inflammatory Activity

Both methanol and ethyl acetate extracts of *R. rugosa roots* showed anti-inflammatory/antinociceptive action in acetic acid-induced writhing and hot plate testing and in a carrageenan-induced paw oedema model in mice and rats (Jung et al. 2005). Repeated chromatography of the ethyl acetate extract led to the isolation of kaji-ichigoside F1 (euscaphic acid 28-*O*-glucoside, 1) and rosamultin (tormentic acid 28-*O*-glucoside, 2). The hydrolyzed fraction when subjected to silica gel column and octadecylsilane column chromatography afforded euscaphic acid (3) and tormentic acid (4). The potencies were observed in the following order: 4 > 3 > 2 > 1. These results suggested 19alpha-hydroxyursane-type triterpenoids to be responsible for the anti-inflammatory/antinociceptive action of *R. rugosa* roots. Among the tested 19α-hydroxyursane-type triterpenoids (kaji-ichigoside F(1), rosamultin, euscaphic acid, tormentic acid (TA)), TA was found to most potently inhibit the production of nitric oxide (NO) in RAW 264.7 cells (An et al. 2011). TA dose dependently decreased the productions of NO, prostaglandin E(2) (PGE(2)) and tumour necrosis factor-α (TNF-α) induced by LPS in RAW 264.7 cells. Further, TA significantly suppressed the LPS-induced expressions of inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and TNF-α at the mRNA and protein levels. TA also inhibited the LPS-stimulated degradation and phosphorylation of inhibitor of kappa B-α (IκB-α). Taken together, the results suggested that the anti-inflammatory activity of TA was associated with the downregulation of iNOS, COX-2 and TNF-α through the negative regulation of the NF-κB pathway in RAW 264.7 cells. Further studies by Kim et al. (2012) showed that euscaphic acid (19α-hydroxyursane-type triterpenoids, EA) isolated from roots of *Rosa rugosa* inhibited lipopolysaccharide (LPS)-induced inflammatory responses by interference with the clustering of TNF receptor-associated factor 6 (TRAF6) with interleukin receptor-associated kinase 1 (IRAK1) and transforming growth factor-β-activated kinase 1 (TAK1) resulting in blocking the activation of IKK (inhibitor kB kinase) and MAPKs (mitogen-activated protein kinases) signal transduction to downregulate NF-κB activations in RAW 264.7 macrophages. EA concentration dependently reduced the production of nitric oxide (NO), prostaglandin E2 (PGE2), tumour necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) induced by LPS in RAW 264.7 macrophages.

Anticancer Activity

Screening of 43 small fruit juices revealed that *Actinidia polygama* Maxim., *Rosa rugosa* Thunb., *Vaccinium smallii* A. Gray and *Sorbus sambucifolia* Roem. strongly inhibited the proliferation of all cancer cell lines examined, and these juices were substantially less cytotoxic towards normal human cell lines (Yoshizawa et al. 2000b). These fruit juices were found to strongly induce differentiation of HL-60 leukemic cells to monocyte/macrophage characteristics in a concentration-dependent manner (Yoshizawa et al. 2000a).

Gallic acid from *Rosa rugosa* was found to be a histone acetyltransferase (HAT) inhibitor with global specificity for the majority of HAT enzymes, but with no activity towards epigenetic enzymes including sirtuin (silent mating type information regulation 2 homologue) 1 (*Saccharomyces cerevisiae*), histone deacetylase and histone methyltransferase (Choi et al. 2009). Gallic acid uncompetitively inhibited p300/CBP-dependent HAT activities. It inhibited p300-induced p65 acetylation, both in vitro and in vivo, increased the level of cytosolic IkappaBalpha, prevented lipopolysaccharide (LPS)-induced p65 translocation to the nucleus and suppressed LPS-induced nuclear factor-kappa B activation in A549 lung cancer cells. Gallic acid treatment inhibited the acetylation of p65 and the LPS-induced serum levels of interleukin-6 in vivo and generally inhibited inflammatory responses caused by other stimuli, including LPS, IFN-gamma and interleukin-1beta, and further down-regulated the expression of nuclear factor-kappa B-regulated antiapoptotic genes. *Rosa rugosa* methanol stem extract inhibited both p300 and CBP (60–70 % at 100 µg/mL) activity, indicating it to be a potent HAT inhibitor (Lee et al. 2008). The extract decreased transcription of androgen receptor (AR)-regulated genes and also reduced histone H3 and AR acetylation in the promoters of prostate-specific antigen (PSA) and beta-2-microglobulin (B2M). Further treatment with the extract reduced the growth of LNCaP, a human prostate cancer cell line. Two galenic preparations (teas and tinctures) of *R. rugosa* root, leaf, nut (seed), hip and flower extracts were evaluated against ovarian (TOV-112D), cervical (HeLa), breast (T47D) and lung cancer (A549) cell lines using the BrdU test (Olech et al. 2012). The root and hip tea decoction and nut tincture at 100 µg/mL had high antitumor effects on human lung and ovary cancer cell lines. Tinctures and decoctions prepared from flowers and leaves showed a considerable antitumour effect on A549 and TOV-112D lines (85–95 % of dead cells), yet the damaging effect on normal fibroblast cell lines was also significant (80–90 %). A significant viability decrease in cervical (HeLa) and breast cancer (T47D) lines was observed after exposure to root decoction (50 % and 75 % for HeLa and T47D, respectively). The significant cytotoxic influence (50 % of dead cells) was observed after incubation of the cervical cell line (HeLa) with flower decoction and breast cancer line (T47D) with nut decoction. A 25 % viability decrease in T47D line after incubation with flower decoction and HeLa line with nut decoction was noticed. Tea obtained from leaves and hips did not exhibit any significant anticancer activity. The data obtained demonstrated considerable impact of polyphenols on the anticancer activity of extracts (ethanolic, in particular). *R. rugosa* petals exhibited cytotoxic effect against cervical (HeLa) and breast cancer (T47D) cell lines (Nowak et al. 2013). All *Rosa rugosa* bee pollen polysaccharides fractions had significant antiproliferative activity in HT-29 and HCT116 human colon carcinoma cell line; the neutral and acidic fractions were shown to have significant synergistic effects which accounted for the antitumour activity of bee pollen polysaccharides from *Rosa rugosa* in vitro (Wang et al. 2013).

Antiviral Activity

Rosa rugosa root extract exhibited potent anti-human immunodeficiency virus (HIV) activity at a concentration of 100 µg/mL (Park et al. 2005a). Rosamultin isolated from the root inhibited HIV-1 protease by 53 % at a concentration of 100 µM.

Among 18 medicinal herbs screened at a concentration of 500 μg/mL, the aqueous extract of dried *R. rugosa* flowers showed the strongest inhibition of human immunodeficiency virus type 1 reverse transcriptase (HIV-1 RT) in vitro (Fu et al. 2006; Ng et al. 2006). Two components, P1-a (Mw150 kDa) and P1-b (Mw 8 kDa), were isolated from the ethanol precipitate of the aqueous extract of *R. rugosa* flowers. They inhibited the activity of HIV-1 RT with an IC_{50} of 158 nM and 148.16 μg/mL (18.5 μM), respectively. Further structural analyses revealed that P1-a was a polysaccharide–peptide complex, and P1-b was a polymer of a condensed tannin consisting of acteoside and acteoside derivatives. Both P(1-a) and P(1-b) possessed antioxidant activity, with the activity of P(1-b) higher than that of P(1-a). Tellimagrandin I together with eugeniin and casuarictin isolated from the methanol flower extract were found to be potent hepatitis C virus invasion inhibitors (Tamura et al. 2010).

Antimicrobial and Probiotic Activities

Growth of intestinal bifidobacteria and lactobacilli was not affected by the addition of *Rosa rugosa* petal in plate cultivation, but the growth of pathogenic bacteria *Bacteroides vulgatus, Escherichia coli, Staphylococcus aureus* and *Bacillus cereus* was completely inhibited by the addition of 0.1, 0.5, 0.1 and 0.05 % (w/v) of the petal, respectively (Kamijo et al 2008). In liquid cultivation, the addition of the petal (0.5 %) stimulated the growth of *Bifidobacterium breve* and slightly inhibited the growth of *Lactobacillus salivarius*, but the growth of *E. coli, S. aureus, B. cereus* and *Salmonella* sp. was inhibited by nearly 50 %. Hydrolyzable tannins isolated from *R. rugosa*, rugosin D and tellimagrandin II showed antibacterial activities against *E. coli, S. aureus, B. cereus* and *Salmonella* sp., but little or no effect against *Bifidobacterium breve* and *L. salivarius. R. rugosa* petal showed selective antibacterial activities against intestinal and pathogenic bacteria, and the selectivity resembled that of prebiotics such as oligosaccharides and dietary fibre. *R. rugosa* petals exhibited notable antimicrobial activity against eight bacterial (i.e. *Staphylococcus epidermidis, Staphylococcus aureus, Bacillus subtilis, Micrococcus luteus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis*) and two yeast strains (*Candida albicans, Candida parapsilosis*) (Nowak et al. 2014).

Of two galenic preparations of *R. rugosa* root, leaf, hip and flower extracts, tinctures were found to be more active than tea decoctions against eight reference bacterial strains (viz., *Staphylococcus epidermidis, Staphylococcus aureus, Bacillus subtilis, Micrococcus luteus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Proteus mirabilis*) with MIC ranging from 0.08 to 2.5 mg/mL and 0.31 to 1.25 mg/mL, respectively (Olech et al. 2012). The best antibacterial properties were found in samples from leaves, followed by flowers and roots, whereas nut and pseudofruit samples exhibited lower antibacterial activity. *Rosa rugosa* extract was one of several plant extracts that had been previously shown to have growth inhibitory activity against a multidrug-resistant clinical strain of *Acinetobacter baumannii*, and the active component was identified to be ellagic acid (Miyasaki et al. 2013).

Antidiabetic Activity

Streptozotocin-induced diabetic rats showed less body weight gain and heavier kidney and liver weights than normal rats, while the oral administration of *Rosa rugosa* at a dose of 100 or 200 mg/kg body weight/day for 20 days attenuated the physiological changes induced by diabetes (Cho et al. 2004). Additionally, *R. rugosa* dose dependently reduced the overproduction of radicals associated with diabetes. *Rosa rugosa* significantly and dose dependently reduced thiobarbituric acid-reactive substance levels in serum, hepatic and renal mitochondria, implying that *Rosa rugosa* would alleviate the oxidative stress associated with diabetes by inhibiting lipid peroxidation. Oral administrations of the *Rosa*

rugosa root extract significantly decreased serum glucose, total cholesterol, triglyceride, AST and ALT levels while increased serum insulin and HDL-C in streptozotocin-induced diabetic rats (Kim and Kin 2010). The hypoglycaemic effect of the *Rosa rugosa* root extract was more effective than normal rat group. *Rosa rugosa* (méiguīhuā) extract was one of the several traditional Chinese medicinal (TCM) herbs permitted to be used as food ingredients that showed hypoglycaemic activity (Feng et al. 2013). The extract exhibited inhibitory activities against both α-amylase and α-glucosidase in vitro. *Rosa rugosa* flowers used as herbal medicine possess many activities. A fraction extracted by the ethyl acetate fraction of *R. rugosa* flowers exhibited strong inhibitory activity in vitro against protein tyrosine phosphatase 1B (PTP1B) suggesting its potential for treating diabetes (Gu et al. 2013). Seventy-five compounds including tannins were found in the fraction.

Antiobesity/Antihyperlipidaemic/ Antihypercholesteromic Activity

Park et al. (2005a) demonstrated that the methanolic extract and its ethyl acetate fraction inhibited the weight increase of the rat body, abdominal fat pad and hyperlipidemia at 200 mg/kg dose induced by high-fat diet for 6 weeks. Further, the triterpenoids, euscaphic acid and tormentic acid, isolated from *R. rugosa* roots, were active at 30 mg/kg in the same assay. Earlier, the results of animal studies suggested an existence of component in the methanol extract of *Rosa rugosa* roots which may ameliorate the accumulation of triacylglycerol in rat liver when the rats were fed the extract at the 1 % level for 4 weeks (Lee et al. 1991). However the extract did not significantly affect the levels of serum and liver total cholesterol.

An ethyl acetate-soluble fraction of methanol extract from the underground parts of *Rosa rugosa* significantly lowered serum cholesterol level in rats (Young et al. 1987a, b). The scientists found that (+)-catechin from the ethyl acetate-soluble fraction could be one of the active principles from this plant.

Antihypertensive Activity

Two different preparations of powdered *R. rugosa* flower extracts, viz. water and ethanol–ethyl acetate preparations, exhibited high angiotensin I converting enzyme (ACE) inhibitory action (Xie and Zhang 2012). The latter extract with higher activity was evaluated in spontaneously hypertensive rats by oral administration for antihypertensive effect. In acute experiment, the decrease in systolic blood pressure (SBP) and the increase in heart rate (HR) were observed at 2 h after administration at high (40 g/kg) and low (20 g/kg) dose; such reductions in SBP were maintained for 12 h. In multiple oral administration chronic experiment, an SBP reduction of 17.5 mmHg was observed after 6 days of administration at low dose, and such reductions were maintained for the next 8 days. The results demonstrated the antihypertensive effect of *Rosa rugosa* flowers, which was attributed to inhibition of angiotensin I converting enzyme.

Anti-allergic Activity

Rosa rugosa petal extract and butanol and hexane fractions effectively reduced systemic anaphylactic reactions and anti-dinitrophenyl (DNP) IgE-mediated passive cutaneous anaphylaxis in mice, with the greatest inhibition observed for the hexane fraction (Jeon et al. 2009). Additionally, a significant reduction of scratching behaviour by mice after histamine injection suggested this fraction's potential anti-allergic effect. At the cell level, the hexane fraction markedly inhibited beta-hexosaminidase release from RBL-2H3 mast cells and suppressed the expressions of mRNA interferon-gamma and interleukin-4 cytokines produced by T helper cells (type 1 and 2). The results strongly suggested that the hexane fraction may have an effect on atopic dermatitis, as these two cell types play central roles in the pathogenesis of atopic dermatitis.

Hepatoprotective Activity

The methanol extract of *R. rugosa* root reduced the activities of aminopyrine *N*-demethylase and aniline hydroxylase, which had been increased by bromobenzene, but rosamultin did not affect the activities of the two enzymes (Park et al. 2004). Both the methanol extract and rosamultin restored the activity of epoxide hydrolase, which had also been decreased by bromobenzene. Hepatic glutathione concentrations were lowered and hepatic lipid peroxides were increased in rats intoxicated with bromobenzene. The hepatic lipid peroxidation induced by bromobenzene was prevented with the methanol extract and rosamultin. However, the decrease in glutathione was not altered by the methanol extract of *R. rugosa*. The results suggested that the extract of *R. rugosa* and its compound, rosamultin, may protect against bromobenzene-induced hepatotoxicity through, at least in part, enhanced activity of epoxide hydrolase. Also antioxidant properties may contribute to the protection of *R. rugosa* against bromobenzene-induced hepatotoxicity. Pretreatment with (+)-catechin isolated from *R. rugosa* roots gave no effects on the activities of aminopyrine N-demethylase and aniline hydroxylase, enzymes forming toxic bromobenzene epoxide intermediates and glutathione S-transferase, an enzyme that removes toxic epoxides in rats treated with bromobenzene (Hur et al. 2007).

Platelet-Aggregating Activity

Among the nine ellagitannins, rugosin E, isolated from *Rosa rugosa*, was the most potent platelet-aggregating agent with an EC_{50} of 1.5 μM in rabbit platelets and 3.2 μM in human platelets (Teng et al. 1997). The aggregations caused by rugosin E and ADP were inhibited by EGTA, PGE1, mepacrine, sodium nitroprusside and neomycin, but not by indomethacin, verapamil, TMB-8, BN52021 and GR32191B. Both rugosin E and ADP did not induce platelet aggregation in ADP (1 mM)-desensitized platelets. In contrast to ADP, rugosin E did not decrease cAMP formation in washed rabbit platelets. Both rugosin E and ADP did not cause phosphoinositide breakdown in [3H]myo-inositol-labelled rabbit platelets. In fura-2/AM-load platelets, both rugosin E and ADP induced increase in intracellular calcium concentration, and these responses were inhibited by ATP and PGE1. All these data suggested that rugosin E may be an ADP receptor agonist in rabbit platelets.

Allergy Problem

Demir et al. (2002) reported that villagers in the lake region, Turkey, reported asthma/allergy symptoms outside the rose season (17.6 %), during the rose season (6.2 %) and both during the rose season and outside the rose season (whole year) (17.6 %). Atopy and specific IgE against *Rosa rugosa* were detected in 12 (19 %) and 8 (19.5 %) of the 41 villagers tested. Villagers who had symptoms the whole year reported more frequently wheezing than those who reported symptoms only outside the rose season (41.2 % vs. 11.1 %).

Traditional Medicinal Uses

Rosa rugosa flowers (petals or buds) have been used for medicinal and food purposes for hundreds of years in China, Korea and Japan (Hur et al 2007; Lee et al 2008; Xie and Zhang 2012). They have been used in traditional Chinese medicine (TCM) to effectively help in expansion of blood vessels and improvement of microcirculation, for treatment of haematemesis (vomiting of blood), haemoptysis (coughing of blood from respiratory tract), hypermenorrhoea (heavy menstruation), apoplexy (bleeding within internal organs), diarrhoea, stomach ache, vaginal discharge, dysentery, mastitis and swellings (Zhu 1989; Lu 2005).

Other Uses

R. rugosa is a widely planted medicinal plant in China, Korea and Japan and also ornamental plant in its native range and elsewhere.

Comments

R. rugosa can outcompete native flora, thereby threatening biological diversity. It has been deemed a noxious weed in the United States.

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Galium odoratum

Scientific Name

***Galium odoratum* (L.) Scop.**

Synonyms

Asperula eugeniae K. Richt., *Asperula matrisylva* Gilib. (inval.), *Asperula odora* Salisb. (illeg.), *Asperula odorata* L., *Asterophyllum asperula* Schimp. & Spenn., *Asterophyllum sylvaticum* Schimp. & Spenn., *Chlorostemma odoratum* (L.) Fourr., *Galium matrisylva* F.H. Wigg. (illeg.)

Family

Rubiaceae

Common/English Names

Catchweed Bedstraw, Hay Plant, Herb Walter, Kiss-Me-Quick, Master of the Forest, Master Of The Woods, Smooth Bedstraw, Star Grass, Sweet Grass, Sweet Woodruff, Sweet-Scented Bedstraw, Wild Baby's Breath, Wood Rove, Woodruff, Wuderove

Vernacular Names

Albanian: Ngjitës Erëmirë
Brazil: Aspérula Odorífera (Portuguese)
Czech: Mařinka Vonná, Svízel Vonný
Danish: Bukar, Bukkar, Grønne Kranse, Mysike. Skovmærke
Dutch: Lievevrouwbedstro, Onze-Lieve-Vrouwbedstro
Estonian: Lõhnav Madar
Esperanto: Asperulo, Asperulo Odora, Galio Odora, Virgulino-Fojno
Finnish: Tuoksumaratti, Tuoksumatara
French: Asperule Odorante, Beille Étoile, Gaillet Odorant, Hépatique Étoilee, Muguet Des Bois, Petit Muguet, Petit Muguet Des Bois, Reine Des Bois
Gaelic: Lus Moileas
German: Echter Waldmeister, Duftlabkraut, Gliedkraut, Herzfreund, Leberkraut, Maiblume, Maichrut, Maikraut, Maitee, Mösch, Teekraut, Waldmeister, Waldermisterkraut, Waldmutterkraut, Waldtee, Wohlriechendes Labkraut
Hungarian: Szagos Müge
Icelandic: Anganmaðra, Ilmmaðra
Italian: Asperula, Caglio Odoroso, Galium, Stellina Odorosa
Japanese: Kurumaba-Sou
Norwegian: Amur, Musk, Mysk, Møske, Myske
Polish: Marzanka Wonna, Marzanna, Przytulia Wonna
Portuguese: Aspérula-Odorífera
Russian: Jasmennik Duschistji
Slovaščina: Dišeča Lakota, Lakota Dišeča
Slovencina: Lipkavec Marinkový
Spanish: Asperula, asperilla de los bisques, Asperilla Olorosa, asperillo, bregandia, hierba de la opilada, Hepática Estrellada, reina de los bisques, rubia menor, Rubilla, ruina de los bosques

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Swedish: Myska, Myskmadra
Welsh: Briwydden Bêr

Origin/Distribution

The native range of *G. odoratum* is reported to be in north and Central Europe southern to the mountains of Italy and of the Balkan Peninsula, northern Africa and north western Asia (W Siberia).

Agroecology

A cool climate, subtemperate to temperate species. In its native range, it is found in woodland, beech forest and shady areas on moist calcareous or rich basic soils. It thrives in partial shade and will tolerate full shade.

Edible Plant Parts and Uses

Galium odoratum is a culinary herb, whose leaves and flowers are used as food and as flavouring for various foods and used for tea (Hedrick 1972; Launert 1981; Facciola 1990; Bown 1995; Elias and Dykeman 2009; Deane 2007–2012). The sweet-scented flowers are eaten or used as a garnish. A fragrant and delicious, herbal tea is made from the green-dried leaves and flowers. The leaves can be eaten raw or cooked and for garnishing. Fruit salads are also flavoured with woodruff leaves. Fresh or dried leaves of woodruff are used as flavouring agents in non-alcoholic, cooling drinks and alcoholic beverages. The leaves are soaked in white wine to make '*Maitrank*', an aromatic tonic drink that is made in Alsace, France. May wine, also called *Maiwei*n and *Maibowle*, and *Korn Schnapps* (vodka) are popular German alcoholic beverages that are flavoured with sweet woodruff. *Korn Schnapps* is a popular party drink among young people. Berliner Weisse beers and brandy are also flavoured with woodruff essential oil. Woodruff-flavoured sherbet powder too is popular. The herb is also used to flavour jams, jellies, ice creams and a Georgian soft drink called *Tarhun*.

Botany

An herbaceous perennial, 20–50 cm high with ascending to erect, branched, 4-angled stems. The leaves are simple, oblanceolate, glabrous above, 2–5 cm long, with prominent midrib, lime green and borne in whorls of 6–9 (Plate 1). Flowers small, 4–7 mm across, produced short pedicels in cymes, funnel-shaped, white with 4–6 mm long, 4-lobed, the lobes about equal to the tube (Plates 1 and 2). Fruits – small nutlets, 2–4 mm long with numerous, short, hooked bristles.

Plate 1 Flowers and leaves (LM Landry)

Plate 2 Close-up of flowers (LM Landry)

Nutritive/Medicinal Properties

G. odoratum plant was found to contain L-ascorbic acid (Wierzchowska-Renke 1969), citric, malic, rubichloric and tannic acids (Grieve 1971), coumarins and flavonoids (Kovac-Besović and Durić 2003); coumarin (0.4–1 %), asperuloside (0.05–0.3 %), monotropein (0.04 %), tannins, iridoids, anthraquinones, flavonoids and traces of nicotinic acid (Kahkeshani et al. 2013). Two methyl caffeoylquinates of chlorogenic acids, namely, methyl 3-caffeoylquinate and methyl 5-caffeoylquinate, were found in maté tea and woodruff (*Galium odoratum*) (Jaiswal and Kuhnert 2011). The following iridoids were found in *G. odoratum*: geniposidic acid, monotropein, 10-deacetylasperulosidic acid, scandoside, asperulosidic acid, deacetylasperuloside and asperuloside (Mitova et al. 2002).

The herb was found to contain 21 free (.07 %) and 19 bound (0.96 %) amino acids, 9 of which were essential (valine, isoleucine, leucine, lysine, arginine, histidine, methionine, threonine, phenylalanine) (Yurchenko et al. 2013). Aspartic and glutamic acids, proline, leucine, alanine, serine, glycine, and arginine dominated in the herb.

Asperuloside is found in seed, seedling, shoot, leaves and fruit (Trim 1952). Monotropein was isolated from the plant (Sticher 1971). On average, fresh woodruff contained 1 % coumarin DW; the highest amount occurred in the leaves, less in the stalks and blossoms, while roots contained no coumarin (Laub and Olszowski 1982).

The roots of *Galium* spp. and *Asperula odorata* contained anthraquinone pigments and one or more ofthefollowingnaphthaleniccompounds:4-methoxy-1-naphthol, 1-naphthyl isopentyl ether, 1-naphthyl isopentenyl ether and 2,2-dimethylnaphtho [1,2-*b*]pyran and its 3,4-dihydro-derivative (Burnett and Thomson 1968). The young leaves contained the glycoside melilotoside; upon damage or withering, coumarin (or 2H-1-benzopyran-2-one) was liberated by enzymatic cleavage.

Wardziak and Osińska (2007) examined the developmental and chemical differentiation of three woodruff populations under natural and cultivated conditions and found that flavonoids and phenolic acids contents depended on the origin and development stage of a plant reaching 0.23 and 1.19 % (at plants from natural habitats) and 0.54 and 1.25 % (at cultivated plants).

A total of 224 volatiles were identified as woodruff constituents and 7,11,15-trimethyl-2-hexadecanone was identified for the first time in nature (Wörner and Schreier 1991). The major compounds were coumarin (>1,000 μg/kg); compounds with contents of 100–1,000 μg/kg included (*Z*)-3-hexen-l-ol; linalool; borneol; benzyl alcohol; 2-phenylethanol, thymol; 8-hydroxylinalool; α-thujone; menthone; camphor; benzaldehyde; carvone; β-ionone; 2-hexadecanone; methyl dihydrocoumarate; pentacosane, dihydroactinidiolide; hexanacid; and anethole; and compounds with contents of 10–100 μg/kg included 2-butanol; 2-methyl-3-buten-2-ol; 2-methyl-1-propanol; 3-penten-2-ol; 1-pentenol; (*Z*)-2- penten-2-ol; 1-hexanol; (*Z*)-2-hexen-l-ol; (*E*)-sabinenhydrate; (*E*)-linalooloxide, furanoid; 1-octanol; 4-terpinen-l-ol; neomenthol; menthol; 1,2-butandiol; isoborneol; α-terpineol; (*E*)-linalooloxide, pyranoid; 1-dodecanol; phenol; 1-tetradecanol; carvacrol;3-methoxybenzylalcohol; farnesol; 4-hydroxyacetophenone; β-thujone; (*E,Z*)-2-4-heptadienal; 2-decanone; (*E,Z*)-3,5-octadien-2-one; pulegone; 2-methylacetophenone; l-phenylpropan-l-one; 5,6,-epoxy-fl-ionone; 4-methoxybenzaldehyde; hexadecanal; 2-methylbutyl-2-butenoate; bornyl acetate; dihydroterpinylacetate; linalylbutanoate; α-terpinylpropanoate; methyl hexadecanoate; tethyl hexadecanoate; α-thujene; camphene; butylcyclohexane; Δ^3-carene; fenchane; aromadendrene; γ-pentalactone; γ-nonalactone; 2,3-dimethyl-2-nonen-4-olide; acetic acid, pentanoic acid, heptanoic acid, octanoic acid, nonanoic acid, benzoic acid; suberin acid, pentadecanoic acid; dihydrocoumaric acid and hexadecanoic acid.

Ninety-six compounds representing 89.1 % of the essential oil *G. odoratum* aerial parts were characterized (Baser et al. 2004). The major components were thymol (30.6 %), isothymol (22.8 %) and isothyml butyrate (5.5 %).

Antioxidant Activity

In 1, 1-diphenyl-2-picryl-hydrazyl (DPPH) assay, both methanolic and aqueous plant extracts

displayed significant antioxidant activity with IC_{50} values of 148 μg/ml and 83 μg/ml, respectively (Kahkeshani et al. 2013).

Wound Healing Activity

Studies found statistically significant improvement in second degree burn wound contraction of rats treated with topical application of methanolic and aqueous extracts of *Galium odoratum* after 14 days in comparison to control (Kahkeshani et al. 2013). The healed wounds in extract-treated animals contained less inflammatory cells and had better re-epithelialization. Wound contraction and histology parameters were relatively better in aqueous extract (90.68 % and 97.18 % for aqueous extracts of 15 % and 30 % in comparison to 79.29 % and 91.94 % for methanolic extracts of 15 % and 30 %, respectively).

Antiviral Activity

Asperula odorata contained an antiviral anthraquinone derivative that showed inhibitory effect against thymidine kinase of herpes simplex virus1 (HSV-1) (Rivola and Guicciardi 1994).

Antimicrobial Activity

Coumarins (1,2-Benzopyrone) found in sweet woodruff had been shown to inhibit a range of fungi and bacteria and it is believed that these cyclic compounds behave as natural pesticidal defence molecules for plants and they represent a starting point for the exploration of new derivative compounds possessing a range of improved antifungal activity (Brooker et al. 2007, 2008).

Traditional Medicinal Uses

The plant is not official but is widely used in folk medicine as a diuretic, sudorific, sedative and wound-healing agent (Yurchenko et al. 2013).

Sweet woodruff was widely used in herbal medicine during the Middle Ages, as an external topical application to wounds and cuts and also administered internally in the treatment of digestive and liver ailments (Grieve 1971). In traditional medicine, woodruff is used as a tonic, antispasmodic, cardiac, diaphoretic, diuretic, sedative and anti-inflammatory agent (Lust 1974; Launert 1981; Huxley et al. 1992; Bown 1995; Chevallier 1996). An infusion of the herb is used in the treatment of insomnia and nervous tension, varicose veins, biliary obstruction, hepatitis and jaundice. A homeopathic remedy of the herb is employed in the treatment of uterus inflammation (Bown 1995). The essential oil of woodruff is used as a carminative and mild expectorant and its leaves and dried plant are widely used as insect repellent and moth deterrent. The dried plant contains coumarins and these act to prevent the clotting of blood—though in excessive doses it can cause internal bleeding, dizziness and symptoms of poisoning (Chevallier 1996).

Other Uses

Woodruff makes an excellent ground-cover plant for growing on woodland edges or in the cool shade of shrubs (Thomas 1990). It is an ideal carpeting plant for bulbs to grow through. Woodruff is used as a strewing herb and is an ingredient of potpourri and hung in bunches to freshen up rooms with its fragrance (Bown 1995). The stems and leaves yield soft-tan and grey-green dyes and the roots a red dye (Grae 1974).

Comments

Woodruff is easily propagated by crown division, separation of the rooted stems or digging up of its shallow subterranean stolons.

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Gardenia jasminoides

Scientific Name

***Gardenia jasminoides* J. Ellis**

Synonyms

Gardenia angusta (L.) Merr., *Gardenia angustifolia* Lodd., *Gardenia angustifolia* var. *kosyunensis* (Sasaki) Masam., *Gardenia augusta* Merr. (Illeg.), *Gardenia augusta* var. *grandiflora* (Lour.) Sasaki., *Gardenia augusta* var. *kosyunensis* Sasaki, *Gardenia augusta* var. *longisepala* Masam., *Gardenia augusta* var. *ovalifolia* (Sims) Sasaki, *Gardenia florida* L. (Illeg.), *Gardenia florida* var. *fortuniana* Lindl., *Gardenia florida* var. *grandiflora* (Lour.) Franch. & Sav., *Gardenia florida* var. *maruba* (Siebold ex Blume) Matsum., *Gardenia florida* f. *oblanceolata* Nakai, *Gardenia florida* var. *ovalifolia* Sims, *Gardenia florida* var. *plena* Voigt, *Gardenia florida* var. *radicans* (Thunb.) Matsum., *Gardenia florida* f. *simpliciflora* Makino, *Gardenia grandiflora* Lour., *Gardenia grandiflora* Siebold ex Zucc. (Illeg.), *Gardenia jasminoides* f. *albomarginata* H. Hara, *Gardenia jasminoides* f. *albovariegata* H. Hara, *Gardenia jasminoides* f. *aureovariegata* Nakai, *Gardenia jasminoides* var. *fortuniana* (Lindl.) H. Hara, *Gardenia jasminoides* f. *grandiflora* (Lour.) Makino, *Gardenia jasminoides* var. *grandiflora* (Lour.) Nakai, *Gardenia jasminoides* f. *longicarpa* Z.M. Xie & M. Okada, *Gardenia jasminoides* var. *longisepala* (Masam.) Metcalf, *Gardenia jasminoides* f. *maruba* (Siebold ex Blume) Nakai ex Ishii, *Gardenia jasminoides* var. *maruba* (Siebold ex Blume) Nakai, *Gardenia jasminoides* f. *oblanceolata* (Nakai) Nakai, *Gardenia jasminoides* f. *ovalifolia* (Sims) H. Hara, *Gardenia jasminoides* var. *ovalifolia* (Sims) Nakai, *Gardenia jasminoides* var. *plena* (Voigt) M.R. Almeida, *Gardenia jasminoides* var. *radicans* (Thunb.) Makino, *Gardenia jasminoides* f. *simpliciflora* (Makino) Makino, *Gardenia jasminoides* f. *variegata* (Carrière) Nakai, *Gardenia jasminoides* var. *variegata* (Carrière) Makino, *Gardenia longisepala* (Masam.) Masam., *Gardenia maruba* Siebold ex Blume, *Gardenia pictorum* Hassk., *Gardenia radicans* Thunb., *Gardenia radicans* var. *simpliciflora* (Makino) Nakai, *Genipa florida* (L.) Baill., *Genipa grandiflora* (Lour.) Baill., *Genipa radicans* (Thunb.) Baill., *Jasminum capense* Mill., *Varneria augusta* L. (Inval.), *Warneria augusta* L. (Inval.)

Family

Rubiaceae

Common/English Names

Cape Jasmine, Cape Jessamine, Common Gardenia, Garden Gardenia, Gardenia, Jasmin

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Vernacular Names

Brazil: Gardênia (Portuguese)
Chinese: Chin Tzu, Shān Zhī Zǐ, Shiu Heng Chi, Shui Heng Zhi, Zhi Zi
Cook Islands: Tiare Taina (Maori)
Czech: Gardénie Jasmínovitá
Danish: Almindelig Gardenia
Estonian: Jasmiingardeenia
French: Gardenia
German: Gardenie, Kap Gardenie, Kap Jasmin, Jasminglanz
India: Gandharaj (Bengali), Gandhraj (Hindi), Suvasane Malle (Kannada), Kaboklei (Manipuri), Gandroya (Marathi), Gulchand (Urdu)
Indonesia: Chepiring, Cheplokpiring, Kacapiring, Pechiring (Javanese), Kacapiring (Sundanese)
Italian: Gardenia
Japanese: Kuchinashi, San Shi Shi
Korean: Chi Ja Na Mu
Laos: Inthavaa, Ph'ud
Malaysia: Buah Patah, Buah Batek, Buah Kuning (Fruit), Bunga Cina, Bunga Susu, Kaca Piring (Flower)
Philippines: Garden Gardenia, Rosal (Tagalog)
Pohnpei: Ioseph Sarawi
Polish: Gardenia Jasminowata
Portuguese: Jasmin-Do-Cabo
Russian: Gardenia
Spanish: Gardenia
Swedish: Gardenia
Thai: Phut, Phut Chin, Phut Son, Phut Yai, Phut-Tharaksaa, Khet-Thawaa
Vietnamese: Dành Dành

Origin/Distribution

Gardenia is native to southern China, Japan, Ryukyu Islands and Taiwan. It is widely cultivated in the tropics and subtropics.

Agroecology

Cape Jasmine is originally a species from subtemperate climates. In tropical areas it grows well, at altitudes of 400–1,200 m. *Gardenia* grows best in a mild, humid climate in partial to full sun. It prefers well-drained, fertile, friable soil with a pH of 5–7 and high organic matter. The plant is salt intolerant and somewhat drought tolerant.

Edible Plant Parts and Uses

An edible yellow dye is obtained from the fruit and is used for colouring food in China, Japan and Korea. In China, the yellow dye is used for colouring bean curd in Guangzhou. In Japan, the dye is used to colour boiled beans, fish eggs, hot cakes, sweets, liquor, noodles, candies, ices and imitation crab (Sangat-Roemantyo and Wirdateti 1992). In Korea, Gardenia yellow dye is used in making yellow mung bean jelly called 'hwangpomuk' (Wikipedia 2013). 'Hwangpomuk' is a noted staple food of Namwon and also Jeonju (both cities in the North Jeolla Province, Korea), where it is a common ingredient of Jeonju-style *bibimbap* in the Jeolla cuisine. The jelly is commonly served in small chunks seasoned with vinegar, soy sauce and other condiments; this side dish is called *hwangpomuk-muchim.*

The mild sweet Gardenia blossoms are edible (Tanaka 1976; Facciola 1990) and used dried or fresh to impart fragrance to jasmine tea in the Far East (Sangat-Roemantyo and Wirdateti 1992; Roberts 2000; Deane 2007–2012). This tea is reported beneficial to people with hepatitis. Fresh Gardenia flowers can be tucked into a tin of tea to scent the tea. Blossoms tucked into rice, oats or sago will impart the same mild sweet fragrance. Gardenia flowers can be added to sugar, drinks, fruit salads, cakes, desserts and syrups (Roberts 2000). Some recipes include Gardenia milk shake, Gardenia chocolate mousse and Gardenia

and litchi fruit salad. Gardenia flowers are also eaten raw as delicacy, pickled or preserved in honey, and they are called *mi-ts'ai*.

Botany

A smooth, unarmed, perennial, evergreen, woody shrub, 1–2 m high. The leaves are opposite, elliptic–ovate, 3–10 cm long, acuminate or obtuse and cuneate at the base, glossy green, smooth and short petioled, 0.2–0.5 cm long. Stipules large, tubular and obliquely opened on one side (Plates 1 and 2). Flowers large and very fragrant, white turning yellowish and solitary at the end of branchlets, pedicels 3–6 mm long with tubular stipule-like bracts, hypanthia turbinate, 6-ridged, 10–12 mm long, sepals 6, obtuse and persistent, corolla salverform, tube 30 mm long, limbs 30–60 mm across deeply 6-lobed, lobes contorted in bud, extended at anthesis, stamens 6, exserted, anthers linear, ovary inferior, disc annular, style slender, stigma clavate (Plates 1 and 2). Fruit berrylike, ellipsoid to ovoid, 10–20 mm long by 10–15 mm, crowned by persistent calyx (Plate 3), orange when ripe with juicy placentae and with numerous discoid seeds with tuberculate testa.

Plate 1 Flower, bud and leaves

Ornamental cultivars have double flowers with petaloid or poorly developed stamens and sterile ovary.

Nutritive/Medicinal Properties

Flower Phytochemicals

Cycloartane triterpenoids gardenic acid and gardenolic acid B were isolated from the flowers (Xu et al. 1987). (R)-Linalyl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside and bornyl 6-*O*-β-D-xylopyranosyl-β-D-glucopyranoside were isolated as aroma precursors of linalool and borneol from *Gardenia jasminoides* flower buds (Watanabe et al. 1994).

Plate 2 Fully opened flower and leaves

Plate 3 Developing fruits with persistent calyx

The major constituents of the essential oil obtained from *G. jasminoides* flower were benzyl acetate, hydroxycitronellal and eugenol (Wang 1979). Fifty-four components were characterized, representing 100 % of the total components detected on Gardenia flower essential oil (Obuzor and Nwaokolo 2010). Gardenia flower oil was composed mainly of sesquiterpenes 49.01 % and monoterpene 44.33 %. The major constituents of sesquiterpenes were identified as α-farnesene (28.41 %) and small amounts of guaiol (5.89 %), (*Z*)-3-hexenyl tiglate (5.47 %), bulnesol (5.03 %) and *cis*-3-hexenyl benzoate (4.21 %). In the case of monoterpene, linalool (22.05 %) was the major constituent and *trans*-β-ocimene (10.59 %) and α-terpineol (9.03 %) with methyl tiglate (2.66 %) as the minor component, while tetracosane (5.64 %) was the only alkane. Sesquiterpenes that occur in small amounts were germacrene D (0.03 %), germacrene B (0.08 %), β-caryophyllene (0.05 %) and calarene (0.14 %) with some monoterpenes such as nerol (0.4 %), α-thujene (0.03 %), *cis*-3-hexenol (0.22 %), myrcene (0.02 %), *allo*-ocimene (0.03 %), α-pinene (0.02 %) and β-pinene (0.02 %). Compounds that occurred in traces included benzaldehyde, 1-octen-3-ol, cymene, α-phellandrene, camphene, terpinolene, sabinene, limonene, benzyl alcohol, γ-terpinene, citral, neral, geranial, isoartemesia, 1,8-cineole, borneol, citronellal, terpinene-4-ol, citronellol, linalyl acetate, borneol acetate, neryl acetate, β-bisabolene, cyperene, α-gurjunene, α-copaene, β-selinene, α-bergamotene, α-selinene, α-bisabolene, τ-muurolene and viridiflorol.

Fruit Phytochemicals

Two iridoid glycosides, geniposide and genipin-1-β-D-gentiobioside, were isolated from *G. jasminoides* fruits (Endo and Taguchi 1973). Earlier gardenoside and geniposide (Inouye et al. 1969), genipin-1-β-D-gentiobioside (Endo and Taguchi 1970) and shanzhiside and deacetylasperulosidic acid methyl ester were isolated (Inouye et al. 1970). From the fruits of *Gardenia jasminoides* forma *grandiflora*, which had been employed as a Chinese crude drug, Shanzhi-I, three new iridoid glucosides, gardenoside, shanzhiside and methyl deacetylasperulosidate, were isolated along with the known geniposide and genipin gentiobioside (Inouye et al. 1974c) and 5β-hydroxygeniposide (Inouye et al. 1974b). From the fruit of *Gardenia jasminoides* forma *grandiflora*, two glucosides, 10-acetylgeniposide and picrocrocinic acid were isolated (Takeda et al. 1976). Enzymatic β-glucosidase hydrolysis of gardenoside yielded its aglucone gardenogenins A and B, while acid treatment of gardenoside gave scandoside methyl ester, deacetylasperulosidic acid methyl ester and 10-dehydrogeniposide (Ishiguro et al. 1983). Two lipoxygenase inhibitors, 3, 4-dicaffeoyl-5-(3-hydroxy-3-methylglutaroyl)quinic acid (Nishizawa and Fujimoto 1986) and 3-*0*-caffeoyl-4-*0*-sinapoyl quinic acid (Nishizawa et al. 1987), were isolated from the fruits. The fruit was found to contain iridoids (Ragasa et al. 2007) and iridoid glucosides, gardoside (8,10-dehydrologanic acid) and scandoside methyl ester (Inouye et al. 1974a). In the first stage of *G. jasminoides* forma *grandiflora* fruit development, i.e. 1–6 weeks after flowering, fruit weight and the geniposide content were found to increase rapidly, and no crocin was detected. In the second stage, 8–23 weeks postflowering, the geniposide content per fresh weight of fruit barely changed, whereas crocin accumulation began and increased linearly with time until full ripeness (Umetani et al. 1980).

Nine new monoterpenoids, gardenamide A, 6α-butoxygeniposide, 6β-butoxygeniposide, 60-*O*-*p*-*cis*-coumaroylgenipin gentiobioside and jasminosides A–E, were isolated from the fruit (Machida et al. 1998). Four new terpenoids, gardenate A, 2-hydroxyethyl gardenamide A, (1*R*,7*R*,8*S*,10*R*)-7,8,11-trihydroxy-guai-4-en-3-one 8-*O*-β-D-glucopyranoside and jasminoside F, were isolated from the fruit (Machida et al. 2000). A new iridoid, gardaloside, and a new safranal-type monoterpene, jasminoside G, together with known compounds geniposide, 6α-hydroxy-geniposide, ixoroside and shanzhiside, were isolated from the fruit (Chang et al. 2005). A new vanillic acid 4-*O*-β-D-(6′-sinapoyl)glucopyranoside and five new quinic acid derivatives, methyl

5-*O*-caffeoyl-3-*O*-sinapoylquinate, ethyl 5-*O*-caffeoyl-3-*O*-sinapoylquinate,methyl5-*O*-caffeoyl-4-*O*-sinapoylquinate, ethyl 5-*O*-caffeoyl-4-*O*-sinapoylquinate and methyl 3,5-di-*O*-caffeoyl-4-*O*-(3-hydroxy-3-methyl)glutaroylquinate, together with three known quinic acid derivatives, two flavonoids, two iridoids and two phenolic compounds, were isolated from the fruit (Kim et al. 2006). A new iridoid glycoside, 6′-*O*-sinapoylgeniposide (Zhou et al. 2007b), and two new monoterpenes named gardenone and gardendiol were isolated from the fruits (Zhao et al. 1994).

Nine compounds, imperatorin; isoimperatorin; crocetin; 5-hydroxy-7,3′,4′,5′-tetrainethoxyflavone; 2-methyl-3,5-dihydroxychromone; Sudan III; geniposide; crocin; and crocin-3, were isolated and identified from *G. jasminoides* fruit (Chen et al. 2007). Five new pyronane-type monocyclic monoterpenoids, jasminodiol, jasminoside H, 6′-*O*-sinapoyljasminoside A, 6′-*O*-sinapoyljasminoside C and jasminoside I, together with four known analogues, jasminoside B, crocusatin C, epijasminoside A and jasminoside A, were isolated from the fruit (Chen et al. 2008a). Seven new iridoid glucosides, 6″-*O*-*trans*-sinapoylgenipin gentiobioside, 6″-*O*-*trans*-*p*-coumaroylgenipin gentiobioside, 6″-*O*-*trans*-cinnamoylgenipin gentiobioside, 6′-*O*-*trans*-*p*-coumaroylgeniposide, 6′-*O*-*trans*-*p*-coumaroylgeniposidic acid, 10-*O*-succinoylgeniposide and 6′-*O*-acetylgeniposide; two new monoterpenoids, 11-(6-*O*-*trans*-sinapoylglucopyranosyl) gardendiol and 10-(6-*O*-*trans*-sinapoylglucopyranosyl) gardendiol; and three known ones, 6′-*O*-*trans*-sinapoylgeniposide, geniposide and 10-*O*-acetylgeniposide, were isolated from the fruit (Yu et al. 2009). The iridoid glycosides, genipin 1-*O*-β-D-isomaltoside and genipin 1,10-di-*O*-β-D-glucopyranoside, together with six known iridoid glycosides, genipin 1-*O*-β-D-gentiobioside, geniposide, scandoside methyl ester (**5**), deacetylasperulosidic acid methyl ester, 6-*O*-methyldeacetylasperulosidic acid methyl ester and gardenoside, were isolated from an ethanol fruit extract (Chen et al. 2009). Eight new monoterpenoids, jasminoside J, jasminoside K, 6′-*O*-*trans*-sinapoyljasminoside B, 6′-*O*-*trans*-sinapoyljasminoside L and jasminosides M–P, together with three known analogues, jasminoside C, jasminol E and sacranoside B, were isolated from the fruit (Yu et al. 2010b). Twelve compounds were isolated from Gardenia fruit ethanol extract and identified as gardenianan A, a lignan; syringaresinol; pinoresinol; syringaresinol-4-*O*-β-D-glucopyranoside; laricinresinol; alangilignoside D; lyoniresinol; lyoniresinol-9-*O*-β-D-glucopyranoside; balanophonin; glycosmisic acid; ficusal; and ceplignan (Yu et al. 2010a). A new lignan glucoside, (+)-(7*S*,8*R*,8′*R*)-lyoniresinol 9-*O*-β-D-(6″-*O*-*trans*-sinapoyl)glucopyranoside, and a new iridoid glucoside, 10-*O*-*trans*-sinapoylgeniposide, together with eight known compounds, were isolated from the fruits (Yu et al. 2012). A new iridoid glycoside, 10-*O*-(4″-*O*-methylsuccinoyl) geniposide, and two new pyronane glycosides, jasminosides Q and R, along with nine known iridoid glycosides and two known pyronane glycosides were isolated from a methanol extract of dried *Gardenia* fruit extract (Akihisa et al. 2012). Thirteen compounds were isolated and identified from the active antiviral fraction from *Gardenia* fruit: shanzhiside, gardenoside, geniposide, geniposidic acid, chlorogenic acid, 10-*0*-acetyl geniposide, shanzhiside methyl ester, scandoside methyl ester or deacetylasperulosidic methyl ester, 6″-*O*-*E*-caffeoyl deacetylasperulosidic methyl ester, 6″-*O*-sinapoyl gardoside, 3-*O*-caffeoyl-5-*O*-sinapoyl quinic acid or 3-*O*-caffeoyl-4-*O*-sinapoyl quinic acid, 3,4-di-O-caffeoyl quinic acid or 3,5-di-*O*-caffeoyl quinic acid and 6″-*O*-sinapoyl geniposide (Yang et al. 2012a). Two new guaiane-type sesquiterpenoid glucosides were isolated from *Gardenia* fruit, and their structures elucidated as (*1R,7R,10S*)-11-*O*-β-D-glucopyranosyl-4-guaien-3-one and (*1R,7R,10S*)-7-hydroxy-11-*O*-β-D-glucopyranosyl-4-guaien-3-one (Yu et al. 2011).

Three new iridoids, gardenal-I, gardenal-II and gardenal-III, together with nine known iridoid glycosides, geniposide, 6-β-hydroxy geniposide, 6-α-hydroxy geniposide, 6-α-methoxy geniposide, feretoside, genipin-1-β-gentiobioside, shanzhiside, lamalbidic acid and picrocrocinic acid, were isolated from *Gardenia*

ethanol fruit extract (Rao et al. 2013). Three new iridoid glycosides, 6″-*O*-*trans*-feruloylgenipin gentiobioside, 2′-*O*-*trans*-*p*-coumaroylgardoside and 2′-*O*-*trans*-feruloylgardoside (3), were isolated from the fruit of *Gardenia jasminoides* var. *radicans* (Qin et al. 2013). Three new iridoid glycosides, 6″-*O*-*trans*-caffeoylgenipin gentiobioside, genipin 1-*O*-β-D-apiofuranosyl (1→6)-β-D-glucopyranoside and genipin 1-*O*-α-D-xylopyranosyl (1→6)-β-D-glucopyranoside, and three new monocyclic monoterpenoids, jasminoside R, jasminoside S and jasminoside T, together with nine known iridoid glycosides and three crocetin glycosides, were isolated from *G. jasminoides* fruit (Peng et al. 2013).

The following carotenoids were isolated and identified from the fruit: crocetin, crocin (crocetin di(β-gentiobiosyl) ester), crocetin mono(β-gentiobiosyl) ester and 13Z-crocin (Pfister et al. 1996). Crocin, an apocarotenoid glycosyl ester, was found to accumulate in fruits of *Gardenia jasminoides* (Pfister et al. 1996; Nagatoshi et al. 2012) and used as a food colouring and nutraceutical owing to its pharmacological benefits. The first step specific to crocin biosynthesis had been reported to be the position-specific cleavage of zeaxanthin to yield crocetin dialdehyde (Pfander and Schurtenberger 1982), and then crocetin dialdehyde was oxidized to crocetin. Two glucosyltransferases UGT75L6 and UGT94E5 that sequentially mediate the final glucosylation steps in crocin biosynthesis in *G. jasminoides* were identified and functionally characterized by Nagatoshi et al. (2012).

Colourless geniposide isolated from Gardenia fruits when hydrolyzed with β-glucosidase yielded genipin that was transformed to blue pigments by reaction with amino acids (glycine, lysine or phenylalanine) (Fujikawa et al. 1987; Paik et al. 2001). Gardenia blue pigments were very stable with regard to pH, temperature and light conditions and may have potential for use as value-added colourants for foods (Paik et al. 2001). Park et al. (2002) obtained Gardenia blue dye through the reaction of methylamine with genipin, the aglycone of geniposide isolated from *G. jasminoides* fruits. Water-soluble intermediates of blue pigments were found to compose of two epimeric isomers. A glycoprotein (GJE glycoprotein) with a molecular weight of 27 kDa was isolated from *G. jasminoides* fruit (Lee et al. 2006b). It comprised a carbohydrate component (57.65 %) and a protein component (42.35 %). Six kinds of fatty acids were found in the Gardenia fruit oil; the major constituents were linoleic acid 43.47 %, palmitic acid 22.72 % and stearic acid 9.98 % (Gan et al. 2009).

Hong and Yang (2013) isolated crocin, crocetin, gentiobiosyl glucosyl crocetin and monogentiobiosyl crocetin from the fruit. Three iridoid glucosides, 6″-*O*-*trans*-feruloylgenipin gentiobioside, 2′-*O*-*trans*-caffeoylgardoside, jasmigeniposide A, and one new bis-iridoid glucoside, jasmigeniposide B, along with six known analogues were isolated from *G. jasminoides* fruit (Li et al. 2013). Two new glycosides, 2-methyl-L-erythritol-4-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside and 2-methyl-L-erythritol-1-*O*-(6-*O*-*trans*-sinapoyl)-β-D-glucopyranoside, along with two known triterpenoids, four quinic acid derivatives and one flavonoid were isolated from *G. jasminoides* fruit (Yang et al. 2013).

Leaf Phytochemicals

Gardenoside and geniposide were found in leaves (Inouye et al. 1974c). Two new iridoid glycosides, 7β,8β-epoxy-8α-dihydrogeniposide and 8-epiapodantheroside, were isolated, together with six known iridoids galioside, gardenoside, deacetylasperulosidic acid methyl ester, scandoside methyl ester, geniposide and ixoroside and three artefact iridoids 8-*O*-methylmonotropein methyl ester, 6-*O*-methyldeacetylasperulosidic acid methyl ester and 6-*O*-methylscandoside methyl ester, from the leaves (Machida et al. 2003). Cerbinal, a pseudoazulene iridoid, was isolated from the benzene leaf extract (Ohashi et al. 1986).

Plant Phytochemicals

Six iridoid glycosides including geniposide, gardenoside, shanzhiside, scandoside methyl ester,

deacetylasperulosidic acid methyl ester and genipin-1-β-D-gentiobioside were isolated and purified from *G. jasminoides* at high purities of over 99 % with approximately 96 % recoveries using reversed-phase two-dimensional preparative high-performance liquid chromatography (Zhou et al. 2007a).

Ten compounds were isolated from *Gardenia jasminoides* and identified as jasminoside A; epijasminoside A; 6-*O*-methylscandoside methyl ester (3); 6-*O*-methyldeacetylasperulosidic acid methyl ester; gardenoside; phenylmethanol; 4-hydroxy-phenylmethol-*O*-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside; 3,4-dihydroxy-phenylmethol-*O*-β-D-glucopyranosyl-(1-6)-β-D-glucopyranoside; 3-hydroxy4-methoxyphenyl-methol-*O*-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside; and 3-hydroxy-4-methoxyphenylmethol-*O*-β-D-glucopyranoside (Zhang et al. 2013b). Ten compounds were isolated from *Gardenia jasminoides* and elucidated as syringic acid (1), syringaldehyde (2), vanillic acid (3), 3-hydroxy-vanillic acid (4), 3,4,5-trimethoxy-phenol (5), 4-hydroxy-3,5-dimethoxy-phenol (6), 4-methoxy-benzaldehyde (7), 7-hydroxy-5-methoxy-chromone (8), crocin-1 (9) and crocin-2 (10) (Zuo et al. 2013).

Cell Suspension Culture, Stem and Root Phytochemicals

From iridoid-producing cell suspension cultures obtained by selection of callus tissues derived from *G. jasminoides* f. *grandiflora* seedlings, tarennoside was isolated along with gardenoside, geniposide and geniposidic acid (Ueda et al. 1981). Oleanolic acid acetate, D-mannitol and stigmasterol were isolated and identified from the stem and root (Wang et al. 1986). Ten compounds were isolated from 70 % ethanol–water extract of *G. jasminoides* roots and identified as betulinic acid, oleanolic acid, oleanolic acid 3-*O*-β-D-glucuronopyranoside-6′-*O*-methyl ester, hederagenin 3-*O*-β-D-glucuronopyranoside-6′-*O*-methyl ester, chikusetsusaponin IVa, stigmasterol, β-sitosterol, daucosterol, vanillic acid and syringic acid (Cao et al. 2011). Three new compounds (gardeniside A–C), 11α,12α-epoxy-3*β*-[(*O*-*β*-D-glucuronopyranoside-6′-*O*-methyl ester)oxy]olean-28,13-olide; siaresinolic acid 3-*O*-*β*-D-glucuronopyranoside-6′-*O*-methly ester; and 3-*O*-*β*-D-glucuronopyranoside-6′-*O*-methly ester-siaresinolic acid-28-*O*-*β*-D-glucopyranoside, with seven known compounds oleanolic acid 3-*O*-*β*-D-glucuronopyranoside-6′-*O*-methly ester, oleanolic acid 3-*O*-*β*-D-glucuropyranoside, hederagenin 3-*O*-*β*-D-glucuronopyranoside-6′-*O*-methyl ester, chikusetsusaponin IVa methyl ester, chikusetsusaponin, chikusetsusaponin IVa butyl ester and siaresinolic acid 28-*O*-*β*-D-glucopyranosyl ester were isolated from the root (Wang et al. 2012).

Numerous studies had shown that *Gardenia jasminoides* fruit and its main constituents crocins and iridoid glycosides possessed antioxidation, anti-inflammatory, antiatherosclerosis, anti-ischaemic brain injuries, antiplatelet aggregation, antihyperglycaemia, antihyperlipidaemia and antihypertension activities (Liu et al. 2013). Many of these activities are elaborated below.

Antioxidant Activity

Crocin, from *G. jasminoides* fruit, with purity of >99.6 % exhibited antioxidative activity at concentrations up to 40 ppm (Pham et al. 2000). At 20 ppm the antioxidative activity of crocin was comparable to that of butylated hydroxyanisole (BHA). The antioxidant property of crocin as evaluated by the thiocyanate method was better than with the thiobarbituric acid method. Another research showed three major crocins from Gardenia that were observed to possess antioxidant activity when tested by four in vitro antioxidant models (Chen et al. 2008b). However, in anti-haemolysis, DPPH radical scavenging and lipid peroxidation assays, Gardenia resin fraction exhibited significantly stronger antioxidant activity than crocins, and no correlation between total crocin contents and antioxidative function was revealed, which implied that ingredients other than crocins in Gardenia gave markedly strong antioxidant activity. A comparison of results indicated that sugars attached to the crocetin

moiety seemed to be beneficial for the antioxidant activity of these water-soluble pigments.

Five new quinic acid derivatives, methyl 5-*O*-caffeoyl-3-*O*-sinapoylquinate, ethyl 5-*O*-caffeoyl-3-*O*-sinapoylquinate, methyl 5-*O*-caffeoyl-4-*O*-sinapoylquinate, ethyl 5-*O*-caffeoyl-4-*O*-sinapoylquinate and methyl 3,5-di-*O*-caffeoyl-4-*O*-(3-hydroxy-3-methyl)glutaroylquinate isolated from the fruits, showed potent DPPH radical scavenging, superoxide anion scavenging and lipid peroxidation inhibition activities (Kim et al. 2006). GJE glycoprotein from Gardenia fruit exhibited dose-dependent scavenging activities for DPPH, lipid peroxyl, superoxide anion and hydroxyl radicals in cell-free systems (Lee et al. 2006b). GJE glycoprotein from Gardenia fruit exhibited dose-dependent blocking activities against glucose/glucose oxidase (G/GO)-induced or hypoxanthine/xanthine oxidase (HX/XO)-induced cytotoxicity and apoptosis in NIH/3T3 cells. 100 μg/ml GJE glycoprotein had an inhibitory effect on PKCα translocation and the DNA binding activity of (NF-κB). The results suggested GJE glycoprotein to be a natural antioxidant and one of the modulators of apoptotic signal pathways in NIH/3T3 cells.

An iridoid glycoside and a crocetin glycoside exhibited strong inhibitory activity on NO production in lipopolysaccharide-activated macrophages with IC_{50} values of 11.14 μM and 5.99 μM, respectively (Peng et al. 2013).

Antiviral Activity

G. jasminoides was one of 27 of the 44 medicinal herbs that showed potent or moderate antiviral activities against respiratory syncytial virus with 50 % inhibition concentration (IC_{50}) values ranging from 6.3 to 52.1 μg/ml and with selectivity index (SI) ranging from 2.0 to 32.1 (Ma et al. 2002). Five new quinic acid derivatives, methyl 5-*O*-caffeoyl-3-*O*-sinapoylquinate, ethyl 5-*O*-caffeoyl-3-*O*-sinapoylquinate, methyl 5-*O*-caffeoyl-4-*O*-sinapoylquinate, ethyl 5-*O*-caffeoyl-4-*O*-sinapoylquinate and methyl 3,5-di-*O*-caffeoyl-4-*O*-(3-hydroxy-3-methyl)glutaroylquinate isolated from the fruits, showed HIV-integrase inhibitory activity (Kim et al. 2006). In vitro studies showed that ZG extracted from Gardenia extract improved Hep-2 cell membrane fluidity, and prevented parainfluenza virus type 1 (PIV-1) infection by protecting the cell membrane (Guo et al. 2007).

The pneumonia induced by influenza virus in mice was inhibited significantly by Gardenia extract reflected by the decrease in mortality rate and increase in life elongation rate (Wang et al. 2006). Also the NO content in serum decreased significantly, and the cytopathic effect induced by six kinds of viruses was inhibited significantly. Oral administration of a fraction from Gardenia fruit extract exhibited antiviral activity against influenza virus strain A/FM/1/47-MA infection in rats (Yang et al. 2012a). Thirteen compounds were isolated and identified from the active antiviral fraction: shanzhiside, gardenoside, geniposide, geniposidic acid, chlorogenic acid, 10-*0*-acetyl geniposide, shanzhiside methyl ester, scandoside methyl ester or deacetylasperulosidic methyl ester, 6″-*O*-*E*-caffeoyl deacetylasperulosidic methyl ester, 6″-*O*-sinapoyl gardoside, 3-*O*-caffeoyl-5-*O*-sinapoyl quinic acid or 3-*O*-caffeoyl-4-*O*-sinapoyl quinic acid, 3,4-di-*O*-caffeoyl quinic acid or 3,5-di-*O*-caffeoyl quinic acid and 6″-*O*-sinapoyl geniposide.

An iridoid glycoside from Gardenia fruit showed moderate antiviral activity against H1N1 with 50 % effective concentration (EC_{50}) value of 104.36 μM and selective index (SI) value greater than 4.79 (Li et al. 2013).

Anticancer Activity

Two lipoxygenase inhibitors 3, 4-dicaffeoyl-5-(3-hydroxy-3-methylglutaroyl)quinic acid (Nishizawa and Fujimoto 1986) and 3-*0*-caffeoyl-4-*0*-sinapoyl quinic acid (Nishizawa et al. 1987) were isolated from the fruits. Animal studies suggested that inhibitors of lipoxygenase may have benefits as preventive agents of lung tumorigenesis (Rioux and Castonguay 1998). In vitro studies showed that pretreating C3H10T1/2 cells with crocetin inhibited benzo[a]pyrene [B(a)P]-induced genotoxicity and neoplastic

transformation by increasing activity of GSH S-transferase and decreasing the formation of B(a)P-DNA adduct (Chang et al. 1996). Pretreatment of CD-1 mice with crocetin, a major component of *G. jasminoides* fruit, suppressed 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced mouse skin carcinogenesis (Hsu et al. 1999). TPA-induced epidermal hyperplasia and TPA-induced expressions of c-Jun, c-Fos and c-Myc in mouse epidermis were reduced by crocetin probably via its antioxidant property. In vitro studies showed that crocetin (5–20 μg/mL) and quercetin (10–40 μg/mL) exhibited selective cytotoxicity, causing intense damage only on the malignant human rhabdomyosarcoma cells, whereas mild toxic effects were observed with cisplatin (60–180 μg/mL), a positive control drug, also on normal (Vero) cells (Jagadeeswarana et al. 2000).

Penta-acetyl geniposide from the fruit was found to play more potent roles than geniposide in the chemoprevention of cancer (Peng et al. 2005a). It decreased DNA damage and hepatocarcinogenesis induced by aflatoxin B1 (AFB1) by activating the phase II enzymes glutathione S-transferase (GST) and GSH peroxidase (GSH-Px). It reduced the growth and development of inoculated C6 glioma cells especially in pretreated rats, exerting its actions on apoptosis and growth arrest, and caused DNA fragmentation of glioma cells. It was not harmful to the liver, heart and kidney. Penta-acetyl geniposide was found to induce JNK activation and c-Jun phosphorylation, thus stimulating the expression of FasL and Fas and apoptosis through the activation of JNK/Jun/FasL/Fas/caspase-8/caspase-3, a mitochondria-independent pathway (Peng et al. 2005b). The JNK pathway was suggested to be the downstream signal of PKCδ. Thus, penta-acetyl geniposide mediated cell death via activation of PKCδ/JNK/FasL cascade signalling. Further they demonstrated that penta-acetyl geniposide induced apoptosis in C6 glioma cells by modulating the activation of neutral sphingomyelinase-induced p75 nerve growth factor receptor and protein kinase Cδ pathway in upstream signals. Further Chang et al. (2004) found that the apoptotic effect of penta-acetyl geniposide, arresting C6 glioma cells at the G_0/G_1 phase, was exerted by inducing the expression of cyclin-dependent kinase (cdk) inhibitor p21 protein that, in turn, repressed the activity of cyclin D_1/cdk 4 and the phosphorylation of retinoblastoma.

The n-butanol fraction of Gardenia ethanol fruit extract showed antiangiogenic activity in the chick chorioallantoic membrane assay (Park et al. 2003). Koo et al. (2004a) also found Gardenia ethanol fruit to have potent antiangiogenic activity in the chick embryo chorioallantoic membrane assay; the extract yielded an active antiangiogenic compound, which was determined to be an iridoid glucoside, geniposide. Geniposide showed antiangiogenic activity in a dose-dependent manner. It also exhibited an inhibitory effect in the range of 25–100 μM on the growth of the transformed NIH3T3 cell line.

Studies by Lim et al. (2010) found that the dichloromethane fraction from Gardenia fruit extract induced apoptotic cell death by DNA topoisomerase 1 inhibition in KB oral cancer cells. Treatment with Gardenia extract dichloromethane fraction also led to the partial increase of caspase-3, caspase-8 and caspase-9 activities and the cleavage of poly(ADP-ribose) polymerase. The following compounds isolated from the roots showed cytotoxic activities against HeLa, A549, MCF-7 and A354-S2 cancer cell lines: 11α,12α-epoxy-3*β*-[(*O*-*β*-D-glucuronopyranoside-6′-*O*-methly ester)oxy]olean-28,13-olide; oleanolic acid 3-*O*-*β*-D-glucuronopyranoside-6′-*O*-methly ester; oleanolic acid 3-*O*-*β*-D-glucuropyranoside; hederagenin 3-*O*-*β*-D-glucuronopyranoside-6′-*O*-methly ester; chikusetsusaponin IVa methyl ester; and chikusetsusaponin IVa butyl ester (Wang et al. 2012). Genipin, a constituent of *G. jasminoides*, significantly induced apoptosis in human breast cancer MDA-MB-231 cells by the downregulation of Bcl-2, up-regulation of Bax, proteolytic activation of caspase-3 and activation of JNK and p38 MAPK (Kim et al. 2012). Further, genipin significantly inhibited invasive and migratory phenotypes of MDA-MB-231 cells.

Anti-inflammatory Activity

G. jasminoides alcohol extract, two fractions and geniposide exhibited anti-inflammatory effects and were comparatively effective in treating soft tissue injuries in animals (Yao et al. 1991). Gardenia fruit ethanol extract and its constituents, genipin and geniposide, exhibited acute anti-inflammatory activities in carrageenan-induced rat paw oedema (Koo et al. 2006). In a dose-dependent manner, Gardenia extract also inhibited vascular permeability induced by acetic acid. Both genipin and geniposide inhibited production of exudate and nitric oxide (NO) in the rat air pouch oedema model. However, genipin possessed stronger anti-inflammatory activity than geniposide. Gardenia fruit extract caused a dose-dependent inhibition of acetic acid-induced abdominal writhing in mice. In an earlier study, genipin exhibited significant topical anti-inflammatory effect shown as an inhibition of croton oil-induced ear oedema in mice (Koo et al. 2004b). Genipin concentration dependently (50–300 μM) inhibited NO production and iNOS expression upon stimulation by lipopolysaccharide/interferon-gamma (IFN-gamma) in RAW 264.7, a murine macrophage cell line. Genipin markedly blocked lipopolysaccharide-evoked degradation of inhibitor-kappaB-beta (IkappaB-beta), indicating that it exhibited inhibitory effect on NO production through the inhibition of nuclear factor-kappa B (NF-κB) activation. Genipin showed concentration-dependent inhibition on lipid peroxidation induced by Fe^{++}/ascorbate in rat brain homogenate. It was also shown to contain potent antiangiogenic activity in a dose-dependent manner, in a chick embryo chorioallantoic membrane assay. Geniposide, a major component of Gardenia fruit, exhibited protective effects against lipopolysaccharide (LPS)-induced acute lung injury in mice by mitigating inflammatory responses which may involve suppression of nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) signalling pathway activation (Yang et al. 2012b). Geniposide substantially inhibited LPS-induced alveolar wall changes, alveolar haemorrhage and neutrophil infiltration in the lung tissue, with evidence of reduced myeloperoxidase (MPO) activity. In a more recent animal study, rats with ankle strain injury treated with geniposide (100 mg/mL) isolated from the fruit showed 21–34 % reduction in swelling ratio compared with the vehicle-treated control rats from the second to the fifth day (Chen et al. 2009).

Crocin, crocetin, gentiobiosyl glucosyl crocetin and mono-gentiobiosyl crocetin isolated from the fruit reduced NO production in a dose-dependent manner in LPS-stimulated RAW 264.7 cells with IC_{50} values of 58.9 μM (1), 29.9 μM (2), 31.1 μM (3) and 37.6 μM (4), respectively (Hong and Yang 2013). They also suppressed the protein and mRNA expressions of iNOS and COX-2 in LPS-activated macrophage. The DPPH radical scavenging activities were increased, and NO productions in LPS-stimulated RAW 264.7 cells were decreased dose-dependently by roast processing. The results suggested that antioxidant and anti-NO production activities of Gardenia were increased by roast processing, and increased anti-inflammatory activities of Gj by processing were due to the increase of crocetin, the aglycone that had greater activity than crocin. Compared with the ova-induced hallmarks of asthma, intraperitoneal geniposide treatment prevented eosinophilic pulmonary infiltration; attenuated the increases in interleukin (IL)-4, IL-5 and IL-13; and reduced eotaxin and vascular cell adhesion molecule 1 (VCAM-1) expression in ova-sensitized and ova-challenged BALB/c mice (Deng et al. 2013). Also, geniposide significantly ameliorated the ova-driven airway hyper-responsiveness, mucus hypersecretion and allergen-specific IgE level, which are the cardinal pathophysiological symptoms in allergic airway diseases. In addition, the efficacy of geniposide was comparable to that of dexamethasone, a currently available antiasthmatic drug. Collectively, their findings revealed that the development of immunoregulatory strategies based on geniposide may be considered as an effective adjuvant therapy for allergic asthma.

Hypoglycaemic Activity

Of four iridoidal glycosides isolated from *Gardenia jasminoides* leaves, deacetylasperulosidic acid methyl ester (DE), scandoside methyl ester (SC), geniposide (GE) and gardenoside (GA), only DE displayed hypoglycaemic activity in test mice (Miura et al. 1996). DE lowered the blood glucose level in normal mice. However, SC, GE and GA did not affect the blood glucose level in normal mice, indicating the absolute configuration of 6-position hydroxy based (OH) to be essential for the biological activity.

Studies showed that genipin inhibited uncoupling protein 2 (UCP2)-mediated proton leak in isolated mouse mitochondria and acutely reversed obesity-induced and high glucose-induced beta cell dysfunction in isolated pancreatic islets and thus may improve type 2 diabetes in mice (Zhang et al. 2006).

In vitro studies by Ma et al. (2013) demonstrated that genipin stimulated glucose uptake in a time- and dose-dependent manner in C2C12 myotubes. The results suggested that genipin activated insulin receptor substrate (IRS)-1, PI3-K and downstream signalling pathway and increased concentrations of calcium, resulting in glucose transporter 4 (GLUT4) translocation and glucose uptake increase in C2C12 myotubes.

Administration of genipin, a compound from *G. jasminoides* fruit, to aging rats ameliorated systemic and hepatic insulin resistance; alleviated hyperinsulinaemia, hyperglyceridaemia and hepatic steatosis; and relieved hepatic oxidative stress and mitochondrial dysfunction (Guan et al. 2013). In addition, genipin not only improved insulin sensitivity by promoting insulin-stimulated glucose consumption and glycogen synthesis and inhibited cellular ROS overproduction and alleviated the reduction of levels of MMP and ATP but also reversed oxidative stress-associated JNK hyperactivation and reduced Akt phosphorylation in palmitate-treated L02 hepatocytes. The authors concluded that genipin ameliorated age-related insulin resistance through inhibiting hepatic oxidative stress and mitochondrial dysfunction.

Anti-pancreatitis Activity

Studies showed that *G. jasminoides* extract increased pancreatic blood flow that was significantly decreased at the early stage of acute necrotizing hemorrhagic pancreatitis in rats (Jia et al. 1993). Extracts of Chinese herbs including *G. jasminoides* used in traditional Chinese medicine could inhibit pancreatic enzymes and improve microcirculation as well as immunoregulation by blocking the pathological progress of severe acute pancreatitis (Zhang et al. 2007). An animal study found that *G. jasminoides* treatment significantly decreased the severity of cerulean-induced acute pancreatitis and pancreatitis-associated lung injury (Jung et al. 2008). *Gardenia* treatment attenuated the severity of acute pancreatitis compared with saline-treated mice, as shown by reduction in pancreatic oedema, neutrophil infiltration, serum amylase and lipase levels, serum cytokine levels and mRNA expression of multiple inflammatory mediators. Studies showed that the combination of Sandostatin and *G. jasminoides* had a protective effect on pancreatic mitochondria injury in severe acute pancreatitis rats (Wang et al. 2011).

Antiatherosclerotic Activity

In an in vitro study of cultured cell line of vascular smooth muscle cell from murine aorta, Gardenia fruit hot aqueous extract stimulated the proliferation of endothelial cells but not of A10 cells and significantly increased the accumulation of basic fibroblast growth factor (Kaji et al. 1991). They postulated that a selective stimulation of endothelial cell proliferation by increasing the production of basic fibroblast growth factor was appropriate for prevention of arteriosclerosis and thrombosis; thus, Gardenia extract may contain a beneficial component as a useful drug. Earlier, they demonstrated that a low molecular mass component of Gardenia fruit hot aqueous extract stimulated endothelial cell proliferation and an increased protein synthesis was an essential component of this response (Kaji et al. 1990).

Gardenia fruit extract may contain a useful compound to stimulate the proliferation of endothelial cells. In vitro studies showed that *G. jasminoides* ethanol extract was able to inhibit TNF-alpha-induced NF-kappa B activation, adhesion molecule expression and monocyte-endothelial interaction in primary cultured human umbilical vein endothelial cells (HUVEC), suggesting an anti-inflammatory role of Gardenia extract, which may be useful in preventing vascular diseases, such as atherosclerosis (Hwang et al. 2010).

Hepatoprotective Activity

Chang et al. (1985) reported that the hepatotoxic activity of oc-naphthylisothiocyanate, in increasing serum bilirubin, glutamic pyruvic transaminase and glutamic oxaloacetic transaminase activities in rats, was significantly reduced by geniposide administered orally. Histopathological observations of the liver gave good agreement with the serological data. However, geniposide appeared unable to reduce the toxic effect of a large dosage of CCl4 or D-galactosamine. Pretreatment with crocetin (10, 20 μM), from Gardenia fruit, suppressed hepatotoxicity in rat primary hepatocytes (Tseng et al. 1995). Crocetin decreased formation of malondialdehyde (MDA) as an index of lipid peroxidation induced by ROS (reactive oxygen species). The addition of crocetin decreased genotoxicity evaluated with unscheduled DNA synthesis by the xanthine–xanthine oxidase (X/XO) and paraquat systems. Crocetin also inhibited the formation of superoxide anion in the X/XO system and bleached the free radical 1,1-diphenyl-2-picrylhydrazyl (DPPH). Oral treatment of geniposide and *G. jasminoides* fruit crude extract of rats for 4 days decreased serum urea nitrogen level but increased liver to body weight ratio, total hepatic glutathione content and hepatic cytosolic glutathione S-transferase activity (Kang et al. 1997). The treatments decreased P-450 content, benzo[a]pyrene hydroxylation, 7-ethoxycoumarin *O*-deethylation and erythromycin N-demethylation activities in liver microsomes without affecting aniline hydroxylation activity. The treatments also decreased the intensity of a P4503A-immunorelated protein. The findings demonstrated that geniposide from *G. jasminoides* had the ability to inhibit a P4503A monooxygenase and increase glutathione content in rat liver. In vitro studies showed that geniposide had a potential for detoxification by inducing GST (glutathione S-transferase) by increasing the transcription of GSTM1 and GSTM2 in primary cultured rat hepatocytes (Kuo et al. 2004). *G. jasminoides* extract significantly inhibited paw oedema in collagen-induced rheumatoid arthritic rats and significantly decreased the levels of serum interleukin (IL)-1 β and tumour necrosis factor (TNF)-α at high dose or medium dose (Zhu et al. 2005).

Lee et al. (2006c) found that *G. jasminoides* glycoprotein inhibited glucose/glucose oxidase-induced toxicity and intracellular reactive oxygen species production in glucose/glucose oxidase-treated murine embryonic liver (BNL CL.2) cells. Further, Gardenia glycoprotein exhibited an antioxidant effect against the lipid peroxidation process in the Fe^{2+}/ascorbic acid system. In CCl_4 (1.0 ml/kg)-treated mice, pretreatment with Gardenia glycoprotein (80 mg/kg) obstructed lactate dehydrogenase release and the formation of thiobarbituric acid-reactive substances. Additionally, in these mice Gardenia glycoprotein resulted in increased nitric oxide production and the activation of antioxidant enzymes, accompanied by the inhibition of the cytotoxic-related signals hepatic cytochrome C, nuclear factor-kappa B and activator protein-1. In both Triton WR-1339 (400 mg/kg) and corn oil (1.0 g/kg)-treated mice, pretreatment with Gardenia glycoprotein (80 mg/kg) lowered the levels of plasma lipoproteins (triglyceride, total cholesterol and low-density lipoprotein).

In vivo studies showed that intraperitoneal injection of geniposidic acid, a constituent of *G. jasminoides*, exhibited cytoprotective activity against D-galactosamine (GalN)/lipopolysaccharide (LPS)-induced fulminant hepatic failure in mice (Kim et al. 2013). The survival rate of the geniposidic acid-treated mice was significantly higher than the control. The results suggested that

geniposidic acid alleviated GalN/LPS-induced liver injury by enhancing antioxidative defence system and reducing apoptotic signalling pathways.

Geniposide, an important constituent of *G. jasminoides*, had exhibited bright prospects in prevention and therapy of hepatic injury (Wang et al. 2013b). A systematic analysis of the therapeutic effects of geniposide using biochemistry, metabolomics and proteomics was conducted to elucidate the working mechanisms of this compound. Geniposide significantly intensified the therapeutic efficacy as indicated by modern biochemical analysis. Metabolomics results indicated 9 ions in the positive mode as differentiating metabolites which were associated with perturbations in primary bile acid biosynthesis, butanoate metabolism, citrate cycle (TCA cycle), alanine, aspartate and glutamate metabolism. Notably, geniposide possessed potential pharmacological effect by regulating multiple perturbed pathways back to normal state. To elucidate the benefits of geniposide based on the proteomics approaches, six identified differential proteins appeared to be involved in antioxidation and signal transduction, energy production, immunity, metabolism and chaperoning. These proteins were closely related in the protein–protein interaction network and the modulation of multiple vital physiological pathways.

Antihyperlipidaemic Activity

Research showed that Gardenia fruit and its component crocin exhibited hypolipidaemic activity that may be due to the inhibition of pancreatic lipase and crocin, and its metabolite, crocetin, could ameliorate hyperlipidaemia (Lee et al. 2005). Crocin and crocetin also showed hypolipidaemic activity in hyperlipidaemic mice induced by high-cholesterol, high-fat or high-carbohydrate diets for 5 weeks. In diet-induced hyperlipidaemic rats, a 10-day treatment with crocin significantly reduced serum triglyceride, total cholesterol, low-density lipoprotein (LDL) cholesterol and very low-density lipoprotein (VLDL) cholesterol level in the daily dose range of 25–100 mg/kg (Sheng et al. 2006). Results of the modified fat-loading method indicated that crocin inhibited the absorption of fat and cholesterol and this inhibition is closely related to the hydrolysis of fat. Crocin increased the faecal excretion of fat and cholesterol in rats, but had no influence on the elimination of bile acids. The findings suggested that crocin exhibited its hypolipidaemic effect by inhibiting pancreatic lipase, leading to the malabsorption of fat and cholesterol.

Chinese herbal extract (*Salvia miltiorrhiza* and *Gardenia jasminoides*) treatment of rats with non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome induced by a high-fat diet (HFD), significantly reduced serum triglycerides and nonesterified fatty acids, enhanced insulin sensitivity and ameliorated the elevated serum hepatic enzymes compared with HFD-saline rats (Tan et al. 2013). HFD rats were obese, hyperinsulinaemic and hyperlipidaemic and have increased hepatic enzymes with the histological images of NAFLD. Herbal extract treatment also attenuated hepatic triglycerides by 18.5 %, normalized macrovesicular steatosis in HFD rats and significantly reduced TNF-α and IL-6 in adipose tissue.

Neuroprotective Activity

Geniposide, isolated from *Gardenia jasminoides*, protected neuronal cells from damage in oxygen and glucose deprivation-exposed hippocampal slice culture (Lee et al. 2006a). Geniposide showed a greater protective effect on the granule cell layer than on the pyramidal cell layer. The results suggested that geniposide may be a therapeutic agent for ischaemia in patients. In vitro studies showed that *G. jasminoides* extract could reduce cytotoxicity of amyloid beta peptide (Abeta) in PC12 cells, possibly by reducing Abeta-induced oxidative stress (Choi et al. 2007).

Research demonstrated that genipin extracted from *Gardenia jasminoides* can be fixed in gelatine and that the genipin-fixed gelatin could be an acceptable extracellular matrix for nerve regeneration (Liu et al. 2004).

Anti-amnesic Activity

The n-butanol fraction of Gardenia fruit extract showed the strongest acetylcholinesterase (AChE) inhibition (43.4 % at a final dose of 0.03 mg/mL) and also exhibited outstanding efficacy (65.9 % at a dose of 250 mg/kg) in an experimental amnesic mouse model of Alzheimer's disease (Nam and Lee 2013). Activity-guided fractionation of the total extracts resulted in the isolation of two glycosides, geniposide and crocin, from the n-butanol fraction and genipin and crocetin from the ethyl acetate fraction. Geniposide showed a 22.8 % AChE inhibitory activity and a potent ameliorating effect on scopolamine-induced memory impairment in amnesic mice of 93.4 % as compared to the control group.

Antiplatelet/Antithrombotic Activity

Geniposide and its metabolite genipin showed an antithrombotic effect in vivo due to the suppression of platelet aggregation by inhibition of phospholipase A (2) activity (Suzuki et al. 2001). In an in vivo model, geniposide and genipin significantly prolonged the time required for thrombotic occlusion induced by photochemical reaction in the mouse femoral artery. In an in vitro study, both geniposide and genipin inhibited collagen-induced, but did not inhibit arachidonate-induced, mouse platelet aggregation.

Studies by Zhang et al. (2013a) indicated that *G. jasminoides* aqueous extract and geniposide demonstrated remarkable antithrombotic activities and supported their therapeutic uses for thrombotic diseases. Gardenia extract (67, 133 and 266 mg/kg) and aspirin (50 mg/kg), respectively, decreased the length of tail thrombus with an average thrombus inhibition rate of 21.9, 55.7, 65.8 and 57.6 % at 48 h after carrageenan injection and improved thrombosis induced by arteriovenous shunt (silk thread) with 36.3, 45.5, 86.4 and 63.7 % inhibition rate of thrombus, respectively, and the ED_{50} of Gardenia extract was 160.8 mg/kg. Additionally, Gardenia extract (67 mg/kg) and geniposide (20 mg/kg) significantly inhibited platelet aggregation induced by thrombin/collagen with 45.1 %/19.3 % and 52.8 %/26.2 % aggregation rate. Geniposide (10–40 mg/kg) and genipin (5–20 mg/kg) inhibited venous thrombosis induced by tight ligation of the inferior vena cava; their ED_{50} values were 18.4 and 8.6 mg/kg, respectively.

Hypotensive Activity

The crude Gardenia seed extract was found to have hypotensive activity (Koo and Li 1977). The hypotensive action was attributable to a reflex phenomenon, involving both the parasympathetic and the sympathetic vasomotor centres, and had minimal cardiac depressant effect. It was demonstrated that the hypotensive and bradycardiac properties of Gardenia extract were entirely abolished in tropinized and vagotomized rats, but only partially attenuated in carotid sinus denervated rats, and that low cervical spinal transection in rats did not inhibit the hypotensive responses.

Anti-hypopigmentation Activity

Geniposide was also reported to enhance melanogenesis by stem cell factor/c-kit signalling in which the expression of c-kit receptor was augmented in norepinephrine-exposed normal human epidermal melanocyte (Lan et al. 2008b). Further, geniposide was found to abrogate the norepinephrine-induced hypopigmentation by the activation of glucagon-like peptide-1 receptor (GLP-1R)-dependent c-kit receptor signalling in which c-kit expression was enhanced in normal human epidermal melanocyte (Lan et al. 2008a).

Antityrosinase Activity

The pyronane monoterpenoid jasminodiol isolated from the fruit exhibited tyrosinase inhibitory activity (IC_{50} 2.2 mM) (Chen et al. 2008a). Three monoterpene glycosides from Gardenia fruit, namely, 6-*O*-*p*-coumaroylgeniposide, 10-*O*-(4″-*O*-methylsuccinoyl)geniposide and

6′-*O*-sinapoyljasminoside, exhibited inhibitory effects on melanogenesis in B16 melanoma cells induced with α-melanocyte-stimulating hormone with 21.6–41.0 and 37.5–47.7 % reduction of melanin content at 30 and 50 μM, respectively, with almost no toxicity to the cells (83.7–106.1 % of cell viability at 50 μM) (Akihisa et al. 2012).

Choleretic Activity

Aqueous and alcohol extracts of Gardenia fruit increased bile secretion in rabbits (Miwa 1953a); the alcoholic fruit extract inhibited the appearance of blood bilirubin when injected into the aural vein of rabbits whose common bile duct had been ligated (Miwa 1953b), and the same alcoholic extract suppressed the bilirubin in peripheral lymph of rabbits (Miwa 1953c). The active principles of Gardenia fruit extract were found to be crocin and crocetin (Miwa 1954). Intravenous injection of crocin or crocetin at a dose of 0.1 g/kg into rabbits increased bile secretion; both compounds suppressed the appearance of blood bilirubin in common bile-duct-ligated rabbit, and the amount of bilirubin in peripheral lymph (popliteal lymph) in common bile-duct-ligated rabbit was suppressed by injection of crocin and crocetin.

Studies showed that erythritol clearance was increased with the increase in bile flow by administration of genipin (Aburada et al. 1978). Genipin showed a significant choleretic action, the concentration of biliary bile acid was decreased inversely. Genipin did not affect the concentration of sodium, potassium, chloride or bicarbonate in the bile collected during the initial stage, in which bile flow was increased, after administration. It was concluded from the results that genipin-induced choleretic action proceeded by a mechanism wherein water was driven along osmotic gradient which originated in the transport of bile acid-independent fraction from hepatocytes into canaliculi, mainly through active Na^+ transport. In further studies they found that genipin and patrinoside decreased biliary concentrations of bile acids, Na^+, Cl^- and $HCO3^-$, corresponding to their rapid choleretic actions which were due to bile acid-independent fraction (Takeda et al. 1981). The main metabolite detected from the bile after administration with genipin was genipin-1-*O*-glucuronic acid (GGA). The periodical pattern of GGA level in the bile was in agreement with that of genipin-induced choleretic action, and quantitatively the cation and anion gap produced was nearly compensated by biliary concentration of GGA.

In vivo studies showed that geniposide, a main iridoid glucoside of Gardenia fruit, was transformed to genipin, a genuine choleretic, in rats (Aburada et al. 1978). Genipin and its glucuronide conjugate were detected at 44 μM and 100 μM in the portal vein and bile, respectively, after intra-duodenal administration of 2 g/kg geniposide in Wistar rats. Akao et al. (1994) reported that after oral administration, geniposide was metabolized by β-D-glucosidases of the enterobacterium, *Eubacterium* sp. A-44, into the aglycone genipin and subsequently to the aglycone of geniposidic acid by esterases. Thus, when geniposide was orally administered, genipin appeared to be effectively produced in the intestine and then absorbed by the liver to act as a genuine choleretic. Zhu et al. (1998) found that at doses of 50 and 100 mg/kg, geniposide could significantly increase the biliary secretion after intra-duodenal administration, while crocins showed no effect. Further, geniposide markedly decreased the content of cholesterol and elevated HCO_3-bicarbonate concentration in bile, but without effect on the level of bilirubin, bile acid and Ca^{2+}. The results showed geniposide was the main choleretic principle in *Gardenia jasminoides*.

Studies showed that the bile secretion in rats was markedly increased by administration of genipin, the aglycone of geniposide, but hardly increased by administration of the extract of Gardenia fruits (Chang et al. 1985). Animal studies showed that intravenous administration of 50 and 100 mg/kg of genipin (GP), gardenogenins (GAR-G), deacetylasperulosidic acid methyl ester genins (DAM-G) and scandoside methyl ester genin (SSM-G) exhibited the bile acid-independent choleretic actions (Miyagoshi et al. 1988). DAM-G exhibited the strongest choleretic

activity, while choleretic action of SSM-G was milder but longer lasting than those of GAR-G and DAM-G.

Immunomodulatory Activity

Geniposide (**3**), 6α-hydroxygeniposide (**5**), ixoroside (**7**) and shanzhiside (**8**) isolated from the fruit showed significant inhibition of interleukin (IL)-2 secretion by phorbol myristate acetate and anti-CD28 monoclonal antibody costimulated activation of human peripheral blood T cells (Chang et al. 2005).

Aflatoxin B1 Cytotoxicity Inhibitory Activity

Pretreatment with crocetin-inhibited aflatoxin B1 activated cytotoxicity and DNA adduct formation in murine C3H10T1/2 fibroblast cells (Wang et al. 1991). The protective effect of crocetin on the aflatoxin B1 cytotoxicity in C3H10T1/2 cells was postulated to be due to the cellular defence mechanisms that elevated the cytosol glutathione and the activities of GSH S-transferase (GST) and GSH peroxidase (GSH-Px).

Antimicrobial Activity

Enzymatic β-glucosidase hydrolysis of galioside yielded an aglucone which showed activity against *Staphylococcus aureus* and *Klebsiella pneumoniae*, but the aglucone of gardenoside was inactive (Ishiguro et al. 1983). Cerbinal, a pseudoazulene iridoid, isolated from leaf, exhibited potent antifungal activity against *Bipolaris sorokiniana*, *Helminthosporium*, *Pyricularia*, *Colletotrichum lagenarium* and *Puccinia* species; it caused 100 % inhibition of germination of spores of *Puccinia* species on oat, wheat, Welsh onion and white clover (Ohashi et al. 1986). The dichloromethane extract of the air-dried flowers of *Gardenia jasminoides* provided a new iridoid natural product and a diastereomeric mixture of two new iridoids (2a and 2b) in a 2:1 ratio (Ragasa et al. 2007). Antimicrobial tests of iridoid 1 indicated that it was moderately active against *Candida albicans* and slightly active against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Trichophyton mentagrophytes,* but inactive against *Bacillus subtilis* and *Aspergillus niger. Gardenia jasminoides* methanol extracts showed the highest level of antifungal activity against *Pleurotus ostreatus*, a wood-rotting fungus, compared to five other methanol plant extracts (Lelono et al. 2009). Two antifungal compounds genipin and geniposide were isolated from n-butanol and ethyl acetate solubles in the methanol extracts of *Gardenia jasminoides* leaves and stems. Both compounds exhibited potent inhibitory effects on two plant pathogenic fungi, *Fusarium oxysporum* and *Corynespora cassiicola*.

Anti-retinal Ischaemic Activity

Crocetin exhibited protective effects against the retinal ischaemia induced by 5 h unilateral ligation of both the pterygopalatine artery and the external carotid artery in anaesthetized mice through its inhibition of oxidative stress (Ishizuka et al. 2013). Crocetin prevented the ischaemia–reperfusion (I/R)-induced reductions in a- and b-wave amplitudes seen at 5 days after I/R and decreased the numbers of TUNEL-positive cells and 8-OHdG-positive cells and the phosphorylation levels of p38, JNK, NF-κB and c-Jun present in the retina after I/R.

Gastroprotective Activity

In an in vivo study on continuous perfusion of rat stomach, genipin, from Gardenia fruit, inhibited only the gastric acid secretion induced by carbachol, but not by tetragastrin, or histamine (Aburada et al. 1978). In isolated organs, genipin showed a weak competitive anti-acetylcholine action on the intestinal contraction. The results suggested that the anticholinergic action at least partly contributed to the genipin-induced inhibitory effect on gastric functions. *G. jasminoides*

extract, and its constituents ursolic acid and genipin, showed the acid-neutralizing capacities, the antioxidant activities and the inhibitory effects on the growth of *Helicobacter pylori* in rats (Lee et al. 2009). Further, Gardenia extract and ursolic acid had cytotoxic activity against AGS and SUN638 gastric cancer cells. The results suggested that Gardenia extract, genipin and ursolic acid may be useful for the treatment and/or protection of gastritis.

Sleep-Promoting Activity

In a double-blind, placebo-controlled, crossover clinical trial of 21 healthy adult men with a mild sleep complaint, administration of crocetin, compound from *G. jasminoides*, reduced the number of wakening episodes compared to placebo (Kuratsune et al. 2010). Subjective data from St. Mary's Hospital Sleep Questionnaire showed that crocetin tended to improve the quality of sleep compared to sleep before its intake. Additionally, no side effects from crocetin intake were observed.

Antifertility Activity

The ethyl acetate flower extract of *G. jasminoides* exhibited significant effects on terminating early pregnancy in rats (Xu et al. 1987). Several compounds were isolated among which 2 cycloartane triterpenoids, namely, gardenic acid and gardenolic acid B, were found to be the active components. The results supported the use of *G. jasminoides* flowers in Chinese folk medicine for birth control. Xiao and Wang (1991) reported gardenic acid and gardenolic acid A (from *Gardenia jasminoides*) to be early pregnancy-terminating agent, for fertility regulation in females.

Cross-Linking Activity

Aglycone geniposidic acid, from Gardenia fruit, a naturally occurring cross-linking agent, was found to have application for the fixation of collagenous tissues (Mi et al. 2007). It was found that the fixation indices and denaturation temperatures of test samples fixed at neutral or basic pH (pH 7.4 or pH 8.5) were significantly greater than at acidic pH (pH 4.0). The results may be used to elucidate the cross-linking mechanism and to optimize the fixation process for developing bioprostheses fixed by aglycone geniposidic acid.

Genipin, the aglycone of geniposide, a major constituent of *G. jasminoides* fruit, is used to prepare blue colourants in food industry and also a cross-linking reagent for biological tissue fixation (Hou et al. 2008). Genipin possessed significant advantages as a natural cross-linking agent over chemical cross-linking agents such as glutaraldehyde, formaldehyde, etc., used in the drug delivery systems as they caused very serious cytotoxic reactions (Manickam et al. 2013). Genipin being less toxic, biocompatible and offering very stable cross-linked products possessed unique potential to be utilized in controlling drug delivery from various formulations. Besides it had been widely used as a traditional Chinese medicine for a long time.

Pharmacokinetic Studies

Hou et al. (2008) found that after oral administration of genipin or Gardenia fruit decoction to rats, genipin sulphate was a major metabolite in the bloodstream, whereas the parent forms of genipin and geniposide were not detected. Importantly, oral administration of 200 mg/kg of genipin resulted in a mortality of 78 % (7/9) in rats.

After per oral administration of geniposide, the peak concentration of geniposide in rat plasma occurred at 1 h, and plasma geniposide was eliminated nearly completely within 12 h (Wang et al. 2013a). The absolute oral bioavailability (%F) of geniposide was calculated as 9.67 %. After per oral administration of geniposide, the AUC0 → 4 h values in tissues were in the order of kidney > spleen > liver > heart > lung > brain. After oral administration of *G. jasminoides* fruit crude extract and Zhi-zi-chi decoction, >88.0 % of geniposidic acid was recovered from

the rat plasma (Long et al. 2013). After oral administration of Zhi-zi-chi decoction (containing Gardenia fruit, bitter orange and soybean) and *G. jasminoides* extract, six iridoid glycosides geniposide, geniposidic acid, scandoside methyl ester, gardenoside, deacetylasperulosidic acid methyl ester and genipin-1-β-gentiobioside were extracted from rat plasma samples (Qu et al. 2013).

Hepatotoxicity Activity

G. jasminoides fruit extract showed no hepatotoxic effects in rats as detected by measurement of alkaline phosphatase, aspartate aminotransferase and lactate dehydrogenase activities in serum and liver (Kong et al. 1977). However in another study, oral administration of Gardenia yellow colour at doses of 800 mg/kg up to 5,000 mg/kg to rats caused diarrhoea and increases in serum alanine aminotransferase and aspartate aminotransferase activities in a dose-dependent manner (Yamano et al. 1988). The toxicity induced by the colourant was stronger by oral administration than by intraperitoneal administration. The content of geniposide, an iridoid compound, was estimated to be 28 % of the colourant, and this iridoid accounted for almost all the hepatotoxic activity of the colourant. It was also shown that hepatotoxic effects of intraperitoneal administration of genipin at a dose of 80 mg/kg body weight were comparable with those of oral administration of geniposide at a dose of 320 mg/kg (Yamano et al. 1990). Buthionine sulphoximine pretreatment enhanced the toxicity of geniposide, while cysteine pretreatment completely suppressed it, suggesting hepatic non-protein sulphhydryls were important in modulating the toxicity. In an earlier study, crocin did not affect hepatic function when given orally to rats in a daily dose of 50 mg/kg for 8 days, and a lower dosage of 10 mg kg for 40 days also did not, but a high dose of 100 mg/kg for 2 weeks induced both hepatic damage and black pigmentation (Lin and Wang 1986). However, the induced black pigmentation and the acute hepatic damage were completely reversible.

The acute toxicity study indicated geniposide at a dose of 574 mg/kg or more could cause hepatic toxicity in rats, and the hepatotoxicity often appeared at 24–48 h after the oral administration (Ding et al. 2013). The hepatotoxicity was associated with oxidative stress with decrease of total superoxide dismutase activity and increase of malondialdehyde concentration in rat livers. Subchronic toxicity study showed geniposide did not cause hepatotoxicity at the doses of 24.3 and 72.9 mg/kg orally for 90 days in rats. Thus, acute hepatotoxicity of geniposide at high doses was likely to be linked to oxidative stress, while geniposide at normal dose of 24.3 mg/kg or less did not cause hepatotoxicity even in the repeated dosing study.

Genotoxicity Activity

Gardenia yellow and its components crocetin, gentiobiose (a component of crocin), geniposide and genipin were found not to be mutagenic in the *Salmonella* reverse mutation assay (Ozaki et al. 2002). Gardenia yellow and genipin caused damage of DNA in the Rec-assay. Gardenia yellow induced a significant dose-dependent increase of sister chromatid exchange frequency, while only genipin induced sister chromatid exchange significantly among the components of Gardenia yellow. The results indicated that genipin possessed genotoxicity.

Contraindications

A 59-year-old woman who had been admitted to the hospital every 2 months for over the past year because of severe right abdominal pain was given a diagnosis of idiopathic mesenteric phlebosclerosis (Nomura et al. 2012). Subsequently, it was found that she had been a long-term user of a Chinese herbal product containing Gardeniae fructus for allergic rhinitis. After discontinuing the product, the patient was free of abdominal pain for a year. However, fibrous thickening and oedematous mucosa with bronze colouring persisted. In an aetiological study of 25 patients,

Hiramatsu et al. (2012) found that long-term use of geniposide in herbal medicines appeared to be associated with mesenteric phlebosclerosis. Only one ingredient, sansisi, was common to the herbal medicines of all 25 patients. This crude drug called geniposide is a major constituent of the Gardenia fruits.

Traditional Medicinal Uses

Cape Jasmine has been used for centuries as a traditional oriental herbal remedy (Burkill 1966; Quisumbing 1978; Le and Nguyen 1999; Herbal Medicine Research Center 2002). The leaves and fruit possess analgesic, antibacterial, antifebrile, demulcent, cholagogic and diuretic properties. They are used in treating fever, inflammation of the eyes, tinnitus, jaundice, epistaxis, sore throat, viral hepatitis, febrile diseases, ophthalmia, haemoptysis, bloody stools, dysuria, burns, boils and impetigo.

Gardenia fruit is used in folkloric traditional medicine as antiphlogistic, diuretic, laxative and choleretic and for treatment of hepatic and inflammatory diseases and for haemostatic purposes in the treatment of trauma by external application (Ozaki et al. 2002; Tang and Eisenbrand 1992). In China the medicinal uses of the smaller fruit are various, such as for fevers, fluxes, dropsies, lung diseases, jaundice and, externally, vulneraries (Quisumbing 1978; Herbal Medicine Research Center 2002). The larger fruit is more particularly used externally, the pulp being applied to swellings and to injuries and to such ailments as wine-nose, dog bite, slight burns and scalds. In China, an infusion of the flowers is used as an emollient and as an antiophthalmic. A poultice of pounded fresh leaves is effective for wounds, phlegmon and acute conjunctivitis. In China it is used as a bitter, febrifuge, stimulant, diuretic, emetic and a styptic. Wee and Hsuan (1990) reported that the fruits are used as a remedy for vomiting of blood, bleeding, jaundice, acute gonorrhoea, sores, boils, abscesses and inflammation; the seeds are used also for jaundice, rheumatism and twisted muscles; and flowers and roots are used to regulate blood flow, to control bleeding and to increase menstrual flow.

In Vietnam, Gardenia fruit is a common drug used in folk medicine; it is employed for treating jaundice, insomnia with restlessness, eye inflammation, tinnitus, dysuria, bloody stools, epistaxis and haemoptysis and useful for relief of sprains and bruises (Le and Nguyen 1999). Poultice of pounded leaves is used for conjunctivitis. In Vietnam, a decoction of *G. jasminoides*, *Adenosma glutinosum* and *Plumeria acutifolia* bark is administered for viral hepatitis. For jaundice and febrile diseases with restlessness, a decoction of *G. jasminoides*, *Phellodendron amurense* and *Glycyrrhiza uralensis* is administered orally. For haemoptysis and haematemesis, a salty decoction of *Gardenia* fruit (torrefied), *Sophora japonica* (torrefied) and *Pueraria thomsonii* is given orally. For burning sensation in the head, ophthalmia, tinnitus and epistaxis, a decoction of Gardenia fruit (torrefied) and *Cassia tora* (torrefied) is taken orally. For haemoptysis and epistaxis, Gardenia fruit and Imperata cylindrical decoction is used. For sprains and bruises, poultice of pounded fruit is applied topically. For burns, carbonized Gardenia fruit is powdered, mixed with egg albumin and made into a paste for external application. Charred, powdered fruit is blown into nostrils for epistaxis.

In Malaysia, the leaves are used in poultices and applied to swollen breasts and used for headache (Burkill 1966). The leaves and roots are used internally; the leaves are crushed with sugar to cure fever and the roots for fever with delirium. A lotion for cooling the heads of children is prepared by boiling Cape Jasmine and *Acacia myriophylla*. The fruit is emetic, stimulant and diuretic and is considered a cooling remedy. They are used for jaundice, for kidney and lung complaints.

Other Uses

Also planted as windbreak, hedge and ornamental. Gardenia flowers are used for cut flowers and in making wreaths, bouquets, etc. It is a favourite in the United States for corsages, being second only to *Cattleya* orchid. An essential oil extracted from the flowers is used in perfumery and cosmetic

preparations. Gardenia fruits also have been used as a yellow dye for staining foods and fabrics. The yellow dye from the fruit is used for textiles in Thailand. The yellow colour components of Gardenia fruits contained carotenoids and related compounds (Tang and Eisenbrand 1992). Colourless components of Gardenia fruits can also produce blue colourants by a simple modification of an enzyme reaction followed by the treatment of primary amines (Park et al. 2002).

The fragrant flowers are used in perfumery; detached flowers are often floated in small containers of water to impart some sweet fragrance to rooms.

Comments

Gardenia can be propagated by soft wood cutting in spring and hard wood cuttings in summer or from seeds.

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Ixora chinensis

Scientific Name

***Ixora chinensis* Lam.**

Synonyms

Bemsetia paniculata Raf., *Gaertnera hongkongensis* Seem., *Ixora blanda* Ker Gawl., *Ixora colei* Gentil, *Ixora crocata* Lindl., *Ixora dixiana* Gentil, *Ixora dubia* Schult., *Ixora flammea* Salisb., *Ixora incarnata* Roxb. ex Sm., *Ixora kroneana* (Miq.) Bremek., *Ixora pallida* Reinw. ex Miq., *Ixora rosea* Wall., *Ixora speciosa* Willd., *Ixora stricta* Roxb., *Ixora stricta* var. *incarnata* Benth., *Ixora stricta* var. *mekongensis* Pierre ex Pit., *Pavetta arborea* Blanco, *Pavetta chinensis* (Lam.) Roem. & Schult., *Pavetta kroneana* Miq., *Pavetta stricta* (Roxb.) Blume, *Sykesia hongkongensis* (Seem.) Kuntze, *Tsiangia hongkongensis* (Seem.) But, H.H. Hsue & P.T. Li.

Family

Rubiaceae

Common/English Names

Chinese Ixora, Jungle Flame, Needle Flower, Prince of Orange, West Indian Jasmine

Vernacular Names

Chinese: Long Chuan Hua
Indonesia: Kembang Soka, Siantan
Japanese: Santanka
Kampuchea: Kam Rontea
Malaysia: Jarum-Jarum Merah, Kayu tentulang, Pechah Priok, Pial Ayam Hutan, Siantan Hutan, Siantan jantan
Philippines: Santan (Bikol), Santan, Santan-Pula, Santan Tsina (Tagalog)
Swedish: Kinesisk Eldboll
Thailand: Kem
Vietnamese: Trang Đỏ

Origin/Distribution

The species is native to Southeast China (Fujian, Guangdong, Guangxi) and Indo-China. It has been introduced and cultivated in Thailand, Malaysia, Indonesia, the Philippines and elsewhere in the tropics.

Agroecology

The species is found in thickets and sparse forests from 200 to 800 m altitude in its native range.

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Edible Plant Parts and Uses

Flowers are consumed in Thailand, used in salad and stir-fried (Wongwattanasathien et al. 2010; Kaisoon et al. 2011).

Botany

A perennial shrub, 0.7–2 m high with many stems and glabrous branches. Leaves opposite, sometimes apparently in whorls of 4 due to reduced stem internodes, sessile or shortly petiolate to 5 mm, glabrous, leathery, oblong–oblanceolate, obovate, obovate–oblong (Plate 1), elliptic–oblong, 6–15 × 3–6 cm, base acute to rounded, apex obtuse to subacute, margin entire, dull green, lateral veins 7–9 pairs; stipules deltoid and persistent. Inflorescence terminal, compact-cymose to compact-corymbiform, many flowered (Plate 2), subsessile to pedunculate, subtend by 2 small leaf-like deltoid bracts. Flowers bisexual, 4-merous; calyx tube 1.5 mm long, lobes 4-dentate; corolla lobes circular–obovate, broadly obtuse to rounded at apex, 6 mm across, orange-red or white, tube 25–35 mm; staminal filaments shorter than corolla tube, anthers reflexed; style filiform, red, with 2 exserted stigma 3–4 mm long, ovary 2-celled (Plate 3). Drupe reddish black, subglobose and shallowly didymous, 6–7 × 6–7 mm, glabrous.

Plate 1 Large oblong–obovate opposite subsessile leaves (S. Wee)

Nutritive/Medicinal Properties

The soluble phenol acids (per g dry weight) identified in *Ixora chinensis* flower extract were gallic acid 66.3 µg, protocatechuic acid 13.1 µg, *p*-hydroxy benzoic acid 26.2 µg, vanillic acid 15.6 µg, chlorogenic acid 54.0 µg, caffeic acid 11.41 µg, syringic acid 6.0 µg, *p*-coumaric acid 7.5 µg, ferulic acid 19.56 µg, sinapic acid 31.4 µg and total phenolic acids 25.1 µg (Kaisoon et al. 2011). The flowers contained 381.4 µg total bound phenolic acids made up of gallic acid 29.8 µg, protocatechuic acid 39.1 µg, *p*-hydroxy benzoic acid 58.7 µg, syringic acid 57.2 µg, *p*-coumaric acid 104.1 µg, ferulic acid 26.9 µg and sinapic acid 64.8 µg. The flowers

Plate 2 Compact corymbose orange-red flower head (S. Wee)

Plate 3 Flowers with 4 obtuse-tipped obovate petals (S. Wee)

contained 251 μg total soluble flavonoid made up of rutin 139 μg, myricetin 5.18 μg, quercetin 102.4 μg, apigenin 0.64 μg and kaempferol 3.77 μg and bound flavonoid 59.6 μg made up of rutin 28.5 μg, myricetin 3 μg, quercetin 13.6 μg and apigenin 14.5 μg. The DPPH radical scavenging activities (% inhibition) of soluble and bound phenolic fraction of the flower were 62.52 % and 33.67 %, respectively. Bound phenolics exhibited lower antioxidant activity than soluble ones. The reducing potential of the soluble and bound phenolic fraction of the flower as evaluated by FRAP (ferric reducing antioxidant power) assay (mmol $FeSO_4$/100 g dry weight) was 14.45 mmol and 15.8 mmol, respectively.

Two iridoid glucosides, ixoroside and ixoside (7,8-dehydroforsythide) along with known geniposidic acid were isolated from leaves and twigs of *Ixora chinensis* (Takeda et al. 1975). A fatty acid found in the seed oil of *Ixora chinensis* was shown to be *cis, cis, cis, trans*-8,10,12,14-octadecatetraenoic acid, named ixoric acid (Huang 1990; Huang and Lu 1999). Another known naturally occurring unusual fatty acid, crepenynic acid (octadec-*cis*-9-en-12-ynoic acid), also occurred in the seed oil. Both acids were major components and comprised up to ca 70 % of the total fatty acids derived from the seed oil.

Antimutagenic Activity

The dichloromethane of *I. chinensis* flowers inhibited the mutagenicity of the reaction product of 1-aminopyrene nitrite model in the absence of metabolic activation on both *Salmonella typhimurium* strains TA 98 and TA 100, while the methanol flower extract exerted similar effect on TA 98 (Wongwattanasathien et al. 2010). The water flower extract exhibited antimutagenic activity on both tester strains. On the basis of such information, it was concluded that these flowers were safe to be consumed and partially satisfied the first step in using the extracts for any purpose in food product development.

Anticancer Activity

Flower decoctions of *I. chinensis* and *I. coccinea* completely inhibited formation of skin, liver and colon tumour initiated by dimethylbenzanthracene and promoted by croton oil in mice (Serrame and Lim-Sylianco 1995).

Traditional Medicinal Uses

In Malaysia, the Malays use a root decoction after childbirth and for urinary problem (Burkill 1966). In the Philippines, an infusion of the fresh flowers is said to be a remedy against incipient tuberculosis and haemorrhage (Quisumbing 1978). An infusion of leaves or flowers is used against headache. In Indonesia, a decoction of the roots is used against bronchial disorders; a decoction of the flowers is prescribed in amenorrhoea and hypertension (Wijayakusuma et al. 1992). In Vietnam, roots, stems, leaves and flowers are used for irregular menses, high blood pressure, tuberculosis, haemoptysis, rheumatism and acne (Perry 1980). In Taiwan, the leaves are used for liver clearance, to improve blood circulation, to lower high blood pressure and to calm uterus movement (Chiu and Chang 1995).

Other Uses

Ixora chinensis is widely cultivated as an ornamental plant and hedges and also used in bonsai.

Comments

The plant is readily propagated by using seeds or stem cuttings.

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Ixora coccinea

Scientific Name

***Ixora coccinea* L.**

Synonyms

Pavetta coccinea (L.) Blume

Family

Rubiaceae

Common/English Names

Burning Love, Flame of the Woods, Ixora, Jungle Flame, Jungle Geranium, Passionate Love, Scarlet Ixora, Scarlet Jungle Flame, Sacred Ixora, Shiva's Flame, West Indian Jasmine

Vernacular Names

Brazil: Iroxa (Portuguese)
Burmese: Pan Sayeik, Poan~Na. Rait, Ponna Yeik, Pone-Na-Yeik, Pundarik
Chinese: Long Chuan Hua
Czech: Ixora Šarlatová
Danish: Ildkugle, Ixora
Dutch: Faja Lobi, Faya Lobi
Estonian: Punane Iksoora
French: Ixora Ecarlate
German: Ixore, Scharlachrote Iora;
India: Rangan, Rangana, Rookmini (Bengali), Rajana, Ranjan, Rugmini (Hindi), Gudda Daasala, Guddedasal, Gudde Dosal, Gurugudu, Holedaasala, Kaepala, Kapala Hoo, Kempu Kaepala, Kempugundu Hoo, Kempukepala, Kempulagida, Kepala, Keppulagida, Kepula, Kepuladai, Kevala, Kevala Gida, Kisagaara Hoo, Kisgara, Kiskar, Kiskara, Kissara, Kissargida, Kisu Kaare, Kisukaare, Kisukare, Kusumaale, Maale Gida, Maale Hoo, Maalehoo Gida (Kannada), Patkali, Podkali (Konkani), Cekki, Cetti, Chekki, Chethi, Chetti, Kattutechi, Schetti, Shekki, Shetti, Tecci, Techi, Tetti, Thechhi, Thechi, Thetti (Malayalam), Bakali, Bakora, Padkali, Pankul, Pendgul, Pendkul, Pentgul, Pitkuli (Marathi), Bondhuko, Romoniphulo, Ruktuka (Oriya), Bandhujivaka, Bandhuka, Bandhujivaka Parali, Binduka, Ishwara, Parali, Paranti, Patali, Raktaka, Raktala (Sanskrit), Attimankicacceti, Attimankicam, Cetarakacceti, Cetarakam, Cetaram, Cetti-Cetti, Cheddi, Cinturacceti, Cinturam, Citaram, Cuvetaki, Cuvetakicceti, Erinakai, Koranpoo, Koran, Koranpu, Kullai, Mayilai, Sedaram, Setti, Sinduram, Tecci, Telli, Vedcci, Vedji, Vellaivetci, Vellaivetcippucceti, Velvetci, Verchi, Vetchi, Vetci, Vitchie, Vitci (Tamil), Bandhuca, Bandhujeevakamu, Bandhujeevamu, Bandhujivakamu, Bandhujivamu, Bandhukamu, Koranam, Korani, Mankana, Manmadhabana, Manmadibanum, Manmathabanamu, Nuru

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Varahalu, Raama Bhanamu, Rama Banamu (Telugu)
Indonesia: Kembang Santen Merah, Soka Merah, Soka Bereum (Sundanese)
Kampuchea: Kam Ron Tea
Malaysia: Pechah Periuk, Todong Periuk
Paluan: Kerdeu Ra Ngebard
Panama: Cache De Tore, Jazmin De Coral (Spanish);
Philippines: Tangpupo (Bisaya), Santan, Santan-Pula (Tagalog)
Portuguese: Amor Ardent, Flor De Coral, Ixora, Ixora Coral, Cruz De Malta, Ixora Coral, Ixora Vermelha, Siderodendro
Spanish: Amor Ardiente, Bola De Coral, Coral, Corallilo, Cruz De Malta, Equisósea, Ixora, Jazmin Del Diablo, Santa Rita
Sri Lanka: Rathmal (Sinhalese), Vedchi (Tamil)
Swedish: Eldboll
Thailand: Khem Baan, Khem Nuu (Bangkok), Khem Farang (Central)
Vietnam: Mẫu Đơn, Cây Đơn Đỏ, Trang Son

Origin/Distribution

The species is a native of India and Sri Lanka. It has been introduced pantropically where it is being cultivated as an ornamental plant.

Agroecology

Ixora grows well in warm humid climates. Ixora thrives best in light-texture, well-drained, fertile, acid soils with pH 5.0–5.5 and rich in organic matter (Staples and Herbst 2005). It does best in full sun but tolerates partial shading. Ixora is mildly tolerant of salt sprays but is intolerant of highly alkaline soils becoming chlorotic.

Edible Plant Parts and Uses

The flowers are edible and used as condiment and for flavouring in India, Sri Lanka and Thailand (Burkill 1966; Altschul 1973; Facciola 1990; Wongwattanasathien et al. 2010). Ripe fruits are edible, eaten by local ethnic communities especially children in Kerala (Nazarudeen 2010).

Botany

A small, dense, multibranched, glabrous evergreen shrub to 2 m high, rounded in form. Leaves sessile, opposite, decussate, simple, leathery, glossy green, ovate to obovate with cordate or obtuse bases, apiculate tips, 3.5–8 cm long by 2.5–3.5 cm wide, margin entire, with interpetiolar, deltoid stipules (Plates 1, 2). Flowers borne in dense terminal, dichasial cymose heads, cymules 3-flowered, occasionally 2–5 flowered (Plates 1–4). Flowers bisexual, actinomorphic, tetramerous, epigynous. Calyx aposepalous, the sepals 4, ovate, reddish. Corolla sympetalous, 3–4.5 cm long, 4-lobed, tubular-rotate, the lobes 4, lanceolate to

Plate 1 Flowers and leaves

Plate 2 Inflorescence head and opposite, decussate leaves

Plate 3 Close up of inflorescence head

Plate 4 Close up of individual flowers

ovate, pointed, reddish, pink or yellow. Androecium polyandrous, stamens 4, exserted. Ovary 2-loculed, syncarpous, style filiform, stigma bifid, ellipsoid, exserted. Fruit a globose berry, reddish-black, 0.5 cm across, with persistent calyx.

Nutritive/Medicinal Properties

Phytochemical studies indicated *Ixora coccinea* plant to contain important phytochemicals such as lupeol, ursolic acid, oleanolic acid, stearic acid, oleic acid, linoleic acids and sitosterol (Ayyanar and Ignacimuthu 2009).

Fruit Nutrients

Nutritive value of the ripe fruit was reported as moisture 82.29 %, protein 0.28 %, fat 0.01 %, reducing sugars 10.15 %, nonreducing sugars 6.05 %, total sugars 16.2 %, fibre 0.9 %, vitamin C trace, energy 66.01 Kcal, mineral matter 0.25 %, Fe trace, Na 9.88 mg/100 g and K 197.69 mg/100 g (Nazarudeen 2010).

Flower Phytochemicals

Two cycloartenol esters (1a and 1b), lupeol fatty ester, lupeol, ursolic acid, oleanolic acid and sitosterol were isolated from *I. coccinea* flowers (Ragasa et al. 2004). Latha et al. 2001) reported the flowers to contain rutin, lecocyanadin glycoside, cyanadin-3-rutinoside and delphinidin monoglycoside. The presence of biochin A, myricetin, quercetin, rutin, daidzein, formononetin and ursolic acid 1.45 % were detected in *Ixora coccinea* methanolic flower extract (Sumathy et al. 2011). Twenty-four other compounds were also found: quinic acid 37.25 %, glycerine 17.58 %, mome inositol 10.17 %, xanthosine 9.40 %, (1R,3R,4R,5R) quinic acid 6.87 %, 4H-pyran-4-one, 2,3 dihydro 3.75 %, 5,5dimethyl1 oxa-5-silacyclononan 2.47 %, 9.12-octadecadienoic acid (*Z*,*Z*) (2-phe) 2.42 %, hydroxymethylfurfural 2.18 %, cymel 1.47 %, 1,3-propanedial, 2-hydroxymethyl 1.34 %, benzenecarboxylic acid 0.78 %, glycerose 0.67 %, 2-cyclopenten-1-one, 2hydroxy 0.57 %, furfuryl alcohol 0.04 %, heptadecane 0.36 %, 9,12,15-octadecatrienoic acid (2-phe) 0.34 %, dimethyl, tetra butoxysilanol 0.33 %, propargyl alcohol 0.29 %, 2,4 dihydroxy-2,5 dimethyl furfural 0.28 %, 2,4 dihydroxy-2,5 dimethyl furfural 0.25 % and furfural 0.23 %. A natural terpenoid, ixoroid, with the structure 21,23-epoxy-tirucall-7-en-3β-ol, was isolated from *Ixora coccinea* flower along with the known constituents stigmast-5-en-3-*O*-β-D-glucoside, 5-*O*-caffeoylquinic acid and D-mannitol (Versiani et al. 2012).

Fifty-four components were identified in the essential oil of *Ixora coccinea* flower (Obuzor and Nwakanma 2011). The oil comprised mainly of triterpenes 62.60 %, monoterpenes 31.73 %, sesquiterpenes 3.35 % and an ester 2.29 %. The major constituents of triterpenes were ursolic

acid (27.34 %), oleanolic (20.16 %) and lupeol (15.10 %). Geranyl acetate (8.74 %) was the major monoterpenes, followed by linalyl acetate (6.79 %), neryl acetate (6.49 %), α-terpineol acetate (4.91 %) and borneol acetate (4.77 %); ethyl cinnamate (2.29 %) is an ester; while the sesquiterpenes were cyperene (2.72 %), α-copaene (0.63 %) and α-cyperone (0.002 %). Other monoterpenes were α-pinene (0.012 %) and β-pinene (0.013 %). Other compounds present in trace amounts included benzaldehyde, 1-octen-3-ol, cymene, α-phellandrene, α-terpinene, citronellol, ascaridole, germacrene B, germacrene D, α-bisabolene, β-bisabolene, α-gurjunene, α-bergamotene, humulene, *trans*-β-ocimene, camphene, terpinolene, sabinene, limonene, benzyl alcohol, *cis*-ocimene, myrcene, allo-ocimene, pinene-2-ol, α-thujene, 2,6,dimethyl-5-heptanal, γ-terpene, citral, neral, geranial, isoartemisia, 1,8-cineole, borneol, citronellal, nerol, a-terpineol, terpin-4-ol and linalool (0.007 %).

Leaf Phytochemicals

Lupeol was isolated from the petroleum ether fraction of ethanol leaf (Zachariah et al. 1994). The ethyl acetate fraction of the methanol extract of *Ixora coccinea* leaves afforded an A-type trimeric proanthocyanidin epicatechin-(2β→*O*→7, 4β→8)-epicatechin-(5→*O*→2β, 6→4β)-epicatechin named ixoratannin A-2 along with seven known compounds, epicatechin, procyanidin A2, cinnamtannin B-1 and four flavon-3-ol rhamnosides, viz. kaempferol-7-*O*-α-l-rhamnnoside, kaempferol-3-*O*-α-l-rhamnoside, quercetin-3-*O*-α-L-rhamnopyranoside and kaempferol-3,7-*O*-α-L-dirhamnoside (Idowu et al. 2010).

Root Phytochemicals

The root bark of *Ixora coccinea* was found to contain a liquid acid, identified as Δ^{9-11}-octadecadinoic acid, myristic acid and mannitol (Sukumaran Kartha and Menon 1943). The bioassay guided fractionation of the saponifiable fraction of the petroleum ether extract of *Ixora coccinea* root was found to contain both saturated and unsaturated fatty acids (Padmaja et al. 1993).

Pharmacological studies suggested the plant to possess antioxidative, antibacterial, gastroprotective, hepatoprotective, antidiarrhoeal, antinociceptive, antimutagenic, antineoplastic and chemopreventive effects, thus lending scientific support to the plant's ethnomedicinal uses (Baliga and Kurian 2012).

Antioxidant Activity

The methanol flower extract of *I. coccine*a showed significant activities in the DPPH free radical scavenging assay, reducing power and total antioxidant capacity using phosphomolybdenum assays compared to the standard antioxidant in a dose-dependent manner (Saha et al. 2008). The high antioxidative property in scavenging reactive oxygen species (ROS) may be attributed to the high amount of hydrophilic phenolics. In DPPH radical scavenging assay, the IC_{50} value of the extract was found to be 100.53 μg/mL while ascorbic acid had the IC_{50} value 58.92 μg/mL.

Antioxidant evaluation of isolated compounds from the leaves revealed that ixoratannin A-2 and cinnamtannin B-1 were the most active compounds in DPPH, inhibition of lipid peroxidation and nitric oxide radical-scavenging assays (Idowu et al. 2010). Among the methanol extracts of various aerial parts of *I. coccinea*, the flower extract exhibited the best antioxidant property, presenting much lower IC_{50} value (6.6 mg/mL for 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay) (Torey et al. 2010). In addition, the highest phenolic content (polyphenols) was found in the flower extract (210.55 μg GAE/mg extract). Furthermore, *I. coccinea* extracts scavenged the superoxide radical generated by the xanthine/xanthine oxidase system. The xanthine oxidase inhibition activity was in the order of allopurinol > leaf > flower > stem with the percentage of inhibition ranged from 39.7 to 77.3 % for the plant parts investigated.

Hypolipidaemic Activity

Ethanol leaf extract of *I. coccinea* showed significant hypolipidaemic effect in Wistar albino rats fed with atherogenic diet by lowering the serum levels of biochemical parameters such as significant reduction in the level of serum cholesterol, triglyceride, LDL, VLDL and HDL level which was similar to the standard drug Atorvastatin (Neelima et al. 2011) The ethanol leaf extract exhibited significant atherogenic index and percentage protection against hyperlipidaemia. Preliminary phytochemical analysis revealed the presence of phytoconstituents such as alkaloids, tannins, flavonoids, carbohydrates, protein and amino acids and reducing sugars.

Antimutagenic Activity

The crude alcoholic extract and the ethyl acetate fraction of *I. coccinea* exhibited antimutagenic activity when tested using the Rec-Assay and the Micronucleus Test (Panlilio et al. 1992). Fractions obtained from the ethyl acetate extract were found to be antimutagenic against a known carcinogen, 4-nitroquinoline, in two *Bacillus subtilis* strains. After purification the antimutagenic fraction was identified as ursolic acid. The activity of ursolic acid was confirmed by the Rec-Assay.

The dichloromethane, methanol and water extract of *Ixora coccinea* flowers were devoid of mutagenic activity on *Salmonella typhimurium* strains TA 98 and TA 100 without metabolic activation (Wongwattanasathien et al. 2010). However, treating the extract with sodium nitrite in acid solution reversed the effects and they became mutagenic. All the three extracts were effective in inhibiting the mutagenic effects of sodium nitrite-treated 1-aminopyrene *on Salmonella typhimurium* strains TA 98. The optimal effect was observed with the dichloromethane followed by methanol and aqueous extract, suggesting that the nonpolar compounds present in the extract were responsible for the observed antimutagenic effects.

Antinociceptive/Analgesic/ Anxiolytic Activities

Studies showed that the aqueous leaf extract of *I. coccinea* possessed appreciable dose-dependent antinociceptive activity when evaluated in hot plate and formalin test but not in tail flick test) (Ratnasooriya et al. 2005a). The antinociceptive action was mediated centrally at the supraspinal level mainly via dopaminergic mechanism, and they postulated that the antioxidant activity of the extract from its quaternary base alkaloid and flavonoid constituents could have played an auxiliary role in inducing antinociception.

The ethanol (50 %) extract of *Ixora coccinea* aerial parts potentiated barbiturate activity and caused semen coagulation (Padmaja et al. 1993).

Cardioprotective Activity

Pretreatment of albino Wistar rats with methanol leaf extract of *Ixora coccinea* followed with the simultaneous treatment with doxorubicin significantly reduced the ST segment elevation and also maintained the blood pressure close to normal (Momin et al. 2012). The extract significantly reduced the elevated level of biomarkers like creatine kinase – MB (CK – MB), lactate dehydrogenase (LDH), serum glutamic oxaloacetic transaminase (SGOT) and glutamate pyruvate transaminase (SGPT), near to normal, and also increased dose-dependently the tissue antioxidant markers, viz. catalase (CAT) and superoxide dismutase, (SOD) and decreased the level of malondialdehyde (MDA) in cardiac tissue. The histopathology of heart also further confirmed the cardioprotection provided by the methanolic leaf extract of *Ixora coccinea*.

Antimicrobial Activity

The 50 % ethanolic extract of *Ixora coccinea* was found to have antimicrobial activity with effective inhibitory concentration of 125 μg/mL for both bacteria and fungi tested (Latha et al. 1995).

Ether and methanol leaf extracts of *Ixora coccinea* dry leaves were found to have antimicrobial activity; the ether extract was more active than the methanol extract (Annapurna et al. 2003). All tested compounds isolated from the leaves, namely, ixoratannin A-2, epicatechin, procyanidinA2,cinnamtanninB-1,kaempferol-7-*O*-α-L-rhamnnoside, kaempferol-3-*O*-α-l-rhamnoside, quercetin-3-*O*-α-L-rhamnopyranoside and kaempferol-3,7-*O*-α-L-dirhamnoside, inhibited the growth of *Bacillus subtilis*, while only epicatechin and quercetin-3-*O*-α-L-rhamnopyranoside inhibited the growth of *Escherichia coli* (Idowu et al. 2010).

Among six extracts (ethanol, aqueous, petroleum ether, benzene, chloroform and ethyl acetate) of *I. coccinea* roots, the ethanolic extract showed highly significant antibacterial activity *Staphylococcus aureus, Bacillus pumilus, Enterococcus faecalis, Escherichia coli, Salmonella typhi* and *Pseudomonas aeruginosa* when compared to standard (Selvaraj et al. 2011). The aqueous extract showed moderate significant inhibition against all bacterial strains when compared to standard. All the extracts elicited negligible activity against the fungi *Candida albicans* and *Aspergillus niger*. The methanol and aqueous extracts of four flower types exhibited considerable antibacterial activity against *Escherichia coli, Staphylococcus aureus, Bacillus subtilis* and *Klebsiella pneumoniae* (Pulipat et al. 2012). The methanol extracts of red and pink flower types exhibited high activity while the orange flower methanol extract exhibited moderate activity and the white flower methanol extract showed low activity. The aqueous extracts were less inhibitory than the methanol extracts.

Wound-Healing Activity

The alcoholic flower extract of *Ixora coccinea* was found to have wound-healing activity in dead space wounds created in rats (Nayak et al. 2003). Increases in the tensile strength of the wound and in the level of lysyl oxidase, the crucial enzyme for collagen maturation, were observed indicating a definite prohealing action. Moreover a highly significant increase in the levels of antioxidant enzymes, namely, catalase, glutathione peroxidase and glutathione reductase, was observed in the extract-treated group. Thus, the gain in tensile strength may be attributed not only to the better cross-linking but also to the antioxidant properties of the extract. The ethanolic root extract of *I. coccinea* showed significant wound-healing activity when compared to standard ointment Nitrofurazone with respect to normal control Wistar albino rat group (Selvaraj et al. 2011) based on enhancement of tensile strength on incision wound model and in terms of wound contraction for excision wound model.

Anticancer Activity

After injecting Dalton's lymphoma cells with an ayurvedic oil preparation containing flowers of *Ixora coccinea* and *Cortus sativum*, tumour development was arrested (Panikar et al. 1986). Flower decoctions of *I. chinensis* and *I. coccinea* completely inhibited formation of skin, liver and colon tumour initiated by dimethylbenzanthracene and promoted by croton oil in mice (Serrame and Lim-Sylianco 1995).

Intraperitoneal administration of 200 mg/kg of the active fraction of *I. coccinea* flower increased the life span of Dalton's lymphoma (ascitic and solid tumours) and Ehrlich ascites carcinoma tumour-bearing mice by 113 and 68 %, respectively (Latha and Panikkar 1998). The fraction showed less activity against solid tumours as compared to ascitic tumours. The same active fraction showed 50 % cytotoxicity to Dalton's lymphoma (ascitic) and Ehrlich ascites carcinoma and Sarcoma-180 (S-180) cells in vitro at concentrations of 18, 60 and 25 μg/mL, respectively. It was toxic to transformed lymphocytes from leukaemic patients, acute lymphoblastic leukaemia (ALL) and chronic myelogenous leukaemia (CML) and K-562 suspension cell cultures but not to normal cells. The active fraction inhibited tritiated thymidine incorporation in cellular DNA. The active fraction was found to contain triterpenoid, ursolic acid.

Two derivatized peptides, designated as ixorapeptide I (1) and ixorapeptide II (2), in addition to 28 other known compounds, were isolated from the methanol extract of *Ixora coccinea* (Lee et al. 2010). Compound 1 exhibited selective potency against Hep3B liver cancer cell line with an IC_{50} value of 3.36 μg/mL, and compound 2 did not show notable cytotoxicity towards cancer cell lines but could inhibit superoxide anion generation and elastase release with IC_{50} values of 0.21 and 0.27 μg/mL, respectively.

Anti-inflammatory Activity

The saponifiable fraction of the petroleum ether extract of *Ixora coccinea* root was found to have anti-inflammatory activity in carrageen-induced paw oedema in albino rats (Padmaja et al. 1993). The bioassay guided fractionation of the saponifiable fraction was carried out, and the active fraction was found to contain both saturated and unsaturated fatty acids. Oral administration of aqueous leaf extract of *Ixora coccinea* (500, 1,000, and 1,500 mg/kg) to rats significantly impaired both early and late phases of the inflammatory response in the carrageenan-induced paw oedema (Ratnasooriya et al. 2005b). In the cotton pellet granuloma test, it significantly suppressed granuloma formation (only highest dose tested). Collectively, these data indicted promising anti-inflammatory activity against both acute and chronic inflammation. The extract showed strong antihistamine and antioxidant activities that could account for its anti-inflammatory potential. In addition, inhibition of prostaglandins and bradykinins may play a role. Methanolic *I. coccinea* leaf extract exhibited dose-dependent anti-inflammatory activity in carrageenan-induced rat paw oedema model (Handunnetti et al. 2009). Oral administration of the extract to rats at a dose of 1,500 mg/kg significantly inhibited peritoneal phagocytic cell infiltration (45.9 %), impaired nitric oxide (NO) production in peritoneal cells (40.8 %) and showed antihistamine activity (54.9 %). In vitro treatment of rat peritoneal cells with the extract inhibited NO production dose-dependently (82.2 % at 400 μg/mL). The extract also possessed significant, dose-dependent in vitro antioxidant activity (IC_{50} value = 8.0 μg/mL), membrane stabilizing activity (IC_{50} value = 6.4 ng/mL) and lipid peroxidation activity (36.7 % at 250 μg/mL). Thirty-day oral treatment of rats with 1,500 mg/kg did not show any adverse signs of toxicity or behavioural changes. The results suggested the anti-inflammatory activity of *I. coccinea* to be mediated via inhibition of NO production, phagocytic cell infiltration, antihistamine effect, scavenging of free radicals, membrane stabilizing activity and lipid peroxidation.

Lupeol, isolated from the leaves, exhibited anti-inflammatory activity in carrageenan-induced paw oedema in albino rats and antimitotic activity in a preliminary cytotoxic study using the *Allium* test of Levan (Zachariah et al. 1994).

In a randomized controlled clinical trial of 20 patients with typical chronic gingivitis, *Ixora coccinea* leaf (Ponna yeik) and chlorhexidine mouthwashes showed significant effectiveness in plague score, bleeding on probing and severity of gingivitis when compared to before treatment. Staining effects were observed in patients who used chlorhexidine but not in patients who used Ponna yeik mouthwash. There were no significant differences between two groups in all scores except staining score after 4 weeks of treatment. The authors concluded that Ponna yeik mouthwash revealed anti-inflammation and antiplague activity without staining.

Antiasmathic Activity

The hydroalcoholic leaf extract of *I. coccinea* extract at doses of 1,000 and 1,500 mg/kg suppressed eosinophilia and significantly inhibited airway hyperreactivity in rat with ovalbumin-induced asthma (Missebukpo et al. 2011). Based on lung histopathological study using hematoxylin and eosin, *I. coccinea* reduced inflammatory cell infiltration and repaired epithelial cells damaged. Further, the extract at the same doses significantly decreased the diameter of the blue spot (16 and 55 %, respectively) compared with the controls and inhibited the skin reactions induced by histamine (23.55 and 53.36 %,

respectively). The findings suggested *I. coccinea* to have antiasthmatic properties supporting its use in folk medicine to treat asthma.

Chemoprotective/Hepatoprotective Activity

The active fractions from *Ixora coccinea* flowers were found to have chemoprotective activity. The flower fraction prevented a decrease in body weight, haemoglobin levels and leucocyte counts of mice treated with cyclophosphamide (Latha and Panikkar 1999) and cisplatin (Latha and Panikkar 2001). Decreased serum glutamate pyruvate transaminase (SGPT) and serum alkaline phosphatase levels in the *Ixora coccinea*-treated groups indicated protection against hepatic toxicity. The fraction significantly prolonged the life span of cisplatin-treated mice and maintained their blood urea nitrogen levels in the near normal range, indicating its chemoprotective effects. The *n*-hexane extract of *Ixora coccinea* flowers showed significant hepatoprotective effect against paracetamol overdose-induced hepatotoxicity in rats, as evidenced by reduction of elevated levels of serum marker enzymes and liver lipid peroxide levels (Latha et al. 2003). Paracetamol-induced alterations in liver histology were markedly decreased by *I. coccinea* treatment. The active fraction from *Ixora coccinea* flowers prevented the decrease in haemoglobin levels and leucocyte counts of Dalton's lymphoma tumour-bearing mice, treated with cyclophosphamide (Latha et al. 2004). It also significantly increased the life span of tumour-bearing mice, treated with cyclophosphamide. Serum glutamate pyruvate transaminase (SGPT) and serum alkaline phosphatase (SAKP) levels of tumour-bearing mice treated with cyclophosphamide were decreased significantly by combination therapy with *I. coccinea* fraction indicating protection against hepatic toxicity.

Oral pretreatment of the rats with the plant ethanolic extract significantly protected against toxin-induced liver damage, determined 72 h after the aflatoxin B1 (challenge (1.5 mg/kg, intraperitoneally) as evidenced by a significant lowering of the activity of the serum enzymes and enhanced hepatic GSH (reduced glutathione) status (Shyamal et al. 2010). Pathological examination of the liver tissues supported the biochemical findings.

Antiplatelet Aggregation Activity

Kaempferol and luteolin isolated from *Ixora coccinea* showed inhibition with IC_{50} values of 3.55 and 2.56 μg/mL, respectively, on platelet aggregation induced by collagen (Lee et al. 2010).

Antidiarrhoeal Activity

The aqueous flower extract of *I. coccinea* showed significant inhibitory activity against castor oil-induced diarrhoea and castor oil-induced enteropooling in albino Wistar rats at the dose of 400 mg/kg (Maniyar et al. 2010). There was also significant reduction in gastrointestinal motility in the charcoal meal test. Results obtained substantiated the antidiarrhoeal effect of the aqueous extract and its use by traditional practitioners in the treatment of diarrhoea.

Gastroprotective Activity

The methanol leaf extract at doses of 100 and 200 mg/kg was found to have protective effect in pyloric ligation (45.86 and 75 %)-induced ulcer model and significantly reduced free and total acidity in albino rats (Arunachalam et al. 2012) In gastric ulcer induced by the hypothermic restraint stress, both doses significantly inhibited gastric ulcer development. Triterpenoids, flavonoids, glycosides, tannins, saponins and reducing sugars were detected in the methanol leaf extract.

Anthelmintic Activity

The chloroform root extract of *I coccinea* elicited higher show anthelmintic activity against

Pheretima posthuma than petroleum ether ethyl acetate and methanol extracts (Surana et al. 2011).

Traditional Medicinal Uses

The flowers, leaves, stem and roots are used to treat various ailments in the Indian traditional system of medicine, the Ayurveda, and also in various folk medicines (Baliga and Kurian 2012) and in southeast Asia (Burkill 1966; Stuart 2012). Decoction of leaves have been used for wounds and skin ulcers. Poulticed fresh leaves and stems have been employed for sprains, eczema, boils and contusions. The bark has been employed for bloodshot eyes. Diluted root tincture have been employed for mouthwash and gargle for sore throat. Root decoction have been administered as a sedative in the treatment of nausea, hiccups and loss of appetite, to stimulate gastric secretion, to act as cholagogue, to control dysenteric diarrhoea and to clarify urine. Moistened powdered roots is applied externally to sores and chronic ulcers.

In Sri Lanka traditional medicine, a decoction of *I. coccinea* flowers is administered for haemophytis, acute bronchitis and dysmenorrhoea; flowers and bark are employed on reddened eyes and eruptions in children; a root decoction is prescribed for dysentery, loss of appetite, fever and gonorrhoea and as a sedative for hiccups and nausea, and the leaves are used for dermatological disorders (Jayaweera and Senaratna 2006). In the Philippines, decoction of roots are used to treat nausea, hiccups and anorexia; powered roots used for sores and chronic ulcers (Quisumbing 1978). The flowers have been used for dysentery, leucorrhoea, bloodshot eyes; a flower decoction have been used to treat hypertension, amenorrhea and irregular menstruation, hemoptysis and catarrhal bronchitis. In Indochina, the root decoction is used to clarify the urine (Petelot 1952–1954, and used as an analgesic, sedative, diuretic and antidysenteric; the flowers have similar but weaker properties (Nguyen 1993) and fresh leaves and stems are used as poultice for sprains, eczema, boils and contusions.

Other Uses

In warm climates, Ixora with flowers in various shades of red, pink, orange, yellow or white is popularly and widely planted as an ornamental for hedges and screens, foundation plantings and mass plantings in flowering beds or grown as a specimen shrub or small tree, in a container in the patio or poolside and in pots around the outside of houses. Dwarf or miniature varieties are also popular. Ixora flowers are also cut and used for flower arrangements.

Comments

Ixora is readily propagated from vigorous growing tip cuttings.

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Ixora javanica

Scientific Name

***Ixora javanica* (Blume) DC**

Synonyms

Ixora amara Steud., *Ixora amoena* Wall. ex G. Don, *Ixora cyathosperma* Wall., (nom. nud.), *Ixora javanica* var. *multinervia* Corner, *Ixora javanica* var. *paucinervia* Corner, *Ixora javanica* var. *retinervia* Corner, *Ixora mutabilis* Reinw. ex Miq., *Ixora stricta* var. *amoena* (Wall. ex G. Don) Ridl., *Ixora stricta* var. *blumeana* Kurz, *Ixora stricta* var. *javanica* (Blume) Kuntze, *Ixora stricta* var. *pubistyla* S. Moore, *Pavetta javanica* Blume

Family

Rubiaceae

Common/English Names

Coral Ixora, Glossy Ixora Javanese Ixora, Jungle Flame, Jungle Geranium, Red Ixora

Vernacular Names

Borneo: Boyu Bukit, Bunga Jarung

Indonesia: Soka, Kembang Soka, Ki Sika (Sundanese)

Malaysia: Jejarum, Siantan

Thai: Khem (Nakhon Si Thammarat), Khem Thong, Khem Saet, Khem Daeng (Peninsular), Pue-Cho-Pu-Yo, Ya-Rang (Malay-Narathiwat)

Origin/Distribution

The species is indigenous to Thailand, Peninsular Malaysia, Sumatra, Java, Borneo (throughout the island) and Celebes (Slik 2006).

Agroecology

In its native range, the species occurs in undisturbed mixed dipterocarp forests, in secondary forests, on hillsides and ridges and on alluvial sites and along rivers and streams. It is found in elevations up to 700 m. It thrives in full sun or light shade and prefers warm and humid conditions.

Edible Plant Parts and Uses

The flowers are used as vegetable in Borneo (Slik 2006) and in vegetable soups in Thailand (King 2007).

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Botany

A shrub 1–3 m high or treelet to 11 m high and with dbh of 26 cm. Leaves, opposite, simple, elliptical, oblong or oblong–ovate, 7.5–17 cm by 2.5–7 cm, herbaceous, base acute, apex acuminate, glabrous, penni-veined (9–10 pairs lateral veins), shortly petiolate (Plate 1), stipules 4 mm long, strongly pointed. Inflorescence, peduncle 1–4 cm long, short-hairy, loose panicle of 4-merous, bisexual, non-fragrant flower of 12 mm diameter. Flower with short calyx tube, ovate lobes, corolla tube 2.5–3.5 cm long, lobes ovate, obtuse or rounded, 6–8 mm long, orange-red sometimes pink or yellow (Plates 1, 2 and 3), anthers pale orange, style 5 mm long slightly exserted. Fruit 10 mm across, reddish-purple.

Plate 1 Leaves and young flower panicle

Plate 2 Flowers with obtuse-tipped ovate corolla lobes

Nutritive/Medicinal Properties

Anticancer Activity

The antitumour fraction from *Ixora javanica* flowers exhibited broad activity against transplantable solid tumours in mice by inhibiting the growth of tumours and arresting the growth of already formed tumours but showed lesser activity against ascites tumours (Nair and Panikkar 1990). It exhibited 50 % cytotoxicity to Dalton's lymphoma (DLA) and Ehrlich Ascites tumour cells in vitro at concentrations of 12 µg and 65 µg, respectively, with no activity against normal lymphocytes but preferential activity for lymphocytes derived from leukaemia patients and K 562 suspension cell culture. The purified fractions contained ferulic acid, pyrocatacheuic acid and caffeic acid. In in-vivo studies, topical application of *I. javanica* flower extract (100 mg/kg body weight) inhibited the growth and delayed the onset of papilloma formation in mice initiated with 7,12-dimethylbenz[a]anthracene (DMBA) and promoted using croton oil (Nair et al. 1991). The extract at the same dose, when administered orally, inhibited the growth of subcutaneously injected 20-methylcholanthrene (MCA)-induced soft tissue fibrosarcomas significantly. Oral administration of 200 mg/kg of the extract inhibited the growth of intraperitoneally transplanted sarcoma-180 and Ehrlich ascites carcinoma tumours besides showing an increase in the life span of the

Plate 3 Loose panicle of yellow flowers

treated mice. Toxicity studies showed that the blood urea nitrogen levels were elevated after treatment. Furthermore, tritiated thymidine incorporation studies indicated that the mechanism of action of the factor was at the site of DNA synthesis. The compounds responsible for antitumour growth were identified as ferulic acid (4-hydroxy-3-methoxycinnamic acid) and its structural isomer, 3-hydroxy-4-methoxycinnamic acid.

Traditional Medicinal Uses

The roots are boiled and consumed to treat tuberculosis in Thailand (Craib 1932; Chuakul et al. 2002)

Other Uses

This Ixora species is widely planted as ornamental plants or hedging plants in tropical and subtropical areas.

Comments

This species is readily propagated from vigorous growing shoot tip cuttings.

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Boronia megastigma

Scientific Name

***Boronia megastigma* Nees ex Bartlett**

Synonyms

Boronia megastigma var. *aurea* auct., *Boronia tristis* Turcz.

Family

Rutaceae

Common/English Names

Brown Boronia, Scented Boronia, Sweet Boronia

Vernacular Names

Estonian: Pruun boroonia
German: Boronia, Boronie

Origin/Distribution

B. megastigma is native to south-western Western Australia occurring from Perth to Albany.

Agroecology

In its native Mediterranean climatic range, it is found in wet or seasonally wet sites, on poor acid soils in often semi-shaded situations. *B. megastigma* requires cool, moist and well-drained, lime free soil, doing best in dappled shade with a good layer of mulch. The plant is sensitive to warm westerly winds in summer, and it is recommended that it be grown on the east side of a wall or behind a wind break of trees or shrubs.

Edible Plant Parts and Uses

Fragrant boronia flowers provide a source of essential oil with an aroma of cinnamon and tobacco, sold as boronia absolute used in food manufacture to create black currant flavour and to enrich other fruit flavours in beverages, ice creams, candy and baked products (Morton 1976; Facciola 1990). Boronia absolute is extracted from *B. megastigma* blossoms primarily for use as a food additive (Plummer et al. 1999). The absolute is used primarily in food flavouring to impart a unique richness to many fruit essences (Davies and Menary 1984; Weyerstahl et al. 1994).

Botany

B. megastigma is a small, dense shrub usually 1 m (–3 m) high. Leaves compound, opposite in whorls along the thin stem, 3–5 leaflets, small,

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Plate 1 Flowers and leaves

Plate 2 Close view of flowers

thick, aromatic linear, to 1.5 cm, apex obtuse. Flowers bisexual, actinomorphic, solitary, axillary, fragrant, pendent, cup-shaped, 8–10 mm in diameter with lysigenous glands in sepals, petals, receptacle, ovary and nectar (Plates 1 and 2). Calyx with 4 basally connate sepals. Corolla comprises 4 connate petals, outer surface of petals usually red-brown or purple glands, inner surface bright yellow. Stamens 8 in 2 whorls, 4 small yellow petaline anthers (fertile) and 4 large red-brown sepaline anthers (sterile). Carpels fused only at apex each containing 2 ovules, style solitary with a large, brown, four-lobed stigma. Nectar disk situated between stamens and the ovary.

Nutritive/Medicinal Properties

Both concrete and absolute are extracted from open *B. megastigma* flowers (Guenther 1974; Davies and Menary 1984; Weyerstahl et al. 1994). At room temperatures concrete is an orange/brown waxy solid and from it absolute, an orange/yellow viscous liquid, is obtained. The concrete is produced by non-chlorinated solvent extraction from the open flowers while traditional alcohol extraction of the concrete produces the absolute (Anonymous undated). Both have an intensely rich, potent, floral aroma. Boronia extract (concrete and absolute) comprised a complex mixture of >160 compounds including monoterpenes; cinnamates; norisoprenoids including ionones; related epoxides and dihydro compounds; acetates of decyl, dodecyl and tetradecyl alcohols; and methyl jasmonate isomers and triterpenes, tiglamides, (*Z*)-heptadec-8-ene, 8-hydroxylinalyl esters and 3-hydroxymegastigm-7-en-9-one (Guenther 1974; Davies and Menary 1984; Weyerstahl et al. 1994, 1995; MacTavish and Menary 1997a). Beta-ionone was found to be the major volatile (12–30 % of total volatiles). The composition of the petroleum ether extract used in commerce had been reported to include β-ionone and related epoxides and dihydro compounds; α-pinene, β-pinene and limonene; fatty acid methyl and ethyl esters; acetates of decyl- and tetra-decyl alcohols; dihydroactinidiolide; isomers of methyl jasmonate and wax hydrocarbons from heneicosane to tritriacontane (Davies and Menary 1984). They found four major volatile β-ionone, dodecyl acetate, (*Z*)-heptadec-8-ene and an unidentified compound 'sesquicineol' that contributed to the typical boronia fragrance. The monoterpenes α-pinene, β-pinene and limonene were also found in some clones but did not provide a favourable effect on the aroma. Ghisalberti (1998) identified the chemical structure of 'sesquicineol' but found it only in one clone and also found (*Z*)-heptadec-8-ene not to have a major role in the aroma.

Weyerstahl et al. (1995) found more than 160 constituents in a commercial boronia absolute of *B. megastigma.* The main constituents were

β-ionone, (*Z*)-heptadec-8-ene, 8-hydroxylinalyl esters (such as 8-hydroxylinalyl isobutyrate, 8-hydroxylinalyl 3-methyl butyrate, 8-hydroxylinalyl decanoate, 8-hydroxylinalyl dodecanoate, 8-hydroxylinalyl heptanoate, 8-hydroxylinalyl isovalerate, 8-hydroxylinalyl nonanoate, 8-hydroxylinalyl propionate, 8-hydroxylinalyl tiglate, 8-hydroxylinalyl tridecanoate, 8-hydroxylinalyl valerate), methyl (*Z,E*)-4-(geranyloxy)cinnamates, methyl (*Z,E*)-4-(5-hydroxygeranyloxy)cinnamates, 3-hydroxymegastigm-7-en-9-ones such as (*E*)-3-hydroxymegastigm-7-en-9-one, (*Z*)-3-hydroxymegastigm-7-en-9-one and *N*-[2-(4-prenyloxyphenyl)ethyl]tiglamide. Some low-volatile constituents of the absolute of *Boronia megastigma* from Tasmania were isolated and characterized (Weyerstahl et al. 1994). Besides (*E*)-β-ionone and many of its derivatives (such as cyclic β-ionone; (*Z*)-retro-α-ionone; 7,8-dihydro-β-ionone; 3-hydroxy-β-ionone; 4-hydroxy-β-ionone; 5,6-epoxy-β-ionone; 4-oxo-β-ionone), the isomeric 3-hydroxymegastigm-7-en-9-ones (namely, (*E*)-3-hydroxymegastigm-7-en-9-one; (*Z*)-3-hydroxymegastigm-7-en-9-one; (*E*)-9-hydroxymegastigm-7-en-3-one) and megastigm-7-en-3,9-dione were isolated. Additionally, the *p*-coumaric acid (*E*, *Z*) derivatives, alkyl esters of 8-hydroxylinalool and *N*-[2-(4-prenyloxyphenyl) ethyl]tiglamide were identified.

Chemical composition of the concrete was reported to contain α-pinene, camphene, sabinene, β-pinene, δ-3-carene, limonene, β-phellandrene, α-terpinene, ethyl octanoate, unknown *cis*-3-hexenyl ester, 2,6-dimethyl 1-2-7 octadiene 1,6, diol, caryophyllene, dihydro β-ionone, dihydro β-ionol, dodecanol, β-ionone, bicyclogermacrene, sesquicineol, spathulenol, dodecyl acetate, methyl jasmonate isomer, methyl isojasmonate, heptadec-8-ene and methyl hydroxyl cinnamate (Anonymous undated).

Twenty-three volatiles were found in the head space of buds and flowers; fully opened flowers emitted the most complex mixture of volatiles and in the greatest quantity, with a rapid decline in senescent flowers (McTavish et al. 2000). Volatiles identified in the headspace of opened boronia flower comprised β-ionone 39.5 %, α-pinene 30.4 %, caryophyllene 10.5 %, bicyclogermacrene 3.5 %, β-pinene 2.7 %, (*Z*)-*n*-heptadec-8-ene 2.3 %, humulene 1.5 %, unknown 1.5 %, unknown 1.2 %, limonene 1.1 %, *n*-pentadecane 0.9 %, myrcene 0.9 %, camphene 0.8 %, hotrienol 0.5 %, *n*-undecane 0.5 %, cyclic β-ionone 0.5 %, *cis*-β-ocimene 0.4 % dodecyl acetate 0.3 % (McTavish et al. 2000). Head space volatile emitted from various floral organs of as percent of whole flowers comprised 11.2 % from calyx/nectar, 26.7 % from petals, 10.5 % stigma, 14 % from sepaline anthers and 37.6 % from petaline anthers. Dodecanol was found in the headspace of petals, sepaline and petaline anthers; (*Z*)-methyl jasmonate in petals, stigma and sepaline anthers; (*Z*)-methyl epi-jasmonate in sepaline anthers; and *n*-heptadecane in petals, sepaline and petaline anthers.

Essential oil of freshly open flowers was found to contain the following compounds (mean and range in μg/g fw): α-pinene 52 μg (0–138 μg), β-pinene 56 μg (0–109 μg), limonene 37 μg (8–88ug), β-ionone 408 μg (115–1,092 μg) and dodecyl acetate 284 μg (112–631 μg) (Bussell et al. 1995). Essential oil of mature fruit was found to contain the following compounds (mean and range in μg/g fw): α-pinene 418 μg (142–877 μg), β-pinene 165 μg (39–240 μg), limonene 1,769 μg (16,996–26,691 ug), β-ionone 14 μg (0–58 μg) and dodecyl acetate 5 μg (0–24 μg). Lysigenous glands were found to be the main volatile oil secreting organs and are found in all plant tissues except the stigma and androecium (Bussell et al. 1995). These glands were the principal sources of monoterpenes α-pinene, β-pinene and limonene. Stigma, staminodes and stamens were found to be the primary sites of accumulation of dodecanol, dodecyl acetate, β-ionone and heptadecene. The receptacle, nectar and ovary were the main sites for α-pinene, β-pinene and limonene. All the mentioned volatile compound were found in the petals and maturing fruit.

The concentrations of floral extract and volatiles in the extract (% by fresh weight) increased as buds mature, the extract concentration being highest in large buds and open flowers and the concentration of volatile compounds being highest

in open flowers (MacTavish and Menary 1997a). Yields of flower material and floral extract per plant and the concentration of total volatiles including β-ionone reach maximum levels when 70 % of flowers have reached anthesis. The petals comprised 50 % of the weight of boronia flowers and the stigma 20 %; however, 70 % of the volatiles in the extract from the whole flower were contributed by the stigma, and only 20 % were present in the petals (MacTavish and Menary 1997b). Proportionately more β-ionone and dodecyl acetate were emitted from the stigma and anthers than were contained in the extract, compared with other volatiles. The calyx, contributed 51 % of total volatiles emitted into the headspace from the whole flower, stigma (16 %), "functional anther" (15 %) "non-functional anther" (14 %) and petals (3 %). Increases in all floral volatile components were greater as a result of postharvest incubation of harvested boronia flowers at 12 °C for 48 h compared with 30 °C for 12 h (Mactavish and Menary 1999b). The volatile portion of the extract increased by between 25 and 117 %, and the concentration of β-ionone increased by between 45 and 181 %. The maximum concentration of total volatiles observed was 0.47 % dw and of β-ionone 0.165 % dw. Four genetically distinct clones of brown boronia had similar concentrations of floral extract when harvested at between 50 and 80 % opened flowers (1.5–2.0 % dw) (Mactavish and Menary 1999a). The concentrations of total volatiles and β-ionone were reduced in pilot scale extractions compared with small-scale extractions. Inter-and intra-sample variability was high; there were no significant trends in the concentration of total volatiles or β-ionone in any clone.

MacTavish and Menary (1998) found that boronia floral extract yield (% of fresh flower weight) could be increased by 90 % by rolling (squashing) frozen flowers prior to extraction. With this process the extraction of volatile compounds increased by 48 %, particularly β-ionone which increased by 23 % per gram of flower material extracted. Selective extraction of β-ionone was optimized when low volumes of solvent were used (4 L of solvent per kg of flowers), producing extracts with enhanced organoleptic qualities. Leaf and flower nitrogen, number of nodes and flower and oil yields as well as the percent volatiles and β-ionone oil content were positively correlated with increased rates of nitrogen application (Roberts and Menary 1994). Ammonium nitrate and calcium nitrate fertilizers gave the highest yields for both boronia clones.

Plummer et al. (1999) found considerable variation existed in the contents of β-ionone, dodecyl acetate, α-pinene, β-pinene and limonene in the flower essential oil extract in *B. megastigma* population. Natural shading was associated with lower levels of monoterpenes but other oils were unaffected. Young plants contained less pinenes than older plants and older plants contained the most dodecyl acetate. Vigorous plants produced more pinenes. Red flowers contained the least β-ionone and dodecyl acetate.

Five C-27 apocarotenoids were detected in acetone boronia flower extracts: hydroxy-apo-10′-carotenoic acid, methyl hydroxy-apo-10′-carotenoate, apo-10′-carotenoic acid, apo-10′-carotenal and methyl apo-10′-carotenoate (Cooper et al. 2003) The results further supported speculation that the C-13 norisoprenoids found in boronia were derived from C-40 carotenoids. Possible parent molecules of β-ionone, an important component of boronia extract, were identified. The C-40 carotenoids β-carotene, zeaxanthin, lutein, and neoxanthin were identified in boronia flowers while two other carotenoids palmitic acid ester of 3-hydroxy-10′-apocaroten-10′-oic acid and 9,15,9′-tri-*cis*-ζ-carotene were also found (Cooper et al. 2009). Significant increases in β-carotene and apocarotenoids that could be derived from cleavage in the 9,10-position, including β-ionone and various C-27 apocarotenoids, were observed at the time of flower opening. An increase in lutein, which was derived through an alternative biosynthetic pathway, was not observed during flower opening, thus indicating the possibility that the β-carotene pathway was activated during flower opening in boronia.

The methanolic extract of marc from *Boronia megastigma* was found to contain both glycosides

and malonyl glycosides of methyl cucurbates, C13 norisoprenoids including megastigmanes, and monoterpene alcohols (Cooper et al. 2011). The following compounds were isolated and identified, (*1R,4R,5R*)-3,3,5-trimethyl-4-[(*1E*)-3-oxobut-1-en-1-yl]cyclohexyl β-D-glucopyranoside (3-hydroxy-5,6-dihydro-β-ionone-β-D-glucopyranoside); 3,7-dimethylocta-1,5-diene-3,7-diol-3-*O*–β-D-glucopyranoside; and a methyl {(1R)-3-(β-D-glucopyranosyloxy)- 2-[(2Z)-pent-2-en-1-yl]cyclopentyl}acetate stereoisomer (a methyl cucurbate-β-D-glucopyranoside), and provided evidence for 3,7-dimethylocta-1,5-diene-3,7-diol-3-*O*-(60-*O*-malonyl)-β-D-glucopyranoside in boronia flowers.

Leaf/Plant Phytochemicals

Compound identified in the head space of boronia leaf/stem included: α-pinene, camphene, myrcene, β-pinene, limonene, β-phellandrene, δ-3-carene, caryophyllene, bicyclogermacrene, sesquieucalyptol, sabinene, unknown, bicycloelemene, α-copaene, α-cubebene, β-elemene, cyperene, β-sesquiphellandrene, humulene, sesquicineole and δ-cadinene (Menary and MacTavish 2000).

Results of studies suggested that cytokinins may influence the rate of boronia flower development by altering the mobilisation of carbohydrates (Day et al. (1995). Within days of transferring boronia plants to cool (17/9 ºC day/night) conditions, a transient increase in zeatin riboside and dihydrozeatin riboside concentrations occurred in root and stem tissue and starch levels increased throughout the plant. A transient decrease in the starch concentration occurred during weeks 1–4 which correlated with early flower differentiation. Between weeks 10 and 12 in cool conditions, cytokinin concentrations increased, carbohydrate concentrations decreased, flower buds became committed to develop through to anthesis and a period of rapid bud expansion ensued.

Beta-ionone, a major volatile component of *B. megastigma* flower had been reported to have anticancer and cytochrome P540 induction activities.

Cytochrome P540 Induction Activity

In vivo studies showed that subcutaneous administration of β-ionone induced liver microsomal levels of several cytochrome P450s: P450 2B1 and 2B2, P450 1A1/2, P450 2C6 and NADPH-P450 reductase by the accumulation of their corresponding mRNAs (Jeong et al. 1995, 1998). The induction of cytochrome P450 2B1 and P450 1A1/2 and 2C by β-ionone was much greater in male rats than in female rats.

Anticancer Activity

Human colon cancer HCT116 cell line treated with subtoxic concentrations of β-ionone underwent dose-dependent cell growth suppression with G1-S-phase growth arrest and significant induction of apoptosis (Janakiram et al. 2008). Beta-Ionone up-regulated expression of retinoid X receptor-alpha mRNA dose-dependently in HCT116 cells. Administration of dietary 0.1 % and 0.2 % β-ionone significantly suppressed total colonic aberrant crypt foci formation up to 34–38 %, respectively, when compared with control group. Furthermore, rats fed β-ionone showed >55 % inhibition of foci containing four or more aberrant crypts. Results from in vitro and in vivo bioassay clearly suggested that β-ionone could be further developed for prevention and treatment of colon cancer. Results of studies by Dong et al. (2013) showed that human gastric adenocarcinoma cancer (SGC-7901) cell growth and DNA synthesis were inhibited and the cell cycle was arrested at the G0/G1 phase in a dose-dependent manner in cells treated with β-ionone (25, 50, 100, and 200 μmol/L) for 24 h. β-ionone significantly decreased the extracellular signal-regulated kinase protein expression and significantly increased the levels of p38 and Jun-amino-terminal kinase protein expression. β-Ionone also inhibited cell cycle-related proteins of Cdk4, Cyclin B1, D1 and increased p27 protein expression in SGC-7901 cells. The results suggested that SGC-7901 cell cycle arrest observed may be regulated through a MAPK pathway by transcriptional down-regulation of cell cycle proteins.

Liu et al. (2008) demonstrated that dietary beta-ionone suppressed 7, 12-dimethylbenz[a] anthracene (DMBA)-initiated mammary cancer in rats. With increasing dietary beta-ionone, the proportions of adenocarcinomas and benign masses, proliferating cell nuclear antigen (PCNA), cyclin D1 and Bcl-2 expression were decreased, and apoptosis, Bax expression and nuclear fragmentation were increased. In further studies, Liu et al. (2010) observed a significant decrease in lipid peroxidation in the mammary tumour-induced rats treated with dietary β-ionone, whereas the plasma activities of antioxidant enzymes such as glutathione peroxidase, glutathione reductase, superoxide dismutase and the nonenzymatic antioxidant glutathione were increased in the β-ionone treated rats when compared to control. The levels of catalase and lactate dehydrogenase were markedly decreased in the β-ionone treated groups compared to the positive control group. These results suggested that dietary β-ionone had biologically relevant antioxidant activity and played a chemopreventive role against DMBA-induced mammary gland tumours.

Data of in vitro studies suggested that β-ionone inhibited cell proliferation, caused cell cycle arrest at the G1-S phase and induced apoptosis in a concentration-dependent manner in human osteosarcoma U2os cells via a p53-dependent mitochondrial pathway (Zhu et al. 2010). Further, beta-ionone up-regulated Bax protein and downregulated Bcl2 protein which led to Bax translocation and cytochrome C release, subsequently activated caspase-3, thus resulting in apoptosis. In vitro studies by Huang et al. (2012) showed that β-Ionone effectively inhibited the metastasis of human hepatocarcinoma SK-Hep-1 cells, via modulation of gene expression and signal pathways related to invasion, adhesion and migration. β-ionone inhibited matrix metalloproteinase (MMP)-2, MMP-9 and urokinase-type plasminogen activator activities and expression of migration-related proteins, including focal adhesion kinase (FAK), phosphorylated form of FAK, Rho, Rac1 and Cdc42. It up-regulated protein expression of the tissue inhibitor of matrix metalloproteinase (TIMP)-1, TIMP-2 and plasminogen activator inhibitor-1 and expression of nm23-H1 protein. In vivo studies showed that β-ionone effectively ameliorated benzo(a)pyrene [B(a)P]-induced lung carcinogenesis in rats (Asokkumar et al. 2012). β-ionone significantly inhibited tumour proliferation, attenuated lipid peroxidation and restored all cancer marker enzymes and antioxidants levels to near normal levels.

Other Uses

The plant is grown commercially for the production of essential oils for perfumes and cut flowers; it is also grown as a garden ornamental.

Comments

Like many Boronias, *B. megastigma* can be quite difficult to grow from seeds as they exhibit dormancy, being covered in a thick coating which prevents germination in all but ideal conditions in the wild. However, the plant can be successfully grown from cuttings.

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Petunia hybrida

Scientific Name

***Petunia hybrida* Vilm.**

Synonyms

Petunia violacea var. *hybrid*a Hook.

Family

Solanaceae

Common/English Names

Common Petunia, Garden Petunia, Petunia

Vernacular Names

Chinese: Aiqianniu, Bidongqie
Dutch: Petunia
Esperanto: Petunio
Finnish: Petunia
French: Pétunia
German: Garten-Petunie, Petunia, Petunien
Italian: Petunia
Japanese: Pechunia
Lithuanian: Petunija
Polish: Petunia Ogrodowa
Portuguese: Petúnia
Romanian: Petunia
Russian: Petúnija
Spanish: Petunia
Turkish: Petunya
Welsh: Petwnia, Petwniâu

Origin/Distribution

Scientist believed that the genus *Petunia* originated from South America.

The first Garden Petunia (*Petunia* × *hybrida* Vilm.) was reported to be an interspecific hybrid of *P. axillaris* (Lam.) Britton, Sterns & Poggenb. (=*P. nyctaginiflora* Juss.) (the large white or night-scented petunia) and *P. integrifolia* (Hook.) Schinz & Thell. (=*P. violacea* Lindl.) (the violet-flowered petunia) (Paxton 1836). Since then, *Petunia inflata* R. E. Fr. and *Petunia parodii* Steere [= *P. axillaris* subsp. *parodii* (Steere) Cabrera] have also been proposed as the likely parents of modern Garden Petunias (Sink 1984).

Agroecology

Garden Petunia will grow in temperature regimes of 4–32 °C. Petunia prefers full sun and will become spindly when grown in shade. Petunias have been reported to require at least 5–6 h of sunlight for optimum flowering. Flower pigmentation (colour intensity) is enhanced within its moderate to lower temperature range. Petunias grow in most soil types but prefer well-drained, moist, light soil of medium fertility in the pH range of 6–7.

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Edible Plant Parts and Uses

Petunia flowers are edible (Coyle 1999; Deane 2007–2012; Rogala and Pothour 2013) The mild-tasting flowers are used in salads or as a garnish.

Botany

Ascending or decumbent, annual herbs, 30–60 cm tall, with soft, glandular hairs. Leaves alternate, shortly petiolate or subsessile; ovate, 3–8 × 1.5–4.5 cm, base cuneate, margin entire, apex acute (Plates 1, 3 and 6). Flowers solitary in axils of leaves or leaf-like bracts on pedicel (3–5 cm) longer than the subtending leaves; calyx deeply 5-parted, 1–1.8 cm by 3.5 mm; corolla funnelform with 5 rounded, spreading lobes 5–7 cm, white, red, yellow, pink, purple, or variegated (Plates 1, 2, 3, 4, 5 and 6) sometimes fragrant; stamens 5–1 short (staminode), 2 medium and 2 long; style slightly exceeding stamens. Capsules conical, 2-valved, 8–12 mm long, dehiscent. Seeds many subglobose, 0.5 mm across.

Nutritive/Medicinal Properties

Flower Phytochemicals

Phenylpropanoids and benzenoids were found to make up the primary volatile constituents of petunia flora volatile emission and to have originated from the aromatic amino acid phenylalanine (Boatright et al. 2004). These compounds were identified as benzaldehyde, phenylacetaldehyde, methyl benzoate, phenylethyl alcohol, benzyl alcohol, isoeugenol and benzyl benzoate, with methyl benzoate being the most abundant volatile in the group (Verdonk et al. 2003; Boatright et al. 2004). Other volatiles identified include phenylethyl benzoate, vanillin, two sesquiterpenes (germacrene D and cadina-3,9-diene), two aliphatic aldehydes (decanal and dodecanal) and two fatty acid derivatives (3-hexenal and 2-hexanal). Schuurink et al. (2006) found the following in petunia flowers: benzoic acid, benzyl alcohol, benzyl benzoate, benzoyl-CoA, methyl benzoate, methyl salicylate, phenylethyl alcohol, phenylethyl benzoate and salicylic acid. ODORANT1 (ODO1), a transcription factor from MYB transcription

Plate 1 Purple single-petal Grandiflora Petunia

Plate 2 Light-red single-petal Grandiflora Petunia

Plate 3 Yellow single-petal Grandiflora Petunia

Plate 4 Hot-pink single-petal Grandiflora Petunia

Plate 5 Maroon-white variegated fringed single-petal Grandiflora Petunia

Plate 6 Crimson-white variegated fringed double-petal Grandiflora Petunia

factor family, had been characterized as a regulator of scent production in *Petunia hybrida* flowers (Verdonk et al. 2005). Suppression of ODO1 in petunia (*Petunia hybrida*) led to decreased levels of emitted volatile phenylpropanoids (Verdonk et al. 2005). Spitzer-Rimon et al. (2010) reported a novel R2R3-MYB-like regulatory factor of phenylpropanoid volatile biosynthesis, Emission of Benzenoids II (EOBII) in petunia flowers. Suppression of EOBII expression led to significant reduction in the levels of volatiles accumulating in and emitted by flowers, such as benzaldehyde, phenylethyl alcohol, benzyl benzoate and isoeugenol. Petunia and snapdragon both synthesize methyl benzoate from benzoic acid and *S*-adenosyl-l-methionine (SAM); however, they used different mechanisms to downregulate its production after pollination (Negre et al. 2003). Petunia floral volatile emission following perception of exogenous or endogenous (postpollination) ethylene included benzaldehyde, benzyl alcohol, phenylacetaldehyde, methyl benzoate, 2-phenylethanol, isoeugenol and benzyl benzoate (Dexter et al. 2007b). Production of these compounds was primarily localized to the petunia corolla and more specifically the petal limb (Underwood et al. 2005). Also, it was found that benzoic acid/salicylic acid carboxyl methyltransferase (PhBSMT1 and 2) genes were responsible for the synthesis of methyl benzoate in petunia. Benzenoid and phenylpropanoid volatiles were found to be synthesized predominantly in the corolla limb, and emission was highly regulated, with a circadian rhythm, during corolla development, pollination and senescence (Clark et al. 2009). *Petunia* × *hybrida* cv. 'Mitchell Diploid' flowers emitted high levels of multiple floral volatile benzenoid/phenylpropanoid (FVBP) compounds from anthesis to senescence in a concerted manner (Colquhoun et al. 2010). Seven genes PhBSMT1, PhBSMT2, PhBPBT, PhPAAS, PhIGS1, PhCFAT *and* PhODO1 were found to be responsible for the production of emitted FVBPs.

Three *Petunia hybrida* cultivars with solid deep-blue flowers that accumulated malvidin in corollas with high tissue pH were found to emit abundant isoeugenol as the principal floral fragrance (Nakamura et al. 2006). Several other cultivars that emitted considerable amounts of methyl benzoate and/or benzyl benzoate from the flower were also identified from the flowers of 40 commercial *Petunia hybrida* cultivars.

Petunia flower petals had been reported to emit large amounts of isoeugenol, which had been shown to be synthesized by isoeugenol synthase (PhIGS1) from an ester of coniferyl alcohol confirmed to be coniferyl acetate (Dexter et al. 2007a).

Three major anthocyanins in red petunias were determined to be cyanidin 3-sophoroside, cyanidin 3-glucoside and peonidin 3-glucoside (Ando et al. 2000). The presence of five anthocyanidins, namely, cyanidin, peonidin, delphinidin, petunidin and malvidin, was confirmed in 195 commercial petunias with floral colours other than white and yellow (Ando et al. 2004). Pelargonidin was not detected, and delphinidin was not a major component. The petunias were classified into three phenotype groups accumulating cyanidin, peonidin or malvidin (plus petunidin) as the major anthocyanidin. A fourth phenotype was segregated in the progeny obtained by self-pollinating an F_1 hybrid of the malvidin group; this accumulated delphinidin 3-glucoside in a markedly crumpled corolla limb (delphinidin group). Such inferior floral traits, associated with the accumulation of delphinidin 3-glucoside, were thought to be the driving force that removed the delphinidin group from commercial petunias.

Different light qualities, far-red, red, blue and dark, were found to influence the accumulation, and the turnover of the 3-monoglucosides of delphinidin, petunidin and malvidin was studied in isolated petals of the delphinidin genotype of *Petunia hybrida* (Steiner 1972b). In the intensity range tested, in white light there was an increase in the accumulation of 3-monoglucosides of delphinidin, petunidin and malvidin with higher illumination in petals of delphinidin genotype of *Petunia hybrida*; in red light no intensity dependency was observed; in far-red and in blue with higher intensities, the accumulation of delphinidin-3-monoglucoside was specifically lowered, whereas the accumulation of petunidin- and malvidin-3-monoglucoside remained about the same (Steiner 1972a). Cornu et al. (1974) found pelargonidin in the flowers of a mutant of *P. hybrida*. In *P. hybrida* flower bud, the anthocyanidin 3(*p*-coumaroyl)rutinosido-5-glucoside was methylated by *O*-methyltransferase using *S*-adenosyl-L-methionine as methyl donor (Jonsson et al. 1982). No methylating activity towards anthocyanidins, anthocyanidin 3-glucosides, anthocyanidin 3-rutinosides, caffeic acid or *p*-coumaric acid was detected. During petunia flower bud development, the increase in anthocyanin content coincided with an increase in activity of three biosynthetic enzymes: chalcone isomerase, uridine diphosphoglucose: flavonoid 3-*O*-glucosyltransferase and S-adenosyl-L-methionine: anthocyanidin 3-(*p*-coumaroyl)-rutinoside-5-glucoside 3′,5′-*O*-methyltransferase (Jonsson et al. 1984). In mature flowers, glucosyltransferase and methyltransferase, both involved in later steps of biosynthesis, were mainly found (93–100 %) in the epidermal layers, whereas chalcone isomerase was evenly distributed between the epidermal and mesophyll tissue. Anthocyanins were found to accumulate in the epidermal layers of the flower. White flowers of the *Petunia hybrida* line W43q were found to accumulate glucosides of 4-coumaric acid and caffeic acid and were able to synthesize anthocyanins from exogenously supplied naringenin (Mol et al. 1983). In white sectors of flowers with a colour pattern, virtually no chalcone synthase (CHS) enzyme activity could be demonstrated. The enzymes chalcone isomerase (CHI), UDPG: flavonoid-3-0-glucosyltransferase (3GT) and SAM: anthocyanin methyltransferase (OMT) were present, although at a more or less reduced level.

Two novel diacylated anthocyanins, malvidin 3-*O*-(6-*O*-(4-*O*-(4-*O*-(6-*O*-caffeoyl-β-D-glucopyranosyl)-*p*-coumaroyl)-α-l-rhamnosyl)-β-D-glucopyranoside)-5-*O*-β-D-glucopyranoside (major pigment) and the malvidin 3-*O*-(6-*O*-(4-*O*-(4-*O*-(6-*O*-caffeoyl-β-D-glucopyranosyl)-caffeoyl)-α-l-rhamnosyl)-β-D-glucopyranoside)-5-*O*-β-D-glucopyranoside (minor pigment), and two known monoacylated anthocyanins were isolated from violet petals of *Petunia hybrida* cv. Surfinia Violet Mini (Fukui et al. 1998). Two acylated anthocyanins were isolated from the petals of petunia (*Petunia hybrida* Surfinia blue), and they were elucidated as malvidin 3-*O*-[6-*O*-(4-*O*-*E*-caffeoyl-a-rhamnopyranosyl)-β-glucopyranoside]-5-*O*-β-glucopyranoside and malvidin 3-*O*-[6-*O*-(4-*O*-*Z*-*p*-coumaroyl-a-rhamnopyranosyl)-β-glucopyranoside]-5-*O*-β-glucopyranoside (Slimestad et al. 1999). Two novel diacylated anthocyanins malvidin 3-*O*-(6-*O*-(4-*O*-

(4-*O*-(6-*O*-feruloyl-β-D-glucopyranosyl)-*E*-*p*-coumaroyl)-α-rhamnosyl)-β-D-glucopyranoside)-5-β-D-glucopyranoside and malvidin 3-*O*-(6-*O*-(4-*O*-(4-*O*-(6-*O*-*E*-*p*-coumaroyl-β-D-glucopyranosyl)-*E*-*p*-coumaroyl)-α-rhamnosyl)-β-D-glucopyranoside)-5-β-D-glucopyranoside and two known anthocyanins 3-caffeoylglucosyl-*p*-coumaroylrutinoside-5-glucosides of malvidin and petunidin were isolated from violet flowers of *Petunia hybrida* cv. Festival (Gonzalez et al. 2001).

Carotenoids were found to be responsible for the increased colour intensity and overall yellow hue of the flowers of three yellow petunia cultivars, 'Summer Sun', 'Bright Yellow' and 'California Girl' (Nielsen and Bloor 1997). Early pigmentation was attributed to a combination of chlorophyll and carotenoid pigments, while mature petal coloration was due to further production of carotenoids and xanthophylls in 'Summer Sun' and 'California Girl'. In 'Bright Yellow', the yellow coloration was attributed to the persistence of high carotenoid levels found in immature flower buds as the flower matured.

Fourteen different flavonol glucosides were identified in flowers from 17 different *Petunia hybrida* cultivars and several *Petunia* species including the 3-glucoside, 3,7-diglucoside, 3-caffeoylsophoroside and 3-caffeoylsophoryl-7-glucoside of quercetin and those of kaempferol (Griesbach and Asen 1990). Petunia flowers were found to contain acylated anthocyanins 3-*p*-coumaroyl-rutinoside-5-glucosides and of 3-rutinoside-5-glucosides acylated with caffeic acid (Griesbach et al. 1991). The red-flowered petunia parent (RHS45A) contained cyanidin-3-glucoside (57.8 %), cyanidin-3-rutinoside and pelargonidin-3-glucoside (8 %), while the violet-flowered (RH S89C) parent contained malvidin-3-caffeoylrutinoside (55 %), malvidin-3-coumarylrutinoside (22.3 %) and petunidin-3-caffeoylrutinoside (22.7 %) (Griesbach 1996).

Endress (1974) established the existence of glucosidized 3,4,2′,4′,6′-penta-hydroxy-chalcone in the biosynthetic pathway of flavonoids in petals of *Petunia hybrida* at the stage of intensive and linear anthocyanin accumulation. A 3′,4′-dihydroxy or a 3′,4′,5′-trihydroxy substitution pattern of dihydroflavonols was required for their conversion into the corresponding anthocyanins in a white flower of *Petunia hybrida* (Kho 1978). In case of a 4′-methoxy substituted dihydroflavonol, a 4′-hydroxyanthocyanin was obtained, suggesting demethylation of this compound. The conversion of synthetic (±)-*trans*-2,3-dihydroflavonols into anthocyanins proceeded almost as well as with natural compounds. In *Petunia hybrida*, 6′-hydroxychalcones were found to be intermediates in the synthesis of flavonoids (Davies et al. 1998). Flavonoids including several different 6′-deoxychalcones accumulated in the petals of chalcone reductase (CHR) transgenics. The major flavonoids in CHR transgenic petals were butein 3-*O*-glucoside, quercetin 3-*O*-sophoroside, butein 4-*O*-glucoside and glucoside of 2′,3′,4′,4-tetrahydroxychalcone, while control petal contained primarily quercetin 3-*O*-sophoroside. The major flavonoids in CHR transgenic pollens were quercetin 3-*O*(2″-*O*-glucosyl) galactoside, isoliquiritigenin, kaempferol 3-*O*(2″-*O*-glucosyl)galactoside and dihydroquercetin, and the flavonoids in control pollen were quercetin 3-*O*(2″-*O*-glucosyl galactoside, kaempferol 3-*O*(2″-*O*-glucosyl) galactoside, dihydroquercetin, naringenin and naringenin chalcone. Chalcone and flavonol levels were highest in young buds and lowest in open flowers. Major flavonoids in the leaves were quercetin-based flavonols, and no chalcones were found. The flavanone 3β-hydroxylase that catalysed the Fe^{2+}/oxoglutarate-dependent hydroxylation of (2*S*)-flavanones to (2*R*,3*R*)-dihydroflavonols in the biosynthesis of flavonoids, catechins and anthocyanidins was partially purified from *Petunia hybrida* and proposed to be active as a dimer of roughly 75 kDa in size (Lukačin et al. 2000). Two flavonoid glucosyltransferases, UDP-glucose:flavonoid 3-*O*-glucosyltransferase (3-GT) and UDP-glucose:anthocyanin 5-*O*-glucosyltransferase (5-GT), were found to be responsible for the glucosylation of anthocyani(di)ns to produce stable molecules in the anthocyanin biosynthetic pathway in *P. hybrida* (Yamazaki et al. 2002).

4,2′,4′,6′-Tetrahydroxychalcone was found in *Petunia hybrida* pollen (De Vlaming and Kho 1976). Pollen extracts from *Petunia hybrida* were found to contain phytic acid (Jackson et al. 1982). The amount of phytic acid was found to increase

in the anthers of young flower buds of *Petunia hybrida*, as the flower developed until anther dehydration, when there was a more rapid increase in phytic acid content (Helsper et al. 1984). Mature pollen contained 2 % phytic acid content by weight of which 90 % was water soluble, while free *myo*-inositol was a relatively low 0.06 % by weight. Phytic acid degradation was initiated soon after pollen germination began, and its degradation products, *myo*-inositol and inorganic phosphate, were rapidly mobilized for phospholipid and pectin biosynthesis. Utilization of labelled *myo*-[2-^{3}H]inositol for phospholipid biosynthesis was about five times that for pectin synthesis during the first few hours of pollen germination. The label in the phospholipid was identified as the *myo*-inositol moiety of phosphatidylinositol, while the pectin material comprised mainly labelled arabinose, with smaller amounts of label in galacturonic acid, glucose and xylose. Labelling germinating pollen with [^{32}P]orthophosphate gave label in phosphatidic acid, phosphatidylinositol, phosphatidylethanolamine and phosphatidylcholine of the phospholipids. Phosphatidylinositol contained 30 % of this label initially, a proportion which declined to 10 % over longer periods of pollen germination. Petunia pollen was found to contain (−)-jasmonic acid and a jasmonate, N-[(−)-jasmonoyl]-tyramine (Miersch et al. 1998). *Petunia hybrida* pollen and stigma were found to contain *vir*E locus inducing compounds, which were released in high concentrations only by pollen (Zerback et al. 1989). In pollen extracts these compounds were identified as the flavonol glycosides kaempferol 3-glucosylgalactoside and quercetin 3-glucosylgalactoside. The expression of the *vir*E locus is also induced by other flavonoid compounds as rutin, myricetin 3-galactoside, narcissin and apigenin 7-glucoside. A histidine domain arabinogalactan protein, PhPRP1, purified from *Petunia hybrida* pistils was shown to be orthologous to TTS-1 and TTS-2 from *Nicotiana tabacum* and NaTTS from *Nicotiana alata* (Twomey et al. 2013).

Petunia floral nectar was shown to contain five proteins (RNase genes), namely, S1 RNase, Sx RNase, peroxidase, endochitinase and a putative fructokinase (Hillwig et al. 2011).

Aerial Part/Leaf/Stem/Cell Suspension Phytochemicals

Non-transgenic petunia plants produced flowers that contained ≈50 ng anthocyanin/100 mg tissue dry weight, and anthocyanin distribution was 63 % cyanidin, 28 % delphinidin and 9 % pelargonidin (Griesbach 1993). In contrast, the transgenic plants expressing the A1 gene of *Zea mays* produced flowers that contained ≈500 ng anthocyanin/100 mg tissue dry weight, with 34 % as cyanidin, 12 % as delphinidin and 54 % as pelargonidin. The increase in anthocyanin production in the transgenic plants resulted in a corresponding molar decrease in flavonol accumulation.

All enzymes of galactose metabolism, namely, galactokinase, hexose-1-phosphate uridyltransferase, UDP-glucose 4-epimerase and galactose-1-phosphate uridyltransferase, were found in *Petunia hybrida* (Dressler et al. 1982). Six new ergostane glycosides, designated as petunioside A, petunioside B, 24-epipetunioside B, petunioside C, 24-epipetunioside C and petunioside D, were isolated from the methanolic extract of the fresh aerial parts of *Petunia hybrida* (Shingu et al. 1994). Seven steroids, 30-hydroxy petuniasterone A (C-30 epimeric mixture); 1α-acetoxy-1,2-dihydropetuniasterone A (designated petuniasterone E); (22*R*,24*S*)-7α,24-dihydroxy-22,25-oxidoergosta-1,4-dien-3-one (petuniasterone F); C-24 epimers of (22*R*)-7α,22,24,25-tetrahydroxyergosta-1,4-dien-3-one (petuniasterones G_1 and G_2); and C-24 epimers of (22*R*)-1-α-acetoxy-7α,22,24,25-tetrahydroxyergost-4-en-3-one (petuniasterones H_1 and H_2), were isolated from *Petunia hybrida* leaves and stem (Elliger et al. 1988).

Trichomes of petunia leaves were found to produce a complex mixture of glucose and sucrose esters with insecticidal properties (Kays et al. 1994). Fourteen different acids from C_2 to C_8 were found esterifed to the sugar (sucrose, glucose) molecules, namely, acetyl (C_2), propionyl, malonyl (C_3), iso-butyryl, n-butyryl (C_4), 2-methyl butyryl, 3-methyl butyryl, valeryl (C_5), 4-methyl valeryl, hexanoyl (C_6), 5-methyl hexanoyl, 4-methyl hexanoyl heptanoyl (C_7), 6-methyl heptanol and octanoyl (C_8).

Three sucrose ester types 2,3,4-*O*-tri-acyl-α-D-glucopyranosyl-1-*O*-malonyl-4-*O*-acyl-6-*O*-acetyl-β-D-fructofuranoside; 2,3,4-*O*-tri-acyl-α-D-glucopyranosyl-4-*O*-acyl-6-*O*-acetyl-β-D-fructofuranoside; and 2,3,4,6-*O*-tetra-acyl-α-D-glucopyranosyl-β-D-fructofuranoside were isolated and identified from the leaf surface lipids of *Petunia hybrida* (Ohya et al. 1996). They contained both unbranched and branched fatty acids (from C2 to C8). Further, one of these sucrose esters contained malonic acids. Three acylated flavonol glycosides, kaempferol-3-*O*-(2-*O*-feruloyl-β-D-glucosyl(1→2)6-*O*-malonylglucoside),quercetin-3-*O*-(2-*O*-caffeoyl-β-D-glucosyl(1 → 2)6-*O*-malonylglucoside) and quercetin-3-*O*-(2-*O*-feruloyl-β-D-glucosyl(1 → 2)glucoside) were found in the leaves of *Petunia hybrida* 'Mitchell' (Bloor et al. 1998). A transgenic Mitchell line expressing the maize leaf colour *(Lc)* cDNA had enhanced levels of anthocyanins, particularly in their leaves. These anthocyanins were determined to be the same acylated petunidin glycosides as those which produce a slight red colouration in the tube of the flowers of *Petunia* Mitchell. Treatment of *P. hybrida* leaves with derivatives of the naturally occurring acylating species caffeic acid resulted in a general increase in flavonol derivatives, especially caffeoylated quercetin-3-*O*-diglucoside (QDG) and kaempferol-3-*O*-diglucoside (KDG) (Cunningham and Edwards 2008). Similarly, methyl ferulate increased the content of feruloylated KDG 40-fold. Treatment with methyl coumarate resulted in the appearance of a coumaroylated derivative of quercetin-3-*O*-glucuronyl-glucoside (QGGA). When the feeding studies were repeated with the equivalent phenylpropanoid isosubstituted with fluorine groups, a semi-synthetic 4-fluorocinnamoyl ester of QGGA was observed.

In *Petunia hybrida* cv. Violet 30 cell suspensions, phenylalanine ammonia lyase (PAL), the first enzyme of the phenylpropanoid pathway (PPP), could be induced by various treatments, e.g. biotic elicitors (sterilized microorganisms, nigeran) or abiotic elicitors (orthovanadate, pH shift) (Hagendoorn et al. 1990). Orthovanadate activated the branch of the PPP, leading to production of lignin-like material such as a guaiacyl-type lignin. Both guaiacyl- and syringyl-type lignins were found in the xylem of the fully grown plants. Increase of the pH in continuous cultures of *Petunia hybrida* cells also led to production of lignin-like material.

Antibacterial Activity

Petunia leaf methanolic extract exhibited higher in vitro inhibition against both human and plant pathogenic bacteria including *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Salmonella* spp., *Streptococcus* spp. and *Staphylococcus aureus* compared to other leaf extracts (petroleum ether, chloroform, ethyl acetate, ethanol and aqueous) (Thenmozhi and Sivaraj 2011). For all the different solvents, leaf extracts only showed highest activity against the test bacteria compare to the callus extract.

Other Uses

Petunias are versatile annual ornamentals. They can be used for colour masses, borders, containers, hanging baskets or as a seasonal groundcover.

Sugar esters from the leaves of *Petunia* × *hybrida* cultivars were found effective against sweet potato whitefly *Bemisia tabaci* (Kays et al. 1994). Treatment concentrations of 1 and 0.5 mg/ml petunia sugar esters gave excellent whitely control on sweet potato leaves. Petunia sugar esters gave significantly lower whitefly egg and adult counts on summer squash, *Cucurbita pepo,* compared to control.

Comments

The *P. hybrida* varieties can be categorized into four main groups (Engebreston and Williamson 2004; Brown 2009):

(a) Grandiflora—large flowered (10–13 cm diameter), consisting of both single and double flowering forms, with ruffled or fringed petals, trailing habit (Plates 1, 2, 3, 4, 5 and 6)

(b) Multiflora—smaller flowers (6–8 cm diameter) and bushier, consisting of both single and double flowering forms, with ruffled or fringed petals
(c) Milliflora—compact, miniature plants with a large number of small flowers (2.5–5 cm)
(d) Hedgiflora or wave—spreading, low-growing ground cover up to 10 cm high with large spread 90–120 cm

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Camellia japonica

Scientific Name

***Camellia japonica* L.**

Synonyms

Camellia bonnardii Berl. ex Lem.; *Camellia florida* Salisb.; *Camellia hayaoi* Yanagita ex Kusaka; *Camellia hozanensis* (Hayata) Hayata; *Camellia japonica* var. *concava* Makino; *Camellia japonica* var. *hexapetala* Makino; *Camellia japonica* var. *hortensis* (Makino) Makino; *Camellia japonica* subsp. *hortensis* (Makino) Masam. & Yanagita; *Camellia japonica* var. *hozanensis* (Hayata) Yamam.; *Camellia japonica* f. *ilicifolia* Makino; *Camellia japonica* f. *lancifolia* H.Hara; *Camellia japonica* f. *leucantha* Makino ex H.Hara; *Camellia japonica* f. *lilifolia* Makino; *Camellia japonica* var. *longifolia* Nakai; *Camellia japonica* var. *macrocarpa* Masam.; *Camellia japonica* f. *macrocarpa* (Masam.) Tuyama; *Camellia japonica* var. *nakaii* (Hayata) Yamam.; *Camellia japonica* f. *otome* Makino; *Camellia japonica* f. *parviflora* Makino; *Camellia japonica* f. *polypetala* Makino; *Camellia japonica* f. *trifida* Makino; *Camellia kaempferia* Reboul; *Camellia mutabilis* Paxton; *Camellia nakaii* (Hayata) Hayata; *Camellia planipetala* Lem.; *Camellia tsubaki* Crantz; *Camellia tuckiana* auct.; *Camellia wabiske* (Makino) Kitam.

Family

Theaceae

Common/English Names

Camellia, Common Camellia, Japanese Camellia

Vernacular Names

Brazil: Camellia, Rosa-Do-Japão
Chinese: Shan Cha, Yuan Bian Zhong
Czech: Kamélie Japonská
Danish: Ægte Kamelia, Kamelia
Estonian: Jaapani Kameelia
French: Camélia, Camélia Du Japon, Rose Du Japon
German: Kamelie, Japanische Kamelie
Japanese: Tsubaki, Housan Tsubaki, Yama Tsubaki, Yabu Tsubaki
Korean: Dong-Baek-Na-Mu, Tteul-Dong-Baeng-Na-Mu
Polish: Kamelia Japonska
Portuguese: Camélia

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Russian: Kameliia Iaponskaia
Spanish: Camelia
Swedish: Tebuske, Kamelia

Origin/Distribution

The species is native to East Asia—China (Shandung), Taiwan, Japan (except Hokkaido) and South Korea.

Agroecology

It is a cool climate crop that occurs in forests and garden in full sun or partial shade from near sea level 300–1,100 m elevation in temperate areas of East Asia.

Edible Plant Parts and Uses

An edible oil known as 'tsubaki oil' is obtained from the seed (Usher 1974; Tanaka 1976; Facciola 1990; Lee et al. 2011). Dried flowers are used as a vegetable cooked or mixed with gelatinous rice to make a Japanese food called 'mochi' (Tanaka 1976; Facciola 1990) or used as a flower tea (Lee et al. 2011; Way et al. 2009). The leaves serve as a substitute for tea and tobacco (Stuart 1979; Kunkel 1984; Facciola 1990).

Botany

An evergreen, branched, glabrous perennial shrub or small tree, 1.5–9 m high (Plate 1). Leaves alternate, coriaceous, glabrous, glossy green, lower surface glandular, borne on short 10 mm long glabrous petioles. Lamina oblong-elliptic, elliptic, broadly ovate, 5–12 cm by 2.5–7 cm; margin serrulate; apex acuminate or obtusely pointed; base broadly cuneate to cuneate, with 6–9 pairs of lateral veins (Plates 1, 2, 3, 4 and 5). Bracteoles and sepals greyish white velutinous. Flowers solitary in 2–5 flowered subterminal clusters. Flower bracteoles 9–13, deciduous, globose, ovate, subglobose; sepals, 9–13, globose, ovate, 2–20 mm long; petals 5–7 obovate, broadly obovate, retuse, round, 30–45 mm long, white, pink, red, variegated or variously coloured (Plates 1, 2, 3, 4, 5 and 6); stamens 25–35 mm long, basal half of outer filaments

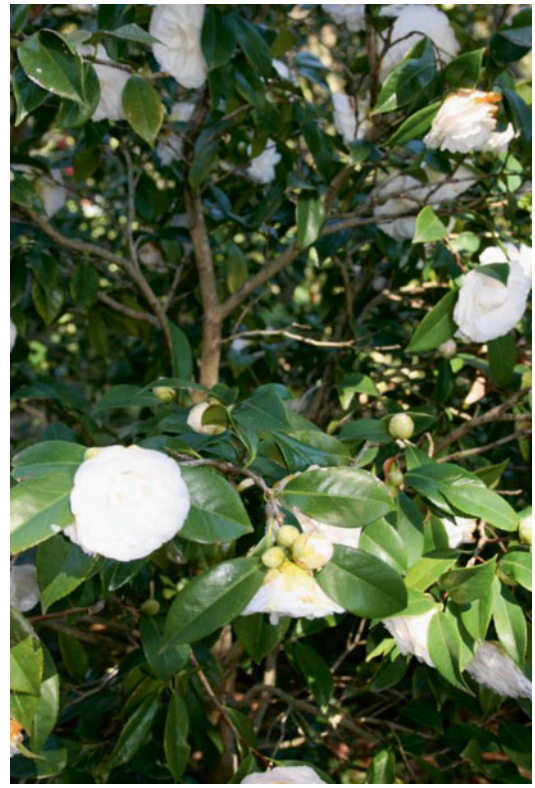

Plate 1 *Camellia japonica* 'First Prom' plant habit

Plate 2 *C. japonica* 'First Prom' white flower

Plate 3 *C. japonica* Madam Louis van Houte flowers and leaves

Plate 6 Pink-white-flowered cultivar

Plate 4 *C. japonica* Madam Louis van Houte (pink flower)

Plate 5 Red flower cultivar

connate, not forming a tube; style, trifid; ovary ovate and 3-locular. Fruit globose capsule, 3–4 cm diameter with 1–3 seed per locule. Seed subglobose to globose, brown.

Nutritive/Medicinal Properties

Flower Phytochemicals

White camellia flowers were found to contain leuco-anthocyanin (Endo 1958a, b). Red and variegated also contain leuco-anthocyanin yielding cyanidin, as well as a glycoside of cyanidin. The major anthocyanin of red flowers of *C. japonica* was determined to be cyanidin 3-*O*-β-D-(6-*O*-*p*-coumaroylglucoside) (Saito et al. 1987). This pigment and cyanidin 3-glucoside are widely distributed in the flowers of *Camellia japonica* and many *Camellia* cultivars. The following acylated anthocyanins were detected in *C. japonica* flowers: cyanidin 3-*O*-β-glucopyranoside, cyanidin 3-*O*-β-galactopyranoside, cyanidin 3-*O*-(6-*O*-*(E)*-*p*-coumaroyl)-β-glucopyranoside, cyanidin 3-*O*-(6-*O*-(*E*)- *p*-coumaroyl)-β-galactopyranoside, cyanidin 3-*O*-(6-*O*-*(E)*-caffeoyl)-β-glucopyranoside, cyanidin 3-*O*-(6-*O*-(*E*)-caffeoyl)-β-galactopyranoside and cyanidin 3-*p*-coumaroylglucoside (Li et al. 2009). In a recent study of chemical taxonomy of red-flowered wild *Camellia* species based on floral anthocyanins, *C. japonica* comprising 3-*O*-β-glucosides of cyanidin was placed in subcluster B (Li et al. 2013).

Cellulose and a β-1,3-glucan (callose) were detected in the pollen tube wall of *C. japonica* (Nakamura and Suzuki 1983). Two triterpenoids from *Camellia japonica* flowers were identified as 3β,18β-dihydroxy-28-norolean-12-en-16-one

and 18β-hydroxy-28-norolean-12-ene-3,16-dione (Itokawa et al. 1981). Camelliin B, a dimeric hydrolyzable tannin, was isolated from *C. japonica* flower buds (Yoshida et al. 1989). Two new dimeric hydrolyzable ellagitannins, camelliins A and B, were isolated from flower buds of *Camellia japonica* (Yoshida et al. 1990). No purine alkaloids (caffeine, theobromine) were detectable in flower buds of *C. japonica* and *C. sasanqua* (Fujimori and Ashihara 1990). The flower of *Camellia sasanqua* yielded tannins, gemin D, pedunculagin and camelliins A and B, which were identical with those of *C. japonica*. From the methanol flower extract, 28-nor-oleanane-type triterpene oligoglycosides; camelliosides A, B and C; and an oleanane-type triterpene oligoglycoside, camellioside D, were isolated together with five known compounds: (−)-epicatechin, oleanolic acid, benzyl B-D-glucopyranoside, methyl gallate and (+)-catechin (Yoshikawa et al. 2007). The following compounds were isolated from the hot aqueous flower bud extract: *p*-hydroxybenzaldehyde; vanillin; dehydroxysynapyl alcohol; 7S,7′S,8R,8′R-icariol A_2; and (−)-epicatechin (Cho et al. 2009). Nine phenolic compounds were identified in the hot water extract of *C. japonica* flowers: 3,4,5-trihydroxybenzoic acid (1), 3,4-dihydroxybenzoic acid (2), 4-hydroxybenzoic acid (3), 2,3-digalloyl-*O*-α-D-glucopyranoside (4), 2,3-digalloyl-*O*-β-D-glucopyranoside (5), quercetin 3-*O*-β-D-galactopyranoside (6), quercetin 3-*O*-α-D-glucopyranoside (7), kaempferol 3-*O*-β-D-galactopyranoside (8) and kaempferol 3-*O*-β-D-glucopyranoside (9) (Lee et al. 2011). Camellia ethanol flower extract contained quercetin, quercetin-3-*O*-glucoside, quercitrin and kaempferol, all antioxidant compounds (Piao et al. 2011).

From the 1-butanol-soluble fraction, of the flower buds, a new 28-nor-oleanane-type and three new oleanane-type triterpene saponins, sanchakasaponins A–D, were isolated together with four known triterpene saponins: primulagenin A 3-*O*-β-D-glucopyranosyl(1 → 2)-[α-L-rhamnopyranosyl(1 → 2)-β-D-galactopyranosyl (1 → 3)]-β-D-glucopyranosiduronic acid, sasanquasaponin II, sasanquasaponin IV and maetenoside B (Fujimoto et al. 2012). Four acylated oleanane-type triterpene oligoglycosides, sanchakasaponins E–H, were isolated from the flower buds, together with four known triterpene oligoglycosides: yuchasaponin A, sasanquasaponin I, sasanquasaponin II and ternstroemiaside C (Nakamura et al. 2012).

Fruit Phytochemicals

From *C. japonica* fruit, camelliagenins A, B and C were isolated and their structures elucidated as 3β, 16α, 22α, 28-tetrahydroxy-(I), 23-oxo-3β, 16α, 22α, 28-tetrahydroxy-(II) and 3β, 16α, 22α, 23,28-pentahydroxy-olean-12-one (III), respectively (Itokawa et al. 1967, 1969). A dimeric hydrolyzable tannin, named camelliatannin H; camelliins A and B; camelliatannins A and F; pedunculagin; (−)-epicatechin; 2,3-(*S*)-hexahydroxydiphenoyl-D-glucose; 1,6-di-*O*-galloyl-B-D-glucose; gallic acid 3-*O*-B-D-(6′-*O*-galloyl)-glucopyranoside; and casuariin (Li et al. 1994); camelliatannins D, B and C, cornusiin B, (−)-epicatechin, tri-*O*-methyl gallate, dimethyl hexamethoxydiphenate and trimethyl octa-*O*-methyl-valonate (Hatano et al. 1995a); and camelliatannin H were isolated from the fruit (Park et al. 2002).

Seed Phytochemicals

Acylated polyhydroxyolean-12-ene triterpene oligoglycosides, camelliasaponins A_1, A_2, B_1, B_2, C_1 and C_2, were isolated from *Camellia japonica* seeds (Yoshikawa et al. 1994, 1996). Acylated polyhydroxyolean-12-ene triterpene oligoglycosides, camelliasaponins A_1, A_2, B_1, B_2, C_1 and C_2, were isolated from *Camellia japonica* seeds (Yoshikawa et al. 1996).

Twenty-seven triterpene alcohols were isolated from the nonsaponifiable lipids of camellia and sasanqua oils from *Camellia japonica* and *C. sasanqua* seeds: tirucalla-5,7,24-trien-3 β-ol (1), lemmaphylla-7,21-dien-3 β-ol (2), isoeuphol (3), isotirucallol (4), (24R)-24,25-epoxybutyrospermol (5), (24S)-24,25-epoxybutyrospermol (6), isoaglaiol (7), aglaiol (8), butyrospermol (9), euphol (10), tirucalla-7,24-

dienol (11), tirucallol (12), dammaradienol (13), 24-methylenedammarenol (14), cycloartenol (15), 24-methylene cycloartenol (16), 24-methyllanosta-8-24(24[1])-dienol (17), 24-methyllanosta-9(11), 24(24[1])-dienol (18), bacchara-12,21-dienol (19), β-amyrin (20), δ-amyrin (21), germanicol (22), α-amyrin (23), taraxerol (24), lupeol (25), 17-epilupeol (26) and ψ-taraster ol (27) (Akihisa et al. 1997). Seven triterpenoids were isolated from seed oil of *C. japonica:* (20S)-3β-hydroxy-25,26,27-trisnordammaran-24,20-olide (1; 3-epicabraleahydroxylactone) (1), 3-epicabraleadiol (2), ocotillol II (3), ocotillol I (4), dammarenediol II (5), (20R)-taraxastane-3β,20-diol (6) and lupane-3β,20-diol (7) (Akihisa et al. 2004). The fatty acid profile of cold-pressed *C. japonica* seed oil comprised 75.75 % oleic acid, 6.0 % linoleic acid, 0.17 % linolenic acid and 18.67 % saturated fatty acids (Salinero et al. 2012). Levels of C_{18} unsaturated fatty acids found in camellia oil were similar to those reported for olive oils. *C. japonica* seed oil was found to be mainly composed of neutral lipids (88.2 %), and the oleic acid (86.3 %) was found to be a major fatty acid of neutral lipids (Noh and Yoon 2012). In the glycolipids and phospholipids, oleic acid was also found to be a major fatty acid at 62.5 % and 54.2 %, respectively. Oleic acid was distributed abundantly in all sn-1, -2 and -3 positions. It was found that the oleic acid was present more at sn-2 (93.6 %) and sn-3 positions (94.7 %) than at sn-1 position (66.0 %).

Leaf Phytochemicals

Camellidin II with the structure 3β,18 β-dihydroxy-28-norolean-12-en-16-one 3-*O* β-D-glucopyranosyl-(1 → 2)-β-D-galactopyranosyl-(1 → 3)-[β-D-galactopyranosyl-(1 → 2)]-β-D-glucuronopyranoside was isolated together with camellidin III, identified as its methyl ester, and three known compounds, quinic acid, 3β,20-dihydroxylupane and 3,3′,4-tri-*O*-methylellagic acid from the leaves (Numata et al. 1987). Complex tannins camelliatannins F and G (Li et al. 1994); camelliatannins C and E (Hatano et al. 1995b); camelliatannins D, B and C, cornusiin B, (−)-epicatechin, tri-*O*-methyl gallate, dimethyl hexamethoxydiphenate and trimethyl octa-*O*-methyl-valonate (Hatano et al. 1995a); a novel flavonol glycoside named camellianoside; and three known flavonol glycosides rutin, hyperoside and isoquercitrin were isolated from the leaves of *Camellia japonica*. The structure of camellianoside was established as quercetin-3-*O*-β-D-xylopyranosyl-(1 → 3)-*O*-α-L-rhamnopyranosyl-(1 → 6)-*O*-β-D-glucopyranoside (Onodera et al. 2006). A novel benzoyl glucoside 4-hydroxy-2-methoxyphenol 1-*O*-β-D-(6″-*O*-*p*-hydroxylbenzoyl)-glucopyranoside (camelliadiphenoside), and 13 known phenolic compounds namely (*E*)-coniferyl alcohol; (−)-epicatechin; 4-hydroxyphenol 1-*O*-β-D-(6-*O*-*p*-hydroxybenzoyl) glucopyranoside; naringenin 7-*O*-β-D-glucopyranoside; quercetin 3-*O*-β-L-rhamnopyranosyl(1 → 6)-β-D-glucopyranoside; kaempferol3-*O*-β-L-rhamnopyranosyl(1 → 6)-β-D-glucopyranoside; (+)-catechin (8), 1,6-di-*O*-*p*-hydroxybenzoyl-β-D-glucopyranoside; phloretin 2″-*O*-β-D-glucopyranoside; quercetin 3-*O*-β-D-glucopyranoside; quercetin 3-*O*-β-D-galactopyranoside;kaempferol3-*O*-β-D-galactopyranoside; and kaempferol 3-*O*-β-D-glucopyranoside were isolated from the leaves (Cho et al. 2008).

An ellagic acid glucoside named okicamelliaside was isolated from the leaves, and its structure elucidated as 3,4-dioxoloellagic acid 4′-*O*-β-D-glucopyranoside (Onodera et al. 2010). Quercetin 3-*O*-β-D-galactopyranoside, quercetin 3-*O*-β-D-glucopyranoside, kaempferol 3-*O*-β-D-galactopyranoside and kaempferol 3-*O*-β-D-glucopyranoside were found in the leaves (Lee et al. 2011). Three aglycone flavonoids (quercetin, kaempferol and apigenin), glycosylated flavonoids (rutin and quercetin) and six fatty acid esters (methyl tridecanoate, methyl tetradecanoate, methyl pentadecanoate, methyl hexadecanoate, methyl heptadecanoate and methyl octadecanoate) were isolated from the leaves (Azuma et al. 2011).

Stem Phytochemicals

Four new 28-nor-oleanane-type triterpene oligoglycosides, camellenodiol 3-*O*-β-D-

galactopyranosyl(1 → 2)[β-D-xylopyranosyl (1 → 2)-β-D-galactopyranosyl(1 → 3)]-β-D-glucuronopyranoside, camellenodiol 3-*O*-4″-*O*-acetyl-β-D-galactopyranosyl(1 → 2)[β-D-xylopyranosyl(1 → 2)-β-D-galactopyranosyl (1 → 3)]-β-D-glucuronopyranoside, camellenodiol 3-*O*-(β-D-galactopyranosyl(1 → 2)[β-D-xylopyranosyl(1 → 2)-β-D-galactopyranosyl (1 → 3)]-6′-methoxy-β-D-glucuronopyranoside and maragenin II 3-*O*-β-D-galactopyranosyl(1 → 2)[β-D-xylopyranosyl(1 → 2)-β-D-galactopyranosyl (1 → 3)]-6′-methoxy-β-D-glucuronopyranoside, along with two known compounds, were isolated from *Camellia japonica* stem bark (Nguyen et al. 2010b). From the ethyl acetate fraction of *Camellia japonica* stem bark, three new triterpenoids, 3β-*O*-acetyl-16β-hydroxy-12-oxoolean, 3β-*O*-acetyl-16beta-hydroxy-11-oxoolean-12-ene and 3β-*O*-acetyl-16β-hydroxyolean-12-ene along with known compounds, 3α-hydroxy-1-oxofriedelan, friedelin, 3β-friedelanol, canophyllol, 3-oxofriedelan-1(2)-ene, β-amyrin, camellenodiol and camelledionol were isolated (Nguyen et al. 2010a).

Antioxidant Activity

The DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging activities of compounds isolated from the hot water extracts of *Camellia japonica* flower buds determined as 50 % scavenging concentration were found to decrease in the order of (−)-epicatechin (20 μM) > α-tocopherol (29 μM) > 7S,7′S,8R,8′R-icariol A_2 (67 μM) > dehydroxysynapyl alcohol (72 μM) > *p*-hydroxybenzaldehyde = vanillin (> 250 μM) (Cho et al. 2009). The DPPH radical scavenging activities of compound isolated from the hot water extracts of *Camellia japonica* flower buds determined as 50 % scavenging concentration decreased in the order of (−)-epicatechin (20 μM) > α-tocopherol (29 μM) > 7S,7′S,8R,8′R-icariol A_2 (67 μM) > dehydroxysynapyl alcohol (72 μM) > *p*-hydroxybenzaldehyde = vanillin (>250 μM) (Cho et al. 2009). DPPH radical scavenging activity (SC50) of the compounds isolated from *C. japonica* flowers in decreasing order was as follows: 2,3-digalloyl-*O*-α-D-glucopyranoside = 2,3-digalloyl-*O*-β-D-glucopyranoside (4.7 μM) > gallic acid (9.8 μM) > quercetin 3-*O*-β-D-galactopyranoside = quercetin 3-*O*-α-D-glucopyranoside (8.2 μM) > α-tocopherol (24.7 μM) > ascorbic acid (25.1 μM) > 3,4-dihydroxybenzoic acid (35.6 μM) > 4-hydroxybenzoic acid = kaempferol 3-*O*-β-D-galactopyranoside = kaempferol 3-*O*-β-D-glucopyranoside (>250 μM) (Lee et al. 2011). The DPPH scavenging activity of red pigment extract from *C. japonica* was comparable to that of standard butylated hydroxyanisole (BHA) with IC_{50} values of 4.55 and 4.17 μg/mL, respectively (Zhang et al. 2011). The pigments showed higher hydroxyl radical scavenging activities than that of mannitol at the same concentration. Following activity-oriented separation, (−)-epicatechin was isolated as an active principle, which exhibited excellent DPPH free radical scavenging activities with IC_{50} 5.08 μg/mL

C. japonica flower ethanol extract exhibited DPPH radical and intracellular reactive oxygen species (ROS) scavenging activity in human HaCaT keratinocytes (Piao et al. 2011). Additionally, Camellia extract scavenged superoxide anion generated by xanthine/xanthine oxidase and hydroxyl radical generated by Fenton's reaction ($FeSO_4 + H_2O_2$) in a cell-free system. Further, Camellia extract increased the protein expressions and activity of cellular antioxidant enzymes, such as superoxide dismutase, catalase and glutathione peroxidase.

The antioxidant activities of *C. japonica* leaf glycosides camellianoside (EC_{50} 25.8 μM), glycosides rutin (EC_{50} 23 μM), hyperoside (EC_{50} 33.1 μM) and isoquercitrin (EC_{50} 27.9 μM) evaluated by the DPPH radical scavenging reaction was higher than those of L-cysteine (EC_{50} 131.9 μM) and L-ascorbic acid (EC_{50} 50.7 μM) used as the reference antioxidants (Onodera et al. 2006). Aqueous leaf extract of *C. japonica* exhibited DPPH radical scavenging and ferric reducing/antioxidant power (FRAP) activities in a dose-dependent manner (Jeong et al. 2010). In neuronal cell viability assay using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide (MTT), the aqueous extract

showed protective effect against H_2O_2-induced neurotoxicity, and lactate dehydrogenase release into medium was also inhibited by the leaf extract. The cell viability of camellia leaf extract was higher than vitamin C (200 μM) at a concentration of 250–1,000 μg/mL. Phenolics of camellia leaf extract amounted to 21.75 mg/g, and major phenolic compounds were quercetin (120.20 mg/100 g) and kaempferol (88.13 mg/100 g). The data suggested that the camellia leaf extract including the above phenolics may be useful as natural antioxidant substances and may reduce the risk of neurodegenerative disease such as Alzheimer's disease.

The methanol extract of young leaf, mature leaf, flower bud, flower, bark and seed of camellia were found to have antioxidant activity (Lee et al. 2005). Total phenolics were the highest in young leaf (74.62 mg), followed by flower buds (65.02 mg) and flowers (62.42 mg) but lower than 20.95 mg per 100 g of dry weight in other parts of *Camellia japonica.*

Antiviral Activity

Of the extracts tested, strong inhibitory effects on human immunodeficiency virus HIV type 1 protease were observed in the acetone extracts of the pericarp and leaves of *Camellia japonica* (Park et al. 2002). Camelliatannin H from the pericarp of *C. japonica* showed a potent inhibitory activity on HIV-1 PR with IC_{50} of 0.9 μM.

Three compounds from the seed oil, dammarenediol II (5), (20R)-taraxastane-3β,20-diol (6) and lupane-3β,20-diol, showed potent inhibitory effects against Epstein–Barr virus early antigen induction by TPA (12-*O*-tetradecanoylphorbol-13-acetate) in Raji cells with IC_{50} values of 277–420 mol ratio/32 pmol TPA (Akihisa et al. 2004).

Anticancer Activity

Camelliin B, a dimeric hydrolyzable tannin isolated from *C. japonica* flower buds, exhibited marked host-mediated antitumour activity (Yoshida et al. 1989). *C. japonica* leaf extract exhibited antiproliferative activity against human leukemic cell line in vitro (Kim et al. 2003). Intraperitoneal injection of camelliin B before intraperitoneal inoculation of sarcoma 180 cells prolonged the life span of sarcoma 180 tumour-bearing mice.

Miura et al. (2007) found that camellia oil, olive oil and cottonseed oil, and their distillate fractions, inhibited connexin 26 (Cx26) mediated gap junction intercellular communications in mposue melanoma BL6 cells. They also showed that daily intraperitoneal injection of camellia oil and its distillate fractions more potently inhibited spontaneous lung metastasis of BL6 cells than oleamide. These oils are being used as foods and were deemed quite safe and could be used as supplements to protect patients from lung metastasis of melanoma.

The triterpenoid 3β-*O*-acetyl-16β-hydroxyolean-12-ene from the stem bark showed cytotoxicity against LLC and HL-60 cancer cell lines with IC_{50} values of 25.2 and 21.7 μM, respectively (Nguyen et al. 2010a). Tea flowers from six different species of *Camellia japonica*, *Camellia tenuifolia*, *Camellia oleifera*, 2 savoury *Camellias* and *Camellia sinensis* exhibited activity against human breast cancer MCF-7 cells with the extract from *C. sinensis* being the most active (Way et al. 2009). *C. sinensis* contained a variety of catechins, while only (+)-catechin and (−)-epicatechin were detected in other tea flowers.

Antimicrobial Activity

Camellidin II, isolated from the leaves, was reported as an antifungal saponin (Numata et al. 1987). Ethanol extract of defatted *Camellia japonica* seeds showed antimicrobial activities not only against several microorganisms tested, but also against lactic acid bacteria (Kang et al. 1998). Minimum inhibitory concentrations (MIC) for yeasts were as low as 1 mg/mL. The water extract exhibited antimicrobial activities for the yeasts tested. The strongest activity for the tested yeasts was found in the butanol fraction of the ethanol extract and for bacteria the

chloroform fraction. *Hansenula anomala* treated with ethanol extract exhibited morphological changes, including the irregularly contracted cell surface and expanded ellipsoidal shape. In another study, the acidic fraction of the methanol petal extract of *C. japonica* was found to be inhibitory in vitro to food-borne pathogens: *Salmonella typhimurium, Escherichia coli, Listeria monocytogenes* and *Staphylococcus aureus* (Kim et al. 2001). An aqueous extract from the petals had an inhibitory effect on growth of all pathogens at 37 °C in microbiological media by increasing the lag phase. Aqueous extract at a concentration of 100 mg/mL was bacteriostatic against all the food-borne pathogens in the milk stored at 25 °C for up to 4 days. Methanol extract, water fraction and butanol fraction of *C. japonica* showed antimicrobial effects in vitro against food-borne pathogens *Escherichia coli, Salmonella typhimurium, Staphylococcus aureus* and *Listeria monocytogenes* (Hahn 2005). The methanol extract exhibited strong antimicrobial effect against *S. aureus* and *L. monocytogenes* and the water, butanol and ethyl acetate fractions against *S. aureus*. No effects were observed in n-hexane and chloroform fractions against all tested microorganisms.

Melanogenesis Inhibition Activity

Triterpene saponins sanchakasaponin B and sasanquasaponin II isolated from the flower buds showed significant inhibitory effects on melanogenesis in theophylline-stimulated B16 melanoma 4A5 cells without cytotoxic effects (Fujimoto et al. 2012). The effects were stronger than the reference compound arbutin. Triterpene saponins sasanquasaponin I and sasanquasaponin II isolated from the flower buds substantially inhibited melanogenesis in theophylline-stimulated B16 melanoma 4A5 cells without cytotoxic effects, while sanchakasaponins E and F and yuchasaponin A also inhibited melanogenesis but had cytotoxic effect at 3 μm (Nakamura et al. 2012) (Nakamura et al. 2012).

Anti-allergic Activity

The leaf extract of *Camellia japonica* exhibited the most potent effect on degranulation in antigen-stimulated rodent and human mast cells of 100 Korean plants screened (Lee et al. 2008). The leaf extract reversibly inhibited degranulation in a dose-dependent manner, with IC_{50} values of ~50 μg/mL for the mast cells, and it also suppressed the expression and secretion of TNF-α (tumour necrosis factor-alpha) and IL-4 (interleukin-4) in rat basophilic leukaemia-2H3 mast cells. The leaf extract also significantly inhibited mast cell-mediated PCA (cutaneous anaphylaxis) in an animal model. The leaf extract inhibited activating phosphorylation of tyrosine Y371 on Syk kinase. In the in vitro kinase assay, the leaf extract directly inhibited Lyn kinase, the major Src-family kinase in mast cells, and suppressed Akt and MAP kinases critical for the production of various proinflammatory cytokines in mast cells. Quercetin-3-β-D-glucoside and eugenol were identified as the major active components. The results strongly suggested that the anti-allergic activity of the leaf extract was mediated through inhibiting degranulation and allergic cytokine secretion by inhibition of Src-family kinase in mast cells and may be useful for the treatment of mast cell-related immediate and delayed allergic diseases.

Oral administration of leaf extracts from *C. japonica* at 1,000 mg/kg for 10 days significantly reduced the vascular permeability of conjunctivas in male S.D. rats which were stimulated with anti-ovalbumin (OVA) serum and challenged with OVA/Evans blue mixture (Kuba et al. 2008). In the second model, male BALB/c mice were stimulated with a Japanese cedar pollen extract and challenged by nasal instillation of the antigen. The sneezing frequency during the 10 min immediately after the challenge tended to decrease by intraperitoneal administration of 0.2 mg/kg of okicamelliaside, a highly potent anti-degranulation ellagic acid glucoside from *C. japonica* leaves, for 24 days. These results suggest that *C. japonica* leaf extracts and okicamelliasid prepared from them could be useful to alleviate the symptoms of an immediate-type

allergy. In further studies, the IC_{50} values for degranulation of rat basophilic leukaemia cells (RBL-2H3) were 14 nM for okicamelliaside and 3 μM for its aglycone, indicating that the two compounds were approximately 2–3 orders of magnitude more potent than the anti-allergic drugs ketotifen fumarate, DSCG and tranilast (0.17, 3 and >0.3 mM, respectively) (Kuba-Miyara et al. 2012). Antigen-induced calcium ion (Ca^{2+}) elevation in the principle signalling pathway, phosphorylation of Syk (Tyr525/526) and PLCγ-1 (Tyr783 and Ser1248) were significantly inhibited by okicamelliaside and aglycone at all concentrations tested. In DNA microarray-screening test, okicamelliaside inhibited expression of proinflammatory cytokines [interleukin (IL)-4 and IL-13], cytokine-producing signalling factors and prostaglandin-endoperoxidase 2, indicating that okicamelliaside broadly inhibited allergic inflammation. During passive cutaneous anaphylaxis in mice, okicamelliaside significantly inhibited vascular hyperpermeability by two administration routes: a single intraperitoneal injection at 10 mg/kg and per os at 5 mg/kg for 7 days. These results suggested the potential for okicamelliaside to alleviate symptoms of immediate-type allergy. Okicamelliaside, isolated from the leaves, was 12,000 times more potent than the antihistaminic drug, ketotifen fumarate, in inhibiting the degranulation of RBL-2H3 cells (Onodera et al. 2010).

Anti-inflammatory Activity

The triterpene alcohols isolated from the seed oil (isoeuphol, isotirucallol, a mixture of (24R)-24,25-epoxybutyrospermoland(24S)-24,25-epoxybutyrospermol and a mixture of isoaglaiol and aglaiol) and eight known triterpene alcohols (butyrospermol; euphol; tirucallol; 24-methylenedammarenol; 24-methyllanosta-9(11), 24(24^1)-dienol; bacchara-12,21-dienol; δ-amyrin and germanicol) exhibited anti-inflammatory activity when evaluated in ear inflammation in mice induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA). The 50 % inhibitory dose of these triterpenes for TPA-induced inflammation (1 μg/ear) was 0.2–0.9 mg/ear (Akihisa et al. 1997). *Camellia japonica* oil inhibited LPS-induced production of NO, PGE(2) and TNF-α in RAW264.7 cells (Kim et al. 2012). In addition, expression of COX-2 and iNOS genes and LPS-induced activation of AP-1 and NF-κB promoters were significantly reduced. These results indicated that *C. japonica* oil exerted anti-inflammatory effects by downregulating the expression of iNOS and COX-2 genes through inhibition of NF-κB and AP-1 signalling.

28-nor-oleanane-type triterpene saponins from *Camellia japonica* stem bark showed inhibitory effects on NO production in RAW264.7 macrophages (Nguyen et al. 2010b).

Hypotriglyceridemic Activity

Fermented mixed tea made with third-crop green tea leaves and camellia leaves was found to contain theasinensins and theaflavins (Tamaru et al. 2013). Rats fed with mixed tea extract (1 %) exerted significantly lower body weight and adipose tissue weight compared to animals fed with third-crop green tea or camellia tea extract alone for 4 weeks. Serum and hepatic triglyceride were significantly and dose-dependently decreased by the mixed tea. This decrease was associated with lowered lipogenic enzyme activities in the liver. Additionally, an oral administration of 4 or 8 % of the mixed tea extract followed by fat emulsion suppressed the increment of serum triglyceride level. The results suggested that the mixed tea had hypotriglyceridemic action, partially via delaying triglyceride absorption in the small intestine and repressing hepatic lipogenic enzymes.

Platelet Aggregation and Gastroprotective Activities

The principal oligoglycosides, camelliosides A and B, from the flower buds (10–100 μg/mL) showed platelet aggregation activity in addition

to the gastroprotective effects on ethanol- or indomethacin-induced gastric mucosal lesions in rats (Yoshikawa et al. 2007). Their gastroprotective effects were equivalent or stronger than reference compounds omeprazole in the ethanol-induced gastric lesion model and cimetidine in the indomethacin-induced gastric lesion model.

Antiosteoporotic Activity

Camelliatannin D isolated from the leaf and fruit was found to be an inhibitor of bone resorption (Hatano et al. 1995a). It inhibited Ca release from mouse calvaria.

It inhibited Ca concentration induced by PTHrp with IC_{50} value of 2.4×10^7 M, while phenols of low molecular weight such as liquitrin showed weak inhibition (IC_{50} value 2.5×10^5 M). Ethanol extract of *Camellia japonica* seeds (0.51 g/kg) was found to markedly enhance weight/length (G/L), bone density of femur, serum calcium and alkaline phosphatase level, with the decreasing of anti-tartaric acid tartrate-resistant acid phosphatase level in osteoporotic rats induced by retinoic acid (Tang et al. 2008). A significant increase of morphological sclerotomal cells and a significant decrease of osteoclasts were observed. The anti-osteoporosis ranking of the various Camellia extracts was ethanol seed extract of *Camellia japonica* > ethanol leaf extract of *C. oleifera* > aqueous leaf extract of *C. oleifera* > aqueous seed extracts of *C. oleifera* > positive control drug > aqueous seed extract of *C. japonica*.

Ethanol Absorption Inhibitory Activity

Camelliasaponins B_1, B_2, C_1 and C2, isolated from the seeds, were found to exhibit inhibitory activity on ethanol absorption after a single oral administration at the dose of 100 mg/kg (Yoshikawa et al. 1994, 1996). Desacyl-camelliasaponins B and C lacked such activity.

Anti-aging Activity

Camellia oil had been proven to have its place in all emulsions used in the cosmetology and dermopharmacy fields (Sabetay 1972). Uses include day or night creams, anti-wrinkle compounds, lipstick, hair creams, make-up, anti-sun preparations, rouge and make-up remover products. Studies showed that *Camellia japonica* leaf extract was one of four plant extracts that completely inhibited the expression of collagenase MMP-1 (matrix metalloproteinase-1) in human fibroblast cells and may have potential for use as natural active ingredient for anti-aging cosmetics (Kim et al. 2007). Further studies on the anti-aging effect of *C. japonica* oil were reported by Jung et al. (2007). They found that camellia oil stimulated human COL1A2 promoter in a concentration-dependent manner and human type I procollagen synthesis while inhibiting matrix metalloproteinase (MMP)-1 activity. In a human skin primary irritation test on 30 volunteers, camellia oil was found to reduce trans-epidermal water loss and did not induce any adverse reactions. They concluded that *C. japonica* oil may be considered as possible wrinkle-reducing candidate for topical application.

Traditional Medicinal Uses

The flowers are astringent, anti-haemorrhagic, haemostatic, salve and tonic in folkloric traditional medicine (Stuart 1979; Duke and Ayensu 1985). When mixed with sesame oil, they are used in the treatment of burns and scalds. The flower has been prescribed in Chinese traditional preparations for the treatment of haematemesis (vomiting of blood) and oketsu syndrome (blood stagnation), and the seed is used as stomachic and anti-inflammatory in Japanese folk medicine (Yoshikawa et al. 1996; Lee et al. 2011). *Camellia*

japonica oil has been used traditionally in East Asia to nourish and soothe the skin as well as help restore the elasticity of skin and on all types of bleeding instances (Kim et al. 2012).

Other Uses

Camellia is cultivated as an oil crop and ornamental. Seeds contain an oleic-rich, nondrying oil, which is used as watchmaker oil, hair oil and vegetable oil and in cosmetics and also used medicinally. In the past it was used as an antirust agent for swords.

Extraction of the fruit hulls also yields useful compounds such as saponin, tannin and pentosan. Saponin is used as an emulsifying agent in pesticides, for foam-forming fire extinguishers and in detergents (Shanan and Ying 1982). Camellia tea oil residues have been used for effective control of the following pests: rice blast, sheath and culm blight of rice, wheat rust, rice hopper, cutworms, cotton aphids, certain scale insects, long-horned beetles and leeches (Shanan and Ying 1982). A green dye is obtained from the pink or red petals.

Camellidin II was isolated from the leaves of *Camellia japonica* as an antifeedant for the larvae of the yellow butterfly, *Eurema hecabe mandarina* (Numata et al. 1987).

Camellia japonica and *Vernicia fordii* seed oils could be employed as a feedstock for production of biodiesel by transesterification with methanol on alkali catalysts (Chung 2010). The fatty acid methyl ester (FAME) contents in the biodiesel produced from the seed oils were above 96 % on KOH catalyst in the reaction and acceptable for the limit of European biodiesel qualities for BD100. Other qualities such as cetane number, acid value, density and kinematic viscosity of the produced biodiesels also matched the biodiesel qualities.

Comments

Camellias can be propagated from seeds, softwood cuttings, air-layering and grafting.

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Tropaeolum majus

Scientific Name

***Tropaeolum majus* L.**

Synonyms

Cardamindum majus (L.) Moench, *Tropaeolum elatum* Salisb., *Tropaeolum hybridum* L., *Tropaeolum quinquelobium* Bergius, *Tropaeolum repandifolium* Stokes, *Tropaeolum schillingii* Vilmorin

Family

Tropaeolaceae

Common/English Names

Climbing Nasturtium, Common Nasturtium, Empress of India, Garden Nasturtium, Indian Cress, Monks Cress, Nasturtium

Vernacular Names

Arabic: Abû Khangar, Abu Khanjar, Nabatu Al-Kabbusin, Tartûr El Bâshâ
Aymara: Alpinku, Tajsawi
Brazil: Chaguinha, Capuchinha, Capuchinha-De-Flores-Grandes (Portuguese)
Breton: Kabusinenn
Bulgarian: Latinka
Catalan: Bequera, Caputxina, Llaguera, Morrissà, Morritort D'indies
Chinese: Han He Hua, Han Jin Lian, Han Jin Lian, Han Lian Hua, He Ye Lian, Jin Si Lian
Croatian: Dragoljub
Czech: Lichooeoišnice Větší, Lichorerisnice Vetsi, Lichořeřišnice Větší
Danish: Baerkarse, Blomsterkarse, Kapuciner Karse, Kapucinerkarse, Landloeber, Nasturtie
Dutch: Capucienerkers, Oostindische Kers
Esperanto: Granda Tropeolo, Tropeolo
Estonian: Suur Mungalill
Finnish: Intiankrassi, Kapusinikrassi, Koeynnoeskrassi, Koristekrassi, Köynnöskrassi, Kukkakrassi, Pensaskrassi
French: Capucine, Capucine Grande, Capucine du Pérou, Capucine Grimpante, Cresson D'Inde, Cresson D'inde, Cresson Du Mexique, Cresson Du Pérou, Grande Capucine
German: Gelbes Vögerl, Große Kapuzinerkresse, Grosse Kapuzinerkresse, Indische Kresse, Kapuzinerkresse, Kapuzinerli, Salatblume, Spanische Kresse
Hawaiian: Pohe Haole
Hebrew: Kova Ha-Nazir
Hungarian: Kapucinusvirág, Kerti Súka, Kerti Sarkantyúka, Nagy Sarkantyúka, Sarkantyúka, Sarkantyúvirág
Icelandic: Skjaldflétta, Skjaldflétta
India: Bilrai (Bengali)
Italian: Cappuccina, Cappucina, Cappucina Maggiore, Crescione Indiano, Fior, Nasturzio, Nasturzio Commune, Nasturzio D'India,

T.K. Lim, *Edible Medicinal and Non Medicinal Plants: Volume 8, Flowers*,
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Nasturzio Del Perù, Nasturzio Del Perù, Nasturzio Indiano, Tropeolo
Japanese: Nasutachumu
Korean: Na-Seu-Teo-Cyum, Na-Seu-Teo-Ti-Um, Nasuteochyum, Nasuteotium
Latvian: Krese
Lithuaian: Mažoji Nasturtė
Maltese: Kapućinella
Mexico: Mastuerzo
Norwegian: Blomkarse, Blomsterkarse
Persian: Gul Ladene, Ladan, Ladn
Peru: Mastuerzo
Polish: Nasturcja, Nasturcja Wieksza
Portuguese: Agrião-Do-México, Agrião-Grande-Do-Peru, Agrião-Maior-Da-India, Capuchinha-Grande, Capuchinha(s), Capuchinho, Chaga Seca, Chagas, Chagas-De-Cristo, Chagas-De-São-Francisco, Chagueira, Cingo Chagas, Flor-De-Chagas, Mastruço-Do-Perú, Nastúrcio, Nastúrio
Quechuan: Tajsa, Tijsaw
Russian: Indejskij Kress, Kapucin-Kress, Kaputsin-Kress, Nasturciâ, Nasturtsiya, Nasturtsiya Bol'Shaya, Nasturtsiya Kul'Turnaya
Sri Lanka: Kakutupala (Sinhalese)
Slovašcinan: Kapucinka, Kapucinček; Velika Kapucinka
Slovencina: Kapucínka Väčšia
Spanish: Cachipillo, Capuchina, Espuela De Galán, Flor De La Sangre, Llagas De Cristo, Marañuela, Mastuerzo, Mastuerzo De Indias, Nasturcia, Nastuerzo, Pajarilla, Pelón, Taco De Reina
Swedish: Buskkrasse, Indiankrasse, Slingerkrasse, Trädgårdskrasse
Turkish: Frenk Teresi, Hind Teresi, Latin Çiç, Lâtin Çiçeği
Vietnamese: Cây Sen Cạn, Địa Liên

Origin/Distribution

The species originated in South America in the Andes from Peru, Bolivia north to Colombia. It was introduced into Europe in the sixteenth century and elsewhere subsequently.

Agroecology

Nasturtium is a temperate or cool climate species. Nasturtiums are suitable for all but the coldest climate zones. Plants need full sun and good drainage and will grow on poor soil and dry conditions.

Edible Plant Parts and Uses

Nasturtium flowers, bud and leaves have a peppery flavour similar to watercress and can be eaten raw (Morton 1976; Small 1997; Friedman et al. 2005, 2007). Nasturtium flower is one of the most popular and best-known edible flowers with attractive blossoms that have a sweet, peppery spicy flavour similar to watercress (Hedrick 1972; Tanaka 1976; Facciola 1990; Larkcom 1980; Garland 1993; Burnie and Fenton-Smith 1996; Lauderdale and Evans 1999; Roberts 2000; Rop et al. 2012; Newman and O'Connor 2009; Deane 2007–2012). Buds and flowers can be added to salads, sandwich spread, vegetable dishes and butter and can be used to flavour vinegar or stuffed or crystallized. Flowers combine well with cream cheese or butter in canapés or in a cheese and tomato sandwich. The buds can be used as caper substitute. The blossoms make a nutritious addition to salads and can be an attractive, decorative garnish to steak and casseroles. They have been reported to have ten times the vitamin C of lettuce (Duke and Ayensu 1985). According to Wilson (2013), nasturtiums are one of the most popular and flexible edible blooms; they are bright and colourful and bursting with a sweet, floral flavour. He recommends to use them as a garnish or to stuff whole flowers. No less than 76 % of consumers awarded nasturtium, borage and viola flowers an acceptable rating based on visual appeal and desire (Kelley et al. 2001). The leaves are also eaten cooked or used as garnish in salads. Leaves and young leafy shoots as well as pickled fruits and flower buds can be used for seasoning. The seeds are also edible and can be used as a caper substitute or can be ground in a pepper mill, and use as you would black pepper. Some recipes with

nasturtium flowers reported include nasturtium salad vinegar, nasturtium cheese dip and grilled aubergine salad with egg and nasturtium flowers (Roberts 2000). The flowers of *T. majus* are excellent functional food sources of lutein and also zeaxanthin, and the leaves are good sources of both lutein and the provitamin A β-carotene (Niizu and Rodriguez-Amaya 2005). Increasing evidence suggests the role of lutein and zeaxanthin in reducing the risk of cataract and macular degeneration.

Botany

A sprawling or climbing, succulent annual or short-lived perennial herb growing up to 30 cm tall with trailing stem growing to 1 m long. The bluish-green orbicular, peltate leaves, 5–15 cm across, are carried on long fleshy petiole 10–30 cm long attached to the centre of the leaf lower surface (Plates 1, 2, 3 and 4). Leaf margin entire, sinuate and slightly undulating, with nine main radiating nerves, lower surface pilose. The showy, orange, red, yellow or creamy-white flowers are trumpet shaped, 2.5–6 cm long with a nectar-filled spur at the base and mildly fragrant borne

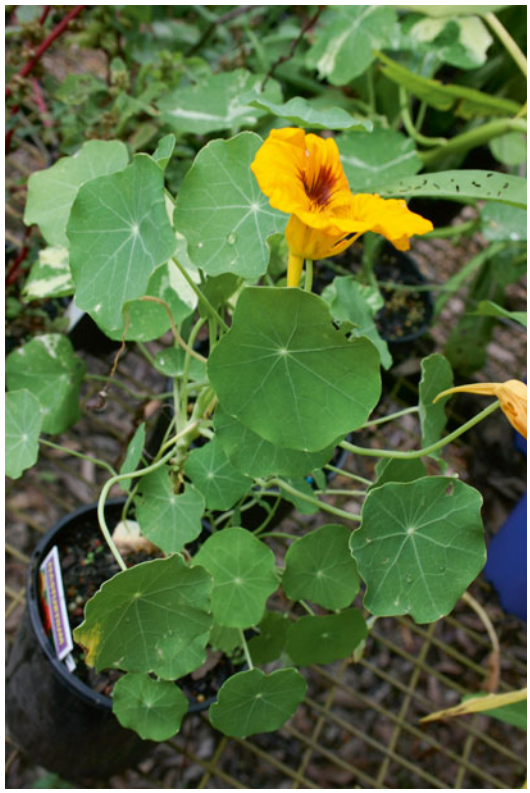

Plate 1 Yellow-flowered nasturtium

Plate 2 Orange-flowered nasturtium

Plate 3 Red-flowered nasturtium

Plate 4 Close view of nasturtium flower and leaves

on 6–14 cm long pedicel. Torus cup-shaped (Plates 1, 2, 3 and 4). Flower with 5 oblong-lanceolate sepals, straight or curved spur 2.5–3.5 cm, 5 petals with rounded apex but sometimes shortly pointed or even toothed, 8 distinct and unequal stamens, 3-loculed ovary and a linear, 3-lobed stigma. Fruit oblate, 2 cm across, separating into three 1-seeded mericarps at maturity. Seed 1–1.5 cm long.

Nutritive/Medicinal Properties

Rop et al. (2012) reported that edible flowers of *Tropaeolum majus* had a dry matter content (%w/w) of 11.27 % and crude protein of 4.74 g/kg and the following elements (mg/kg fresh mass (FM)): P 481.31 mg, K 2,453.39 mg, Ca 337.23 mg, Mg 149.38 mg, Na 88.52 mg, Fe 6.47 mg, Mn 5.85 mg, Cu 1.17 mg, Zn 9.07 mg and Mo 0.29 mg. The flowers had total antioxidant capacity of 5.12 g ascorbic acid equivalents/kg FM, total phenolic content of 3.31 g gallic acid/kg FM and total flavonoid content of 1.35 g rutin/kg FM. *Tropaeolum majus* flower was found to contain 7.9 % DM, 34.4 total mg/100 g FW flavonoids made up of 32.8 mg quercetin and 1.6 mg kaempferol (Yang et al. 2008).

Eight carotenoids were identified in *T. majus* flowers: violaxanthin (5,6,5′, 6′-diepoxy-5,6,5′, 6′tetrahydro-β,β-carotene-3,3′-diol), antheraxanthin (5,6-epoxy-5,6-didehydro-β,β-carotene-3,3′diol), lutein (β,ε-carotene-3,3′-diol), zeaxanthin (β,β-carotene-3,3′-diol), zeinoxanthin (β,ε-carotene-3-ol), β-cryptoxanthin (ββ-caroten-3-ol), α-carotene (β,ε-carotene) and β-carotene (β,β-carotene) (Niizu and Rodriguez-Amaya 2005). The flowers were found to be excellent food sources of lutein and the leaves good sources of both lutein and the provitamin A β-carotene. The yellow and brownish-orange flowers of *T. majus* were found to have 450 μg/g and 350 μg/g lutein, respectively. Violaxanthin, antheraxanthin, zeaxanthin, zeinoxanthin, β-cryptoxanthin, α-carotene and β-carotene were also detected at very low levels. The leaves had 136 μg/g lutein, 69 μg/g β-carotene, 74 μg/g violaxanthin and 48 μg/g neoxanthin. Lutein was partly esterified in the flowers and unesterified in the leaves.

Chromoplasts of unfolding petals showed differently oriented bundles of tubules with variable diameters (mean 17 nm) intermingled with numerous isodiametric bodies of ca. 50 nm diameter (Falk 1976). Chromoplasts of unfolding petals of *Tropaeolum majus* contained large amounts of filaments (tubules) and uneven-shaped, isodiametric to elongated bodies (Winkenbach et al. 1976). These structural elements were the major sites of the chromoplast pigments. Fractions of these elements contained 15–33 % protein, large amounts of carotenoids and their esters, glyco- and phospholipids, as well as minor amounts of tocopherols. The polypeptide pattern was very similar in all three fractions. One main polypeptide, with an MW of about 30,000, accounted for up to 80 % of the protein of each fraction. Tubulous chromoplasts were isolated in pure form from *Tropaeolum majus* petals (Liedvogel et al. 1978). Whole chromoplasts as well as substructures have been tested for their activities. The following activities of whole chromoplasts as well as substructures in lipid synthesis were found: fatty acid synthesis from acetate, glycosyl transfer reactions from UDP-galactose and UDP-glucose to galactolipids and sterols, acyltransferase reactions from palmitoyl-CoA and a very active acyl-CoA hydrolase. Fatty acid synthesis was restricted to whole chromoplasts. Glycosyl- and acyltransferases were essentially confined to envelope membranes, whereas acyl-CoA hydrolase was found in all fractions. The lipid bodies consisted mainly of galactolipids and carotenoid esters in a 1:1 ratio, together with small amounts of protein.

The volatile oil obtained from hydrodistillation of the aerial parts (leaves and flowers) contained 136 μg/g lutein, 69 μg/g β-carotene, 74 μg/g violaxanthin, 24 μg/g heterotransglycosylation and 48 μg/g neoxanthin (Butnariu and Bostan 2011). Antheraxanthin, zeaxanthin, zeinoxanthin, β-cryptoxanthin, α-carotene and β-carotene were detected in small concentrations. Saponins were present on average of 2.153 % comprising ester saponins, bisdesmosides and monodesmosides of hederagenol. Fatty acids, such as palmitic, oleic, stearic, linoleic, linolenic and docosahexanoic acid were

present in a concentration of 9.5 %, sterols 6.6 % and sterol esters 8.4 %. Flavonoids, tannins and the antibiotic tromalyte were also detected.

The petals and seeds were found to contain large proportions of (*Z*)-11-eicosenoic (gondoic) and (*Z*)-13-docosenoic (erucic) acids, fatty acids of the triglycerides and polar lipids (Radwan 1976). In the lipids of the other floral organs as well as in those of vegetative organs, only traces of these fatty acids were detected. (*Z*)-9,12-octadecadienoic (linoleic) and (*Z*)-9,12,15-octadecatrienoic (linolenic) acids, which occurred only in traces in lipids of the seeds, were major constituent fatty acids of lipids in floral and vegetative organs as well as those of callus cultures.

Tropaeolum majus oil was found to contain the highest levels of erucic acid of known seed oils (75–80 %) (Carlson and Kleiman 1993) with a significant portion of the acid being attached to the 2-position of the glycerol. Trierucin (50 %) was also a major component. Oil contents of seeds of 11 commercial varieties ranged from 6 to 11 % and erucic acid levels from 62 to 80 %. Composition of the deffated meals consisted of moisture (9.40–13.95 %), crude protein (21.7–30.8 %), crude fibre (9.4–12.9 %), ash (5.17–7.25 %), nitrogen free extract (40.9–49.8 %), non-protein nitrogen (0.5–1.1 %) and oil (5.9–10.5 %). Within *T. majus*, the varieties could be grouped into essentially three sets by oleic acid content (<2, 4–8 and 17.5 %) or by erucic acid content (<68, 68–74 and >76 %). Eicosenoic acid levels were least variable of the three major monoenes (mean = 14.9 %). NCAUR 64477 had relatively high oleic acid (17.5 %) content at the expense of erucic acid (62.3 %), whereas NCAUR 47180 had the highest eicosenoic acid content (21.1 %) at the expense of erucic acid (68.1 %). The fatty oil from *T. majus* seeds contained a good amount of keto fatty acid (38.2 %) (9-keto-octadec-*cis*-12-enoic acid) and palmitic (20.8 %), stearic (13.5 %), oleic (19.2 %), linoleic (6.7 %) and linolenic (1.6 %) acids (Daulatabad, and Jamkhandi 2000). The storage triacylglycerols of nasturtium (*Tropaeolum majus*) seeds were found to compose mainly of *cis*-13-docosenoatic acid (erucic acid) 66–78 % and 17–25 % *cis*-11-eicosenoic acid (gondoic acid) (Pollard and Stumpf 1980). Incubation with(14)C-labelled precursors such as [1-(14)C]acetate produced primarily *cis*-11-[1-(14)C]eicosenoate and *cis*-13-[1,3-(14)C]docosenoate in the triacylglycerol fraction, and the odd-carbon [U-(14)C]oleate also formed from [(14)C] acetate was in the polar lipid fraction. Under suitable conditions, nasturtium seed could also produce [(14)C]stearate, [(14)C] eicosenoate and [(14)C]docosenoate from [1-(14) C]acetate. Seeds were reported to accumulate large amounts of non-fucosylated xyloglucan as a seed storage polymer (Jensen et al. 2012).

Studies found that the leaves were the primary site of benzylglucosinolate synthesis (Lykkesfeldt and Moller 1993). The content increased from 5 mg of benzylglucosinolate in the fresh seed to between 200 and 400 mg in the adult plant. The high amounts of benzylglucosinolate accumulating in other tissues (e.g. developing seeds) reflected transport of benzylglucosinolate from the leaves. Du and Halkier (1996) isolated an in vitro enzyme system that actively converted phenylalanine to phenylacetaldoxime in the biosynthesis of glucotropaeolin in *T. majus* seedlings. Low biosynthetic activity was enhanced by the combined treatment of seedlings with light and 50 μM jasmonic acid dissolved in 50 % ethanol.

Young, developing *Tropaeolum majus* fruits were reported to accumulate large deposits of non-fucosylated xyloglucan in periplasmic spaces of cotyledon cells (Desveaux et al. 1998). Mature nasturtium seeds were found to contain cell wall polysaccharide xyloglucan (amyloid), protein and lipid as storage substances (Hoth et al. 1986). The following glycosidases were identified in *T. majus* seeds: a thioglucosidase, a β-glucosidase, a fructofuranosidase and an enzyme causing partial hydrolysis of amylopectin and glycogen (Snowden and Gaines 1969). Hydrolytic activity also indicated the presence of an α-1,1-glucosidase and possibly the presence of a β-galactosidase. The transitory occurrence of starch during the process of seed development was also confirmed. A β-D-glucosidase was purified from the cotyledons of germinated nasturtium seeds (Crombie et al. 1998). The purified protein (Mr 76, 000; a glycoprotein; apparent pH optimum 4.5; temperature optimum 30 °C)

catalyzed the hydrolysis of *p*-nitrophenyl-β-D-glucopyranoside, cello-oligosaccharides, β-linked glucose disaccharides and certain xyloglucan oligosaccharides. An alpha-D-xylosidase involved in the mobilization of xyloglucan was isolated and characterized from the cotyledons of germinated nasturtium fruit (Crombie et al. 2002). It was active against several alpha-(1 → 4) and alpha-(1 → 6)-linked substrates, the former being hydrolyzed faster. Polypeptide assemblies cross-linked by S-S bonds (molecular mass >200 kDa) and single polypeptides folded with internal S-S cross-links (<41 kDa) were found in particulate membranes and soluble extracts of developing cotyledons of nasturtium seed (*Tropaeolum majus*) (Faik et al. 2000). These polypeptides were found to facilitate the channelling of uridine diphosphate (UDP)-activated sugars from the cytoplasm through Golgi vesicle membranes to lumenal sites, where they could be used as substrates for glycosyltransferases to synthesize products such as xyloglucan. Besides xyloglucan endotransglycosylase/hydrolase (XTH/XET) activity, involving the transfer of xyloglucanosyl residues from xyloglucan to xyloglucan-derived oligosaccharides, a glycosyl transfer from xyloglucan to sulforhodamine-labelled cello-oligosaccharides and laminarioligosaccharides was detected in nasturtium extract (Mohand and Farkas 2006). Five forms of xyloglucan endotransglycosylase/hydrolase (XTH) differing in their isoelectric points were detected in crude extracts from germinating nasturtium seeds (Stratilová et al. 2010). All five forms behaved as typical endotransglycosylases since they exhibited only transglycosylating (XET) activity and no xyloglucan-hydrolyzing (XEH) activity and were glycoproteins with identical molecular mass, and deglycosylation led to a decrease in molecular mass from approximately 29–26.5 kDa. The major enzyme form designated as TmXET(6.3) exhibited broad substrate specificity by transferring xyloglucan or hydroxyethylcellulose fragments not only to oligoxyloglucosides and cello-oligosaccharides but also to oligosaccharides derived from β-(1,4)-D-glucuronoxylan, β-(1,6)-D-glucan, mixed-linkage β-(1,3; 1,4)-D-glucan and at a relatively low rate also to β-(1,3)-gluco-oligosaccharides.

The compound responsible for the fruity/red fruit and sulphury odour noted in *T. majus* was identified as *O,S*-diethyl thiocarbonate (Breme et al. 2009). They identified 44 odorant compounds in Indian cress among which two molecules, (*E*)-hex-2-enal (fruity) and diethyl trisulfide (alliaceous, sulphury, cabbage), had the highest odour impact (Breme et al. 2010).

A xanthoxin-like inhibitor was found in *T. majus* plant growing under direct sunlight (Alaniz and Sivori 1979). Indole-3-acetic acid (IAA), indole-3-butyric acid (IBA) and phenylacetic acid (PAA) were identified as endogenous compounds with auxin activity in *Tropaeolum majus* (Ludwig-Müller and Cohen 2002). PAA occurred at concentrations about 10- to 100-fold lower than IAA, whereas IBA occurred in the same concentration range as IAA. Free IAA was highest in roots followed by young leaves. IBA was also highest in the roots, and relatively high concentrations were found in young leaves and flowers. The presence of a nitrilase gene family and nitrilase activity in extracts from *T. majus* suggested that PAA might be synthesized by the nitrilase pathway using benzylglucosinolate as precursor.

Irrespective of the incubation temperature, the lipids in cultures of *T. majus* contained as predominant classes steryl glycosides, esterified steryl glycosides, sterols, steryl esters and fatty acids and, as minor constituents, various proportions of triacylglycerols, phospholipids and several unidentified fractions (Radwan et al. 1978). Erucic acid, the major constituent fatty acid of the seed lipids, occurred only in trace amounts in the lipids of callus cultures. In contrast, linoleic and linolenic acids, which occurred only in traces in the seed lipids, were the major constituent fatty acids in the lipids of callus cultures derived from nasturtium seedlings. The levels of constituent polyunsaturated fatty acids in the diacylglycerophosphorylethanolamines and the diacylglycerophosphorylcholines increased with time, whereas in the triacylglycerols, only linolenic acid was slightly increased. Nasturtium hairy root cultures were found to produce higher content of glucotropaeolin and had higher myrosinase activity than in callus, cell suspensions and leaves of intact plant (Wielanek and Urbanek 1999). Glucotropaeolin production by hairy roots was

stimulated markedly by cysteine and less by phenylalanine and methyl jasmonate. Myrosinase activity was stimulated by methyl jasmonate.

Antioxidant Activity

Antioxidant activity of yellow and orange nasturtium flowers of the climbing mix cultivar was similar and lower than that in red flowers Friedman et al. 2005). Storage of lowers at 2–5oC did not alter the antioxidant activity. The petals of orange Nasturtium flowers were found to contain 72 mg/100 g FW of anthocyanin, and pelargonidin 3-sophoroside represented 91 % of the total anthocyanin content (Garzón and Wrolstad 2009). The ascorbic acid content was 71.5 mg/100 g, and the total phenolic content as determined by the Folin–Ciocalteau method was 406 mg GAE/100 g FW. The radical scavenging activities against ABTS (2,2′-azino-bis 3-ethylbenzthiazoline-6-sulphonic acid) and DPPH (2-diphenyl-1-picrylhydrazyl) radicals were 458 and 91.87 μm trolox eq/g FW, respectively. The excellent free radical scavenging activities along with high phenolic and ascorbic acid content of Nasturtium flowers suggest that they could be a good source of natural pigments and antioxidants for applications in functional foods.

Antimicrobial Activity

Leaves of *Tropaeolum majus* were found to contain high amounts of the glucosinolate glucotropaeolin (Kleinwächter et al. 2008). When Tropaeolum leaves are consumed, glucotropaeolin is hydrolyzed to yield mustard oils, which are absorbed in the intestine and excreted in the urine, exhibiting their antimicrobial activity. The findings supported their use in traditional medicine to treat infections of the urinary tract.

Anticancer Activity

Tropaeolum majus produce significant amounts of benzyl glucosinolate which, through enzymatic hydrolysis, resulted in the production of benzyl-isothiocyanate (BITC). BITC showed promising cytotoxicity in the low micromolar range (0.86–9.4 μM) against four human ovarian carcinoma cell lines (SKOV-3, 41-M, CHl, CHlcisR), a human lung tumour (H-69), a murine leukaemia (L-1210) and a murine plasmacytoma (PC6/sens). The L1210 cells were most sensitive (Pintão et al. 1995).

Diuretic Activity

Tropaeolum majus also has natriuretic and diuretic activity (Gasparotto et al. 2009). The oral administration of 300 mg/kg of hydroethanolic extract of *Tropaeolum majus* increased significantly the urinary and Na+ excretion. Prolonged administration of the extract (300 mg/kg) significantly increased diuresis and the urinary excretion of Na+, with no signs of toxicity, and the mechanism could involve the prostaglandin system. Beside the plant extract, its main compound isoquercitrin also exhibited pronounced diuretic effects (Gasparotto et al. 2011a). An active fraction from the hydroethanolic extract (TMLR) (25–100 mg/kg) and isoquercitrin (5–10 mg/kg) orally administered to spontaneously hypertensive rats dose-dependently increased urinary excretion rate. No evidence of renal toxicity or other adverse effects in these animals were observed even after prolonged treatment with TMLR or isoquercitrin. The results supported the ethnomedicinal use of *T. majus* as diuretic. They found that the mechanisms by which isoquercitrin and extracts of *Tropaeolum majus* increased diuresis in spontaneously hypertensive rats were mainly related to angiotensin converting enzyme (ACE), increased bioavailability of bradykinin, prostaglandin 12 (PGI2) and nitric oxide, besides an inhibitory effect on Na(+)/K(+)-ATPase (Gasparotto et al. 2012).

Hypotensive Activity

Oral administration of hydroethanolic extract (HETM) and semi-purified fraction (TMLR) obtained from *T. majus* significantly reduced, in a

dose-dependent manner, the mean arterial pressure (MAP) in both normotensive and SHR spontaneously hypertensive rats (SHR) (Gasparotto et al. 2011b). Additionally, the intravenous administration of isoquercitrin, but not kaempferol, decreased MAP in rats. The oral administration of the HETM, TMLR or isoquercitrin reduced angiotensin converting enzyme (ACE) activity in serum samples at 90 min after administration. Also, the intravenous administration of ISQ caused a significant reduction in the hypertensive response to angiotensin I, but not angiotensin II in normotensive rats. The results suggested that the hypotensive effects caused by the HETM, as well as by its TMLR, may be associated with the high levels of the flavonoid isoquercitrin found in this plant. In addition, isoquercitrin-induced hypotension in rats was found to be dependent on the inhibition of angiotensin II generation by ACE.

Antithrombin Activity

Methylene chloride and methanol extracts of the six plants *Hedychium gardnerianum, Tropaeolum majus, Gunnera tinctoria, Hedera helix, Festuca juhata* and *Laurus azorica* elicited antithrombin activity of 78 % or higher in the chromogenic bioassay system (De Medeiros et al. 2000).

Hepatoprotective Activity

Koriem et al. (2010) found that pretreatment with either *T. majus* methyl alcohol extract or vitamin E provided protection against blood and liver toxicity induced by diethyl maleate in rats; these results were confirmed by histopathological examinations. *T. majus* methyl alcohol extract or vitamin E prior to diethyl maleate injection shift blood and liver toxicity induced by diethyl maleate towards normal values and preserved hepatic lobular architecture.

Anti-inflammatory Activity

The volatile oil extracted by hydrodistillation from *T. majus* aerial parts prevented (oedema) inflammation in mice especially after 24 and 48 h (Butnariu and Bostan 2011). It elicited 85 % inhibition of skin irritation induced by sodium lauryl sulphate. The integrity of the hydric layer of the skin was significantly improved 30 min after the application of the oil.

Antimicrobial Activity

T. majus volatile oil, methanol, ethanol and hexanol extracts of the aerial plant parts all exhibited good in vitro antimicrobial activity against *Pseudomonas aeruginosa, Listeria monocytogenes, Escherichia coli, Salmonella* sp. *Staphylococcus aureus, Bacillus subtilis* and *Candida albicans* (Butnariu and Bostan 2011).

Toxicological Studies

No significant alterations in the animal's body weight gain, relative organs weight, serum biochemical analysis and haematological or histopathological analyses of liver, kidneys and spleen were observed in male and female Wistar rats which were administered with three doses of hydroethanolic extract of *T. majus* (HETM) (75, 375 and 750 mg/kg) for 28 days (Gomes et al. 2012). The results demonstrated the absence of subchronic toxicity due to oral treatment with HETM for 28 days in Wistar rats. The hydroethanolic extract of *T. majus* did not elicit any (anti)oestrogenic or (anti)androgenic activities in pregnant Wistar rats nor altered uterine contractility at the end of pregnancy (Lourenço et al. 2012)

Pharmacokinetic Studies

Feed supplementation with *T. majus* had no effect on growth performance of piglets (Bloem et al. 2008). *T. majus* was supplemented at an upper dosage of 1 g/kg with the feed, equaling 48.7 mg/kg glucotropaeolin, which resulted in a benzyl-isothiocyanate concentration in the urine of up to 16 µmol/L, which ought to be high enough to control a broad range of bacteria. Up to 7.3 % of the glucotropaeolin taken up by the animals was excreted as bioactive benzyl-isothiocyanate.

After consumption of nasturtium, containing 1,000 μM glucotropaeolin, the primary source of benzyl-isothiocyanate (BITC), quantifiable levels of BITC-cysteinylglycine, BITC-cysteine and BITC-*N*-acetyl-L-cysteine were found in human urine samples (Platz et al. 2013). Maximum levels in urine were determined 4 h after the ingestion of nasturtium. With regard to the human plasma samples, all metabolites were determined including individual distributions.

Allergy Problem

Several cases of contact dermatitis (Maurice 1997; Derrick and Darley 1997; Perez-Crespo et al. 2009) and bullous contact dermatitis (Wetzig et al. 2000). Diamond et al. (1990) suggested that nasturtium should be added to list of plants capable of causing allergic contact dermatitis as it contained mustard oil.

Traditional Medicinal Uses

Nasturtium (*T. majus*) is a herbal plant that meets the German 'Commission E' standards of herbal medicines in 1978 (Blumenthal et al. 1998). *T. majus* has a very broad range of action. The plant is antiseptic, diuretic, antiscorbutic and expectorant and therefore good for head colds (Lust 1974; Chiej 1984; Bown 1995). The plant is ingested internally in the treatment of genito-urinary diseases, respiratory infections, scurvy and poor skin and hair conditions (Bown 1995). Externally it makes an effective antiseptic wash and is used in the treatment of baldness, minor injuries and skin eruptions. *Tropaeolum majus* is a medicinal herb popularly used in Brazil for treatment of inflammatory and cardiovascular diseases (Lourenço et al. 2012). Nasturtium has long been used in Andean herbal medicine as a disinfectant and wound-healing herb and as an expectorant to relieve chest conditions by reducing catarrh formation and stimulate the clearing and coughing up of phlegm (Chevallier 1996).

Fresh leaves of *T. majus* were used in traditional medicine for the treatment of infected wounds and the gall bladder, as diuretic, as aphrodisiac and as remedy against chronic diseases such as obstructive pulmonary disease, cystitis, pyelitis and infections of kidneys and bladder (Madaus 1938; Muller 1979; Weiss 1980; Winter 1955). The leaves are reported to possess antibacterial, antifungal, antiseptic, aperient, depurative, diuretic, emmenagogue, expectorant, purgative, aphrodisiac, vulnerary, rejuvenative, antineoplastic, demulcent, laxative and stimulant activities.

Other Uses

Garden nasturtium is a popular ornamental garden plant; many hybrids and horticultural cultivars have been developed. Garden nasturtiums are also widely considered as useful companion plants as they repel many insect pests and attract beneficial predatory insects, they are also useful as trap crop against black fly aphids. The seeds yield a high percentage of a drying oil that can be used in making paints, varnish, etc.

Comments

Nasturtium is regarded as an invasive species in several countries.

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Typha orientalis

Scientific Name

***Typha orientalis* C. Presl**

Synonyms

Typha angustifolia subsp. *muelleri* (Rohrb.) Graebn., *Typha japonica* Miq., *Typha latifolia* var. *orientalis* (C.Presl) Rohrb., *Typha muelleri* Rohrb., *Typha orientalis* var. *brunnea* Skvortsov, *Typha shuttleworthii* Lehm. [Illeg.], *Typha shuttleworthii* subsp. *orientalis* (C.Presl) Graebn.

Family

Typhaceae

Common/English Names

Asian Bulrush, Broad Leaf Cumbungi, Broad-Leaf Cumbungi, Broad-Leaf Cumbungi, Broad-Leaved Cumbungi, Bull Rush, Bull-Rush, Bullrush, Bulrush, Cat-Tail, Cumbungi, Japanese Cattail Lesser Reed Mace, Oriental Bulrush, Oriental Cattail, Raupo, Raupo Bulrush

Vernacular Names

Chinese: Dong Fang Xiang Pu
Czech: Orobinec Východní
Indonesia: Asiwung Raja Matri, Embet, Heikre, Walini, Wawalingian
Japanese: Ko-Gama
Korean: Bu-Deul
Malaysia: Lembang
Philippines: Balangot
New Zealand: Raupō (Maori)
Vietnamese: Bồn Bồn; Bồn Bồn Lá Rộng, Hương Bồn Lá Rộng, Cỏ Nến Lá Rộng

Origin/Distribution

The species is native to Eastern and Southeastern Asia (i.e. eastern Russia, Korea, Mongolia China, Japan, Taiwan, the Philippines, Myanmar and Papua New Guinea), Australia and New Zealand (Sun and Simpson 2010).

Agroecology

T. orientalis is a wetland plant that grows in fresh or brackish waters on the edges of ponds, lakes, channels, swamps and slow-flowing rivers and streams.

Edible Plant Parts and Uses

Young flowering spikes before the pollen is shed can be eaten either raw or cooked; they are best served with butter like corn on the cob, the hard central core being discarded (Cribb and Cribb

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1987). The young flowering, green stalk is eaten raw or cooked (Tanaka 1976; Low 1991). Pollens released from the stamens can be collected, eaten raw or cooked or baked into cakes, and the protein-rich pollens can be mixed with milk or flour and fried into crumbly pancakes or made into bread and porridge (Launert 1981; Cribb and Cribb 1987; Brooker et al. 1989; Crowe 1990; Low 1991). The young new shoot that arises from the spongy underground stem can be cut and cooked, they taste like asparagus but older parts of the stem are fibrous (Tanaka 1976; Cribb and Cribb 1987; Crowe 1990; Low 1989, 1991).

The starchy rhizomes can be cooked and eaten (Tanaka 1976; Brooker et al. 1989; Low 1989, 1991; Facciola 1990). The rhizomes can be boiled and eaten like potatoes or macerated and then boiled to yield sweet syrup. They can also be dried, ground into a powder and then used as a thickener in soups, porridges and broths, or added to cereal flours. Rich in protein, this flour is used to make biscuits, bread, cakes etc.

Botany

A vigorous, emergent monoecious aquatic perennial to 2 m high with submerged underground rhizome of 20 mm diameter and stout cylindrical stems to 20 mm diameter. Leaves stiff, flat, strap-like linear up to 2 m long and 20–30 mm wide (Plate 1), upper leaves with sheath of the 2–4 uppermost leaves usually distinctly auriculate. Flowers are arranged into a dense cylindrical chestnut to brown spike on tall erect stems above the foliage (Plate 1). Male flower spike is less than 2 cm above the female flower spike that is 7–30 cm in length and 15–20 mm in width. Male flowers: stamens 3, rarely 2 or 4; anthers about 3 mm; pollens shed as single grains. Female flowers without bracteoles; ovary fusiform to lanceolate; stalk 2.5 mm, slender; styles 1.2–2 mm; stigmas spatulate, 0.5–0.8 mm. Fruit small, one seeded, elliptic follicle surrounded by silky hairs. Spikes can contain up to 200, 000 follicles.

Plate 1 Flowering spike and foliage

Nutritive/Medicinal Properties

Typha orientalis root extract was found to have high contents of polysaccharides, protein and amino acid (Tang et al. 2010). *Typha orientalis* was found to have xyloglucan oligosaccharides in its cell walls (Hsieh and Harris 2009). The xyloglucan oligosaccharides found were 1.4 % XXG, 49.1 % XXXG, 0.7 % XLXG, 10.6 % XXLG, 0.7 % XLLG and 37.5 % XXFG where the letters G, X, S, L and F referred to the following structures: G = unsubstituted β-D-Glc*p*; X = α-D-Xyl*p*-(1 → 6)-β-D-Glc*p*; S and L = X with α-L-Ara*f*-(1 → 2)- and β-D-Gal*p*-(1 → 2)-attached, respectively, and F = L with α-L-Fuc*p*-(1 → 2) attached.

The best growth of *Typha orientalis* occurred in plants at 25 °C water temperature supplied

with 70 mg N/L and 20 mg P/L (Cary and Weerts 1984). Biomass production at 16 and 20 °C was about 33 and 66 %, respectively, of that at 24 °C. Production at 30 °C was about 25 % less than that at 25 °C. On a dry weight basis, leaves accumulated up to 3.56 % N, 0.50 % P, 5.78 % K, 1.26 % Ca, 0.34 % Mg and 0.59 % Na, according to nitrogen and phosphorus treatment. Rhizomes and roots, generally, had lower concentrations of N, K, Ca and Mg but higher concentrations of P and Na. Roots, in particular, had higher Na concentrations (up to 1.36 % of dry weight).

Immunosuppressive Activity

The ethanol extract of Pollen Typhae (*T. latifolia, T. angustifolia, T. orientalis*) consisting of a mixture of flavonoids, steroids and volatile oils exhibited immune-suppressive activity in mice (Qin and Sun 2005). The pollen extract significantly suppressed concanavalin A (Con-A)-induced and lipopolysaccharide (LPS)-induced splenocyte proliferation in vitro, in a concentration-dependent manner. In OVA-immunized mice, the extract EEPT significantly suppressed Con A-, LPS- and OVA-induced splenocyte proliferation in a dose-dependent manner. It also significantly reduced the OVA-specific total IgG, IgG1 and IgG2b levels in the OVA-immunized mice. The results suggested that the pollen extract could suppress the cellular and humoral response in mice and could have potential to be developed as immunosuppressant.

Other Uses

The leaves were used for roofs and walls and occasionally for canoe sails (Metcalf 1998). The stem and leaf fibres were used as a string and to weave baskets. Activated carbon was prepared from an inexpensive and renewable carbon source, *Typha orientalis*, by H_3PO_4 activation and then impregnated with different manganese salts (Zhang et al. 2008). The prepared Mn-modified activated carbons were found to be promising adsorbents for the removal of Neutral Red from wastewater.

Comments

The length and diameter of the female inflorescence, and gap between the inflorescences could be used to identify the two Australian species of *Typha* (*T. domingensis* and *T. orientalis*) (Finlayson et al. 1985). The presence or absence of an auriculated leaf sheath was also found to be a useful character, while leaf shape was not.

Broad-leaved cumbungi (*Typha orientalis*) is regarded as an environmental weed in south-western Australia.

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Viola hederacea

Scientific Name

***Viola hederacea* Labill**

Synonyms

Erpetion hederaceum (Labill.) G. Don, *Viola hederacea* Labill. forma A, *Viola hederacea* Labill. forma B, *Viola hederacea* Labill. forma C, *Viola hederacea* Labill. forma D, *Viola hederacea* Labill. forma E, *Viola hederacea* Labill. forma F, *Viola hederacea* Labill. forma G

Family

Violaceae

Common/English Names

Curtis'violet, Ivy-Leaf Violet, Ivy-leaved, Native Violet, Violet

Vernacular Names

None recorded

Origin/Distribution

A native of Australia, found in north-east Queensland, Central Queensland, New South Wales, South Australia and Tasmania.

Agroecology

In its native range, it occurs in an altitudinal range from 70 to 1,160 m and grows in moist shady places in Eucalypt forest, Syncarpia forest and closed Eucalypt woodland. *Viola hederacea* grows in soils ranging from a pH of 6.5 (slightly acidic ranges from 6.1 to 6.5) to 8 (slightly alkaline ranges from 7.6 to 8). It is adapted to chalk, clay loam, loam, loamy sand, sandy clay, sandy clay loam and sandy loam soils.

Edible Plant Parts and Uses

Flowers are edible (King 2007). The flowers are eaten as bush food (Haslam 2011) and can be used in salad or as a garnish desserts (Schaeffer and Fletcher 2012). Flowers are coated with beaten egg white and dusted with icing sugar—great for cakes or with ice cream for children.

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Botany

A perennial, pubescent, prostrate herb with short erect stem, 40–60 mm high, rooting at leaf nodes. Leaves in a basal rosette; petiole up to 60 mm; lamina variable in outline, reniform to suborbicular with deeply cordate base (Plate 1), 14–23 by 9–11 mm, dull-greyish-green, sparsely pubescent on upper surface, margin crenate to obscurely serrated; stipules reddish-brown. Solitary flower on scape to 10 cm, pubescent, curved downwards before flowering; flowers rather pale and spent-looking (Plates 1 and 2).

Plate 1 Flowers and leaves

Plate 2 Close view of flower

Bracteoles two near middle of scape. Sepals 4–5 mm long with basal appendages. Corolla 7–11 mm long, concolorous, white with pale violet centres, anterior petals obovate, lateral petals twisted and bearded. Top of anthers forming a hood-like structure. Style 2 mm long. Ovary 1.5–2 mm, green with purplish spots near the tip. Fruit 3-valved, ovoid capsule, 9 by 4 mm. Seeds ovoid and brown, 1–1.5 mm.

Nutritive/Medicinal Properties

Viola hederacea was found to contain at least 57 novel cyclotides including one cyclotide expressed only in underground parts, named cyclotide *Viola hederacea* root cyclotide or 1V hr (Trabi and Craik 2004). Plant cyclotides are a family of 28–37 amino acid miniproteins characterized by their head-to-tail cyclized peptide backbone and six conserved cysteine residues arranged in a cystine knot motif. This knotted disulfide arrangement, together with the cyclic peptide backbone, renders the cyclotides extremely stable against enzymatic digest as well as thermal degradation, making them interesting targets for both pharmaceutical and agrochemical applications. They proposed that cyclotides constituted a new family of plant defense peptides with more diverse biological function than the well-known plant defensins. In *Viola hederacea*, the relative peptide levels of some cyclotides remained almost constant throughout the year, while other cyclotides were present only at certain times of the year (Trabi et al. 2004).

Other Uses

Native violet is excellent ground cover for shaded moist areas forming a dense mat. It is useful in ferneries, as a ground cover in cottage gardens, in wood land margins, in banks and slopes, in containers, in flower border and beds, under shrub and in hanging baskets.

Comments

Native violet is readily propagated by seeds or divisions, cutting through the plant and planting out the divisions.

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Viola odorata

Scientific Name

***Viola odorata* L.**

Synonyms

Viola odora Neck, *Viola odorata* f. *odorata, Viola wiedemannii* Boiss

Family

Violaceae

Common/English Names

Apple Leaf, Bairnworth, Banworth, Blue Violet, Common Blue Violet, Common Violet, Devon Violet, English Violet, Florist's Violet, Garden Violet, Ordinary Violet, Parma Violet, Purple Violet, Russian Violet, Sweet Blue Violet, Sweet Dog-Violet, Sweet-Scented Violet, Sweet Violet, Violet

Vernacular Names

Albanian: Manushaqja
Arabic: Asarun, Banafasaj, Banafsag, Banafsaj, Banafshaj, Banafshaj Banafsaj, Behussej, Benephig, Farfeera
Brazil: Viola, Violeta (Portuguese)
Chinese: Hu Chin Tsao, Xiang Jin Cai
Czech: Violka Vonná
Danish: Marts-Viol, Viol
Dutch: Maarts Viooltje
Estonian: Lõhnav Kannike
Esperanto: Violo Heĝa
Finnish: Tuoksuorvokki
French: Violette, Violette De Mars, Violette Odorante
Gaelic: Sailchuach Chumhra
German: Duft-Veilchen, Echtes Veilchen, Märzveilchen, Veilchen, Wohlriechendes Veilchen
Hungarian: Illatos Ibolya
Icelandic: Ilmfjóla
India: Bag-Banosa, Banafsa, Banafsha, Banafshah, Banaphsa (Hindi), Bagabanosa (Marathi), Banafsha, Banapsa, Nilapuspa, Vanaphsa, Vanspika (Sanskrit), Curiyakan Ti, Orital-T-Tamarai, Ratna Purus, Ratnapurucu, Vayilethe, Vayilettu (Tamil), Abroo, Banafsha, Banafshah, Gul Banafsha, Gul Banafshah, Gul-E-Banafsha (Urdu)
Indonesia: Antanan (Javanese)
Italian: Mammola, Roseviole, Viola Mammola, Viola Zopa, Violetta
Japanese: Nioi-Sumire
Norwegian: Marsfiol
Persian: Baanfshah, Banafsha, Banafshah, Gule Banafsha, Kookash
Philippines: Bayoleta (Cebu Bisaya), Violeta (Tagalog)
Polish: Fiolek, Fiołek Wonny
Russian: Fialka, Fialka Duschistaja

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Slovascina: Dišeča Vijolica, Vijolica Dišeča
Slovencina: Fialka Voňavá
Spanish: Viola, Violeta
Swedish: Äkta fiol, Äkta viol, Doftviol, Luktviol
Thai: Waiolet
Turkish: Dört Mevsim Menekşe
Vietnamese: Hoa Tím Thơm
Welsh: Fioled Bêr

Origin/Distribution

The species is indigenous to Europe, North Africa and Western Asia. The plant is grown elsewhere in the temperate and sub-temperate areas, often escaped and naturalized. They are now naturalized throughout North America and Australia. The plant has been grown for erosion control in the mountains of Java and as medicinal herb in India and Cuba.

Agroecology

Sweet violet grows in the cool climate and dislikes the hot tropics, hot dry summers and hot dry winds. In its native range, sweet violet can be found near the edges of forests or in clearings, hedge-banks; it is also a common weed in shaded lawns or elsewhere in gardens. It tolerates full sun in winter and where summers are mild and dappled or partial shade in other seasons and situations. It does best in moist, free-draining, deep soil rich in organic matter, preferably from composted fallen leaves.

Edible Plant Parts and Uses

Young leaves, flower buds and flowers are edible raw or cooked (Macnicol 1967; Harrington 1974; Morton 1976; Facciola 1990; Garland 1993; Burnie and Fenton-Smith 1996; Barash 1997; Lauderdale and Evans 1999; Newman and O'Connor 2009; Mlcek and Rop 2011; Anonymous 2012). The flowers have a sweet mild, lettuce-like flavour with a delicate fragrance and can be used in salads, desserts, butter and vinegar. They can be added to drinks or can be used as a decorative addition to a green salad or to garnish a pâté or dessert. Flowers are also used fresh to flavour and colour confectionery. They can be crystallized and used on cakes, cookies or creamy desserts or eaten as sweet treats. Flower infusion with added sugar is used to flavour cream puddings, sorbets, syrup, cakes or ices. Young leaves have a mild flavour and are used in salads and soups and as flavouring in puddings. A leaf extract is used to flavour sweets, baked goods and ice cream. A soothing tea can be made from the leaves and flowers. In Italy it is grown as a culinary herb for flavouring. Sweet violet stunning petals make a wonderful garnish for drinks, desserts and salads (Wilson 2013). They add a subtle, sweet and perfumed flavour. In the recent Chelsea Flower Show, top chef Marcus Wareing used sweet violet flowers to garnish his gin and tonic granita, an unusual take on the famous English tipple (Wilson 2013).

Botany

A hardy, prostrate, perennial herb growing to 15 cm tall, stems short and erect, spreading by sparsely hairy stolons. The leaves are dark green, cauline and borne on long, slender petioles up to 12 cm long. Lamina more or less circular to broad-ovate, 2–7 cm long, deeply cordate at base; margins finely crenate; glabrous to somewhat pubescent (Plates 1, 2 and 3). Stipules are entire stipules ovate to lanceolate, glandular, ciliate, 10–13 mm long. Flowers solitary and axillary; scapes 6–12 cm long, axillary; bracteoles near middle. Sepals 5–6 mm long; petals 5, white to violet, the lower petal 1.2–1.6 cm long including the 3–4-mm long pouched spur, the lower 3 not bearded, the lateral pair usually bearded; sepals 5, lanceolate; style heads hooked (Plates 1, 2 and 3). Fruit small, smooth capsule with cream-coloured, tiny seeds.

Plate 1 Flowers and leaves

Plate 2 Close-up of flower

Plate 3 Pinkish-purple flowers

Nutritive/Medicinal Properties

Flower Phytochemicals

V. odorata flowers contained C 47.26 %, O 42.39 %, Mg 0.9 %, Al 0.45 %, Si 1.37 %, Cl 0.64 %, K 5.06 %, Ca 1.53 % and Fe 0.39 % (Bibi et al. 2006). From the flowers, 3,4-dimethylheptane was isolated (Beierbeck and Saunders 1980). Flowers of *Viola odorata* contained 4.0 % anthocyanins, 1.1 % flavonoids, 0.4 % outside, 18.0 % mucilage and 8.5 % ash (Lamaison et al. 1991). Essential oil of *V. odorata* was found to contain ionine, saponins, glycoside, methyl salicylate, mucilage, vitamins A and C and alkaloids (Keville 1991).

The following flavonol glycosides were identified in *V. odorata* flowers (Karioti et al. 2011): quercetin-3-*O*-α-rhamnopyranosyl-(1 → 2)-[α-rhamnopyranosyl(1 → 6)]-β-glucopyranoside-7-*O*-α-rhamnopyranoside; kaempferol 3-*O*-α-rhamnopyranosyl-(1 → 2)-[α-rhamnopyranosyl (1 → 6)]-β-glucopyranoside-7-*O*-α-rhamnopyranoside; violanin [delphinidin-3-(4″-*p*-coumaroyl)-rutinoside-5-glucoside]; quercetin-3-*O*-α-rhamnopyranosyl(1 → 2)-[α-rhamnopyranosyl-(1 → 6)]-β-glucopyranoside; cyanidin-3-(coumaroyl)-methylpentosyl-exosyl-5-exoside; kaempferol-3-*O*-α-rhamnopyranosyl(1 → 2)[α-rhamnopyranosyl-(1 → 6)]-β-glucopyranoside; quercetin-3-*O*-rutinoside (rutin); quercetin-3-*O*-glucopyranoside; kaempferol-3-*O*-rutinoside (nikotiflorin); kaempferol-3-*O*-glucopyranoside; kaempferol-7-*O*-glucopyranoside; and apigenin-7-*O*-glucopyranoside.

V. odorata flower essential oil was found to contain 63 different compounds amounting to 83.05 % of total oil (Hammami et al. 2011). The oil contained high percentages of monoterpenes and sesquiterpenes. The dominant components were 1-phenyl butanone (22.43 %), linalool (7.33 %%), benzyl alcohol (5.65 %), α-cadinol (4.91), globulol (4.32 %) and viridiflorol (3.51 %). Pulegone (3.33 %), epi-α-cadinol (3.05 %), terpinen-4-ol (2.31 %), germacrene A (1.99 %), benzyl benzoate (1.67 %), 1,10-di-epi-cubenol

(1.44 %) and *p*-methyl anisole (1.09 %) were found to be minor components of the oil. Other minor components (<1 %) included furfural (0.18 %), α-thujene (0.12 %) α-pinene (tr), sabinene (0.13 %), myrcene (0.15 %), α-terpinene (0.14 %), β-phellandrene (0.37 %), δ-3-carene (0.15 %), *Z*-β-ocimene (0.52 %), γ-terpinene (0.15 %), acetophenone (0.15 %), *Z*-sabinene hydrate (tr), *Z*-linalool oxide (furanoid) (0.16 %), methyl benzoate (0.14 %), 1,3,8-*p*-menthatriene (0.43 %), 1,3,8-*O*-menthatriene (0.55 %), *Z*-*p*-menth-2-en-1-ol (0.65 %), 1-terpineol (0.8 %), ethyl benzoate (tr), geranil (0.57 %), δ-elemene (0.22 %), α-cubebene (tr), isoledene (0.37 %), α-copaene (0.22 %), β-bourbonen (0.26 %), β-cubebene (0.24 %), α-gurjunene (0.225), *Z*-caryophyllene (0.84 %), β-duprezianene (0.14 %), α-guaiene (0.17 %), γ-elemene (0.26 %), aromadendrene (0.66 %), α-humulene (0.15 %), allo-aromadendrene (0.45 %), germacrene D (0.42 %), β-selinene (0.24 %), bicyclogermacrene (0.6 %), *E*-β-guaiene (0.53 %), γ-cadinene (0.12 %), β-sesquiphellandrene (0.17 %), germacrene B (0.34 %), germacrene D-4-ol (0.12 %), spathulenol (0.47 %),10-epi-γ-eudesmol (0.27 %), eremoligenol (tr), *Z*-methyl epijasmonate (0.1 %) and *Z*-α-bisabolene epoxide (0.54 %). Wahba and El Gait (1994) identified the following compounds in the flower essential oil: linalool, terpineol, benzyl acetate, methyl salicylate, eugenol, pentadecanoic acid ethyl ester, pentaoxahexadecan-1-ol, tetraoxahexadecan-1-ol, octadecadienal, octadecatrienoic acid ethyl ester, pentaoxanonadecan-1-ol and hexadecanoic acid. Besides volatiles, the flowers also contained an emetic compound called violin and several flavonoids such as viola-quercetin and rutin (Schmelzer and Horsten 2001).

The unique, fine, sweet fragrance of the violet flowers was reported to be dominated by ionones: α-ionone, β-ionone and β-dihydroionone (Brunke et al. 1996). Also, hydroquinone dimethyl ether or 1,4-dimethoxybenzene was another major constituent, with a powerful sweet herbal anisic odour, acting as synergist to the ionones (at least as perceived by human beings). Among the trace components, a number of secondary metabolites of linoleic and linolenic acids were detected, e.g. (*Z*)-3-hexenal with a powerful grassy odour and (*E,Z*)-2,6-nonadienol with a powerful cucumber-like odour. The fragrance of *V. odorata* flowers was attributed to ionone compounds such as β-ionone and (*E*)-4-(2,6,6-trimethyl-1-cyclohexenyl)but-3-en-2-one which originated from enzymatic degradation of carotenoids (Meusinger 2012). From several ionone isomers, the three double-bond position isomers α-ionone, β-ionone and γ-ionone with two stereoisomeric γ isomers with different olfactory properties existed. The odour of (R)-(−)-γ-ionone was described as weak green, fruity and pineapple-like with metallic aspects, quite different from the typical ionone odour, whereas the odour of (S)-(+)-γ-ionone was described as very pleasant, floral, green and woody with a very natural violet tonality. However, β-ionone was a more significant contributor. In conjunction with the ring structure and the equivalent (geminal) methyl groups, only two isomers were possible: (2,6,6-trimethylcyclohex-enyl)butanone and (2,3,3-trimethylcyclohex-enyl)butanone. *Viola odorata* is used as a source for the perfume industry; however, 1 t of fresh flowers yields only 28–43 g of violet essential oil.

Hydroalcoholic solution could extract more melatonin from *Tanacetum parthenium, Tripleurospermum disciforme* and *V. odorata* flowers than hot water (Ansari et al. 2010). The presence of melatonin in these plant tissues may provide some explanation for the anecdotal evidence of their physiological effects in humans with regards to their efficacy in the treatment of neurological and antioxidant deficiency-related disorders for their melatonin content.

Leaf Phytochemicals

V. odorata leaves contained C 48.86 %, O 44.60 %, Mg 0.51 %, Al 0.0 %, Si 0.49 %, Cl 0.48 %, K 3.96 %, Ca 1.10 % and Fe 0 % (Bibi et al. 2006).

More than 100 compounds were separated, of which 23 compounds have been identified in the violet leaf volatiles, representing 95 % of the total (Cu et al. 1992). Some of the components

included 1-dodecanol; pentadeca-5,10-dien-1-ol; pentadec-5-en-1-ol; 3-pentadecenal; 2,5-heptadien-1-ol; 2,4-dimethyldodecane; 1-octadecene; 1-eicosene; and octadeca-9,12-dienoic acid, plus the terpene friedelin was also detected. Twenty-five compounds were identified in the leaf essential oil representing 92.77 % of the oil with butyl-2-ethylhexylphthalate (30.10 %) and 5,6,7,7a-tetrahydro-4,4,7a-trimethyl-2(4H)-benzofuranone (12.03 %) being the two major components (Akhbari et al. 2012). (*Z*)-3-hexenal with a powerful grassy odour and (*E,Z*)-2,6-nonadienol with a powerful cucumber-like odour were also the prominent compounds in violet leaf oil imparting a sparklingly intense 'green' odour being much appreciated in fine perfumery (Brunke et al. 1996). This steam-volatile leaf oil was reported to consist of 30–50 % of 2,6-nonadien-1-al (the violet leaf aldehyde), 2,6-nonadien-1-ol, *n*-hexanol, *n*-hexenol, *n*-heptenol, *n*-octenol, traces of eugenol, as well as several acids (Schmelzer and Horsten 2001).

Stem and Root Phytochemicals

The roots and rhizomes were reported to contain saponins, which were active as an emetic and expectorant, and also salicylic acid, methyl salicylic ester and gaultherin, a glycoside of methyl salicylic acid (Schmelzer and Horsten 2001). In addition they contained an essential oil closely resembling that of the flowers and an alkaloid, odoratine, with a marked hypotensive activity. The stems contained C 43.92 %, O 47.13 %, Mg 0.76 %, Al 0.55 %, Si 1.91 %, Cl 0.58 %, K 2.32 %, Ca 2.20 % and Fe 0.62 % (Bibi et al. 2006). The roots contained C 43.49 %, O 45.96 %, Na 0.28 %, Mg 0.78 %, Al 0.89 %, Si 3.02 %, Cl 0.47 %, K 2.10 %, Ca 2.16 % and Fe 0.85 % (Bibi et al. 2006).

Plant Phytochemicals

Elemental analysis showed the presence of C, O, Na, Mg, Al, Si, Cl, K, Ca and Fe in different parts of *Viola odorata* (Bibi et al. 2006). Sodium was found only in the roots and aluminium and iron were absent in the leaves.

2,2,6,6-Tetramethyl-4-piperidinone was isolated from *V. odorata* (Rodrigues et al. 2007). *V. odorata* was found to contain cyclotides, mini-proteins of 28–37 amino acid residues having the unusual feature of a head-to-tail cyclic backbone surrounding a cystine knot of three disulfide bonds (Craik et al. 1999; Ireland et al. 2006a, b; Ireland et al. 2008). Craik et al. (1999) found cycloviolacins O 1,3,4,6,7,8,9,10,11 in *V. odorat*a and established that structure of cycloviolacin O1 consisted of a distorted triple-stranded beta-sheet and a cystine knot arrangement of the disulfide bonds. The structure was similar to kalata B1 and circulin. Three cyclotides, varv A, varv F and cycloviolacin 02, were isolated from *V. odorata* (Lindholm et al. 2002). Two polypeptide cyclotides named vodo M and vodo N, both of 29 amino acids, were isolated from *Viola odorata* (Svangård et al. 2003). It was confirmed that vodo M (cyclo-SWPVCTRNGAPICGESCFT-GKCYTVQCSC) and vodo N (cyclo-SWPV-CYRNGLPVCGETCTLGKCYTAGCSC) formed a head-to-tail cyclic backbone and that six cysteine residues were involved in three disulphide bonds The cyclotide, cycloviolacin O2, was isolated from *Viola odorata* plant (Göransson et al. 2004). It exhibited potent effects against fouling barnacles (*Balanus improvisus*), with complete inhibition of settlement at a concentration of 0.25 μM. The effect of cycloviolacin O2 against barnacles was reversible and nontoxic in the bioassay employed. *V. odorata* was found to have a linear cyclotide violacin A (Ireland et al. 2006b). Cyclotides cycloviolacin O2, cycloviolacin O3, cycloviolacin O8, cycloviolacin O13, cycloviolacin O14, cycloviolacin O15 and cycloviolacin O16 were extracted from *Viola odorata* (Colgrave et al. 2008). Thirteen new cyclotide sequences were found from the plant *V. odorata*, practically doubling the number of cyclotides to 30 characterized from this species (Ireland et al. 2006a). The 30 cyclotides found included cycloviolacin 0 1–25, Varv A, Kalata B1, Vodo M, vodo N and violacin A (a linear cyclotide derivative) . Cycloviolacin 012 was also named varv E. Prototypic cyclotides, including the Möbius

kalata B1 and the bracelet cycloviolacin O2 (cyO2), were isolated from *V. odorata* (Pränting et al. 2010).

The cyclotide content was determined to be 23.5–14,200 μg/g (dry weight) in the plants *Oldenlandia affinis* and *Viola odorata* (Ovesen et al. 2011). The highest content of cyclotide was found in wild Danish *V. odorata*, presenting the highest content of cyclotide in a plant reported hitherto. Candied violets contained 0.00–8.66 μg/g (dry weight), while no cyclotides were detected in commercial violet tea. From the petroleum ether extract of the plant, stigmasterol, β-sitosterol and lupeol were isolated (Mittal 2013).

Cyclotides, a large family of cyclic peptides, had been reported to have broad range of biological activities, including defence against insect pests and pathogens (Jennings et al. 2001, 2005), and cytotoxic, uterotonic (Gran 1973), insecticidal, anti-HIV, antimicrobial, antineurotensive, cytotoxic and haemolytic activities (Ireland et al. 2006a, b; Huang et al. 2009; Henriques et al. 2011).

Antioxidant Activity

Water extracts of *V. odorata* flowers were shown to possess concentration-dependent free radical scavenging activity when evaluated by the DPPH assay (Stojković et al. 2011). Leaf extract of *V. odorata* exhibited antioxidant activity in vitro (Ebrahimzadeh et al. 2010). In the DPPH radical scavenging assay, its IC_{50} value was 245.1 μg/mL. In the Fe^{2+} chelating ability, its IC_{50} value was 188 μg/mL. The extract showed weak nitric oxide scavenging activity and exhibited very low and moderate concentration-dependent antioxidant activity in ferric thiocyanate methods. The IC_{50} for scavenging of H2O2 was 640 μg/mL.

Anticancer Activity

The acetone extract of *V. odorata* exhibited chemopreventive effects against 7,12-dimethylbenz(a) anthracene (*DMBA*)-induced skin cancer in mice (Perwaiz and Sultana 1998).

Three cyclotides, varv A, varv F and cycloviolacin O2, isolated from *Viola arvensis* and *Viola odorata*, exhibited strong cytotoxic activities, which varied in a dose-dependent manner against a panel of 10 human tumour cell lines, namely, four sensitive parental cell lines [CCRF-CEM (T-cell leukaemia), NCI-H69 (small cell lung cancer), RPMI-8226/s (myeloma) and U-937GTB (histiocytic lymphoma)], five drug-resistant sublines [CCRF-CEM/VM-1(T-cell leukaemia), NCI-H69AR (small cell lung cancer), RPMI-8226/Dox40 (myeloma), RPMI-8226/LR-5 (myeloma) and U-937VCR(histiocytic lymphoma)] and one cell line with primary resistance [ACHN (renal adenocarcinoma)] (Lindholm et al. 2002). Cycloviolacin O2 was the most potent in all cell lines (IC_{50} 0.1–0.3 μM), followed by varv A (IC_{50} 2.7–6.35 μM) and varv F (IC_{50} 2.6–7.4 μM). Herrmann et al. (2006) showed that the single glutamic acid of cyclotide cycloviolacin O2 played a key role for the cytotoxicity: methylation of this residue produced a 48-fold decrease in potency. Further the activity was dependent on an intact disulfide network and that the short sequences between the six cysteine residues, namely, the backbone loops, were devoid of cytotoxic activity.

Studies showed cyclotides to have specific membrane-disrupting activity (Svangård et al. 2007). Disruption of cell membranes played a crucial role in the cytotoxic effect of the cyclotide cycloviolacin O2, isolated from *Viola odorata*. Cell viability and morphology studies on the human lymphoma cell line U-937 GTB showed that cells exposed to 1 displayed disintegrated cell membranes within 5 min. Functional studies on calcein-loaded HeLa cells and on liposomes showed rapid concentration-dependent release of their respective internal contents. Studies by Huang et al. (2009) confirmed kalata B1 to be a membrane-active and pore-forming peptide, characteristics that explained its lytic ability towards membrane mimetics and electrophysiological properties. Cycloviolacin O2 (CyO2), from *Viola odorata*, had been found to have antitumour effects in the breast cancer line, MCF-7,

and caused cell death by membrane permeabilization but did not produce significant membrane disruption in primary human brain endothelial cells, which suggested cyclotide specificity towards induced pore formation in highly proliferating tumour cells (Gerlach et al. 2010).

Antimicrobial Activity

Aqueous plant extracts of *Anethum graveolens*, *Elettaria cardamomum*, *Foeniculum vulgare*, *Trachyspermum ammi* and *Viola odorata* were found to be better/equally effective compared to standard antibiotics against reference strains of human pathogenic bacteria *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella typhi, Salmonella typhimurium, Shigella flexneri* and *Staphylococcus aureus* (Arora and Kaur 2007). *V. odorata* was the most effective antibacterial with minimum inhibitory concentration values ranging from 1 to 2 %. Studies found significant synergistic inhibitory effect of a combination of two aqueous extracts of violet, *Viola odorata*, and the rue, *Ruta graveolens*, at concentrations of 0.15625, 0.3125 and 10–20 mg/cm^3 on the growth of *Trichomonas vaginalis* cultured in (CM161) medium (Al-Heali and Rahemo 2006). *Trichomonas vaginalis* is the most common curable sexually transmitted infection. Trichomoniasis is an important health problem in developing countries. Complete inhibition was seen with a concentration of 10 mg/cm3 for 48 h. During the 96 h period, 81 % inhibition was achieved at a concentration of 0.3125 mg/cm^3 and 75 % at a concentration of 0.15625 mg/cm^3. Significant synergism was achieved at a concentration of 20 mg/cm^3, and a suggestive synergism was achieved at 10 mg/cm^3. *V. odorata flower* essential oil showed strong antifungal activity against the fungal phytopathogen *Botrytis cinerea* (Hammami et al. 2011). When the oils at doses of 25, 12.5 and 6.25 µl/mL concentrations were applied to tomatoes seven days before pathogen inoculation, it completely prevented fruit decay in storage.

Cycloviolacin O2 (cyO2) was the most active cyclotide in *V. odorata* and efficiently inhibited the growth of *Salmonella enterica* serovar *Typhimurium LT2* and *Escherichia coli*, while the other peptides were less active (Pränting et al. 2010). In time-kill assays, cyO2 also had bactericidal activity against the Gram-negative species *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. In contrast, none of the cyclotides had high activity against *Staphylococcus aureus.* Chemical masking of the charged Glu and Lys residues in cyO2 caused a near total loss of activity against *Salmonella*, while masking Arg caused a less pronounced activity reduction. Cyclotides from Iranian *V. odorata* were found to have potent antimicrobial activity against human pathogenic bacteria *Staphylococcus aureus* and plant pathogenic bacteria (Zarrabi et al. 2013).

V. odorata plant extracts and fractions showed in vitro activity against extended spectrum beta lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* (Ziad et al. 2012). The ethyl acetate and aqueous fractions showed inhibitory and bactericidal effects on *Escherichia coli*. Only ethyl acetate fraction exerted inhibitory and bactericidal effects on *Klebsiella pneumoniae*. The concentrations at which most of the strains were inhibited were 5 µg/µL for ethyl acetate fraction and 80 µg/µL for the aqueous fractions. The lowest MIC was recorded for the ethyl acetate fraction with *Escherichia coli* at 2.5 µg/µL. The MIC_{90} was determined with ethyl acetate fraction at 10 µg/µL for *Escherichia coli* and at 5.5 µg/µL for *Klebsiella pneumoniae*. Crude extract, petroleum ether and dichloromethane fractions did not show any inhibitory effect within the tested concentrations. Although the aqueous fraction showed antibacterial activities with *Escherichia coli*, it did not exhibit any activity on *Klebsiella pneumoniae*.

Antipyretic Activity

The hexane-soluble extract of *V. odorata* exhibited prominent antipyretic effects against subcutaneous yeast-induced pyresis in rabbits (Khattak et al. 1985). No obvious toxic effects were noted

for the plant extracts up to doses of 1.6 g/kg. The effect could be related to the salicylic acid content of the plant.

Analgesic Activity

The aqueous and methanolic extract of *V. odorata* aerial parts at a dose level of 400 mg/kg, p.o. showed a significant analgesic effect in the peripheral and central models of pain (tail immersion and hot plate method), while n-hexane and butanolic extracts did not show any significant effect (Antil et al. 2011).

Antihyperlipidemic Activity

Viola odorata leaf extract caused a reduction in total cholesterol and triglyceride levels in tyloxapol- induced dyslipidemia (Siddiqi et al. 2012). In high-fat diet-induced dyslipidemia model, the plant extract caused a significant decrease in total cholesterol, LDL-C and atherogenic index and prevented the increase in average body weights, while it increased HDL-C.

Antihypertensive activity

Viola odorata leaf extract induced a dose-dependent (0.1–1.0 mg/kg) decrease in mean arterial blood pressure in anaesthetized rats (Siddiqi et al. 2012). In isolated guinea pig atria, the extract inhibited force and rate of spontaneous atrial contractions. On the baseline of rat thoracic aortae (endothelium-intact and denuded), the leaf extract caused phentolamine-sensitive vasoconstriction. When tested on phenylephrine and K^+-induced vasoconstriction, the extract exerted a concentration-dependent relaxation and also caused a rightward shift of Ca^{2+} concentration-response curves as well as suppression of phenylephrine control peaks in Ca^{2+}-free medium, similar to that caused by verapamil.

Antiviral Activity

Cyclotides have anti-HIV activity (Gustafson et al. 2004; Ireland et al. 2008). Henriques et al. (2011) reported that the anti-HIV activity of the cyclotide kalata B1 could be attributed to its ability to target and disrupt the membranes of HIV particles; raft-like membranes are very rich in phosphatidylethanolamine phospholipids. Ireland et al. (2008) showed that Möbius cyclotides (e.g. kalata B1) had comparable inhibitory activity against HIV infection to bracelet cyclotides (cycloviolacin O2) and that they were generally less cytotoxic to the target cells.

Anti-inflammatory Activity

Water-soluble polysaccharides extracted from *Viola odorata* were found to possess anti-inflammatory activity, which was manifested by suppression of the exudation and proliferation stages of inflammation and by a change in the capillary permeability (Drozdova and Bubenchikov 2005).

Haemolytic Activity

The haemolytic activity of the various cyclotides cycloviolacins O2, 024, 013, 02, 014 and 015; varv A; and kalata B1 did not vary considerably (Ireland et al. 2006a). At a concentration of 25 μM, a more than 6-fold difference existed between the most haemolytic cyclotide, cycloviolacin O24 (~75 % haemolysis), and the least haemolytic cyclotide, cycloviolacin O14 (~11 % haemolysis).

Diuretic Activity

An infusion of the leaves was found to have diuretic activity when administered to rabbits by gastric intubation at a dose of 2 g/animal (Rebuelta et al. 1983). The aqueous extract of *Viola odorata* aerial parts (200 and 400 mg/kg, p.o.) showed significant diuretic activity in rats (Vishal et al. 2009).

Laxative Activity

Butanolic and aqueous extracts of *Viola odorata* aerial parts (200 and 400 mg/kg, p.o.) showed good laxative effect in rats (Vishal et al. 2009).

Pulmnoprotective Activity

Viola odorata aqueous extract given prophylactically was partially effective in preventing formalin-induced lung damage in rats and was comparable to that of hydrocortisone (Koochek et al. 2003).

Mosquito Repellency Activity

The essential oil of *V. odorata* was induced with a maximum protection time of 8 h and a100% repellency on human skin against the yellow fever mosquito, *Aedes aegypti*; the malaria vector, *Anopheles stephensi*; and the filariasis and encephalitis vector, *Culex quinquefasciatus* (Amer and Mehlhorn 2006).

Molluscicidal Activity

Crude cyclotide extracts from both *Oldenlandia affinis* and *Viola odorata* plants showed molluscicidal activity against golden apple snails (*Pomacea canaliculata*) comparable to the synthetic molluscicide metaldehyde (Plan et al. 2008). Individual cyclotides from each extract demonstrated a range of molluscicidal activities. The cyclotides cycloviolacin O1, kalata B1 and kalata B2 were more toxic to golden apple snails than metaldehyde, while kalata B7 and kalata B8 did not cause significant mortality. The toxicity of the cyclotide kalata B2 on a nontarget species, the Nile tilapia *(Oreochromis niloticus*), was three times lower than the common piscicide rotenone.

Anthelmintic Activity

Cyclotides cycloviolacin O2, cycloviolacin O3, cycloviolacin O8, cycloviolacin O13, cycloviolacin O14, cycloviolacin O15 and cycloviolacin O16 extracted from *Viola odorata* showed up to 18-fold greater anthelmintic potency than the prototypic cyclotide kalata B1 in *Haemonchus contortus* and *Trichostrongylus colubriformis* larval development assays (Colgrave et al. 2008). Cycloviolacin O2 and cycloviolacin O14 were significantly more potent than kalata B1 in adult *H. contortus* motility assays. The lysine and glutamic acid residues of cycloviolacin O2, the most potent anthelmintic cyclotide, were chemically modified to investigate the role of these charged residues in modulating the biological activity. The single glutamic acid residue, which was conserved across all known cyclotides, was shown to be essential for activity, with a sixfold decrease in potency of cycloviolacin O2 following methylation. The three lysine residues present in cycloviolacin O2 were acetylated to effectively mask the positive charge, resulting in an 18-fold decrease in anthelmintic activity.

Toxicity Studies

The acute toxicity of all four extracts, i.e. n-hexane, butanol, methanol and aqueous extracts of *V. odorata* aerial parts, was orally evaluated in rats and was found to be higher than 2,000 mg/kg (Vishal et al. 2009).

Traditional Medicinal Uses

Sweet violet has been used since ancient times in traditional folk medicine especially in the treatment of cancer and whooping cough (Grieve 1971; Duke and Ayensu 1985). The whole plant is regarded anti-inflammatory, diaphoretic, diuretic, emollient, antiphlogistic expectorant, antitussive and laxative (Grieve 1971; Chiej 1984; Lust 1974; Uphof 1968). Tea made from the entire plant is used to treat digestive disorders. It is administered internally for the remedy of chronic bronchitis, upper respiratory catarrh, whooping coughs, asthma, pertussis and cancer of the breast, lungs or digestive tract and externally to treat mouth and throat infections (Bown

1995). The plant has been used as diaphoretic and febrifuge and for infantile disorder and lung troubles (Ahmad et al. 2009).

The fresh whole plant is used in a homeopathic remedy (Grieve 1971). The plant contains salicylic acid and is effective in the treatment of headaches, migraine and insomnia and is used as a sedative (Phillips and Foy 1992). The plant is also used for impetigo, rheumatism and ulcers.

Flowers are listed in many pharmacopoeias around the world for their expectorant and diuretic properties. Syrup made from the flowers is a well-known medicine for cough, colds, asthma and hoarseness. The flowers are demulcent and emollient and used in the therapy of biliousness and lung troubles; petals are prepared in syrup and administered for infantile disorders (Chopra et al. 1986). Celtic women used to mix violet and goat's milk to make a beauty lotion (Grieve 1971). Violet petals can be made into a cough syrup, and a tea will relieve bronchitis and dry mouth. Flowers are also used as a gargle for sore throats. An essential oil from the flowers is used in aromatherapy in the treatment of bronchial complaints, exhaustion and skin complaints (Bown 1995). The seeds are diuretic and purgative and have been used in the treatment of urinary complaints and for gravel (Grieve 1971).

Violet leaves are also considered good remedy traditionally in bronchitis, mucus, coughs, asthma and cancer of the breast, stomach, lungs and digestive tract (Bown 1995). Crushed aerial plant parts are used for rheumatism and applied to ulcers, sores, swelling and cuts (Schmelzer and Horsten 2001). Leaves are emollient and used internally and externally for cancer. An infusion of the leaves relieves congestion and sore throat, makes a hot compress and, in larger doses, is emetic (Grieve 1971). Fresh leaves are crushed and used externally to reduce swellings and soothe irritation. The leaves are also considered to be effective in case of hoarseness, sore throat, impairments of sleep and neurosis. The leaves and roots of *Viola odorata* have mucolytic, sweltering, blood-cleansing effect, and the flower has mucolytic, depressant and blood pressure lowering effect. The root is a more potent expectorant than other parts of the plant; they also contain the alkaloid violin which at higher doses is strongly emetic and purgative (Grieve 1971; Phillips and Foy 1992; Chevallier 1996). In large doses, rhizome and seeds are poisonous.

Other Uses

Sweet violets are often grown as an ornamental plant and as a ground cover and are effective in erosion and weed control. An essential oil distilled from the flowers and leaves is used in perfumery; 1 t of fresh flowers yields only 28–43 g of violet essential oil. The fragrant flowers are also used to flavour breath fresheners. A pigment extracted from the flowers is used as a litmus test for acids and alkalis.

The observation that kalata B2 inhibited the growth and development of *Helicoverpa armigera* larvae suggested a role for the cyclotides in plant defense (Jennings et al. 2005). Barbeta et al. (2008) reported that ingestion of the cyclotide kalata B1 severely retarded the growth of *Helicoverpa armigera* larvae. They confirmed that kalata B1 induced disruption of the microvilli, blebbing, swelling and ultimately rupture of the cells of the *Helicoverp*a gut epithelium.

Comments

Propagation of *Viola odorata* is by division, cuttings from well-developed runners or seeds.

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Viola tricolor

Scientific Name

***Viola tricolor* L.**

Synonyms

Jacea tricolor (L.) Opiz, *Mnemion agreste* Fourr., *Mnemion alpestre* Fourr., *Mnemion contemptum* Fourr., *Mnemion elegans* Spach, *Mnemion gracilescens* Fourr., *Mnemion nemausense* Fourr., *Mnemion sagotii* Fourr., *Mnemion segetale* Fourr., *Mnemion sudeticum* Fourr., *Mnemion tenellum* Webb, *Mnemion tricolor* Spach, *Mnemion variatum* Fourr., *Viola tricolor* var. *hortensis* DC.

Family

Violaceae

Common/English Names

Banewort, Banwort, Bird's Eye, Bouncing Bet, Bullweed, Call-me-to-you, Cat's Face, Cuddle Me, Cull Me, European Wild Pansy, Field Pansy, Garden Pansy, Flower-o-luce, Godfathers And Godmothers, Heart's Ease, Heartease, Hens-and-roosters, Herb Constancy, Jack-jump-up-and-kiss-me, Johnny Jumpup, Johnny-jump-up, Jump-up, Kiss-her-in-the-buttery, Kit-run-about, Kit-run-in-the-fields, Live-in-idleness, Love-in-idleness, Love-lies-bleeding, Loving Idol, Meet-me-in-the-entry, Miniature Pansy, Pansy, Pink-eyed-john, Pink-o-the-eye, Stepmother, Three-colour Violet, Three-coloured violet, Three-faces-under-a-hood, Trinitaria, Trinity Violet, Wild Pansy

Vernacular Names

Albanian: Menekshe
Brazil: Amor Perfeito, Amor Perfeito Bravo, Violeta-tricolor (Portuguese)
Chinese: San Se Jin
Czech: Maceška trojbarevná, Maceška trojbarevná pravá, Violka trojbarevná
Danish: Almindelig stedmoderblomst, Almindelig Stedmorsblomst, Stedmoderblomst, Vild stedmoder, Vild stedmoderblomst
Dutch: Driekleurig Viooltje
Estonian: Aaskannike
Esperanto: Penseo, Trikoloreto, Violo trikolora
Faroe Islands: stjúkmóðurblóma, trílitt blákolla
Finnish: Äidinsilmä, Keto-orvokki
French: Fleur De La Trinité, Pensée, Pensée Sauvage, Pensée tricolore, Violette Tricolore
German: Acker-Stiefmütterchen, Acker-Veilchen, Ackerstiefmütterchen, Ackerveilchen, Dreifaltigkeitskraut, Feld-Stiefmütterchen, Freisamkraut, Gewöhnliches Stiefmütterchen, Stiefmütterchen, Stiefmütterchenkraut, Wildes Stiefmütterchen
Hungarian: Háromszínű árvácska
Icelandic: Þrenningarfjóla, Þrilit fjóla
Italian: Viola, Viola Del Pensiero

T.K. Lim, *Edible Medicinal and Non Medicinal Plants: Volume 8, Flowers*,
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Japanese: Sanshiki-Sumire
Norwegian: Dag og natt, Kattaue, Natt og dag, Sjukmorblom, Skjereblom, Stedmorsblomst, Stemorsblom, Stemorsblomst, Stømorblom, Styggmorblom
Polish: Bratek, Fiołek trójbarwny
Portuguese: Amor Perfeito
Romanian: trei fraţi pătaţi
Russian: Anjutiny Glazki
Slovašcina: Divja vijolica, Sorta, Vijolica divja
Slovencina: Fialka trojfarebná
Spanish: Flor de la Trinidad, Pensamiento, Pensamiento salvaje Trinitaria
Swedish: Natt och dag, Styvmorsviol, Trefaldighetsblomster
Thai: dtôn paen see
Turkish: Hercai Meneks, Şifalı Menekşe
Vietnamese: Hoa tím ba màu; Hoa tím tam sắc; Hoa bướm; Hoa bươm bướm; Tư tường; Hoa păng xê

Origin/Distribution

The plant is indigenous to Europe and West Asia eastwards to Western Siberia and India. It has been introduced into North America, Australia and other subtropical and temperate countries.

Agroecology

Heartease is a cool climate natural woodland plant that grows in temperate to sub- temperate areas. They are tough and adaptable and occur commonly in pastures and in disturbed moist sites. They are easily grown in full sun or shade, but a position in semi-shade is best, with moist, well-drained, humus-rich soils. Depending on the growth form, propagation is from seed, by division, or from basal cuttings.

Edible Plant Parts and Uses

Young tender leaves, flower buds and flowers are eaten raw or cooked (Tanaka 1976; Launert 1981; Facciola 1990; Barash 1993; Mackin 1993; Lauderdale and Evans 1999; Anonymous 2012). The attractive small flowers are added to salads or used as a garnish and to embellish desserts—frosted cakes, sorbets and iced drinks. They also can be crystallized, eaten as a sweet treat and used on cakes, cookies or creamy desserts. Some common recipe names include crystallized violets, triple violet salads, violet-lavender sorbet and wild spring flower salad. The leaves are tasty when cooked like spinach, and a tea can be made from the leaves. Studies by Kelley et al. (2003) found that edible flowers of *Viola tricolor* 'Helen Mount' stored in polyethylene bags at 0 and 2.5 °C for 2 weeks still retained the highest quality and were marketable.

Botany

Annual or biennial herb with decumbent, angular stems, often with short retrorse hairs and fibrous roots. Leaves broad-ovate to narrow-elliptic, 10–35 mm long, 5–15 mm wide, margins obtusely toothed to crenate; petiole 10–20 mm long; stipules to 4 cm long, deeply lobed (Plates 1, 2 and 3). Scapes 3–8 cm long axillary, bracteoles just below the flower. Sepals 5 broadly lanceolate, ciliate with prominent basal appendages, 6–10 mm long. Petals 5 broadly lanceolate, with earlike lobes at the base, 5–10 mm long, the lower shortly spurred, variable coloured, white, violet, yellow, creamy-white with yellow-orange base, sometimes with violet around the edges (Plates 1, 2, 3, 4 and 5). Capsules, smooth, egg shaped, 5–8 mm long; seeds light brown.

Plate 1 Heartease flowers and leaves

Plate 2 Deep purple flowers and leaves

Plate 3 Yellow flowers and leaves

Plate 4 Purple-yellow bicoloured flowers

Plate 5 White-purple variegated flowers

Nutritive/Medicinal Properties

Plant Phytochemicals

Violaxathin, auroxanthin and flavoxanthin were isolated from the flowers (Karrer and Rutschmann 1944). A *cis*-isomer of violaxanthin 15-*cis*-(=central-mono-*cis*)-violaxanthin and natural violaxanthin (5,6,5′,6′-diepoxy-5,6,5′,6′-tetrahydro-β,β-caroten-3,3′-diol) were found in the flowers (Molnár and Szabolcs 1980). Fatty acid esters of violaxanthin and the minor xanthophylls were found in the petals of *Viola tricolor* (Hansmann and Kleinig 1982). β-hydroxy acids (12:0, 14:0, 16:0) were found to be involved in the esterification in addition to the usual acids (12:0, 14:0, 16:0, 18:0). Saito et al. (1983) reported the anthocyanins violanin, platyconin and violanin chloride in *V. tricolor* flowers. Platyconin was found to be delphinidin 3-rutinoside-5-glucoside with two mols of glucosylcaffeic acid attached to the glucose moiety of rutinose in a branched-chain arrangement. Radics et al. (1983) confirmed the geometrical configuration of central-mono-*cis*-violaxanthin in *V. tricolor*. From blossoms of *Viola tricolor*, four new naturally occurring geometrical isomers of violaxanthin (5,6,5′,6′-diepoxy-5,6,5′,6′-tetrahydro-β,β-carotene-3,3′-diol) were isolated (Molnár et al. 1985). The new pigments were shown to be the 9,9′-, 9,13′-, 9,15- and 9,13-di-*cis* violaxanthins.

The aerial parts of *V. tricolor* were found to contain saponins (5.98 %), mucilages (14.20 %)

and total carotenoids (18.46 mg/100 g); 8 carotenoids: violaxanthin (352 μg/100 g), antheraxanthin (711 μg/100 g), lutein (1575 μg/100 g), zeaxanthin (1488 μg/100 g), α-cryptoxanthin (66 μg/100 g), β-carotene 5,6-epoxide (133 μg/100 g), β-carotene (1678 μg/100 g) and 9*Z*-β-carotene (312 μg/100 g) (Toiu et al. 2009a).

The main flavonoid compounds of heartease were identified as rutin (3-*O*-rhamnoglucosylquercetin), violanthin (6-*C*-rhamnosyl-8-*C*-glucosylapigenin), vicenin-2 (6-*C*-glucosyl-8-*C*-glucosylapigenin), orientin (8-*C*-glucosylapigenin) and isoorientin (6-*C*-glucosylapigenin) (Vukics et al. 2008a). The two main flavonoid components in *V. tricolor* were violanthin (6-*C*-glucosyl-8-C-rhamnosyl apigenin) and rutin (3-*O*-rutinosyl quercetin) (Vukics et al. 2008a, d). Heartsease herb contained 420 μg/g rutin. Four flavonol *O*-glycosides, nine flavone-*C*-glycosides and three flavone C, *O*-glycosides were characterized in heartsease methanol extract (Vukics et al. 2008c). All of these glycoconjugates were found to be the derivatives of six aglycones: apigenin, chrysoeriol, isorhamnetin, kaempferol, luteolin and quercetin.

The expression of cyclotides, macrocyclic plant peptides, in six violets, *Viola cotyledon, V. biflora, V. arvensis, V. tricolor, V. riviniana* and *V. odorata*, was found to express notably complex mixtures, with single species containing ></50 cyclotides (Göransson et al. 2003). Cyclotides, small lipophilic proteins having a head-to-tail cyclic backbone, with six cysteine residues being involved in three disulfide bonds (Ireland et al. 2008), found in *Viola tricolor* included cyclo-GESCVWIPCITSAIGCSCKSKVCYRNGIPC (vitri A), cyclo-GETCVGGTCNTPGCSCSWPVCTRNGLPVC (varv A) and cyclo-GETCVGGTCNTPGCSCSWPVCTRNGLPIC (varv E) (Svangård et al. 2004). The cyclotide violapeptide I isolated from *V. tricolor* was found to have haemolytic activity (Schoepke et al. 1993). Cyclotides cycloviolacin O2, kalata B1 and vary peptide A were isolated from *V. tricolor* (Xu et al. 2008). A suite of 14 cyclotides, comprising seven novel cyclotides [vitri B, vitri C, vitri D, vitri E, vitri F, varv Hm and varv He], together with seven known cyclotides [varv A, varv D, varv E, varv F, varv H, vitri A and cycloviolacin O2], was isolated from *Viola tricolor* (Tang et al. 2010). The cyclotides could be classified into two subfamilies: vitri B, C, D, E, varv Hm, He, H, A, D, E and F belonging to the Möbius subfamily and vitri A, F and cO2 belonging to the bracelet subfamily.

The following phenolic acids were extracted from the herbage of both species harvested during flowering local species *Viola tricolor* and *Viola arvensis*: caffeic, protocatechuic, genistic, *p*-hydroxybenzoic, 4-hydroxyphenylacetic, *p*-coumaric (*trans* and *cis* forms), vanillic and salicylic acids (Komorowski et al. 1983). Bioactive compounds reported in *V. tricolor* included rutin, quercetin, luteolin, luteolin-7-glycoside, scoparin, saponarin, saponaretin, violantin, orientin and isoorientin, vicenin-2, vitexin, violeoxanthin, lutein, luteinepoxide and neoxanthin; triterpene saponins based on uriolic acid and containing galactose and galacturonic acid as the sugar component; phenolcarboxylic acids and the derivatives thereof: *trans*-coumaric acid, *cis*-coumaric acid, gentisic acid, *p*-hydroxybenzoic acid, 4-hydroxyphenylacetic acid, *trans*-caffeic acid, protocatechuic acid, vanillic acid, salicylic acid and derivatives; polysaccharides based on glucose, galactose, arabinose, rhamnose, xylose and uronic acid; vitamins E and C; and triacylglycerol (Hansel et al. 1996).

V. tricolor was found to have polyphenolic compounds such as flavonoids, polyphenol carboxylic acids, anthocyanins and proanthocyanins (Toiu et al. 2007b, 2008a). The aerial parts of *V. tricolor* were found to have 112.23–112.27 mg/100 g of salicylic acid (Toiu et al. 2008a). The flavonoids were the major polyphenolic compounds in all the 10 % tinctures of air-dried flowering aerial parts from three *Viola* species, the richest species being *V. tricolor* (Toiu et al. 2008b). *V. tricolor* was found to contain flavonoids (2.108 %), polyphenol carboxylic acids (0.921 %) and salicylic acid (91.83×10^{-3} %) and trace amounts of caffeic acid derivatives. Various flavonol aglycones, flavon-glycosides, flavonol-glycosides and flavonol-diglycosides were detected in herbs of *Solidago canadensis* chemovarieties, in leaves of *Filipendula ulmaria*

and in the herb of *Viola tricolor* species (Papp et al. 2004).

Essential oil of fresh and dried *V. tricolor* herb was found to comprise sesquiterpenes (59.27 %, 4.79 %), aliphatics (29.81 %, 42.21 %), shikimic acid derivatives (8.05 %, 11.20 %) and monoterpenes (0.30 %, 2.23 %), respectively (Toiu et al. 2009b). Components of the essential oil of fresh and dried *V. tricolor* were respectively as follows: limonene (0.12 %, nd (not detected)), 2-pentyl-furan (nd, 0.71 %), eucalyptol (tr (traces), nd), α-methyl-benzene ethanol (0.15 %, nd), *n*-nonanal (0.33 %,1.99 %), 2-methyl benzyl alcohol (5.64 %, nd), menthone (nd, 0.43 %), *neo*-menthol (nd, 0.38 %), methyl salicylate (1.47 %, 1.22 %), β-cyclocitral (tr, 0.51 %), thymol (tr, nd), geranyl acetone (nd, 0.98 %), *trans*-β-farnesene (4.01 %, nd), β-ionone (0.13 %, 1.0 %), β-bisabolene (tr, nd), lauric acid (nd, 0.47 %), spathulenol (0.76 %, nd), caryophyllene (0.18 %, nd), bisabolol oxide B (2.28 %, nd), bisabolol oxide (43.25 %, nd), bisabolol oxide A (7.78 %, nd), myristic acid (0.30 %, 1.72 %), hexahydrofarnesyl acetone (1 %, 4.06 %), benzyl salicylate (0.63 %, nd), farnesyl acetone C (nd, 0.73 %), palmitic acid (12.57 %, 21.62 %), phytol (6.46 %, 7.27 %), linoleic acid (1.50 %, 0.29 %), *n*-tricosane (2.37 %,3.05 %) and *n*-pentacosane (4.51 %, 1.56 %).

Thirty-five compounds representing 97.76 % of the total essential oil were obtained from fresh aerial parts of *V. tricolor*, as follows: 8 sesquiterpenes, 17 aliphatics, 6 shikimic acid derivatives and 4 monoterpenes. Sesquiterpenes were the major component (59.27 %), followed by aliphatics (29.81 %), shikimic acid derivatives (8.05 %) and monoterpenes (0.30 %) (Anca et al. 2009). The main components found were bisabolone oxide (43.25 %), palmitic acid (12.57 %), bisabolol oxide A (7.78 %), phytol (6.46 %), 2-methyl benzyl alcohol (5.64 %), *n*-pentacosane (4.51 %), *trans*-β-farnesene (4.01 %), *n*-tricosane (2.37 %) and bisabolol oxide B (2.28 %). In the essential oil obtained from dried aerial parts of 24 compounds representing 60.53 % of the total oil were identified as follows: 14 aliphatics, 4 shikimic acid derivatives, 2 sesquiterpenes and 4 monoterpenes. The main components found were palmitic acid (21.62 %), phytol (7.27 %), hexahydrofarnesyl acetone (4.06 %), *n*-tricosane (3.05 %), *n*-nonanal (1.99 %), myristic acid (1.72 %), *n*-pentacosane (1.56 %), methyl salicylate (1.22 %) and β-ionone (1.00 %). Aliphatics were the major components (42.21 %), followed by shikimic acid derivatives (11.20 %), sesquiterpenes (4.79 %) and monoterpenes (2.32 %).

Plastoglobules were isolated in pure form from petals of the heartease, *V. tricolor* (Hansmann and Sitte 1982). Triacylglycerols (57 %) as well as carotenoids such as violaxanthin and their esters (23 %) were the main constituents. Polar lipids, proteins, alkanes, phytyl esters, plastid quinones and steryl esters were also detected in smaller amounts. The mean diameter of chromoplast globules was 280 nm (corresponding to a volume of 11.7×10^6 nm^3) and their buoyant density 0.93 g/cm–^{3}. The plastoglobules were devoid of a surrounding unit membrane.

Antioxidant Activity

Studies in Britain also confirmed the antioxidant activities of *Viola tricolor* (Mantle et al. 2000). Heartease herb was found to be a promising source of natural antioxidants (Vukics et al. 2008b). A significant correlation was found between the flavonoid content and antioxidant activity as determined by the trolox equivalent antioxidant capacity (TEAC) assay. The flavonoid content of heartease was 0.50 g rutin/100 g sample, anthocyanin content 0.02 g cyanidin-3-glucoside per 100 g sample and antioxidant activity IC_{50} value of 4.17×10^{-5} g/mL. The antioxidant capacity of different flavonoid fractions of heartease was determined using both Trolox equivalent antioxidant capacity (TEAC) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) in vitro antioxidant assays (Vukics et al. 2008a). The highest electron-donor capacity was found for the major flavonoid component (rutin), whereas one minor component-rich flavonoid fraction exhibited the highest hydrogen-donor activity.

Alcoholic extract obtained from *Viola tricolor* showed the highest concentration on flavonoid

compounds among three medicinal plants tested (Durdun et al. 2009). The Fe^{2+} chelating abilities of its alcoholic extract was the highest at 63.35 %. Fe^{3+} reducing capacity was higher for ethanolic extract of *Viola tricolor* (1.3 mM $FeSO_4$ equivalent/g of dry plant). Mo(VI) reducing power of the extract was found to be 159.32 μg ascorbic acid/g and lipid peroxidation of the alcoholic fraction was 68.91 %.

Gonçalves et al. (2012) demonstrated the antioxidant capacity of *V. tricolor* fractions by 1, 1-diphenyl-2-picrylhydrazyl (DPPH) scavenging method and thiobarbituric acid-reactive species (TBARS) assay. IC_{50} DPPH values ranged from 13.40 to 14.18 mg/mL in flowers and 32.84–284.87 μg/mL for the leaves/roots. The fractions showed inhibition against TBARS, following order ethyl acetate fractions > butanolic fractions > dichloromethane fractions. In the flower fractions the phenolic content varied from 12.84 to 0.23 mg/g and 7.49–0.63 mg/g for leaves/roots. HPLC results indicated a very high content of rutin (177.46 mg/g) in this species. *V. tricolor* flower extract with IC_{50} of 16 μg/mL was found to have better antioxidant capacity than the standard ascorbic acid (IC_{50} of 16.57 μg/mL) (Piana et al. 2013b). This was attributed to the presence of amounts of polyphenols (109.32 mg of Gallic acid equivalent/g of extract), flavonoids and condensed tannins.

Anticancer Activity

The methanol extract of *V. tricolor* exhibited >90 % inhibition of mouse leukaemia cells L1210 in vitro (Goun et al. 2002). Among the small lipophilic proteins isolated from *V. tricolor*, cytotoxic compounds showing the lowest IC_{50} values against two human cancer cell lines, U-937 GTB (lymphoma) and RPMI-8226/s (myeloma), were three cyclotides: vitri A (IC_{50} = 0.6 μM and IC_{50} = 1 μM, respectively), varv A (IC_{50} = 6 μM and IC_{50} = 3 μM, respectively) and varv E (IC_{50} = 4 μM in both cell lines) (Svangård et al. 2004). Several of the cyclotides isolated from *V. tricolor* exhibited cytotoxic activities against five human cancer cell lines: U251, MDA-MB-231, A549, DU145 and BEL-7402 (Tang et al. 2010). Three cyclotides, vitri A, vitri F and cycloviolacin O2, and all bracelet cyclotides were the most cytotoxic with IC_{50} values of 2.74–17.05 μg/mL against all tested cancer cell lines. The IC_{50} values of the Möbius cyclotides against U 251 vary from 37/18 to 74.39 μg/mL. The cytotoxic activity of the cyclotides did not correlate well with their haemolytic activity (human type O red blood cells), indicating that different interactions, most likely with membranes, were involved for cytotoxic and haemolytic activities.

Antimicrobial Activity

The infusion, decoction and ethanol extract of *V. tricolor* herb were found to be most effective against the tested microorganisms: *Staphylococcus aureus*, *Staphylococcus epidermidis, Bacillus cereus, Enterococcus faecalis and Candida albicans (*Witkowska-Banaszczak et al. 2005).

Anti-inflammatory Activity

Viola tricolor (aerial parts) extract (50 mg tincture/100 g b.w.) significantly reduced polymorphonuclear leucocytes and monocytes percentages and the activation of circulating phagocytes in male Wistar rats (Toiu et al. 2007a). There was a slight decrease of nitric oxide synthesis. This was attributed to its high antioxidant property. The study concluded that *Viola tricolor* extract had anti-inflammatory effect on bone marrow acute phase response.

Viola tricolor gel was found to have an antinociceptive and anti-inflammatory effect in the ultraviolet-B-induced burn (Piana et al. 2013a). This was reflected by changes in threshold in the static and dynamic mechanical allodynia (Imax = 100 and 49 %, respectively), paw oedema (Imax = 61 %) and myeloperoxidase activity (Imax = 89 %) models. Such effects may be attributed, in part, to rutin, salicylic and chlorogenic acids and others compounds found in this species.

Immunosuppressive Activity

An aqueous *Viola tricolor* herbal extract inhibited proliferation of activated lymphocytes by reducing IL-2 cytokine secretion without affecting IL-2 receptor expression (Hellinger et al. 2014). Similarly, effector functions were affected as indicated by the reduction of IFN-γ and TNF-α production; degranulation capacity of activated lymphocytes remained unaffected. Cyclotides were identified as the bioactive components

Antidermatitic Activity

A double-blind, vehicle-controlled, randomized, half-side comparison study of 88 patients with mild-to-moderate atopic dermatitis, treatment with an ointment containing *Mahonia aquifolium, Viola tricolor* and *Centella asiatica* reduced the primary and secondary endpoints slightly more than the base cream which was used as vehicle; however, the differences were not statistically significant (Klövekorn et al. 2007). However, a subanalysis indicated that the cream might be effective under conditions of cold and dry weather.

Haemolytic Activity

A protein designed as violapeptide I was reported to be responsible for the haemolytic property of *V. tricolor* (Schoepke et al. 1993). Haemolytic activity of 9 cyclotides from *V. tricolor* was measured on human type O blood cells (Tang et al. 2010). The HD_{50} values calculated were 8.91 μm for vitri A, 225.90 μm for vitri B, 11.53 μm for vitri C, 4.29 μm for vitri D, 27.06 μm for vitri E, 10.00 um for vitri F, 6.96 μm for varv E, 33.04 μm for varv F and 7.52 μm for varv H. Vitri B showed the least haemolysis and vitri D was the most potent.

Antithrombin Activity

V. tricolor plant extract exhibited 90 % or higher activity in the inhibition of thrombin (Goun et al. 2002).

Photoprotective Activity

Among the ethyl acetate extracts of 16 medicinal plants tested, extracts of leaves of *Dracocephalum moldavica* and flowering tops of *Viola tricolor* had the highest sun protection factors (SPFs), i.e. 24.79 and 25.69, respectively (Khazaeli and Mehrabani 2008). Both plants contained high amounts of phenolic compounds and flavonoids which could be the cause for their high SPF. *V. tricolor* was reported to contain flavonoids, including violanthin, rutin, violaquercitrin and salicylates. Both salicylates and rutin contained in the plant had been reported to be anti-inflammatory agents. Due to the high concentration of rutin in the flowers, *V. tricolor* may be used to prevent UV-induced oxygen free radical generation (Khazaeli and Mehrabani 2008). *V. tricolor* is an especially valued remedy for treating skin diseases. Used both internally and topically, it is good for eczema, psoriasis and acne.

Diuretic Activity

A tincture of *V. tricolor* aerial parts showed a moderate diuretic activity (diuretic index 1.103, saluretic index of Na^+ 1.181 and saluretic index of K^+ 1.365) (Toiu et al. 2009a).

Pediculicidal Activity

Viola tricolor was one of four Ukrainian medicinal plants that exhibited significant pediculicidal properties (Iryna and Tarasyuk 2009). The rate of lice *Pediculus humanus* death amounted to 84.00–100 % when test insects were plunged into the ethanol extract. Pediculicidal effect of the ethanol extract persisted up to a year.

Contraindications

A case of haemolysis in a 9-month-old infant with a history of glucose-6-phosphate-dehydrogenase (G6PD) deficiency was reported in Tehran, Iran, which was caused by ingestion of boiled watery

extract of *Viola tricolor* (Behmanesh and Abdollahi 2002). After 24 h of routine interventions, the infant recovered his health.

Traditional Medicinal Uses

Heartease is regarded as anodyne, antiasthmatic, anti-inflammatory, cardiac, demulcent, depurative, diaphoretic, diuretic, emollient, expectorant, laxative and vulnerary (Uphof 1968; Grieve 1971; Lust 1974; Chiej 1984; Launert 1981; Toiu et al. 2009b; Hellinger et al. 2014; Piana et al. 2013a), and the root is emetic (Chiej 1984). Heartsease has been used for a long time in herbal folk medicine as treatments for epilepsy, asthma, skin diseases like eczema and cutaneous eruptions; respiratory problems such as bronchitis, asthma and whooping cough and cold; rheumatism, cystitis, bed-wetting and difficulty in passing urine (Grieve 1971; Launert 1981; Chevallier 1996; Rimkiene et al. 2003; Toiu et al. 2009b). *Viola tricolor* has been reported to have expectorant, diuretic, astringent, antiphlogistic and blood-cleansing effect (Keville 1994; Hansel et al. 1996), and teas or extracts prepared from the aerial parts of the plant are often used in case of cold as well as inflammatory, skin and arthritic diseases (Leporatti and Ivancheva 2003). It is a component of some prepared antitussives, cholagogues, dermatological medicines, roborants and tonics, alternatives and anti-phlebitis remedies.

Heartsease (*Viola tricolor*) has a long history as a medicinal plant and has been documented in the Pharmacopoeia of Europe (Hellinger et al. 2014). Due to its anti-inflammatory properties, it is regarded as a traditional remedy against skin diseases, for example, for treatment of scabs, itching, ulcers, eczema or psoriasis; it is also used in the treatment of inflammation of the lungs and chest such as bronchitis or asthma and burns (Piana et al. 2013a).

Other Uses

The flowers yield yellow, green and blue-green dyes. The leaves can be substituted for litmus in testing for acids and alkalis. *Viola tricolor* was used as a symbol of Athens. It is a popular and attractive ornamental plant in gardens and pots.

Comments

Studies found that violets of the section Melanium (zinc violets, *Viola lutea* ssp. *calaminaria* and *V. lutea* ssp. *westfalica;* heartsease or wild pansy, *Viola tricolor*; and mountain pansy, *Viola lutea*) are heavy-metal excluders and not accumulators (Hermann et al. 2013). When these violets were grown in low-metal soils, higher concentrations of the heavy metals were found in the roots and shoots than in the soil, whereas the opposite was seen in samples from high-metal soils. Under all field conditions examined, the roots of all of these species were colonized by arbuscular mycorrhizal fungi.

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Viola × *wittrockiana*

Scientific Name

***Viola* × *wittrockiana* Gams**

Synonyms

Viola* × *hortensis auct.

Family

Violaceae

Common/English Names

Garden Pansy, Ladies' Delight, Pansy, Violas, Wittrock's Violet

Vernacular Names

Japanese: Panji
Portuguese: Amor-Perfeito (Brazil)
Spanish: Pensamiento
Swedish: Pensé

Origin/Distribution

Garden pansy, known only in cultivation, is a complex hybrid resulting from extensive hybridizing and selecting involving the species of *Viola tricolor, V. lutea, V. altaica* and others. Most, if not all, of the parent species are native to Europe and Asia Minor.

Agroecology

Garden Pansy is a cool climate hybrid species. They are hardy biennial grown as annual. They are generally very cold hardy plants surviving freezing even during their blooming period. They can survive light freezes and short periods of snow cover; in areas with prolonged snow cover, they survive best with a covering of dry winter mulch. They grow best in sunny or partially sunny positions in free-draining, moist, humus-rich, acidic, sandy loams, loams or clayey loams. Pansies are not very heat tolerant; they are best used as a cool season planting; warm temperatures inhibit blooming, and hot humid and wet conditions cause rot and death.

Edible Plant Parts and Uses

The flowers are edible (MacNicol 1967; Larkcom 1980; Facciola 1990; Lauderdale and Evans 1999; Newman and O'Connor 2009; Rop et al. 2012). The attractive flowers are added to salads or used as a garnish and to embellish desserts—frosted cakes, sorbets and iced drinks. They also can be crystallized and eaten as a sweet treat.

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Botany

Pansies are hardy, small, compact herbaceous plants growing to 10–20 cm high with a spread of 10 cm. The leaves are deep green, alternate, ovate to lanceolate–oblong, simple, margins obtusely toothed to crenate, finely hairy on 10–20 mm long petiole (Plates 1, 2 and 3). Scapes are axillary, flowers showy and attractive, bisexual, subrotund in outline, 2.5–4.5 cm across. Sepals 5 and petals 5—the two top petals overlapping slightly, two side petals and a single bottom petal with a slight indentation, as well as beards where the three lower petals join the centre of the flower. Petals come in a myriad of rainbow pastel colours and hues from yellow, white, blue, pink, purple, orange, lavender, rust, bronze or black, in monotone or multi-toned and with blotches of other dark colours (Plates 1, 2, 3, 4 and 5). Stamens 5 filaments connate that in a ring around the ovary and a 3-carpellate compound pistil with a superior ovary.

Plate 1 Garden pansy—yellow flowers and leaves

Plate 2 Garden pansy—pink-maroon flowers

Plate 3 Garden pansy—yellow-brown flowers

Plate 4 Garden pansy—yellow with dark radiating lines

Plate 5 Garden pansy—yellow-brown flowers

Nutritive/Medicinal Properties

Rop et al. (2012) reported that edible flowers of *Viola* × *wittrockiana* had a dry matter content (%w/w) of 10.01 %, crude protein of 6.70 g/kg and the following elements (mg/kg fresh mass (FM)): P 514.62 mg, K 3964.84 mg, Ca 486.44 mg, Mg 190.05 mg, Na 131.97 mg, Fe 7.29 mg, Mn 7.93 mg, Cu 1.95 mg, Zn 11.52 mg and Mo 0.84 mg.

Garden pansy being a complex hybrid derived from *Viola tricolor* × *V. lutea* × *V. altaica* would have similar cyclotides, flavonoids and carotenoids and other compounds common to its parents and share similar biological activities. Four anthocyanins identified in pansy (*Viola* × *wittrockiana)* were Dp3RG (delphinidin 3-rhamnosylglucoside) (tulipanin), Cy3RG = cyanidin-3-*O*-(6″-*O*-α-rhamnopyranoside-β-D-glucopyranoside), Dp3pCRG5G = delphinidin-3-(*p*-coumaroylrutinoside)-5-glucoside (nasunin) and Cy3pCRG5G = cyanidin-3-*(p*-coumaroyl*)*-rutinoside-5-glucoside (Hase et al. 2005). One of the flavonols was identified as quercetin-3-*O*-rutinoside (rutin). Yellow and white lines did not contain anthocyanin. Nasunin, rutin and five flavonols were detected in bluish-coloured flowers. Another anthocyanin cyanidin-3-*(p*-coumaroyl*)*-rutinoside-5-glucoside was detected in reddish-purple line. Pansy petals had been reported to contain carotenoids and flavonoids (flavonols and anthocyanins) (Gamsjaeger et al. 2011). Using Fourier Transform Raman spectroscopy, the distribution of carotenoids, anthocyanins and flavonols from the outer layer of the petals could be discriminated, and their relative concentration could approximately be determined. *Viola* × *wittrockiana* petals primarily contain a complex mixture of xanthophylls from which violaxanthin was isolated from the yellow variety.

The most complex cyclotide pattern was found in the roots of *Viola wittrockiana*, the humble garden pansy (Trabi and Craik 2004). Of Viola species screened in their study, *V. wittrockiana* produced the largest cyclotide with a mass of 3481 D. The most hydrophobic cyclotides was also found in *V. wittrockiana*, specifically in the root; the main component had a mass of 3126D and was accompanied by a second peptide (mass 3096 D).

Antioxidant Activity

Pansy flowers had total antioxidant capacity of 6.65 g ascorbic acid equivalents/kg FM, total phenolic content of 5.11 g gallic acid/kg FM and total flavonoid content of 1.99 g rutin/kg FM (Rop et al. 2012).

Garden pansy (*V.* × *wittrockiana*) especially the flower was found to be a promising source of natural antioxidants (Vukics et al. 2008). A significant correlation was found between the flavonoid content and antioxidant activity as determined by the trolox equivalent antioxidant capacity (TEAC) assay. The flavonoid content of violet pansy flower was 1.21 g rutin/100 g sample, anthocyanin content 1.52 g cyanidin-3-glucoside per 100 g sample and antioxidant activity IC_{50} value of 1.57×10^{-5} g/mL; the flavonoid content of violet-white pansy flowers was 2.58 g rutin/100 g sample, anthocyanin content 0.19 g cyanidin-3-glucoside per 100 g sample and antioxidant activity IC_{50} value of 8.59×10^{-5} g/mL; the flavonoid content of white pansy flowers was 2.01 g rutin/100 g sample, anthocyanin content 0.09 g cyanidin-3-glucoside per 100 g sample and antioxidant activity IC_{50} value of 6.35×10^{-5} g/mL; and the flavonoid content of yellow pansy flowers was 2.93 g rutin/100 g sample, anthocyanin content 0.31 g cyanidin-3-glucoside per 100 g sample and antioxidant activity IC_{50} value of 6.98×10^{-5} g/mL.

Other Uses

Pansies make good container or above-ground planter and as border or edge plants. They are also used as cut flowers. The flowers yield yellow, green and blue-green dyes.

Comments

The pansy is the flower of Osaka, Japan.

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Hemerocallis fulva

Scientific Name

***Hemerocallis fulva* (L.) L.**

Synonyms

Hemerocallis lilioasphodelus var. fulva L.*; Hemerocallis lilioasphodelus var. fulvus* L.

Family

Xanthorrhoeaceae, also placed in Hemerocallidaceae and Liliaceae

Common/English Names

Coastal Day Lily, Common Yellow Day Lily, Ditch Daylily, Fulvous Daylily, Orange Daylily, Tawny Daylily, Tiger Daylily

Vernacular Names

Chinese: Xuan Cao, Chang Ban Xuan Cao, Chang Guan Xuan Cao, Chang Lu Xuan Cao
Czech: Denivka Forrestova, Denivka Plavá
Danish: Brun Daglilje, Rødgul Daglije, Rødgul Daglilje
Dutch: Bruine Daglelie
Estonian: Ruuge Päevaliilia
Finnish: Punakeltainen Päivänlilja, Rusopäivänlilja
French: Hémérocalle Fauve
German: Bahnwärter-Taglilie, Braunrote Taglilie, Gelbrote Taglilie, Rotgelbe Taglilie
India: Swarnlili
Italian: Giglio Di San Giuseppe
Japanese: Akino-Wasuregusa, Hama-Kanzō, Oni-Kanzo, Yabu-Kanzo
Korean: Heutowanchuri, Khnwonchuri, Nomnamul, Wangwonchuli, Wonch'uri
Norwegian: Brun Daglilje
Polish: Liliowiec Rdzawy
Russian: Krasodnev Buro-Želtyj, Krasodnev Ryžij
Slovašcina: Maslenica Rumenorjava, Rumenorjava Maslenica
Slovencina: Ľaliovka Žltá
Swedish: Branddaglilja, Brunröd Daglilja
Thai: DtôN-Jam-Chàai
Vietnamese: Hoa Hiên; Huyên Thảo; Hoàng Hoa; Kim Trâm Thái; Lộc Thông

Origin/Distribution

The species is native to East Asia—China (Anhui, Fujian, Guangdong, Guangxi, Guizhou, Hebei, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Shaanxi, Shandong, Shanxi, Sichuan, Taiwan, Xizang, Yunnan, Zhejiang). It is cultivated in China, Taiwan, Korea, India, Vietnam and Japan and, as an ornamental, in many temperate and subtropical countries.

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Agroecology

It is a cool climate species. In its native area, it occurs naturally in forests, thickets, grasslands and stream-sides from 300 to 2,500 m elevations.

Edible Plant Parts and Uses

The dried flowers are used as spice and root tubers, young leaves and young shoots and flower buds are eaten as vegetable (Read 1946; Polunin 1969; Harrington 1974; Stuart 1979; Facciola 1990; Erhardt 1992; Roberts 2000; Woodward 2000; Hu 2005; Tanaka and Nguyen 2007; Newman and O'Connor 2009). The thick petals can be eaten raw. The flowers can also be dried and used as a thickener in soups or as relish. Tuber especially the young tubers are eaten cooked.

Botany

A herbaceous perennial, deciduous in winter, 40–120 cm high, with fleshy globose-ellipsoid, swollen, tuberous part near tip and stolons (Plate 1). Leaves are linear, 50–90 cm long and 1–2.8 cm broad. Flowers borne in a helicoidal, usually 2–5-flowered cyme with linear scale-like bracts, pedicel short, 5 mm long (Plates 1–2), Flowers unscented, opening in morning and closing in evening of same day. Perianth single, occasionally double, orange to reddish orange; tube 2–4 cm; segments spreading, with a purple or reddish orange patch towards the tube and pale central line, 5–12 × 1–3 cm; margin sometimes crinkly undulate, inner segments wider than outer ones. Filaments dark orange colour with purplish-black anthers. Capsule ellipsoid, 3-valved, 2–2.5 cm by 1.2–1.5 cm dehisces at maturity to release the seeds.

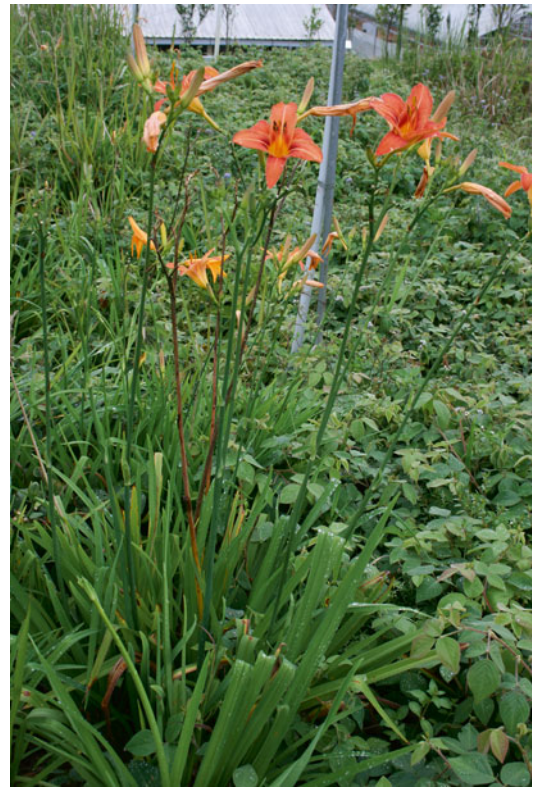

Plate 1 Clumpy of orange day lilies

Plate 2 Close-up of flower and buds

Nutritive/Medicinal Properties

Flower Phytochemicals

The flowers were reported to have the following nutrient composition: protein 9.3 %, fat 25 %, ash 0.9 % and carbohydrate 60 % (rich in sugars) (Read 1946).

From the methanol and aqueous methanol extracts of lyophilized edible *Hemerocallis* cv. Stella de Oro flowers, kaempferol, quercetin and isorhamnetin 3-*O*-glycosides (1–9); phenethyl β-D-glucopyranoside (10); orcinol β-D-glucopyranoside (11); phloretin 2′-*O*-β-D-glucopyranoside (12); phloretin 2′-*O*-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside (13);

a new naphthalene glycoside, stelladerol (14); and an amino acid (longitubanine A) (15) were isolated (Cichewicz and Nair 2002). Three polyphenols, n-butyl 4-*trans*-*O*-caffeoylquinate (1), kaempferol 3-*O*-{α-L-rhamnopyranosyl(1 → 6)[α-l-rhamnopyranosyl(1 → 2)]}-β-D-galactopyranoside (2) and chrysoeriol 7-*O*-[β-D-glucuronopyranosyl(1 → 2)(2-*O*-*trans*-feruloyl)-β-D-glucuronopyranoside (3), together with four caffeoylquinic acid derivatives (4–7); eight known flavones (8–15); one naphthalene glycoside, stelladerol (16); one tryptophan derivative (17); adenosine (18); and guanosine (19) were isolated from the bioactive fractions of the aqueous ethanol extract of *H. fulva* flowers (Lin et al. 2011).

Various forms of *Hemerocallis fulva* differed in their relative anthocyanin:carotenoid ratios and the type of anthocyanin present (Griesbch and Batdorf 1995). *Hemerocallis fulva* fm. *fulva* contained a single anthocyanin (cyanidin-3-rutinoside) and two carotenoids (zeaxanthin and lutein). *Hemerocallis fulva* fm. *rosea* contained a single anthocyanin (cyanidin-3-rutinoside) and traces of carotenoids. *Hemerocallis fulva* fm. *disticha* contained a single anthocyanin (delphinidin-3-rutinoside) and two carotenoids (zeaxanthin and lutein).

Twenty-one pigments were found in the flowers of daylily (*Hemerocallis disticha*), of which 14 carotenoids were identified, including neoxanthin, violaxanthin, violeoxanthin, lutein-5,6-epoxide, lutein, zeaxanthin, β-cryptoxanthin, all-*trans*-β-carotene and their *cis* isomers (Tai and Chen 2000). Prior to hot-air-drying (50 °C) or freeze-drying, some of the daylily flowers were subjected to soaking in a sodium sulphite solution (1 %) for 4 h. Under either the hot-air- or the freeze-drying treatment, the amounts of most carotenoids were higher in the soaked daylily flowers than in those that were not soaked. With hot-air-drying, the amount of *cis* carotenoids showed a higher yield in soaked samples than in non-soaked samples. However, with freeze-drying, only a minor change of each carotenoid was observed for both soaked and nonsoaked samples. Also, air-drying resulted in a higher loss of carotenoids than freeze-drying.

Konar and Stanley (1969) reported a peak in cellulase activity in the pistil just prior to anthesis, followed by a 62 % diminution in the enzyme activity at the time of anthesis. Cellulase activity, per mg protein, was about twice as high in the upper (stigma) portion as in the middle and lower one-third of the pistil tissues. No pectinase activity was detected in the pistil at all stages of development. Extractable pectinase occurred at a maximum level in the very young ovary and decreased rapidly as the ovary developed. Cellulase remained at a moderate level of activity throughout the development of the ovary, except for an increase of about 50 % at pollination. Soluble cellulase and pectinase were found in mature pollen.

Dynamin, a protein with molecular weight 100 kD, was isolated from the pollens; it was found to have GTPase activity (Wu et al. 2002). Tubulins of high purity (93.7 %) were prepared from *H. fulva* pollen grains Liao et al. 2006). The molecular weight of α-tubulin and β-tubulin from daylily pollen was about 56 and 58 kD. Circular dichroism spectrum analysis showed that the percentage of α-helix, β-sheet and random coil of daylily tubulin is 27.24 %, 24.48 % and 48.28 %, respectively, indicating a typical feature of globulin. Motor dynamin-like protein with molecular weight of 100 kD was purified and identified from daylily (*Hemerocallis fulva*) pollens (Liao et al. 2007). It contained tryptophan and tyrosine residues.

Leaf Phytochemicals

Aqueous methanol extracts of fresh *Hemerocallis fulva* leaves afforded 1′,2′,3′,4′-tetrahydro-5′-deoxy-pinnatanine, pinnatanine, roseoside, phlomuroside, lariciresinol, adenosine, quercetin 3-*O*-β-D-glucoside, quercetin 3,7-*O*-β-D-diglucopyranoside, quercetin 3-*O*-α-L-rhamnopyransol-(1 → 6)-β-D-glucopyranosol-7-O-β-D-glucopyranoside, isorhamnetin-3-*O*-β-D-6′-acetylglucopyranoside and isorhamnetin-3-*O*-β-D-6′-acetylgalactopyranoside (Zhang et al. 2004).

Two novel amino acid amides connected with the fructopyranose, kwansonine A (1) and kwansonine B (2), together with three known amino acid amides, (longitubanine A, longitubanine B and pinnatanine) from the methanol leaf extract of *Hemerocallis fulva* var. *semperviren*s (Ogawa and Konishi 2009). The structures of 1 and 2 were determined as N(2)-(1-β-D-fructopyranosyl)-N(5)-(2′,5′-dihydro-2′-furyl-3′-hydroxymethyl)-γ-hydroxyglutamine and N(2)-(1-β-D-fructopyranosyl)-N(5)-(2-hydroxymethylbutadienyl)-γ-hydroxyglutamine.

Aerial Plant Parts Phytochemicals

A 2,5-dimethoxytetrahydrofuran, fulvanol, has been extracted from *Hemerocallis fulva* var. *kwanso* along with fulvanines, 2,5-dihydrofuryl-γ-lactams (Konishi et al. 1966). The structure of fulvanol was established as 3-hydroxymethyl-2,5-dimethoxy- 3,4-dihydroxytetrahydrofuran. The structure of fulvanol was closely related to the branched-chain tetrofuranose apiose, occurring in the form of UDP-glycoside or as other cell components. The chloroform extract of *H. fulva* afforded chrysophanol, methyl rhein, 1,8-dihydroxy-3-methoxy-anthraquinone and rhein (Sarg et al. 1990). The unsaponifiable fraction yielded a long chain hydrocarbon, a long chain ester, a long chain alcohol and β-sitosterol. The aqueous fraction yielded choline.

Three novel 2,5-dihydrofuryl-γ-lactam derivatives, fulvanine A, B and C, were extracted from *H. fulva* var. *kwanso,* along with another compound (Inoue et al. 1990). Their respective structures were established as 1-(3-hydroxymethyl-2,5-dihydrofuryl)-azacyclopenta-3,5-dihydroxy-2-one, 1-(3-methyl-2,5-dihydrofuryl)-azacyclopenta-3,5-dihydroxy-2-one and 1-(3-methyl-2,5-dihydrofuryl)-azacyclopenta-3-hydroxy-5-methoxy-2-one. Another two 2,5-dihydrofuryl-γ-lactam derivatives, fulvanine D and E, were isolated from *Hemerocallis fulva* L. var. *kwanso* along with fulcanine A, B and C (Inoue et al. 1994). The structures of fulvanine D and E were established as 1-(3-hydroxymethyl-2,5-dihydro-2-furyl) and hydro-1,5-dioxa-8a-aza-asym-indacen-7-hydroxy-8-one.

Two steroidal saponins, hemeroside A and B, were isolated from the aerial part of *Hemerocallis fulva* var. *kwanso*, and their structures were established as 24S-hydroxy-neotokorogenin 1-*O*-α-L-arabinopyranosyl 24-*O*-β-D-glucopyranoside (1) and isorhodeasapogenin 3-*O*-β-D-glucopyranosyl-(1 → 3)-[β-D-xylopyranosyl-(1 → 2)]-β-D-glucopyranosyl-(1 → 4)-β-D-galactopyranoside (Konishi et al. 2001). Chlorogenic acids, namely, three caffeoylquinic acids (3-CQA 3-*O*-caffeoylquinic acid (I), 4-CQA 4-*O*-caffeoylquinic acid (III) and 5-CQA 5-*O*-caffeoylquinic acid (II)), three *p*-coumaroylquinic acids (3-*p*CoQA 3-*O*-*p*-coumaroylquinic (IV), 4-*p*CoQA 4-*O*-*p*-coumaroylquinic (VI) and 5-*p*CoQA5-*O*-*p*-coumaroylquinic (V)) and two feruloylquinic acids (3-FQA 3-*O*-feruloylquinic acid (VII) and 4-FQA4-*O*- feruloylquinic acid (IX)) were identified a methanolic extract of freeze-dried *Hemerocallis* (Chinese daylily) (Clifford et al. 2006).

Root Phytochemicals

Two anthraquinones, 7-hydroxy-1,2,8-trimethoxy-3-methylanthraquinone and 7,8-dihydroxy-1,2-dimethoxy-3-methylanthraquinone, were isolated from *Hemerocallis fulva* roots (Huang et al. 2003). The chloroform extract of *Hemerocallis fulva* dried roots afforded a novel diterpene named hemerocallal A, a naturally occurring diterpene with a *trans*-bicyclo[5.1.0]octane system (Yang et al. 2003). The butanol extract afforded a new glycoside named hemerocalloside. Seven new anthraquinones, kwanzoquinones A, B, C, D, E, F and G; two known anthraquinones, 2-hydroxychrysophanol and rhein; one new naphthalene glycoside, 5-hydroxydianellin; one known naphthalene glycoside, dianellin; one known flavone, 6-methylluteolin; and α-tocopherol were isolated from *Hemerocallis fulva* 'Kwanzo' roots (Cichewicz et al. 2002, 2004). From the n-butanol fraction of the ethanol root extract of *H. fulva*,

9 glycosides were isolated and identified as sweroside, laganin, picraquassioside C, puerarin, 3′-methoxypuerarin, 7-hydroxylnaphthalide-*O*-*β*-D-glucopyranoside, orcinol-3-*O*-β-glucopyranoside, HN saponin F and hederagenin-3-*O*-β D-glucopyranosyl-(1–3)-α-L-arabinopyranoside-28-*O*-β-D-glucopyranosyl ester (Yang et al. 2008).

Antioxidant Activity

Both water and ethanol extracts from hot-air-dried and freeze-dried daylily flowers exhibited strong antioxidant activity, in terms of total antioxidant activity, reducing capacity, superoxide anion scavenging activity and chelating activity (Que et al. 2007). Freeze-dried flowers had the strongest antioxidant activity with the highest content of phenolic compounds. Rutin, (+)-catechin and gallic acid were identified in daylily flowers and highly correlated with the antioxidant activities. Animal experiment also indicated that that freeze-dried flowers significantly reduced lipid peroxidation and enhanced the activity of antioxidant enzyme in blood and liver of mice. In the macrophage model system, the water extracts from fresh daylily flower, sponge gourd, pea sprout and eggplant exhibited over 80 % inhibition on NO (nitric oxide) generation stimulated by lipopolysaccharide (Bor et al. 2006). The extract from fresh daylily flower that expressed the strongest inhibition on NO production was attributed to the ability to reduce the inducible nitric oxide synthase (iNOS) induction. In addition, the water extracts from fresh daylily flower, sponge gourd, pea sprout and eggplant also showed over 40 % inhibitory effect on DNA damage induced by sodium nitroprusside in RAW 264.7 macrophage.

Studies showed that the growth area, flower age and processing method all significantly influenced the functional components and antioxidant activities of *H. fulva* grown in mountainous areas of Taiwan (Liu et al. 2010). The total phenols and anthocyanins of the methanol flower extracts of F1DF samples were 2.64 mg GAE/100 g dried basis (db) and 0.102 μmol/100 g db, which were significantly higher than the others. The total flavonoid contents of F1DF, F2DF, F3DF and D3DF were 20.83, 29.67, 31.65 and 22.30 mg QE/100 g db, respectively, with the F1DF level as the lowest. The reducing power showed that both the fresh and dried flowers were very weak. The amounts of most flavonoids in the flowers from Hualien were greater than those from Taidon.

Stelladerol isolated from the flowers was found to possess strong antioxidant properties, inhibiting lipid oxidation by 94.6 % at 10 μM in an in vitro assay (Cichewicz and Nair 2002). Several of the flavonol 3-*O*-glycoside isolates also demonstrated modest antioxidant activities at 10 μM. None of the isolates inhibited cyclooxygenase activity at 100 μM. Compounds roseoside, phlomuroside, lariciresinol and quercetin 3-*O*-β-D-glucoside,quercetin3,7-*O*-β-D-diglucopyranoside, quercetin 3-*O*-α-L-rhamnopyransol-(1 → 6)-β-D-glucopyranosol-7-O-β-D-glucopyranoside, isorhamnetin-3-*O*-β-D-6′-acetylglucopyranoside and isorhamnetin-3-*O*-β-D-6′-acetylgalactopyranoside isolated from the leaves were found to possess strong antioxidant properties, inhibiting lipid oxidation by 86.4, 72.7, 90.1, 79.7, 82.4, 89.3, 82.2 and 93.2 %, respectively, at 50 μg/mL (Zhang et al. 2004). Caffeoylquinic acid derivatives isolated from the flowers were found to be the major components with potent free radical scavenging activity in HepG2 cells (Lin et al. 2011).

Antiobesity Activity

Studies found *H. fulva* plant extract to be a novel lipolysis-promoting material that sensitized the lipolytic response of isolated adipocytes from rat subcutaneous fat to catecholamine and suggested that *H. fulva* could amplify the intracellular signalling pathway related to PKA (phosphokinase A) or modify the other mechanism-regulating lipase activity (Mori et al. 2009). The results suggested that *H. fulva* material could contribute to improvement of adipose mobility in obesity-related disorder or in subcutaneous adiposity and to suppression of body fat accumulation.

Anticancer Activity

Extracts of *Hemerocallis fulva* plant parts caused marked dose-dependent growth inhibition of human colon carcinoma cell lines, with IC_{50} values in the range of 10–80 μg/ml (Kaneshiro et al. 2005). With the HCT116 cell line, the extracts of *Hemerocallis fulva* induced G1 cell cycle arrest after 48 h of treatment.

Kwanzoquinones A–C and E, kwanzoquinone A and B monoacetates (1a and 2a), 2-hydroxychrysophanol and rhein, isolated from the roots, inhibited the proliferation of human breast, CNS, colon and lung cancer cells with GI_{50} values between 1.8 and 21.1 μg/mL (Cichewicz et al. 2004). However, upon exposure of the cancer cells to the GI_{50} concentrations of the bioactive anthraquinones, most of the cancer cell lines exhibited higher than anticipated levels of cell viability. Co-incubation of the anthraquinones with vitamins C and E increased the viability of breast cancer cells. In contrast, vitamins C and E potentiated the cytotoxic effects of the anthraquinones against the colon cancer cells. None of the anthraquinones inhibited the activity of topoisomerase.

Sleep-Promoting Activity

Studies showed that mice fed freeze-dried flowers of the Akinowasuregusa (*Hemerocallis fulva* var. *sempervirens*) had significant sleep-promoting effect compared with control mice (Uezu 1998). The slow wave sleep and paradoxical sleep of the H*emerocallis*-treated mice increased during the dark period. The Hemerocallis feeding did not cause a change in sleep time during the light period. As a result, there was no significant change in the sleep-time percentage over a 24-h period.

Antiparasitic Activity

Compound 2-hydroxychrysophanol isolated from the roots immobilized all cercariae of human pathogenic trematode *Schistosoma mansoni* within 15 s at 3.1 μg/mL (Cichewicz et al. 2002). However, upon removal of the compound, 20 % of the immobilized cercariae recovered after 24 h. In contrast, kwanzoquinone E immobilized cercariae within 12–14 min at 25 μg/mL. Following removal of the compound, all cercariae died within 24 h. The adult worms were also immobilized within 16 h by both compounds at 50 μg/mL. None of the compounds had an effect on the schistosomula stage.

Antimicrobial Activity

H. fulva plant extracts as well as some isolated compounds showed antimicrobial activity against Gram-negative and Gram-positive bacteria and *Candida albicans* (Sarg et al. 1990). *Hemerocallis fulva* 'Stella Deora' leaf extract was found to be most effective in inhibiting in vitro growth of bacteria *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis* and *Saccharomyces cerevisiae* yeast (Li et al. 2009).

Traditional Medicinal Uses

The results of herbal textural research showed that the original plants of the Chinese drug Xuancaogen in ancient times were *Hemerocallis fulva*, *H. fulva* var. *kwanso*, *H. citrina*, *H. lilioasphodelus* and *H. minor* (Zhang 1993). The erroneous scientific names of Beihuanghuacai and Shexiangcao in contemporary literature were corrected. Daylilies have been recorded to exhibit antidepressant affects, and it was ascribed as 'forget one's sorrow plant' in Japan and China (Tobinaga 1999). The plant has diuretic, febrifuge, laxative properties (Stuart 1979; Erhardt 1992). The flowers are anodyne, antiemetic, antispasmodic, depurative, febrifuge and sedative (Duke and Ayensu 1985). A flower extract is used as blood purifier and as an anodyne for women in childbirth in China (Chopra et al. 1986). A tea made from boiled rhizomes is used as a diuretic (Duke and Ayensu 1985; Erhardt 1992); the rhizome has a folk history of use in the treatment of cancer (Duke and Ayensu

1985). The juice from the rhizome is used as an antidote in cases of arsenic poisoning (Erhardt 1992). In Korea, the rhizome is used to treat oppilation, jaundice, constipation and pneumonia (NPRI-SNU 1998) and has antimicrobial, tuberculostatic and anthelmintic activity against parasitic worms that cause filariasis (NPRI-SNU 1998).

Other Uses

The plant is widely grown as an ornamental plant and is used in soil erosion control.

Comments

Four varieties of *H. fulva* are recognized in China (Chen and Noguchi 2000):

(a) var. *kwanso* with double perianth and petaloid stamens
(b) var. *aurantiaca* evergreen plant with single perianth and normal stamens
(c) var. *fulva* deciduous plant, single perianth, with rather short, stout perianth tube, 2–3 cm; inner segments 2–3.5 cm wide; stamens normal
(d) var. *angustifolia* plant deciduous, single perianth, tube long >4 cm, slender; inner segments 1–2.5 cm wide, stamens normal.

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Hemerocallis lilioasphodelus

Scientific Name

***Hemerocallis lilioasphodelus* L.**

Synonyms

Cameraria lilioasphodelus (L.) Boehm. *Hemerocallis flava* (L.) L., *Hemerocallis flava* var. *aurantiaca* A.I. Baranov & Skvortsov, *Hemerocallis lilioasphodelus* f. *aurantiaca* (A.I. Baranov & Skvortsov) Kitag., *Hemerocallis lilioasphodelus* var. *flava* L. (nom. illeg.), *Hemerocallis lilioasphodelus* var. *major* hort., *Hemerocallis lilioasphodelus* var. *nana* L, *Hemerocallis lutea* Gaertn.

Family

Xanthorrhoeaceae, also placed in Hemerocallidaceae, Liliaceae

Common/English Names

Golden Needles, Lemon Daylily, Lemon Lily, Yellow Daylily

Vernacular Names

Chinese: Kum Chan, (Cantonese), Jīnzhēn, Jin-Zhen Cai, Chin-Chen-T'sai, Huang-Hua-Cai, Huang-Hua T'sai, Bei Huang Hua Cai
Czech: Denivka Žlutá
Danish: Gul Daglilje
Dutch: Gele Daglelie
Estonian: Kollane Päevaliilia
Finnish: Keltapäivänlilja
French: Lis Asphodèle, Lis Jaune, Hémérocalle Jaune
German: Gelbe Taglilie
Hungarian: Sárgaliliom
Italian: Giglio Dorato
Japanese: Ezo Ki-Suge, Kanzou
Korean: Kohleep-Wonch'uri
Norway: Gul Daglilje
Russian: Krasodnev Želtyj
Swedish: Gul Daglilja, Klargul Daglilja
Vietnamese: Hoa Hiên Nhỏ

Origin/Distribution

The species is native to Russia (Siberia), Mongolia, China (Gansu, Hebei, Heilongjiang, Henan, Jiangsu, Jiangxi, Jilin, Liaoning, Shaanxi,

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Shandong, Shanxi), Korea, Japan and Europe; it is introduced and now naturalized in North America and elsewhere. Cultivated in China, Japan, Taiwan, India and Vietnam for its flowers used as vegetable and condiment.

Agroecology

Its natural habitat is found in forests, thickets, meadows, grasslands and slopes along valleys from 100 to 2,000 m altitude. Yellow daylily prefers full sun and rich, well-drained soil with a pH of 6–7.

Edible Plant Parts and Uses

All parts of the lemon lily are edible: root tubers, young leaves, young shoots, flower buds and flowers are eaten as vegetable. Flower buds and flowers (Plates 1, 2, 3 and 4) are eaten raw or cooked (Tanaka 1976; Gessert 1983; Facciola 1990; Erhardt 1992; Roberts 2000; Hu 2005; Tanaka and Nguyen 2007; Tanaka 1976; Gessert 1983; Facciola 1990; Erhardt 1992; Roberts 2000; Hu 2005; Tanaka and Nguyen 2007). They are mildly sweet and are used for crowning a frosted cake or used as a dramatic garnish, or the succulent petals can be added to spring salads. Flowers and buds are dipped in batter of milk, flour and eggs and seasoned and browned like fritter in oil or butter. In China and Southeast Asia, the flowers are harvested just before they open and are boiled or steamed and then dried as a traditional food (spice or condiment) called *Kum Cham* in Cantonese or *Jīnzhēn*, in pinyin, meaning 'golden needles'. Dried flowers give

Plate 1 Clumps of lemon lily

Plate 2 Close-view of flower and buds

Plate 3 Harvested lemon lily buds

Plate 4 Fleshy harvested lemon lily buds sold in a Thai local market

flavour to soups, stir-fries and noodle dishes. The fresh flower buds are available in local markets in Asia and the dried stuff sold in Asian food market stores in America, Europe and Australia. Two popular Chinese dishes are '*Mu xu rou*' (Daylily Egg-shred pork) and a vegetarian dish called *Luo-Han zhai* (Buddha Disciples' delight). Young leaves and young shoots about 6–8 cm high can be used as substitute for asparagus and cooked like asparagus or celery. The swollen roots are bland and sweetish and eaten cooked or roasted. When cooked, the small roots taste somewhat like sweet corn or salsify.

Botany

A small herb, 70–100 cm tall, deciduous in winter, with roots slightly fleshy sometimes with a swollen, tuberous part. Leaves linear, 20–70 × 0.3–1.2 cm, apex acuminate, dark green. Scape closely branched distally, 8–12 flowered, solid; main axis distinct; sterile lanceolate bracts present. Flowers showy, strongly sweet fragrant, yellow perianth tube shortly funnelform, 1.5–2.5 cm; tepals uniformly pale to bright lemon yellow or orangey-yellow, 5–7 cm by 1.3–1.6 cm, inner tepals slightly wider than the outer ones, margins smooth (Plates 1 and 2); filaments 5–5.5 cm; anthers 2–3 mm, yellow; ovary 5–6 mm; style white to yellow, 7–8 cm; pedicel 2–4 mm. Capsules ellipsoid, 2.5 by 1.2 cm. Seeds black, round or angular, 3–5 mm, shiny.

Nutritive/Medicinal Properties

Fifty-one components were identified in the essential oil of *Hemerocallis flava* daylily, constituting approximately 92 % of the oil; the main constituents of the essential oil were 3-furanmethanol (47.9 %) and 2-furancarboxaldehyde (10.4 %) (Lin et al. 2003).

Chlorogenic acids, namely, three caffeoylquinic acids (3-CQA 3-*O*-caffeoylquinic acid (I), 4-CQA 4-*O*-caffeoylquinic acid (III) and 5-CQA 5-*O*-caffeoylquinic acid (II)), three *p*-coumaroylquinic acids (3-*p*CoQA 3-*O*-*p*-coumaroylquinic (IV), 4-*p*CoQA 4-*O*-*p*-coumaroylquinic (VI) and 5-*p*CoQA5-*O*-*p*-coumaroylquinic (V)) and two feruloylquinic acids (3-FQA 3-*O*-feruloylquinic acid (VII) and 4-FQA4-*O*- feruloylquinic acid (IX) were identified in a methanolic extract of freeze-dried *Hemerocallis* (Chinese daylily) (Clifford et al. 2006).

Neuropharmacological Activity

Studies showed that the water extract of daylily as active in reducing motility in rats and that this effect may be related the decrease in the concentration of norepinephrine in the cortex and the concentration of dopamine and serotonin in brainstem (Hsieh et al. 1996).

Traditional Medicinal Uses

Dried flowers are significant as remedy in folk medicine for the circulatory system and diseases of the brain, the blood vessels and the skin, arthritis, rheumatism and various pains (Duke and Ayensu 1985; Chopra et al. 1986). The flowers have cooling and tranquilizing properties, are diuretic and antipyretic and said to improve appetite. In Vietnam, they are used to treat nosebleeding (Tanaka and Nguyen 2007). Root decoction is used to treat haematuria, nosebleeding, hepatitis otitis and mastitis. The juice of the roots has been reported to be an effective antidote in cases of arsenic poisoning. The root also has a folk history of use in the treatment of cancer—extracts from the roots have shown antitumour activity. A tea made from the boiled roots is used as a diuretic and possess anti-swelling property.

Other Uses

The tough dried foliage is plaited into cord and used for making footwear. Plants form a spreading clump and are suitable for ground cover when spaced about 45 cm apart each way. There are many cultivars of considerable interest as

ornamentals. In the lower Yellow River Region in China, many yellow or orangey varieties are grown as cash crop.

Comments

In some books, *Kum cham* has been erroneously identified as *Hemerocallis fulva*, the red or tawny daylily, the flowers of which are orange with red tone near the centre. Also according to Prof Hu, the flower buds of *H. fulva* are rarely used as food in China and the young leaves are eaten by some people living on the hillsides in China.

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Etlingera elatior

Scientific Name

***Etlingera elatior* (Jack) R.M. Smith**

Synonyms

Alpinia acrostachya Steud., *Alpinia diracodes* Loes. nom. illeg., *Alpinia elatior* Jack, *Alpinia magnifica* Roscoe, *Alpinia javanica* (Blume) D. Dietr., nom. illeg., *Alpinia speciosa* (Blume) D. Dietr., *Amomum magnificum* (Roscoe) Benth. & Hook.f. ex B.D.Jacks., *Amomum tridentatum* (Kuntze) K.Schum., *Bojeria magnifica* (Roscoe) Raf., *Cardamomum magnificum* (Roscoe) Kuntze, *Cardamomum speciosum* (Blume) Kuntze, *Cardamomum tridentatum* Kuntze, *Diracodes javanica* Blume, *Elettaria speciosa* Blume, *Etlingera elatior* var. *alba* Todam & C.K.Lim, *Etlingera elatior* var. *pileng* Ongsakul & C.K. Lim, *Geanthus speciosus* Reinw. ex Blume, nom. nud., *Hornstedtia imperialis* (Lindl.) Ridl., *Nicolaia elatior* (Jack) Horaninow, *Nicolaia imperialis* Horan., *Nicolaia intermedia* Valeton, *Nicolaia magnifica* (Roscoe) K.Schum. ex Valeton, *Nicolaia speciosa* (Blume) Horan., *Phaeomeria imperialis* Lindl., nom. inval., *Phaeomeria magnifica* (Roscoe) K. Schum., *Phaeomeria speciosa* (Blume) Koord.

Family

Zingiberaceae

Common/English Names

Ginger Bud, Ginger Flower, Ginger Flower Buds, Indonesian Tall Ginger, Javanese Aromatic Ginger, Philippine Waxflower, Pink Ginger Bud, Porcelain Ginger, Red Ginger Lily, Torch Ginger, Torch Lily, Torch Nicola Flower Buds, Wild Ginger

Vernacular Names

Brazil: Rosa-De-Porcelana
Chinese: Huo Ju Jiang, Xiang Bao Jiang, Xiang Hua Ya Jiang
French: Gingembre Aromatique, Gingembre Aromatique De Java, Gingembre Aromatique Des Malais
German: Malayischer Fackelingwer
Hawaiian: ‘Awapuhi-Ko’oko’o
Indonesian: Bunga Combrang, Bunga Kantan, Bunga Siantan, Combrang, Kantan, Kecumbrang, Kecombrang, (Javanese), Honje, Honje Benar, Hnonje Berem (Fruit Blood Red), Honje Bodas (Fruit Yellowish-White), Honje Laka (Fruit Dark Carmine Red), Honje Leweng, Honje Jangkring, Combrang, Rombeh (Sudanese), Ptikala (Maluku)
Malaysia: Bunga Kantan, Kantam, Tepus Kampong (Peninsular), Tuhau, Tikaloh, Kechala (Iban), Ubad Udat (Kelabit)
Marquesas: Opuhi, Eka, Pua Vao
Spanish: Antorcha, Boca De Dragón
Tahitian: ‘Awapuhi, Opuhi
Thai: Kaa Laa

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Origin/Distribution

The species is native to Southeast Asia—Indonesia, Malaysia and South Thailand; it is widely cultivated pantropically and naturalized in Southeast Asia.

Agroecology

In its native range, it occurs in open areas, at margins of primary and secondary forest at low elevations, and is not found in montane forest areas. It is also cultivated as an ornamental garden plant. It thrives in partial shade, in fertile, well-drained, moist soil rich in humus. It will grow on acid soils.

Edible Plant Parts and Uses

Flower petal, and receptacle, hearts of young leafy pseudostems, flower buds, fruit (Plates 5, 6, 7, 8, 9, 10 and 11), seed and rhizome are used as condiments, eaten raw as salad, cooked in various ways or pickled (Burkill 1966; Tanaka 1976; Facciola 1990; Ochse and Bakhuizen van den Brink 1980; Noweg et al 2003; Wetwitayaklung et al. 2008; Chan et al. 2011b). Flower petals and half-ripe fruiting shoots are widely used in curries, particularly in Penang laksa, nasi ulam, nasi kerabu, rojak or cooked in mixed vegetables. They are also eaten fresh as ulam. Less commonly the heart of young vegetative shoots is used for flavouring dishes or eaten raw as ulam with rice. The Sudanese used the heart of the young shoots called humbut or boros as *lalap*; the large inflorescence is used for *sayor* or *ange* (in Sundanese), especially in *sayur lodeh* (vegetable dish with red shallots, garlic, chilli, pepper, pounded shrimps, tamarind, salt, sugar), raw or cooked for *lalap* (dish of raw vegetables with spicy sauce) or *urab* (steamed vegetable side dish). The Javanese also used the flowers for making *pejak* where the inflorescence is first roasted, mixed with santan (coconut milk), lombok (chilli), trasi (pounded dried shrimps) and kencur. Half-ripe fruits are also used in cooking, either added to sayor or as pejak with dengdeng (dried beef). The mature fruits of *Etlingera elatior* are edible but sour and are reputed for their antihypertensive activity. They are also processed into candies or *manisan*. The ripe seeds are also eaten raw. In North Sumatra, the flower buds are used for a dish called *arsik ikan mas* (Andaliman peppercorn spiced carps). In North Sumatra, another common Karo dish with the flower bud is *asam cekala* (asam meaning 'sour'), and the ripe seed pods, which are packed with small black seeds, are an essential ingredient of the Karo version of *sayur asam* which is cooked with fresh fish.

Botany

A coarse tall, perennial herb with closely grouped pseudostems reaching 3–4 m high (Plates 1, 2 and 4). Ligule is bilobed and glabrous; petiole

Plate 1 Plant habit of red torch ginger

Plate 2 Red torch ginger inflorescences

Plate 3 Close up of red torch ginger inflorescences

3–4 cm; leaf blade lanceolate, glabrous, 80 cm long by × 18 wide. Inflorescence is borne on a robust, long (0.8–15 m) peduncle (scape) raised well above ground and is surrounded by red, tapering, glabrous involucral bracts, 2–3 × ca. 1 cm; floral bracts are similar to involucral bracts but pinkish and smaller (Plates 1, 4, 5 and 6). The bracteoles are tubular, 2 cm, deeply split on 1 side. Calyx is 3–4 cm, with 3-toothed apex. Corolla is pink to red, sometimes white (Plates 2, 3, 4, 5, 6, 7 and 8). Labellum is deep red with a yellow margin. Filament is short, flat, whitish and pubescent; anther is long and red. Fruiting head (infructescene) is greenish, yellowish orangey or reddish, ellipsoid (Plates 9 and 10) sometimes subglobose, about 2.5 cm across containing many small black seeds.

Nutritive/Medicinal Properties

Nutrient and Phytochemical in the Flowers

Flowers of *Etlingera elatior* were reported to contain the following per 100 g edible portion: water 91 g, protein 1.3 g, fat 1.0 g, carbohydrates 4.4 g, fibre 1.2 g, K 541 mg, P 30 mg, Ca 32 mg, Mg 27 mg, Fe 4 mg, Mn 6 mg, Zn 0.1 mg and Cu 0.1 mg (Ibrahim and Setyowati 1999). The edible hearts of young vegetative shoot comprised 20–325 % of the total weight of unpeeled young shoots. A recent study by Wijekoon et al. (2011b) reported the following proximate

Plate 4 Habit Pink torch ginger

Plate 5 Half-opened pink torch ginger flowering head

Plate 6 Fully opened torch ginger inflorescence

Plate 7 Unopened torch ginger inflorescences on sale in a local market

Plate 8 Opened and unopened torch ginger inflorescences on sale in a local market

Plate 9 Infructescence of pink torch ginger

nutrient composition of torch ginger inflorescence (g/100 g dry weight basis): crude protein 12.6 g, crude lipid 18.2 g, crude fibre 17.6 g, ash 15.5 g, nitrogen-free extract 36.3 g and energy value 1,322.3 kJ/100 g; elements (mg/100 g dry weight) including Ca 775.3 mg, K 1,689 mg, P 286 mg, Mg 327.1 mg, S 167 mg, Mn 8.3 mg, Zn 2.8 mg, Na 4.5 mg, Fe 2.4 mg, B 2.6 mg, Fl 1.4 mg, Cu 0.6 mg, Se <0.1 mg, Co <0.1 mg, Cr <0.1 mg and Mo <0.1 mg; total saturated fatty acids 57.8 %, total unsaturated fatty acids 42.2 %, myristic acid (C14:0) 47.6 %, palmitic acid (C16:0) 9.0 % and stearic acid (C18:0) 1.2 %; palmitoleic acid (C16:1n7) 16.4 %, hexadecadienoic acid (C16:2n4) 1.1 %, hexadecatrienoic acid (C16:3n4) 0.1 %, hexadecatetraenoic acid (C16:4n3) 0.4 %, oleic acid (C18:1n9) 5.2 %, *cis*-vaccenic acid (C18:2n7) 0.8 %, linoleic acid (C18:2n6 14.5) %, octadecatrienic acid (C18:3n4) 1.1 %, α-parinaric acid (C18:4n3) 3.2 %, *cis*-11-eicosenoic acid/gondoic acid (C20:1n9) 0.1 %, eicosatetraenoic acid (C20:4n3) 0.2 %, cetoleic acid (C22:1n11) 0.7 %, docosapentaenoic acid/cupanodoic acid

Plate 10 Infructescence of red torch ginger

Plate 11 Hearts of young pseudostems peeled above and unpeeled below

(C22:5n3) 0.4 %; and amino acids (mg/100 mg) including histidine 2.3 mg, isoleucine 4.2 mg, leucine 7.2 mg, lysine 7.9 mg, methionine 0.8 mg, phenylalanine 4.1 mg, threonine 4.4 mg, valine 5.0 mg, alanine 5.1 mg, arginine 6.2 mg, aspartic acid 9.4 mg, cysteine 4.7 mg, glutamic acid 10.1 mg, glycine 4.2 mg, proline 3.0 mg, serine 4.8 mg and tyrosine 2.5 mg. Antinutrients (mg/100 g dry weight) included saponin 3,496 mg, phytic acid 2,851 mg, Cd <0.1 ppm, Pb <0.1 ppm, Ni <0.1 ppm, As <0.01 pm and Hg <0.01 ppm.

Proximate nutrient composition (g/100 g DW) of *Etlingera elatior* was reported as: moisture (94.9 g/100FW), energy 225 kcal, carbohydrate 36.4 g, protein 16.2 g, fat 1.6 g, fibre 19.8 g, ash 17.6 g, macroelements (mg/g) (Na 5.2 mg, K 39.0 mg, Mg 2.91 mg, Ca 11.5 mg) and microelements (Fe 3.6 mg/100 g, Zn 183.9 μg/g, Cu 107.7 μg/g, ascorbic acid 272.2 μg/g, γ-tocopherol 11.5 μg/g, α-tocopherol 12.3 μg/g, thiamin 3.2 μg/g and riboflavin 4.4 μg/g) (Ng et al. 2012).

Ethanol and acetone extract of the flowers were determined to have 1,928 mg and 244 mg GAE (gallic acid equivalent)/100 g fresh plant of total phenol content (TPC), 324.8 and 17.6 mg QE (quercetin equivalent)/100 g fresh plant of total flavonoid content (TFC), and 0 and 1.05 mg of CGE (cyanidin- 3-glucoside)/100 g fresh plant of total anthocyanin content, respectively (Mai et al. 2009). Of all the solvents employed, namely, methanol, acetone and distilled water, 50 % acetone extract showed highest amount of total phenols (687.0 mg GAE/100 g) and total flavonoids (1,431 mg QE/100 g), while 50 % methanol extract showed maximum (5.9 mg cynidin-3-glucoside equivalent/100 g) recovery for anthocyanins from *E. elatior* inflorescence (Wijekoon et al. 2011a). Tannin extractability was found to be highest with 100 % methanol (467.8 mg CE/100 g). The results obtained suggested the use of bunga kantan inflorescence as a potential source of natural antioxidants for food and nutraceutical applications.

Among the 49 compounds identified in the young flower shoots, the major chemical classes were the aliphatic alcohols (42.1 %) and aldehydes (21.4 %), while terpenoid compounds constituted 18.2 % of the oil (Wong et al. 1993). Monoterpenes hydrocarbons were the major type of compounds present in the essential oils of the flowers of *E. elatior* with 47.20 % followed by oxygenated monoterpene derivatives 30.83 % (Faridahanim et al. 2007). The dominant constituents were cyclododecane (40.32 %), 1,1-dodecanediol diacetate (24.38 %) and α-pinene (6.30 %). Other constituents included caryophyllene (4.45 %), (*E*)-2-hexenal (4.37 %),

(*Z*)-hexadecene (3.72 %), decanal (3.62 %), β-pinene (0.10 %), D-limonene (0.33 %), 9-octadecenal (0.45 %0, α-caryophyllene (0.27 %, (*Z*)-β-farnesene (0.30 %), 1,13-tetradecadiene (0.72 %), 1-heptadecene (0.04 %), dodecanoic acid tetradecyl ester (0.44 %), elaidic acid (0.43 %), 2,3,dihydroxypropyl octadec-9-enoate (glyceryl) palmitoleate) (0.04 %),oleic acid (0.25 %) and glyceryl monooleate (0.05 %). The major volatile components identified in the oils of inflorescence and inflorescence axis of *E. elatior* were dodecanol (42.5 %, 34.6 %), dodecanal (14.5 %, 21.5 %) and α-pinene (22.2 %, 6.3 %), respectively (Zoghbi and Andrade 2005).

Leaf Phytochemicals

Ethanol and acetone extract of the leaves were determined to have 3,064 and 902 mg GAE (gallic acid equivalent)/100 g fresh plant of total phenol content (TPC); 320.4 and 13.9 mg QE (quercetin equivalent)/100 g fresh plant of total flavonoid content (TFC), respectively (Mai et al. 2009). Flavonoids of kaempferol 3-glucuronide, quercetin 3-glucuronide, quercetin 3-glucoside and quercetin 3-rhamnoside had been reported in the leaves (Williams and Harborne 1977). Three caffeoylquinic acids including chlorogenic acid (CGA) and three flavonoids quercetin, isoquercetin and catechin were isolated from the leaves (Chan 2009). Caffeoylquinic acids (CQA), namely, 3-*O*-caffeoylquinic acid and 5-*O*-caffeoylquinic acid methyl ester, including chlorogenic acid CGA (5-*O*-caffeoylquinic acid), were isolated from the leaves (Chan et al. 2009b). The content of CQA of *E. elatior*, *Etlingera fulgens* and *Etlingera rubrostriata* leaves was significantly higher than that of the leaves of *Ipomoea batatas* and comparable to the flowers of *Lonicera japonica*. Also they reported that leaves of *Etlingera* species were rich in total phenols and CQA and non-cytotoxic to normal human liver and African green monkey kidney cells. Chlorogenic acid found only in the leaves of *E. elatior* and *E. fulgens* was significantly higher in content than that of the flowers of *L. japonica* and the commercial source and may have great potential to be developed into functional food and other health products (Chan et al. 2009b, 2011a).

Sesquiterpene hydrocarbons dominated the essential oils of the leaves of *E. elatior* with 45.06 %, followed by monoterpene hydrocarbon 29.75 % (Faridahanim et al. 2007). Major components were (*E*)-β-farnesene (27.90 %), β-pinene (19.17 %) and caryophyllene (15.36 %). Other components included α-thujene, α-pinene (6 %), camphene (0.11 %), sabinene (0.13 %), β-myrcene (2.49 %), α-terpinolene (0.06 %), 1,3,8-*p*-menthatriene (0.04 %), α-terpinene (0.15 %), cyclododecane (1.57 %), eucalyptol (3.85 %), 2-ethyl fenchone (0.27 %, camphor (0.12 %), borneol (4.24 %), dihydrocavreol (0.55 %), α-terpineol (1.84 %), 1,1,dodecanediol diacetate (1.45 %), β-elemene (0.34 %), α-caryophyllene (1.46 %), *trans*-nerolidol (0.68 %) and octadac-9-enoic acid (0.16 %). Abdelmageed et al. (2011) found 73 compounds in the leaf essential oil of *E. elatior*. The most abundant components included β-pinene (24.92 %), 1-dodecene (24.31 %), bicyclo[3.1.1] hept-2-ene,2,6,6-trimethyl (11.59 %), dodecanal (8.15 %), acetic acid (3.49 %), *trans*-(*Z*)-α-bisabolene epoxide (2.56 %), β-farnesene (2.49 %), 1,6,10,-dodecatriene, 7,11-dimethyl-3-meth-ylene (2.41 %), 1,3-propanediol, 2-dodecyl (2.27 %), α-caryophyllene (1.99 %), 3-bromo-7-methyl-1-adamantanecarboxylic acid (1.38 %) and 2-pentadeyn-1-ol (1.22 %).

Phytochemicals in Stem and Rhizomes

Ethanol and acetone extract of the stems were determined to have 556 and 228 mg GAE (gallic acid equivalent)/100 g fresh plant of total phenol content (TPC), 37.9 and 16 mg QE (quercetin equivalent)/100 g fresh plant of total flavonoid content (TFC), respectively (Mai et al. 2009). Ethanol and acetone extract of the rhizomes were determined to have 642 and 393 mg GAE (gallic acid equivalent)/100 g fresh plant of total phenol content (TPC); 0 and 23.7 mg QE (quercetin equivalent)/100 g fresh plant of total flavonoid content (TFC), respectively (Mai et al. 2009).

Oxygenated monoterpene derivatives were the major type of compounds in the essential oils of the stems and rhizomes of *E. elatior* with 53.99 % and 47.28 %, respectively (Faridahanim et al. 2007). The rhizome contained 34.45 % cyclododecane, 24.38 % 1,1,dodecanediol diacetate and minor constituents 2,3,dihydroxypropyl octadec-9-enoate (glyceryl) palmitoleate) (0.45 %),oleic acid (0.52 %) and glyceryl monooleate (0.12 %). Dominant components in the essential oil of the stem were 1,1,dodecanediol diacetate (34.26 %), (*E*)-5-dodecene (26.92 %), decanal 16.53 % and caryophyllene 6.60 %.

From the rhizomes, 1,7-bis(4-hydroxyphenyl)-2,4,6-heptatrienone; demethoxycurcumin; 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one; 16-hydroxylabda-8(17),11,13-trien-15,16-olide; stigmast-4-en-3-one; stigmast-4-ene-3,6-dione; stigmast-4-en-6β-ol-3-one; 5α,8α-epidioxyergosta-6,22-dien-3β-ol; tetracosanoic acid; and a mixture of stigmasterol and β-sitosterol were isolated (Habsah et al. 2005a).

Antioxidant Activity

Etlingera elatior also possesses antioxidant activities. Three diarylheptanoids, 1,7-bis(4-hydroxyphenyl)-2,4,6-heptatrienone, demethoxycurcumin and 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one, isolated from the rhizomes were found to inhibit lipid peroxidation in a more potent manner than alpha-tocopherol (Habsah et al. 2005a). The total antioxidant activity of *E. elatior* extract was 89.23 % as evaluated by β-carotene/linoleic acid system (Ng et al. 2012). The effective concentration, EC_{50}, value of the *E. elatior* extract in DPPH scavenging activity was 1.80 mg extract/ml, and EC_{50} value of the ferrous ion chelating activity was 2.26 mg extract/ml. Total phenolic content of the extract was 4.1 mg GAE/g FW and total flavonoid 1.4 mg RE/g FW.

The whole plant of *E. elatior* had lower DPPH scavenging activity (995 ug/ml) than that of the leaves of *Cinnamomum pubescens* (77.2 ug/ml) although *E. elatior* had a higher total flavonoid content of 244.83 g RE (rutin equivalent)/Kg compared to *C. pubescens* with 205.65 g RE/Kg (Abdelmageed et al. 2011). Total phenolic content of *E. elatior* was 3341.2 g GAE/Kg.

The percent yield of extract and the amount of total polyphenols in g/100 g calculated as gallic acid on dried flowers, and crude methanolic extract bases for *E. elatior* were reported as 18.68 (% yield), 0.37 g total polyphenols (g/100 g dried flower) and 2.00 g total polyphenols (g/100 g crude extract) (Wetwitayaklung et al. 2008). Antioxidant capacity for *E. elatior* flowers expressed in TEAC (trolox equivalent antioxidant capacity) = 0.04 and IC_{50} = 279.32 μg/50 μl. There was a good linear relationship between antioxidant activity and flower extract concentrations with $R^2 = 0.9709$.

Of the 26 ginger species screened, leaves of *Etlingera* species had the highest total phenol content and ascorbic acid equivalent antioxidant capacity (AEAC) (Chan et al. 2008). For total phenol content (mg GAE/100 g) ranking was in the order of *E. elatior* (2390) > *Etlingera rubrostriata* (2250) > *Etlingera littoralis* (2150) > *Etlingera fulgens* (1280) > *E. maingayi* (1110). In terms of AEAC (mg ascorbic acid/100 g), ranking sequence was *E. rubrostriata* (2290) > *E. elatior* (2280) > *E. littoralis* (1990) > *E. maingayi* (963) > *E. fulgens* (845). In an earlier study of five *Etlingera* species, highest total phenolic content (TPC), ascorbic acid equivalent antioxidant capacity (AEAC) and ferric reducing antioxidant power (FRAP) were found in leaves of *Etlingera elatior* and *E. rubrostriata* (Chan et al. 2007). Leaves of *E. maingayi*, with the lowest TPC, AEAC and FRAP, had the highest ferrous ion chelating (FIC) ability and β-carotene bleaching (BCB) activity. Ranking of TPC and AOA (antioxidant activity) of different plant parts of *E. elatior* was in the order leaves > inflorescences > rhizomes. Leaves of highland populations of *Etlingera* species displayed higher values of TPC and AEAC than those of lowland counterparts. Leaves of *Etlingera* species exhibited antibacterial activity against Gram-positive of *Bacillus cereus, Micrococcus luteus* and *Staphylococcus aureus* but not Gram-negative bacteria. In another study with five Zingiberaceae species, freeze-drying resulted in significant gains in TPC,

AEAC and FRAP for *Alpinia zerumbet* and *Etlingera elatior* leaves (Chan et al. 2009a). After 1 week storage, AOP of freeze-dried *E. elatior* leaves remained significantly higher than those of fresh control leaves. Freeze-dried tea of *A. zerumbet* was superior to the commercial tea for all antioxidant activities studied.

Treatment of rats with *E. elatior* pre- or post-treatment after lead acetate exposure decreased lipid hydroperoxides and protein carbonyl contents and significantly increased total antioxidants and antioxidant enzymes (Nagaraja et al. 2010b). Treatments with *E. elatior* extract also reduced lead-induced histopathological damage in bone marrow. The results suggested *E. elatior* to have a powerful antioxidant effect and could protect lead acetate-induced bone marrow oxidative damage in rats. Supplementation of rats exposed to lead acetate in the drinking water with *E. elatior* ethanol flower extract for 14 days reduced serum lipid hydroperoxides and protein carbonyl contents and significantly increased total antioxidants and antioxidant enzyme levels (Tan et al. 2011). The results suggested that flower extract of *Etlingera elatior* had powerful antioxidant effect against lead-induced oxidative stress and the extract may be a useful therapeutic agent against lead toxicity.

Anticancer Activity

The flower shoot extract showed also promising antitumour-promoting activity (Murakami et al. 2000). $CHCl_3$ and MeOH extracts of *E. elatior* possessed high antitumour-promoting activity, with 92.18 and 85.9 % inhibition rate, respectively (Habsah et al. 2005b). Both hexane and ethyl acetate were cytotoxic against Raji cell at initial concentration (200 mg/ml). Among the compounds isolated from the rhizome, stigmast-4-en-3-one and stigmast-4-en-6β-ol-3-one, a mixture of β-sitosterol and stigmasterol and tetracosanoic acid showed high antitumour-promoting activity, with inhibition rate of 78.4 %, 80.6 %, 85.1 % and 72.4 %, respectively. Compound stigmast-4-ene-3,6-dione only showed moderate activity with an inhibition rate of 56.9 %. The ethyl acetate extract of the rhizome showed a very significant cytotoxic activity against CEM-SS (human T lymphoblastoid) and MCF-7 breast cancer cell lines (4 mg/ml and 6.25 mg/ml, respectively) as determined through MTT assay. The other extracts, including the hexane, $CHCl_3$ and methanol extracts, also showed significant cytotoxicity against both MCF-7 and CEM-SS cell lines. In an earlier study, demethoxycurcumin from *Curcuma zedoaria* exhibited cytotoxicity effect against ovarian cancer OVCAR-3 cells (Syu et al. 1998).

Ethanol extract of *E. elatior* flower shoots exhibited cytotoxic activity against glandular cervix cancer cells with curative dose CD_{50} values in the range of 10–30 µg/ml (Mackeen et al. 1997). Among the acetone extracts of *E. elatior* leaves, rhizomes, stems and flowers, the leaf extract was the most potent against human colorectal cancer cells (HT29) with IC_{50} value of 170 µg/ml (Mai et al. 2009). Cell death was mediated via apoptosis. The extract did not inhibit proliferation of Chinese hamster ovary cells up to 250 µg/ml.

Tyrosinase Inhibition Activity

Of five *Etlingera* spp., tyrosinase inhibition activity was strongest in leaves of *E. elatior* (55.2 %), which was significantly higher than that of the positive control of *Hibiscus tiliaceus* (43.9 %) (Chan et al. 2008). Inhibition activities of leaves of *E. fulgens* (49.3 %) and *E. maingayi* (42.6 %) were comparable. Activities of leaves of *E. rubrostriata* (29.5 %) and *E. littoralis* (22.0 %) were significantly lower.

Hepatoprotective Activity

Studies found that co-treatment of male Sprague–Dawley rats with lead acetate and *Etlingera elatior* extract significantly reduced lipid hydroperoxides and protein carbonyl content in serum and increased the antioxidant enzyme levels in the liver (Nagaraja et al. 2010a). Treatment with *E. elatior* significantly reduced lead-induced alterations in hepatic architecture, which also

reduced the blood lead levels. The results suggested *E. elatior* to have a potent effect against lead-induced hepatotoxicity. Demethoxycurcumin (also isolated from *E. elatior* rhizome (Habsah et al. 2005b)) displayed DPPH free radical scavenging activity and showed significant hepatoprotective effects on tacrine-induced cytotoxicity in human liver-derived Hep G2 cells (Song et al. 2001)

Testicular Protective Activity

Etlingera elatior was found to be effective against oxidative damage caused by lead acetate in the testis (Haw et al. 2012). Studies showed that *E. elatior* treatment only, concurrent treatment of lead acetate and *E. elatior* and posttreatment of lead acetate followed by *E. elatior* or pretreatment (preventive) of *E. elatior* in rats, improved the histology of the testis when compared to the lead acetate-treated group. *E. elatior* induced a significant reduction in the testis protein carbonyl content activity, while at the same time it significantly increased the activities of superoxide dismutase and glutathione peroxidase in the testis and the testosterone level in the serum.

Traditional Medicinal Uses

In folkloric medicine in Malaysia (Burkill 1966), a decoction of the fruit is dropped into the ear for earache. A decoction of the leaves is used for cleaning wounds. A decoction of young shoots with other herbs is used to reduce body odour after giving birth.

Other Uses

In Sumatra the stem is made into matting. The stem also has potential for paper manufacture. The rhizome yields a yellow dye. The plant is grown commercially as a decorative cut flower for its long scape and attractive, unique inflorescence which has a vase life of several weeks.

Comments

E. elatior is normally propagated by division of the rhizome, but this affords a low proliferation rate. An efficient protocol for complete plant regeneration from suckers has been developed by Yunus et al. (2012). Also *E. elatior* can be micropagated using plantlets derived from axillary bud explants cultured on Murashige and Skoog (MS) basal medium, supplemented with various concentrations of cytokinin (BAP, 6-benzylaminopurine) or auxin (IAA, indole acetic acid) as plant growth regulators (Abdelmageed et al. 2011).

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Etlingera hemisphaerica

Scientific Name

***Etlingera hemisphaerica* (Blume) R.M. Sm.**

Family

Zingiberaceae

Synonyms

Alpinia hemisphaerica (Blume) D. Dietr., *Amomum anthoidioides* (Teijsm. & Binn.) Koord., *Amomum eriocarpum* (Kuntze) K. Schum., *Amomum hemisphaericum* (Blume) K. Schum., *Cardamomum anthodiodes* (Teijsm. & Binn.) Kuntze, *Cardamomum eriocarpum* Kuntze, *Cardamomum hemisphaericum* (Blume) Kuntze, *Elettaria anthodioides* Teijsm. & Binn., *Elettaria atropurpurea* Teijsm. & Binn., *Elettaria hemisphaerica* Blume, *Nicolaia anthodioides* (Teijsm. & Binn.) Valeton, *Nicolaia atropurpurea* (Teijsm. & Binn.) Valeton, *Nicolaia hemisphaerica* (Blume) Horan., *Nicolaia rostrata* Valeton *Nicolaia rostrata* var. *talangensis* Valeton, *Nicolaia sanguinea* Valeton, *Phaeomeria anthodioides* (Teijsm. & Binn.) Koord., *Phaeomeria atropurpurea* (Teijsm. & Binn.) K. Schum., *Phaeomeria hemisphaerica* (Blume) K. Schum., *Phaeomeria rostrata* (Valeton) Loes., *Phaeomeria sanguinea* (Valeton) Koord.

Common/English Names

Helani Tulip Ginger, Tulip Ginger

Vernacular Names

Indonesia: Sikala (Bengkulu), Sekala (East Sulawesi), Honje Leuweung, Honje Hejo, Honje Laka (Sundanese); Honje Hutan
Malaysia: Kantan Liar
Thailand: Kaa Laa

Origin/Distribution

It is found in the lower mountainous forest in Java and perhaps also in Sumatra. It has been introduced and naturalized in other areas in Malesia and is also now grown elsewhere in the tropics.

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Agroecology

A wet tropical plant species, it thrives in partial shade in moist, well-drained, fertile soil rich in organic matter. It will grow in warm and wet subtropical areas.

Edible Plant Parts and Uses

The plant is used as a spice (Ibrahim and Setyowati 1999). In Indonesia, the inflorescence is used for *sayur lodeh* (Malay) or *angen lodeh* (Sundanese); the half-ripe fruits are mixed raw into various sayur while the ripe fruits are made into *manisan* (fruit comfit), the soft heart of the stem called *hubut* or *boros* is eaten raw, cooked or steamed (Ochse and Bakhuizen van den Brink 1980).

Botany

A clumping, robust, terrestrial, geophyte with copiously branched subterraneous or partly superterraneous rhizome. Leafy, spurious, dark green pseudostems, erect, 3–5.5 m high, thickened at the base, 3–5 cm thick (Plate 2). Leaves distichous, alternate, upper leaves larger than the lower leaves, lamina to 77 × 16 cm, ovate–oblong to elliptic–linear, glabrous on both surfaces, dark green above, red beneath, base more or less auriculate, costa red above on young leaves (Plate 1). Petiole short 2 cm long, broadly furrowed on anterior side, with a broadly rounded or ovate–oblong green ligule at the base. Inflorescence lateral, arising from the base, obovoid or turbinate with a flat or depressed apex; peduncle robust, erect, 35–100 cm long closely embraced by large green amplexicaul bracts; uppermost bracts enclosing base of spike (Plates 2 and 3). Spike

Plate 1 Foliage—dark green above, reddish below

Plate 2 Red inflorescences on long peduncles

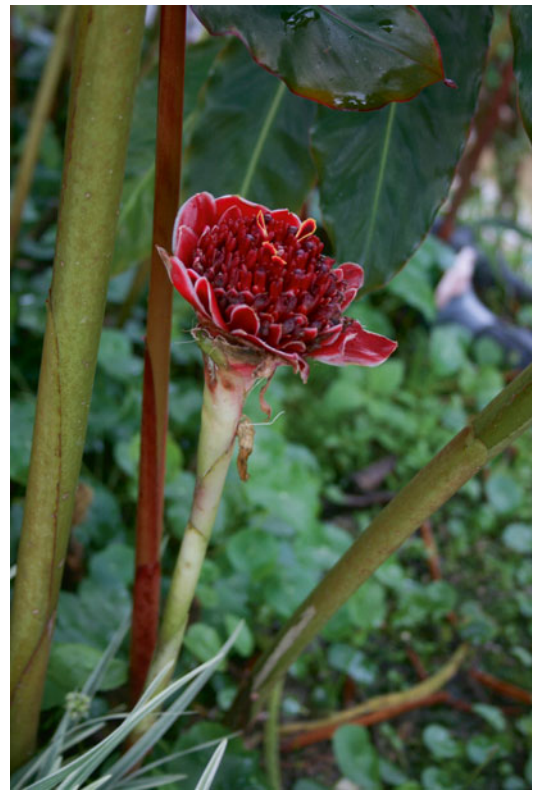

Plate 3 Close view of inflorescence

Plate 4 Ripening infructescence

6–7 × 3–6 cm with five sterile bracts, white tinged green at base and pink at apex. Receptacle 1.2–1.5 cm with 38–49 closely crowded flowers. Fertile bract short-lived, tinged red—also inside. Bracteole cream tinged red. Calyx narrowly tubular, red with yellow-green apex. Corolla tubular 3-fid, white; segments dark red (burgundy) with white margin. Labellum broadly ovate, cymbyform with rounded apex, dark red with white undulating margin laterally, yellowish at apex. Filament cream. Anther red, darker at apex. Style terete, pilose, red. Stigma purple. Infructescence to 5.5 × 8 cm, with 2–20 fruits. Fruit green, ripening yellowish-green, apex truncate to slightly depressed (Plate 4). Seeds numerous, ovoid, angular, brownish-black, hard, arillate.

Nutritive/Medicinal Properties

No information on its nutritive and medicinal properties has been published. Refer to notes on a closely related species, *Etlingera elatior*.

Other Uses

It is grown as an ornamental in parks and gardens for its foliage with wine red undersurface and unusual inflorescence.

Comments

The plant is normally propagated by division of the rhizome. Studies showed that *Etlingera hemisphaerica* cv. 'Red Tulip' and 'Black Tulip' can be micropropagated from explants derived from apices of terminal and lateral buds cultured in the Murashige and Skoog medium, supplemented with various cytokinin and growth regulators (benzyladenine) (Barra and Mogollon 2007).

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Hedychium coronarium

Scientific Name

***Hedychium coronarium*. J. König.**

Synonyms

Amomum filiforme Hunter ex Ridl., *Gandasulium coronarium* (J. König) Kuntze, *Gandasulium lingulatum* (Hassk.) Kuntze, *Hedychium chrysoleucum* Hook., *Hedychium coronarium* var. *baimao* Z.Y. Zhu, *Hedychium coronarium* var. *chrysoleucum* (Hook.) Baker, *Hedychium coronarium* var. *maximum* (Roscoe) Eichler, *Hedychium gandasulium* Buch.-Ham. ex Wall., *Hedychium lingulatum* Hassk., *Hedychium maximum* Roscoe, *Hedychium prophetae* Buch.-Ham. ex Wall., *Hedychium spicatum* Lodd., nom. illeg., *Hedychium sulphureum* Wall. inval., *Kaempferia hedychium* Lam., illeg.

Family

Zingiberaceae

Common/English Names

Butterfly Flower, Butterfly Ginger, Butterfly Ginger Lily, Butterfly Lily, Butterfly-Ginger, Butterfly-Lily, Cinnamon-Jasmine, Common Ginger Lily, Garland Flower, Garland Lily, Garland-Flower, Ginger Lily, Ginger-Lily, White Garland-Lily, White Ginger, White Ginger-Lily, White-Ginger, Wild Ginger

Vernacular Names

Afrikaans: Witgemmerlelie
Brazil: Borboleta, Lágrima-de-vênus, Lírio do Brejo (Portugese)
Chinese: Jiang Hua
Chuukese: Sinser, Sinsér, Tolon, Tunun
Cook Islands: Kaopui Teatea, Kōpī, Kōpī Teatea, Re'A, Re'A Teatea (Maori)
Cuba: Flor De Mariposa
Estonian: Lõhnav hedühhium
Fijian: Cevuga Vula, Dalasika, Ndrove, Thevunga
French: Hédychie Couronnée
French Reunion: Longose Blanc, Longoze
German: Garland Blume, Schmetterlingslilie Zingiberaceae Ingwergewächs, Weisse Ingwerlilie
Hawaiian: 'Awapuhi Ke'Oke'O
India: Dolan Champa (Hindi), Takhellei, Takhellei Angouba (Manipuri), Sontaka, Sonttaka (Marathi), Suruli Sugandhi (Kannada), Cankitam, Cantikantam, Cantiramulikai, Cimaikkiccilikkilanku, Kaccolam, Kaccoram, Kaccuram, Kaiccolam, Kaiccoram, Kantapalaci, Karppuraver, Kentimulam, Kiccili (Tamil), Kicciligadda, Vasa Vasanthi (Telugu)
Indonesia: Gondasuli (Javanese), Gandasoli (Sundanese)

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Japanese: Hanashukusha
Malaysia: Gandasuli, Suli
Nepalese: Dudh Kevara, Suli
Philippines: Kamia (Bikol), Banai, Katkatan, Katotant (Bisaya), Donsuli (Bukidnon), Kamia (Cebu Bisaya), Gandasuli (Moro), Kamia (Tagalog)
Pohnpeian: Sinter Pwetepwet
Samoan: Teuila, Teuila Paepae
Tahitian: Opuhi Tea
Thai: Hanghong, Mahahong, Tha-Hern
Tongan: Teuila, Thevunga

Origin/Distribution

The species is probably native to the Himalayas—India and Nepal, Myanmar, Taiwan and south-western China. It is now found naturalized throughout the warm tropics, in eastern Australia, southern Africa, southeastern United States, Central America and many oceanic islands.

Agroecology

Butterfly Ginger Lily likes moist habitats and is found in shaded areas in rainforests, mesic forests, pastures, roadside and stream sides, from near sea level to 3,000 m altitude. It also grows in full sun to partial shade in fertile, moist soil. It is tolerant of mild frost.

Edible Plant Parts and Uses

Young buds and flowers are eaten as vegetables or used as a flavouring, and rhizomatous roots are cooked and eaten as a famine food (Tanaka 1976; Kunkel 1984; Facciola 1990; Sirirugsa 1997; Hu 2005).

Botany

An erect, rhizomatous, perennial shrub, 0.5–1.5 m tall with fleshy, aromatic rhizomes, 2.5–5 cm across and erect pseudostems (Plates 1 and 2).

Plate 1 Plant habit

Plate 2 Pseudostems and rhizome

Leaves alternate, distichous, glabrous, oblanceolate or narrowly elliptic, acuminate, about 30–60 cm long, 10 cm wide, petioles short (Plates 1, 3 and 4). Ligule prominent, 1–3 cm long. Flowers white, sweetly fragrant, to 6–8 cm long, corolla fused with tepals to form a slender tube cleft on one side, labellum obovate, apically notched, white with a

Plate 3 Terminal inflorescence

Plate 4 Open flowers and buds

darker yellow patch near the base (Plates 1 and 4). Flowers formed in dense spikelike, terminal, bracteate inflorescences; bracts oblong–obovate or oblong, imbricate, green. Staminodes are white, oblong–elliptic, narrowed at the base. Capsule oblong with numerous seeds.

Nutritive/Medicinal Properties

Flower Phytochemicals

Two new labdane-type diterpene glycosides, coronalactosides I (1) and II (2), and a new labdane-type trinorditerpene, coronadiene (3), were isolated together with 8 known compounds: (E)-labda-8(17),12-diene-15,16-dial; coronarins B, C and D; 15-hydroxylabda-8(17),11,13-trien-16,15-olide; 16-formyllabda-8(17),12-dien-15,11-olide; kaempferol 3-*O*-(2′-α-L-rhamnopyranosyl)-β-D-glucuronopyranoside; and ferulic acid from 80 % aqueous acetone extract of *H. coronarium* flowers (Nakamura et al. 2008).

One hundred thirty-one compounds were identified in the flower essential oil (Omata et al. 1991). The ginger flower has a diffusive, sweet, spicy and floral scent, and linalool, methyl jasmonate, eugenols, *cis*-jasmone, β-ionone and lactones were found to make a major contribution to the odour of this flower. Of the 175 volatile compounds identified in the flowers, linalool, methyl benzoate, *cis*-jasmone, eugenol, (*E*)-isoeugenol, jasmin lactone, methyl jasmonate, methyl epi-jasmonate, indole, nitriles and oximes were found to make a great contribution to the scent of the flowers (Matsumoto et al. 1993). A total of 113 compounds were identified in the headspace.

A total of 29 components were identified in the flower essential oil of *H. coronarium* (Lu et al. 2009). The main constituents were β-*trans*-ocimenone (28.05 %), linalool (18.52 %), 1,8-cineole (11.35 %), α-terpineol (7.11 %), 10-epi-γ-eudesmol (6.06 %), sabinene (4.59 %) and terpinen-4-ol (3.17 %). The minor constituents included (*E*)-β-farnesene 2.28 %, γ-terpinene 2.21 %, limonene 2.02 %, β-pinene 2.01 %, α-pinene 1.37 %, nerolidol 1.25 %, borneol 1.13 %, unknown 1.10 %, geraniol 1.03 %, *p*-menthen-9-al 0.78 %, patchoulane 0.61 %, β-cedrene 0.41 %, carvacrol 0.37 %, α-terpinene 0.36 %, β-myrcene 0.35 %, isocyclocitral 0.33 %, β-eudesmol 0.28 %, α-phellandrene 0.20 %, α-gurjunene 0.18 %, α-thujene 0.14 %, fenchyl alcohol 0.13 %, β-phellandrene-8-ol 0.13 % and camphene 0.12 %.

A total of 39 compounds were identified in the flower oil accounting for 98 % of the entire amount (Báez et al. 2011). The volatile fraction was characterized by monoterpene hydrocarbons (34.9 %), oxygenated monoterpenes (34.4 %) and sesquiterpene hydrocarbons (13.2 %). The major components were (E)-β-ocimene (28.7 %), linalool (19.3 %) and 1,8-cineole (14.5 %), and they were found to make a major contribution to the typical scent of the flower.

Leaf Phytochemicals

Ali et al. (2002) found the leaf oil in Fiji to be rich in α-pinene (20.9 %), β-pinene (53.6 %), 1,8-cineole (11.9 %) and β-caryophyllene (17.7 %). Leaf essential oil from Brazil was found to be rich in β-caryophyllene (43.0 %), caryophyllene oxide (12.1 %) and β-pinene (11.6 %,) (dos Santos et al. 2010). β-Pinene (33.9 %), α-pinene (14.7 %), 1,8-cineole (13.3 %), r-elemene (11.0 %) and carotol (9.1 %) were the main components in the *H. coronarium* leaf oil, including 82.0 % terpenoid compounds (Ho 2011).

Rhizome Phytochemicals

Two labdane-type diterpenes, coronarin E and coronarin F, were isolated from the rhizomes (Itokawa et al. 1988b). Four new labdane-type diterpenes, coronarins A, B, C and D, and one known labdane-type diterpene, (*E*)-labda-8(17), 12- diene-15,16-dial, were isolated as cytotoxic principles from the rhizomes (Itokawa et al. 1988a). Singh et al. (1991) isolated coronarin D, coronarin D ethyl ether, coronarin E and a new diterpene identified as (+)-14β-hydroxylabda-8(17),12-dieno-16,15-lactone, assigned the trivial name of isocoronarin D from the rhizome of *H. coronarium* grown in Nepal. Two new diterpenes identified as coronarin D methyl ether, a labdane diterpene, and 14,15,16-trinorlabda-8(17),11-(*E*)-dien-13-al, an unusual trinorditerpene catabolite, were isolated from the rhizomes (Singh et al. 1993). Three new labdane diterpenes, labda-8(17),11,13-trien-15(16)-olide, an ester of labda-8(17),11,13-trien-15-al-16-oic acid and isocoronarin D, and 7β-hydroxycoronarin B were isolated together with four known diterpenes, viz. (*E*)-labda-8(17),12-diene-15,16-dial; coronarins B and D; and isocoronarin D from the rhizomes of *H. coronarium* (Nakatani et al. 1994).

Three new labdane-type diterpene lactones, hedychilactones A (1), B (2) and C (3), together with six known diterpenes coronarin D (4), coronarin D methyl ether (5), coronarin E(6), labda-8(17),13(14)-dien-15,16-olide (7), hedychenone (8) and 7-hydroxyhedychenone (9); three farnesene-type sesquiterpenes, (+)-nerolidol (10), hedychiol A (11) and hedychiol B 8,9-diacetate (12); and a flavonol, 5-hydroxy-3,7,4′-trimethoxyflavone (13), were isolated from the methanolic extract of the fresh rhizome of Japanese *H. coronarium* (Matsuda et al. 2002a, b) Two new farnesane-type sesquiterpenes, hedychiol A and hedychiol B 8,9-diacetate, together with 10 constituents coronarin D; coronarin D methyl ether; coronarin E; labda-8(17),13(14)-dien-15, 16-olide; hedychenone; 7-hydroxyhedychenone; and (+)-nerolidol including hedychilactones A–C, were isolated from the methanolic extract of the fresh rhizome of *Hedychium coronarium* cultivated in Japan (Morikawa et al. 2002). Benzoyl eugenol along with the C-14 epimers of the labdane diterpene isocoronarin D and the C-15 epimers of the ethoxyl derivative from coronarin D were isolated from the rhizomes (Taveira et al. 2005). A new labdane diterpenoid, (E)-labda-8(17),12-dien-15,16-olide (1), together with eight known compounds, coronarin D (2), coronarin D methyl ether (3), coronarin D ethyl ether (4), isocoronarin D (5), coronarin B (6), labda-8(17),11,13-trien-15,16-olide (7), (E)-labda-8(17), 12-diene-15,16-dial (8) and 16-hydroxylabda-8(17),11,13-trien-15,16-olide (9), were isolated from the rhizomes (Chimnoi et al. 2008, 2009). Compounds 2–4, 5 and 9 are isolated as mixtures of C-15, C-14 and C-16 epimers, respectively.

Two new labdane-type diterpenes, hedychicoronarin A and hedychicoronarin B, and ten known compounds were isolated from the rhizome

(Chen et al. 2010). Three new labdane-type diterpenes 1–3, named coronarins G–I, as well as seven known compounds, coronarin D, coronarin D methyl ether, hedyforrestin C, (*E*)-nerolidol, β-sitosterol, daucosterol and stigmasterol, were isolated from the rhizomes (Phan et al. 2011). Two new labdanes, 15-methoxylabda-8(17),11E,13-trien-16,15-olide and 16-methoxylabda-8(17),11E, 13-trien-15,16-olide, named hedycoronen A and hedycoronen B, as well as four known compounds, labda-8(17),11,13-trien-16,15-olide; 16-hydroxylabda-8(17),11,13-trien-15,16-olide; coronarin A; and coronarin E, were isolated from the rhizomes (Phan et al. 2011). Two new labdane diterpenoids, namely, hedycoronals A and B, together with eight known diterpenoids and a known diarylheptanoid, were isolated from the rhizomes (Zhan et al. 2012).

Ali et al. (2002) found the rhizome oil of *H. coronarium* in Fiji to be rich in α-pinene (10.6 %), β-pinene (31.4 %) and 1,8-cineole (55.9 %). Rhizome essential oil from Brazil was found to be rich in 1,8-cineole (34.8 %), β-pinene (16.7 %) and α-terpineol (13.1 %) (dos Santos et al. 2010). Gurib-Fakim et al. (2002) found the rhizome essential oil from Mauritius to be rich in α-muurolol (16.8 %), α-terpineol (15.9 %), 1, 8-cineole (11.2 %), an unknown sesquiterpene alcohol (7.0 %), α-fenchyl acetate (5.6 %), citronellal (5.5 %) and (*E*)-methyl cinnamate (5.1 %). 1,8-Cineole was found as the most abundant component of the rhizome essential oil in south India (Sabulal et al. 2007). Joshi et al. (2008) found *trans*-meta-mentha-2,8-diene and linalool as major components in the rhizome essential oil. The major constituents of *H. coronarium* rhizome oil were 1,8-cineole (37.3 %), β-pinene (23.0 %), α-terpineol (10.4 %) and α-pinene (9.9 %), comprising 80.6 % of the oil (Ho 2011).

The essential oil from fresh and dried rhizomes of *H. coronarium* afforded 44 and 38 constituents representing 93.91 % and 95.41 %, respectively (Joy et al. 2007). The major components of the essential oil from fresh and dried rhizome were 1,8-cineole (41.42 %, 37.44 %), β-pinene (10.39 %, 17.4 %) and alpha-terpineol (8.8 %, 6.7 %), respectively.

Antioxidant Activity

The rhizome essential oil from *Hedychium* species including *H. coronarium* exhibited moderate-to-good Fe(2+) chelating activity (Joshi et al. 2008). The polar extracts of *H. coronarium* were found to possess antioxidant activity as evaluated using DPPH scavenging, chelating effect of ferrous ions and reducing power assay (Ho 2011). Appreciable total phenolic content (18.5–26.3 mg/g) was also detected by Folin–Ciocalteu test.

Anti-inflammatory Activity

The methanolic extract from the rhizome of *Hedychium coronarium* was found to inhibit the increase in vascular permeability induced by acetic acid in mice and nitric oxide production (IC_{50} = 45 μg/ml) in lipopolysaccharide (LPS)-activated mouse peritoneal macrophages (Matsuda et al. 2002a, b). The ethyl acetate-soluble fraction was more inhibitory on NO production with an IC_{50} of 13 μg/ml. In addition, constituents, coronarin D and its methyl ether were found to show an inhibitory effect on the increase in vascular permeability induced by acetic acid in mice. They also reported the inhibitory effects of labdane-type diterpene constituents including hedychilactones (1–3) against NO production and/or induction of inducible nitric oxide synthase (iNOS) in LPS-activated mouse peritoneal macrophages. The results supported the traditional effects of this herbal medicine for the treatment of inflammation. In carrageenan-induced rat paw oedema test, the chloroform and methanol rhizome extracts at a dose of 400 mg/kg body weight showed statistically significant inhibition of paw oedema by 27.46 and 32.48 %, respectively, at the third hour after carrageenan injection (Shrotriya et al. 2007). Among the compounds isolated from the rhizome, coronarin G, coronarin H, 15-methoxylabda-8(17),11E,13-trien-16,15-olide (hedycoronen A) and labda-8(17),11,13-trien-16,15-olide, and hedyforrestin C were significant inhibitors of lipopolysaccharide (LPS)-stimulated production of proinflammatory cytokines TNF-α, IL-6 and IL-12 p40 in bone

marrow-derived dendritic cells with IC_{50} ranging from 0.19 to 10.38 μM (Phan et al. 2011). Further they reported that hedycoronens A and B isolated from the rhizomes were potent inhibitors of LPS-stimulated interleukin-6 (IL-6) and IL-12 p40, with IC_{50} ranging from 4.1 to 9.1 μM. Hedycoronens A and B showed moderate inhibitory activity on the tumour necrosis factor-α (TNF-α) production with IC_{50} values of 46.0 and 12.73 μM. Their results indicated the potential anti-inflammatory benefits of labdane diterpenes from *H. coronarium*.

The flower essential oil (100 mg/kg p.o.) produced significant inhibition of paw oedema, but showed poor antioxidant activity with the DPPH IC_{50} value of 1,091.00 μg/ml and FRAP (ferric reducing/antioxidant power assay) value of 0.22 μmol Fe^{2+}/mg (Lu et al. 2009). There was no direct correlation between anti-inflammatory effect and antioxidant activity of the essential oil.

Antitumour Activity

Studies showed that coronarin D [E-labda-8(17),12-diene-15-ol], a labdane-type diterpene, from *Hedychium coronarium* inhibited both constitutive and inducible nuclear factor-kappa B pathway activation, which led to inhibition of inflammation and invasion, potentiation of apoptosis and suppression of osteoclastogenesis (Kunnumakkara et al. 2008). Coronarin D was found to be more potent than its analogue coronarin D acid. Two new labdane diterpenes isolated from the rhizomes were found to be cytotoxic against the A-549 (lung cancer), SK-N-SH (human neuroblastoma), MCF-7 (breast cancer) and HeLa (cervical cancer) cell lines (Suresh et al. 2010). Two diterpenoids isolated from the rhizome exhibited potent cytotoxic activities against four cancer cell lines and displayed promising inhibitory activities against human umbilical vein endothelial cell (HUVEC) proliferation with the IC_{50} values of 6.4 to 3.3 μM (Zhan et al. 2012).

A new labdane diterpenoid, (E)-labda-8(17),12-dien-15,16-olide (1), together with coronarin D (2), coronarin D methyl ether (3), coronarin D ethyl ether (4), isocoronarin D (5), coronarin B (6), labda-8(17),11,13-trien-15,16-olide (7), (E)-labda-8(17),12-diene-15,16-dial (8) and 16-hydroxylabda-8(17),11,13-trien-15,16-olide (9), was isolated from the rhizomes (Chimnoi et al. 2008, 2009). Some of the isolated compounds showed significant cytotoxicity with IC_{50} values lower than 4 μg/ml when tested against the following cancer cell lines: S102, hepatocellular carcinoma; HuCCA-1, cholangiocarcinoma; A549, lung adenocarcinoma; MOLT-3, T-lymphoblast (acute lymphoblastic leukaemia); KB, epidermoid carcinoma; HeLA, cervical carcinoma; MDA-MB231, hormone-independent breast cancer; T-47D, hormone-dependent breast cancer; HL-60, human promyelocytic leukaemia cell; P388, mouse lymphoid neoplasm; and HepG2, hepatoblastoma.

Analgesic Activity

In the acetic acid-induced writhing test, the chloroform and methanol extract of *H. coronarium* rhizomes at doses of 400 mg/kg body weight elicited 27.23 and 40.59 % inhibition of writhing reflex, respectively (Shrotriya et al. 2007). Both extracts showed significant elongation of tail-flick time (41.15 and 61.32 % elongation, respectively) at 400 mg/kg body weight.

Hepatoprotective Activity

The 80 % aqueous acetone extract of *Hedychium coronarium* flowers exhibited a protective effect on D-galactosamine-induced cytotoxicity in primary cultured mouse hepatocytes (Nakamura et al. 2008). In addition, its constituents, labdane-type diterpene, coronarin C, coronarin D, 15-hydroxylabda-8(17),11,13-trien-16,15-olide and 16-formyllabda-8(17),12-dien-15,11-olide, exhibited hepatoprotective effects. Coronarin C and 15-hydroxylabda-8(17),11,13-trien-16,15-olide displayed hepatoprotective effects, which were stronger than that of the hepatoprotective agent, silybin.

Anti-allergic Activity

Hedychilactone A and coronarin D isolated from the methanol extracts of *H. coronarium* rhizome inhibited the release of β-hexosaminidase from rat basophilic leukaemia RBL-2H3 cell line cells (Morikawa et al. 2002). Coronarin D (6) especially showed strong inhibitory activity (IC_{50} = 57 μm). In addition, hedychenone (10) enhanced the release of β-hexosaminidase from RBL-2H3 cells. RBL-2H3 cells are tumour analogues of mucosal mast cells.

Antihypertensive Activity

Oral administration of *H. coronarium* leaf lamina aqueous ethanol extract (40 ml/kg) exerted antihypertensive effects in conscious unrestrained SHR rats (Ribeiro et al. 1986).

Diuretic Activity

Of 32 medicinal plants tested, oral administration of the aqueous ethanol of *H. coronarium* leaf blade and sheath (40 ml/kg) exerted the most significant diuretic effect in conscious unrestrained rats (Ribeiro et al. 1988).

Antiasthmatic Activity

Of the 19 Brazilian species investigated, *Hedychium coronarium*, *Xylopia frutescens* Aubl. and *Hymenaea courbaril* L. exhibited a high 5-lipoxygenase inhibitory activity (Braga et al. 2000). 5-Lipoxygenase is a human enzyme that plays a key role in regulating the production of leukotrienes.

Antimicrobial Activity

The rhizome essential oil was reported to have antimicrobial activity (Joy et al. 2007). It was found that the antimicrobial activity was higher in the fresh sample than the dried. Both samples showed a better activity against *Trichoderma* sp. and *Candida albicans* than against the bacteria *Bacillus subtilis* and *Pseudomonas aeruginosa*. *H. coronarium* rhizome oil exhibited antimicrobial activity against *Salmonella typhi*, *Escherichia coli*, *Proteus vulgaris* and the fungi *Candida albicans* and *Candida glabrata* (Sabulal et al. 2007).

The methanol and dichloromethane rhizome extracts exhibited antibacterial activity against both Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus megaterium* and *Sarcina lutea* and Gram-negative (*Escherichia coli*, *Shigella sonnei*, *Shigella shiga*, *Pseudomonas aeruginosa* and *Salmonella typhi*) bacteria (Aziz et al. 2009). Dichloromethane extract showed comparatively higher activity than the other extracts. The minimum inhibitory concentrations (MICs) of the extracts were found to be in the range of 08–128 μg/ml. The LC_{50} cytotoxicity against brine shrimp nauplii (*Artemia salina*) was also evaluated and found to be 34.85 μg/ml for methanol extract, 62.59 μg/ml for ethyl acetate extract and 55.59 μg/ml for dichloromethane extract.

The leaf and rhizome essential oil of *H. coronarium* displayed significant antimicrobial activity, inhibiting the growth of all five fungal and four bacterial strains tested (Ho 2011). The antimicrobial nature of the essential oil was related to high terpenoid contents. Among the compounds isolated from the rhizome, (+)-coronarin A and coronarin D methyl ether exhibited antitubercular activities against *Mycobacterium tuberculosis* $H_{37}Rv$ in vitro, with MICs = 80 and 50 μg/ml, respectively (Chen et al. 2010).

Coronarin D was effective against *C. albicans* with a minimum inhibitory concentration (MIC) of 2 mg/ml and a minimum fungicidal concentration (MFC) of 4 mg/ml (Kaomongkolgit et al. 2012). The *C. albicans* fungicidal activity of coronarin D was higher than that of clotrimazole and nystatin at 2 × MFC and 4 × MFC, respectively.

Larvicidal Activity

The leaf oil exhibited the mosquito larvicidal activity with 2 h and 24 h LC_{50} values of 111 and 90 ppm, respectively, while the rhizome oil showed the

larvicidal activity with 2 h and 24 h LC_{50} values of 86 and 47 ppm, respectively (Ho 2011). β-Pinene, α-pinene and 1,8-cineol in *H. coronarium* serve as the principal larvicidal components of both oils.

Leishmanicidal Activity

Hedychium coronarium ethanolic plant extract was found to exhibit good leishmanicidal activity against *Leishmania amazonensis* amastigotes with IC_{50} <10 μg/ml (Valadeau et al. 2009).

Anthelmintic Activity

The rhizome oils of *Hedychium coronarium* and *H. spicatum* exhibited higher anthelmintic activity than piperazine phosphate against earthworms and tapeworms, but the activity against hookworms and nodular worms was lower than hexylresorcinol (Dixit and Varma 1975).

Cercaricidal Activity

The cut stem of *Hedychium coronarium* exuded a cercaricidal substance, active against the cercariae of *Schistosoma mansoni* (Warren and Peters 1968).

Traditional Medicinal Uses

Hedychium coronarium has been used in folkloric medicine in Asia for a variety of ailments (Burkill 1966; Duke and Ayensu 1985; Chopra et al. 1986; Matsuda et al. 2002a, b; Morikawa et al. 2002; Nakamura et al. 2008) such as to treat cold, headache, arthritis and injuries. The seed is aromatic, carminative and stomachic. Juice from the stem is used for swellings and a decoction used as a gargle. The rhizome contains 1.7 % essential oil and is used medicinally in Ayurvedic medicine as antirheumatic, anthelmintic, carminative, excitant and tonic. The ground root is used as a febrifuge and for treating diabetes. In India, rhizomes are sold in bottles of extract called Gulbakawali Ark, used as eye tonic and for the prevention of eye cataracts. In Chinese medicine, the rhizome is used for headache, inflammatory pains, rheumatism and contusion. The plant has been used as a remedy for foetid nostril. In Hawaii, the natives used the juice of mature seed head as hair and skin treatment. In the Moluccas, the base of the stem is chewed and the juice placed on swellings and a decoction used as a gargle. The rhizomes of *Hedychium coronarium* are used in the treatment of diabetes by the Siddis of Uttara Kannada district, Karnataka, India (Bhandary et al. 1995). They have been used for the treatment of inflammation, skin diseases, headache and sharp pain due to rheumatism in traditional Vietnamese medicine (Phan et al. 2011).

Other Uses

The plant is popularly grown as an ornamental. The plant has been used in occult activities where the rhizome prescribed in an embrocation was used to treat emaciation ascribed to the influence of an evil spirit. The stems contain 43–48 % cellulose and are useful in making paper. The fragrant flowers are popularly used in the making of bridal bouquets, leis and wreaths. An essential oil obtained from the fragrant flowers is valued in high-grade perfumes.

Comments

In Cuba, *H. coronarium* is the national flower, known as 'Flor de Mariposa', literally 'Butterfly Flower', due to its similarity with a flying white butterfly. In Australia, *H. coronarium* is deemed a potential weed of native bushland, rainforests and other closed forests, forest margins and riparian zones.

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Zingiber zerumbet

Scientific Name

***Zingiber zerumbet* (L.) Roscoe ex Smith**

Synonyms

Amomum silvestre Poir, *Amomum sylvestre* Lam. (illeg.), *Amomum zerumbet* L., *Zerumbet zingiber* T. Lestib., *Zingiber sylvestre* Garsault (inval.)

Family

Zingiberaceae

Common/English Names

Broad-Leaved Ginger, Martinique Ginger, Pine Cone Ginger, Pinecone Lily, Shampoo Ginger, Wild Ginger, Zerumbet Ginger

Vernacular Names

Arabic: auruq-ul-kafoor, satwal, zadwar, Zurunbah, Zurunbâd
Bangladesh: Jangli Adha
Brazil: Gengibre Amargo
Burmese: Linne-Gyi
Chinese: Hong Qiu Jiang
Fijian: Cagolaya, Drove, Layalaya
French: Amome Sauvage, Zérumbet, Gingembre Fou, Gingembre Blanc
German: Wilder Ingwer, Zerumbet
Hawaiian: Awapuhi, Awapuhi Kuahiwi, Ophui
India: Ghatian (Assamese), kulanjan, Mahabari bach, narkachur (Bengali), banadrak, mahabari-bach, mahabaribach, nar-kachur, narkachur (Hindi), agale shunti, agaleshunthi, agalesunthi, agalu shunti, agalusunthi, kaadu kolinjana, kaadu shuntee, kaadu shunti, kallu shunti, kallusunthi, kallusunti (Kannada), kathu-inshi-kua, katinci, katouinschikua, kattinchi, kattinci, kattincikuva, kattinji, kattinjikuva, kattu-inschi-kua (Malayalam), yaimu, singkha (Manipuri), kaali halad, narakchora, ran-alem (Marathi), Gada, Pasukedar, viranam (Oriya), Kachur, Narkachur (Punjab), ahava, avanti, karpuraharidra, kolanjana, kumbhika, sthulagranthi, viranam (Sanskrit), araniyacaranai, aniyacaranai, cirrinci, kattinci, vanaarttirakam (Tamil), kaarallamu, kaarupasupu, karallamu, karupasupu, santapasupu (Telugu), Kallusonti (Tulu), kapur kachri, kapur-kachri, kapurkachri, narkachoor (zurumbad), narkachur, narkachur nim koafta, narkachur nim kofta, zarambad, zaranbad, zaranbad nim kofta, zarnabad, zarnabad nim kofta (Urdu)
Indonesia: Lempuyang, Lampuyang emprit, Lampuyang prit, Lampuynag rum, Lampuyang wangi (Javanese), Lampojang, Lampojang paek (Madurese), Lampoyan gajah, Lampuyan kapur, Lampuyan kebo, Lampuyang wangi (Malay), Lampuyang badak, Lampuyang ruum, Lampuyang wangi (Sundanese)

T.K. Lim, *Edible Medicinal and Non Medicinal Plants: Volume 8, Flowers*,
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Italian: Zenzero Bianco, Zenzero Salvatico
Japanese: Niga Shouga
Khmer: Khnei Phtu, Prateal Vong Prenh Atit
Laotian: Hva:Nz Ph'ai Chai Hluang
Malaysia: Lampoyang, Lampuyan, Lempoyang
Persian: kazhur, zaranbad, zhuranbad
Philippines: Balauag, Layag Sasulug (Bikol), Barik, Langkawas, Luiang-Usiu, Tumbong-Aso (Tagalog), Lampuyana, Tandok (Bukidnon)
Portuguese: Gengibre Amargo
Samoan: 'Ava'avaaitu sosolo, 'ava'avaaitu tu, 'avapui'
Spanish: Jengibre, Jengibre Amargo
Sri Lanka: Waliguru
Thailand: Haeo Dam, Hiao Kha, Hiao Daeng, Kaen, Ka Thue, Ka Thue Pa, Ka Waen, Kra Thue, Ple Pho (Karen), Wanfai (Don Daeng)
Turkish: Yabani zencefil, Zurunbad, Zerunebat, Zernebat
Vietnamese: Gừng dại, Gừng gió, Ngải mặt trời, Ngải xanh

Origin/Distribution

The species is a native of tropical Indo-Malesian–India, Malaysia and Indonesia. It is widely cultivated in the Asian tropics—Cambodia, India, Laos, Indonesia, Malaysia, Myanmar, Sri Lanka, Thailand, Vietnam, Pacific Islands including China (Guangdong, Guangxi, Yunnan) and Taiwan. It is now pantropical in distribution.

Agroecology

The plant thrives in the humid and hot tropical areas in rainforests and thickets and beaches and mangroves at low and medium (600 m) altitudes, under full shade to partial shade in rich, moist, well-drained soil rich in humus.

Edible Plant Parts and Uses

The flower buds are boiled and eaten as vegetables (Sirirugsa 1997). The young shoots and rhizome are used as a spice/condiment in much the same way as ginger. The young ends of rhizomes, peeled or unpeeled, are eaten raw as *lalab* with rice in Java (Ochse and Bakhuizen van den Brink 1980).

Botany

A tall erect, herbaceous plant with pseudostems growing in clumps up to 0.6–2 m tall (Plate 1) with a subterranean tuberous rhizome which is pale yellow inside (Plate 2). Leaves are numerous, distichous, sessile or shortly petiolate, green, simple, entire, lanceolate or oblong–lanceolate, 15–40 cm by 3–8 cm, glabrescent or abaxially somewhat pilose, base narrowed, apex acuminate (Plates 1, and 3). Inflorescences conical or ovoid–oblong, 6–15 cm by 3.5–5 cm, with obtuse apices (Plates 1, 3, and 4), occurring at the end of

Plate 1 Flowering clumps of pine cone gingers

Plate 2 Harvested rhizomes

Plate 3 Pine cone inflorescences, flower and peduncles

Plate 4 Close-up of pine cone inflorescence and flower

peduncles 10–30 cm with 5–7scalelike sheaths which arise from rhizomes. Bracts are closely imbricate, green when young, red when old, slightly hairy, margin membranous, and bracteoles are 1.5 cm. Calyx 1.2–2 cm, membranous, split on 1 side, apex 3 toothed. Corolla tube 2–3 cm, slender; lobes pale yellow, lanceolate, central one 15–25 mm. Labellum pale yellow, 15×25 mm; central lobe suborbicular or subobovate, 15–20 mm by 15 mm, apex emarginate; lateral lobes obovate, 10 mm, free nearly to base. Stamen 10 mm; connective appendage beaklike. Ovary glabrous. Capsule ellipsoid, 12 mm long. Seeds oblong, black.

Nutritive/Medicinal Properties

The volatile flower oil was found to contain more than 60 components, of which 45 compounds, making up 85 % of the oil, were identified (Nguyên et al. 1995). (*Z*)-nerolidol (36.3 %) and β-caryophyllene (13.2 %) were the major constituents. Flower essential oil was rich in (*E*)-nerolidol (34.9 %), β-caryophyllene (10.2 %) and linalool (17.1 %) (Chane-Ming et al. 2003).

The major components of the leaf oil were (*Z*)-nerolidol (22.3 %), β-caryophyllene (11.2 %), zerumbone (2.4 %) and *trans*-phytol (12.6 %). Predominant minor constituents included β-pinene (5.2 %), α-humulene (2.9 %), caryophyllene oxide (5.5 %) and linalool (2.4 %) (Nguyên et al. 1995). Leaf essential oil was rich in β-pinene (31.4 %), (*E*)-nerolidol (21.4 %), α-pinene (10.3 %), linalool (7.7 %) and β-caryophyllene (6.9 %) (Chane-Ming et al. 2003). Twenty-nine components were identified in the leaf essential oil of *Z. zerumbet* grown in Bangladesh (Bhuiyan et al. 2009). The leaf oil was rich in zerumbone (36.98 %), α-caryophyllene (16.35 %), camphene (9.24 %), 1,2-dihydropyridine,1-(1-oxobutyl), -(5.82 %), 3-cyclo hexen-1-carboxaldehyde, 3,4-dimethyl-(3.91 %), caryophyllene (3.25 %), camphor (2.72 %), caryophyllene oxide (2.54 %), α-pinene (2.23 %), eucalyptol (1.69 %) and *trans*-longipinene (1.65 %). Minor leaf oil constituents included the following: limonene (1.14 %), 1,5-cycloundecadien, 8,8-dimethyl-9-methylene (1.13 %), 3-carene (1.02 %), agarospirol (0.97 %), linalool (0.85 %), borneol (0.81 %), 3α,9-dimethyldodecahydrocyclohepta [D] inden-3-one (0.72 %), 3-isopropyltricyclo [4.3.1.1] (2,5) undec-3-en-l0-ol (0.78 %), β-eudesmol (0.71 %), 2,6-dimethylbicyclo [3,2,1]octane (0.69 %), 7-octylidenebicyclo [4.1.0] heptane-(0.69 %), cycloheptane, 4-methylene-1-methyl-2-(2-methyl-1-propen-1-1-yl)-1-vinyl (0.68 %), tricyclene (0.56 %), 1,6,10-dodecatrien-3-ol,

3,7,11-trimethyl, -[*S*-(*Z*)] (0.53 %), borneol (0.52 %) andazulene1,2,3,4,5,6,7,8-octahydro-1,4-dimethyl-7-(1-methylethylidene), -(IS-cis)- (0.48 %).

The major components of the stem oil were (*Z*)-nerolidol (16.8 %), β-caryophyllene (10.4 %), zerumbone (21.3 %) and *trans*-phytol (7.0 %). Predominant minor constituents included β-pinene (5.4 %), α-humulene (2.5 %), caryophyllene oxide (1.1 %) and linalool (1.1 %) (Nguyên et al. 1995).

Two oxygenated derivatives of humulene, viz. humulene monoxide and humulene dioxide, were isolated from the sesquiterpene fractions of *Z. zerumbet* oil (Ramaswami and Bhattacharyya 1962). Zerumbone and 4″-*O*-acetylafzelin were obtained from organic extracts of entire plants of *Z. zerumbet* (Dai et al. 1997).

Phytochemicals in Rhizome

From the rhizome essential oil, humulene was identified (Varier 1944), monoterpenes and zerumbone (Balakrishnan et al. 1956) were also found, the structure of zerumbone was elucidated as 2,6,9,9-tetramethyl-2,6,10-cycloundecatrien-1-one (Dev 1960). Two oxygenated derivatives of humulene, viz. humulene monoxide and humulene dioxide, were isolated from the sesquiterpene fractions of *Z. zerumbet* oil (Ramaswami and Bhattacharyya 1962). Nigam and Levi (1963) isolated β-pinene, Δ^3-carene, β-caryophyllene, *ar*-curcumene, linalool, borneol and α-terpineol from the oil. The essential oil from *Zingiber zerumbet* rhizomes was found to contain sesquiterpenoids: dihydro-ψ-photozerumbone, ψ-photozerumbone, humulene epoxide-I, humulene epoxide-11, caryophyllene oxide, β-caryophyllene, the sesquiterpene alcohols (+)-humulenol-I and (+)-humulenol-II (Damodaran and Dev 1968a, b, c) and zerumbone oxide, a sesquiterpene epoxy ketone (Chhabra et al. 1975). Zerumbone, zerumbone epoxide, diferuloylmethane, feruloyl-*p*-coumaroylmethane, di-p-coumaroylmethane and 3″,4″-*O*-diacetylafzelin were isolated from the pentane and ether extracts of *Z. zerumbet* rhizome (Matthes et al. 1980). Yu et al. (2008) reported approximately 86 % sesquiterpenoids with zerumbone being the major component in the ethanol rhizome extract. They also found β-caryophyllene, caryophyllene oxide and β-eudesmol. Duve (1980) reported that the local Fijian variety contained 56.7 % zerumbone, while the Indian variety had 37.5 % zerumbone. A sesquiterpene, zederone, was isolated from the crude ethanolic extract of *Z. zerumbet* rhizomes (Kader et al. 2010).

Two flavonoid glycosides, kaempferol-3-*O*-(3,4-*O*-diacetyl-α-L-rhamnopyranoside) and kaempferol-3-*O*-(2,4-*O*-diacetyl-α-l-rhamnopyranoside), and two flavonols, kaempferol-3,4′-*O*-dimethylether and kaempferol-3-*O*-methylether, were isolated from the CH_2Cl_2-soluble part of the extract of fresh rhizomes of *Zingiber zerumbet* along with zerumbone, zerumbone epoxide and curcumin (Nakatani et al. 1991). A humulene sesquiterpene, 5-hydroxyzerumbone (5-hydroxy-2E,6*E*,9*E*-humulatrien-8-one), and zerumboneoxide (Jang et al. 2005), two isomers of 6-methoxy-2*E*,9*E*-humuladien-8-one (1 and 2) and stigmast-4-en-3-one (Jang and Seo 2005), were isolated from the rhizomes. Three new acetylated and one known kaempferol glycosides were isolated from fresh *Zingiber zerumbe*t rhizomes and their structures determined to be the kaempferol-3-*O*-(2-*O*-acetyl-α-l-rhamnopyranoside), kaempferol-3-*O*-(3-*O*-acetyl-α-L-rhamnopyranoside), kaempferol-3-*O*-(4-*O*-acetyl-α-l-rhamnopyranoside) and kaempferol-3-*O*-α-l-rhamnopyranoside (Masuda et al. 1991). Among Fijian edible food plants, *Z. zerumbet*, a widely used herb taken before meals, was found to provide the richest source of kaempferol (240 mg/100 g) (Lako et al. 2007).

Two aromatic compounds, *p*-hydroxybenzaldehyde and vanillin, and six flavonoids, kaempferol derivatives, kaempferol-3,4′,7-*O*-trimethylether, kaempferol-3-*O*-methylether, kaempferol-3,4′-*O*-dimethylether, 4″-*O*-acetylafzelin, kaempferol-3-*O*-(4-*O*-acetyl-α-l-rhamnopyranoside), 2″,4″- *O*-diacetylafzelin, kaempferol-3- *O*-(2,4-*O*-diacetyl-α-l-rhamnopyranoside), 3″,4″- *O*-diacetylafzelin and kaempferol-3-*O*-(3,4-*O*-diacetyl-α-l-rhamnopyranoside),

were isolated from the chloroform-soluble fraction of *Zingiber zerumbet* rhizome (Jang et al. 2004). Five flavonoids, kaempferol 3-*O*-rhamnoside, kaempferol 3-*O*-(2″-*O*-acetyl) rhamnoside or kaempferol 3-*O*-(3″-*O*-acetyl) rhamnoside, kaempferol 3-*O*-(4″-*O*-acetyl)rhamnoside, kaempferol 3-*O*-(3″,4″-*O*-diacetyl)rhamnoside and kaempferol 3-*O*-(2″,4″-*O*-diacetyl) rhamnoside, were found in the active fraction from *Z. zerumbet* rhizome (Ruslay et al. 2007). Zerumbone, 3-*O*-methyl kaempferol, kaempferol-3-*O*-(2, 4-di-*O*-acetyl-α-L-rhamnopyranoside) and kaempferol-3-*O*-(3,4-di-*O*-acetyl-α-L-rhamnopyranoside) were isolated from the rhizome of *Z. zerumbet* (Chien et al. 2008).

Oliveros and Cantoria (1982) found that the dried rhizome of *Z. zerumbet* yielded a dextrorotatory volatile oil with zerumbone as its major constituent which congealed at 3 °C. In contrast, they found a proposed variety which yielded a levorotatory volatile oil with 4-terpinenol as its main constituent and congealed at −27 °C. The essential oil of Z. *zerumbet* rhizome was found to be rich in oxygenated derivatives of α-humulene, in particular zerumbone (65.3 %) (Lechat-Vahirua et al. 1993). More than 30 components were identified in the essential oil of *Zingiber zerumbet* rhizome, of which zerumbone was the major constituent (72.3 %) (Nguyêñ et al. 1993).

The essential oil of *Zingiber zerumbet* rhizomes afforded 36 compounds (Srivastava et al. 2000). Curzerenone (14.4 %), zerumbone (12.6 %), camphor (12.8 %), isoborneol (8.9 %) and 1,8-cineole (7.1 %) were found as major compounds. Another study found the essential oil obtained from the rhizome to be rich in zerumbone (37 %), α-humulene (14.4 %) and camphene (13.8 %) (Chane-Ming et al. 2003). Thirty components were identified in rhizome essential oil of *Z. zerumbet* grown in Bangladesh (Bhuiyan et al. 2009). The rhizome oil was rich in zerumbone (46.83 %), α-caryophyllene (19.00 %), 1,5,5,8-tetramethyl-12-oxabicyclo[9.1.0]dodeca-3,7-diene (4.28 %), caryophyllene (3.98 %), caryophyllene oxide (3.70 %), camphene (3.56 %), camphor (2.80 %), kauran-18-al, 17-(acetyloxy)-,(4β) (2.16 %), 1H-cycloprop[e] azulen-4-ol, decahydro-1,1,4,7-tetramethyl-, [1ar-(1aα, 4β,4aβ, 7α.,7aβ,7bα)]- (1.89 %), eucalyptol (1.27 %) and α-pinene (1.17 %). Minor compounds included the following: 2-methylenecholestan-3-ol (1.02 %), carveol (0.92 %), limonene (0.88 %), bicyclo[3.1.0] hexane-6-methanol, 2-hydroxy-1,4,4-trimethyl- (0.88 %), 3-carene (0.82 %), linalool (0.57 %), *trans*-nerolidol (0.45 %), cycloheptane, 4-methylene-1-methyl-2-(2-methyl-1-propen-1-yl)-1-vinyl- (0.46 %), 2,4-diisopropenyl-1-methylcyclohexane (0.45 %), bicyclo[5.3.0] decane, 2-methylene-5-(1-methylvinyl)-8-methyl- (0.43 %), anisole, *p*-styryl- (0.41 %), 2-naphthalenemethanol, 1,2,3,4,4α,5,6,7-octahydro-α, α,,4α,8-tetramethyl- (0.37 %), (2R-cis)-β-terpinyl acetate (0.30 %), borneol (0.29 %), norethynodrel (0.24 %), 4-terpineol (0.23 %), β-cymene (0.21 %), 4-isopropenyl-4,7-dimethyl-1-oxaspiro[2.5]octane (0.21 %) and germacrene D-4-ol (0.20 %). The most abundant component of *Z. zerumbet* rhizome oil was zerumbone, 73 % of the total oil, other major components were α-humulene (5.9 %), camphene (2.8 %) and caryophyllene oxide (2.7 %) (Sri Nurestri et al. 2005).

Thirty-three compounds, accounting for 93.6 % of the essential oil of *Z. zerumbet* var. *darcyi* rhizome, were identified including 20 compounds in minor (0.1–0.6 %) and eight in trace (<0.05 %) amounts (Rana et al. 2012). The major constituents were zerumbone (69.9 %), α-humulene (12.9 %), humulene epoxide-II (2.5 %), caryophyllene oxide (1.1 %) and camphene (1.9 %). Two terpene synthases involved in the production of terpenoids, namely, α-humulene synthase and β-eudesmol synthase, were found in *Z. zerumbet* rhizome (Koo and Gang 2012). β-Eudesmol synthase was also isolated from the rhizome by Yu et al. (2008). 6-Gingerol ((*S*)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-3-decanone) was one of the pungent constituents of *Zingiber zerumbet* rhizome (Tzeng and Liu 2013). Nik Norulaini et al. (2009) found that extraction of zerumbone, α-caryophyllene and camphene from *Z. zerumbet* could be optimized by using SC-CO_2 at 30 °C and 55 MPa with total amount of 30 g of CO_2.

Anticancer Activity

Many studies, in vivo and in vitro, had highlighted the potent anticancer properties of zerumbone, a cyclic 11-membered sesquiterpene from *Z. zerumbet*, via different cell signalling pathways, reporting its chemopreventive/therapeutic effects in different tumour models (Prasannan et al. 2012). The multi-targeted actions of zerumbone are a very desirable property for cancer therapy, as carcinomas typically involve dysregulation of multiple genes and associated cell signalling pathways at various stages of initiation, progression and metastasis. However, preclinical and clinical studies are lacking and are warranted.

In Vitro Studies

Zerumbone, zerumbone epoxide, diferuloylmethane, feruloyl-*p*-coumaroylmethane, di-*p*-coumaroylmethane and 3″,4″-*O*-diacetylafzelin isolated from *Z. zerumbet* rhizome exhibited cytotoxic activity (Matthes et al. 1980). Zerumbone was found to be a potent inhibitor of tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate-induced Epstein-Barr virus activation (Murakami et al. 1999). The IC_{50} value of zerumbone (0.14 μM) was markedly lower than those of the antitumour promoters. Further, α-humulene lacking the carbonyl group at the 8th position in zerumbone was inactive (IC_{50} >100 μM), while 8-hydroxy-α-humulune was markedly active (IC_{50}=0.95 μM). *Z. zerumbet* rhizome extract inhibited 12-*O*-tetradecanoyl phorbol-13-acetate (TPA)-induced Epstein-Barr virus early antigen (EBV-EA) in Raji cells but had no cytotoxicity effect in Raji cells (Vimala et al. 1999).

Zerumbone from *Z. zerumbet* notably inhibited free radical generation, proinflammatory protein production and cancer cell proliferation in a variety of cell culture experiments (Murakami et al.; 2002). Zerumbone effectively suppressed 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced superoxide anion generation from both NADPH oxidase in dimethyl sulfoxide-differentiated HL-60 human acute promyelocytic leukaemia cells and xanthine oxidase in AS52 Chinese hamster ovary cell. The combined lipopolysaccharide- and interferon-γ-stimulated protein expressions of inducible nitric oxide synthase and cyclooxygenase (COX)-2, together with the release of tumour necrosis factor-α, in RAW 264.7 mouse macrophages were considerably diminished by zerumbone. These suppressive events were accompanied with a combined decrease in the medium concentrations of nitrite and prostaglandin E2, while the expression level of COX-1 was unchanged. Zerumbone inhibited the proliferation of human colonic adenocarcinoma cell lines (LS174T, LS180, COLO205 and COLO320DM) in a dose-dependent manner, while the growth of normal human dermal (2F0-C25) and colon (CCD-18 Co) fibroblasts was less affected. It also induced apoptosis in COLO205 cells, as detected by dysfunction of the mitochondrial transmembrane. Their results indicated zerumbone to be a food phytochemical with distinct potentials for use in anti-inflammation, chemoprevention and chemotherapy strategies. Studies by Takada et al. (2005) found that zerumbone abrogated NF-kappaB and IkappaBalpha kinase activation induced by tumour necrosis factor (TNF), okadaic acid, cigarette smoke condensate, phorbol myristate acetate and H_2O_2. This led to suppression of anti-apoptotic and metastatic gene expression, up-regulation of apoptosis and downregulation of invasion, providing a molecular basis for the prevention and treatment of cancer by zerumbone. In another study, zerumbone exhibited antiproliferative effect on the growth of human breast carcinoma cell lines (Rumiza and Azimahtol Hawariah 2005). Zerumbone was found to mediate its activity through the inhibition of activation of nuclear factor NF-κB and NF-κB-regulated gene expression induced by carcinogens such as tumour necrosis factor (TNF), okadaic acid, cigarette smoke condensate, phorbol myristate acetate and H2O2 NF-κB activation. Sung et al. (2008) found that zerumbone downregulated CXC chemokine receptor 4 (CXCR4) expression leading to inhibition of ligand CXCL12-induced invasion of breast and pancreatic tumour cells.

Zerumbone significantly showed an antiproliferative activity upon human hepatocellular liver carcinoma HepG2 cells with an IC_{50} of

3.45 μg/mL by inducing apoptosis (Sharifah Sakinah et al. 2007). Apoptosis was mediated by the up-regulation of pro-apoptotic Bax protein and the suppression of anti-apoptotic Bcl-2 protein expression and was independent of functional p53 activity. Recent studies by Kamalidehghan et al. (2012) found that apoptosis in zerumbone-induced HepG2 cells was not associated with DNA fragmentation. Apoptosis was mediated by low and high expression of Bcl2 and Bax proteins, respectively. Another study demonstrated that zerumbone significantly suppressed the proliferation of promyelocytic leukaemia NB4 cells among several leukaemia cell lines, but not human umbilical vein endothelial cells (HUVECs), by inducing G2–M cell cycle arrest followed by apoptosis with 10 μM of IC_{50} (Xian et al. 2007). It was found that zerumbone induced apoptosis by triggering the Fas/CD95- and mitochondria-mediated apoptotic signalling pathway.

Zerumbone from *Zingiber zerumbet* had been reported as one of the promising chemopreventive agents against colon and skin cancer (Nakamura et al. 2004). In cultured rat normal liver epithelial cell line, exposure to zerumbone activated phase II drug-metabolizing enzymes such as glutathione *S*-transferase. Zerumbone was found to potentiate the gene expression of several Nrf2/ARE-dependent phase II enzyme genes, including gamma-glutamylcysteine synthetase, glutathione peroxidase and hemeoxygenase-1. The findings suggested the antioxidant role of this detoxification system activation by zerumbone in the neutralization of lipid peroxidation in hepatocytes, providing a new insight for cancer prevention

Zerumbone exerted an antiproliferative effect towards cervical cancer cell line (HeLa) in a time-dependent manner (24, 48 and 72 h) (Abdul et al. 2008). Zerumbone was found to be cytotoxic on human cervical cancer (HeLa) cells (Abdelwahab et al. 2009). The apoptogenic effects of zerumbone were characterized by nuclear and chromatin condensation, cell shrinkage, multinucleation, abnormalities of mitochondrial cristae, membrane blebbing, holes, cytoplasmic extrusions and formation of apoptotic bodies in HeLa cells. Weng et al. (2010) demonstrated that zerumbone (10–50 μM) induced apoptosis in human glioblastoma multiforme (GBM8401) cells in a dose-dependent manner via inactivation of IKKα, followed by Akt and FOXO1 phosphorylation and caspase-3 activation. Studies showed that zerumbone suppressed the viability of pancreatic carcinoma PANC-1 in a concentration- and time-dependent manner by induction of apoptosis (Zhang et al. 2012). The expression of p53 protein and the p21 level was elevated in zerumbone-treated PANC-1 cells. Further, zerumbone also produced the same antitumour activity in pancreatic carcinoma cell lines SW1990 and AsPC-1.

Recent studies by Ohnishi et al. (2013) reported that the potent bioactivities of zerumbone, a promising chemopreventive agent, was dependent on the electrophilic moiety of its α,β-unsaturated carbonyl group and to its chemical potential for binding to cellular proteins through a Michael reaction. They showed that zerumbone insolubilized cellular proteins in vitro and induced ubiquitination and aggregation of cellular proteins. In Hepa1c1c7 cells, zerumbone activated the ubiquitin–proteasome system and autophagy and conferred resistance to toxicity of 4-hydroxy-2-nonenal, an endogenous lipid peroxidation product via p62 induction. Their results suggested that protein modifications by zerumbone caused mild proteo-stress, thereby activating intracellular proteolytic machineries to maintain protein homeostasis. They considered these effects on proteolytic mechanisms to be hormesis, which provides beneficial functions through mild biological stresses.

Histone deacetylase (HDAC) inhibitors that inhibit proliferation and induce differentiation and/or apoptosis of tumour cells were isolated from *Z. zerumbet* rhizomes (Chung et al. 2008). The n-hexane-soluble fraction from the rhizome yielded two major sesquiterpenoids, 6-methoxy-2E,9*E*-humuladien-8-one (1) and zerumbone (2). Compound 1 exhibited growth-inhibitory activity on six human tumour cell lines and showed potential inhibitory activity in histone deacetylase (HDAC) enzyme assay (GI_{50} = 1.25 μM). It also exhibited growth inhibitory activity on five

human tumour cell lines and higher inhibitory activity on the MDA-MB-231 breast tumour cell line (IC_{50} = 1.45 μM).

Of six kaempferol derivatives extracted from *Z. zerumbet*, kaempferol-3-*O*-methyl ether and kaempferol-3,4′-*O*-dimethylether showed a potent P-glycoprotein inhibitory effect as great as verapamil, a well-known P-glycoprotein inhibitor, in multidrug-resistant (MDR) human breast cancer cells, MCF-7/ADR (Chung et al. 2007). The P-glycoprotein inhibitory activity of these two compounds was through a threefold increase of the level of [(3)H]-daunomycin accumulation and a decrease of P-glycoprotein-mediated efflux. These results suggested that the kaempferol derivative components of *Z. zerumbet* could be used as a scaffold for developing agents that reverse P-glycoprotein-mediated MDR in human cancer chemotherapy.

Among 17 zerumbone derivatives synthesized, derivative 5 showed the most potent antiproliferative activity against cholangiocarcinoma cell line (KKU-100) with an IC_{50} value of 16.44 μM (Songsiang et al. 2010). Docking studies with different enzymes and receptor proteins revealed that the compound 5 exhibited better binding interaction to EGFR than CDK-2, CDK-5 and GSK-3, indicating that compound 5 could be a promising candidate for treatment of cancer.

The inclusion complex of zerumbone with hydroxypropyl-β-cyclodextrin (HPβCD) was found to retain its cytotoxic activity as shown by in vitro cell survival assay on human cervical cancer (HeLa), breast cancer (MCF7 and MDA-MB-231) and human leukaemic (CEM-SS) cell lines (Eid et al. 2011). The study showed HPβCD to be a suitable encapsular capable of forming thermodynamically stable complex with zerumbone for safe delivery of the compound as an anticancer drug in the future. Zerumbone encapsulated with hydroxypropyl-β-cyclodextrin (HPβCD) afforded a highly soluble inclusion complex that was found to be a promising anticancer agent for the treatment of hepatocellular carcinoma in humans (Muhammad Nadzri et al. 2013). It induced apoptosis in liver hepatocellular HepG2 cells via caspase-8/BID cleavage switch and modulating Bcl2/Bax ratio. Sobhan et al. (2013) substantiated that mitochondrial permeabilization and cytochrome c-dependent caspase activation dominated in zerumbone-induced cancer cell death and that Bax was essential for mitochondrial permeabilization. Bax activation, the essential and early event of cell death, was independently activated by reactive oxygen species (ROS) as well as calpains. Mammary epithelial cells, endothelial progenitor cells and smooth muscle cells were relatively resistant to zerumbone-induced cell death with lesser ROS accumulation than cancer cells.

Animal Studies

Dietary administration of zerumbone to male F344 rats exposed to the carcinogen azoxymethane (AOM) caused a reduction in the frequency of aberrant crypt foci (ACF): 72 (14 % reduction) at a dose of 0.01 % and 45 (46 % reduction) at a dose of 0.05 % (Tanaka et al. 2001). AOM exposure produced 84 ACF/rat at the end of the study. Feeding of zerumbone significantly reduced expression of COX-2 and prostaglandins in the colonic mucosa and significantly lowered the number of nucleolar organizer region protein (AgNORs) in colonic crypt cell nuclei. The findings suggested possible chemopreventive ability of zerumbone, through suppression of COX-2 expression, cell proliferating activity of colonic mucosa and induction of phase II detoxification enzymes in the development of AOM-induced colonic aberrant crypt foci. A single topical pretreatment of zerumbone to the mouse skin (2 μmol) 24 h before application of dimethylbenz[a]anthracene (0.2 μmol) markedly suppressed tumour incidence by 60 % and the number of tumours by 80 % per mouse (Murakami et al. 2004). Repeated pretreatment (16 nmol) twice weekly during the post-initiation phase reduced the number of 12-*O*-tetradecanoylphorbol-13-acetate (TPA, 1.6 nmol)-induced tumours by 83 % as well as their diameter by 57 %. They found zerumbone to be a promising agent for the prevention of both tumour-initiating and tumour-promoting processes, through induction of antioxidative and phase II drug-metabolizing enzymes as well as attenuation of proinflammatory signalling pathways.

Huang et al. (2005) found that the diethyl ether extract of *Z. zerumbet* rhizome could induce DNA fragmentation in P-388D1 cells in vitro and significantly prolong the life of P-388D1-bearing CDF1 mice (ILS% = 127.8) at a dosage of 5 mg/kg body weight. Zerumbone isolated from the diethyl ether extract also inhibited the growth of P-388D1 cells, induced DNA fragmentation in culture and significantly prolonged the life of P-388D1-bearing CDF1 mice (ILS% = 120.5) at a dosage of 2 mg/kg. Further, zerumbone inhibited the growth of a human leukaemia cell line, HL-60 cells, in a time- and concentration-dependent manner, with IC_{50} values of 22.29, 9.12 and 2.27 µg/mL for 6, 12 and 18 h, respectively, via induction of G2–M cell cycle arrest in HL-60 cells. In a separate study, zerumbone was found to have cytotoxic effect against T-cell acute lymphoblastic leukaemia, CEM-SS cells in vitro with an IC_{50} of 8.4 µg/mL (Abdelwahab et al. 2011). Zerumbone induced apoptosis of CEM-SS cells as evidenced by abnormalities such as membrane blebbing, holes and cytoplasmic extrusions.

Using two different preclinical mouse models, Kim et al. (2009) found that oral administration of zerumbone at 100, 250 and 500 ppm significantly inhibited the multiplicity of colonic adenocarcinomas and suppressed colonic inflammation. In the lung carcinogenesis, zerumbone feeding at 250 and 500 ppm significantly inhibited the multiplicity of lung adenomas in a dose-dependent manner. Feeding with zerumbone resulted in inhibition of proliferation, induction of apoptosis and suppression of NF-kappaB and heme oxygenase (HO)-1 expression in tumours developed in both colon and lung tissues. Topical application of zerumbone onto the dorsal skin of hairless mice and mouse epidermal JB6 cells induced activation of NF-E2-related factor 2 (Nrf2) and expression of heme oxygenase-1 (HO-1) (Shin et al. 2011). This afforded a mechanistic basis for the chemopreventive effects of zerumbone on mouse skin carcinogenesis.

In vivo studies showed that zerumbone protected the rat liver from the carcinogenic effects of diethylnitrosamine (DEN) and dietary 2-acetylaminofluorene (AAF) (Taha et al. 2010). Serum alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (AP) and alpha-fetoprotein (AFP) were significantly lower in zerumbone-treated than untreated rats with liver cancer. There was also significant reduction in the hepatic tissue glutathione (GSH) concentrations. The liver sections of untreated DEN/AAF rats also showed abundant proliferating cell nuclear antigen (PCNA), while in zerumbone-treated rats the expression of this antigen was significantly lowered. By the TUNEL assay, there were significantly higher numbers of apoptotic cells in DEN/AAF rats treated with zerumbone than those untreated. Zerumbone treatment had also increased Bax and decreased Bcl-2 protein expression in the livers of DEN/AAF rats, which suggested increased apoptosis. The results suggested that zerumbone reduced oxidative stress, inhibited proliferation and induced mitochondria-regulated apoptosis, thus minimizing DEN/AAF-induced carcinogenesis in the rat liver.

Anti-inflammatory Activity

Anti-inflammatory effects were observed against an acute (PGE2-induced paw oedema) model of inflammation when rats were pretreated with 50 and 100 mg/kg water extracts of *Zingiber zerumbet* rhizome (Somchit and Shukriyah Nur 2003). The extracts were devoid of any toxicity up to 500 mg/kg in rats. The anti-inflammatory effect of water extract was similar to the reference mefenamic acid. The ethanolic rhizome extract was devoid of any anti-inflammatory effect from 25 to 100 mg/kg concentrations. *Z. zerumbet* water extract decreased the release of tumour necrosis factor-alpha and interleukin-4 (IL-4) in vitro and effectively suppressed leukotriene C4 (LTC4) release from lung tissue in vivo (Chaung et al. 2008). Additionally, BALB/c mice treated with the extract expressed higher ratios of interferon-gamma/IL-4 mRNA in their splenocytes than that of the control group. The results showed that *Z. zerumbet* water extract should have beneficial effects for the treatment of asthmatic patients through its capabilities to inhibit the synthesis of

LTC4 and through the immunomodulation of Th1/Th2 cytokine production.

The methanol extract of *Zingiber zerumbet* rhizomes at doses of 25, 50 and 100 mg/kg showed significant antioedema activity when assessed using the carrageenan-induced paw oedema test and the cotton pellet-induced granuloma test in mice (Zakaria et al. 2010). The extract exhibited significant antinociceptive activity when assessed by the writhing, hot plate and formalin tests. Pretreatment with naloxone (5 mg/kg) significantly decreased the latency of discomfort produced by the 100 mg/kg dose of the extract in the hot plate test. The anti-inflammatory and antinociceptive activities may involve the inhibition of bradykinin-, prostaglandin-, histamine- and opioid-mediated processes.

Essential oil of *Z. zerumbet*, at doses of 30, 100 and 300 mg/kg, administered intraperitoneally to rats induced significant anti-inflammatory activity both in acute and chronic animal models in the carrageenan-induced paw oedema and cotton pellet-induced granuloma tests (Zakaria et al. 2011). The essential oil also inhibited inflammatory- and noninflammatory-mediated pain when assessed using the formalin test. The results indicated that the essential oil of *Z. zerumbe*t possessed anti-inflammatory activity, in addition to its antinociceptive activity, which may explain its traditional uses to treat inflammatory-related ailments.

Studies showed that pretreatment with zerumbone lowered inflammatory markers IL-1beta, tumour necrosis factor (TNF)-alpha and prostaglandin (PG)E(2) and suppressed dextran sodium sulphate (DSS)-induced ulcerative colitis in mice (Murakami et al. 2003). In contrast, nimesulide (a selective COX-2 inhibitor) suppressed the histological changes induced by DSS without affecting inflammatory biomarkers. However, their combination treatment was most effective for suppressing these biomarkers. The results suggested a combination of agents, with different modes of actions, may be an effective anti-inflammatory strategy. In vitro studies showed that zerumbone suppressed expression of pro-inflammatory genes (COX-2 and iNOS) and induced detoxification genes (GSTP1 and NQO1) in RAW 264.7 macrophages (Ohnishi et al. 2009). Zerumbone was found to covalently bind to proteins, Keap1 and HuR, that played key roles in these molecular mechanisms.

Of the following compounds zerumbone (1), 3-*O*-methyl kaempferol (2), kaempferol-3-*O*-(2, 4-di-*O*-acetyl-α-L-rhamnopyranoside) (3) and kaempferol-3-*O*-(3,4-di-*O*-acetyl-α-L-rhamnopyranoside) (4) isolated from *Z. zerumbet* rhizome, compounds 1 and 2 demonstrated potent inhibition of NO production, with IC_{50} values of 4.37 and 24.35 μM, respectively, and also significantly suppressed iNOS expression in a dose-dependent manner (Chien et al. 2008). However, 1 and 2 could inhibit PGE2 production only at high doses (20 and 40 μM, respectively), and COX-2 protein level was not affected. In in-vivo studies, mice administered with zerumbone (10 mg/kg) 1 h before carrageenan injection significantly attenuated oedema and were compared to the vehicle control. Separate studies demonstrated that intraperitoneal administration of zerumbone at doses of 5, 10, 50 and 100 mg/kg to mice produced significant dose-dependent inhibition of paw oedema induced by carrageenan (Sulaiman et al. 2010a). At similar doses, zerumbone significantly suppressed granulomatous tissue formation in the cotton pellet-induced granuloma test.

The humulene sesquiterpene, 5-hydroxyzerumbone (5-hydroxy-2*E*,6*E*,9*E*-humulatrien-8-one), and zerumbone oxide, isolated from *Zingiber zerumbet* rhizomes, were found to inhibit lipopolysaccharide (LPS)-induced nitric oxide production in murine macrophage RAW 264.7 cells with IC_{50} values of 14.1 and 23.5 μM, respectively (Jang et al. 2005). Results of further studies suggested that downregulation of LPS-induced NO production by 5-hydroxyzerumbone was mediated by the suppression of iNOS expression through the modulation of NF-κB activation and HO-1 induction in macrophage cells (Min et al. 2009).

Antinociceptive Activity

Zerumbone, isolated from *Z. zerumbet*, administered intraperitoneally produced significant

dose-dependent antinociceptive effect in acetic acid-induced abdominal writhing test and hot plate test in mice (Sulaiman et al. 2009). The antinociceptive effect in the hot plate test was reversed by the nonselective opioid receptor antagonist naloxone, suggesting that the opioid system was involved in its analgesic mechanism of action. Studies demonstrated that intraperitoneal administration of the *Z. zerumbet* essential oil at the doses of 30, 100 and 300 mg/kg produced significant dose-dependent inhibition of acetic acid-induced abdominal writhing, comparable to that of obtained with acetylsalicylic acid (100 mg/kg) (Sulaiman et al. 2010b). At similar doses, the essential oil produced significant dose-dependent increases in the latency time in the hot plate test with respect to controls, and in the formalin-induced paw licking test, the essential oil also significantly reduced the painful stimulus in both neurogenic and inflammatory phase of the test. The antinociceptive effect of the essential oil in the formalin-induced paw-licking test as well as hot plate test was reversed by the nonselective opioid receptor antagonist naloxone, suggesting that the opioid system was involved in its analgesic mechanism of action. It was shown that *Zingiber zerumbet* essential oil administered to mice via intraperitoneal and oral routes at doses of 50, 100, 200 and 300 mg/kg produced significant dose-dependent antinociception when assessed using acetic acid-induced abdominal writing test (Khalid et al. 2011). Similarly intraperitoneal administration of the oil produced significant dose-dependent inhibition of neurogenic pain induced by intraplantar injection of capsaicin (1.6 μg/paw), glutamate (10 μmol/paw) and phorbol 12-myristate 13-acetate (1.6 μg/paw). The antinociception activity was reversed by pretreatment with L-arginine (100 mg/kg, i.p.) and administration of glibenclamide (10 mg/kg, i.p.), indicating that the essential oil-induced antinociceptive activity was possibly related to its ability to inhibit glutamatergic system and TRPV1 receptors as well as through activation of L-arginine/nitric oxide/cGMP/protein kinase C/ATP-sensitive K(+) channel pathway.

Antihyperlipidemic/Anti-adipogenic Activities

Oral administration of *Z. zerumbet* ethanol extract (300 mg/kg/day) to rats fed with a high-fat diet (HFD) for 2 weeks produced effects similar to fenofibrate (100 mg/kg) in reducing body weight gain, visceral fat pad weights and plasma lipid levels (Chang et al. 2012d). The extract caused reductions in hepatic triglyceride and cholesterol content and lowered hepatic lipid droplet accumulation and the size of epididymal adipocytes. HFD-induced reductions in the hepatic proteins of peroxisome proliferator-activated receptor (PPAR)-α, acyl-CoA oxidase (ACO) and cytochrome P450 isoform 4A1 (CYP4A1) were reversed by the extract. The results suggested that the extract reduced the accumulation of visceral fat and improved hyperlipidaemia in HFD-fed rats by increasing fatty acid oxidation, mediated via up-regulation of hepatic PPARα.

Results of recent in vitro studies suggested that 6-gingerol isolated from *Z. zerumbet* effectively suppressed adipogenesis and that it exerted its role mainly through the significant downregulation of PPARγ and C/EBPα and subsequently inhibiting FAS and aP2 expression (Tzeng and Liu 2013). 6-Gingerol also inhibited the differentiation in 3T3-L1 cells by attenuating the Akt/GSK3β pathway.

Antiatherosclerotic Activity

In THP-1 human monocytic cells, zerumbone suppressed phorbol ester-induced expression of multiple scavenger receptor genes governing macrophage scavenger receptors like lectin-like ox-LDL receptor-1 (LOX-1), a key event in atherosclerosis which up-regulated the uptake of oxidized low-density lipoproteins (ox-LDL) (Eguchi et al. 2007). Further, zerumbone attenuated the expression of SR-A, SR-PSOX and CD36, but not that of CD68 or CLA-1, leading to a blockade of DiI-Ac-LDL uptake, while it also inhibited the transcriptional activities of activator protein-1 and nuclear factor-kappaB.

Their results indicated zerumbone to be a potential phytochemical for regulating atherosclerosis with reasonable action mechanisms.

Nephroprotective Activity

Studies showed that zerumbone attenuated cisplatin-induced nephrotoxicity in rats (Ibrahim et al. 2010). Zerumbone reduced kidney damage and preserved renal functions and reduced elevated malondialdehyde (MDA) levels induced by cisplatin. It was concluded that zerumbone was beneficial in cisplatin-induced renal dysfunction and organ damage in rats possibly via the prevention of lipid peroxidation and preservation of antioxidant glutathione. Treatment of rats with *Z. zerumbet* ethyl acetate extract at doses of 200 and 400 mg/kg prevented the paracetamol-induced nephrotoxicity and oxidative impairments of the kidney, as evidenced by a significantly reduced level of plasma creatinine, plasma renal malondialdehyde (MDA), plasma protein carbonyl and renal advanced oxidation protein product (AOPP) (Abdul Hamid et al. 2012). Further, both doses were also able to induce a significant increment of plasma and renal levels of glutathione (GSH) and plasma superoxide dismutase (SOD) activity. *Z. zerumbet* extract administered at 400 mg/kg was found to show greater protective effects than that at 200 mg/kg. The nephroprotective effects of *Z. zerumbet* extract were confirmed by a reduced intensity of renal cellular damage.

Studies showed that *Z. zerumbet* rhizome ethanol extract displayed similar characteristics to those of metformin in reducing hyperglycaemia and renal dysfunction in streptozotocin-induced diabetic rats (Tzeng et al. 2013). The histological examinations revealed amelioration of diabetes-induced glomerular pathological changes following *Z. zerumbet* treatment. Additionally, protein expressions of renal nephrin and podocin in diabetic rats were significantly increased following the treatment with the extract. The AMP-activated protein kinase (AMPK) protein phosphorylation and expression levels were remarkably reduced in diabetic renal tissues. *Z. zerumbet* treatment significantly rescued the AMP-activated protein kinase phosphorylation compared to non-treated diabetic group.

Antiviral Activity

Zerumbone and 4″-*O*-acetylafzelin were obtained from organic extracts of entire plants of *Z. zerumbet* (Dai et al. 1997). Zerumbone exhibited HIV (human immunodeficiency virus) inhibitory and cytotoxic activities, while 4″-*O*-acetylafzelin was inactive in both assays.

Antibacterial Activity

Staphylococcus aureus, methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus mutans* and *Salmonella typhi* were found to be susceptible in vitro to *Z. zerumbet* chloroform extract (Voravuthikunchai et al. 2005). The chloroform extract inhibited the growth of *S. aureus* in vitro with MIC (minimum inhibitory concentration) of 0.79 mg/mL and MBC (minimum bactericidal concentration) of >12.5 mg/mL (Voravuthikunchai et al. 2006). The chloroform extract of *Z. zerumbet* rhizome inhibited the growth of *Mycobacterium tuberculosis* in vitro with MIC of 125 μg/mL (Phongpaichit et al. 2006). The crude ethanol extract and its petroleum ether and chloroform fractions of *Z. zerumbet* rhizome at 400 μg/disc showed mild-to-moderate antibacterial activity (Kader et al. 2011). The crude ethanol extract showed the highest activity against *Vibrio parahaemolyticus*. The minimum inhibitory concentration (MIC) of the crude ethanol extract and its fractions was within the value of 128–256 μg/mL against two Gram-positive and four Gram-negative bacteria, and all the samples showed the lowest MIC value against *V. parahaemolyticus* (128 μg/mL).

Zerumbone isolated from *Z. zerumbet* rhizome exhibited a dose-dependent antibacterial effect on *Salmonella choleraesuis*, while no antifungal activity was observed (Abdul et al. 2008). Several zerumbone derivatives were found to be selective

inhibitors of the growth of Gram-positive bacteria (Kitayama et al. 2001). Zederone isolated from the crude ethanolic extract of *Z. zerumbet* rhizomes exhibited antibacterial activity against a number of multidrug-resistant and methicillin-resistant *Staphylococcus aureus* strains with minimum inhibitory concentration (MIC) values from 64 to 128 μg/mL. (Kader et al. 2010).

Two new compounds, viz. azazerumbone 1 and azazerumbone 2, were synthesized by $ZnCl_2$-catalysed Beckmann rearrangement of the zerumbone oxime (Santosh Kumar et al. 2013). Azazerumbone 2 exhibited higher antibacterial activity than zerumbone. Among the tested bacteria, *Bacillus cereus* was the most sensitive and *Yersinia enterocolitica* was found to be the most resistant.

Immunomodulatory Activity

Lymphocyte proliferation assay showed that zerumbone was able to activate dose dependently mice thymocytes, splenocytes and human peripheral blood mononuclear cells, (PBMC) and the best dose is 7.5 μg/mL (Keong et al. 2010). Zerumbone also stimulated the production of human interleukin-2 and human interleukin-12 cytokines in lymphocytes, indicating its potential to be used as an immunomodulatory agent. The chloroform extract of *Z. zerumbet* rhizome significantly stimulated T lymphocytes to express CD69 antigen by 31.6 % as compared to the control group (6.2 %), while the methanol and aqueous extracts gave the percentage stimulation of CD69 antigen of 5.8 % and 2.3 %, respectively (Vuddhakul et al. 2004). None of the crude extracts stimulated the migration of polymorphonuclear cells, but the chloroform and methanol extracts did suppress polymorphonuclear cell migration.

Antihyperglycaemic Activity

Recent studies by Chang et al. (2012a) suggested that the ethanol extract of *Zingiber zerumbet* may be used as ethnomedicine for improving insulin sensitivity. In rats fed with a high-fructose diet for six weeks and treated with the extract (300 mg/kg/day) for 8 weeks, the extract reduced insulin resistance indicated by a reduction on the homeostasis model assessment (HOMA-IR) and enhanced composite whole-body insulin sensitivity index (ISIcomp) and hepatic glycogen accumulation. Elevated glycosylated haemoglobin levels and hyperinsulinaemia were ameliorated by the extract. The extract also enhanced the action of insulin on muscle glucose transporter subtype 4 translocation and attenuated hepatic phosphoenolpyruvate carboxykinase expression.

In an earlier study, administration of an aqueous *Z. zerumbet* extract (50, 100 and 150 mg/kg body weight) did not significantly lower blood glucose level in normoglycaemic and streptozotocin-induced hyperglycaemic rats (Husen et al. 2004). Similarly Lal et al. (2012) found that aqueous extract of *Z. zerumbet* exerted no significant activity in streptozotocin-induced diabetic rats.

Antiplatelet Aggregating Activity

Studies by Jantan et al. (2005) showed that the methanol extract of *Z. zerumbet* rhizome at a concentration of 18 μg/mL exerted approximately 96.4 % inhibitory effect on platelet-activating factor (PAF) receptor binding. The inhibitory effect of the methanol extract was greater than Cedrol, a known PAF antagonist (85.2 %), which was used as the standard drug. The IC_{50} value obtained for the active methanol extract was 1.2 μg/mL, which was the lowest compared to Cedrol (2.4 μg/mL) and *Boesenbergia pandurata* (8.6 μg/mL). The methanol extract of *Z. zerumbet* rhizome also showed strong antiplatelet aggregation activity in human whole blood in vitro at 100 μg/mL (Jantan et al. 2008).

Among all tested compounds, zerumbone showed strong inhibition on platelet aggregation at 100 μg/mL caused by arachidonic acid (100 % inhibition), ADP (100 % inhibition) and collagen (64.7 % inhibition).

Antiprotozoal Activity

The chloroform extracts from *Zingiber zerumbet* exhibited anti-giardial activity against trophozoites of *Giardia intestinalis* with an IC_{50} of <100 μg/mL (Sawangjaroen et al. 2005). The chloroform extracts from *Z. zerumbet* exhibited moderate anti-amoebic activity against trophozoites of *Entamoeba histolytica* with IC_{50} of 196.9 μg/mL (Sawangjaroen et al. 2005).

Anti-allergic Activity

The ethanol and aqueous extracts of *Z. zerumbet* rhizome inhibited the release of β-hexosaminidase from RBL-2H3 cell line at doses between 10 and 100 μg/mL with the percentage inhibition of 8.4–53.7 % and 10.9–59.1 %, respectively (Tewtrakul and Subhadhirasakul 2007).

Larvicidal Activity

The essential oil of *Z. zerumbet* rhizome was toxic against both pyrethroid-susceptible and pyrethroid-resistant *Aedes aegypti* laboratory strains at LC_{50}, LC_{95} and LC*99* levels (Sutthanont et al. 2010). The major components of the oils were α-humulene (31.93 %) and zerumbone (31.67 %). The dichloromethane and methanol extracts of the *Zingiber zerumbet* rhizomes exhibited higher inhibitory against *Anopheles nuneztovari* larvae than against *Aedes aegypti* larvae (Bücker et al. 2013).

Anthelmintic Activity

The alcoholic extract of *Z. zerumbet* rhizome exhibited good in vitro anthelmintic activity against *Ascaris lumbricoides* (Raj 1975). The ethanol extract of the rhizome exhibited potent in vitro anthelmintic activity against *Pheretima posthuma* (Goswami et al. 2011). They also reported that *Z. zerumbet* exhibited better anthelmintic activity against *Pheretima posthuma* than *Cucurbita maxima* seed extract at a higher concentration (100 mg/mL) compared to standard albendazole (100 mg/mL) (Pandey et al. 2011).

Antimutagenic Activity

Analogues of zerumbone, viz. azazerumbone 1 and azazerumbone 2, exhibited strong protection against sodium azide-induced mutagenicity of *Salmonella typhimurium* strains TA 98 and TA 1531 (Santosh Kumar et al. 2013). Azazerumbone 2 showed better antimutagenic activity than azazerumbone 1.

Genotoxicity/Toxicity Study

Studies using chromosomal aberration assay and micronuclei test showed that zerumbone was cytotoxic but not clastogenic in cultured human peripheral blood lymphocytes (Al-Zubairi et al. 2010). Studies found that there were no increases in the number of revertant colonies with the ethanol rhizome extract of *Z. zerumbet* at concentrations of 150–5,000 μg per plate, regardless of the metabolic activation system (S9 mix) used in the histidine-dependent auxotrophic mutants of *Salmonella typhimurium* (strains TA97, TA98, TA100, TA102 and TA1535), compared to the vehicle control (Chang et al. 2012b). Additionally the extract, at doses of 150–5,000 μg/mL, did not increase the number of structural aberrations in Chinese hamster lung cells in the presence or absence of S9 mix. An oral administration of the extract to ICR mice, with doses of up to 2,000 mg/kg, caused no significant increases in the number of micronucleated polychromatic erythrocytes (MNPCEs) and mean ratio of polychromatic erythrocytes to total erythrocytes. Also, the extract did not increase the incidence of MNPCEs in the bone marrow. The extract was found to contain zerumbone (200.3 μg/g) and 6-gingerol (102.5 μg/g). Based on these findings, they concluded that the use of ethanol rhizome extract of *Z. zerumbet* in traditional medicine poses no risk of genotoxicity.

In the acute toxicity study in Wistar rats, the ethanol extract of *Z. zerumbet* rhizomes at a

single dose of 15 g/kg did not produce any toxic signs or deaths indicating the 50 % lethal dose must be higher than 15 g/kg (Chang et al. 2012c). In the subchronic toxicity study, the extract administered by gavage at doses of 1,000, 2,000 and 3,000 mg/kg daily for 4 weeks did not alter either the body weight gain or the food and water consumption. The haematological and biochemical analysis did not show significant differences in any of the parameters examined in female or male groups. Necropsy and histopathological examination did not reveal any remarkable and treatment-related changes. The no-observed adverse-effect level for the extract was determined at 3,000 mg/kg for rats under the conditions of this study, implying consumption of the ethanol rhizome extract of *Z. zerumbet* for various medicinal purposes to be safe.

Traditional Medicinal Uses

Rhizomes have been used as traditional medicine in many Asian countries as carminative, anti-inflammatory, antipyretic, stomachic, anodyne, antihypertensive, stimulant and depurative, for the treatment of inflammation, asthma, stomach ache, dyspnoea, dyspepsia, thrush, diabetes, coughs, bacterial infections, fever, toothache, indigestion, constipation, diarrhoea, severe sprains, pain, boils, fish poisoning, wounds and haemorrhoids, as well as antispasmodic, anti-rheumatic and diuretic agents (Wutthithamavet 1997; WHO 1998; Norhayati et al. 1999; Bhuiyan et al. 2009; Zakaria et al. 2010, 2011; Sulaiman et al. 2010a, b; Stuart 2012). Malays in Malaysia commonly used the rhizome to relive gastralgia, debility, vertigo and constipation (Norhayati et al. 1999). Malays used the fresh rhizomes as a cure for oedema, stomach ache and sores, while the juice of the boiled rhizomes is used to treat worm infestation in children (Somchit and Shukriyah Nur 2003; Ruslay et al. 2007; Sulaiman et al. 2010a, b). A decoction of the rhizome is used as appetizer and for stomach ache in Indonesia (Burkill 1966). In the Philippines, decoction is prescribed for asthma and as a topical for rheumatism (Stuart 2012). The Chinese macerate the rhizomes in alcohol and use it as a tonic, depurative or stimulant, while the Taiwanese used the plant as an anti-inflammatory adjuvant for stomach ache, sprain and fever (Stuart 2012). In Thailand, the fresh rhizomes are also used as antiflatulent agent (Wutthithamavet 1997). In India, the rhizome powder is mixed with ripe *Morinda citrifolia* for the treatment of severe pain; the cooked and softened rhizome is used to treat toothache, cough, asthma, worms, leprosy and other skin diseases; and the ground and strained rhizome is mixed with water and drank to treat stomach ache (Tushar et al. 2010; Zakaria et al. 2011) In Hawaii, compressed rhizomes are used for bruises and cuts and to treat headaches, toothaches, ringworm, joint sprains and abdominal colic (Abbott 1992; Chun 1994). In addition, they also used ashes from burnt *Z. zerumbet* leaves, which are combined with a mixture of ashes of *Schizostachyum glaucifolium*, nut sap of *Aleurites moluccana* and rhizome sap of *Z. zerumbet*, as a remedy for cuts and bruised skin. In Polynesia it is an ingredient of several medical preparations used to treat ear inflammation and diarrhoea (Petard 1986).

Other Uses

Zingiber zerumbet and *Curcuma xanthorrhiza* are two of the most commonly used ingredients in Indo-Malaysian traditional medicines, health supplements and tonics (Ruslay et al. 2007). Recently, a number of products derived from the aqueous extracts of these species have appeared in the market in the form of spray-dried powder packed in sachet or bottle. The milky sap from the inflorescence cone has been employed as a shampoo in Hawaii (Wagner et al. 1999).

The plant is cultivated as an ornament for its unique inflorescence which has become a popular cut-flower with long shelf life of several weeks.

Comments

Z. zerumbet is propagated by divisions of the clumps or rhizome pieces. Recent studies showed that the plant can be efficiently micropropagated from plantelets derived from rhizome bud explants (Faridah et al. 2011).

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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 100 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 programmes 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, the United States 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 and 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 1,000 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

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and pharmacological properties of the plants. This work will be of significant interest to 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 Allergic 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.

Abdominal Distension Referring to generalized 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.

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.

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-sulphonic acid, a type of mediator in chemical reaction kinetics of specific enzymes.

ACAT Acyl CoA: cholesterol acyltransferase.

ACE See angiotensin-converting enzyme.

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 catalyses 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.

Acidosis Increased acidity, an excessively acid condition of the body fluids.

Acne Vulgaris 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.

Acquired Immunodeficiency Syndrome (AIDS) An epidemic disease caused by an infection by human immunodeficiency virus (HIV-1, HIV-2), a 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.

ACTH (Adrenocorticotropic Hormone) Also known as 'corticotropin', is a polypeptide tropic hormone produced and secreted by the anterior pituitary gland.

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

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expression in response to a variety of stimuli, 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.

Actoprotective Increasing the body's physical performance.

Actoprotectors Preparations that increase the mental performance and enhance body stability against physical loads without increasing oxygen consumption. Actoprotectors are regarded as a subclass of adaptogens that hold a significant capacity to increase physical performance.

Acute Otitis Media (AOM) See otitis media.

Acyl-CoA Dehydrogenases A group of enzymes that catalyses 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. A_1 receptors and A_{2A} play roles in the heart, regulating myocardial oxygen consumption and coronary blood flow, while the A_{2A} receptor also has broader anti-inflammatory 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 A_{2B} and A_3 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).

Adrenal Glands Star-shaped endocrine glands that sit on top of the kidneys.

Adrenalectomized Having had the adrenal glands surgically removed.

Adrenergic Having to do 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.

Agalactia Lack of milk after parturition (birth).

Agammaglobulinaemia An inherited disorder in which there are very low levels of protective immune proteins called immunoglobulins. *cf.* x-linked agammaglobulinaemia.

Age-Related Macular Degeneration (AMD) A medical condition of elderly adults that results in a loss of vision in the centre of the visual field (the macula) because of damage to the retina.

Agglutination Clumping of particles.

Agglutinin A protein substance, such as an antibody, that is capable of causing agglutination (clumping) of a particular antigen.

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 Signalling Pathway Akt are protein kinases involved in mammalian cellular signalling which inhibits apoptotic processes.

Akt/FoxO Pathway Cellular processes involving Akt and FoxO transcription factors that play a role in angiogenesis and vasculogenesis.

Akt/GSK-3β/eNOS Phosphorylation Amplifies serotonin 5-HT2B receptor blockade mediated anti-hypertrophic effects.

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.

Albuminuria Excessive amount of albumin in the urine, a symptom of severe kidney disease.

Alcohol Dehydrogenase (ADH) An enzyme involved in the breakdown of alcohol.

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.

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.

Allodynia A painful response to a normally innocuous stimulus.

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 behavioural 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, alpha-linked polysaccharides, such as starch and glycogen, yielding glucose.

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.

Amenorrhaea 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.

Amygdalitis Inflammation of one or both tonsils, tonsilitis.

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.

Anaphrodisiac Or antiaphrodisiac is something that reduces or blunts the libido.

Anaphylactic *Adj*. See anaphylaxis.

Anaphylatoxins 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.

Anaphylaxis A severe, life-threatening allergic response that may be characterized by symptoms such as reduced blood pressure, wheezing, vomiting or diarrhoea.

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.

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.

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.

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.

Angioedema Rapid swelling of the dermis, subcutaneous tissues, mucosa and submucosal tissues caused by small blood vessels leaking fluid into these tissues.

Angiogenic *Adj*. See angiogenesis.

Angiogenesis A physiological process involving the growth of new blood vessels from pre-existing vessels.

Angioplasty Medical procedure used to open obstructed or narrowed blood vessel resulting usually from atherosclerosis.

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.

Anguillulosis A parasitosis caused by the intestinal nematode *Strongyloides stercoralis* (round worm).

Anisakiasis A human parasitic infection of the gastrointestinal tract caused by the consumption of raw or undercooked seafood containing larvae of the nematode *Anisakis simplex*.

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.

Anosmia Inability to perceive odour, reduced sense of smell.

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.

Antiasthmatic 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 buildup 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.

Antidopaminergic A term for a chemical that prevents or counteracts the effects of dopamine.

Antidote A remedy for counteracting a poison.

Antidrepanocytary Anti-sickle cell anaemia.

Antidysenteric An agent used to reduce or treat dysentery and diarrhoea.

Antidyslipidaemic Agent that will reduce the abnormal amount of lipids and lipoproteins in the blood.

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.

Antifilarial Effective against human filarial worms.

Antifungal An agent that kills or inhibits the growth of fungi.

Antiganacratia Anti-menstruation.

Antigastralgic Preventing or alleviating gastric colic.

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.

Antihaemorrhagic An agent which stops or prevents bleeding.

Antihematic Agent that stops vomiting.

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.

Antihypercholesterolaemia Term to describe lowering of cholesterol level in the blood or blood serum.

Antihypercholesterolaemic Agent that lowers cholesterol level in the blood or blood serum.

Antihyperlidaemic 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).

Anti-inflammatory 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.

Antileukaemic Anticancer drugs that are used to treat leukaemia.

Antilithiatic An agent that reduces or suppresses urinary calculi (stones) and acts to dissolve those already present.

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.

Antinutrient Are natural or synthetic compounds that interfere with the absorption of nutrients and are commonly found in food sources and beverages.

Anti-oedematous Reduces or suppresses oedema.

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 (converted 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).

Antioxytocic Inhibiting premature labour. *cf.* tocolytic.

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.

Antiplasmodial Suppressing or destroying plasmodia.

Antiplatelet Agent Drug that decreases platelet aggregation and inhibits thrombus formation.

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 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.

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.

Apnoea Suspension of external breathing.

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.

Apoplexy Unconsciousness or incapacity of the brain to function resulting from a cerebral haemorrhage or stroke.

Apoprotein The protein moiety of a molecule or complex, as of a lipoprotein.

Apoptogenic Ability to cause death of cells.

Apoptosis Death of cells.

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.

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, seborrhoea and vascularization.

Aromatase An enzyme involved in the production of estrogen that acts by catalysing 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.

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.

Aromatic Having a pleasant, fragrant odour.

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.

Arthrodynia An affection characterized by pain in or about a joint.

Arthus Reaction An allergic reaction of the immediate hypersensitive type that results from the union of antigen and antibody, with complement present, in blood vessel walls.

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.

ASAT or 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 coordination) 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.

Atelectasis The collapse or closure of the lung resulting in reduced or absent gas exchange.

ATF-2 Activating transcription factor 2.

Atherogenesis The formation of lipid deposits in the arteries.

Atherogenic Having the capacity to start or accelerate the process of atherogenesis.

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 buildup 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.

Athlete's Foot A contagious skin disease caused by parasitic fungi affecting the foot, hands, causing itching, blisters and cracking. Also called dermatophytosis.

Athymic Mice Laboratory mice lacking a thymus gland.

Atonic Lacking normal tone or strength.

Atony Insufficient muscular tone.

Atopic Dermatitis An inflammatory, noncontagious, pruritic skin disorder of unknown aetiology; often called eczema.

Atresia A congenital medical condition in which a body orifice or passage in the body is abnormally closed or absent.

Atretic Follicle Follicular atresia is the breakdown of the ovarian follicles.

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; the most serious consequence of atrial fibrillation is ischaemic stroke.

Atrioventricular Node A node of specialized heart muscle located in the septal wall of the right atrium; receives impulses from the sinoatrial node and directs them to the walls of the ventricles.

Attention-Deficit Hyperactivity Disorder (ADHD, ADD or AD/HD) Is a neurobehavioral developmental disorder, primarily characterized by the coexistence 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 hydrolyses 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.

Babesia A protozoan parasite (malaria-like) of the blood that causes a haemolytic disease known as Babesiosis.

Babesiosis Malaria-like parasitic disease caused by Babesia, a genus of protozoal piroplasms.

Back Tonus Normal state of balanced tension in the tissues of the back.

Bactericidal Lethal to bacteria.

BAFF A cytokine that belongs to the tumour necrosis factor (TNF) ligand family.

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 Oesophagus (Barrett Oesophagitis) A disorder in which the lining of the oesophagus 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.

B-Cell Activating Factor (BAFF) Also called tumour necrosis factor ligand superfamily member 13B. It plays an important role in the proliferation and differentiation of B cells.

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 leukaemia.

Bechic A remedy or treatment of cough.

Bed Nucleus of the Stria Terminalis (BNST) Acts as a relay site within the hypothalamic–pituitary–adrenal axis and regulates 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 B_1) 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 signalling 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, $(1 \rightarrow 3)$, $(1 \rightarrow 4)$-β-D-glucan, soluble, viscous component of fibres found in cereals like oats.

Beta-Lactamase Enzymes produced by some bacteria that are responsible for their resistance to beta-lactam antibiotics like penicillins.

Beta-Thalassemia An inherited blood disorder that reduces the production of haemoglobin.

BHT Butylated hydroxytoluene (phenolic compound), an antioxidant used in foods, cosmetics, pharmaceuticals and petroleum products.

BID The only known Bcl-2 family member that can function as an agonist of proapoptotic Bcl-2-related proteins such as Bax and Bak.

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 eighteenth and nineteenth 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 malaria whereby the red blood cells burst in the bloodstream, (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 (haemorrhage) due to a defect in the system of coagulation.

Blennorrhaea Inordinate discharge of mucus, especially a gonorrhaeal discharge from the urethra or vagina.

Blennorrhagia Gonorrhea.

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.

Blood Stasis Syndrome Blood stagnation or slowing of blood, an important underlying

pathology of many disease processes according to traditional Chinese medicine.

BMPs (Bone Morphogenetic Proteins) A family of secreted signalling molecules that can induce ectopic bone growth.

BNIP3 A proapoptotic BH3-only protein which is associated with mitochondrial dysfunction and cell death.

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 downwards.

Bouillon A broth in French cuisine.

Bowman–Birk Inhibitors Type of serine proteinase inhibitor.

Bradycardia 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 Neurotrophic Factor (BDNF) A protein member of the neurotrophin 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 the 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.

Bursa A fluid-filled sac or saclike cavity situated in areas subjected to friction.

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-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-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-Kit Receptor A protein tyrosine kinase receptor that is specific for stem cell factor. This interaction is crucial for the development of haematopoietic, gonadal and pigment stem cells.

C-Myc Codes for a protein that binds to the DNA of other genes and is therefore a transcription factor.

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-akpha) 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.

Ca^{2+} ATPase (PMCA) Is a transport protein in the plasma membrane of cells that serves to remove calcium (Ca^{2+}) 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.

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 towards the urinary bladder.

Calculosis The tendency or deposition to form calculi or stones.

Calculus (Calculi) Hardened, mineral deposits that can form a blockage in the urinary system.

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 signalling cascade used in cell communication in living organisms.

CAMP Factor Diffusible, heat-stable, extracellular protein produced by Group B streptococcus that enhances the hemolysis of sheep erythrocytes by *Staphylococcus aureus*. It is named after Christie, Atkins and Munch-Peterson, who described it in 1944.

Campylobacteriosis Is a gastrointestinal disease (gastroenteritis) caused by bacteria called *Campylobacter* which is frequently associated with the consumption of contaminated poultry.

Cancer A malignant neoplasm or tumour in any 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.

Cannabinoid Receptor Family Includes CB1 cannabinoid receptors found predominantly in the brain and nervous system and CB2 cannabinoid receptors mainly associated with immune tissues and expressed at low levels in the brain.

Cannabinoid Receptor Type 2 (CB 2 Receptor) A G protein-coupled receptor from the cannabinoid receptor family that are mainly expressed on T cells of the immune system, on macrophages and B cells and in haematopoietic cells.

Carboxypeptidase An enzyme that hydrolyses 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.

CB-1 Receptor Cannabinoid receptor type 1 held to be one of the most widely expressed G protein-coupled receptors in the brain.

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.

CD4T Cell Helper T cell with CD4 receptor that recognizes antigens on the surface of a virus-infected cell and secretes lymphokines that stimulate B cells and killer T cells.

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, haematopoietic 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 extracellular 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.

Cephalalgia 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 travelled to the brain.

Cerebral Infarction Is the ischaemic kind of stroke due to a disturbance in the blood vessels supplying blood to the brain.

Cerebral Ischaemia Is the localized reduction of blood flow to the brain or parts of the brain due to arterial obstruction or systematic hyperfusion.

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.

CGRP Calcitonin Gene-Related Peptide A vasodilator neuropeptide that is expressed in a subgroup of small neurons in the dorsal root and trigeminal and vagal ganglia. This neuropeptide has been postulated to play a role in the pathophysiology of migraine.

Chalcones A subgroup of flavonoids.

Chancre A painless lesion formed during the primary stage of syphilis.

Chaperones Are proteins that assist the noncovalent folding or unfolding and the assembly or disassembly of other macromolecular structures.

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 peripheral neurons that are sensitive to chemical stimuli.

Chemosensitizer A drug that makes tumour cells more sensitive to the effects of chemotherapy.

Chemosis Oedema 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 anaemia 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.

Cholelithiasis Presence of gall stones (calculi) in the gall bladder.

Cholera An infectious gastroenteritis caused by enterotoxin-producing strains of the bacterium *Vibrio cholera* and characterized by severe, watery diarrhoea.

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 from the liver to the duodenum.

Cholesterol A soft, waxy, steroid substance found among the lipids (fats) in the bloodstream and in all our body's cells.

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 signalling roles for cell membranes, cholinergic neurotransmission (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, also called parasympathomimetic.

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.

Chromoblastomycosis A chronic fungal infection of the skin and the subcutaneous tissue caused by traumatic inoculation of a specific group of dematiaceous fungi (such as *Fonsecaea pedrosoi, Phialophora*

verrucosa, Fonsecaea compacta) through the skin.

Chromosome Long pieces of DNA found in the centre (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.

Chronotropic Affecting the time or rate, as the rate of contraction of 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.

Chylous 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.

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.

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.

Colibacillosis Infection with *Escherichia coli*.

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.

Collagen Protein that is the major constituent of cartilage and other connective tissues; comprises the amino acids hydroxyproline, proline, glycine and hydroxylysine.

Collagenases Enzymes that break the peptide bonds in collagen.

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 Hyperaemia Enlarged blood vessels in the eyes.

Conjunctivitis Sore, red and sticky eyes caused by eye infection.

Constipation A very common gastrointestinal disorder characterized 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 homeostasis.

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 centres 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 anaemia-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.

Cor Pulmonale Or pulmonary heart disease is enlargement of the right ventricle of the heart as a response to high blood pressure or increased resistance in the lungs.

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.

Cornification Is the process of forming an epidermal barrier in stratified squamous epithelial tissue.

Corpora Lutea A yellow, progesterone-secreting body that forms from an ovarian follicle after the release of a mature egg.

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.

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 signalling 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.

Creatine 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's Disease An inflammatory disease of the intestines that affect any part of the gastrointestinal tract.

CRP (C-Reactive Protein) A substance produced by the liver that increases in the presence of inflammation in the body.

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).

Cryptococcal Meningitis A fungal infection of the membranes covering the brain and spinal cord (meninges).

Crytorchidism (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.

Cystorrhoea 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 catalyses 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 signalling 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 and ulcers.

Decidual Stromal Cells Like endometrial glands and endothelium, express integrins that bind basement components.

Deciduogenic Relating to the uterus lining that is shed off at childbirth.

Deciduoma Decidual tissue induced in the uterus (as by trauma) in the absence of pregnancy.

Deciduomata Plural of deciduoma.

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 diminishes 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 characterized 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.

Desquamative Gingivitis Red, painful, glazed and friable gingivae which may be a manifestation of some mucocutaneous conditions such as lichen planus or the vesiculobullous disorders.

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 Foot Any pathology that results directly from diabetes mellitus or any long-term or chronic complication of diabetes mellitus.

Diabetic Neuropathy A neuropathic disorder that is associated with diabetes mellitus. It affects all peripheral nerves including pain fibres, 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 Refers to a clinical trial or experiment in which neither the subject nor the

researcher knows which treatment any particular subject is receiving.

Douche A localized 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.

Drug-Metabolizing Enzymes Play central roles in the biotransformation, metabolism and/or detoxification of xenobiotics or foreign compounds that are introduced to the human body.

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.

Dysbiosis Also called dysbacteriosis, refers to a condition with microbial imbalances on or inside the body.

Dysentery (Formerly known as flux or the bloody flux) is a disorder of the digestive system that results in severe diarrhoea 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.

Dyshomeostasis An imbalance or other breakdown of a homeostasis system.

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.

Dysmenorrhoea 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 (oesophagus, stomach, small and large intestines).

Dyspareunia Painful sexual intercourse.

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 centred 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-Cadherin Has traditionally been categorized as a tumour suppressor.

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 catalysing the dismutation of superoxide radicals.

Ectopic Heartbeats Small changes in an otherwise normal heartbeat that lead to extra or skipped heartbeats.

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 oedema, 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.

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 signalling 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 oedematous tissue on the genitals and legs due to various causes.

Embrocation Lotion or liniment that relieves muscle or joint pains.

Embryonation Formation of embryo in the egg.

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 caused by a virus.

Encephalocele Protrusion of brain tissue through a congenital fissure in the skull.

Encephalomalacia Cerebral softening, a localized softening of the brain substance, due to haemorrhage 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.

Endosteul Pertaining to the endosteum.

Endosteum The thin layer of cells lining the medullary cavity of a bone.

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.

Endotoxaemia The presence of endotoxins in the blood, which may result in shock. *adj*. endotoxaemic.

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.

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.

eNOS (Endothelial Nitric Oxide Synthase) The enzyme responsible for most of the vascular nitric oxide produced.

Enteral Term used to describe the intestines or other parts of the digestive tract.

Enteralgia Pain in the intestines; intestinal colic.

Enteral Administration Involves the oesophagus, 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.

Enterohaemorrhagic Causing bloody diarrhoea 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 localized 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.

Epidermal Growth Factor Receptor (EGFR) Belongs to the ErbB family of receptor tyrosine kinases (RTK). EGFR are involved in the pathogenesis and progression of different carcinoma types.

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.

Epistaxis Acute haemorrhage from the nostril, nasal cavity or nasopharynx (nosebleed).

Epithelial-Mesenchymal Transition or Transformation (EMT) A process by which epithelial cells lose their cell polarity and cell–cell adhesion and gain migratory and invasive properties to become mesenchymal cells.

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.

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 labour especially by eliminating fatigue symptoms.

ERK (Extracellular Signal-Regulated Kinases) Widely expressed protein kinase intracellular signalling 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.

Eryptosis Suicidal death of erythrocytes, characterized by cell shrinkage, membrane blebbing, activation of proteases and phosphatidylserine exposure at the outer membrane leaflet.

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; characterized 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 needs 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.

Exfoliative Cheilitis Is a reactive process, in which upper, lower or both lips become chronically inflamed, crusted and sometimes fissured.

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.

Experimental Allergic Encephalomyelitis (EAE) Is an animal model of brain inflammation.

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 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 and 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 Adenomatous Polyposis (FAP) Is an inherited condition in which numerous polyps form mainly in the epithelium of the large intestine.

Familial Amyloid Polyneuropathy (FAP) Also called Corino de Andrade's disease, a neurodegenerative autosomal dominant genetically transmitted, fatal, incurable disease.

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.

Felon A purulent infection in the bulbous distal end of a finger.

Fetotoxic Toxic to the fetus.

Fibrates Hypolipidaemic 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.

Fibrinolytic 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 threadlike nematode worm.

Filariasis A parasitic and infectious tropical disease that is caused by threadlike filarial nematode worms in the superfamily Filarioidea.

Fistula An abnormal connection between two organs 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, hydrolyses 5′-nucleotides to their corresponding nucleosides.

5-HT1A Receptor A serotonin protein that binds to 5-5-hydroxytryptamine (5-HT) with high affinity to exert subtle control over emotion and behaviour.

Flash Electroretinogram or Flash ERG (fERG) Is a test which measures the electrical response of the eye's light-sensitive cells (rods and cones). It also checks other cell layers in the retina.

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.

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.

Flavans A subgroup of flavonoids. See flavonoids.

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 that 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 and heavy menstrual bleeding and are also anti-inflammatory.

Fluorine 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. Also called FMVD (flow-mediated vasodilation).

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 breakdown 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 plays 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.

G Protein-Coupled Receptor Kinases (GRKs, GPCRKs) A family of protein kinases which regulate the activity of G protein-coupled receptors (GPCRs) by phosphorylating their intracellular domains after their associated G proteins have been released and activated.

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 proapoptotic gene.

Galactagogue A substance that promotes the flow of milk.

Galactophoritis Inflammation of the milk ducts.

Galactopoietic Increasing the flow of milk; milk producing.

Galctifuge Or lactifuge, causing the arrest of milk secretion.

Gall Bladder 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, cholecystitis.

Gallic Acid Equivalent (GAE) Measures the total phenol content in terms of the standard gallic acid by the Folin–Ciocalteu 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.

Gastroprokinetic See prokinetic.

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 agents that damage cellular DNA, resulting in mutations or cancer.

Geriatrics Is a subspecialty of internal medicine that focuses on healthcare 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 characterized 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 gonorrhoea) 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.

Glioblastoma Common and most lethal form of brain tumour.

Glioblastoma Multiforme Most common and most aggressive type of primary brain tumour in humans, involving glial cells.

Glioma Is a type of tumour that starts in the brain or spine. It is called a glioma because it arises from 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-6-Phosphate Dehydrogenase (G6PD or G6PDH) Is a cytosolic enzyme in the pentose phosphate metabolic pathway.

Glucose Transporter Type 4 (GLUT 4) Insulin-regulated glucose transporter found in adipose tissues and striated muscles that modulate 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 enables 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) Catalyses 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 x 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. goitre.

Goitrogenic *Adj*. causing goitre.

Gonadotroph A basophilic cell of the anterior pituitary specialized to secrete follicle-stimulating hormone or luteinizing hormone.

Gonadotropins 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 buildup 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 Sandlike 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 prepares for mitosis and where chromatids and daughter cells separate.

Guillain–Barre Syndrome Is a serious disorder that occurs when the body's defence (immune) system mistakenly attacks part of the nervous system, leading to nerve inflammation, muscle weakness and other symptoms.

Gynecomastia Enlargement of the gland tissue of the male breast, resulting from an imbalance of hormones.

Gynecopathy Any or various diseases specific to women.

Gynoid Adiposity Fat distribution mainly to the hips and thighs, pear-shaped.

Haemagglutination A specific form of agglutination that involves red blood cells.

Haemagglutination–Inhibition Test Measures of the ability of soluble antigen to inhibit the agglutination of antigen-coated red blood cells by antibodies.

Haemagglutinin Refers to a substance that causes red blood cells to agglutinate.

Haemagogic Promoting a flow of blood.

Haemangioma Blood vessel.

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.

Haematocrit Is a blood test that measures the percentage of the volume of whole blood that is made up of red blood cells.

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.

Haematopoietic 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.

Haematuria, Hematuria Is the presence of blood in the urine. Haematuria 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 catalyses 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.

Haemoglobinopathies Genetic defects that produce abnormal haemoglobins and anaemia.

Haemolysis Lysis of red blood cells and the release of haemoglobin into the surrounding fluid (plasma), *adj*. haemolytic.

Haemolytic Anaemia Anaemia due to haemolysis, the breakdown of red blood cells in the blood vessels or elsewhere in the body.

Haemolytic-Uremic Syndrome Is a disease characterized by haemolytic anaemia, acute renal failure (uraemia) and a low platelet count.

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.

Haemorheology Study of blood flow and its elements in the circulatory system. *adj*. haemorheological.

Haemorrhage, Hemorrhage Bleeding, discharge of blood from blood vessels.

Haemorrhagic Colitis An acute gastroenteritis characterized by overtly bloody diarrhoea that is caused by *Escherichia coli* infection.

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 sulphur-producing bacteria that live within the surface of the tongue and in the throat.

Hallucinogen Drug that produces hallucinogen.

Hallucinogenic Inducing hallucinations.

Hallux Abducto Valgus Commonly called bunion is an abnormal bending of the big toe towards the other toes of the foot.

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.

HBD-2 (human β-defensin 2) A member of the defensin family of antimicrobial peptides that plays important roles in the innate and adaptive immune system of both vertebrates and invertebrates.

HBeAg Hepatitis B e antigen.

HBsAg Hepatitis B s antigen.

Heartburn Burning sensation in the stomach and oesophagus 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.

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.

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, characterized 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 and 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 a 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 Circinatus Dermatitis herpetiformis (resembling herpes).

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.

HGPRT, HPRT (Hypoxanthine–Guanine Phosphoribosyl Transferase) An enzyme that catalyses 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.

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 bloodstream. 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.

Hippocampal Pertaining to the hippocampus.

Hippocampus A ridge in the floor of each lateral ventricle of the brain that consists mainly of grey matter.

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.

Histone Acetyltransferases (HAT) Are enzymes that acetylate conserved lysine amino acids on histone proteins by transferring an acetyl group from acetyl-CoA to form e-N-acetyl lysine. HATs act as transcriptional co-activators.

Histone Lysine Demethylases (KDMs) Enzymes that play a key role in the amplification of hypoxia-inducible-factor signalling and expression of pro-angiogenic genes in cancer and neurological disorders.

HIV See human immunodeficiency virus.

Hives Urticaria, is a skin rash characterized 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-methylglutaryl-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 anaemia.

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.

Hormesis A term used by toxicologists to refer to a biphasic dose response to an environmental agent characterized by a low dose stimulation or beneficial effect and a high dose inhibitory or toxic effect.

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, estrogen and progesterone and sometimes testosterone.

HSF-1 Factor Major regulator of heat shock protein transcription in eukaryotes.

HSP27 Is an ATP-independent, 27 kDa heat shock protein chaperone that confers protection against apoptosis.

HSP70 Heat shock protein chaperone that confers protection against heat-induced apoptosis.

HSP90 A 90 kDa heat shock protein chaperone that has the ability to regulate a specific subset of cellular signalling proteins that have been implicated in disease processes.

HSPD 1 Heat shock 60 kDa protein 1

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 sulphates.

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.

Hydrocoele Abnormal accumulation of fluid inside the scrotum.

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.

Hyperaemia Is the increased blood flow that occurs when tissue is active.

Hyperammonemia, Hyperammonaemia A metabolic disturbance characterized by an excess of ammonia in the blood.

Hypercalciuria (*Idiopathic*) Presence of excess calcium in the urine without obvious cause.

Hypercholesterolaemia High levels of cholesterol in the blood that increase a person's risk for cardiovascular disease leading to stroke or heart attack.

Hyperemesis Severe and persistent nausea and vomiting (morning sickness) during pregnancy.

Hyperfibrinogenaemia Excessive fibrinogen in the blood.

Hyperglycaemia Hyperglycaemic High blood sugar, is a condition in which an excessive amount of glucose circulates in the blood plasma.

Hyperglycaemic A substance that raises blood sugar levels.

Hyperhomocysteinaemia Is a medical condition characterized by an abnormally large level of homocysteine in the blood.

Hyperinsulinaemia A condition in which there are excess levels of circulating insulin in the blood; also known as prediabetes.

Hyperkalaemia Is an elevated blood level of the electrolyte potassium.

Hyperkeratosis Abnormal thickening of the outer layer of the skin. *adj*. hyperkeratotic.

Hyperkinesis Enhanced itch to pricking.

Hyperleptinaemia Increased serum leptin level.

Hyperlipoproteinaemia A metabolic disorder characterized by abnormally elevated concentrations of lipid/lipoprotein in the plasma, also known as hyperlipidaemia and hyperlipaemia.

Hypermenorrhoea Abnormally heavy or prolonged menstruation.

Hypermethylation An increase in the inherited methylation of cytosine and adenosine residues in DNA.

Hyperoxaluria An excessive urinary excretion of oxalate.

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 in muscle tension and a reduced ability of the muscle to stretch.

Hypertriglyceridaemia or Hypertriglycaemia A disorder that causes high triglycerides in the blood.

Hypertrophy Enlargement or overgrowth of an organ.

Hyperuricaemia Is a condition characterized by abnormally high level of uric acid in the blood.

Hypoadiponectinaemia 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.

Hypoalbuminaemia A medical condition where levels of albumin in blood serum are abnormally low.

Hypocalcaemic 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 Refers to states where the production of gastric acid in the stomach is absent or low.

Hypocholesterolaemic 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 Characterized 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.

Hypoxia-Inducible Factors (HIFs) Transcription factors that respond to changes in available oxygen in the cellular environment, specifically to deficiency in oxygen.

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 Mesenteric Phlebosclerosis (IMP) A rare disease, characterized by thickening of the wall of the right hemicolon with calcification of mesenteric veins.

Idiopathic Sudden Sensorineural Hearing Loss (ISSHL) Is a 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 signalling.

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 prediabetic state of dysglycaemia 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 injuries, 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 vapour 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 physiological 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 signalling 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 behaviour.

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, among others. 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 signalling 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. It usually occurs with walking and disappears after rest.

Interoceptive Relating to stimuli arising from within the body.

Interstitial Pertaining to the interstitium.

Interstitium The space between cells in a tissue.

Intertrigo An inflammation (rash) caused by microbial infection in skin folds.

Intima Innermost layer of an artery or vein.

Intimal Hyperplasia The thickening of the tunica intima of a blood vessel as a complication of a reconstruction procedure.

Intoxicant Substance that produces drunkenness or intoxication.

Intracavernosal Within the corpus cavernosum, 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.

Ischaemia 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.

Janus Kinase (JAK)-Signal Transducer and Activator of Transcription (STAT) Signalling Are essential molecules in cytokine signal transduction pathways involved in cancer development and progression.

Jaundice Refers to the yellow colour 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 leukaemia.

Kainate Receptors Or KARs, are non-NMDA (N-methyl-D-aspartate) ionotropic receptors which respond to the neurotransmitter glutamate.

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 human 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.

KB Cell A cell line derived from a human carcinoma of the nasopharynx, used as an assay for antineoplastic (antitumour) agents.

Keloids Benign dermal tumours characterized by fibroblastic proliferation and excessive accumulation of collagen.

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.

Keratolysis Softening and separation of the horny layer of the epidermis.

Keratolytic Pertaining to keratolysis.

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 catalyses 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.

Larvicidal 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 LD 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, easing pain or discomfort.

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 leukaemia, causing leukaemia.

Leukocytopenia Abnormal decrease in the number of leukocytes (white blood cells) in the blood.

Leukocytosis Increase in white blood cell count above its normal range.

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.

Levarterenol See norepinephrine.

LexA Repressor Or repressor LexA, is a repressor enzyme that represses SOS response genes coding for DNA polymerases required for repairing DNA damage.

Leydig Cells Also called interstitial cells of Leydig, are found adjacent to the seminiferous tubules in the testicle. They produce testosterone in response to luteinizing hormone.

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.

Liposomes Artificially prepared vesicles made of lipid bilayer.

Lipotoxicity Refers to tissue diseases that may occur when fatty acids spill over in excess of the oxidative needs of those tissues and enhance the 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).

Lithontriptic Removes stones from kidney, gall bladder.

Liver X Receptors Nuclear hormones that function as central transcriptional regulators for lipid homeostasis.

Lotion A liquid 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 the 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 signalling 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-centred 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 Degeneration of the corpus luteum and ovarian luteinized tissues at the end of the luteal phase of both the estrous and menstrual cycles in the absence of pregnancy. *adj*. luteolytic.

Luteotropic Stimulating the formation of the corpus luteum.

Lymphadenitis The inflammation or enlargement of a lymph node caused by microbial infection.

Lymphadenitis, Cervical Inflammation of the lymph nodes in the neck, usually caused by an infection.

Lymphadenomegaly Is the enlargement of the lymph node/nodes.

Lymphadenopathy A term meaning 'disease of the lymph nodes', lymph node enlargement.

Lymphatitis Inflammation of lymph vessels and 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 separation 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 colour 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.

Mammalian Target of Rapamycin (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 physiological 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, dysregulated 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 three 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 disc, muscle, tendon and skin. They respond to a noxious (damaging) mechanical load.

Medial Preoptic Area Is located at the rostral end of the hypothalamus; it is important for the regulation of male sexual behaviour.

Megaloblastic Anaemia An anaemia 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.

Melaena (Melena) Refers to the black, 'tarry' feces that are associated with gastrointestinal haemorrhage.

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 Refers to permanent cessation of menstruation.

Menorrhagia Is heavy bleeding and that's usually defined as periods lasting longer than 7 days or excessive bleeding.

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.

Meta-analysis A statistical procedure that combines the results of several studies that address a set of related research hypotheses.

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.

Metabolomics Is the scientific study of chemical processes involving metabolites.

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.

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.

Metestrus The quiescent period of sexual inactivity between oestrus cycles.

Metropathy Any disease of the uterus especially of the myometrium.

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.

Microphthalmia-Associated Transcription Factor (MITF) A basic helix–loop–helix leucine zipper transcription factor protein that plays a role in the development, survival and function of melanocytes and osteoclast.

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.

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.

mTOR, the Mammalian (or Mechanistic) Target of Rapamycin Regulates a wide range of cellular and developmental processes by coordinating signalling responses to mitogens, nutrients and various stresses.

MTTP Microsomal triglyceride transfer protein that is required for the assembly and secretion of triglyceride-rich lipoproteins from both enterocytes and hepatocytes.

MUC 5AC Mucin 5AC, a secreted gel-forming protein mucin with a high molecular weight of about 641 kDa.

Mucolytic Capable of reducing the viscosity of mucus, or an agent that so acts.

Mucositis Painful inflammation and ulceration of the mucous membranes lining the digestive tract.

Mucous Relating to mucus.

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.

Musculotropic Affecting or acting upon muscular tissue.

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 muscle 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 Ischaemia 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 fibres.

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 A symptom of certain neuromuscular disorders characterized by the slow relaxation of the muscles after voluntary contraction or electrical stimulation.

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 fibre or cell with a tubular appearance and a centrally located nucleus.

Myringosclerosis Also known as tympanosclerosis or intratympanic tympanosclerosis, a condition caused by calcification of collagen tissues in the tympanic membrane of the middle ear.

N-Nitrosomorpholine 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 causes 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 constitutes 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.

Neovascularization Is the development of tiny, abnormal, leaky blood vessels inside the eye.

Neovasculature Formation of new blood vessels.

Nephrectomized 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 cleave 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.).

Neurectomy Surgical cutting through or removal of a nerve or a section of a nerve.

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 post-mitotic 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 behaviour of antipsychotic drugs that reduce confusion, delusions, hallucinations and psychomotor agitation in patients with psychoses.

Neuroma Is a growth or tumour of nerve tissue.

Neuropathy A collection of disorders that occurs when the peripheral nervous systems are damaged causing pain and numbness in the hands and feet.

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 the nutrition and maintenance of nervous tissue (neurons).

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 induces 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.

Nicotinamide Adenine Dinucleotide Phosphate (NADP) A coenzyme comprising nicotinamide mononucleotide coupled by pyrophosphate linkage to adenosine 2′,5′-bisphosphate; it acts as an electron carrier in numerous reactions, being alternately oxidized (NADP+) and reduced (NADPH).

NIH3T3 Cells A mouse embryonic fibroblast cell line used in the cultivation of keratinocytes.

Nidation Implantation.

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 constitutes 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.

Nocebo 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.

Nociceptive Causing pain, responding to a painful stimulus.

Nociceptors Specialized peripheral sensory neurons that respond to potentially damaging stimuli by sending nerve signals to the spinal cord and brain.

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.

Non-osteogenic Fibromata of bone, a benign tumour of bone which shows no evidence of ossification.

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.

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.

Nycturia Excessive urination at night, especially common in older men.

Nystagmus Fast, involuntary movements of the eyes.

Obsessive–Compulsive Disorder (OCD) A common psychiatric disorder defined by the presence of obsessive thoughts and repetitive compulsive actions, self-grooming.

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 12 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.

Oedematogenic Producing or causing oedema.

Oligoanuria Insufficient urine volume to allow for administration of necessary fluids, etc.

Oligoarthritis An inflammation of two, three or four joints.

Oligoasthenoteratozoospermia Male infertility refers to the inability of a male to achieve a pregnancy in a fertile female.

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.

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.

Oppilation Obstruction particularly of the lower intestines.

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.

Orchidectomized 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 non-inflammatory 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 referred to as bone gamma-carboxyglutamic acid-containing protein.

Osteoclastogenesis The production of osteoclasts.

Osteoclasts A kind of bone cell that removes bone tissue by removing its mineralized matrix.

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.

Osteosarcoma 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.

Otitis Media Inflammation of the middle ear.

Otopathy Disease of the ear.

Otorrhoea Running drainage (discharge) exiting the ear.

Ovariectomized 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 labour 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.

P65 Transcription Factor Is a protein that in humans is encoded by the RELA gene. Its alternative name is nuclear factor NF-kappa-B p65 subunit.

P300/CBP Are transcriptional co-activators that play critical roles in integrating multiple signal-dependent transcription events and may have specific roles in tumour suppression pathways.

p21waf1/cip1 Encodes a cyclin-dependent kinase inhibitor that is transcriptionally activated by the p53 tumour 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 haematological 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 fingerlike 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.

Paraesthesia 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'.

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.

Parasitaemia Presence of parasites in blood. *adj*. parasitaemic.

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.

Parenteral Administration Administration by intravenous, subcutaneous or intramuscular routes.

Paresis A condition characterized by partial loss of movement or impaired movement.

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 an important role in the remodeling of chromatin and the regulation of gene expression, transcription, cell cycle 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 delta 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.

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.

PDGR Receptor (Platelet-Derived Growth Factor Receptor) Are cell surface tyrosine kinase receptors for members of the platelet-derived growth factor (PDGF) family.

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.

Percutaneous 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.

Perineum The region between the thighs inferior to the pelvic diaphragm.

Perineal Pertaining to the perineum.

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 pyorrhoea.

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 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, paraesthesia, dysaesthesia, spasm, weakness, hypoesthesia or anaesthesia.

Peripheral Neuropathy Refers to damage to nerves of the peripheral nervous system.

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.

Peyer's 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 a process the human body uses to destroy dead or foreign cells.

Pharmacodynamics Branch of pharmacology dealing with the effects of drugs and the mechanism of their action.

Pharmacognosis The branch of pharmacology that studies the composition, use and history of drugs.

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.

Phase II Drug-Metabolizing Enzymes Play an important role in biotransformation of endogenous compounds and xenobiotics to more easily excretable forms as well as in the metabolic inactivation of pharmacologically active compounds. Phase II drug-metabolizing enzymes are mainly transferases.

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.

Phloroglucinol 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 colour, also called hypophosphataemia.

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 hydrolyses 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 cleave 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 and 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 provide 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 towards light.

Phthisis An archaic name for tuberculosis.

Phytohaemagglutinin 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 contains no pigment.

Piles See haemorrhoids.

PI3K Phosphoinositide 3-kinase.

PI13K/AKT Signalling 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 characterized 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.

Plantar Verruca Wart occurring on the sole of the foot.

Plasma The yellow-coloured liquid component of blood, in which blood cells are suspended.

Plasma Kallikrein 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.

Platelet-Derived Growth Factor (PDGF) Is one of the numerous growth factors, or proteins, that regulate cell growth and division.

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 characterized by the production of too many red blood cells.

Polymorphonuclear 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.

Polyneuropathy Simultaneous malfunction of many peripheral nerves throughout the body.

Polyp A growth that protrudes from a mucous membrane.

Polyphagia Medical term for excessive hunger or eating.

Polyposis Describes a condition where there are a lot of polyps.

PolyQ Disease Polyglutamine repeat diseases are neurodegenerative ailments elicited by glutamine-encoding CAG nucleotide expansions within endogenous human genes.

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) 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.

PR Interval Is the time (in seconds) from the beginning of the P wave (onset of atrial depolarization) to the beginning of the QRS complex.

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-eclampsia Toxic condition of pregnancy characterized by high blood pressure, abnormal weight gain, proteinuria and oedema.

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.

Prenidatory Phase Pre-implantation phase.

Prenylated Flavones Flavones with an isoprenyl group in the 8-position, has been reported to have good anti-inflammatory properties.

Prepubertal Before puberty, pertaining to the period of accelerated growth preceding gonadal maturity.

Primiparous Relating to a woman who has given birth once.

Pro-angiogenic Promote angiogenesis (formation and development of new blood vessels).

Probiotication Enhancement with beneficial probiotic 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 proanthocyanidin, oligomeric proanthocyanidin, 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.

Prokinetic Or gastroprokinetic, substance that enhances gastrointestinal motility by increasing the frequency of contractions in the small intestine or making them stronger.

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.

Prolapsus 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, characterized 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 Leukaemia A subtype of acute myelogenous leukaemia (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.)

Prostanoid EP 4 A prostaglandin receptor that may be involved in the neonatal adaptation of circulatory system, osteoporosis, as well as initiation of skin immune responses.

Prostate A gland that surrounds 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.

Protheolithic Proteolytic see proteolysis.

Prothrombin Blood-clotting protein that is converted to the active form, factor IIa, or thrombin, by cleavage.

Prothyroid Good for thyroid function.

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.

Pruritus 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 behaviour.

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 behaviour.

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 Signalling Pathway Shown to be important for an extremely diverse array of cellular activities—most notably cellular proliferation and survival.

Phthisis 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 Postpartum 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.

Pyelitis Acute inflammation of the pelvis of the kidney caused by bacterial infection.

Pyelonephritis An ascending urinary tract infection that has reached the pyelum (pelvis) of the kidney.

Pyoderma Bacterial skin infection.

Pyodermatitis Refers to inflammation of the skin.

Pyorrhoea 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.

QSR Complex Series of deflections in an electrocardiogram that represent electrical activity generated by ventricular depolarization prior to contraction of the ventricle.

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.

Radiodermatitis A skin disease associated with prolonged exposure to ionizing radiation.

Radiolysis The dissociation of molecules by radiation.

Radioprotective Serving to protect or aiding in protecting against the injurious effect of radiations.

RAD23B UV excision repair protein RAD23 homolog B

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 urticaria.

Reactive Oxygen Species Species such as superoxide, hydrogen peroxide and hydroxyl

radical. At low levels, these species may function in cell signalling 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.

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 defences 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.

Respiratory Burst Is the rapid release of reactive oxygen species (superoxide radical and hydrogen peroxide) from different cells.

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.

Reticulocyte Non-nucleated stage in the development of the red blood cell.

Reticulocyte Lysate Cell lysate produced from reticulocytes, used as an in vitro translation system.

Reticuloendothelial System Part of the immune system, consists of the phagocytic cells located in reticular connective tissue, primarily monocytes and macrophages.

Retinal Ischaemia Is a common cause of visual impairment and blindness.

Retinitis Pigmentosa (RP) An inherited, degenerative eye disease that causes severe vision impairment and may lead to blindness.

Retinoblastoma Protein A tumour suppressor protein that is dysfunctional in several major cancers.

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.

Reye's Syndrome A potentially fatal disease that has numerous detrimental effects to many organs, especially the brain and liver, occurs commonly in children after a viral infection.

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 anaemia.

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.

Rhinorrhoea 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 is 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 diarrhoea (gastroenteritis) in young children and infants, one of several viruses that cause 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 subcutaneous, 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 ischaemia or injury and coronary artery disease.

Salve Medical ointment used to soothe the head or body surface.

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.

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 behaviours.

Schwann Cells Or neurolemmocytes, are the principal supporting cells of the peripheral nervous system, they form the myelin sheath of a nerve fibre.

Sciatica A condition characterized 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 behaviour 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 Bradyacusia Hearing impairment of the inner ear resulting from damage to the sensory hair cells or to the nerves that supply the inner ear.

Sepsis Potentially fatal whole-body inflammation caused by severe infection.

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 systemic 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.

Sialylation 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 haemoglobin S, an abnormal type of haemoglobin. 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 Serum Institut 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.

Sirtuin Also called Sir2 proteins a class of proteins that possess either histone deacetylase or mono-ribosyltransferase activity.

6-Keto-PGF1 Alpha A physiologically active and stable hydrolysis product of epoprostenol, found in nearly all mammalian tissues.

Sjögren's Syndrome An autoimmune disease that mainly affects the eyes and salivary glands, but can affect different parts of the body.

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 signalling by members of the TGF-beta (transforming growth factor beta) superfamily.

Smad2/3 A key signalling 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.

SOCE (Store-Operated Ca^{2+} Entry) Is a receptor-regulated Ca^{2+} entry pathway.

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.

Sphingolipid A member of a class of lipids derived from the aliphatic amino alcohol, sphingosine.

Spina Bifida A congenital birth defect caused by the incomplete closing of the embryonic neural tube.

Spinocerebellar Ataxia (SCA) Is a progressive, degenerative, genetic disease with multiple types.

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, a transcription factor, 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.

Steatohepatitis Liver disease, characterized by inflammation of the liver with fat accumulation in the liver.

Steatorrhoea Is the presence of excess fat in feces which appear frothy, foul smelling and floats because of the high fat content.

Steatosis Refers 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.

Steroidogenesis The production of steroids, as by the adrenal glands.

Steroidogenic Relating to steroidogenesis.

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 sulphate (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 Haemorrhage Is bleeding in the area between the brain and the thin tissues that cover the brain.

Substance P A neuropeptide 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 plays an important role in reward, addiction and movement.

Sudatory Medicine that causes or increases sweating; also see sudorific.

Sudorific A substance that causes sweating.

Sulphur Sulphur is an essential component of all living cells. Sulphur is important for the synthesis of sulphur-containing amino acids, all polypeptides, proteins and enzymes such as glutathione an important sulphur-containing tripeptide which plays a role in cells as a source of chemical reduction potential. Sulphur 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 STDs. 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.

Systemic 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 plays 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.

Tachykinins Neuropeptide transmitters that are widely distributed and active in the central nervous system and periphery, rapidly acting secretagogues and cause smooth muscle contraction and vasodilation (hypotension).

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 tapeworm or flatworm of the genus, *Taenia*.

Taeniacide An agent that kills tapeworms.

Tardive Dyskinesia A disorder characterized by repetitive, involuntary, purposeless movements in the body such as grimacing, tongue protrusion, lip smacking, puckering and pursing of the lips and rapid eye blinking. Rapid, involuntary movements of the limbs, torso and fingers may also occur.

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.

Teletherapy A noninvasive procedure using external beam radiotherapy treatments.

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 the inflammation of a tendon.

Tenesmus A strong desire to defecate.

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.

Th 1 Cells Helper cells that play an important role in the immune system.

Th 17 Cells A subset of T helper cells producing interleukin 17.

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.

Thermogenesis Is the process of heat production in organisms.

Thermogenic Tending to produce heat, applied to drugs or food (fat burning food).

Thermonociceptors Or thermal nociceptors, sensory receptors that are stimulated by noxious 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.

3-β-HSD Or 3-β-hydroxysteroid dehydrogenase/δ-5-4 isomerase, is an enzyme that catalyses the synthesis of progesterone from pregnenolone.

3-Nitrotyrosine (3-NT) Protein Used as a marker for oxidative damage or nitrosative stress.

Thrombocythaemia A blood condition characterized 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 bloodstream 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 cruris Ringworm of the groin.

Tinea favosa See favus.

Tinea imbricata Also called Tokelau, an eruption characterized by concentric rings of overlapping scales forming papulosquamous patches scattered over the body; it occurs in tropical climates especially prevalent in southwest Polynesia and is caused by the fungus *Trichophyton concentricum*.

Tinea pedis Fungal infection of the foot, also called athletes' 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 (tPA) 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 labour.

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.

Topoisomerase Inhibitors A new class of anti-cancer 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.

Toxaemia 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 pre-eclampsia.

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 catalyses 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 six 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 *Trichophyton*.

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 bloodstream.

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).

TRPV1 See transient receptor potential vanilloid 1.

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 hydrolyses 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.

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 Eardrum.

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 myringosclerosis.

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 two 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 one 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.

Uricaemia 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.

Urinary Incontinence Sudden and strong need to urinate because of poor bladder control.

Urinogenital Relating to the genital and urinary organs or functions.

Urodynia Pain on urination.

Urokinase Also called urokinase-type plasminogen (uPA), is a serine protease enzyme in human urine that catalyses the conversion of plasminogen to plasmin. It is used clinically as a thrombolytic agent.

Urokinase-Type Plasminogen (uPA) 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 Myomas Also called fibroids, tumours that grow from the uterine wall.

Uterine Prolapse Occurs when weakened or damaged muscles and ligaments allow the uterus to slip into the vagina.

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.

Vaginal Dystrophy A condition in which the outer part of the vagina becomes dry and the skin thickens or thins.

Vaginitis Infectious or non-infectious inflammation of the vaginal mucosa.

Vaginopathy Any disease of the vagina.

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, wind-pipe, lungs, heart and most of the digestive system.

Varicose Veins Are veins that have become enlarged and twisted.

Variola Or smallpox, a contagious disease unique to humans, caused by either of two virus variants, *Variola major* and *Variola minor*. The disease is characterized by fever, weakness and skin eruption with pustules that form scabs that leave scars.

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 stimulate 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 characterized by hot flushes and night sweats.

Vasospasm Refers to a condition in which blood vessels spasm, leading to vasoconstriction and subsequently to tissue ischaemia 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 A contagious and painful wart on the sole of the foot.

Verruca plana Is a reddish-brown or flesh-coloured, 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 resulted from or worsened by genetic or environmental conditions.

Vestibular Schwannoma Also called acoustic neuroma is a benign tumour that may develop from an overproduction of Schwann cells that press on the hearing and balance nerves in the inner ear.

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.

Vimentin A type III intermediate filament protein that is expressed in mesenchymal cells.

Viraemia 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 colourful 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, dissolves 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 functions 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 haemoglobin 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 and 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 prevents anaemia. 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 hypocalcaemic 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 helps prevent or delay the chronic diseases associated with free radicals. Besides its antioxidant activities, vitamin E is involved in immune function, cell signalling, regulation of gene expression and other metabolic processes. Deficiency is very rare but can cause mild haemolytic anaemia in newborn infants.

Vitamin K A group of fat-soluble vitamin and consists of vitamin K_1 which is also known as phylloquinone or phytomenadione (also called phytonadione) and vitamin K_2 (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 haemorrhage.

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.

Vulva–Vaginal Erythema Abnormal redness and inflammation of the skin in the vagina.

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 affect 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 Signalling Pathway Is a network of proteins involved in embryogenesis and cancer and also in normal physiological processes.

Xanthine Oxidase A flavoprotein enzyme containing a molybdenum cofactor (Moco) and (Fe_2S_2) clusters, involved in purine metabolism. In humans, inhibition of xanthine oxidase reduces the production of uric acid and prevents hyperuricaemia 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.

Xerostomia Dryness in the mouth due to lack of saliva production.

X-Linked Agammaglobulinaemia Also known as X-linked hypogammaglobulinaemia, XLA, Bruton type agammaglobulinaemia, Bruton syndrome or sex-linked agammaglobulinemia; a rare x-linked genetic disorder that affects the body's ability to fight infection.

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 skin, bone and joints, also called framboesia.

yGCN5 A histone acetyl transferase (HAT) that plays a role in regulation of transcription, cell cycle 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 haemorrhagic 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.

ZK1 Krueppel-type zinc finger protein, binds DNA and, through this binding, regulates gene transcription.

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.

Abortive Imperfectly formed.

Abscission Shedding of leaves, flowers or fruits following the formation of the abscission zone.

Acaulescen tLacking 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° before terminating in a point as of leaf apex and base.

Adaxia lSide closest to the stem axis.

Adelphous 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 and 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.

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.

Alternate Leaves or buds that are spaced along opposite sides of stem at different levels.

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 fibres.

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 forms 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 specs 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 leaflike 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 candlestick.

Canescent Covered with short, fine whitish or greyish 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).

Caruncle (Bot) fleshy structure attached to the seed of certain plants.

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.

Chamaephyte A low-growing perennial plant whose dormant overwintering buds are borne at or just above the surface of the ground.

Chartaceous Papery, of paper-like texture.

Chasmogamous Describing flowers in which pollination takes place while the flower is open.

Chatoyant Having a velvety sheen or lustre.

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 coloured 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, refers 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, montmorillonite-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 genetic 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 Specialized 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.

Crested Frilled and ruffled edge.

Crispate Weakly undulating edge.

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 Gramineae (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 specialized 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 removes 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.

Diadelphous Having stamens in two bundles as in Papilionaceae flowers.

Diageotropic The tendency of growing parts, such as roots, to grow at right angle to the line of gravity.

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.

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.

Diplochory Seed dispersal involving two or more modes.

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.

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.

Dipterocarpus 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 shape. *cf*. discoid, radiate.

Discoid Resembling a disc; having a flat, circular form; disc-shaped *cf*. disciform, radiate.

Discolorous Having two colours, as of a leaf which has different colours 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.

Elaioplasts A type of leucoplast that is specialized for the storage of lipids in plants.

Elaiosome Fleshy lipid-rich structures that are attached to the seeds of many plant species.

Ellipsoid A 3-dimensional shape; elliptic in outline.

Elliptic Having a 2-dimensional shape of an ellipse or flattened circle.

Elongate 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.

Ensiform Shaped like the blade of a sword, long and narrow with sharp edges and a pointed tip.

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.

Epithet Name.

Equitant In a loose fan pattern.

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 fertilization 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 Leaflike.
Foliage Leaves of the plant.
Foliar Pertaining to a leaf.
Foliolate Pertaining to leaflets, used with a number prefix to denote the number of leaflets.
Foliose Leaflike.
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.
Foveolate Surface pitted with shallow depressions.
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.
Frutescent Shrubby.
Fugacious Shedding off early.
Fulvous Yellow, tawny.
Funiculus (Botany) short stalk which attaches the ovule to the ovary wall.
Fuscescent Dusky.
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 does not develop into a fruit but is 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 the 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.
Geniculate Bent like a knee, refers to awns and filaments.
Genome Complete set of genetic material of an organism.
Geocarpic Where the fruit is 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, extrafloral 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 colour due to wetland conditions.

Globose Spherical in shape.

Globular A three-dimensional shape, spherical or orbicular; circular in outline.

Glochidiate Having glochids.

Glochidote Plant having glochids.

Glochids Tiny, finely barbed hair-like spines found on the areoles of some cacti and other plants.

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, fibre-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 Refers to palms which flower 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 outwards 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 disc 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). Refers 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, thereby facilitating 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. Refers 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.

Hybridization 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 Sore-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. *adj.* relating to or of the nature of a hypanthium.

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 inwards or downwards, 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.

Infundibulum Funnel-shaped cavity or structure.

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 is 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.

Lacerate Irregularly cleft.

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 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.

Ligneous Woody.

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.

Lipotubuloids Are cytoplasmic domains containing aggregates of lipid bodies surrounded by a network of microtubules, which join one lipid body with the others.

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 made 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.

Lorate Strap-shaped with obtuse tip.

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, becomes 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 fertilization.

Microsporangium The sporangium containing microspores in pteridophytes. *cf*. megasporangium.

Midvein The main vascular supply of a simple leaf blade or lamina, also called midrib.

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 Refers 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.

Monostichous Forming one row.

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 defence 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.

Myrmecochory Seed dispersal by ants.

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 contains *Rhizobium* bacteria which fix 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.

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.

Nucellus Central portion of an ovule in which the embryo sac develops.

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 downwards.

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 towards 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°.

Ochraceous A dull yellow colour.

Ocreate Having a tube-like covering around some stems, formed of the united stipules; sheathed.

-oid Suffix denoting a 3-dimensional shape, e.g. spheroid.

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 fertilization. *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 throughout 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 2 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 Refers 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 midrib 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 Refers 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, grey 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.

Pulviniform Swelling or bulging.

Pulvinus Swelling at the base of leaf stalk.

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.

Purpurascent Purple or becoming purple.

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 downwards.

Regosol Soil that is young and undeveloped, characterized by medium to fine-textured unconsolidated parent material that may be 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°.

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 enrolled 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 vigour by altering water uptake and causing ion-specific toxicities or imbalances.

Salinity Is characterized 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 because of scattered rough hairs.

Scale Dry bract or leaf.

Scandent Refers 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 forwards.

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 Refers 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 characterized 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 refers 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.

Sporangium A spore-bearing structure found in ferns, fern allies and gymnosperms. *pl*. sporangia. *adj*. sporangial.

Sporidia Asexual spores of smut fungi.

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 fertilization 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 leaflike, 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

Strophile An appendage at the hilum of certain plant seeds.

Strophiolate Furnished with a strophile or caruncle.

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.

Subfamily 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.

Suffrutescent Stem Stem woody at the base.

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.

Tomentellose Mildly tomentose.

Tomentose Refers to plant hairs that are bent and matted forming a wooly coating.

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, angular ovate.
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 downwards, 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.
Vaginate Forming or enclosed in a sheath.
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.
Veinlets Small veins.
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 fro 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 colour 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.

Zygoten The fist cell formed by the union of two gametes in sexual reproduction. *adj*. zygotic.

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