# Senna auriculata

## **Scientific Name**

Senna auriculata (L.) Roxb.

## Synonyms

Cassia auriculata L., Cassia densistipulata Taub.

# Family

Fabaceae also placed in Caesalpiniaceae

## Common/English Names

Avaram Senna, Matara Tea, Styptic Weed, Tanner's Cassia, Tarwar

# **Vernacular Names**

*Burmese*: Peikthingat *Chinese*: Er Ye Jue Ming

*French*: Avaram

*India*: Tangedu (<u>Andra Pradesh</u>), Awala (<u>Gujarati</u>), Anwal, Aval, Awai, Tarawar, Taroda, Tarval, Tarvar, Tarwan, Tarwar (<u>Hindi</u>), Aavarike, Athi, Avara, Avara-Gida, Avarakka, Avarike, Avarikke, Bobbade, Cakusina, Chaknsiva, Chakoosina Gida, Charma Hada Aavarike, Chookusina Gida, Honnaavare, Honnaavarike, Honnarike, Honnavari Gida, Honnavarike, Olaniyaro, Olle Thangadi, Olletangadi, Olletangedi, Olletangedu, Sakusina, Tangadi, Tangadi-Gida, Tangedi, Taravada, Taravada-Gida, Thangadi (Kannada), Avara, Avarakka, Avaram, Aveeram, Aviram, Jimute, Ponnaviram (Malayalam), Arsuai, Avul, Taravada, Taroda, Tarvad, Tarwad, Tarwar, Tharoda (Marathi), Timirihari (Oriya), Adarisimbi, Ahula, Ahulya, Ahulyam, Avartaki, Avarttaki, Awarteki, Bhumyahulya, Carmaranga, Charamranga, Charmaranga, Mandari, Mayahari, Mayharie, Pitakalika, Pitakilaka, Pitapuspa, Talopota, Timirihari, Visanika (Sanskrit), Aavaarai, Aavarai, Akuli, Anakavarai, Anakavaraicceti, Avarai, Avarai, Avarai, Avaraicceti, Avaram, Avary, Avavirai, Avaviraicceti, Avirae, Avirai, Avirai Arici, Aviraittol, Aviraiyilai, Avirantol, Aviri, Aviricceti, Cakacaka, Cakuli, Canakkirampul, Caruvantirakam, Catilaka, Catilakacceti, Catinakam, Catinam, Catirakuli, Caturkkalicceti, Caturkkuli, Caturkuli, Cemmai, Cemmala, Cemmalai, Cemmalaviraicceti, Ceppalai, Cicuravikam, Cittiraippal, Corikkattai, Cularai, Cummai, Cutcumapattiram, Cuvarnaputpatam, Emaputpi, Ilanci, Kapalacanti, Kapalatti, Kapalatticceti, Kari, Karikacceti, Katavukacikacceti, Katavukacikam, Kotaikkuvatan, Kotakacalai, Mancalavarai, Mekacatturu, Mekamaki, Mekari, Mikupattam, Mikupattavarai, Muntakaveni, Muntakavenicceti, Nattavarai, Nattunilavarai, Patarai, Pataraicceti, Periyaavirai, Periyatakarai, Peyaviram, Pitantavarai, Pitaputpi, Pitattavarai, Rukkumam, Sadurguli, Sadurgulu,

Semmalai, Summai, Talapattiram, Talapetam, Talapotakam, Talapotam, Talapotam, Talapotavirai, Tamirakari, Tankamavarai, Tavapotakam, Turonikai, Turonikaivirai, Tuvakai, Vanamakiyamuli, Vanamakumuli, Vanamikumuli, Vanamikuntamulicceti, Vanamulikai, Vanatteri, Vanattericceti, Varnaputpakam (<u>Tamil</u>), Avaray, Merakatangedu, Merakathangedu, Merikatangaru, Merka Tangedu, Tangar, Tangedu, Tangera, Tanghedu, Tangheroo, Thangedu, Thangera (<u>Telugu</u>)

*Portuguese*: Avúl *Sri Lanka*: Ranawara (Sinhalese)

# **Origin/Distribution**

Senna auriculata is a native of India, Myanmar and Sri Lanka and has been successfully introduced into several African countries. It has been suggested that it is indigenous in Tanzania, but an early introduction and naturalization seem more likely. It is cultivated in India and Sri Lanka and occasionally elsewhere.

## Agroecology

Under natural or naturalized conditions, *Senna auriculata* is found in woodlands and wooded grasslands up to 600 m altitude. It usually grows wild in dry regions with a minimum annual precipitation of 400 mm, but it also tolerates wet climates with an annual precipitation of up to 4,300 mm. It grows well in areas with mean annual temperature range of 16–27 °C. *Senna auriculata* needs full sun. It tolerates many soil types, including saline soils but prefers fairly rich, well-drained, friable soils.

# **Edible Plant Parts and Uses**

The flowers, young leaves and young tender pods are edible (Watt 1908; Burkill 1966; Facciola 1990; Rahmansyah 1991; Reddy et al. 2007). Flowers are eaten as vegetables in Andhra Pradesh, India (Reddy et al. 2007). The leaves are made into a refreshing cooling drink in India. The leaves are sometimes used to make tea, dried flowers serve as a coffee substitute, and in times of food scarcity, the young tender pods, young leaves and flowers are eaten as a vegetable (Rahmansyah 1991). A fermented mixture of pounded bark and dissolved molasses serves as an alcoholic beverage in some parts of India.

#### Botany

A branched shrub or small tree 1.5–5 m high (Plate 1), with a trunk diameter up to 20 cm and with thin, brown, lenticellate bark. Leaves alternate, paripinnately compound with 6-13 pairs leaflets (Plates 1 and 2); stipules large and leafy, broadly reniform, 7-22 mm wide, persistent; petiole 10-14 cm long; rachis provided with a gland between each pair of leaflets. Leaflet oblongelliptical to obovate-elliptical,  $10-35 \times 5-12$  mm, rounded and mucronate at apex, glabrous to pubescent. Inflorescence an axillary raceme, 2-8 flowered (Plates 1 and 3). Flower (Plate 4) bisexual, zygomorphic, pentamerous, 4-5 cm across; sepals rounded at apex, imbricate, glabrous; petals free, imbricate, unequal, 1.5-3 cm long, yellow; stamens 10, the 3 lower ones largest and fertile, others usually sterile; ovary superior, falcate, with 1.5 cm long, stalked, style (fruit a flattened cylindrical pod 5-18×1-2 cm, transversely undulate between the 10-20 seeds, indehiscent, green turning to brown when mature.



Plate 1 Flowers and foliage (GF Chung)



**Plate 2** *Upper* and *lower* surface of pinnate leaves (GF Chung)



Plate 3 Inflorescence with yellow flowers (GF Chung)



Plate 4 Close up of flower (GF Chung)



Plate 5 Ripe and mature pods (GF Chung)

Seeds compressed ovoid-cylindrical,  $7-9 \times 4-5$  mm, with a distinct areole on each surface (Plate 5).

# **Nutritive/Medicinal Properties**

## Leaf Phytochemicals

Five compounds were isolated from the leaves (Varshney et al. 1973). Compounds A, B and C were found to be saturated higher aliphatic fatty alcohols and formed 2:4-dinitrophenylhydrazone derivatives, compound D gave all characteristics of a sterol, and compound E was identified as an anthraquinonepigment, emodin(1,6,8-trihydroxy-Di-(2-ethyl) 3-methylanthraquinone). hexyl phthalate was isolated from Cassia auriculata leaves (Nageswara Rao et al. 2000). Leaves were reported to contain carbohydrates, phenols, lipids, proteins, saponins, flavonoids, tannin, terpenoids and cardiac glycosides (Senthilkumar and Vijayakumari 2012). Thirteen bioactive compounds were identified in the ethanol leaf extract, and the major constituents were phytol, octadecane 1-(ethenyloxy)- and E-10-pentadecenol. Other components included resorcinol; 3-O-methyl-1,14-tetradecanediol; 3,7,11,15-D-glucose; tetramethyl-2-hexadecen-1-ol; 2H-cyclopropa[a] naphthalen-2-one,1,1a,4,5,6,7,7a,7b-octahydro-, 1,7,7-tetramethyl-(1aa,7a,7aa,7ba)-; azulene, 1,2, 3,5,6,7,8,8a-octahydro-1,4-dimethyl-7-(1methylethenyl)-, [1*S*-(1a,7a,8aa)]-; 1,2-benzene dicarboxylic acid, diisooctyl ester; squalene; 1-cyclohexylnonene; and 1-4-[(2-diethylamino] ethylamino[-6-methyl-2-pyrimidinyl]-3-[3,4,5-trimethoxyphenyl] guanidine.

Twenty-nine compounds were found in C. auriculata leaves (Anandan et al. 2011). The main constituents were 3-O-methyl-D-glucose  $(48.50\%), \alpha$ -tocopherol- $\beta$ -D-mannoside (14.22%),resorcinol (11.80%), *n*-hexadecanoic acid (3.21%), 13-octadecenal, (Z)- (2.18 %), 1,2,3,4-tetrahydroisoquinolin-6-ol-1-carboxylic acid (1.98 %), unknown (3.29 %), unknown (2.61 %) and unknown (1.14 %). Other minor constituents were glycerine (0.16 %), thymine (0.11 %), 1-butanol, 3methyl-, formate (0.17 %), 4H-pyran-4-one,2,3dihydro-3,5-dihydroxy-6-methyl (0.46 %), benzaldehyde,4 methyl- (0.83 %), 2-propenoic acid, 4-methylpentyl ester (0.125), sucrose (1.2 %), 1,6,anhydro- $\beta$ -D-glucopyranose (levoglucosan) (0.3 %),  $\beta$ -D-glucopyranoside, methyl (0.36 %), 1,2-benzenedicarboxylic acid, bis(2-methylpropyl) ester (1 %), benzenamine,2,3,4,5,6-pentamethyl (0.87), unknown (0.57 %), hexadecanoic acid, ethyl ester (0.1 %), 1-tridecyne (0.3 %), 13-oxabicyclo[10.1.0] tridecane (0.42 %), phytol (0.61 %), 1-E,11,Z-13-octadecatriene (0.56 %), 1 octadecanoic acid (0.46 %), a-tocopherol (1.16 %) and *N*-acetyl tyramine (1.24 %).

#### Seed/Pod Phytochemicals

Sterols, anthracene derivatives, triterpenoid and tannins were isolated from the ethanol extract of the pods (Suresh et al. 2007).

The following chemicals were identified in the seed extract: *n*-hexadecanoic acid (21.31 %), grapeseed oil (linoleic and oleic acids) (31.02 %), *E*,*Z*-1,3,12-nonadecatriene (12.27 %), stearic acid (9.39 %), benzoic acid, 2-hydroxy-methyl ester (0.07 %), β-ethoxypropionaldehyde diethyl acetal (0.86 %), ethyl caprylate (0.14 %), 2-methoxy-4-vinylphenol (0.36 %), glycine, *N*-(trifluoroacetyl)-, 1-methylbutyl ester (0.10 %), 2,3-dihydro-3,5-dihydroxy-6-methyl-4*H*-pyran-4-one (0.12 %), capric acid ethyl ester (0.16 %), resorcinol (0.21 %) dodecanoic acid

(0.48 %), 3'5'-dimethoxyacetophenone (0.58 %), 9-octadecenoic acid, (*E*)-(12.60 %), palmitic acid  $\beta$ -monoglyceride (2.95 %), dl- $\alpha$ -tocopherol (1.22 %) and stigmasta-5,23-dien-3-ol,(3 $\beta$ )-(1.21 %) (Raj et al. 2012).

Polyphenols quantified in the hydroalcoholic seed extract of *C. auriculata* were epicatechin (14 %), catechin (4.5 %) and procyanidin B1 (1 %), while the supercritical fluid extract contained catechin (6 %) and epicatechin gallate (20 %) (Puranik et al. 2011).

#### Flower Phytochemicals

The flower of *C. auriculata* was found to contain a flavonol glycoside 5-*O*-methylquercetin 7-*O*-glucoside (Manogaran and Sulochana 2004). The hydromethanolic extract and its ethyl acetate and *n*-butanol fractions of the flowers were found to contain phenolic compounds, carbohydrates, tannins, steroids and amino acids (Surana et al. 2009).

#### Root Phytochemicals

Phytochemical analysis of the crude root extracts revealed the presence of an array of active chemical constituents such as tannins, flavonoids, glycosides, carbohydrates, steroids and triterpenoids (Wadekar et al. 2011).

#### Plant Phytochemicals

*C. auriculata* was reported to contain leucopelargonidins, flavan-3,4-diols of the 'phloroglucinol series' (Paris and Cubukcu 1962). From the aerial plant parts, the following compounds were isolated: kaempferol-3-*O*-rutinoside, rutin, kaempferol, quercetin and luteolin (Juan-Badaturuge et al. 2011; Habtemariam 2013), and oleanolic acid (Senthilkumar and Reetha 2011).

Some of the reported pharmacological properties of the various plant parts of *Cassia auriculata* are elaborated below.

#### Antioxidant Activity

The ethanol and methanol extracts of C. auricu*lata* flowers showed antioxidant activity in both 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assays (Kumaran and Karunakaran 2007). The flower powder of Cassia auriculata significantly decreased the thiobarbituric acid reactive substances (TBARS), hydroperoxide and conjugated dienes and increased the (catalase, antioxidant enzymes superoxide dismutase and glutathione peroxidase) and nonenzymatic antioxidants (ascorbic acid, vitamin E and reduced glutathione) in streptozotocininduced diabetic rats (Jeyashanthi and Ashok 2010). The antioxidative effect of 200 mg/kg body weight (bw) of the extract was significantly better than 100 mg/kg body weight extract and the reference drugs (tolbutamide and metformin). Antioxidative effect was not observed in normoglycemic rats in the experiment. In another study, oral administration of C. auriculata aqueous leaf extract to streptozotocin-induced mild diabetic (MD) and severe diabetic (SD) rats (100, 200 and 400 mg/kg bw per day for a period of 21 days) produced significant fall in fasting blood glucose (FBG) in a dose-dependent manner (Gupta et al. 2009c). Treatment with the extract (400 mg/kg) showed significant reduction in serum levels of thiobarbituric acid reactive substances (TBARS) and oxidized low-density lipoprotein (OxLDL) in both MD and SD rats. The antioxidant defence system was also found to be improved in extracttreated (400 mg/kg) MD and SD rats, as revealed by significant increase in activities of erythrocyte's antioxidant enzymes, that is, superoxide dismutase (SOD) and catalase (CAT) with a concomitant elevation in erythrocyte's reduced glutathione (GSH) content. Moreover, there were no toxic signs in rats treated with high doses of the extract (1,000 and 2,000 mg/kg bw per day for 21 days). Blood glucose, hepatic and renal function parameters in these rats were found within normal limits.

The alcoholic extract of the aerial part of *C. auriculata* exhibited potent antioxidant activity when assessed by DPPH radical scavenging,

lipid peroxidation and reducing power analysis (Juan-Badaturuge et al. 2011). Fractionation of the crude extract showed that the ethyl acetate fraction was the most active followed by the chloroform fraction, while the petroleum ether, n-butanol and water fractions were less active than the crude extract.

# **Anticancer Activity**

*Cassia auriculata* leaf ethanol extract dosedependently inhibited the growth of human breast adenocarcinoma MCF-7 and human larynx carcinoma Hep-2 cell lines in vitro with IC50 values of 400 and 500 µg through induction of apoptosis (Prasanna et al. 2009). The MCF-7 and Hep-2 cells showed decreased expression of antiapoptotic Bcl-2 protein and increased expression of Bax/Bcl-2 ratio upon treatment. When *Cassia auriculata* extract and curcumin were combined, a synergistic effect of anticancer activity at a much lower concentration of both was noted (Prasanna et al. 2011).

## Antimicrobial Activity

Cassia auriculata leaf extract exhibited significant broad spectrum activity in-vitro against Bacillus subtilis and S. aureus (Samy and Ignacimuthu 2000). Studies conducted in birds with Escherichia coli infection showed that C. auriculata herbal extract had more potent microbicidal activity compared to Piper betle (Prakash 2006). The methanol leaf extract (5 mg/disc) and methanol flower extract (2.5 mg/disc) showed invitro growth inhibitory activity against Bacillus subtilis, Staphylococcus aureus, Staphylococcus epidermidis and Enterococcus faecalis (Duraipandiyan et al. 2006). The methanol flower extract (5 mg/disc) showed antibacterial activity against all four bacteria and Escherichia coli.

The ethanol, methanol and aqueous extracts of dry flowers and ethanol, methanol and acetone extracts of fresh flowers of *Cassia auriculata* exhibited in-vitro antibacterial activity against *Staphylococcus aureus, Enterococcus faecalis,*  Bacillus subtilis, Salmonella typhi, Salmonella paratyphi A, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Klebsiella pneumoniae, Vibrio cholerae and *Shigella* dysenteriae (Maneemegalai and Naveen 2010). The maximum activity was observed against all organisms except Pseudomonas aeruginosa and Klebsiella pneumoniae. The minimum inhibitory concentration ranged between 12.5 and 75 mg/mL depending on microorganism and various extract. Presence of phytochemicals such as terpenoids, tannins, flavonoids, saponin, cardiac glycosides and steroids was observed. Of several plant species, Cassia auriculata was selected as the efficient plant, which showed antibacterial activity against Escherichia coli, Salmonella typhi, Proteus mirabilis and Klebsiella pneumoniae at different concentrations Senthilkumar and Reetha 2011).

## Antiinflammatory Activity

The 50 % acetone flower extract of *C. auriculata* showed marked antiinflammatory activity (56 %) in carrageenan-induced oedema in rats (Manogaran and Sulochana 2004).

#### Antidiabetic Activity

Administration of aqueous Cassia auriculata flower extract at 0.45 g/kg significantly decreased blood glucose, glycosylated haemoglobin and gluconeogenic enzymes and increased plasma insulin, haemoglobin and hexokinase activity in streptozotocin diabetic rats (Latha and Pari 2003a). The elevated gluconeogenesis during diabetes was reverted to normal by the extract in enhancing the utilization of glucose through increased glycolysis. The effect of the extract was more prominent than that of glibenclamide. The methanol flower extract of C. auriculata was found to have potential alpha-glucosidase inhibitory activity in vitro, preferably on maltase with a low IC<sub>50</sub> value of 0.023 mg/mL and inhibited the maltase activity competitively (Abesundara et al. 2004). Oral administration of C. auriculata methanol extract in Sprague-Dawley rats significantly and potently lowered blood glycemic response towards maltose ingestion which was observed at 30 minutes after dosing of 5 mg/kg, thus concurrently suppressed insulin activity. The  $ED_{50}$  of the extract (4.9 mg/kg) clearly indicated that the antihyperglycemic effect was as potent as that of the rapeutic drug, acarbose ( $ED_{50}$ 3.1 mg/kg). In another study, oral administration of water-soluble fraction of the ethanol extract of C. auriculata flowers to alloxan diabetic rats significantly reduced blood glucose level and elevated plasma insulin level compared to the aqueous extract-treated rats and diabetic control (Hakkim et al. 2007). Treatment with water-soluble fraction of ethanol extract and aqueous extract of C. auriculata flowers restored altered hyperlipidaemic parameters and enzymatic markers in diabetic animals. The water-soluble fraction of the ethanol extract exerted a more efficient antihyperglycemic effect compared to the aqueous extract. Surana et al. (2009) reported that the n-butanol fraction of the hydromethanol flower extract exhibited significant reduction in blood glucose levels and was also found effective in restoring the blood lipids and proteins to normal level. The activity was found comparable with standard drug phenformin. The flower and leaf extracts of Cassia auriculata exerted a significant reduction in the serum glucose and triglycerides and cholesterol levels and increase in the plasma insulin levels in alloxan-induced diabetic rats when compared to root and stem extracts (Umadevi et al. 2006).

An aqueous leaf extract of *Cassia auriculata* was found to lower the serum glucose level in normal rats and alloxan-induced diabetic rats (Sabu and Subburaju 2002). The extract was also found to inhibit the body weight reduction induced by alloxan administration. Glucose uptake and glycogen deposition studies suggested that *C. auriculata* leaf extract probably had no direct insulin-like effect which can enhance the peripheral utilization of glucose. In separate studies, oral administration of aqueous leaf extract of *Cassia auriculata* (100, 200, 400 and 600 mg/kg bw daily for 21 days) to alloxan-induced mild diabetic (MD) and severe diabetic (SD) rabbits produced dose-dependent fall in

fasting blood glucose up to 400 mg/kg dose from day 3 to day 21 (Gupta et al. 2009b). Further, a significant increase in insulin levels and fall in glycosylated haemoglobin (HbA1c) was observed in both MD and SD rabbits when treated with 400 mg/kg dose of the extract. The extract also caused a significant decrease in serum levels of triglycerides (TG), total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) with a concomitant increase in high-density lipoprotein cholesterol (HDL-C) in MD and SD rabbits. Atherogenic indices (TG/HDL-C, TC/ HDL-C and LDL-C/HDL-C) were also significantly reduced in both diabetic models of rabbits fed with the extract. Effect of the extract at 400 mg/kg dose was comparable to that of glibenclamide (600  $\mu$ g/kg), a reference antidiabetic drug. Similar results were obtained with the leaf extract in streptozotocin (STZ)-induced mild diabetic (MD) and severe diabetic (SD) rats (Gupta et al. 2009a). In another study, Gupta et al. (2010) found that aqueous leaf extract of C. auriculatatreated mildly diabetic (MD) and severely diabetic (SD) rats showed significant reduction in fasting blood glucose. Assessment of plasma insulin and C-peptide following treatment with the leaf extract revealed significant elevation in their levels. Administration of the leaf extract enhanced the activity of hepatic hexokinase and phosphofructokinase and suppressed glucose-6phosphatase and fructose-1,6-bisphosphatase in both MD and SD rats. A significant rise in glycogen content was also observed in both liver and muscles of leaf extract-fed MD and SD rats. Histopathological examination of pancreatic sections revealed increased number of islets and  $\beta$ -cells in leaf extract-treated MD as well as SD rats. The results of the study suggested that the antidiabetic effect of the leaf extract could be due to its insulinogenic action as well as through pancreatic as well as extrapancreatic action. In another recent study, supplementation of C. auriculata aqueous leaf extract to the streptozotocin-induced diabetic rats produced significant reduction in fasting blood glucose along with significant reversal in altered serum lipid profile and apolipoprotein B (Gupta et al. 2011). Lipid peroxidation was found to be significantly

suppressed in extract-fed diabetic rats. Significant reduction in serum levels of oxidized low-density lipoprotein, soluble vascular cell adhesion molecule and plasma fibrinogen with a concomitant elevation in serum nitric oxide was observed in diabetic rats following treatment with extract. Histopathological examination of heart myocardium of extract-treated diabetic rats revealed reversal of fatty change towards normal. The results suggested that *C. auriculata* aqueous leaf extract exhibited anti-atherosclerotic role in the diabetic state and may help to prevent the progression of cardiovascular diseases.

Gold nanoparticles (AuNPs) using *Cassia auriculata* aqueous leaf extract were synthesized, and the stabilizing and reducing molecules of nanoparticles may promote antihyperglycemic effect but required further testing (Kumar et al. 2011). Green leafy *Cassia auriculata* porridge should not be recommended as breakfast meals for diabetics because of its high GI (77) compared to other green leafy porridges (Anuruddhika and Ekanayake 2013).

Oral administration of ethanol (400 mg/kg) and aqueous extract (250, 500 mg/kg) of whole plant of *C. auriculata* to streptozotocin-induced neonatal model of non-insulin-dependent diabetes mellitus (NIDDM) rats led to suppression in elevated glucose, cholesterol and triglycerides levels (Juvekar and Halade 2006).

Diamed an herbal formulation composed of the aqueous extracts of three medicinal plants (*Azadirachta indica, Cassia auriculata* and *Momordica charantia*) was found to have antihyperglycaemic action in alloxan-induced experimental diabetes in rats (Pari et al. 2001). Oral administration of Diamed resulted in a significant reduction in blood glucose, glycosylated haemoglobin, and an increase in plasma insulin and total haemoglobin. Diamed also prevented a decrease in body weight.

### Antihyperlipidaemic Activity

The crude extract of *C. auriculata* aerial parts displayed in-vitro inhibitory activity against pancreatic lipase with  $IC_{50}$  of 6.0 µg/mL (Habtemariam 2013). The most active antilipase compound in the extract was kaempferol-3-*O*-rutinoside with IC<sub>50</sub> value (2.9  $\mu$ M) only about twice weaker than the standard antilipase drug, orlistat (IC<sub>50</sub>=1.45  $\mu$ M). Luteolin, quercetin and rutin were found to be weak pancreatic lipase inhibitors (IC<sub>50</sub>>100  $\mu$ M), whereas kaempferol showed no activity up to 250  $\mu$ M.

Cassia auriculata flowers were found to possess antihyperlipidaemic effect in addition to antidiabetic activity (Pari and Latha 2002). Oral administration of aqueous flower extract of C. auriculata suppressed the elevated blood glucose and lipid levels in streptozotocin-induced diabetic rats. The effect was found to be comparable to glibenclamide. Administration of the ethanol extract of C. auriculata flowers to triton WR 1339 induced hyperlipidaemic rats to revert the parameters of hyperlipidaemia to normal (Vijayaraj et al. 2011, 2013). Treatment with the extract significantly reduced the total cholesterol (TC), triglycerides (TG) and low-density lipoprotein cholesterol (LDL) levels and significantly increased the high-density lipoprotein (HDL) level associated with reduction of atherogenic index in hyperlipidaemic rats. Lipid peroxidation decreased whereas the activities of superoxide dismutase, glutathione peroxidase and catalase increased in extract treated rats. Pronounced changes were comparable to the standard drug lovastatin.

## Hepatoprotective Activity

The study of Kumar et al. (2002) showed that treatment with *C. auriculata* leaf extract had a lipid-lowering effect in rats with experimentally induced, alcohol-related liver damage. This was associated with a reversal of steatosis in the liver and of spongiosis in the brain. They reported that administration of *C. auriculata* leaf extract to rats with alcohol-induced hepatotoxicity significantly lowered the levels of thiobarbituric acid reactive substances (TBARS) and hydroperoxides and elevated the activities of superoxide dismutase (SOD) and catalase (CAT) and the levels of reduced glutathione (GSH) in the liver, brain, kidney and intestine compared to unsupplemented alcohol-treated rats (Kumar et al. 2003). The leaf extract restored the serum vitamin E and vitamin C levels also to near those of the experimental control animals. Histopathological studies of the liver and brain confirmed the beneficial role of *Cassia auriculata* leaf extract.

#### Nephroprotective Activity

The ethanol root extract of *Cassia auriculata* at doses of 300 and 600 mg/kg body weight reduced elevated blood urea and serum creatinine and normalized the histopathological changes in the curative regimen in cisplatin-induced renal injury in male albino rats (Annie et al. 2005). In the gentamicin-induced renal injury model, the ethanol extract at a dose of 600 mg/kg body weight reduced blood urea and serum creatinine effectively in both the curative and the preventive regimen. The probable mechanism of nephroprotection by *C. auriculata* against cisplatin- and gentamicin-induced renal injury could be due to its antioxidant and free radical scavenging property.

#### Immunomodulatory Activity

Polyphenols derived from *Cassia auriculata* were found to boost T-cell immunity by increasing the number of T cells and B cells percentage along with enhanced proliferation of splenocytes in both resting and LPS-stimulated cells in aged rats (John et al. 2011). *Cassia* polyphenol supplementation reduced the oxidative burst activity of neutrophils in response to PMA (phorbol myristate acetate) and *Escherichia coli* activation that could potentially harm multiple biological systems in aged rats.

### Neuroprotective Activity

Streptozotocin diabetic rats treated with aqueous flower extract of *Cassia auriculata* or glibenclamide

showed significant decrease in thiobarbituric reactive substances (TBARS) and hydroperoxide formation in the brain, suggesting the role of the extract in protection against lipid peroxidation-induced membrane damage by antiperoxidative efficacy (Latha and Pari 2003b).

## Laxative Activity

Studies showed that the ethanol pod extract of *C. auriculata* (200 mg/kg p.o.) exhibited laxative activity in rats (Suresh et al. 2007). The ethanol extract induced an increase in gastrointestinal transit as compared to control. It was also concluded that the anthracene derivatives present could be attributed for the laxative activity.

## Antipyretic Activity

The flower and leaf extracts of *C. auriculata* were reported to have antipyretic activity (Vedavathy and Rao 1991).

## Herbal Drug–Drug Interaction

Studies demonstrate that a significant increase (32.5 %) in the steady state levels of theophylline occurred when this drug was administered concurrently with herbal tea-prepared dried flowers of Cassia auriculata (Thabrew et al. 2004b). They cautioned that herbal teas prepared from C. auriculata should therefore be avoided by patients treated with theophylline as these herbal teas had the potential to influence the bioavailability of the prescription drug. They also found that C. auriculata tea had the potential to influence the bioavailability of carbamazepine and hence its therapeutic actions. They demonstrated that in rats receiving the Cassia auriculata tea and carbamazepine, the blood levels of the prescription drug were significantly enhanced by 47.1 %, when compared with the levels in animals receiving only carbamazepine for the same time period, with no apparent changes in toxicity. Concurrent ingestion of carbamazepine with herbal teas containing *Cassia auriculata* was therefore best avoided by patients under treatment for epilepsy.

## Antiplasmodial Activity

The methanol leaf extract of *C. auriculata* showed promising antiplasmodial activity against blood stage CQ-sensitive (3D7) and CQ-resistant (INDO) strains of *Plasmodium falciparum* in culture with IC<sub>50</sub> value of 14 µg/mL. The high TC<sub>50</sub> in mammalian cell cytotoxicity assay and the low IC<sub>50</sub> in antimalarial *P. falciparum* assay indicated selectivity and good resistance indices for the leaf extract.

## Insecticidal Activity

Benzene root extract was found to be most potent among all extract showing comparable paralysis of Pheretima posthuma and death time comparable to the standard anthelmintic drug albendazole (Wadekar et al. 2011). Phytochemical analysis of the crude root extracts revealed the presence of an array of active chemical constituents such as tannins, flavonoids, glycosides, carbohydrates, steroids and triterpenoids. The petroleum ether, ethyl acetate, ethanol and aqueous extracts of Cassia auriculata leaves exhibited dosedependent anthelmintic activity against the earthworm, Eisenia foetida (Kainsa et al. 2012). The decreasing order of activity of extracts was ethyl acetate, ethanol, petroleum ether and aqueous extracts.

## Insecticidal Activity

The acetone, chloroform, ethyl acetate, hexane, methanol and petroleum ether extracts of leaf, flower and seed of *Cassia auriculata* showed moderate larvicidal effects; however, the highest mortality was found in leaf petroleum ether, flower methanol extracts of *C. auriculata*, against the larvae of *Anopheles subpictus* ( $LC_{50}$ =44.21, 44.69 ppm;  $LC_{90}$ =187.31, 188.29 ppm, respectively) and against the larvae of *Culex tritaeniorhynchus* ( $LC_{50}$ =69.83, 51.29 ppm;  $LC_{90}$ =335.26, 245.63 ppm, respectively) (Kamaraj et al. 2009).

The leaf ethyl acetate and flower methanol extracts of *C. auriculata* exerted highest mortality of the larvae of cattle tick *Rhipicephalus* (*Boophilus*) *microplus*; the leaf methanol exhibited antiparasitic activity against adult hematophagous fly, *Haemaphysalis bispinosa* (Kamaraj et al. 2010).

#### Safety/Toxicity Studies

Animal studies by Puranik et al. (2011) found that the traditional hydroalcoholic extract and technology-based supercritical extract of Cassia auriculata (CA) seeds to be pharmacologically safe and did not show any significant adverse reactions at the tested doses (250 mg to 1,000 mg/kg). The traditional hydroalcoholic extract did not show any significant effect on pharmacokinetics; however, the technology-based supercritical extract caused a significant reduction in absorption of metformin when co-administered. No rat mortality was observed during the treatment period of 12 weeks in either the control or treated groups. No significant change in total bilirubin, TC, TG, glucose and creatinine was observed. There was no significant difference between both systolic and diastolic blood pressure between CA extract-dosed animals and controls. ECG variables like heart rate (R-R interval), QT interval (diastolic dysfunction) and ventricular hypertrophy (R wave amplitude) were normal in all the groups.

*Cassia auriculata* was found to have pyrrolizidine alkaloids (Arseculeratne et al. 1981). Feeding trials in rats with materials from the plant produced liver lesions—disruption of the centrilobular veins, congestion or haemorrhage in the centrilobular sinusoids, and centrilobular or focal hepatocellular necrosis—and histopathology in the lungs and kidneys which were in accord with the action of pyrrolizidine alkaloids. The researchers suggested that the consumption of herbal medicines that contain pyrrolizidine alkaloids could contribute to the high incidence of chronic liver disease including primary hepatocellular cancer in Asian and African countries.

# Traditional Medicinal Uses

The leaves, flowers, seeds, roots and bark are used for medicinal purposes in traditional medicine. The plant is used for the treatment of skin diseases, asthma, conjunctivitis and renal disorders by the tribal communities of the Chittoor district of Andhra Pradesh (Vedavathy et al. 1997). The Lambadis use the leaves for bone fractures; the Chenchus use the seeds to treat inflammations, diarrhoea, infertility, fever, migraine, night blindness, scorpion sting, leucorrhoea, ulcers and fissures in the mouth, and the stem and root for renal ailments; the Yanadis use the root bark and stem bark for stomach ache and earache. The leaves and fruit are ground into a paste and given as pills orally with limewater for leucorrhoea and menorrhoea in women by the Adivasis tribe of the Eastern Ghats, Andhra Pradesh (Ratnam and Raju 2005). The leaves are used in folk medicine for scorpion bites by the Chencu and Yanadi tribes in Gundla Brahmeswaram Wildlife Sanctuary, Andhra Pradesh (Ratnam and Raju 2008). They also use the whole plant for leucorrhoea and menorrhoea, similarly prepared and the pills are taken orally with milk. In South Travancore, India, the tribal communities use the leaves as a paste with vinegar for external application for various skin diseases (Jeeva et al. 2007). The indigenous communities of Kanyakumari district of Tamil Nadu use a dried leaf paste in vinegar as application on skin diseases once a day till cured (Kingston et al. 2009). In the Haveri district of Karnataka state, India, the village folks use tender cassia leaves mixed with lime in tablet form for stomach ache (Nagnur et al. 2009). Leaves and flowers are used for diabetes and religious function by the community in the sacred grove of Pallapatti in the Madurai district of Tamil Nadu, India (Ganesan et al. 2009). Traditional healers in the Kancheepuram district of Tamil Nadu prescribe ingestion of the dried flower powder mixed with goat milk to prevent white discharge (Muthu et al. 2006).

The roots and bark are astringent and are used for gargles, as an alterative, and to cure skin diseases, eye troubles and rheumatism (CSIR 1950; Chopra et al. 1986; Duke 1981; Rahmansyah 1991). A decoction of the flowers and the seeds is recommended for diabetes; seeds are used to cure eye diseases, gonorrhoea and gout. In Tanzania the plant is used to treat impotence, which may be related to diabetes (Jansen 2005). Leaves and fruits serve as an anthelmintic and diuretic.

## **Other Uses**

The plant is utilized for green manuring in India and is used for revegetating erodible and sodic soils. The bark is used in India to stupefy fish. The bark yields a valuable tanning material for heavy hides, and goatskin and sheepskin, a black dye and bast fibres can be made into ropes. Handles of small tools can be made from the wood. Branches are used as chewing sticks and toothbrushes. In southern India the flowers are used as a fast yellow dye for leather. In Gujarat, India, the flower buds are used with madder roots (*Rubia cordifolia*) in the galling process prior to dyeing cotton cloth and chintzes red, pink or purple. Boiled seeds are an important ingredient in indigo vats where bacterial fermentation converts the insoluble indigo into soluble leuco-indigo, facilitating the impregnation of the dye by textile fibres.

## Comments

The plant is propagated from seeds. Acid scarification or manual scarification of seeds will facilitate germination. The tree also produces root suckers freely.

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