2.4: *Eugenia jambolana* Lam.

A. Classification:

- **Kingdom:** Plantae
- **Division:** Magnoliophyta
- **Class:** Magnoliopsida
- **Family:** Myrtaceae
- **Genus:** Eugenia
- **Species:** jambolana Lam.

C. Synonym’s:

- **English:** Black plum, Jaman
- **Hindi:** Jamun
- **Marathi:** Jambhul
- **Kannad:** Ama-Phala, Jambunerale, Nayinerale
- **Sanskrit:** Brahaspati, Jambavam
- **Telugu:** Goyya-Pandu, Jam-Pandu

D. Parts Used: Fruit, Pulp, Seed, Leaves, bark

E. Botanical description

It is a large evergreen tree up to 30 m high. Bark pale brown, slightly rough on old stems. Leaves opposite, simple, entire, elliptic to broadly oblong, smooth, glossy, somewhat leathery, 7.5-15 cm long, short pointed at tips. Flowers white 7.5-13 mm across in branched clusters at stem tips, calyx cuplike; 4 petals, fused into a cap; many stamens. Fruit variable in size up to 2.5 cm long, ellipsoid or oblong, crowned with truncate calyx-limb, black with pink juicy pulp. It is widely distributed throughout India, Ceylon-Malaya and Australia and known as Jamun, Jam, Jambul in India. It has been valued in Ayurveda and Unani system of medication for possessing variety of therapeutic properties (Kirtikar & Basu, 1975).
Figure 2.7 Important parts of *Eugenia jambolana* plant

- **Fruit**
- **Leaves**
- **Bark**
F. Traditional Uses:

Most of the plant parts of *Eugenia jambolana* are used in traditional system of medicine in India. According to Ayurveda, its bark is acrid, sweet, digestive, astringent to the bowels, anthelmintic and in good for sore throat, bronchitis, asthma, thirst, biliousness, dysentery, blood impurities and to cure ulcers (Kirtikar & Basu, 1975). The fruits are acrid and sweet, cooling, dry and astringent to bowels. They increase “Vata” and remove bad smell from the mouth. As per Unani system of medicine they acts as liver tonic, enriches blood, strengthens teeth and gums and forms good lotion for removing ringworm infection of the head. The vinegar prepared from the fruit is tonic, astringent, carminative and useful in spleen diseases. The seeds are sweet, astringent to bowels and good for diabetes. The sprouts are refrigerant, carminatives & astringent to bowels (Kirtikar & Basu, 1975, Sharma & Mehta 1969). In Unani medicine system the ash of leaves is used for strengthen the teeth and the gums. The seeds are astringent, diuretic and stops urinary discharge (Kirtikar & Basu, 1975). Its bark, with or without the addition of other astringents like cardamom and cinnamon, is used as decoction in case of chronic diarrhoea and dysentery. It is also acts as a gargle in sore throat; spongy gums etc. and when externally used, bark shows good wound healing properties (Nadkarni 1954, Sharma & Mehta 1969). Juice of the tender leaves of *Eugenia jambolana* together with mango leaves and myrobalan is administered along with goat’s milk and honey to cure dysentery with bloody discharge (Chakardata) where as juice of tender leaves alone or in combination with carminatives is given along with goat’s milk to cure diarrhoea in children. Powdered seeds are used as a remedy in diabetes (Nadkarni 1954) and in metrorrhagia (Sharma & Mehta 1969). Seed powdered in combination with mango kernels were administered with curd to overcome the problem of diarrhoea and dysentery, enlargement of spleen and as diuretic in scanty or suppressed urine and oil of leaves is useful in skin diseases. Juice of black jamun and mangoes in equal parts relieves thirst and has been found very effective in diabetes. The riped fruits are considered to be the good diet in convalescence diarrhoea and dysentery and syrup or vinegar prepared from them is also useful in spleen enlargement and it is effective in chronic diarrhoea (Nadkarni 1954).
G. Phytochemistry

**Seeds**

Seeds of *Eugenia jambolana* contain glycosides, a trace of pale yellow essential oil, fat, resin, albumin, chlorophyll (Nadkarni 1954), an alkaloid- jambosine (Chopra et al., 1956), gallic acid, ellagic acid, corilagin and related tannin, 3,6- hexahydroxydiphenoylglucose and its isomer 4,6- hexahydroxydiphenoylglucose, 1- galloylglucose, 3- galloylglucose, quercetin (Bahtia & Bajaj, 1975) and elements such as zinc, chromium, vanadium, potassium and sodium (Ravi et al., 2004). Unsaponifiable matter of seed fat contains β-sitoterol (Gupta & Agrawal, 1970). Dry seeds of *Eugenia jambolana* have been reported with 11.67% alcohol soluble extractive, 3.397% inorganic (Kar et al., 1999), 40% of water-soluble gummy fiber and 15% of water insoluble neutral detergent fibers (Pandey & Khan, 2002).

**Fruits**

Fruits of *Eugenia jambolana* have been reported with raffinose, glucose, fructose (Srivastava, 1953), citric acid (Winton, 1935), mallic acid (Lewis, 1956) and gallic acid. The sourness of fruits may be due to presence of gallic acid. Venkateswarla (1952) and Rastogi & Mehrotra (2001) reported that the color of the fruits might be due to the presence of anthocyanins namely delphinidin-3-gentiobioside and malvidin-3- laminaribioside along with petunidin-3- gentiobioside.

**Leaves and Stems**

Gupta & Sharma (1974) isolated sitosterol, betulinic acid and crategolic (maslinic) acid and also detected hepatcosane, n-nonacosane, n-hentriacontane, noctacosanol, ntriacontanol and n-nodotricontanol by GLC and sugars- glucose, fructose, acids- oxalic, citric, glycolic acids and amino acids- glycine, alanine, tyrosine and leucine by co paper chromatography in the leaves of *Eugenia jambolana*. Subsequently Mahmoud et al., (2001) isolated 15 polyphenols and two acetylated flavonol glycosides identified as 3-O- (4”-Oacetyl)- alpha-L-rhamnopyranosides of mearnsetin (myricetin 4’-methyl ether) and myricetin 3-O- (4”- acetyl- 2”-O-galloyl)–alpha-Lrhamnopyranoside from leaves of *Eugenia jambolana* and subsequently Timbola et al., (2002) isolated quercetin (0.0085%), myricetin (0.023%), myricitrin (0.009%), and a flavonol glycosides myricetin 3-O-(4”-acetyl)-α-L-rhamnopyranosides (0.059%) from its leaves. Leaves, stems and fruits of *Eugenia jambolana* have been reported with essential oil respectively yields of 0.11, 0.20 and 0.03 (%v/w) and the GC-MS analysis of these oils,
revealed that except bornyl acetate the common components of essential oil are mono- or sesqui- terpenes (Craveiro et al., 1983).

**Flowers:** Flowers of *Eugenia jambolana* contain oleanolic acid; two other triterpenoids ellagic acids and flavonols isoquercetin, quercetin, kampferol and myricetin are present in small amounts where as myricetin-3-L arabinoside, dihydromyricetin and quercetin galactosides have also been isolated (Subramanian & Nair, 1972).

**H. Pharmacology**

Although *Eugenia jambolana* has been prescribed in various complications including diabetes, diarrhea and dysentery etc. in folklore and traditional system of medication but scientific proof of its efficacy are still lacking.

**Antidiabetic activities**

Although earlier reports stated that administration of powdered seeds of *Eugenia jambolana* do not produce appreciable difference in blood sugar levels in rabbits but according to Brahmcari et al., (1961) its ethanolic extract shows hypoglycaemic activities in albino rabbits. Latter French scientists Sigogneau- Jagodzin-ski et al., (1967) proved that constituents isolated from ethanolic extract had hypoglycemic action on alloxan induced diabetic rats. According to Bansal et al., (1981) observed that oral feeding of seeds at 170, 240 and 510 mg/rat for 15 days caused maximum reduction in blood glucose of normal fasted rats at 240 mg/rat doses as comparison to chlorpropamide treatment. In addition there was a 2.4-6.8 fold and 9.2 fold increase in cathepsin B activity pertaining to proteolytic conversion of proinsulin to insulin by seed extracts of *Eugenia jambolana* and chlorpropamide respectively in rats. From a preliminary study Mahapatra et al., (1985) reported hypoglycemic effect from seeds. Muna et al., (1991) investigating the hypoglycemic activity in normal and streptozotocin-induced diabetic rats, and results were compared to those obtained using the sulfonylurea, glibenclamide and reported significant decrease in blood glucose level by oral administration of *Eugenia jambolana* seeds. Achrekar et al.,(1991) reported that oral administration of pulp extract of fruits of *S. cumini* to normoglycaemic and streptozotocin induced diabetic rats exhibited hypoglycemic activity in 30 min which was possibly mediated by insulin secretion. In addition the extract inhibited insulinase activity in the liver and kidney. Indira and Mohan Ram (1992) reported hypoglycemia and reduced glucosuria on oral administration of alcoholic extracts of dried seeds of *Eugenia jambolana*. Teixeira et al., (1992) reported
decoction of dry leaves of *S. cumini* exhibiting hypoglycemic effect. Later they also observed no anti-hyperglycemic action of the leaves (in the form of tea) of *Eugenia jambolana* collected in South Brazil at 16–32 g leaves per liter of water, to normal and diabetic rats for 14–95 days (Teixeira et al., 1997). Prince et al., (1998) reported prominent hypoglycemic (>glibenclamide) and antioxidant activity at the dose of 5.0 gm/kg for 6 days of aqueous extract of *Eugenia jambolana* seeds however the low dose of 2.5 gm/kg had no significant effect. Kar et al., (1999) reported inorganic constituents of *Eugenia jambolana* possessing more pronounced action of glucose tolerance factor compared to their corresponding organic components extracted from 95% ethanol. In subsequent study Teixeira et al., (1997) found no antihyperglycemic action when aqueous extract of leaves (0.25–1.0 g/100g b.wt.), was given to normal rats for 14 days and to diabetic rats for 4 days, and when nondiabetic young volunteers ingested a decoction prepared from 2 g dry leaves in 250mL of water. According to Grover et al., (2000) daily administration of lyophilized powder of *Eugenia jambolana* seeds (200 mg/kg) showed maximum reduction of blood glucose level to 73.51, 55.62 and 48.81% as compared to their basal value in mild (21 days), moderate (120 days) and severe (60 days) in diabetic condition in rats.

In addition the treatment also partially restored altered hepatic and skeletal muscle glycogen content and hepatic glucokinase, hexokinase, glucose-6-phosphate and phospho-fructokinase levels. Pepato et al., (2001) observed no significant difference in biochemical and physiological parameter when decoction of *Eugenia jambolana* leaves (15% w/v) was given to streptozotocin induced diabetic rats as a substitute for water. Vats et al., (2001) has reported that treatment with aqueous extracts of *Eugenia jambolana* at 400 mg per day for 15 days substantially prevented hyperglycemia and hyperinsulinemia induced by high fructose diet in rats. Pandey & Khan, (2002) observed that the hypoglycemic effect of *S. cumini* (*Eugenia jambolana*) seeds is due to water-soluble gummy fiber and not because of water insoluble neutral detergent ber and other constituents of the seeds. Kar et al., (2003) observed blood glucose lowering effect within 1 week dosing of 250mg/kg/day of the ethanolic extracts of *Eugenia jambolana* in alloxan induced diabetic rats. Sharma and co-worker (2003) investigated that hypoglycemic and hypolipidemic effect of ethanolic extracts (100mg/kg, P.O.) of seeds in alloxan induced sub diabetic, mild diabetic and severe diabetic rabbits showed significant fall in the fasting blood glucose level on 15 days administration. They also observed 32.85 and 26.95% increase in insulin level in mild and severe respectively and fall
in total serum cholesterol / HDL ratio. Prince et al.,(2004) have reported a significant reduction in blood glucose and urine sugar and lipids in serum and tissues in alloxan diabetic rats by the administration of alcoholic extracts (100mg/kg) of Eugenia jambolana. The extract also increased total haemoglobin level. In a comparative study Jasmine et al., (2004) noticed greater hypoglycemic effect due to aqueous extracts of Eugenia jambolana seeds compared to Phyllanthus niruri leaves. Karnick et al., (1991) reported a polyherbal preparation containing Eugenia jambolana to be clinically effective in the treatment of diabetes. Kohli et al., (1993) has carried out clinical trial of Eugenia jambolana seed powder in NIDDM

**Effect on diabetic complication**

As per Grover et al.,(2001) extracts of Eugenia jambolana significantly (P<0.05) prevented renal hypertrophy as compared to diabetic controls. Rath et al., (2002) has reported lyophilized aqueous extract of Eugenia jambolana seeds preventing the development of cataract in alloxan induced diabetic rats. According to Prince et al. (2003), oral administration of an alcoholic seed extract (100 mg/kg) for 6 weeks brought back all the parameters to near normal. According to them the effect of both these extracts was better compared to glibenclamide (600 μg/kg) in reducing tissue damage in diabetic rat brain. After giving lyophilized fruit-pulp extract of Brazilian Eugenia jambolana (50 mg/kg) for 41 days to streptozotocine diabetic rats, found no observable difference in body weight, food or water intake, urine volume, glycaemia, urinary urea and glucose, hepatic glycogen, or on serum levels of total cholesterol, HDL cholesterol or triglycerides (Pepato et al., 2005). Grover et al., (2002) Oral administration of aqueous extracts of Eugenia jambolana for 50 days caused a significant increase in gastric transit percentage compared to streptozotocin induced diabetic control and significant decrease in serum sugar level (21% reduction) without any euglycaemic state. They also reported insignificant prevention in the rise in basal tail flick latency by daily administration of aqueous extracts of Eugenia jambolana in comparison to diabetic controls.
**Mechanism of action**

The antidiabetic action of *Eugenia jambolana* is not fully understood. It exerts a dual effect namely a combination of mechanism of action of sulfonylurea and biguanids (Grover et al., 2000) on the other hand, as per Archekar et al., and Ravi et al., *Eugenia jambolana* may bring about its hypoglycemic action through stimulation of surviving β cells of islets of langerhans to release more insulin (Achrekar et al., 1999; Ravi et al., 2004). However according to some other studies it increases G-6-P content in liver indicating an overall increase in glucose influx thus it is having an overall effect in increasing glucose utilization (Grover et al., 2000) and as per Bansal et al., (1981) it may be acting as hypoglycemic agent by increased the insulin content through increasing activity of cathepsin B. Anti oxidants Ravi et al., (2004, 2004a) has observed that oral administration of ethanolic extracts of *Eugenia jambolana* seed kernel to streptozotocin induced diabetic rats significantly decreased the levels of glycosylated hemoglobin, increased the body weight and hemoglobin, restored the activities of superoxide dismutase, catalase, glutathione peroxidase to the normal level. They also found an increase in glutathione content and increased levels of lipid peroxidation and hydroperoxides in liver and kidney. The same group in the plasma and pancreas observed later similar results along with the capacity to bring level to near normal of vitamin C concomitant to vitamin E and ceruloplasmin in plasma.

*Anti-bacterial activity*

Shafi et al., (2002) reported good antibacterial properties from essential oil of *Eugenia jambolana* leaves. Shaikh et al., (1994) have reported antibacterial activity of ethanolic extracts of *Eugenia jambolana* against gram positive and gram-negative organisms. Bhuiyan et al., (1996) has determined antibacterial activity of methanol and ethyl-acetate extracts of the seeds of *Eugenia jambolana* at a concentration of 200 μg/disc against five gram positive bacteria (Bacillus creus, B.subtilis, B. megaterium, Streptococcus β-haemolyticus, Staphylococcus aureus) and nine gram-negative bacteria (Shigella dysenteriae, Sh. shiga, Sh. boydii, Sh. flexneriae, Sh. sonnei, E.coli, S.typhi B, S. typhi B- 56 and Klebsicella species) by disc diffusion method where the MIC for methanol extract was 64, 128 and 64μg/ml against Bacillus creus, E. coli and Sh. flexneria respectively where as those for ethyl acetate extract MIC were 256, 256 and 64 μg/ml against Bacillus creus, E. coli and Sh. flexneria respectively.

*Anti-inflammatory activity*
Ethanolic extract of *Eugenia jambolana* bark extract has a potent anti-inflammatory action against different phases of inflammation without any side effect on gastric mucosa (Muruganandan et al., 2000, 2001). Muruganandan et al., (2002) stated that ethanolic extracts of *Eugenia jambolana* exhibiting inhibitory role on inflammatory response to histamine, 5-HT and PGE2. Chaudhuri et al., (1990) reported chloroform fractions of its seeds significantly inhibit carrageenan, kaolin and other mediator induced edema. They also observed significant antipyretic action of the extracts against yeast-induced pyrexia.

**Antifertility activity**

Rajasekaran et al., (1988) has revealed antifertility effect of oleanolic acid isolated from the flowers of *Eugenia jambolana* significantly decreased the fertilizing capacity of the male albino rats without any significant change in body or reproductive organ weights. It causes significant reduction in conversion of spermatocytes to spermatides and arrest of spermatogenesis at the early stages of meiosis leading to decrease in sperm count without any abnormality to spermatogenic cells, leyding interstitial cells and sertoli cells.

**Gastroprotective effects**

Mukherjee et al., (1998) has reported that ethanolic extract of the bark of *Eugenia jambolana* at dose of 400 mg/kg p.o. reduced diarrhea by inhibiting gastrointestinal motility (P<0.001) and PGE2 – induced enteropolling (P<0.001) in castor oil induced rats. The work carried out by Ramirez et al., (2003) suggests that tannins extracted from *Eugenia jambolana* bark have gastroprotective and anti-ulcerogenic effects. Other uses Krikorian et al., (1967) found anorexigenic power of *Eugenia jambolana* was approximately equal to that of amphetamine. According to Ahmed et al., (1995) seed extracts of *Eugenia jambolana* produce alteration in the general behavior of test animal such as reduction in locomotion, decrease in aggressiveness and increase in phenobarbitone induced sleeping time in dose dependent fashion in a stress reducing study. They also found significant analgesic effect against acetic acid induced writhing movement and reduction in body temperature and also reduces plasma cortisone level, which was elevated due to stress. Jagetia et al., have reported radiation-induced DNA damage protection by the leaf extract of *Eugenia jambolana*. Later they reported that this extract provide protection against the gastrointestinal death by increasing the survival by 66.66% compared to 12% survival in control group. Similarly 30- mg/kg b.wt. of extract provided protection against the radiation-induced bone marrow death in mice (Jagetia & Baliga, 2002,2003).
Table 2.5 Various combination studies of *jambolana* (Leaves & Seeds)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Combination</th>
<th>Effect/ Investigation</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td><em>Syzygium cumini</em> and <em>Aegles mormelos</em></td>
<td>Activate glucose transport in a PI3 fashion</td>
<td>R. Anandharajana, <em>et al.</em>, 2006</td>
</tr>
<tr>
<td>2</td>
<td><em>Syzygium cumini</em> and <em>Baccharis trimera</em></td>
<td>Evaluation of metabolic parameter</td>
<td>Antanio carlos <em>et al.</em>, 2005</td>
</tr>
<tr>
<td>3</td>
<td><em>Eugenia jambolana</em> and <em>Tinospora cardifolia</em></td>
<td>Effect on metabolic enzyme and carbohydrate metabolism</td>
<td>Graver JK <em>et al.</em>, 2000</td>
</tr>
<tr>
<td>4</td>
<td><em>Eugenia Jambolana</em> <em>Vinca rosea</em> and <em>Cassia auriculata</em></td>
<td>Hypoglycemic properties</td>
<td>Shrotri DS <em>et al.</em>, 1963</td>
</tr>
<tr>
<td>5</td>
<td><em>Syzygium cumini</em> and <em>Ficus bengalensis</em></td>
<td>Mechanism of action in hypoglycemic action</td>
<td>Achrekar S <em>et al.</em> 1991</td>
</tr>
<tr>
<td>6</td>
<td><em>Syzygium cumini</em> and <em>Pterocarpus marsupium</em></td>
<td>Antidiabetic properties</td>
<td>Sepaha GC <em>et al.</em>, 1956</td>
</tr>
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From the above mentioned thorough literature survey it can be concluded that *Eugenia jambolana* preparations are widely available and employed by practitioner of natural health for treatment of diabetes and related complications, antioxidant, antiinflammatory, and antifertility agents. *Eugenia jambolana* plant serves varies purposes in diabetic patients such as lowering blood glucose level, delaying diabetic complications such as neuropathy and cataract etc. Most of the studies have been conducted using crude preparation of *Eugenia jambolana* without mention of their chemical profile. Although the studies on *Eugenia jambolana* have proved its efficacy in several complications including the management of diabetes, the detailed research work on standardization is seriously required on this potential plant of Ayurveda. Although many studies have claimed it for the treatment of the diabetes but in the Ayurveda it is mentioned for several ailments like diarrhoea and dysentery.
However most pharmacological work was carried out with seeds but the pharmacological potential of the other parts like leaves, stem bark, roots of the plant are required to explore. Taking all the consideration for stem bark of *Eugenia jambolana* as an alternative medicine in the treatment of diabetes, it has been decided to carry out pharmacological finding, preliminary phytochemical nature and estimation of chemical components like phenolic compounds followed by standardisation. Additionally, objective has been set to find out the combined effect of *Eugenia jambolana* stem bark and *Momordica charantia* when administered orally in the proportion of 50:50.

### 2.5 *Momordica charantia:*

**A. Classification:**
- Kingdom: Plantae
- Order: Cucurbitales
- Family: *Cucurbitaceae*
- Genus: *Momordica*
- Species: *charantia*

**B. Synonyms:** Karela, bitter gourd, korola

**C. Parts Used:** Fruit, Leaves

**D. Botanical description:**
It bears simple, alternate leaves 4–12 cm across, with three to seven deeply separated lobes. Each plant bears separate yellow male and female flowers. The fruit has a distinct warty exterior and an oblong shape. It is hollow in cross-section, with a relatively thin layer of flesh surrounding a central seed cavity filled with large, flat seeds and pith. The fruit is most often eaten green, or as it is beginning to turn yellow. The skin is tender and edible. Seeds and pith appear white in unripe fruits. When the fruit is fully ripe, it turns orange and mushy, and splits into segments which curl back dramatically to expose seeds covered in bright red pulp.
E. Traditional uses

The native country of *Momordica charantia* is uncertain, but the plant is cultivated throughout the tropics, particularly in India, China, East Africa and Central and South America. It is occasionally grown as an ornamental creeper, but more commonly cultivated for the use of the unripe fruit as a vegetable. The fruit has a number of different local names – karela, Karle, bitter gourd, bitter-melon, balsam-pear. The term karela is used throughout this chapter to denote all varieties of the fruit since in the majority of studies the type used has not been specified. When used as an anti-diabetic remedy, karela juice prepared by crushing and straining the unripe fruit (eq. 50 ml) is taken once or twice a day. Fried karela may also be consumed (Bailey et al., 1986).

F. Phytochemistry:

Since the early 1960’s a number of phytochemicals have been isolated from *Momordica charantia* fruit, seeds and whole plants. A review of the known constituents was published in
1989. In some cases biological activities such as insulinomimetic properties, protein synthesis inhibition, or insect attractant effects have been associated with the pure compounds e.g. saponins or proteins. Possible identities, which emerge for the hypoglycaemic principle in Momordica charantia, are steroidal glycosides, insulinomimetic kectins and alkaloids: the evidence relating to each of these is discussed below.

**Steroidal Glycosides:** The earliest reported active constituent of karela fruit was “Charantin” a mixture of glucosides of sitosterol and 5.25 stig mastadien-3β-ol. However, it is important to note that the dose of charantin required to elicit a hypoglycaemic response in rabbits was equivalent to 180 to 315 g of fruit orally and 81 g fruit intravenously, whereas the hypoglycaemic effect can be seen in rabbits with about 10 to 15 g of the fruit per kg body weight. In 1975, Olaniyi isolated a substance “foetidin,” from the whole plant of *Momordica foetida*, which was found to be identical in composition to charantin. Marquis et al. (1977) claimed that at 18 hours from administration, foetidin lowered blood glucose in fasting rats in an effect comparable to insulin. This claim is often quoted in the literature as support that the steroidal mixture is the active principle of *Momordica charantia*. However, a closer examination of the original data presented in the paper shows that foetidin was not significantly different from control at time points other than the 18-hour sample. It is known that *Momordica charantia* fruit, seeds and vines contain other steroidal glycosides. A saponin fraction from the seeds of karela showed insulinomimetic effects in vitro (Wong et al., 1985; Ng et al., 1986 b). The contribution of steroidal constituents other than charantin to the in vivo anti diabetic effects of *Momordica charantia* has not been evaluated.

**Insulinomimetic proteins.**

In vitro insulinomimetic effects have been observed with fruit proteins. The active seed protein is believed to be a galactose binding lectin. Khanna et al., (1981) reported that an 11 k Dalton protein (p-insulin or v-insulin) caused hypoglycaemia in man and laboratory animals on parenteral administration. Proteins are generally considered to be inactive when administered by the oral route, as they would undergo extensive digestion by proteolytic enzymes. Thus the possibility of a polypeptide being responsible for the hypoglycaemic effects of the fruit or seeds when given orally must be viewed with some skepticism. However, against this, there is some evidence (Pusztai, 1986) that lectins may be absorbed into the
bloodstream from the gastro-intestinal tract. Khanna et al., (1985) has stated without any supporting data that p-insulin is also effective orally.

**Alkaloids.** Day et al., (1990) reported that hypoglycaemic activity of fractionated karela fruit juice resided in an alkaloid-rich fraction. The alkaloids have not been isolated or characterized. The pyrimidine nucleoside vicine has been isolated from the seeds (Dutta et al., 1981; Barron et al., 1982). This “alkaloid” has been found to induce hypoglycaemia in rats in an intraperitoneal dose equivalent to 16 g seeds per kg body weight. Thus vicine may not account for all the activity of the seeds.

**Kakra compounds.** Srivastava et al., (1993) isolated three non-steroidal hypoglycaemic compounds (Kakra 1 b, 111 a and 111 b) from the fruit which differ from earlier reported principles, ie. p-insulin or charantin. The structure of these compounds was not elucidated.

**G. Pharmacology:**

**Karela fruit**

To date, no large-scale clinical trial has been reported on the anti-diabetic effects of karela, but a number of studies using small groups of diabetic patients have been conducted. Both non-insulin-dependent diabetes mellitus (NIDDM, Type II, maturity onset) and insulin-dependent (IDDM, Type I, juvenile onset) patients have participated. Kirti et al. (1982) have described some early studies (1950-1974) carried out in India and the Caribbean, in which karela’s anti-diabetic activity was observed. More recent interest was aroused when Aslam and Stockley (1979) reported a case of a possible interaction, in the form of decreased glycosuria, between a curry containing karela and the anti-diabetic drug chlorpropamide taken by the Asian NIDDM patient. Following this, Leatherdale et al. (1981) carried out a study in 9 Asian NIDDM outpatients living in the United Kingdom. Acute administration of karela juice with a glucose load resulted in a significant improvement in glucose tolerance without increasing the insulin levels in the blood. Daily consumption of fried karela for 8 to 11 weeks had a similar, through not statistically significant, effect. Nevertheless, there was a significant reduction in glycosylated haemoglobin, indicating an improved control of blood glucose levels over this period. Further evidence for a beneficial chronic effect is that an improvement in both glucose tolerance, and fasting blood glucose levels was observed in 8 NIDDM patients.
following 7 weeks of daily consumption of powdered karela fruit (Akhtar, 1982). Srivastava et al. (1993) reported that 3-7 weeks treatment of diabetics with powdered fruit, led to a mean fall of 25% (range 11-48%) in post-prandial blood glucose levels. There was a marked fall in both blood and urine sugar over 7 weeks in a group treated with an aqueous extract of the fruit. Glycosylated haemoglobin showed a significant reduction by the end of the trial. By contrast, Kirti et al. (1982) reported that whilst karela (acute or chronic) resulted in a reduction in glycosuria, there was no effect on blood glucose. However in their experiments, blood glucose levels were measured two hours after the administration of karela extract and by this time any effects of the fruit may have diminished. The earlier work of Leatherdale et al. (1981), suggested that improved glucose tolerance is most marked within the first 90 minutes of karela administration. Inter-patient variation may also explain a poor response to karela; Welihinda et al. (1986) reported that karela juice significantly improved glucose tolerance in only 13 of the 18 patients tested.

P-insulin.

In 1974, Khanna et al., isolated a polypeptide (p-insulin or v-insulin) from karela. A significant hypoglycaemic effect was observed in 6 IDDM, 1 NIDDM and 2 asymptomatic diabetics administered p-insulin subcutaneously (Baldwa et al., 1977). In a later study by Khanna et al. (1981) subcutaneous p –insulin led to a significant fall in blood glucose in 11 IDDM patients, whereas a similar effect in 8 NIDDM patients did not reach statistical significance. One IDDM patient was reported to have been maintained on p-insulin for 5 months with no complaints of side effects.

Karela seeds: Oral administration of powdered karela seeds produced a significant reduction in post-prandial blood sugar values in 14 NIDDM and 6 IDDM patients (Grover and Gupta, 1990).

Effects on tissue and enzymes; possible mode of action

Attempts have been made to obtain further information on the mode of action of karela fruit and seeds through experiments using enzymes, tissues or cells in vitro or examining organs isolated from karela treated animals. Karela fruit and seed preparation have a number of biological effects in vitro, which may give an indications of their mode of action.
Glucose Absorption

A theoretical means by which glucose tolerance can be improved is by decreased absorption of glucose from the gut. Meir and Yaniv (1985) reported that glucose uptake by inverted gut was inhibited in the presence of extracts of karela fruit. However, from the in vivo work of Day et al. (1990) and Higashino et al. (1992) it would appear that this is not the mechanism involved in the action of karela since tolerance of intraperitoneally administered glucose is also improved. There have been no studies reported to date on effects of karela on enzymes involved in the digestion of carbohydrates, e.g. α-amylase.

Insulin secretion: In a number of in vitro studies (Welihinda et al., 1982; Ali et al., 1993; Mosihuzzaman et al., 1994), extract from the fruit have been found to stimulate insulin release from isolated pancreatic islet cells. The responsiveness of STZ and alloxan treated animals to karela, would seem to suggest that pancreatic stimulation is not involved. However, it must be noted that STZ and alloxan treatment may not result in complete destruction of pancreatic β-cells. For instance, in the study by Kedar and Chakrabarti (1982), STZ-treated animals were responsive to glibenclamide, which acts by stimulation of insulin release from the pancreas. In addition, some studies (Sharma et al., 1960; Tiangda et al., 1987) alloxan treated rabbits were more responsive to karela extracts than normal animals. This may include a sensation of the β-cells to karela by alloxan. However, it should be noted that increased insulin levels have not been observed in karela treated mice (Day et al., 1990), rats or humans (Leatherdale et al., 1981) in vivo.

Insulinomimetic effects

Karela juice shows certain insulinomimetic effects such as increased glucose uptake into muscle, stimulation of lipogenesis, and inhibition of lipolysis on tissue preparation in vitro. In vitro tests on tissues taken from animals treated with karela have also shown a depression of hepatic glucogenetic enzymes, and increased liver and muscle glycogen. There is conflicting data on effects of karela extracts on tissue respiration. Welihinda and Karunanayake (1986) found that karela juice did not show any effect on tissue respiration by diaphragm muscle in vitro. However, Meir and Yaniv (1985) reported that karela inhibited the oxidation of glucose by liver tissue, possibly at the first step in glycolysis i.e. phosphorylation by hexokinase. These contradictory results may be due to difference in the tissue, methodology and type of karela preparation used. A more reliable indicator of effect of karela on tissue respiration may be that demonstrated by Shibib et al. (1993). Liver glucose –6-
phosphate dehydrogenase (G6PD) activity was elevated on in vivo administration of karela ethanolic extract by gastric intubation. This would enhance the utilization of glucose by the liver leading to a lower in blood glucose.

The lipogenic and anti-lipolytic effects of karela juice in vitro are shared by seed extracts. A saponin (not identified) and proteins have been found to account for the in vitro effects of the seeds. The proteins are believed to be lectins; the abortifacient proteins α- and β-momorcharin also found in the seeds are not active in this assay (Wong et al., 1985 a, b). However, against this, Welihinda and Karunanayake (1986) reported that adipose tissue of karela treated rats did not differ significantly in triglyceride content from that of control animals. Thus, inhibition of glucose absorption, insulin secretagogue activity and insulinomimetic effects have been attributed to karela in in vitro tests. However, not all of these have been fully supported by in vivo data, probably due to the compounds showing activity in vitro not being bioavailable in vivo.

Other pharmacological and toxicological properties

A number of effects of Momordica charantia unrelated to diabetes have been investigated. No data is available on standard toxicity parameters e.g. LD50 values of the juice, seeds or plants. However some information on toxicity is available from observations made during experimental or clinical use of Momordica charantia extracts in animals or humans.

Anti-cancer: Protein fractions obtained from the fruit and seed of Momordica charantia have the ability to inhibit cell growth, guanylate eyelase activity and ribosomal activity. West et al., (1971) demonstrated inhibitory effects of whole plant extracts on seedling root growth, division of fertilized sea urchin eggs, rat foetal growth (if injected on day of mating) and the growth of Hep2 cells in culture. They also report a single case study of a leukemia patient in whom regular intake of the extract led to a fall in white blood cell count, and an increase in blood haemoglobin.

Antivirals: The growth of herpes simplex virus I (Foa Tomasi et al., 1982) and human immunodeficiency virus I (Lifson et al., 1988; Lee-Huang et al., 1990) is inhibited by karela extracts. Increased T-cell count and a normalization of the CD 4/CD 8 ratio seemed to occur in three HIV positive patients given regular doses of karela juice (Zhang, 1992). The juice was
administered as a retained enema i.e. rectally. This may explain its apparent effectiveness since the active anti-viral components of *Momordica charantia* are believed (Zhang, 1992) to be the proteins α and β- momorcharin and MAP, which would be expected to undergo hydrolysis by pancreatic enzymes if administered by the oral route.

**Analgesic Effects:** A methanolic extract of the seeds from unripe fruit has been shown to produce a marked dose-dependent analgesic effect in mice and a much weaker effect in rats (Biswas et al., 1991), but using different test systems for the two species. Naloxone pretreatment failed to modify the analgesic response, suggesting the opioid receptors were not involved.

**Anti-inflammatory effects:** A dose related anti-inflammatory effect has been demonstrated using carrageenin-induced rat hind-paw oedema (Lal et al., 1990). Free radical scavenging activity of the juice in vitro (Rao, 1991) may be involved.

**Hypotensive action:** “Cerasee” (aerial parts of *Momordica charantia*) extract showed a marked transient depressor effect on injection to the anesthetized dog (Feng et al., 1962). Gamma amino butyric acid has been suggested to be responsible for this effect (Durand et al., 1962).

**Anti-fertility effects:** Oral administration of karela fruit extract (1.75 g/day for 60 days) to male dogs resulted in testicular lesions and mass atrophy of spermatogenic elements (Dixit et al., 1978). Serum enzyme were normal implying that an infertility state was induced without altering general metabolic activity in the animal. A study by Stepka et al. (1974) found that daily oral administration of the fresh juice *Momordica* (species not stated) leaves to a group of female mice reduced the fertility rate. This was reversed on withdrawal of the treatment. No pathological changes were seen in any of the maternal organs, but in some cases, concepti were seen as necrotic masses. In more recent work proteins capable of inducing abortions (α and β momorcharins) and necrosis of placental trophoblasts have been isolated from *Momordica charantia* seeds. It is possible that similar proteins occur in the leaves. Uterine bleeding has been induced in pregnant rats given karela juice (6 ml/kg) orally (Zhang 1992),
while 2 pregnant rabbits given karela juice (6 ml/kg) suffered uterine haemorrhage and death within a few hours (Sharma et al., 1960). No such effect was noted in non-pregnant females.

**Effects on growth, blood and serum lipids:** Chronic administration of karela extract (1.75 g orally per day for 20-60 days) to dogs resulted in elevated levels of serum cholesterol and non-esterified fatty acids, but no significant changes in body weight or serum enzymes (Dixit et al., 1978). Rats maintained on a diet containing freeze-dried karela for 8 weeks showed no change in food consumption rate or growth rate (Platel et al., 1993). At the end of this period, organ weights (liver, kidney, testes, spleen, adrenals and heart) were similar to those of control animals. Blood cell counts, cell volume and haemoglobin parameters showed no significant difference to controls and remained within the normal range. However in this study, there was a significant decrease in blood cholesterol.

**Hepatotoxicity:** Following the administration of karela juice and seed extract to rats (10 ml/kg body weight daily for 30 days), serum γ-glutamyl transferase and alkaline phosphatase was significantly elevated, but consistent histopathological defects were not observed in the liver (Tennekoon et al., 1994). Therefore the elevated enzymes could either be due to mechanisms not obvious at the histological level or to enzyme induction. The prevalence of dilatation and/or congestion in the hepatic central veins and associated sinusoids was twice as high in the juice treated group as in the seed extract treated and control groups. Ng et al. (1994) have found that α- and β- momorcharins can induce cytoplasmic blebs and other morphological changes in rat hepatocyte *in vitro*. Secretion of various enzyme markers of cell damage is also raised.

**Fatal doses in animals:** Continuous single or twice daily oral administration of karela juice (6 ml/kg body weight) to 6 rabbits, died within a few hours of receiving this dose (Sharma et al., 1960). Rats given karela juice (18-40 ml/kg body weight, by intraperitoneal route) became sluggish and died within 6-18 hours. Zhang (1992) reported that pregnant rats died within a few hours of receiving karela juice (6 ml/kg body weight) orally. In normal and alloxan diabetic rats given the same dose daily, 80-90% died within 5-23 days. Abdominal injection of the juice at (15 ml/kg body weight) caused death in 6-18 hours. In rabbits receiving 10 ml/kg orally per day, the majorities were reported to have shown toxic effects, although the nature of these effects was not given in the paper.
**Toxicity in humans:** Although toxicity has been observed in some animal studies, if extrapolated to humans, the relevance of the dose and route of administration must be considered. A dose of 6-10 ml/kg would represent a dose of 400 ml-1000 ml for an adult. The normal adult dose is 50 ml, given orally. There are no published reports of fatal or serious effects in adults at this dose. Patel et al. (1968) reported that administration of the juice or dried juice powder (equivalent to 250-500 g of the fruit) to diabetic patients led to abdominal pain and diarrhea. Zhang (1992) has used orally or rectally administered fruit juice to treat HIV-positive patients. He reports that there is very low clinical toxicity. A patient who had been given the juice daily for over three years did not show any change in the blood chemistry or any other untoward effect. Liver, kidney, heart or blood abnormalities have not been reported in any of Zhang’s patients despite long term use of *Momordica charantia* fruit juice. The only report of a potential fatal reaction in humans is hypoglycaemic coma induced in two small children (Hulin et al., 1988). The children aged three and four required urgent medical attention following ingestion of a water extract of *Momordica charantia* leaves and vines.

Overall, the fruit seeds and aerial parts of *Momordica charantia Linn* have been used as an anti-diabetic remedy in a number of areas of the world notably India, Sri Lanka, China and the West Indies. Limited studies on humans have shown that karela fruit juice reduces fasting blood glucose and improves glucose tolerance on acute administration. Prolonged administration causes a lowering of glycosylated haemoglobin in the blood and decreasing glycosuria and basal glycaemia. The hypoglycaemic and anti-hyperglycaemic effects of karela fruit and seeds have also been demonstrated in animal models. Through evidence from animal and *in vitro* studies, there is support for both insulin secretagogue and insulinomimetic activity of the fruit. However, enhanced insulin levels *in vivo* in response to administration of karela have not been observed.

A wide range of compounds has been isolated from *Momordica charantia* fruit, seeds and vines, notably saponins and proteins. Suggested hypoglycaemic compounds include a polypeptide (p-insulin), a steroid mixture (charantin) and a pyrimidine nucleoside (vicine). However, none of these is fully supported as a sole active constituent by the scientific data available. It is possible that a number of active constituents with a range of biological effects beneficial to diabetes are present in the fruit. Principal toxic properties of karela juice noted in animals are anti-fertility effects and hepatotoxicity, with death occurring on chronic oral treatment with doses of the order of 6 ml/kg body weight. Pregnant females were particularly
susceptible. Encouragingly, similar effects have not been reported in humans despite widespread use of the fruit juice both as a medicinal plant and as a vegetable. After the thorough literature review for both the plants it has been observed that both EJ & MC have been used for long time to treat various stages of diabetes and other ailment related to diabetes. The plant parts other than the stem bark of EJ have been well explored for phytochemical as well as pharmacological activities. There is no reports on bark available for its use in diabetes or related metabolic disorders except the anti-inflammatory activity. So it has been concluded to explore the use of EJ in treatment of diabetes. As mentioned in table 2.4 various combination studies have been reported and showed very impressive results by means of additive effect. With these supportive references for combinations of EJ seeds, leaves or MC fruit, we have decided to evaluate the combination of EJ stem bark which is first time combined with MC fruit as per the literature we have reviewed.
Table 2.6 Various combinations studied using with *Momordica charantia*

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Combination</th>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><em>Momordica charantia</em> and <em>Phyllanthus urinaria</em></td>
<td>Decreased BGL by 23% and 39% at the doses of 10 and 30 mg/kg</td>
<td>Higashino H, Suzuki A 1992</td>
</tr>
<tr>
<td>2.</td>
<td><em>Sesamum indicum</em> (gingili), <em>Emblica officinalis</em> and <em>MC</em></td>
<td>hypolipidaemic and hypoglycaemic activities</td>
<td>Anila, Vijayalakshmi 2000</td>
</tr>
<tr>
<td>3.</td>
<td><em>Momordica charantia</em> (MC) and <em>Eugenia jambolana</em> seeds</td>
<td>Treatment with 400 mg per day of aqueous extracts of MC and EJ for 15 days substantially prevented hyperglycemia and hyperinsulinemia</td>
<td>Grover et.al., 2001</td>
</tr>
<tr>
<td>4.</td>
<td>Cactus, aloe Vera and <em>Momordica Charantia</em></td>
<td>cactus, aloe Vera and <em>Momordica charantia</em> juice for 21 days, the serum glucose concentration of these diabetic mice were significantly lower than STZ diabetic model group (P &lt; 0.01) but still higher than the normal control group</td>
<td>Shen X, Long Z, 2001</td>
</tr>
<tr>
<td>5.</td>
<td><em>Momordica charantia</em> (MC) and <em>Mucuna pruriens</em> (MP)</td>
<td>Antihyperglycaemic effect occurred with an aqueous extract of MC and MP at week 6 at a dose of 200 mg/kg/day. MP individually ineffective</td>
<td>Rathi SS et al., 2002</td>
</tr>
<tr>
<td></td>
<td><strong>Literature</strong></td>
<td><strong>Activities</strong></td>
<td><strong>References</strong></td>
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<tr>
<td>7.</td>
<td><em>Momordica charantia</em> (MC) seeds, <em>Eugenia jambolana</em> (EJ) seeds, <em>Tinospora cordifolia</em> (TC) stems and <em>Mucuna pruriens</em> (MP) seeds</td>
<td>MC and EJ prevented the development of cataract while the protective effect was less with TC and MP along with a significant reduction of plasma glucose levels</td>
<td>Rathi SS et al., 2002</td>
</tr>
<tr>
<td>8.</td>
<td><em>Momordica charantia</em> and Sodium orthovanadate (SOV)</td>
<td>The results suggest that <em>Momordica</em> fruit extract and SOV exhibit hypolipidaemic as well as hypoglycemic effect in diabetic rats and their effect is pronounced when administered in combination.</td>
<td>Yadav UC, 2005.</td>
</tr>
<tr>
<td>9.</td>
<td><em>Momordica charantia</em> and <em>Andrographis paniculata</em></td>
<td>Results suggest that the anti-diabetic potentials of <em>Momordica charantia</em> and <em>Andrographis paniculata</em> could restore impaired estrous cycle in Alloxan-induced diabetic rats.</td>
<td>Reyes BA, Bautista ND, 2006.</td>
</tr>
<tr>
<td>10.</td>
<td>Bitter gourd and spent turmeric</td>
<td>The observed beneficial effects in glycosaminoglycans (GAGs) metabolism during diabetes</td>
<td>Kumar GS et.al., 2006</td>
</tr>
</tbody>
</table>
2.6: *Gmelina arborea* Roxb. (Verbenaceae):

**Classification:**

- Kingdon: Plantae
- Genus: *Gmelina*
- Species: *arborea*

**Synonyms:**

- Assame: Gomari
- Bengali: Gamari, Gumari, Gumbar
- English: Candahar tree, Cashmere tree, Coomb teak, White teak
- Gujarati: Savan, Shivan, Sivan
- Hindi: Gamari, Gambari, Gambhar, Gamhar, Gumbhar,
- Kannada: Kulimavu, Kumbuda, Kumulu
- Kasmiri: Mara, Shivani
- Konkani: Niuvon, Sivony
- Malayalam: Kumbili, Kumbulu, Kumil, Kumiska
- Marathi: Gamar, Kamar, Shivan, Shewan
- Oriya: Gambari, Bhodroparni
- Punjabi: Gumhar, Kumhar
- Sanskrit: Ashveta, Bhadra, Bhadraparni, Gambhari, Gandhari,
- Telugu: Adavigummudu, Challagummudu, Gummadi, Gummudu,

**Parts used:** Steam bark

**Botanical Description**

An unarmed (without branches) tree has about 60 ft. height, clear bole (the lower part of the stem upto a point where the main branches are given off) upto 20-30 ft. and a girth of 5-7 ft. It is found scattered in deciduous forests throughout the greater part of India and the Andamans upto an altitude of 5000 ft. It is also planted in gardens and avenues (Anonymous, 2003).

Leaves are 10-20-7.5-15 cm, broadly ovate, acuminate, entire, glabrous above when mature. Petioles are 5-7.5 cm long, cylindric, puberulous glandular at top. Flowers appear with or sometimes before the young leaves, usually in small cymes of about 3 flowers arranged along
the branches of a densely fulvous-hairy panicle reaching 30 cm long; buds clavate, angular; bracts 8 mm long, linear lanceolate. Calyx 5 mm long, broadly campanulate, densely fulvous-hairy. Corolla brownish yellow, densely hairy outside, reaching 3.8 cm long, 5-lobed, 2-lipped; upper lip rather more than 1 cm long, deeply divided into two oblong, obtuse lobes; lower lip nearly 2.5 cm long, 3-lobed, the middle lobe projecting forward, ovate, subobtuse, with irregularly crenulate margin, much longer and broader than the obovate rounded lateral lobes. Drupe is 2-2.5 cm long, ovoid or pyriform, smooth, orange-yellow when ripe (Kirtikar and Basu, 1999). The wood is yellowish to reddish white when first exposed, aging to light russet or yellowish brown, occasionally with roe and mottle figuring. It is light to moderately heavy (sp. gr. 0.47, wt. 30 lb./cu.ft.), hard, strong, elastic, lustrous with smooth feel.

Figure: 2.9: Plant of Gmelina arborea

Medicinal Uses
The root, fruit, bark and leaves of the plant are being used in medicine (Chopra et al., 1994; Anonymous 2003). The root is stomachic, laxative, anthelmintic; improves the appetite; useful in hallucinations, thirst, piles, abdominal pains, burning sensations, fevers, tridosha (Kirtikar
and Basu, 1999). Root is an ingredient of the Dasamulas of the vaidyas. It is used in the form of infusion or decoction in fever, in indigestion, anasarca. With liquorice, sugar and honey added it is given as galactagogue (Nadkarni, 2000). The root bark improves thirst and relieves abdominal pain (Asolkar et al., 2005). Pulverised root is applied locally for gout (Anonymous, 2003). The flowers are sweet, cooling, bitter, acrid; astringent; useful in leprosy and blood diseases (Kirtikar and Basu, 1999). The fruit is acrid, sour, bitter, cooling, diuretic, aphrodisiac, alterative, astringent to the bowels. It promotes growth of hairs, useful in vata, thirst, anaemia, leprosy, ulcers, consumption, vaginal discharges (Kirtikar and Basu, 1999). Fruit forms an ingredient of several cooling and refrigerant decoctions (Anonymous, 2003), e.g. i) Take of the fruits of Gmelina arborea, Grewia asiatica, liquorice root, red sandal wood and root of Andropogon muricatus, equal parts in all two tolas, water 32 tolas, and boil till reduced to one-half. This decoction is used as a drink in bilious fever. ii) Take of the fruit of Gmelina arborea 10, Raisins 10, Indian Sarsaparilla 6, Delphinium saniculaefolium 5, and Cocculus cordifolius 8 parts. Mix and make a decoction. When ready add jaggery 2 parts; dose 1 to 1.5 ounces. This is used in remittent fever (Nadkarni, 2000). The juice of the leaves is used to remove foetid discharges and worms from ulcers (Kirtikar and Basu, 1999). Juice of tender leaves added to cow’s milk and sweetened with sugar-candy is given with much benefit in gonorrhoea and catarrh of bladder. Leaves grounded into paste with water are applied to forehead for headaches in fevers (Nadkarni, 2000).

To prevent abortions in early stage of pregnancy a powder of the bark of black gingelly seeds, manjistha and shatavari is given in milk (Nadkarni, 2000). The plant is used in treatment of diabetes (Kapoor, 1939; Soumyanath, 2006; Khan and Khanum, 2005), in snake-bite and scorpion sting (Nadkarni, 2000, Chopra et al., 2002). In snake-bite a decoction of the roots and bark (1 in 16) is given internally (Kirtikar and Basu, 1999).

**Phytochemical studies**

**Leaves**

Rao et al. (1967) isolated luteolin from alcoholic extract of leaves. Chemical examination of the leaves of Gmelina arborea has resulted in the isolation of apigenin, quercetin, hentriacontanol and β- sitosterol as the crystalline components. The presence of glycosides of the flavones has been detected (Rao and Rao, 1970).
Nair and Subramanian (1975) isolated kaempferol-3-rutinoside, apigenin-7-rutinoside, apigenin-7-glucoronide, luteolin-7-rutinoside from leaves. Besides the known iridoids 6-O-α-L-rhamnopyanosylcatapol, 6-O-(3”-O-transferuloyl)-α-L-rhamnopyanosylcatapol, 6-O-(2”-4”-O-di-trans-cinnamoyl)-α-L-rhamnopyanosylcatapol and the known phenylpropanoid glycosides verbascoside and martynoside, 12 new acetylated iridoid glycosides named gmelinosides A-L have been isolated from leaves (Hosny and Rosazza, 1998). An isoxazole alkaloid, premnazale was isolated by Barik and coworkers (1992) from leaves of the plant.

**Heartwood**
Joshi and coworkers (1970) isolated n-hexacosanol and n-octacosanol, alongwith β-sitosterol from the benzene extract of hertwood of *Gmelina arborea*. Isolation of nhentriacontanol from benzene extract of heartwood of *Gmelina arborea* was done by Joshi et al.(1971). The isolation of arboreal, a tetrahydrofuranoid lignan from the heartwood of *Gmelina arborea* is reported by Govindachari and coworkers (1972). By a combination of spectral and degradative evidence, arboreal is shown to be 1-hydroxy-2-methoxy-2,6-bis(3,4-methylenedioxyphenyl)-3-7-dioxobicyclo octane. Anjaneulu et al. (1972) reported isolation of arboreol and gmelinol form heartwood of the plant. Paulownin, isoarboreol, ethyl arboreol and gmelanone, lignans from *Gmelina arborea* which have a rearranged carbon skeleton relative to other lignans like arboreol and gmelinol was isolated by Row and coworkers (1974).

**Root:**
Satyanarayana et al. (1985) described isolation of an apiose containig glycoside which contain structure similar to that of umbelliferone as aglycone with carbohydrate moiety being 6-linked β-glucoside and a terminal apiioside.

**Pharmacological studies**
Ethahnolic extract (50%) of bark and stem of wood showed hypoglycemic and antiviral action (Asolkar et al., 2005). Barik et al.(1992) studied effect of plant extracts in inflammation. Wound healing activity of leaves of *Gmelina arborea* was evaluated by Shirwaikar and coworkers (2003). The aqueous methanol extract of bark was studied for antidiarrhoel activity by Agunu and coworkers (2005). This study was carried out on perfused isolated rabbit...
jejunum and castor oil-induced diarrhoea in mice. *Gmelina arborea* showed concentration dependent relaxation at low doses (0.5, 1.0 mg/ml), but showed no significant relaxation at higher doses (2.0, 3.0 mg/ml). The effect of *Gmelina arborea* Roxb. (Verbenaceae) bark and fruit aqueous extracts on paraquat- and hydrogen peroxide–induced oxidative stress was investigated using liver slice culture. Both paraquat and hydrogen peroxide were found to be cytotoxic as measured by release of lactate dehydrogenase from liver slice culture. Addition of bark and fruit extracts along with these cytotoxic agents led to a decrease in lactate dehydrogenase release. Activities of three antioxidant enzymes, namely superoxide dismutase, catalase, and glutathione reductase, were found to increase on treatment with these prooxidants. Addition of the plant extracts along with the pro-oxidants suppressed the enzyme activities. The extracts also displayed antioxidant activity in vitro radical scavenging assays.

Results indicate that *Gmelina* bark and fruit extracts protected liver slice culture cells by alleviating oxidative stress–induced damage to liver cells (Sinha et al., 2006). The effect of hydroalcoholic extracts of leaves of *Gmelina arborea* on gastric ulcers was evaluated by using different experimental models such as aspirin induced ulcer, pylorus ligation induced ulcers, ethanol induced ulcers and cold restrain stress induced ulcers. In all these models the common parameter determined was ulcer index. The hydroalcoholic leaf extracts of *Gmelina arborea* (286 mg/kg and 667 mg/kg) showed a significant effect on ulcer induced by different ulcer induced models. The leaf extract of *Gmelina arborea* was effective in ulcer healing. It was concluded that leaves of *Gmelina arborea* increases healing of gastric ulcers and also prevent the development of gastric ulcers in rats (Giri et al., 2009).

The antioxidant and free radical scavenging activity of defatted and fractionated methanolic extract of *Gmelina arborea* (MEGA) was evaluated using in vitro methods like 1, 1-diphenyl, 2- picryl hydrazine (DPPH) radical scavenging activity, H2O2 scavenging activity, Nitric oxide (NO) radical scavenging activity, Nitro Blue Tetrazolium (NBT) reduction assay, β-carotene-lineolate bleaching assay and Total reduction ability by Fe3+-Fe2+ transformation. In DPPH radical scavenging activity, H2O2 scavenging activity, NO scavenging activity and NBT reduction assay the IC 50 values obtained for MEGA were found to be 434.56 μg/ml, 60.36 μg/ml, 49.54 μg/ml and 67.11 μg/ml respectively and for Ascorbic acid the IC 50 values were found to be 511.36 μg/ml, 33.06 μg/ml, 42.40 μg/ml and 94.82 μg/ml respectively. In the reduction power assay increase in absorbance was observed in a dose dependant manner. Measurement of total phenolic content using Folin-Ciocalteu phenol reagent showed that 1
mg of the extract contained 85.95 μg/ml total phenolics equivalent to gallic acid. The results obtained in study indicated that MEGA can be a potential source of natural antioxidants and the activity may due to the presence of phenolics (Shukla et al., 2009).