

## **Aegle marmelos: Bael**

The bael is one of the sacred trees of the Hindus. Leaves are offered in prayers to Shiva and Parvathi since ancient times. It has its own place in indigenous systems of medicine. The bael fruit, *Aegle marmelos* Correa (syns. *Feronia pellucida* Roth., *Crataeva marmelos* L.), is also called Bengal quince, Indian quince, golden apple, holy fruit, stone apple, bel, bela, sirphal, maredoo and mapin in Thailand; phneou or pnoi in Cambodia; bau nau in Vietnam; bilak, or maja pahit in Malaya; modjo in Java; oranger du Malabar in French; marmelos in Portuguese.

### **BOTANICAL DESCRIPTION & CULTURE:**

#### **Description**

The bael fruit tree is slow-growing of medium size, up to 40 or 50 ft (12-15 m) tall with short trunk, thick, soft, flaking bark and spreading sometimes spiny branches the lower ones drooping. Young suckers bear many stiff straight spines. A clear gummy sap, resembling gum arabic exudes from wounded branches and hangs down in long strands, becoming gradually solid. The deciduous, alternate leaves, borne singly or in 2'S or 3'S, are composed of 3 to 5 oval, pointed, shallowly toothed leaflets, 1 1/2 to 4 in (4-10 cm) long, 3/4 to 2 in (2-5 cm) wide, the terminal one with a long petiole. New foliage is glossy and pinkish-maroon. Mature leaves emit a disagreeable odor when bruised. Fragrant flowers, in clusters of 4 to 7 along the young branchlets, have 4 recurved, fleshy petals, green outside, yellowish inside and 50 or more greenish-yellow stamens. The fruit round, pyriform, oval or oblong, 2 to 8 in (5-20 cm) in diameter may have a thin, hard, woody shell or a more or less soft rind, gray-green until the fruit is fully ripe when it turns yellowish. It is dotted with aromatic minute oil glands. Inside there is a hard central core and 8 to 20 faintly defined triangular segments. With thin dark-orange walls filled with aromatic pale-orange, pasty, sweet, resinous, more or less astringent, pulp. Embedded in the pulp are 10 to 15 seeds. Flattened-oblong, about 3/8 in (1 cm) long, bearing woolly hairs and each enclosed in a sac of adhesive, transparent mucilage that solidifies on drying.

#### **Origin and Distribution**

The tree grows wild in dry forests on hills and plains of central and Bangladesh also in mixed deciduous and dry dipterocarp forests of former French Indochina. Mention has been found in writings dating back to 800 B.C. it is cultivated throughout India, mainly in temple gardens, because of its status as a sacred tree; also in Ceylon and northern Malaya, the drier areas of Java and to a limited extent on northern Luzon in the Philippine Islands where it first fruited in 1914. It is grown in some Egyptian gardens and in Surinam and Trinidad.

#### **Climate**

The bael fruit tree is a subtropical species. In the Punjab, it grows up to an altitude of 4,000-ft (1,200-m) where the temperature rises to 120° F (48.89° C) in the shade in summer and descends to 20° F (-6.67° C) in the winter and prolonged droughts occur. It will not fruit where there is no long, dry season, as in southern Malaya.

#### **Soil**

The bael fruit is said to do best on rich, well-drained soil, but it has grown well and fruited on the oolitic limestone of southern Florida. It grows luxuriantly in the soils having pH range from 5 to 8". In India it has the reputation of thriving where other fruit trees cannot survive.

#### **Propagation**

The bael fruit is commonly grown from seed in nurseries and transplanted into the field. Seedlings show great variation in form size texture of rind quantity and quality of pulp and number of seeds. The flavor ranges from disagreeable to pleasant. Therefore superior types must be multiplied vegetatively.

#### **Culture**

The tree has no exacting cultural requirements, doing well with a minimum of fertilizer and irrigation. The spacing in orchards is 25 to 30 ft (6-9 m) between trees. Seedlings begin to bear in 6 to 7 years, vegetatively propagated trees in 5 years. Full production is reached in 15 years. In India flowering occurs in April and May soon after the new leaves appear and the fruit ripens in 10 to 11 months from bloom-March to June of the following year.

#### **Harvesting**

Normally, the fruit is harvested when yellowish-green and kept for 8 days while it loses its green tint. Then the stem readily separates from the fruit. The fruits can be harvested in January (2 to 3 months before full maturity) and ripened artificially in 18 to 24 days by treatment with 1,000 to 1,500 ppm etrel (2-chloroethane phosphonic acid) and storage at 86°F (30°C). Care is needed in harvesting and handling to avoid causing cracks in the rind.

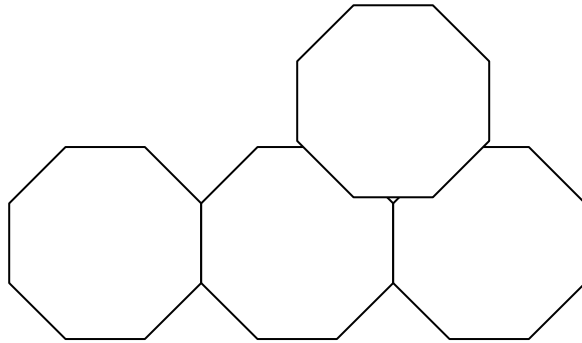
A tree may yield as many as 800 fruits in a season but an average crop is 150 to 200, or, in the better cultivars, up to 400.

### **PHYTOCHEMICALS:**

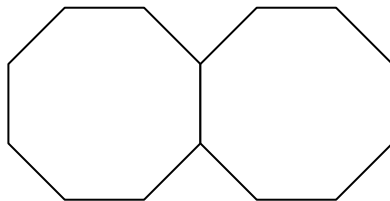
The dry pulp of fruit contains chiefly mucilagepectin like substance. The root, stem and leaves have been shown to contain tannins. Alkaloids, sterols, coumarin and aromatic components have been isolated. Aegelin, marmelosine, marmelin, o-methyl hayordinol, alloimperatorin methyl ester, o-isopentanyl hayordinol and linoleic acid have been identified.

Aegelin, formerly identified as sterol but clarified as a neutral alkaloid, rutacine,  $\gamma$ -sitosterol, aegelimine and aegeline were identified from the leaves. Marmin, marmesin, umbelliferine, skimmianine were identified from the bark and roots. A major constituent of the fruit is the mucilage and marmelosin (0.5%) a coumarin, in addition to the minor constituents like reducing sugar essential oils, ascorbic acid and various minerals. A bitter, light-yellow oil contains 15.6% palmitic acid, 8.3% stearic acid, 28.7% linoleic and 7.6% linolenic acid. The seed residue contains 70% protein.

### **MARMELOSIN**



### **COUMARIN**



### **TRADITIONAL MEDICINAL USES:**

The fresh ripe pulp of the higher quality cultivars, and the "sherbet" made from it, are taken for their mild laxative, tonic and digestive effects. A decoction of the unripe fruit, with fennel and ginger, is prescribed in cases of hemorrhoids. It has been surmised that the psoralen in the pulp increases tolerance of sunlight and aids in the maintaining of normal skin color. It is employed in the treatment of leucoderma. Marmelosin derived from the pulp is given as a laxative and diuretic. In large doses, it lowers the rate of respiration, depresses heart action and causes sleepiness.

For medicinal use, the young fruits, while still tender, are commonly sliced horizontally and sun-dried and sold in local markets. They are much exported to Malaya and Europe. Because of the astringency, especially of the wild fruits, the unripe bael is most prized as a means of halting diarrhea and dysentery, which are prevalent in India in the summer months. Bael fruit was resorted to by the Portuguese in the East Indies in the 1500's and by the British colonials in later times.

A Bitter, light-yellow oil extracted from the seeds is given in 1.5g doses as a purgative.

The bitter, pungent leaf juice, mixed with honey, is given to allay catarrh and fever. With black pepper added, it is taken to relieve jaundice and constipation accompanied by edema. The leaf decoction is said to alleviate asthma. A hot poultice of the leaves is considered an effective treatment for ophthalmia and various inflammations, also febrile delirium and acute bronchitis.

A decoction of the flowers is used as eye lotion and given as an antiemetic. The bark decoction is administered in cases of malaria. Decoctions of the root are taken to relieve palpitation of the heart, indigestion and bowel inflammations; also to overcome vomiting.

The fruit, roots and leaves have antibiotic activity. The root leaves and bark are used in treating snakebite.

Following uses described in folk medicine (not supported by experimental or clinical data):

**Abdominal discomfort:** Boil together 50 g bark of *Aegle marmelos*, 25 g flower of caraway, 25 g of dried ginger and take the decoction twice daily in empty stomach for two to three days.

**Acidity:** Grind together the leaves of *Aegle marmelos* and black pepper (2 g) with water. Take this paste orally once only.

**Burning sensation:** While urinating: grind together the leaves of *Aegle marmelos* and entire plants of *Cynodon dactylon* with a little water. Take this paste in the morning with a glass of water (in which sugar candy has already been dissolved) in empty stomach once a day for 15 day.

**Constipation:** Make a drink (shrabat) of the fruit pulp of *Aegle marmelos*. With 50 g sugar take this sharbat orally early in the morning once a day till it cures. (or) Grind roots of *Aegle marmelos* with cold water and make a paste. Take the paste orally in empty stomach once a day early in the morning till it cures.

**Diarrhoea:** Boil the bark of *Aegle marmelos* in water. Filter this and add some powdered long pepper to it. Take the decoction twice daily for two to three days.

**Epilepsy:** Grind together the leaves of *Aegle marmelos*, *Cassia fistula*, *Lagerstroemia reginae*, *Premna mucronata*, whole plants of *Solanum xanthocarpum*, *Tribulus terrestris*, *Desmodium gangeticum*, *Desmodium pulchellum* and branches and leaves of *Solanum indicum*. Boil the paste in water. Filter with a cloth. Administer orally with honey. Dosage: one teaspoonful twice daily for seven days or till it cures.

**Fever:** Make a paste of 50 g leaves of *Aegle marmelos*. Apply the paste on head and chest daily till it cures. (or) Boil 100 g leaves of *Aegle marmelos* with water. Filter and take the decoction orally twice daily for two days. (or) grind together the barks of *Aegle marmelos*, *Cassia fistula*, *Gmelina arborea*, *Premna mucronata* and the whole plants of *Solanum xanthocarpum*, *Tribulus terrestris*, *Desmodium gangeticum*, *Desmodium pulchellum* and the twigs of *Solanum indicum* all in equal proportion. Boil these plants/plant parts with water. Filter with a cloth. Administer one teaspoonful of this decoction twice daily orally with honey for seven days or until cured. (or) Boil the bark of *Aegle marmelos* with water and filter it. Add a little juice of garlic to this decoction. Take this orally twice daily for two days.

**Indigestion:** Grind the leaves of *Aegle marmelos* with 7 nos. of black pepper. Take this orally twice or thrice for one day only.

**Leprosy:** Sun-dry the leaves of *Aegle marmelos* and then powder them. Sprinkle this powder on the wound after taking bath. Continue this process till it cures. Avoid taking dried fish, pumpkin and tomato in diet.

**Myalgia:** Grind the roots of *Aegle marmelos* with cold water and make a paste. Take this paste orally in early morning in empty stomach.

**Smallpox:** powder the leaves of *Aegle marmelos*. Take one teaspoonful of this paste orally once a day with water till it cures.

**Spermatorrhoea:** Grind together the leaves of *Aegle marmelos* and a few plants of *Cynodon dactylon* with water. Take this paste orally in the morning with a glass of water (in which sugar candy has already been dissolved) in empty stomach. Continue this process for 15 days. (or) Powder together a fruit of *Aegle marmelos*, 10 g tuber of *Salvia malabarica*, 5 g dried ginger, 5 g long pepper, 5 g aniseed, 5 g fenugreek,

1 g cloves and 1 g cinnamon. Take orally one teaspoonful of this powder with cold water twice daily for seven days.

**Food value per 100 g of Edible Portion\***

Water	54.96-61.5 g
Protein	1.8-2.62 g
Fat	0.2-0.39 g
Carbohydrates	28.11-31.8 g
Ash	1.04-1.7 g
Carotene	55 mg
Thiamine	0.13 mg
Riboflavin	1.19 mg
Niacin	1.1 mg
Ascorbic Acid	8-60 mg
Tartaric Acid	2.11 mg

- Fresh bael fruit, as analyzed in India.

**OTHER TRADITIONAL USES:**

**Fruit:** The fruit pulp has detergent action and has been used for washing clothes. The bael fruit is employed to eliminate scum in vinegar making. The gum enveloping the seeds is most abundant in wild fruits and especially when they are unripe. It is commonly used as a household glue and is employed as an adhesive by jewelers. Sometimes it is resorted to as a soap-substitute. It is mixed with lime plaster for waterproofing wells and is added to cement when building walls. Artists add it to their watercolors and it may be applied as a protective coating on paintings.

The limonene-rich oil has been distilled from the rind for scenting hair oil. The shell of hard fruits has been fashioned into pill- and snuff boxes, sometimes decorated with gold and silver. The rind of the unripe fruit is employed in tanning and also yields a yellow dye for calico and silk fabrics.

**Leaves:** In the Hindu culture, the leaves are indispensable offerings to the 'Lord Shiva' the leaves and twigs are lopped for fodder.

**Flowers:** A Cologne is obtained by distillation from the flowers.

**Wood:** The wood is strongly aromatic when freshly cut. It is gray-white, hard, but not durable; has been used for carts and construction, though it is inclined to warp and crack during curing. It is best utilized for carving, small-scale turnery, tool and knife handles, pestles and combs, taking a fine polish.

**PHARMACOLOGICAL ACTIVITIES AND CLINICAL TRIALS:**

**Antidiabetic activity**

The study evaluates the antidiabetic effect of an aqueous extract of Aegle marmelos fruits (AMFEt) in diabetes. Female albino Wistar rats were randomly divided into five groups; normal (untreated), normal + AMFEt, streptozotocin (STZ)-treated, STZ-treated + AMFEt, and STZ-treated + glibenclamide. Rats were rendered diabetic by STZ (45 mg/kg) administered intraperitoneally. AMFEt (250 mg/kg) was given twice daily for 1 month. Blood glucose, plasma insulin, glycosylated hemoglobin, liver glycogen, and change in body weight were determined. Food intake and water intake were monitored daily. An oral glucose tolerance test was also performed to determine the effect of this extract. The results show that glucose level and glycosylated hemoglobin were increased and plasma insulin and liver glycogen were decreased in diabetic rats, and that treatment with AMFEt reversed the effects of diabetes on these biochemical parameters to near normal levels.

**Antidiarrhoeal activity**

A study was undertaken to evaluate the effect of aqueous and methanolic plant extracts of Acorus calamus rhizome, Pongamia glabra leaves, Aegle marmelos unripe fruit and Strychnos nux-vomica root bark for their antidiarrhoeal potential against castor-oil induced diarrhoea in mice. The methanolic plant extracts were more effective than aqueous plant extracts against castor oil induced diarrhoea. The methanolic plant

extracts significantly reduced induction time of diarrhoea and total weight of the faeces. The results obtained establish the efficacy of these plant extracts as antidiarrhoeal agents.

#### **Antifungal activity**

The antifungal activity of essential oil isolated from the leaves of bael (*Aegle marmelos* (L.) Correa ex Roxb., Rutaceae) has been evaluated using spore germination assay. The oil exhibited variable efficacy against different fungal isolates and 100% inhibition of spore germination of all the fungi tested was observed at 500 ppm. However, the most resistant fungus, *Fusarium udum* was inhibited 80% at 400 ppm. Kinetic studies showed concentration as well as time dependent complex inhibition of spore germination by the essential oil.

#### **Antiperoxidative activity**

Relative importance of *Bacopa monnieri* (200 mg/kg), *Aegle marmelos* (1.00 g/kg) and *Aloe vera* (125 mg/kg) leaf extracts in the regulation of thyroid hormone concentrations in male mice was investigated. While serum levels of both T(3) and T(4) were inhibited by *A. vera*, *A. marmelos* extract could decrease only T(3) concentration. On the other hand, T(4) concentration was increased by *B.monniieri* extract suggesting its thyroid stimulating role. When the relative potency of each plant extract was calculated in terms of percent increase or decrease in thyroid hormones, as compared to the control value, the decrease in T(3) concentration by *A. marmelos* was about 62% indicating its possible use in the regulation of hyperthyroidism. *B. monnieri* could increase T(4) concentration by 41% without enhancing hepatic lipid peroxidation (LPO) suggesting that it can be used as a thyroid-stimulating drug. In fact, hepatic LPO was decreased and superoxide dismutase (SOD) and catalase (CAT) activities were increased by *B.monniieri* and *A.marmelos* leaf extracts showing their antiperoxidative role. It is thus suggested that *A. marmelos* and *A. vera* may be used in the regulation of hyperthyroidism, while *B.monniieri* in hypothyroidism.

#### **Antiprotozoal activity**

Antiprotozoal activity has also been shown by Henry and Brown.

#### **Antiproliferative activity**

The extracts from *Aegle marmelos* Correa are able to inhibit the in vitro proliferation of human tumor cell lines, including the leukemic K562, T-lymphoid Jurkat, B-lymphoid Raji, erythroleukemic HEL, melanoma Colo38, and breast cancer MCF7 and MDA-MB-231 cell lines. Molecules present within the studied *Aegle marmelos* C. extracts were identified by gas-chromatography/mass-spectrometry analysis; three derivatives (butyl p-tolyl sulfide, 6-methyl-4-chromanone and butylated hydroxyanisole) were found to exhibit strong activity in inhibiting in vitro cell growth of human K562 cells. The antiproliferative activity of these compounds was found to be comparable to that of known antitumor agents, including cisplatin, chromomycin, cytosine arabinoside and 5-fluorouracil. In addition, the antiproliferative activity of butyl-p-tolyl sulfine, 6-methyl-4-chromanone and 5-methoxypsolaren was associated to activation of the differentiation pattern of K562 cells.

#### **Antiulcer activity**

Oral administration of bergenin and norbergenin, two isocoumarins isolated from the leaves and roots of *Flueggea microcarpa* and luvangetin, a pyranocoumarin isolated from the seeds of *Aegle marmelos* Correa, showed significant protection against pylorus ligated and aspirin-induced gastric ulcers in rats and cold restraint stress-induced gastric ulcers in rats and guinea pigs. The study on prostaglandins release by human colonic mucosal incubates, indicated a concentration dependent (1-10 micrograms/ml) stimulatory effect of bergenin and norbergenin, while luvangetin (1-10 micrograms/ml) did not produce any effect. The results suggest that gastroprotective effects of bergenin and norbergenin could be due to increased prostaglandin production while some other mucosal defensive factors may be involved for luvangetin.

#### **Cardiotonic activity**

In Indian Systems of Medicine there are many plants having high medicinal values. In a study it is observed the efficacy of *Aegle marmelos* Corr.(AM) as a Cardiotonic drug and an attempt has also been made to elucidate the mechanism of action of the same. The total aqueous extract of the leaves of AM was perfused to in-situ frog's heart preparation. The mechanical activity of heart was studied by kymographic drum. The experiment showed that AM increases the force of contraction of cardiac muscles and also its action is not blocked by Calcium channel blockers and Beta blockers. As the doses of AM extract increases there is a graded decrease in the heart rate and increase in the force of contraction. Thus the study proves the Cardiotonic action of *Aegle marmelos* Corr. On amphibian heart.

### **Effect on biotransformation enzyme systems**

The effect of hydroalcoholic (80% ethanol, 20% water) extract of leaves of *Aegle marmelos* was examined on carcinogen metabolizing phase-I and phase-II enzymes, antioxidant enzymes, glutathione content, lactate dehydrogenase and lipid peroxidation, using two doses of dried extract (50 and 100 mg kg<sup>-1</sup> daily for 14 days), in the liver of mice. The modulatory effect of the extract was also examined on extrahepatic organs (lung, kidney, fore-stomach) for effects on the activity of glutathione S-transferase, DT-diaphorase, superoxide dismutase and catalase. Extract treatment significantly increased the basal levels of acid-soluble sulphhydryl (-SH) content, cytochrome P450, NADPH-cytochrome P450 reductase, cytochrome b5, NADH-cytochrome b5 reductase, glutathione S-transferase, DT-diaphorase, superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase in the liver. *Aegle* acted as a bifunctional inducer since it induced both phase-I and phase-II enzyme systems. Both doses significantly decreased the activity of lactate dehydrogenase and formation of malondialdehyde in liver, suggesting a role in cytoprotection as well as protection against pro-oxidant-induced membrane damage. Butylated hydroxyanisole (positive control) induced almost all the antioxidative parameters measured in this study. The extract was effective in inducing glutathione S-transferase, DT-diaphorase and superoxide dismutase and catalase in lung, glutathione S-transferase, DT-diaphorase and superoxide dismutase in fore-stomach, and DT-diaphorase and superoxide dismutase in lung. These significant changes in the levels of drug-metabolizing enzymes and antioxidative profiles are strongly indicative of the chemopreventive potential of this plant, especially against chemical carcinogenesis.

### **Effects on spontaneous beating and calcium-paradox**

Effects of methanolic extract of root bark of *Beli* (*Aegle marmelos* Corr.), an Ayurvedic crude drug used for heart diseases, and constituents isolated from the extract on spontaneous beating of cultured mouse myocardial cells were examined. The extract at a concentration of 100 micrograms/ml inhibited the beating rate by approximately 50%. Among the isolated constituents, auraptin was the most potent inhibitor the IC<sub>50</sub> of auraptin is 0.6 microgram/ml, which is comparable with that of verapamil, a calcium antagonist. Addition of auraptin at concentrations higher than 1 microgram/ml significantly reduced the ratio of morphologically changed myocardial cells which originated from calcium overload caused by successive treatment with calcium free and calcium-containing solutions.

### **Hypoglycaemic activity**

*Aegle marmelos* Corr. (Rutaceae) is widely used in Indian Ayurvedic medicine for the treatment of diabetes mellitus. The hypoglycaemic effect of the water extract of the fruits of *Aegle marmelos* was examined in streptozotocin-induced diabetic Wistar rats. Oral administration of the water extract (125 and 250 mgkg<sup>-1</sup>) twice a day for 4 weeks resulted in significant reductions in blood glucose, plasma thiobarbituric acid reactive substances, hydroperoxides, ceruloplasmin and alpha-tocopherol and a significant elevation in plasma reduced glutathione and Vitamin C in diabetic rats. The effect of the extract at a dose of 250 mgkg<sup>-1</sup> was more effective than glibenclamide in restoring the values of these parameters. The results of this study clearly show the hypoglycaemic activity of the fruit extract.

In an effort to test the hypoglycaemic activity of *Aegle marmelos* and *Hibiscus rosa sinensis* in glucose induced hyperglycaemic rats, their alcoholic leaf extracts were studied. Both the groups of animals receiving either *A. marmelos* or *H. rosa sinensis* leaf extract for seven consecutive days, at an oral dose equivalent to 250 mg kg<sup>-1</sup> showed significant improvements in their ability to utilize the external glucose load. Average blood glucose lowering caused by *A. marmelos* and *H. rosa sinensis* was 67% and 39% respectively which shows that former significantly ( $P < 0.0001$ ) improves the glucose tolerance curve. The magnitude of this effect showed time related variation with both the plants. Efficacy of *A. marmelos* and *H. rosa sinensis* was 71% and 41% of glibenclamide, respectively. These data throw some light on the possible mechanism of hypoglycaemic activity of both the plants. The mechanism of action could be speculated partly to increased utilization of glucose, either by direct stimulation of glucose uptake or via the mediation of enhanced insulin secretion.

Investigations were carried out to evaluate the oral hypoglycaemic activity of some Sri Lankan medicinal plants. Approximately 40 plants available locally are reputed to have oral hypoglycaemic activity of these the mostly widely used are (a) *Salacia reticulata* (Celastraceae) (b) *Aegle marmelos* (Rutaceae) and (c) *Momordica charantia* (Cucurbitaceae). Aqueous decoctions of these plants were investigated for their ability to lower the fasting blood glucose level and improve the glucose tolerance in laboratory animals. The results indicate that the aqueous decoctions of all three plants possess significant hypoglycaemic effect. The magnitude of this effect showed time related variation with the three plants. The highest oral hypoglycaemic activity and the maximum improvement of the oral glucose tolerance were associated with the extract of *Momordica charantia* while the least but significant effects were shown by *Salacia reticulata*.

### **Irritable bowel syndrome**

Among 169 patients with irritable bowel syndrome (IBS), standard therapy (with clidinium bromide, chlordiazepoxide and isaphaghulla), a compound Ayurvedic preparation (with *Aegle marmelos* corra plus *Bacopa monniere* Linn) along with a matching placebo were given in a double blind randomised trial for 6 wk. The Ayurvedic preparation in 57 patients was found effective in 64.9 per cent, while standard therapy (60 patients) was useful in 78.3 per cent. Patients on placebo (52 patients) showed improvement in 32.7 per cent only. Ayurvedic therapy was particularly beneficial in diarrhoea predominant form as compared to placebo. The standard therapy was more useful in the painful form of IBS as compared to placebo and Ayurvedic preparation. In gas predominant form the effect of standard as well as Ayurvedic therapy, was similar to placebo. Long-term follow-up (greater than 6 months) showed that both forms of therapy were no better than placebo in limiting the relapse.

### **Radioprotective effect**

The radioprotective effect of a hydroalcoholic extract of *Aegle marmelos* (AME) was evaluated in cultured human peripheral blood lymphocytes (HPBLs) by the micronucleus assay. The optimum protective dose of the extract was selected by treating HPBLs with 1.25, 2.5, 5, 6.25, 10, 20, 40, 60, 80 and 100 microg/ml AME before exposure to 3 Gy gamma-radiation and then evaluating the micronucleus frequency in cytokinesis blocked HPBLs. Treatment of HPBLs. With different doses of AME reduced the frequency of radiation-induced micronuclei significantly, with the greatest reduction in micronucleus induction being observed for 5 microg/ml AME. Therefore this dose of AME was considered as the optimum dose for radioprotection and further studies were carried out treating the HPBLs with 5 microg/ml AME before exposure to different doses (0, 0.5, 1, 2, 3, and 4 Gy) of gamma-radiation. The irradiation of HPBLs with different doses of gamma-radiation caused a dose-dependent increase in the frequency of lymphocytes bearing one, two and multiple micronuclei while treatment of HPBLs with 5 microg/ml AME significantly reduced the frequency of lymphocytes bearing one, two and multiple micronuclei when compared with the irradiated control. The dose-response relationship for both groups was linear. To understand the mechanism of action of AME separate experiments were conducted to evaluate the free radical scavenging of OH, O<sub>2</sub><sup>-</sup>, DPPH, ABTS(+) and NO in vitro. AME was found to inhibit free radicals in a dose dependent manner up to a dose of 200 microg/ml for the majority of radicals and plateaued thereafter. The study demonstrates that AME at 5 microg/ml protected HPBLs against radiation-induced DNA damage and genomic instability and its radioprotective activity may be by scavenging of radiation-induced free radicals and increased oxidant status.

### **Toxicity**

The leaves are said to cause abortion and sterility in women. The bark is used as a fish poison in the Celebesw. Tannin ingested frequently and in quantity over a long period of time, is antinutrient and carcinogenic.

The study was undertaken to investigate the toxic effect of aqueous extracts of *Aegle marmelos* (AM), *Stevia rebaudiana* (SR) *Pouteria cambodiana* (PC) and *Clausena excavata* (CE) on rats by dominant lethal test. The data of 8-week treatment suggested that none of the extracts adversely affected male body and testicular weights as well as cauda epididymal sperm counts. No notable changes in sperm morphology and motility were observed. On the other hand sperm count in the CE group was significantly higher as compared to both control and other treatment groups. There were no abnormal changes in the number of implantation sites, number of viable feruses and number of dead fetuses in females mated with plant extract-treated males relative to controls. Based on these results it could be concluded that all the investigated plant extracts have no toxic effect on male rat reproduction and progeny outcome.

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