



## **AEGLE MARMELOS (LINN.): A THERAPEUTIC BOON FOR HUMAN HEALTH**

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### ABSTRACT

Traditional system of medicine consist large number medicinal plants, which conveyed their potential therapeutic utilities. *Aegle marmelos* (Linn.) is commonly known as Bael belongs to Rutaceae Family, widely grown in India, Tropical and subtropical Countries. In India, *Aegle marmelos* (Linn.) possess great mythological significance and medicinal significant in ancient system of medicine as well. Number of studies on photochemistry of the plat suggest no of bioactive chemical entity like,  $\gamma$ -sitosterol, aegelin, lupeol, rutin, marmesinin,  $\beta$ -sitosterol, flavone, glycoside, O-isopentenyl halfordiol, marmeline and phenylethyl cinnamamides. A priceless tank of bioactive molecule of the plant exploit its medicinal properties such as antidiabetic, antiulcer, antioxidant, antimalarial, anti-inflammatory, anticancer, radioprotective, antihyperlipidaemic, antifungal, antibacterial and antiviral activities. Present review highlights the present Ethno-pharmacological uses, and chemical properties of *Aegle marmelos* (Linn.)

**Keywords:** *Aegle marmelos*, Rutaceae, Phytochemical constituents, Pharmacological activity.

### INTRODUCTION

Herbalism is a traditional medicinal or folk medicine practice based on the use of plants and plant extracts. Herbalism is also known as botanical medicine, medical herbalism, herbal medicine, herbology, herblore, and phytotherapy<sup>1</sup>. Plants are considerably useful and economically essential. They contain active constituents that are used in the treatment of many diseases. Plants are rich source of ecologically developed secondary metabolites, which are potential remedies for different ailments<sup>2</sup>.

*Aegle marmelos* (L.) Correa commonly known (Table 1) as Bael or Bilva belonging to the family Rutaceae has been widely used in indigenous systems of Indian medicine due to its various medicinal properties<sup>3</sup>. *Aegle marmelos* (L.) tree is held sacred by Hindus and offered in prayers to deities Lord Shiva and Parvati and thus the tree is also known by the name Shivaduma (the tree of Shiva). The Bael tree has its origin from Eastern Ghats and Central India. It is Indigenous to Indian subcontinent and mainly found in tropical and subtropical regions. The tree is also found as a wild tree, in lower ranges of Himalayas up to an elevation of 500 meters. Bael is found growing along foothills of Himalayas, Uttaranchal, Jharkhand, Madhya Pradesh, and the Deccan Plateau and along the East coast<sup>4</sup>.

### Discription

*Aegle marmelos* is a slow-growing, medium sized tree, up to 12 to 15 m tall with short trunk, thick, soft, flaking bark, and spreading, sometimes spiny branches, the lower ones drooping<sup>5</sup>. Fruit, Leaf, Bark and Decoction of the bark have been used in traditional medicinal system for the treatment of various diseases (Figure 1).



Figure 1: *Aegle marmelos* plant

### Leaves of *Aegle marmelos*

The deciduous, alternate leaves, borne singly or in 2's or 3's, are composed of 3 to 5 oval, pointed, shallowly toothed leaflets 4-10 cm long, 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. (Figure 2.1)



Figure 2.1: Leaves of *Aegle marmelos*

Table 1: Different name of *Aegle marmelos*

Language	Vernacular name
Hindi.	Bel, Beli, Belgiri.
Sanskrit.	Bilva, Shivdruma, Shivaphala, Vilva.
Urdu.	Bel, Belk ham.
Assamese and Marathi	Bel.
Gujarati.	Bilavaphal.
Malyalam.	Marredy.
Oriya.	Belo.
Tamil.	Vilva marum, Vilvama.

### Fruit and Seeds

Fruits, yellowish green, with small dots on the outer surface, oblong to globose, 5.3 cm to 7.2 cm in diameter; weight, 77.2 g; volume, 73.7 ml; pulp, yellow and mucilaginous, the pulp of dried fruits retains its yellow, and also remains intact; rind woody, 4 to 5 mm thick<sup>6</sup>.

The Seeds are, numerous, embedded in the pulp, oblong, compressed, with white, cotton-like hairs on their outer surface. (Figure 2.2)



Figure 2.2: Fruit and Seed of *Aegle marmelos*

### Flower

Flowers are greenish white in colour, and sweetly scented in nature and have bisexual, actinomorphic, ebracteate, hypogynous, stalk. The stalk is about 8 mm long and has a diameter of a fully open flower of about 1.8 cm. The flowers are borne in lateral panicles of about 10 flowers, arising from the leaf axil. The calyx is gamosepalous, five-lobed, pubescent, light green, very small in comparison with petals. The corolla is polypetalous, with 5 petals, imbricate, leathery and has pale yellow colour from above and green color from beneath and length is about 4 mm. The androecium is polyandrous, numerous, basifixed and 4 mm long, dehiscing longitudinally. The gynoecium is light green in color, and about 7 mm long, having capitate stigma and terminal style<sup>6</sup>. (Figure 2.3)

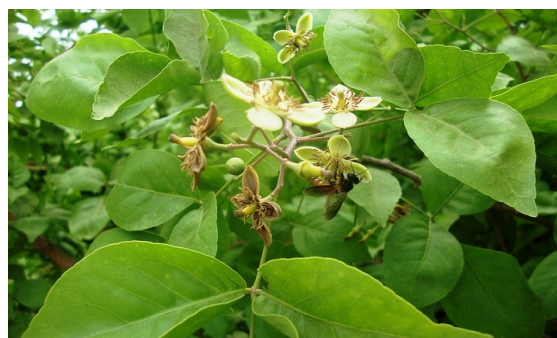


Figure 2.3: Flower of *Aegle marmelos*

### Traditional Uses

Bael leaves are useful in jaundice and in the treatment of wounds. The extract of leaves is beneficial in the treatment of leucorrhoea, conjunctivitis and deafness. Fruits give feeling of freshness and energy. It is used as carminative and astringent. It finds good utility in thyroid related disorder. The other fine therapeutic uses reported in cardiac stimulant, swollen joints, pregnancy trouble, typhoid and coma. The dried powder of leaf is used in the treatment of irritable bowel syndrome<sup>7</sup>.

### Chemical Constituent

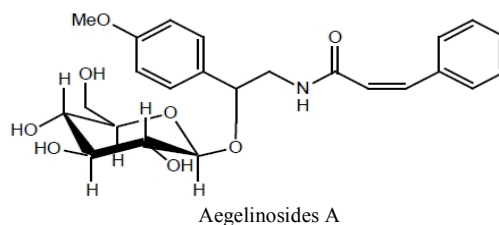
Extensive investigations have been carried out on different parts of *Aegle marmelos* and as a consequence, varied classes of compound viz., alkaloids, coumarins, terpenoids, fatty acids and aminoacids have been isolated from its different parts.

*Aegle marmelos* leaves contained  $\gamma$ -sitosterol, aegelin, lupeol, rutin, marmesinin,  $\beta$ -sitosterol, flavone, glycoside, Oisopentenyl halfordiol, marmeline and phenylethyl cinnamamides.

The detailed investigations on isolated compound classes are as under,

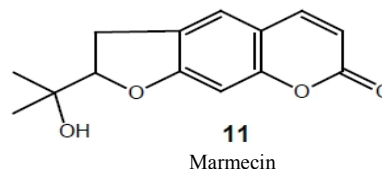
#### Alkaloids

The alkaloids comprise the largest single class of secondary plant substances. New alkaloids from the leaves of *A. marmelos* were reported viz., halfordino, ethylcinnamamide, ethylcinnamamide, ethylcinnamamide and marmeline. Recently, series of phenylethyl cinnamides, which included new compounds named anhydromarmeline, aegelinosides A and B were isolated from *Aegle marmelos* leaves as  $\alpha$ -glucosidase inhibitors<sup>8</sup>.



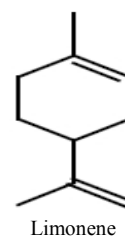
#### Phenylpropenoids

These are naturally occurring phenolic compounds, which have an aromatic ring to which three carbon side chain is attached. Among the phenylpropenoids are included hydroxycoumarins, phenylpropenes and lignans.



#### Terpenoids

The essential oil of *A. marmelos* (L.) Correa leaves were studied very much extensively in India by various workers since 1950.  $\alpha$ -Phellandrene was found to be the common constituent of the essential oil from leaves, twigs and fruits.  $\alpha$ -Phellandrene (56%) and p-cymene (17%) were reported from leaf oil. Limonene (82.4%) was reported as the main constituent from *A. marmelos* leaves and it was shown that limonene is characteristic marker for identification of *A. marmelos* oil samples<sup>8</sup>.



### **Tannins**

The maximum tannin content in bael fruit was recorded in the month of January. There is as much as 9% tannin in the pulp of wild fruits, less in cultivated type. Tannin is also present in leaves as skimmianine, it is also named as 4, 7, 8-trimethoxyfuro, quinoline.

### **Carotenoids**

Carotenoids are responsible for imparting pale colour to fruit. Marmelosin, skimmianine and umbelliferone are the therapeutically active principles of bael plant. Minor constituents like ascorbic acid, sitosterol, crude fibres, tannins,  $\alpha$ -amyrin, carotenoids, and crude proteins are also present<sup>6</sup>.

### **Pharmacological Activity of Leaves**

#### **Contractile activity**

The effect of the alcoholic extract of the leaves of *Aegle marmelos* (L.) on guinea pig isolated ileum and tracheal chain was investigated, as this plant is used traditionally to treat asthma and related afflictions. Dose of 1 mg/ml and 2 mg/ml of the alcoholic extract as a low and high dose respectively witnessed a positive relaxant effect in isolated guinea pig ileum and tracheal chain, respectively. From the above statement, it can be concluded that relaxations induced by *A. marmelos* in both guinea pig ileum and tracheal chain were due to the depression of H1- receptors<sup>9</sup>.

#### **Anti-microfilarial activity**

Methanolic extract of roots of *Vitex negundo* L. and extracts of leaves of *Vitex negundo* L. *Ricinus communis* L. and *Aegle marmelos* (L.) corr. were explored for possible antifilarial effect against *Brugia malayi* microfilariae. It was observed that among the herbal extract, root extract of *Vitex negundo* L and leaves extract of *Aegle marmelos* Corr. At 100 mg/ml concentration showed complete loss of motility of microfilariae after 48 hrs of incubation<sup>10</sup>.

#### **Analgesic Activity**

The methanol extract of leaves of *Aegle marmelos* (L.) corr. at a dose level of 200 and 300 mg/kg showed significant analgesic activity on acetic acid-induced writhing and tail flick test in mice<sup>11</sup>.

#### **Anti-inflammatory, antipyretic and analgesic Activity**

The serial extracts of the leaves of *Aegle marmelos* (L.) were investigated for anti-inflammatory property. The analgesic and antipyretic properties were also evaluated. The most of the extracts derived from the plant *Aegle marmelos* (L.) caused a significant inhibition of the carrageenan-induced paw edema and cotton-pellet granuloma in rats. The extracts also produced marked analgesic activity by reduction the early and late phases of paw licking in mice. A significant reduction in hyperpyrexia in rats was also produced by the most of the extracts. This study was established anti-inflammatory, antinociceptive and antipyretic activities of the leaves of *Aegle marmelos* (L.)<sup>9</sup>.

#### **Anti ulcer activity**

The anti-ulcer activity of the polyherbal formulation was investigated by ethanol induced gastric ulcer model in wistar rats. The formula contains *Glycyrrhiza glabra* rhizome part (200mg), *Aegle marmelos* (L.) Corr. leaf part (150mg), *Hemidesmus indicus* root part (75mg) and *Cuminum cyminum* fruit part (75mg) with varying

proportion. The developed formulation was evaluated (as per WHO guidelines) and was standard under Ayurvedic pharmacopoeial limits. The formulation with 500mg/kg per oral produced significant inhibition of the gastric lesions in ethanol induced ulcer model with respect to standard 20mg/kg of Omeprazole administration. The dose fixation was made with the help of acute toxicity studies with varying doses in wistar rats and the result shows that the formulation might be useful in severe gastric ulcer, antiulcerogenic and as well as ulcer healing properties, which might be due to its anti-secretory activity. The formulation is non-toxic even at relatively high concentration<sup>12</sup>.

#### **Anticonvulsant activity**

The anticonvulsant effect of ethanolic extract of the leaves of *Aegle marmelos* (L.) Corr. on maximal electroshock (MES) and pentylenetetrazole (PTZ) in male mice was examined. The extract of *Aegle marmelos* (L.) Corr. (orally) was administered in mice at the doses of 100 and 200 mg/kg. The Extract suppressed hind limb tonic extensions (HLTE) induced by MES and also exhibited protector effect in PTZ-induced seizures, at 200 mg/kg dose. Since the ethanolic extract of *Aegle marmelos* (L.) Corr. delayed the occurrence of MES and PTZ convulsions, it is concluded that it interfere with gabanergic mechanism(s) to exert their anticonvulsant effect in addition it reveals the presence of flavonoid attributed to their anti-convulsant action<sup>13</sup>.

#### **Antidepressant and Anxiolytic activity**

The anxiolytic and antidepressant activities of methanol extract of *Aegle marmelos* (L.) Corr. leaves and its interaction with conventional anxiolytic and antidepressant drugs using elevated plus maze and tail suspension test in mice was carried out. Effects were observed on, (a) time spent on, (b) number of entries into, (c) number of stretch attend postures and (d) number of head dips in arms of elevated plus maze and on duration of immobility in tail suspension test. It is concluded that *Aegle marmelos* (L.) Corr. possess potential anxiolytic and antidepressant activities and it enhances the anxiolytic and antidepressant activities of imipramine and fluoxetine<sup>14</sup>.

#### **Antifertility Activity**

Study was carried out to evaluate the effective concentration of aqueous extract of *Aegle marmelos* (L.) Corr. leaves on male reproductive system of albino rats. According to study protocol animals were administered the aqueous leaf extract of *Aegle marmelos* (L.) Corr. daily at 250mg/kg, and 350mg/kg respectively for a period of 45days. Significant decreases in the weight of testis, epididymes and seminal vesicle were observed. A dose related reduction in the testicular sperm count, epididymal sperm count and motility and abnormal sperm count were observed. The results showed that *Aegle marmelos* (L.) Corr. has effects on male rat reproduction, affecting the sexual behavior and epididymal sperm concentration<sup>15</sup>.

#### **Antifungal Activity**

The in vitro study of anti fungal activity of *Aegle marmelos* (L.) Corr. leaf extract was carried out on clinically isolates of dermatophyteic fungi like *Trichophyton Mentagrophytes*, *Trichophyton rubrum*,



*Microsporium canis*, *Microsporium gypseum*, using the minimum inhibitory concentration (MIC) & Minimal fungicidal concentration (MFC) of various extract and fractions of leaves of *Aegle marmelos* (L.) Corr.. The MIC and MFC was found to be high in water and ethyle alcohol extract and methanol fraction (200 µg/ml) against dermatophytic fungi studied. *Aegle marmelos* (L.) Corr. leaf extract significantly inhibits the growth of all dermatophytic fungi<sup>16</sup>.

#### **Hepatoprotective activity**

The hepatoprotective effect of *Aegle marmelos* (L.) Corr. leaf extract in alcohol induced liver injury in albino rat was evaluated using essential biochemical parameters. The experimental animals were administered with 30% ethyl alcohol for a period of 40 days and the fine crude plant leaves powder was fed to animals for next 21 days. The results were compared with the standard herbal drug silymarin (133.04 µg/g tissue). The experimental results indicate that, the Bael leaves have excellent hepatoprotective effect. A similar experimental result was also observed in other biochemical parameters. The proposed hepatoprotection result from the antioxidant properties of the *Aegle marmelos* (L.) Corr. leaf extract<sup>17</sup>.

#### **Radioprotective Activity**

The radioprotective activity of a leaf extract of *Aegle marmelos* (L.) Corr. in mice was carried out by exposing it to different doses of  $\gamma$ -radiation. Different doses of leaf extract of *Aegle marmelos* (L.) Corr. was administered to the animal for 5 days. The animal was then exposed to  $\gamma$ -radiation at an intensity of 10 Gy 60Co. The animals were monitored for symptoms of radiation sickness and mortality up to 30 days post-irradiation. Glutathione and lipid peroxidation were estimated in the surviving animals of both groups on day 31 post-irradiation. *Aegle marmelos* (L.) Corr. leaf extract treatment reduced the symptoms of radiation-induced sickness and increased survival. The radioprotective action might be due to free-radical scavenging and arrest of lipid peroxidation accompanied by an elevation in glutathione<sup>18</sup>.

#### **Hypolipidemic activity**

The lipid lowering property of an aqueous extract of *Aegle marmelos* (L.) Corr. leaves was carried out on streptozotocin (STZ) induced diabetic rats. The lipid profiles such as serum total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), and very low density lipoprotein (VLDL) were studied. Extracts were administered orally at increasing dose levels of 250mg, 350mg, 450mg/kg body wt., to STZ induced diabetic rats. The levels of TC, TG, LDL, HDL, and VLDL were found to be reduced significantly when compared to that of diabetic control rats. These results further suggest that *Aegle marmelos* (L.) Corr. may be useful in the therapy and management of hyperlipidemia by reducing lipid levels<sup>19</sup>.

#### **Immuno modulatory activity**

The efficacy of different dietary doses of *Aegle marmelos* (L.) Corr. leaf extract was carried out for the immune response and the disease resistance of the freshwater fish, *Cyprinus carpio* Linn. (Cyprinidae) infected by *Aeromonas hydrophila* Chester (Aeromonadaceae). Fish were challenged with *Aeromonas hydrophila* at a dose of  $1.5 \times 10^4$  cells/mL through intraperitoneal injection, and

the hematological changes, the immune response, the enzyme activity and the disease resistance of *Cyprinus carpio* against the pathogen were also studied for 20 days at 5-day intervals. The results obtained from the study demonstrated that the fish fed with leaf extract of *Aegle marmelos* incorporated into feed significantly enhanced the red blood cell count, white blood cell count, hemoglobin, phagocytic activity, nitroblue tetrazolium chloride assay, lysozyme, pathogen clearance and enzyme activity compared with the control group. The survivability was higher in the fish which consumed leaf extract-incorporated feed, and the fish group fed with 5 g diet showed highest percentage survival of the fish. These results indicate that *Aegle marmelos* stimulates the immunity and makes the freshwater fish *Cyprinus carpio* more resistant to *Aeromonas hydrophila*<sup>20</sup>.

#### **Pharmacological Activity of Fruit**

##### **Hypoglycaemic Activity**

The hypoglycaemic effect of the water extract of the fruits of *Aegle marmelos* (L.) Corr. was examined in streptozotocin-induced diabetic Wistar rats. The effect of the extract at a dose of 250 mg kg<sup>-1</sup> was more effective than glibenclamide in restoring the values of these parameters. The results of this study clearly showed the hypoglycaemic activity of the fruit extract.

S Brijesh *et al*, studied an anti diarrhoeal activity of *Aegle marmelos* unripe fruit<sup>21</sup>.

##### **Pharmacological Activity of Seed**

##### **Hypoglycaemic Activity**

The aqueous extract of *Aegle marmelos* (L.) Corr. seeds was administered orally at different doses (100, 250 and 500 mg/kg) to normal as well as sub (fasting blood glucose (FBG) normal; glucose tolerance abnormal) and mild (FBG 120–250 mg/dl) diabetic rats. It brought about fall in level of total cholesterol (TC) by 25.49% with increase of 33.43% in high density lipoprotein (HDL) and decrease of 53.97 and 45.77% in low density lipoprotein (LDL) and triglyceride (TG), respectively. These results clearly indicate that aqueous seed extract of *Aegle marmelos* (L.) Corr. possesses antidiabetic and hypolipidemic effects in diabetic rats<sup>22</sup>.

##### **Antifungal activity**

A new anthraquinone, 1-methyl-2-(3'-methyl-but-2'-enyloxy)-anthraquinone has been isolated from seeds of *Aegle marmelos* (L.) Correa. The compound exhibited significant antifungal activity against pathogenic strains of *Aspergillus species* and *Candida albicans* in disc diffusion assay (MIC value of 6.25 µg/disc), microbroth dilution and percent spore germination inhibition assays (MIC value of 31.25–62.5 µg/ml)<sup>79</sup>. The antifungal activity of essential oil isolated from the leaves of bael (*Aegle marmelos* (L.) Correa, Rutaceae) 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 400ppm. Kinetic studies showed concentration as well as time dependant complex inhibition of spore germination by essential oil<sup>23</sup>.

## CONCLUSION

The extensive literature survey revealed that *Aegle marmelos* (Linn.) having diverse pharmacological spectrum due to it possesses wide range of chemical entity. As a consequence of which it is conclude that *Aegle marmelos* (Linn) is an important herb in human life. The evaluation needs to be carried out on *Aegle marmelos* (Linn) in order to uses and formulation of the plant in their practical clinical applications, which can be used for the welfare of the mankind.

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