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Review Article

Beal (Aegle Marmelos) Extracts, Pharmacological Insights & Clinical Potential

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ABSTRACT

Aegle marmelos, commonly known as Bael, is a traditional medicinal plant with a rich history of use in Ayurvedic and folk medicine. Its bioactive compounds, including alkaloids, flavonoids, and essential oils, exhibit diverse pharmacological activities, such as antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and hepatoprotective effects. Recent studies highlight its potential in managing gastrointestinal disorders, metabolic conditions like diabetes, and liver diseases. The fruit, leaves, and bark of Aegle marmelos are the primary sources of its therapeutic properties. Clinical evidence supports its safety and efficacy, though further randomized controlled trials are required to establish standardized dosages and treatment protocols. This review consolidates pharmacological insights and explores the clinical potential of Aegle marmelos extracts in modern medicine.

INTRODUCTION

Humans depend heavily on plants for survival, as their products and active compounds serve essential roles in sustaining life on Earth [1]. Over recent years, researchers have focused on identifying and validating plant-derived substances for the treatment of various diseases [2]. India is widely known as the "world's botanical garden" due to its status as the largest producer of medicinal plants [3]. The World Health Organization estimates that 80% of people in developing countries depend on traditional medicines, primarily derived from natural plants, to meet their basic healthcare needs [4].

Humans rely on a diverse range of plants and plant-based products to manage and treat numerous physical and mental health conditions. These plants are integral to traditional systems of medicine such as Chinese, Ayurveda, Siddha, Unani, and Tibetan practices. Ancient texts like the *Rigveda*, *Yajurveda*, *Atharvaveda*, *Charak Samhita*, and *Sushrut Samhita* also highlight the use of herbs for addressing various health issues [5].

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The global demand for medicinal plants has surged as natural products gain greater recognition. These plants offer minimal toxicity, are cost-effective, pharmacologically active, and provide straightforward remedies for numerous human ailments, in contrast to synthetic drugs, which are often subject to adulteration and side effects [6].

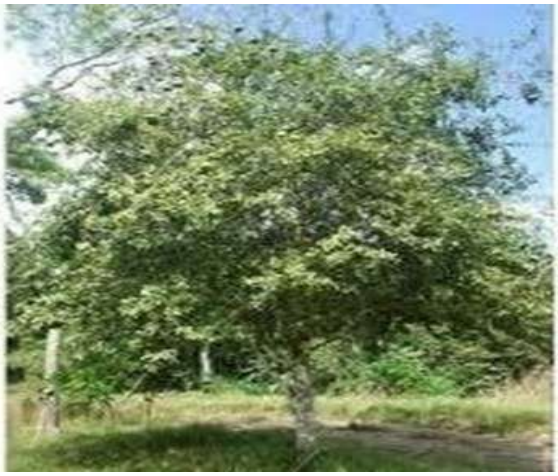


Figure A: Bael Plant Tree

Figure B: Bael Plant Leaf

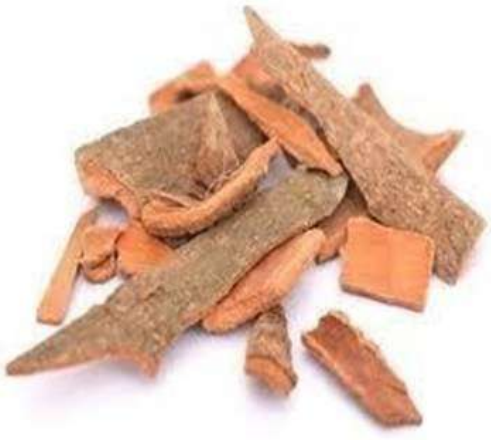


Figure C: Bael Plant Bark Extract

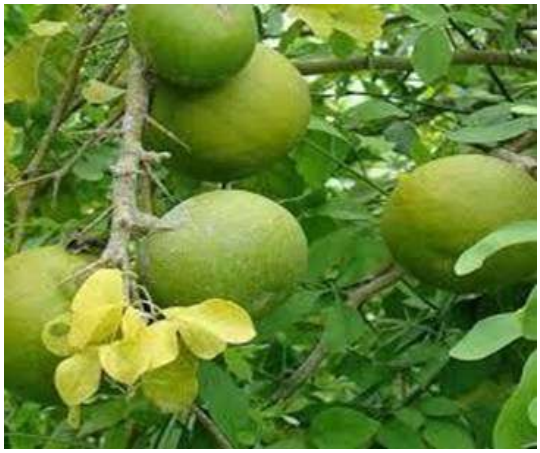


Figure D: Bael Plant Fruit

Since the time of Charak (1500 B.C.), Bael (*Aegle marmelos*) has been acknowledged as one of India's most important medicinal plants [7]. Bael is a medium-sized, thorny deciduous tree belonging to the Rutaceae family. Native to India, it is now cultivated across many Southeast Asian countries [8]. In India, *Aegle marmelos* is commonly grown in temple gardens, with its leaves often used in worship to Lord Shiva. It holds great significance as a medicinal plant, playing a key role in traditional and folk medicine systems for various ethnomedicinal applications [9]. The leaves, roots, stems, and fruits of this tree, at every stage of maturation, are used in ethnomedicine to treat a wide range of human ailments [8]. The primary chemical compounds found in the fruit of *Aegle marmelos* include marmelosin, luvangetin, psoralen, tannins, and marmin [10]. *Aegle marmelos* contains various phytoconstituents, including marmenol, marmin, marmelosin, marmelide, psoralen, alloimperatorin, rutaretin, scopoletin, aegelin, marmelin, fagarine, anhydromarmelin, and limonene [11].

Taxonomical classification:

Kingdom	Plantae
Order	Sapindales
Family	Rutaceae
Subfamily	Aurantioideae
Genus	*Aegle*
Species	*A.marmelos*

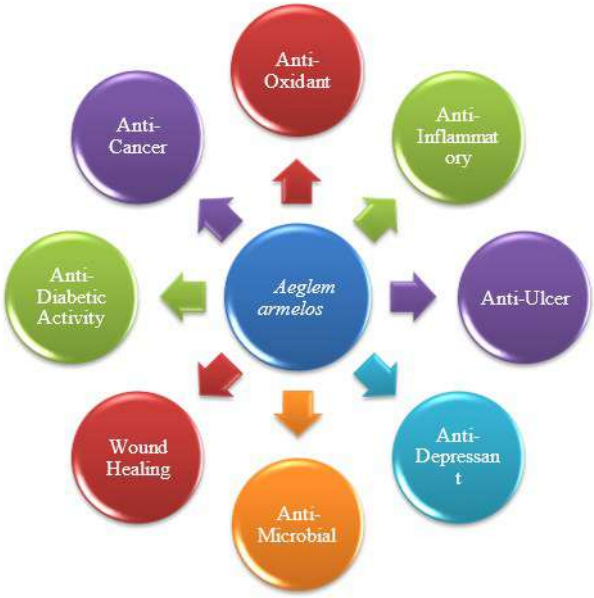
Botanical classification:

The *Aegle marmelos* tree is a medium-sized, aromatic, and slender medicinal plant that grows slowly, reaching a height of approximately 762 cm and a diameter of 90 to 120 cm [12].

- **Leaf:**
  The leaves are arranged alternately and are typically trifoliate, with 3 to 5 leaflets. Each leaflet measures 4 to 10 cm in length and 2 to 5 cm in width [13]. The flowers are greenish-white in color, and as they mature, the leaves develop a dark green hue [14]. Bael leaves effectively help eliminate mucilage secretion from the bronchial tubes. They are used to treat conjunctivitis and are also beneficial in relieving constipation, deafness, and leucorrhea. Additionally, bael leaf powder can be used to manage bowel syndrome [15].
- **Bark:**
  The bark of the *Aegle marmelos* tree is thick and flaky, often featuring spiny branches. When the bark is wounded, it secretes a gum that thickens upon exposure to air [13]. A decoction made from the root and bark of the *Aegle marmelos* tree is beneficial for treating melancholia, heart palpitations, and intermittent fever. Additionally, the root of the Bael tree is a key ingredient in the popular Ayurvedic medicine known as *Dashmula* [16]. A decoction of the bark, leaf extract combined with honey, and bael extract are utilized for treating fever, serving as a febrifuge, and managing intermittent fever [17].
- **Fruits:**
  The fruit of *Aegle marmelos* is primarily yellowish-green and features a hard, woody exocarp. It has a diameter of approximately 5 to 7 cm, weighs around 77.2 grams, and has a volume of 73 mL. The fruits are either spherical or oval in shape, with a sphericity of 93.72 ± 2.78% [18]. The fruit extract of *Aegle marmelos* has been found to enhance the treatment of thyroid issues. It has also shown effectiveness in curing chronic gastrointestinal disorders, treating piles, and reducing rectal inflammation [19]

Pharmacological activity:

1. Anti-OxidantActivity:



Antioxidants are compounds that scavenge free radicals and protect cells from oxidative stress. These beneficial compounds can be sourced from nature, particularly plants. The antioxidant activity of these plants is attributed to the presence of flavones, isoflavones, flavonoids, anthocyanins, coumarins, lignans, catechins, and isocatechins. *Aegle marmelos* has been extensively documented to exhibit antioxidant activity against a wide range of free radicals [20]. Research indicates that unripe fruits demonstrate more pronounced antioxidant activity compared to ripe fruits. Both chloroform and aqueous extracts of bael exhibit significant free radical scavenging activity and inhibit the lipoxygenase enzyme [21].

The radical scavenging activity of the hydroalcoholic extract of bael has been demonstrated against 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) and DPPH radicals. Additionally, bael extract can inhibit oxidation caused by the 2,2'-azobis(2-amidinopropane) dihydrochloride radical, which affects biomolecules like plasmid DNA, bovine serum albumin, and lipids [22].

2. Anti-Inflammatory Activity

Various organic extracts of *Aegle marmelos* leaves exhibit significant acute and subacute anti-inflammatory activity [19]. These effects are attributed to the presence of lupeol and skimmianine in the leaves, as both compounds have demonstrated similar properties in their pure forms [23]. Bael fruit extract exhibits anti-inflammatory properties, stabilizes mast cells, and possesses antioxidant effects. It increases superoxide dismutase levels and reduces malondialdehyde levels, providing protection against mast cell degranulation [24]. The alcoholic extract of *Aegle marmelos* leaves counteracts histamine-induced contractions and exhibits a relaxant effect in isolated guinea pig ileum and tracheal chains, suggesting potential H1 receptor inhibition [19].

3. Anti-Ulcer Activity

Ulcers, a common gastrointestinal condition, result from an imbalance between mucosal protective and aggressive factors, often caused by oxidative stress, Helicobacter pylori infection, or reduced mucosal protection [25]. Luvangetin, a pyranocoumarin found in bael seeds, has shown protective effects against gastric ulcers induced by aspirin and pylorus ligation in animal studies [26].

4. Antidepressant Activity

Depression, a mood-related disorder, is often treated with synthetic drugs that can cause adverse effects like drowsiness, ataxia, insomnia, and libido issues. Natural sources, including bael, are considered safer alternatives [27]. Studies using tail suspension and elevated plus maze tests on mice treated with anxiolytic medications showed that bael enhanced the antidepressant activity of fluoxetine and imipramine [28]. Its mechanism is associated with agonistic action on serotonin receptors [29].

5. Antimicrobial Activity

Aegle marmelos has been traditionally used to treat infectious diseases and has been reported to inhibit a wide range of pathogenic microorganisms. Numerous in vitro studies have demonstrated its antimicrobial potential against bacteria and fungi [30].

Marmelide extracted from bael has exhibited antiviral activity against Coxsackieviruses B1–B6 in plaque inhibition assays conducted over 96 hours, showing no toxic effects on host cells [31]. The inhibition rate of bael extract varies with concentration: a 0.05% extract dose can eliminate 100% of fungi, while 0.04% and 0.03% doses can inhibit 90% and 75%, respectively [32].

6. Wound Healing Activity

The wound-healing process involves inflammation, cell proliferation, and contraction, leading to the formation of a collagen lattice. Bael contains flavonoids, alkaloids, essential oils, and sterols, which enhance epithelialization, promote wound contraction, increase tensile strength, and elevate hydroxyproline content [33, 34]. *Aegle marmelos* exhibits wound-healing properties comparable to nitrofurazone. Its phytochemicals enhance antioxidant activity, contributing to faster healing [35, 8].

7. Antidiabetic Activity

Diabetes mellitus is a prevalent metabolic disorder often triggered by stressful lifestyles, poor diets, and genetic factors [36]. *Aegle marmelos* extract reduces blood glucose and glycosylated hemoglobin levels while increasing plasma insulin and liver glycogen in diabetic rats [37]. The dietary fiber and amino acids in bael help moderate sugar absorption. At a dosage of 250 mg/kg, bael

has shown greater effectiveness than glibenclamide [37].

8. Anti-Cancer Activity

Cancer is a major global health concern, with treatments often being expensive and associated with severe side effects [39]. Bael has shown potential as an affordable and non-toxic alternative for cancer treatment. It demonstrates cytotoxicity against tumor cell lines in assays such as the brine shrimp lethality assay and methyl thiazolyl tetrazolium (MTT) assay [40].

Bael suppresses the proliferation of several human cancer cell lines, including leukemic K562, T-lymphoid Jurkat, beta-lymphoid Raji, and erythroleukemic HEL20. While it is antiproliferative, its effects on breast cancer cell lines like MCF-7 and MDA-MB-231 occur only at higher concentrations [40]. The phytochemicals marmesin and marmelosin in bael interact with HSULF-2 at its active site, potentially producing anticancer effects [41].

CONCLUSION

The review paper on Aegle marmelos (Bael) extensively covers the medicinal importance of this plant, recognized for centuries in traditional systems like Ayurveda. Originating in India, Aegle marmelos holds a significant place in the ethnomedicinal landscape of South Asia, with various parts of the tree, such as the leaves, bark, and fruits, being used to treat numerous ailments.

The paper highlights the major chemical constituents and their pharmacological activities. Bael exhibits a wide range of therapeutic effects, including antioxidant, anti-inflammatory, and anti-ulcer properties. Its antioxidant activity is particularly notable and is attributed to compounds like flavonoids and coumarins, which have demonstrated potential in scavenging free radicals and preventing oxidative stress. Furthermore, the anti-inflammatory action of bael is supported by studies demonstrating its efficacy in mast cell stabilization and enzyme inhibition.

In addition to these activities, the plant shows potential in wound healing, antimicrobial effects, and antidiabetic action. Its ability to modulate blood glucose levels and aid in glycemic control underscores its relevance in managing diabetes. Moreover, bael has been explored for its anticancer properties, with research indicating cytotoxic effects on cancer cell lines, albeit at higher concentrations.

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