

SYSTEMATIC REVIEW OF THERAPEUTIC POTENTIAL OF AEGLE MARMELLOS (LINN) IN THE MANAGEMENT OF ULCERS: EFFICACY, MECHANISMS AND CLINICAL APPLICATIONS

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ABSTRACT

Many people suffer from ulcers, a common gastrointestinal ailment characterized by the erosion of the stomach and duodenal lining. These ulcers are classified into two categories: duodenal and stomach ulcers, collectively referred to as stomach ulcers. Synthetic medicines can treat ulcers, but they are more expensive and may have more side effects compared to herbal remedies. Recent research has linked *Helicobacter pylori* infection of the gastrointestinal tract lining to stomach ulcers. Various herbs and herbal preparations have been found effective in protecting against or treating peptic and gastric ulcers. In ancient India, the plant *Aegle marmelos*, also known as Bael, was revered in mythology and traditional medical systems like Ayurveda. Every part of the tree, including the root, bark, fruit, leaf, and flower, is valued for its therapeutic properties in treating various conditions. Native to India, *Aegle marmelos* belongs to the monotypic genus *Aegle* of the Rutaceae family and is renowned for its numerous nutraceutical and therapeutic qualities.

KEYWORDS: *Aegle marmelos*, Peptic ulcer, Gastric ulcer, *Helicobacter pylori*, Bael

INTRODUCTION

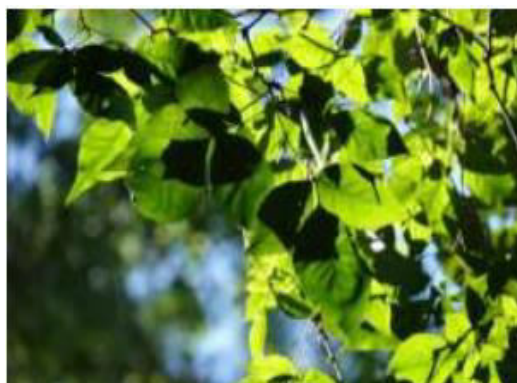
In traditional medical systems, *Aegle marmelos*, known as Bael and belonging to the Rutaceae family, is believed to offer numerous therapeutic benefits. Considered sacred in Hinduism, Bael leaves have been offered to deities Shiva and Parvati as a sign of prayer since ancient times. This sacred deciduous tree is associated with gods and is reputed for its medicinal qualities, especially as a cooling agent. Bael can be grown in any home and is popular in temples dedicated to Shiva and Vishnu[1].

Plants are highly significant to humans due to the variety of active chemicals they contain, which form the basis for many medications. In India, flora have been used as herbal or natural remedies for millennia, with many plants in Indian medicine being rich in pharmacologically active principles and substances [2]. Bael, also known as Bengal-quince, golden apple, stone apple, and sacred tree in Hindu communities, is valued for its therapeutic properties. It contains various phytochemicals, including tannins, gums, resins, essential oils, polysaccharides, and alkaloids, making it beneficial for a range of illnesses and environmental significance [3].

Historically, Bael has been used for its anti-tumor, anti-diabetic, and anti-lipidemic properties. The bark can stop diarrhea in both adults and children, and the fruit is used to create hair tonic. Gastric ulcers, one of the most common gastrointestinal disorders, affect 5–10% of people at some point in their lives[4]. The primary causes of peptic ulcers include Gram-negative *Helicobacter pylori* infection, increased hydrochloric acid output, and insufficient mucosal defense against gastric acid, along with factors like acidic and cholinergic medications, NSAIDs, and inappropriate eating habits[5].



Figure No.1: Aegle marmelos fruits



**Figure No.2: Aegle marmelos
Morphological characteristics**

Plant part	Morphological characters
bark	The bark grey or brownish in colour, and it bears a number of long, straight spines. It includes gums, which form from wounded branches and harden over time. The easiest way to describe these gums is as a transparent, sticky sap. It tastes good at first, but it quickly gets irritating to the throat.
Leaf	Its leaves are trifoliate, with a pointy tip and a round base. Young leaves are pale green, whereas adult leaves are dark green.
Flower	The bisexual flowers have a greenish or yellowish hue. New leaves generally make it obvious
Fruit	The Bael fruit has an outer jacket that is robust and measures between 5 and 12 cm in diameter. When unripe, it is green; when ripe, it turns yellow-brown. There are up to 20 orange pulps inside of it.
Seed	They are hard, hairy, flattened-oblong, and tiny (almost 1 cm long), with an adhesive sac encircling each one. ^[2]

BOTANICAL DESCRIPTION: Aegle marmelos, commonly known as Bael, is a medium-sized, slow-growing tree that can reach heights of 12 to 15 meters. It has a short trunk with thick, soft bark that flakes and branches that spread out, sometimes being prickly, with the lower branches often sagging[6]. Young suckers are characterized by many straight, hard spines. The plant parts include the bark, leaf, flower, fruit, and seed. The bael tree's branches are spiky, and the leaves are usually trifoliate, consisting of three to five leaflets per leaflet. Each leaflet measures four to ten centimeters in length and two to five centimetres in width. Young leaves are lighter green and darken as they mature. The tree's bark is thick and separates easily, with often spiky limbs and gum discharge visible from injured bark[7].

The bael flower is greenish-white and pleasantly fragrant. The bael fruit is primarily yellowish-green, with a diameter of 5.3–7.2 cm, an approximate weight of 77.2 g, a volume of 73.7 mL, and a sphericity of $93.72 \pm 2.78\%$. The fruit's pulp is yellow and mucilaginous, containing several spots on the exterior and many firm seeds covered with white thread-like hairs on the outer surface[8].

TYPE OF SOIL: Bael thrives best in rich, well-drained soil but has also been found to grow and produce fruit on southern Florida's oolitic limestone. Additionally, it can flourish in marshy conditions[9].

APPLICATIONS OF PARTS

Seed: Bael seeds contain a pyranocoumarin called ligangetin, which exhibits protective properties against pylorus- and aspirin-induced conditions. They are also used as a febrifuge.

Leaf: Bael leaves have been proven effective in treating asthma and jaundice. They help clear bronchial tubes of secreted mucilage. Additional applications include treating conjunctivitis, diarrhea, constipation, deafness, sore throats, spinal pain, eye grievances, stomach problems, vomiting, cuts and wounds, ulcers, dropsy, beriberi, heart weakness, cholera, and diarrhea. Bael leaf powder may also be used to treat bowel syndrome, act as a cardiogenic, regulate glucose levels, treat animal wounds, neurological issues, intense bronchitis, and serve as a hair tonic[10].

Fruit: Bael fruit extracts have been shown to expedite thyroid treatment. When consumed with boiling rice water during pregnancy, they are believed to be highly effective in treating vomiting. Unripe fruit pulp powder is particularly beneficial for curing pustules. The fruit has astringent, antidiarrheal, and stomachic properties. It is used to treat loose stools, stomach problems, constipation, and acts as a purgative, tonic, and stomachic agent. It also has effects on the mind and heart, and can treat gonorrhoea, epilepsy, intestinal parasites, ulcers, and serves as an antiviral medication.

Flowers: Bael flowers possess astringent and antibacterial qualities and are used to treat epilepsy. Marmala water, distilled from the flower, is beneficial for treating conjunctivitis. Bael flower extract has been examined for its wound-healing abilities.

Bark: Bael bark is used to treat stomach problems, heart issues, and intermittent fever.

PLANT PART CHEMICAL CONSTITUTE:

Leaf	Skimmianine, Aeglin, Rutin, -sitosterol, -sitosterol, Flavone, Lupeol, Cineol, Citral, Glycoside, O-isopentenyl, Hallordiol, Madeline Citronellal, Cuuminaldehyde phenylmethyl cinnamates Eugenol,
Fruit	Psoralen, Marm elide, Tannin, Phenol, Marmelosin, Luvangetin, Auraptene, Tannin, Phenol, Tannin, Tannin,
Bark	Alkaloids, Fagarine, Marmin, Furoquinoline
Seed	D-limonene, A-D-phellandrene, Cineol, Citronellal, Citral, PP-Cyrene, and Cumin aldehyde are essential oils.
Roots	Terpenes, Halopine, Coumarins, and Alkaloid. ^[6]

TYPES OF ULCERS:

- Duodenum (called duodenal ulcer)
- Esophagus (called esophageal ulcer)
- Stomach (called gastric ulcer)
- Meckel's diverticulum (called Meckel's diverticulum ulcer; very tender with palpation).

SIGNS AND SYMPTOMS: The symptoms of ulcers include nausea and frequent vomiting, bloating and fullness in the abdomen, loss of appetite, weight loss, and severe abdominal discomfort that worsens around mealtimes and about three hours after eating. Additional symptoms are nausea, copious vomiting, loss of appetite, and weight loss **【3,10†source】** .

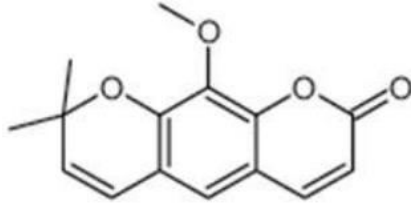
ULCER HEALING ACTIVITY OF AEGLE MARMELOS: Aegle marmelos, commonly known as the Bael tree and a member of the Rutaceae family, is predominantly found in India and regionally referred to as "vilvam." This plant contains chemical components such as flavonoids, tannins, and saponins.

Numerous studies have demonstrated Bael's anti-ulcer properties. Oral administration of Bael methanolic extract has been used to treat gastric ulcers in rats induced by lipopolysaccharides. According to the study, a dose of 500 mg/kg of Bael's methanolic extract effectively reduces stomach ulcers by 93.98% . Additionally, aqueous leaf extract administered orally for 21 days at a dose of 1 gram per kg of body weight significantly reduced the number of ulcer lesions in pylorus-ligated and aspirin-sensitive rats compared to the control group .

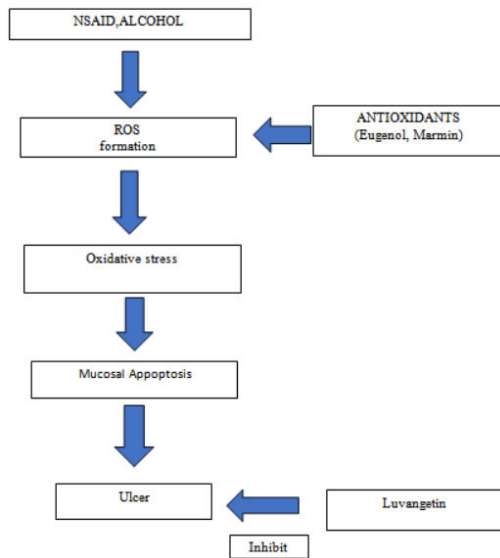
Aegle marmelos contains "Luvangetin" as an active constituent, which shows action against ulcers .

Chemical structure of Luvangetin:

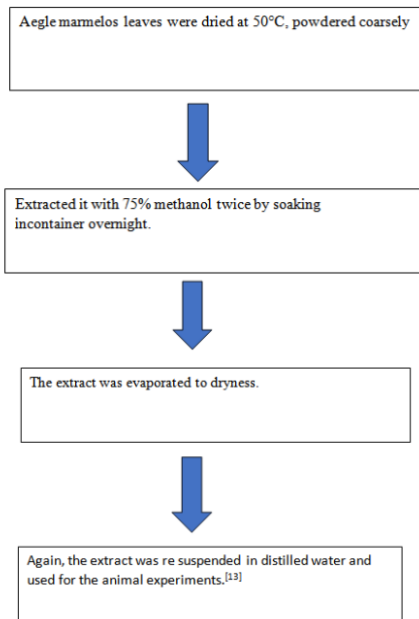
$C_{15}H_{14}O_4$



Mechanism of Action



Preparation of methanolic extract



PHARMACOLOGICAL USES: Several scientists have documented various biological activities of *Aegle marmelos*. These are listed under the following categories:

- Antibacterial
- Ulcer healing
- Antihistaminic
- Antifungal
- Anti-inflammatory
- Antipyretic and analgesic
- Hepatoprotective
- Insecticidal
- Hypoglycemic and antioxidant
- Antidiarrheal
- Antimicrobial and antiviral
- Diuretic
- Antithyroid
- Immunomodulatory
- Myocardial infarction
- Anxiolytic and antidepressant
- Wound healing
- Antimalarial
- Antistress adaptogenic
- Antifertility .

Antimalarial activity: The methanol extract of *A. marmelos* leaves demonstrated significant activity against *Plasmodium falciparum* in vitro with minimal cytotoxicity. The antiplasmodial activity showed an IC₅₀ of 7 µg/ml, indicating its potential. Infected mice showed suppressed parasite infection when treated with *A. marmelos* at doses of 20 and 40 mg/kg body weight, unlike those treated with *C. longa*.

Anticancer activity: *A. marmelos* extract has been found to effectively inhibit the in vitro proliferation of human tumor cell lines, including leukemic K562, T-lymphoid Jurkat, beta-lymphoid Raji, and erythroleukemia HEL.

Anti-inflammatory and analgesic activity: The anti-inflammatory properties of *Aegle marmelos* leaf extracts have been studied extensively. The extracts significantly inhibited carrageenan-induced paw edema and cotton-pellet granuloma in rats. They also reduced paw licking in mice and demonstrated notable analgesic efficacy. Additionally, the extracts brought about a significant decrease in hyperpyrexia in rats.

Antipyretic activity: *A. marmelos* demonstrated antipyretic activity in rodents with Brewer's yeast-induced pyrexia. At dosages of 400 mg/kg and 200 mg/kg body weight, the ethanolic extract caused a dose-dependent significant ($P < 0.001$) reduction in elevated body

temperature. The antipyretic efficacy of the extracts was comparable to that of paracetamol (100 mg/kg body weight) .

Antifungal activity: Studies suggest that the essential oil from *Aegle marmelos* leaves may interfere with the Ca²⁺-dipicolonic acid metabolic pathway, potentially inhibiting spore development. Leaf extracts in ethanol, methanol, and water showed adequate antifungal activity against dermatophyte organisms.

CONCLUSION

Aegle marmelos, also known as Bael, is recognized for its numerous pharmacological and nutritional properties, making it a significant plant in traditional medicine. This study's conclusions indicate that the ethanolic extract of *Aegle marmelos* leaves exhibits ulcer-preventing effects, warranting further research. Clinical studies have shown Bael's non-toxic behavior, confirming its safety for pharmaceutical applications without adverse effects. Bael has demonstrated highly promising therapeutic properties, making it a candidate for more extensive research.

The observed anti-ulcer action is attributed to its mucosal defense factor, suggesting its potential in peptic ulcer therapy. Peptic and other types of ulcers are commonly seen, often caused by high doses of NSAIDs, junk food, *Helicobacter pylori*, and excessive caffeine consumption. This review attempts to outline the scientific evidence supporting the anti-ulcer properties of herbal agents, specifically *A. marmelos*.

Aegle marmelos contains various phytoconstituents that significantly contribute to its therapeutic efficacy. Nearly all parts of the plant, including leaves, fruits, seeds, bark, and roots, are used to treat a wide range of ailments. Given the Bael tree's immense potential, it should be cultivated and utilized to its fullest extent, promising profit and the development of novel, potent herbal remedies.

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