

Aegle Marmelos : A Comprehensive Review of its Phytochemical, Pharmacological and Health Benefits

Sakshi Rajendra Kamble¹; Lokesh Vyas²; Abhishek Kumar Sen³; Dr. Sonali Uppalwar⁴
Ideal Institute of Pharmacy, Posheri, wada, Maharashtra, India; Mumbai University

Abstract:-

➤ *Background:*

Aegle marmelos (L.) Corr. Serr, commonly known as the wood apple plant, is a medicinal plant belonging to the Rutaceae family. It has been used in traditional medicine for centuries, particularly in Ayurveda, Unani, and Siddha systems, to treat various diseases. Recent advances in scientific techniques have led to the isolation and pharmacological analysis of bioactive compounds from different parts of the plant.

➤ *Objective:*

This study aims to evaluate the medicinal efficacy of Aegle marmelos extracts across various health conditions, focusing on its pharmacological activities and potential therapeutic applications.

➤ *Method:*

A comprehensive review of existing literature was conducted to gather information on the morphology, distribution, phytochemistry, traditional uses, and biological activities of Aegle marmelos. Various scientific databases, including PubMed, Scopus, and Web of Science, were searched using keywords such as “Aegle marmelos,” “phytochemistry,” “traditional medicine,” and “biological activities.”

➤ *Result:*

This review can be related to the biological activities of isolated chemicals from A. Marmelos that are being studied utilizing extracts. According to the findings of this study, A. Marmelos holds great promise for the treatment and prevention of a variety of illnesses, such as cancer, infectious diseases, and diabetic problems. These evaluations cover a wide range of issues, including spermatogenic, analgesic and antipyretic, inflammatory, antiulcer, and malaria treatment medications.

➤ *Conclusion:*

Aegle marmelos is a valuable medicinal plant with a rich history of traditional use and scientifically validated biological activities. Its bioactive compounds offer potential therapeutic applications, warranting further research and development of pharmaceutical formulations and nutraceutical products.

Keywords:- Aegle Marmelos, Phytochemistry, Traditional Medicine and Biological Activities.

I. INTRODUCTION

In traditional medical systems, Aegle marmelos, a member of the Rutaceae family, is referred to as Bael and is said to provide a number of therapeutic benefits. The bael tree is considered sacred by Hindus [1]. Hypoglycemic, antifungal, antibacterial, analgesic, anti-inflammatory, antipyretic, antidiabetic, immunomodulatory, anti-proliferative, wound-healing, antifertility, and insecticidal properties are few of its pharmaceutical applications [2]. In many traditional formulas, every component of the plant—fruit, seed, bark, leaves, and root is employed as an ingredient. It is one among India’s most beneficial medicinal herbs because of its healing qualities. Bael is beneficial for a variety of conditions because it includes a variety of phytochemicals, including alkaloids, tannins, essential oils, gums, resins, coumarin, and polysaccharides. Its nutritional value is far more important than that of other fruits [7]. For thousands of years, people have used plants as a natural supply of therapeutic chemicals [8]. Many plants and products derived from them are used by humans to treat and alleviate a variety of physical and mental ailments [9-18]. Traditional Chinese, Ayurvedic, Siddha, Unani, and Tibetan remedies all make use of these herbs. Plants can be used to treat a variety of health issues, according to ancient texts like the Rigveda, Yajurveda, Atharvaveda, Charak Samhita, and Sushrut Samhita. Another Indian medicinal plant is bael (Aegle marmelos(L.) Corr.), which has been used traditionally to treat a wide range of illnesses and from which numerous bioactive components have been extracted[22].



Fig 1 Aegle Marmelos Flowers



Fig 2 Aegle Marmelos Fruits



Fig 3 Aegle Marmelos Leaves

➤ *Plant Profile*

Table 1 Scientific Classification

Kingdom	Plantae
Order	Sapindales
Family	Rutaceae
Subfamily	Aurantioideae
Genus	Aegle
Species	Aegle Marmelos
Biological Name	Aegle Marmelos

II. BOTANICAL DESCRIPTION

The medium-sized, slow-growing Aegle marmelos tree can reach a height of 12 to 15 meters. It has a short trunk, thick, soft, flaking bark, and spreading, occasionally prickly branches, with the bottom ones drooping [1]. The leaflets are 4–10 cm long and 2–5 cm wide, with an oval or lancet form. Three to five leaflets make up the leaves. The terminal leaflet has a lengthy petiole, but the lateral leaflets lack one. The round, pyri-form, oval, or rectangular fruits have a diameter of 5 to 20 cm and might have a thin, woody shell or a more or less soft rind. They remain grey-green until they are fully ripe, at which point they turn yellowish. There are several compressed, oblong, Testa mucous seeds [2].

➤ *Flowers*

April and May see flowering shortly after the new leaf appears. Fragrant blooms with four fleshy, recurved petals that are green on the outside and yellowish on the inside, borne in clusters of four to seven along the young branchlets, and at least fifty greenish-yellow stamens [7].

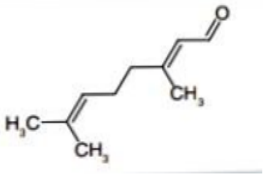
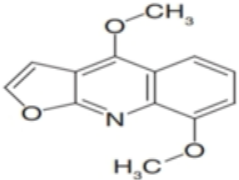
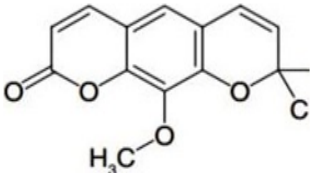
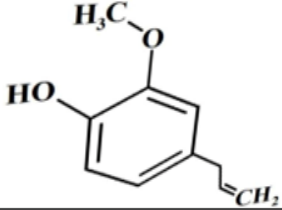
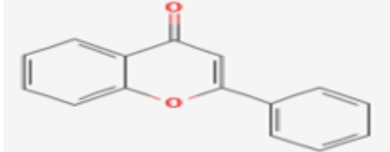
III. CHEMICAL CONSTITUENTS

Aegle marmelos contains a variety of portions from which different phytoconstituents have been extracted. These parts can be classified as [19].

Table 1 Phytoconstituents Isolated from Various Parts of Aegle Marmelos

Sr. No	Parts	Phytoconstituents
1	Leaf	Skimmianine, Aegeline, Lupeol, cineol, Citral, Citronella, Cuminaldehyde, Eugenol
2	Bark	Simonise, Fagarine, Marmin
3	Fruit	Marmelosin, Luvangetin, Aurapten, Psoralen, Marmelide, Tannin

Table 2 Chemical Structure of Compound Present in Aegle Marmelos

Chemical constituents	Structure	Pharmacological Activity	Reference
Citral		Antibacterial, Antifungal, Antiparasitic	72
Fagarine		Antiplasmodial	73
Luvangetin		Antiulcer	74
Eugenol		Antimicrobial	71
Flavone		Antifungal	69

➤ Citral

Bale's main ingredient, 3,7-dimethyl-2,6-octadien-1-al, has been demonstrated to cause apoptosis in a number of hematological cancer cell lines. This apoptotic action is similar to that of staurosporine, a powerful antibiotic produced from *Streptomyces staurosporeus*. Citral has also been shown to exhibit antiproliferative properties, to hinder cell cycle progression in the G2/M phase, to promote apoptosis in the human breast cancer cell line MCF-7, and to reduce the synthesis of prostaglandin E(2). These findings were reported by Chaouki et al. Recently [23].

➤ Cineole

A terpene found in many aromatic plants, including eucalyptus, mugwort, sweet basil, rosemary, sage, and cardamom, is called cineole (1,8-cineole), or eucalyptol. Cineole also promotes apoptosis in human leukemia cell lines Molt 4B and HL-60 cells, but not in human stomach cancer KATO III cells, according to in vitro research. In both Molt 4B and HL-60 cells, the scientists saw a concentration- and time-dependent apoptosis (as determined by the DNA fragments), demonstrating that the activity of 1,8-cineole

against cancer is cell-specific and is mediated by induction of apoptosis [3].

➤ Limonene

One monoterpene that can be found in the peel of citrus fruits, dill, caraway, fennel, and celery is called limonene. Research has demonstrated that d-limonene exhibits chemotherapeutic properties against malignancies of the pancreas, breast, and prostate. Mechanistic investigations suggest that the effects that have been seen are caused by many mechanisms. Most importantly, though, is the finding that monoterpenes prevent proteins like Ras from being posttranslationally isoprenylate [4].

➤ Phenylpropanoids

These are phenolic compounds that occur naturally. They have an aromatic ring with a three-carbon side chain attached [24]. Phenylpropanoids include lignans, phenylpropenes, and hydroxycoumarins. The parent chemical, coumarin itself, which is found in more than 27 plant groups, is the most widely distributed coumarin in plants [25]. Marmesin, a component of heartwood and roots,

was discovered to be a novel substance derived from leaves [26].

➤ *Carotenoids*

Fruit's light coloration is attributed to carotenoids. Umbelliferone, marmelosin, and skimmianine are the bael plant's three therapeutically active constituents [27]. There are also minor constituents such as carotenoids, ascorbic acid, sitosterol, crude proteins, tannins, α -amyrin, and crude fibers. It has also been discovered that the tree's roots contain scopoletin, xanthotoxin, and psoralen (Farooq, 2005)[28]. There have also been reports of compounds such montanin, praecaltin D, trans-cinnamic acid, 4-methoxy benzoic acid, and betulonic acid (Ali and Pervez, 2004)[29]. Many bioactive substances have been extracted from different Bael tree parts; a selection of these are shown in Table 1. The structures of some Of these bioactive chemicals are given in Figure 1[30].

➤ *Alkaloids*

Alkaloids are naturally occurring, physiologically active secondary metabolites of plants that contain nitrogen. Marmeline (Z)-N-[2-hydroxy-2-[4-(3-methylbut-2-enoxy) phenyl]ethyl] is present in A. Marmelos. 3-phenylprop-2-enamide, aegeline ((2E)-N-[2-hydroxy-2-(4-hydroxyphenyl)ethyl]ethyl, phenylethyl cinnamides (N-2-[4-(3,3-dimethylallyloxy) phenyl]ethylcinnamide, N-2-hydroxy-2-(4-hydroxyphenyl) ethylcinnamide, and N-4-methoxystyryl cinnamide) 2-enamide (3-phenylpropyl)[31]. The antidiabetic effects of A. Marmelos are caused by phenolphthaleins that were extracted from its leaves and had α -glucosidase inhibitory action. The visual system, pre-frontal cortex, thalamus activity, insecticidal, demulcent, antiplasmodic, hepatoprotective, and anti-inflammatory properties are all enhanced by these alkaloid compounds [32].

➤ *Tannins*

January was the month in which the highest tannin concentration in bael fruit was recorded. The pulp of wild fruits contains up to 9% tannin, but farmed fruits contain less. Tannin, also known as 4, 7, 8-trimethoxyfuro-quinoline, is found in leaves as well as skimmianine [33].

➤ *Terpenoids*

Since 1950, several workers in India have conducted in-depth research on the essential oil of A. Marmelos (L.) Correa leaves. A-phenellandrene was shown to be the common component of the essential oil extracted from leaves, twigs, and fruits.[34] A-Phellandrene (56%) and p-cymene (17%) have been reported in leaf oil.18 Many workers later found the same findings about leaf essential oil. P-Menth-1-en-3,5-diol was isolated and described from A. Marmelos leaves [35]. It was discovered that limonene (82.4%) was the main constituent of A. Marmelos leaves and that it was also a distinguishing characteristic for recognizing A. Marmelos oil samples. The leaves' sitosterol was identified. A- and β -amyrin and B-sitosterol was found in the stem bark, leaves, fruit, and root [36].

IV. PHARMACOLOGICAL ACTIVITIES

➤ *Anti-Cancer Activity*

One of the most serious illnesses in the modern world is cancer. Both the medical procedure and the medications are quite expensive. Three distinct chemicals that were extracted from the extract have been found to be highly significant in suppressing K562 cells: 6-methyl-4-chromanone, butyl ptoyl sulfide, and butylated hydroxyanisole [37]. The cytotoxic effects of bael extract on MDA-MB-231 and MCF-7 breast cancer cells have been confirmed by an in vitro experiment conducted on medicinal plants in Bangladesh [38]. Bael extract may prevent the growth of T-lymphoid Jurkat, Leukemic K562, B-lymphoid Raji, melanoma Colo38, erythroleukemic HEL, and MDA-MB-231 and MCF7 cell tumors. In another study, 400 mg/kg of hydroalcoholic bael extract was administered intraperitoneally to Swiss albino mice suffering from Ehrlich ascites cancer [39]. A noteworthy finding indicates that the median survival time was extended for 28 days, which is significantly longer than the group that received saline treatment as a control. Bael's carotenoids, phytochemicals, and polyphenols may be able to lessen cell mutation, which would lessen DNA damage [40]. According to a study, bael's lupeol extends ER α expression in ER α -negative MDA-MB-231 cells, which can stop cancer cells from proliferating and has a significant influence on the sequencing of RA4 DNA [41]. Bael extract aids in anti-cancer activities by strengthening the body's immune system. Bael extract may be able to postpone the genotoxic effects of doxorubicin treatment on mouse bone marrow. Before doxorubicin is administered, treatment is administered for a maximum of five days at a time [42]. This reduces the increase in normochromatic erythrocyte and micro nucleated polychromatic frequency that is brought on by doxorubicin treatment. Three compounds derived from bael extract have demonstrated anti-neoplastic properties: citral, eugenol, and D-limonene [43].

➤ *Anti-Inflammatory Activity*

Due to the presence of skimmianine and luteol, organic extracts of A. Marmelos leaves have strong anti-inflammatory properties (Angajala, Ramya, & Subashini, 2014). Histone receptor activation is crucial in cases of asthmatic and allergic symptoms [44]. The alcoholic extract made from A. Marmelos leaves has a good relaxant effect on the isolated tracheal chain and guinea-pig ileum, and it can oppose histamine-induced contractions that lead to H1 receptor inhibition (Balakumar et al., 2011). When carrageenan-induced paw edema in rats was induced at a dose of 50 mg/kg, it was found that ethanol, acetone, diethyl ether, petroleum ether, and chloroform extracts of leaves showed highly significant acute anti-inflammatory effects (Arul et al., 1999) [45].

➤ *Analgesic Activity*

Pain-relieving action Using writhing and tail immersion tests in mice, the antinociceptive response to A. Marmelos leaves methanol extract was reported [46]. In comparison to other dosages, the maximum effect of methanolic extract (200 mg/kg p.o.) was more statistically significant. It is concluded

that there is a notable analgesic effect from the methanol extract of *A. Marmelos* leaves [47].

➤ *Antimalarial Activity*

The best antimalarial efficacy against *Plasmodium falciparum* was demonstrated by *A. Marmelos* leaf methanol extract in vitro, which also exhibited little cytotoxicity and a promising antiplasmodial activity with an IC₅₀ of 7 g/ml [48]. Treatment with *C. Longa* did not affect infected mice that had a suppressive effect on the parasite; however, *A. Marmelos* at doses of 20 and 40 mg/kg body weight prevented parasite infection. Lastly, *A. Marmelos* showed potent antiplasmodial and antioxidant qualities; it may be one of the traditional herbs used to cure malaria [49]. When compared to crude leaf extracts of *A. Marmelos* Correa, standard *Temephos* shows superior larvicidal activity against *Anopheles Stephensi*, with an IC₅₀ of 500.06 ppm [50].

➤ *Hypoglycemic Activity*

Anhydroaegeline, with an IC₅₀ value of 35.8 μM, demonstrated the most effective inhibitory activity against α-glucosidase among the phenylethyl cinnamides described by Phuwapraisirisan et al. [51]. *Aegle marmelos*'s ability to act as an antioxidant and its ability to combat experimental diabetes were both studied by Sabu et al. [52]. *Aegle marmelos* extract substantially reduced the oxidative stress induced by alloxan and provided a reduction in blood sugar [53]. Upadhyaya et al. examined the levels of glucose, urea, and GST (glutathione-S-transferase) in plasma as well as GSH (glutathione) and MDA (malondialdehyde) in the erythrocytes of diabetic rats given alloxan. They discovered the hypoglycemic and antioxidant properties of the aqueous extract of *Aegle marmelos* leaves [54].

V. TRADITIONAL USES

Every part of the *Aegle marmelos* plant, including the leaves, fruit pulp, flower, stem bark, root bark, and so on, has therapeutic value.

➤ *Leaves*

Asthma, mucous membrane inflammation with a free discharge, and mild laxatives are all treated with leaves. The leaf decoction acts as an expectorant, encouraging the elimination of mucus discharge from the bronchial tubes, and as a febrifuge, aiding in the eradication of fever [55]. Leaf juice is administered when there is dropsy, or an abnormal buildup of liquid in the cellular tissue, along with jaundice and constipation [56]. When treating ophthalmia or severe conjunctival inflammation accompanied by acute bronchitis and other regions of the body inflamed, a heated poultice of the leaves is used [57].

➤ *Fruits*

Fruit extract has been shown to accelerate the treatment of thyroid in many body areas. When consumed with boiling rice water during pregnancy, it is believed to be highly useful in treating vomiting. Unripe fruit pulp powder is particularly beneficial in abscess curing [58]. Unripe fruit's starch is converted to sugar by heat treatment; the fruit extract is then added, filtered, and mixed with hot water and anise. The

resulting extract is shown to be beneficial. In dysentery. Fruit pulp in milk coupled with sugar is useful in urinogenital diseases [59]. It can be applied as a stomatic and antiscorbutic agent. It is possible to treat indigestion, persistent constipation, and stomach ulcers. It can also be used to treat epilepsy, gonorrhoea, and heart tonics. Because of its bitter taste, extract from ripe fruit juice lowers blood sugar levels. It has also been discovered that treating piles, rectum irritation, and chronic gastrointestinal disorders can all be cured [60].

➤ *Roots and Bark*

Heart palpitations, intermittent fever, and melancholy can all benefit from the root and bark infusion. *Dashmula* bael tree root is one of the substances used in the manufacture of a well-known ayurvedic medicine. An equal mixture of Bael Root extract with onion and turmeric has been found to be beneficial for ear secretions (Kala 2006). It is among the components of *Chyavanprash* [61]. While bark decoction, leaf extract with honey, and bael extract are used to treat fever, they can also be used as a febrifuge for intermittent fever and fish poisoning [62-64].

➤ *Therapeutic uses*

- Digestive diseases (constipation, diarrhea, dysentery)
- Breathing problems (cold, cough, bronchitis)
- Skin disorders (wounds, eczema, acne)
- Cardiovascular disorders (high blood pressure, high cholesterol)
- Fungal and antimicrobial illnesses
- Antitumor and anticancer characteristics
- Anti-inflammatory and neuroprotective properties
- The antioxidant and hepatoprotective properties [71].

➤ *Importance, uses and Significance*

Fruits have a high importance in Ayurvedic treatment. In recent years, there has been a growing body of research finding and verifying plant-derived compounds for the treatment of a wide range of human ailments. Astringent, antidiarrheal, antidycentric, antipyretic, antiulcerantidiabetic, antibacterial, antiviral, antifungal, anticancer, analgesic, radioprotective, antiviral, antimicrobial, and antihelminthic are just a few of the uses for various plant parts in ethnomedicine [65]. Additionally, compounds extracted from various bael tree sections have demonstrated repressive actions against a number of illnesses (Maity et al. 2009, Patkar et al. 2012 [68]). The root is also a key component in "*dasmula*" (10 roots), an Ayurvedic concoction that is renowned for being a cure-all for digestive problems [66]. Leaf poultice is applied on ulcers and ophthalmia. Additionally, fresh leaves are used as a treatment for catarrh, beriberi, dropsy, and asthma [67].

➤ *Clinical Studies of Aegle Marmelos*

Researchers Kumari, Suresh, Samarasinghe, Handunnetti, and Samaranayake (2013) looked into how *Aegle marmelos* flower extract affected people with diabetes. They observed improved oral glucose tolerance test (OGTT) results and a considerable drop in fasting blood glucose when the extract was taken regularly. It's interesting to note that after consuming glucose, the patients' insulin levels increased

by 62%. Important markers including creatinine, glycated hemoglobin (HbA1c), and certain enzymes did not change substantially after a month, despite these positive modifications. The ability of *A. Marmelos* flower extract to lower blood sugar and boost insulin production in people with type II diabetes was the main focus of the investigation. Over 65% of the population is affected by obesity, which continues to be a global health epidemic and a contributing factor to numerous serious health problems.

In rats given a high-fat diet, research by Karmase, Birari, and Bhutani (2013) demonstrated the potential anti-obesity effects of *A. Marmelos* leaf extracts, specifically dichloromethane, ethyl acetate, and n-butanol. The two main substances that were most successful in lowering these animals' body weight, triglycerides, cholesterol, and glucose levels were umbelliferone and esculetin [69]. Using clinical studies, Yaheya and Ismail (2009) investigated the antidiabetic properties of powdered *A. Marmelos* leaves. Twenty noninsulin dependent diabetic mellitus (NIDDM) patients were divided into five groups, while five individuals served as the study's control group. When compared to patients receiving normal oral hypoglycemic medication, patients receiving powdered *A. Marmelos* leaves showed a substantial change in their postprandial blood glucose level (PPBGL). A clinical investigation including 120 NIDDM patients split into four groups was carried out by Singh and Kochhar (2012). Group I served as the control, while groups II, III, and IV received doses of 2 g of leaf powder, pulp, and seed powder, respectively, for three months. For the following three months, they received nutritional supplements [71].

➤ Toxicological Studies of *Aegle Marmelos*

Marmelos is generally regarded as safe, and not much research has been done on how harmful it is. Veerappan et al. Investigated the harmful effects of the leaves of *A. Marmelos*. Histopathological analyses of the heart, liver, kidney, testis, spleen, and brain revealed no appreciable alterations following intraperitoneal administration of 50 mg/kg body weight of *A. Marmelos* extracts for 14 days in a row. There were no obvious pathological abnormalities or changes to the histology. Additionally, these researchers discovered that male and female Wistar rats did not exhibit any short-term toxicity when given extracts of *A. Marmelos* leaves intraperitoneally at doses of 50, 70, 90, and 100 mg/kg body weight for 14 consecutive days.

Furthermore, it has been observed that the aqueous extract of *A. Marmelos* fruit is not mutagenic to *Salmonella typhimurium* strain TA 100 in the Ames assay. However, there were no published animal studies. Pharmacological research on animal models further confirmed that up to a maximum dosage of 250 mg/kg body weight, doses of *A. Marmelos* fruit extract administered over a 30-day period have not been associated with any negative side effects [70].

VI. RESULT AND DISCUSSION

This review can be related to the biological activities of isolated chemicals from *A. Marmelos* that are being studied utilizing extracts. According to the findings of this study, *A.*

Marmelos holds great promise for the treatment and prevention of a variety of illnesses, such as cancer, infectious diseases, and diabetic problems. These evaluations cover a wide range of issues, including spermatogenic, analgesic and antipyretic, inflammatory, antiulcer, and malaria treatment medications. Development of clinical research on this medicinal herb is therefore imperative, as is learning from traditional healers who have amassed expertise over many generations of trial and error. Worldwide use of bael has increased as more study is done on its advantageous properties in hopes of creating novel treatment.

VII. CONCLUSION

These studies have demonstrated the therapeutic potential of *A. Marmelos* and the presence of components that may be utilized to create novel drugs for the treatment, mitigation, or prevention of diabetes, cancer, and other pathogenic disorders. *A. Marmelos* has been historically utilized for a range of ethno botanical applications. Sadly, a thorough evaluation of the majority of compounds is still required in order to explore new lead molecules or pharmacophores. Furthermore, the mechanisms of a few bioactive compounds have been discovered so far. To determine the mechanisms of action, the bioactivity of various phytochemicals, and the efficaciousness of *A. Marmelos* medicinal properties, extensive research is required.

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