



A COMPREHENSIVE REVIEW OF MEDICINAL USES AND PHARMACOLOGICAL PROPERTIES OF AEGLE MARMELLOS

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Abstract

The present era is fast-moving and everyone believes in allopathic medicines, which provide rapid relief but the darkest side is there. Severe side effects and contraindications on other side plants are excellent substitutes for those medicines because of their fewer side effects and cure the problem directly from the root. Therefore, herbalists most frequently use medicinal plants for healthcare purposes, and they are widely accessible in rural and tribal communities as well. In this review, we attempt to compile information on the pharmacological applications and medicinal properties of the important plant *Aegle marmelos*. Extensive research and clinical investigations reveal that *Aegle marmelos* has a variety of medicinal qualities, including those that are antibacterial, anti-diarrheal, and anti-cancer. In comparison to the entire *Aegle marmelos* the fruits of *Aegle marmelos* are producing the best results compared to the leaves and peels, therefore it is important to assess their medicinal qualities to provide scientists with a general idea of where they stand.

Keywords - *Aegle marmelos*, Golden apple, Bael, Phytoconstituents, Ethnobotany.

INTRODUCTION

Human uses varieties of plants and products derived from plants to treat and relieve a wide range of physical and mental issues. Traditional Chinese, Ayurvedic, Siddha, Unani, and Tibetan remedies all use these herbs. Rigveda, Yajurveda, Atharvaveda, Charak Samhita, and Sushrut Samhita are sources of ancient literature, that describe the use of plants to cure a variety of health issues. These plants have been thoroughly investigated over the past 50 years using cutting-edge scientific methods, and they have been found to have a variety of medicinal properties, including anticancer, antibacterial, antifungal, antidiabetic, antioxidant, hepatoprotective, hemolytic, larvicidal, and anti-inflammatory effects.

Since ancient times, people have used plants as a natural supply of therapeutic chemicals. India is home to the native plant *A. marmelos*. The current study seeks to provide information on the morphology, phytochemistry, and therapeutic characteristics of *A. marmelos* as well as its potential for future scientific research leading to the creation of potent medications [1] study on *Aegle* leaf extract According to Marmelos' research on diabetes caused by alloxan, the extract employed was sufficient to lower oxidative stress by scavenging lipid peroxidation and boosting specific anti-oxidant levels, which lowers increased blood glucose levels. [2] examined the effects of an *Aegle marmelos* leaf extract on alcohol-induced liver damage in albino rats and offered evidence of its superior hepatoprotective properties. Similar findings were made by [3,4] who showed that an ethanol extract from its leaves has antifungal, anti-diarrheal, and antibacterial properties. [5] assessed the antifungal properties of essential oils.

PLANT PROFILE

SCIENTIFIC CLASSIFICATION [6]

Kingdom – Plantae Order- Sapindales Family- Rutaceae Subfamily-Aurantioideae Genus- *Aegle*
Species- *Aegle Marmelos* Botanical name- *Aegle marmelos*

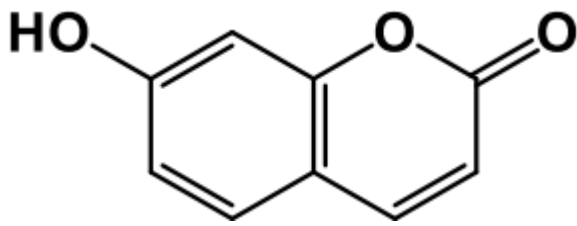
Vernacular names [7]

English – Bengal quince, Beal fruit, Golden Apple. Hindi- Bael, Sirphal.
Sanskrit- Adhararutha, Atimangaliya, Bilva. Asholam.

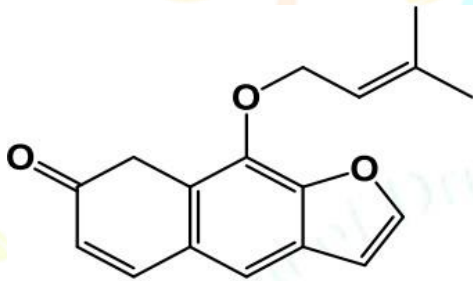


Fig.1. *Aegle marmelos*

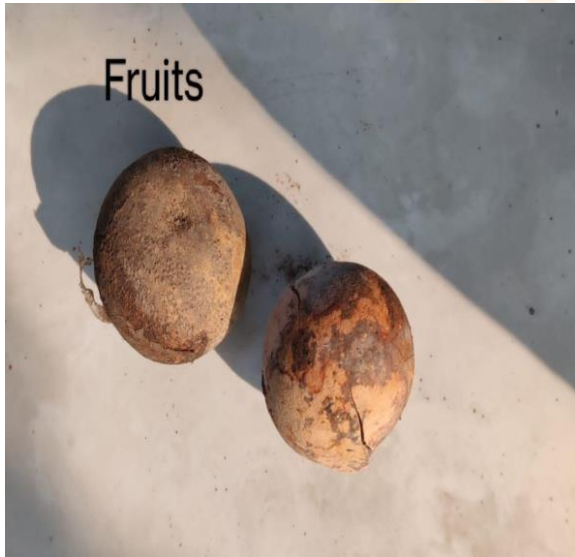
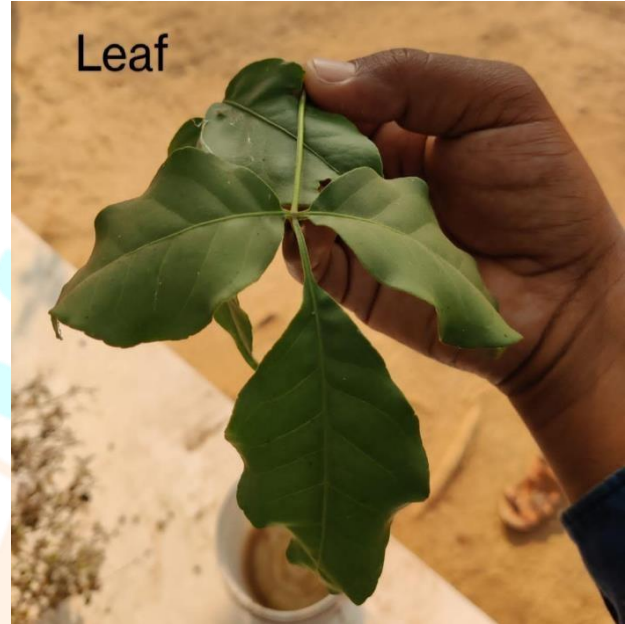
OVERVIEW OF PHYTOCONSTITUENTS PRESENT IN A. MARMELOS WITH THEIR STRUCTURES ^[8]



Umbelliferone



ACTUAL IMAGES OF GOLDEN APPLE TREE, LEAVES, FRUIT



MORPHOLOGY

The tree is medium to large in structure, deciduous, glabrous, and armed, with axillary 2.5cm long alternative trifoliate leaves, small flowers, and globular fruits^[9]

ETHNOBOTANICAL USES OF AEGLE MARMELLOS

Many Indian Ayurvedic practitioners and traditional herbalists claim that different portions of *A. marmelos* are used to cure a variety of health risks. Every component of the plant is used for the creation of many drugs. Fruit is one of the essential portions that can treat the most diseases out of all the other parts. Different kinds of powder, paste, and tablets made from the Bael plant are used.

Bael is a key component in the creation of dasamula, chyavanprash, etc. It is used to treat several disorders because of its digestive and carminative qualities. Bael is a key treatment in Ayurveda for conditions like chronic diarrhea, dysentery, cerebral tonic, etc.

The components of bael, including the root, and bark. Bael fruit powder has anti-cancer and anti-proliferative effects^[10] Vomiting during pregnancy can be treated with a twice-daily dose of boiled rice water and unripe fruit pulp^[11] Urogenital problems can be treated by combining milk, sugar, and unripe fruit pulp from bael. Half-roasted, unripe pulp combined with sugar is crucial for the treatment of both dysentery and abscesses^[10] By taking it twice daily, bael leaf extract treats intestinal worms, ulcers, and ophthalmia^[10] Urogenital problems can be treated by combining milk, sugar, and unripe fruit pulp from bael. Half-roasted, unripe pulp combined with sugar is crucial for the treatment of dysentery and abscesses^[10] By taking it twice daily, bael leaf extract treats intestinal worms, ulcers, and ophthalmia^[12] A poultice made from betel leaf is needed for cure of eye problems^[13] Leaf juice has several pharmacological benefits, especially for managing diabetes. Patients with fever and a cold are given a decoction of bael root. Fever and heart conditions can both be treated with a decoction of root and bark^[10]

Table 1- Ethnobotanical Uses.

Plantparts	ETHANOBOTANICAL USES
LEAF	Abscess, backpain, eye complaints, gastrointestinal issues, vomiting, cut and wound, ulcer, diarrhea, cardiotoxic, blood sugar, nervous disorders, hair tonic, bronchospasm, child birth. ^{14,17,18,20,23,25}
	Veterinary medicine for wounds, killing worms, stimulation of respiration and contraction of denervated nectitating membrane in anaesthetized cats ^{14,20,22,24}
Fruit	Astringent, diarrhea, gastric troubles...antiviral, intestinal parasites, gonorrhoea, epilepsy ^{14,18,19,20,23} , edible, jam preserve ^{16,20,21}
Root	Dog bites, gastric troubles, heart disorders, anti-amoebic, hypoglycemic, rheumatism ^{17,23}
bark	Stomach disorder, intermittent fevers, heart disorder ^{23,25}
Seed	Febrifuge ¹⁴
Flower	Expectorant, epilepsy ^{18,19}
Wholeplant	Abdominal pain, astringent, dog bite, breast pain, cholera, jaundice, laxative, snakebite, cut and wounds ^{14,15,14,20,23,25}
Root, Bark	Fish poison ²⁰
Seed mucilage	Plaster for walls ²⁴
Seed oil	Laxative ¹⁹
wood	Special couches for rheumatic patients ^{16,21,24}

Gum around seed	In order to improve strength of water paints ^{16,21,24}
Unripe fruits rind and bark	Yellow dye ^{21,24}
Stem	Pestles of oil sugar mills ^{21,24}

PREPARATION OF PLANT EXTRACT^[26]

1. An extract is a combination of phytochemicals made from any plant and produced by extracting particular plant components.
2. The leaves, fruits, and peels of aegle marmelos were washed with distilled water, incubated for 3–4 days at 37°C, and then ground into a fine powder.
3. The plant material was then dissolved in a mixture of ethanol and methanol (70:80), ethyl acetate, and hot water (1:10).
4. One gram of the sample should dissolve in ten milliliters of solvent. (10 cc of solvent should be added to 1 g of sample to dissolve it.).
5. In sterile beakers, mixtures were maintained at room temperature for three days in the dark.
6. To prevent evaporation and exposure to sunlight, the food was wrapped in aluminum foil.
7. After three days, the mixtures were filtered using Whatman No. 1 filter paper and maintained in an incubator at 37 °C until all of the solvents had fully evaporated from the mixtures. 8. All mixes were now dissolved in DMSO (dimethyl sulfoxide).

TEST MICRO-ORGANISMS

1. 1-gram positive culture of staphylococcus aureus (MTCC 2940)
2. 2-gram negative cultures- pseudomonas aeruginosa (MTCC 2453)
3. E. coli (MTCC 739)

PHYTOCHEMICAL ANALYSIS (Table no.2)

Sr.no.	Tests	Leaves	Fruits	Peels
1	Reducing sugar	-	+	+
2	Tannins	+	+	+
3	Phlobatannins	+	+	+
4	Saponin	+	+	+
5	Terpenoids	+	+	+
5	Alkaloids	+	-	-
6	Flavonoids	-	-	-
7	Polyphenol	+	+	+

Above table showing that the phytochemicals mainly found in *Aegle marmelos* were tannins, phlobatannins, saponin, triterpenoids, alkaloids and polyphenols.

PHARMACOLOGICAL USES

1. Anti-microbial activity

The presence of leaf constituents such as cuminaldehyde and eugenol may be responsible for antimicrobial activity.²⁷

Anti-bio gram analysis

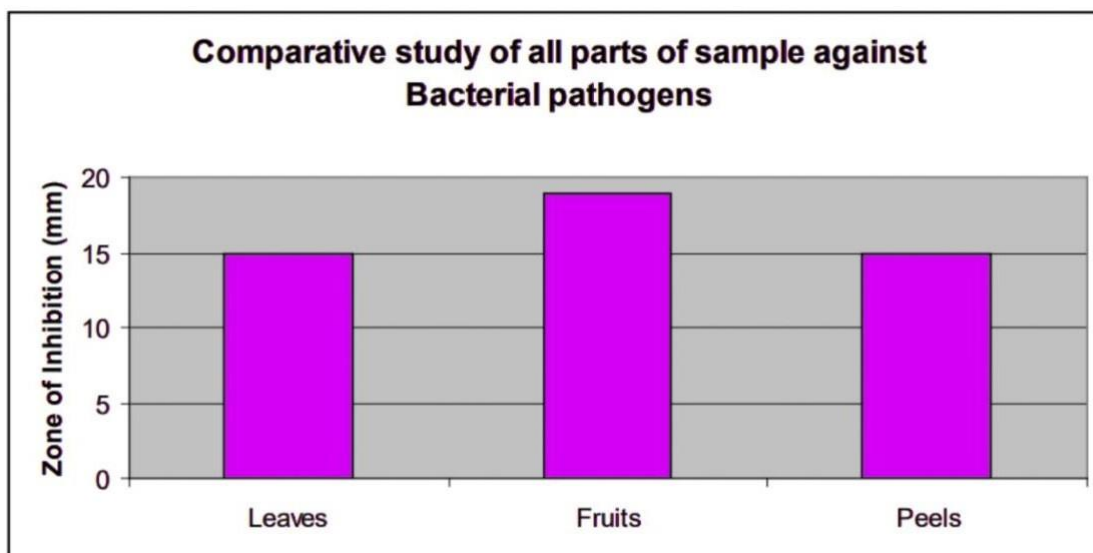
Using hot water, ethanol, methanol, ethyl acetate, and extracts of *Aegle marmelos*, the anti-bacterial activity of species was assessed against bacterial strains. Diffusion technique using agar wells²⁸.

For all extracts, nutrient agar plates were prepared. 50 l of the chosen bacteria inoculums were evenly distributed over the plates using a glass spreader. Three wells, each measuring about 5 mm in diameter, were then drilled into the agar after five minutes. Tetracycline, distilled water, and plant extract were all added in an equal volume (50µL) and put into the wells. For 24 hours, plates were incubated at 37°C.

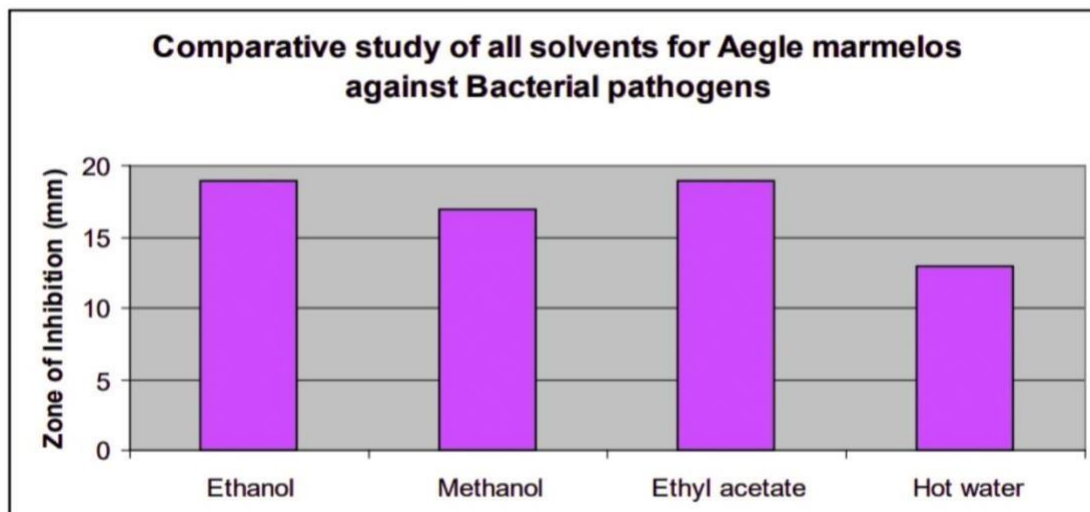
Determination of MIC of several extract such as methanolic ethanolic and ethylacetate and hot water extract

The MIC is defined as the lowest concentration of anti-microbial agent that will inhibit the visible growth of microorganism after overnight incubation at temperature condition of 37 degree Celsius for 24 hrs. in shaker incubator.^{29,30}

Graph No 1 : Given graph shows that *A.Marmelos* Fruits are having maximum anti bacterial activity, compare to leaves and peels.



Graph No 2 : Given graph shows that ethanol and ethyl acetate are having maximum anti bacterial activity.



2. Antibacterial activity of *A. marmelos* crude extract

Significant action against *S. aureus* has been observed for the aqueous extracts of *A. marmelos*. *Corynebacterium* was inhibited by the leaf extract's antibacterial activity.

Diphtheriae, Pneumococcus, Streptococcus pyrogens, *E. coli*, Salmonella typhimurium, Proteus vulgaris, Staphylococcus aureus, and Klebsiella pneumoniae³¹ *S. aureus* is a notable human pathogen, and almost everyone will develop an infection from it at some point in their lifetime. The severity of these infections ranges from mild to severe. food poisoning, mild skin infections, and infections that require life-saving treatment. In order to replace the current commercial antibacterial medications that cause numerous forms of toxicity in patients, the discovery of these potential herbal antibacterial agents is exciting. The crude extract from *Eagle Marmelos* displayed poor susceptibility to *P. vulgaris*. Up to 125 mg/ml, *P. aeruginosa* and *V. cholerae* had no action. There is one class of natural substances called acetogenins whose powerful biological activity and unique structural characteristics have been noted by some researchers, who also isolated flavonoids from the plant's leaves, aporphine alkaloids^{32,33,34}, terpine derivative, glycosides³⁵, and a novel diazepine, squamolone Numerous acetogenins having antimicrobial, antiparasitic, antimalarial, cell growth inhibitory, and cytotoxic pesticidal activities.

One such substance that demonstrated antitumor and pesticidal action in vivo was bullatacin. It has been demonstrated that methanolic extracts of *Aegle marmelos* seed possess antiparasitic properties.

3. Anti-fungal Action of *aegle marmelos*

A. marmelos crude extract should possess a strong anti-fungal activity against *C. albicans* are most often implicated in the infection of genital urinary tract; due to its inhibitory effects against group of fungal diseases its consequently reputed useful in treating venereal diseases.³⁶

4. Anti-constipating effect

Most ripe fruits that are readily available are regarded as a natural alternative to various laxatives. Fruits from *A. marmelos* are typically used to cleanse and tone the gut. Consuming this fruit consistently for 2 to 3 months results in the bowels' old, accumulated feces being evacuated. It is typically consumed as "sherbat," a beverage prepared from ripe fruit pulp.³⁷

5. Anti-diarrheal activity

A. marmelos is extensively employed for controlling chronic cases of diarrhea and dysentery due to astringent properties unripe Bael fruit, which was prevalent in India in summer months.^{37,38,39} The ethanolic extract showed

excellent activities against *Shigella boydii*, moderate activity against *S. dysenteries*.⁴⁰

6. Diuretics

The alcoholic extract of *A. marmelos* produces significant increase in level of sodium at higher dose (450-500mg/kg). pet.ether, chloroform, and ethyl acetate fractions are also effective.⁴¹

7. Antiproliferative activity

Stem bark of *A. marmelos* show Antiproliferative activity against many human tumor cell lines. Which includes melanoma colo38 and Breast cancer MCF7 and MDAMB – 231 cell lines.⁴²

8. Anti-cancer

As leading cause of mortality in both industrialized and developing nations men and women⁴³, cancer is serious public health issue. A total of 7.6 million cancer fatalities and 12.7 million new cancer diagnoses were reported in 2008, with 56% of these instances occurring in developing nations. According to the projection there will be three-fold increase in incidence of cancer by the year 2020, with a disproportionate increase in cancer cases and fatalities occurring in developing nation with insufficient resources to combat the issue.⁴⁴

According to preclinical trials results *A. marmelos* leaf extracts effectively slowed the growth of leukemic K562, T- lymphoid Jurkat, B-lymphoid Raji, erythroleukemic HEL.

9. Cytoprotective Action

Cyprinus carpio, or freshwater fish, were subjected to this impact. For 1, 8, 16, and 32 days, experimental fish were maintained at sublethal metal ion concentrations. These fish were given 500mg/kg of *Aegle marmelos* crude powder after 32 days. Following treatment, the outcome is Stabilization of the plasma membrane and control of the antioxidant enzyme system have a cytoprotective impact.⁴⁵

10. Hepatoprotective effect

Hepatoprotective effects of *A. marmelos* leaf can protect albino rats' livers from harm caused by alcohol use. A bacterial suspension containing 5×10^6 CFU/0.1 ml is administered to rats intraperitoneally. For 15 days, the rats were given a 100 mg/kg body weight alcohol extract of *marmelos* in physiological saline. The animals went without food for 12 hours after the 15-day period.

Following a quick chloroform sedation, scarification Organs are taken out and thoroughly cleaned in ice-cold saline after blood is extracted to separate the serum. Alkaline phosphate⁴⁶, SGOT⁴⁷, SGPT⁴⁷, total bilirubin⁴⁷, and protein⁴⁸, among other biochemical indicators, were examined.⁴⁹ Blood glutathione was calculated with the aid of DTNB.⁵⁰ These albino rats were fed plant leaf powder for the following 21 days after receiving daily doses of 30% ethyl alcohol for 40 days. The *A. marmelos* leaf has a great hepatoprotective effect, according to the experimental data.⁵¹

11. Analgesic activity

Methanolic extract of *Aegle marmelos* produce significant analgesic activity.⁵²

12. Anti-arthritis activity

Wistar albino rat gives positive result for anti-arthritis activity of *A. marmelos* leaves.^{53,54,55}

13. Anti-diabetic and antioxidant activity

The hypoglycemic and anti-oxidant effect of an aqueous extract of Golden Apple leaves carried out by using albino rats. Owing to its hypoglycemic and anti-oxidant properties aq. Extract of marmelos may be useful in long term management of diabetes.^{56,57}

14. Wound healing activity

Injection and ointment of methanolic extract of *A. marmelos* shows significant effect on both excision and incision wound models in rats. The results were also compared with those of standard drug Nitrofurazone⁵⁸

15. Anti-fertility activity

The aqueous extract of marmelos leaves have effect on male reproductive system, (experiment carried out on rat) that affects the sexual behavior, epididymal sperm concentration.⁵⁹

16. Antipyretic potential

A dose of 200 mg/kg body weight of *A. marmelos* eugenol extract resulted in a significant (P 0.001) alleviate rise in body temperature in a dose-dependent manner. This effect was compared with paracetamol (100 mg/kg body weight).^{60,61}

17. Antiviral activity

A virus is seen as both a living and nonliving entity, depending on where it is located in the host body. It causes seasonal outbreaks and doesn't react well to the majority of synthetic medications. As a result, there is a growing need for natural bioresources to solve this issue. Antiviral activity is produced by hydroalcoholic bael fruit extract against the Ranikhet sickness virus. Also disclosed is interferon-like activity against the same pathogen. As a result, fruit having a greater viricidal capability and may one day be employed as a powerful antiviral agent.⁶²

18. Immunomodulatory activity

The immunomodulatory action of methanolic extract of *A. marmelos* fruit in experiment of immunity testing was carried by

- a. Neutrophil adhesion test
- b. Carbon clearance assay

Whereas humoral immunity was analyzed by

- a. mice lethality test
- b. an indirect hemagglutination assay

so it is concluded that methanolic extract of *A. marmelos* has the capacity to boost immunological function through cellular and humoral mechanism more at small dose (100mg/kg body weight) than high dose (500mg/kg body weight).⁶³

FUTURE PERSPECTIVE

1. aegle marmelos loaded Herbosome will be prepared successfully for safe and efficacious delivery of the formulations.
2. preparation of phytosomes containing methanolic extract of leaves of *A. marmelos* which will show

following effects

- a. Anti-oxidant
 - b. Anti-proliferative
3. Micro-sphere as a drug carriers for controlled drug delivery of formulation containing A.marmelos in treatment of diseases such as diabetes.
 4. Nanoparticles are are colloidal particles size ranging from about 10nm to 1000nm, as they are biodegradable and biocompatible use for delivery of preparation containing A. marmelos in treatment of diseases such malaria.
 5. Phytosomes containing methanolic extract of leaves of a.marmelos can showed huge anti-cancer activity against human breast (MCF7) cell line compared to pure extract.

CONCLUSION

Man aspires to lead in our fast-moving generation and no one wants to be seated last. We deal with this neck chopping battle because a brand new, intricate health issue, and today we are depending more and more on modern medicines. Or the artificial medicines which are undoubtedly provides the quick outcomes, but creates various new issues such as unfavorable effects and side effects. On the other hands natural medications like A. marmelos (Bael) is significantly safer and more valuable in comparison to those chemical observers, broad view of the Bael tree, one should either cultivate it or make it an effort to protect it for the right usage and to get the freshest, most potent natural medicine.

The use of various A. marmelos components by traditional healers to treat a variety of human afflictions has been described. These have anti-inflammatory, anti-cancer, anti-viral, anti-ulcer, anti-diarrheal, anti-fungal, antiproliferative, cytoprotective, hepatoprotective, antifertility, analgesic, anti-arthritis, contractile, anti-hyperlipidemic, immunomodulatory, and immunostimulatory properties. Wrist-healing qualities. Several chemically diverse chemicals that are biologically active are identified in distinct A. marmelos sections. Alkaloids, terpenoids, vitamins, coumarins, tannins, carbohydrate, flavonoids, fatty acids, essential oils, and other diverse chemicals are among the isolated components. The majority of this review's attention was given to a number of phytochemical and pharmacological studies that described the phytoconstituents, medicinal and therapeutic potential of A. marmelos.

ABBREVIATIONS

A.marmelos- Aegle marmelos (Bael)

MIC – Minimum Inhibitory Concentration
Pet. Ether - Petroleum ether

SUMMARY

The present review highlights medicinal, phytochemical and pharmacological aspects of Aegle marmelos that may be fruitful for future researches.

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