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<u>Review Article</u>

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PHYTOCHEMISTRY, PHARMACOLOGY AND ETHNOMEDICINAL USES OF AEGLE MARMELOS PLANT: A COMPENDIOUS REVIEW

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ABSTRACT

In an ancient time, the plants were used as medicine in various diseases. In India various medicinal system uses parts of plants (leaves, barks, seed, fruit, flower, stem, root) to cure and treat number of various human ailments. Aegle marmelos is one of the medicinal plant, also known as bael have spiritual as well as medicinal importance. The leaves of Bael are used during the worship of lord shiva. Bael belongs to family Rutaceae. In peninsular India, the tree is very commonly found in dry forest hills and central & southern Indian plains. The present review article aims to reveal an updated and explicit information the botanical aspect, ethnomedicinal on uses. phytochemical and pharmacological activities of Aegle marmelos. Marmelos has been extensively studied for their medicinal activity, and

different phytochemical were isolated from various parts of the plant using various advanced pharmacological technologies.

KEYWORDS: Aegle marmelos, Ecology, Phytochemistry, Ethanpharmacology.

INTRODUCTION

Bael is the most commonly known plant of Indian origin from ancient times and has been pointed in the old traditional system of medicine. Bael plant has great mythological importance as well. Due to its preventive measures, it is one of the most important medicinal plants in India. The utilization of the bael plant has been improved day by day life in different forms. The various products obtained from bael having a great ethnomedical and nutritive value so getting more popular in India as well as the international market. By absorbing poisonous gases from an environment and converting them into neutral, by improving oxygen content of atmosphere bael plant act as a 'drop' for the harmful chemical pollutant. Bael plant is also known as 'climate purifier' by emitting a large amounts of oxygen in the atmosphere. Aegle marmelosa plant also considered under the species frangent category, the flower of plant, and also volatile content neutralize the bad odor of air.^[1] Hindu religions grasp the bael leaves with great esteem. This plant is generally grown near the temple, bael leaves mostly loved by lord Shiva. According to Hindus mythology, lord Shiva's prayer is incomplete without the use of bael leaves. Hindu have a lot of faith in that, lord shiva lived under the bael tree, so it is also known as the "Shivadurma" tree of Shiva. It is the responsibility of all Hindus to plant and foster the bael tree, planting of this tree gives long to life. The bael plant is held blest by Hindus and offered in worship of lord shiva. Nowadays post harvested technologies play important role in the production of a large number of byproducts like toffee, candy, jam, jelly, juice, etc. from bael fruit. These technologies help to a number of postharvest losses which helps in the improvement of bael product shelf life so, it is one of the best profitable income sources for the destitute farmers.^[2] Bael plant is composed of numerous phytochemicals from various plant parts like root, stem, fruit, leaves, seeds, etc. Aegle marmelosa is commonly known as 'wood apple'.

The earliest literature such as Yajurveda, Atharvaveda, Chark Samhita, Rigveda also briefly explain the importance of the bael plant for the treatment of various health problems.^[3] This plant has several ethnomedical uses in the folk medicinal system and traditional medicinal system. Nutritional aspects of bael plant are more much notable as compared to other plants.^[4]

Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Rosidae
Order	Sapindales
Family	Rutaceae
Genus	Aegle
Species	Aegle marmelos

Table 1: Taxonomica	l classification of	f Aegle marmelosa L. ^[5]
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Bael leaf "Fig. 1"

Bael plant "Fig .2"

Table 2: Vernacular names of Aegle marmelos L.^[6]

Name	Language
Aegle marmelos:	Latin
Wood/Stone apple, Bengal Quince, IndianQuince	English
Mbau Nau, Trai Mam	Vietnamese
Bel, Gudu	Nepali
Toum	Lao (Sino-Tibetan)
Bnau	Khmer
Modjo	Javanese
Oranger du Malabar	French
Ohshit, opesheet	Burmese
Mojo tree	Indonesian
Pokok Maja Batu	Malay
Mapin, Matum, Tum	Thai
Shreephal, Bilva, Bilwa	Sanskrit
Sir Phal	Old Hindi
Bel, Shreefal	Bengali
Kaveeth	Marathi
Vilva Maram, Vilva Pazham	Tamil
Maredu	Telugu
Bel	Urdu

History of Bael plant

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Ecology^{[2][7][8]}

Bael has Indian origin generally found in various other countries like Egypt, Bangladesh,

Myanmar, Malaysia, Sri Lanka, Pakistan, and Thailand. The bael plant wildly grows on dry forests hills and plains of southern as well as central India, Bangladesh, Pakistan, and Burma, also in mixed deciduous and dry forests. Bael (Aegle Marmelos (Linn), family Rutaceae, is also known as Bale fruit tree, wood apple is a moderate-sized, slender, fragrant tree, 6.0 -7.5 m in height, and 90 to 120 cm in circumference, with a somewhat fluted trunk of the tree of 3.0-4.5 meter growing wild throughout the deciduous forests of India, have an ascending altitude of 1200 meters in the western Himalayans and also occurring in Andaman Island.

Bael tree is generally referred to as a sacred tree by Hindus, the leaves are offered in the worship of Lord Shiva. According to Hindu mythology, the tree is another form of Lord Kailashnath. Leaves, fruit, stem, and roots of this tree at all stages of maturity are used as ethnomedicine against various human diseases.

A REVIEW OF LITERATURE^{[1][2][5][6][7][9]}

Table 3: Review of literature.

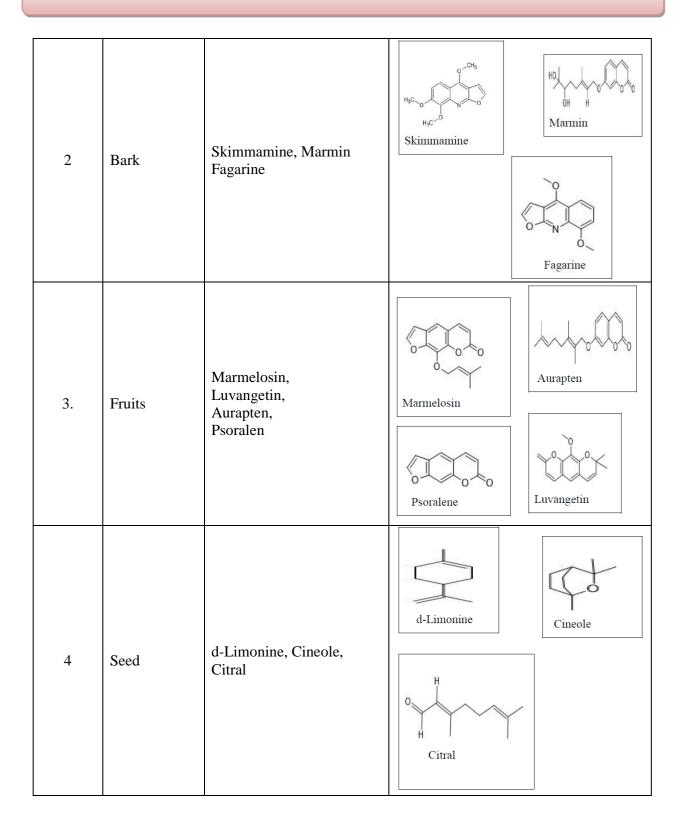
SrNo	Title of review	Author name	Objective of study	Issue
1	Medicinal Values of Bael (Aegle marmelos) (L.) Corr.: A Review	Ganesh N. Sharma, Susheel K. Dubey, Piush Sharma, Nitin Sati	Aegle marmelos contains a number of phytoconstituents which reveals its uses for various therapeutic purposes.	(IJCPR) International Journal of Current Pharmaceutical Review and Research
2	A review on pharmacologicaland phytochemical properties of Aegle marmelos(L.) Corr. Serr. (Rutaceae)	Dinesh Kumar Sekar, Gaurav Kumar, L. Karthik and K. V. Bhaskara Rao*	Traditional use, Phytochemical composition, pharmacological study and nutritional value of Aegle marmelos	Asian Journal of Plant Science and Researcher
3	A Review onBael Tree	Prabodh Chander Sharma, Vivek Bhatia, Nitin Bansal and Archana Sharma	Looking upon wide prospectsand potential of bael for various purposes, it is worthwhile to cultivate this plant on large scale especially on unproductive and wasteland. This will helpin financial upliftment of poor and landless farmers.	Natural product Radiance
4	Phytochemical And PharmacologicalReview Of Maja(Aegle Marmelos)	Alfiah Putri Mulyaningsih1, Rina Desni Yetti And Harrizul Rivai	The result of this review shows that the view of the pharmacological activities of the phytochemical content of the medicinal plant Maja provides a solid basis for developing traditional	World Journal of Pharmacy And Pharmaceutical Sciences

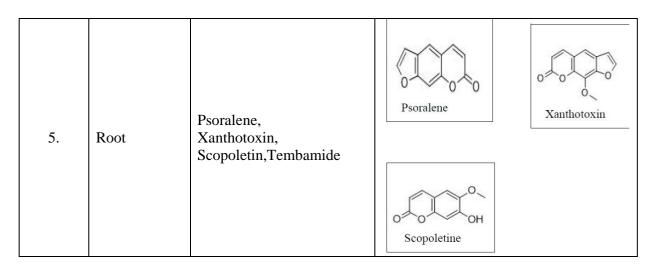
			medicines.	
5	An Eye- Catching Review of Aegle marmelos L. (GoldenApple	Kausik Bhar, Sumanta Mondal, Padilam Suresh	This review mainly focused on several phytochemical and pharmacological studies which have explained phytoconstituents and therapeutic potential of A. marmelos.	Pharmacognosy Journal,
6	A Systematic Review on Aegle marmelos(Bael)	Savita S. Mali, Rekha L. Dhumal, Vijay D. Havaldar, Snehal S. Shinde, Nilam Y. Jadhav, Bhagyashri S. Gaikwad	The present review elaborates various therapeutic and innovative approaches to find out the perspective on globalization of the Bael tree.	Research Journal ofPharmacognosy and Phytochemistry

Phytochemical Constituents

Table 4: Phytoconstituents isolated from various parts of Aegle marmelos.^[5]

Sr. No.	Part	Phytoconstituents	Structure
1	Leaf	Skimmianine, Aegeline, Lupeol, Cineole, Citral, Citronellal, Cuminaldehyde, Eugenol	$ \begin{array}{c} \underset{H_{0} \leftarrow \\ H_{0} $





Several research works have been performed on various parts of the bael plant to identify active chemical constituents. Spacious surveys have been performed out on various parts of Bael and significance, diverse modules of the compound have been separated from various parts of plants like coumarins, fatty acids, alkaloids, amino acids and terpenoids. Especially, the majority of report works have been done on the isolation, identification, evaluation, and characterization of compound by many Indian workers. Extraction performed on leaves of Aegle marmelos using different organic solvents have been reported to possess alkaloids, cardiac glycosides, terpenoids, saponins, tannins, flavonoids, and steroids. The fruit pulp of Aegle marmelos has been reported for the availability of steroids, terpenoid, flavonoids, phenolic compounds, lignin, fat and oil, inulin, proteins, carbohydrates, alkaloids, cardiac glycosides, and flavonoids.

Ethnopharmacology^{[10][11][12][13]}

In conformity with a number of Indian Ayurveda practitioners and traditional herbal healers, several parts of Aegle marmelos were utilizing for the prevention and treatment of various health issues. Among different parts of the plant, fruit has more importance that can a prevent maximum number of disorders. There are numbers of different types of pills, paste, powder, are used which are generally obtained from various parts of the bael plant. Bael plant is the main active ingredient used in the formulation of Dasamula, Chyavanprash, etc. The digestive and carminative properties of bael make it useful to treat and prevent various diseases. Bael can be considered as an important medicine in Ayurveda for treating chronic diarrhea, dysentery, brain tonic, etc. A perfect combination of five parts of bael like root, bark, leaf, flower, and fruit can be highly preferred as an effective agent to cure certain mental disorders. Antiproliferative and anticancer activity produced by fruit powder of bael. Vomiting during pregnancy can be prevented by using a mixture of boiled rice water and

unripe fruit pulp by taking twice daily, also the mixture of bael unripe fruit pulp with milk and sugar cures urogenital disorders. Half roasted unripe pulp mixed with sugar is essential for preventing dysentery and abscess. Leaf extract of bael can be used to treat ophthalmia, ulcer, and intestinal worms by taking twice daily. Bael leaf poultice that is used to cure eye diseases. Leaf juice of bael having a great medicinal value especially to maintain blood sugar level in diabetes. Bael root decoction is given to a patient suffering from fever, cold as well as heart disorders.

Therapeutic application of aegle marmelos

1) Antidiabetic and anti-hyperlipidemic activity^{[2][14][15][16][17]}

According to Indian Ayurvedic, Siddha, Unani traditional system of medicine, bael plant has been used for control and management of diabetes mellites. Some literature surveys investigates that antidiabetic effect of the plant may be due to the presence of coumarin as a chemical constituent in fruit. Aqueous extract of bael seed help to reduce blood glucose level in severe diabetic cases. In vivo, scientific study has been performed using an animal model to show antidiabetic effect of various organic extracts and juice of bael fruit extract of bael plant effectively reduce the blood cholesterol and urea level in diabetic induced rat. Leaf extract of Aegle mermelos has been enough competent to lower the oxidative stress by lipid peroxidation scavenging and improving the certain level of antioxidant which results in dropping of elevated blood glucose level. An alkaloidal-amide, aegeline (table 4) has been isolated from the leaves of Aegle mermelos, aegeline has antihyperglycemic activity, as demonstrated by lowering blood glucose levels at 12.9% and 16.9% for 5 and 24 hours, respectively. Aegeline also has anti-hyperlipidemic activity because it significantly reduced plasma triglyceride (Tg) levels by 55% (P < 0.001), total cholesterol (TC) by 24% (P < 0.05), and free fatty acids(FFA) by 24%. Accompanied by an increase in HDL-C by 28% and HDL-C/TC ratio by 66% in dyslipidemic hamster models at a dose of 50 mg/kg body weight. The bael plant's lipidlowering property has been investigated by administering aqueous leaf extract in albino Wistar rats. This activity was measured by using serum lipid profiles that is high-density lipoprotein (HDL), very low-density lipoprotein (VLDL), total cholesterol (TC), and triglyceride (TG) profiles.

2) Analgesic, anti-inflammatory and antipyretic activity^{[7][9][18][19]}

The various organic extracts of the leaves of Aegle marmelos Corr. Were evaluated for their anti-inflammatory, analgesic, and antipyretic activity. The analgesic and antipyretic

properties were also evaluated. The sequential extracts derived from the plant Aegle marmelos shows a noteworthy inhibition of the carrageenan-induced paw edema and cottonpellet granuloma in rats. The reduction in the early and late phases of paw licking in mice has also produced a marked analgesic activity by bael plant. Hyperpyrexia in rats can also be significantly reduced by most of the extracts of Aeglemarmelos. The investigation of the anti-inflammatory activity of aqueous extracts of dried flowers of Aegle marmelos has also been performed. The mechanism of the anti-inflammatory effect was assessed by inhibition of nitric oxide (NO) production by rat peritoneal cells, rat peritoneal cell infiltration, antihistamine effects, membrane stabilization activity, antioxidant capacity, and inhibition of lipid peroxidation by aqueous extract of Aegle marmelos. Aqueous extract of bael protects the membrane from heat, which promotes lysis in a dose-dependent manner and shows a significant antioxidant effect and inhibitory effect on lipid peroxidation.

3) Diarrhoea and dysentery^{[9][20][21]}

Half ripe or unripe fruit acts as a remedy to cure chronic diarrhoea and dysentery without fever. The half ripe fruit is considered as good for this purpose but fully ripe fruits or uniform powder of fruit has shown better results. The unripe fruit can also be taken by baking and then mixing with brown sugar or jaggery. The amount of blood passed in the fecal matter gets reduced, and the fecal matter gets a more solid form afterconsumption of fruit. This study was evaluated to verify the gastroprotective and antidiarrheal effects of Aegle marmelos raw fruit extracts. This gastro protective action of bael extract was evaluated in rats besides damage to the gastric mucosa triggered by hypothermic buffer stress, absolute ethanol, and indomethacin. In similarity, the antidiarrheal property was examined by studying the effect on gastrointestinal transit as measured by charcoal indicators on the accumulation of castor oil-induced from intestinal fluid in rats. In the isolated Guinea-pig ileum acetylcholine, histamine, serotonin, and barium chloride cause the contractile response. Raw fruit extracts significantly inhibit both intestinal transit and intestinal fluid accumulation caused by castor oil in mice, at the same dose. Additionally, extracts show contractile responses produced by different agonists on intestinal absorption of Guinea-Pig in vitro. The druginhibition potential is in the order of acetylcholine > histamine > serotonin > barium chloride. These results designate the possible antidiarrheal effect of A. marmelos raw fruit extracts from inhibition of intestinal motility to secretion can prevent clinical diarrhea.

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4) Antimicrobial and antifungal activity^{[22][23][24][25]}

Traditionally A. marmelos have been used for the treatment of numerous infectious diseases and have been extensible stated to kill the broad range of pathogenic microorganisms. Many literature surveys evaluated the antimicrobial potential of A. marmelos extracts against pathogenic microorganisms including bacteria and fungi. The agar well diffusion method has been used to identify the antimicrobial activity of A. marmelos leaves. The aqueous, petroleum ether and ethanol extract of the leaves of Aegle marmelos demonstrated effective antimicrobial activity against Proteus Vulgaris, Escherichia coli, Streptococcus pneumoniae, Salmonella typhi, and Klebsiella pneumoniae. Disc diffusion method has been done to identify the antimicrobial activity. The petroleum ether extract of leaves was tested against multiresistant strains of Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Salmonella typhi, Proteus vulgaris, Pseudomonas aeruginosa, and Klebsiella pneumonia. Gram-negative strains show higher antimicrobial activity than of gram-positive strains. Bael leaves have been described as an antifungal against clinical isolates of dermatophytes. A. marmelos leaf extracts and fractions were found to have fungicidal activity against Trichophyton mentagrophytes, T. rubrum, Microsporum canis, M. gypseum, Epidermophyton floccosum. The antifungal and antibacterial activity of the fruit of A. marmelos was reported. The antimicrobial activity was performed by using the tube dilution MIC method. The fruit decoction of bael indicated activity against Aspergillus niger, Aspergillus fumigatus, Candida albicans and Staphylococcus aureus and the MIC results for the above individual organisms were 19.5 μ g/ml, 39 μ g/ml, 625 μ g/ml, and 1.25 mg/ml. The antimicrobial activity was checked against Bacillus subtilis, Staphylococcus aureus, Klebsiella pneumoniae, Proteus mirabilis, Escherichia coli, Salmonella paratyphi A, and Salmonella paratyphi B. The methanol extract showed considerably high activity against the above-mentioned bacteria as compared to other extracts. The hexane, cold methanol, hot methanol, and ciprofloxacin extracts presented high antibacterial activity against Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris, Micrococcus luteus, Enterococcus faecalis, and Streptococcus faecalis.

5) Antioxident activity

Oxidative stress can be facilitated by the compound having free radicals scavenging activity and the ability to prevent cells from free radicals. Natural sources such as plants show the presence of the antioxidant compound and the presence of flavones, isoflavones, flavonoids, anthocyanin, coumarin, lignans, catechins, and isocatechins facilitate the antioxidant activity. Antioxidant activity of the fruit of A. marmelos was demonstrated. Some literature reviews compares antioxidant activity and free radical scavenging activity of the ripe and unripe fruit. Results designate that the enzymatic antioxidants enlarged in ripe fruit as compared to extract of unripe fruits (except glutathione peroxidase) also shown a higher percentage of free radical inhibition in unripe fruit than that of the ripe fruit. On administration of Bael fruit extract at a dose of 250mg/kg of body weight, indicate better results than glibenclamide (36µg/kg).

6) Hepatoprotective activity^{[26][27]}

The present work has been done to study the hepatoprotective activity of aqueous extract of bael at different doses, which shows a toxic effect in mice. The hepatoprotective effect of the A. marmelos leaves and was described in alcohol-induced liver injury in albino rats. For that 30% of ethyl alcohol were administered to rat for 40 days and the induced rats were fed with leaves of A. marmelos for 21 days. It has been also investigated that aqueous extract of bael fruit pulp and seeds have a better effect in the treatment and prevention of CCI4 induced hepatic toxicity.

7) Anticancer activity^[28]

Literature survey demonstrates the anticancer activity of folk medicine used in Bangladeshi and used extracts of Aegle marmelos for cytotoxic action using brine shrimp lethality assay; sea urchin eggs assay, and MTT assay using tumor cell lines. The extract of Aegle marmelos was found to be effectively toxic to all used assays. Similarly, the anticancer activity of hydroalcoholic extract of bael leaves in the animal model of Ehrlich ascites carcinoma and suggested that the presence of skimmianine in the extract exerts induction of apoptosis.

8) Antiviral activity^{[29][30] [31]}

Viruses are is deliberated as an alive substance inside the host body and as nonliving outside the host body. It may lead to the regular outbreak and does not react appropriately to most of the synthetic drugs. Therefore the natural bio-resources is in increasing demand to disabling this problem. Bael fruit hydro-alcoholic extract have better antiviral activity against Ranikhet disease virus, which have been also determining Interferon like activity against the same virus. Therefore, bael fruit can be reported to have a better viricidal activity and in the near future it may exploited as a potent antiviral agent. It is also establishing that; bael has antiviral activities during the early stages of viral replication with minimum host cytotoxicity in contrast to recent vermicidal chemotherapeutic agents (i.e ribavirin), which usually effective in the advanced stages of viral infection.

9) Anti-ulcer activity^{[32][33]}

By preparing polyherbal formulation antiviral activity of bael plant was examined by using ethanol induced gastric ulcer model in Wistar rats. This formulation consists of Glycyrrhizia glabra rhizome part (200mg), A. marmelos (L.) Corr leaf part (150 mg), Hemidesmus indicus root part (75mg) and Cumimum cyminum fruit part (75mg). This formulation at the dose of 500 mg/kg was effective to produce moderate inhibition of gastric lesions in ethanol induced ulcer model in wistar rats and compared withOmeprazole 20 mg/kg as standard. The result shows that the effectiveness of this polyherbal formulation in severe gastric ulcer. Even it is non-toxic at relatively high doses. Pyranocoumarin isolated from the seeds of Aegle marmelos, has protective effect against pylorus-ligated and aspirin-induced gastric ulcers on oral administration. A significant inhibition of absolute ethanol induced gastric mucosal damage can be produced by unripe bael fruit extract. Peptic ulceration in the most significant adverse effect produced by NSAIDs. Even though H2 blockers and proton pump inhibitors effectively prevent NSAID induced peptic ulcers, but both of them have measurable side effects. Therefore, it is necessary to prevent the NSAIDs induced peptic ulcers producing side effects. In traditional Indian medicine there are two products which are commonly used to treat peptic ulcers namely Aloe vera leaf extract and Aegle marmelos leaf extract. Therefore, this study was directed to evaluate the anti ulcerogenic potential of combining the two drugs compared with standard drug ranitidine in preventing NSAID-induced peptic ulcers.

10) Antiarthritis activity^[34]

A. Marmelos leaves were stated to have antiarthritis activity against collagen induced arthritis in Wistar rats. Methanol extract of A. marmelos showed the significant reduction of the paw swelling and arthritic index in rats. Also, reduction in Radiological and histopathological changes were also significantly showed in methanol extract treated rats.

11) Radioprotective Activity^[7]

Exposure of different doses of gamma-radiation in mice and found after oral administration of extract of Aegle marmelos results in an increase in radiation toleranceby 1.6 Gy. Effects of plant extract on the peripheral blood and small intestine of Swiss albino mice has also been studied. They proved that on exposure of animals to gammaradiation and collected the data against radiation-induced alterations in the peripheral blood, spleen colony forming units, and intestinal mucosa, informed that Aegle marmelos extract considerably lowers the harmful effect of radiation in the intestine and bone marrow of a mouse.

12) Antispermatogenic Activity^[35]

Ethanolic extract of Aegle marmelos leaves reported to have antispermatogenic activityin rats. Again anti motility of rat sperms through In Vitro study has been also presented. The in vitro effect of ethanol extracts of leaves of A. marmelos on sperm motility has been stated and was recommended a significant effect of extract on the motility of sperm. It was also suggested that if there is increase in concentration of the extracts leads to decrease in motility of sperms.

Miscellaneous uses^{[1][36][37]}

- The bael plant has diuretic and laxative effect, due to the presence of marmelosin derived from pulp. It depresses cardiac action, causes sleepiness and reduce therate of respiration, in increasing dose.
- A mild laxative, tonic and digestive effects produced by the "sherbet" and freshripe pulp of higher value cultivars made from bael.
- In cases of haemorrhoids, the unripe fruit decoction, with fennel and ginger, is prescribed.
- It has been concise that the psoralen in the pulp rises tolerance of sunlight and helps to maintain of normal colour of skin. It is active to cure leucoderma.
- In India in the summer month, the unriped bael fruit is most prized as means of halting diarrhea and dysentery because of astringency, especially of the wild fruits.

CONCLUSION

From the above review, it can be resolved that Aegle marmelos is used traditionally for many years as described in various literatures. Much of the traditional uses has been authenticated by scientific research. Researchers have exploited the plant to expose its medicinal values successfully. It is an important species that has economic and ecological significance and should be preserved for ecological perspectives. Several new activities were reported by researchers and hence the plant is now gaining importance to improve some more new search for the future development. Therefore by considering its versatile medicinal uses, there is an ample scope for future research on bael, and hence further pharmacological investigations are warranted. Further research can be carried out to explore the unexploited and unexplored prospective of these plant and study mechanism of action and therapeutic activities.

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