



EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

<u>Review Article</u> ISSN 2394-3211 EJPMR

A COMPREHENSIVE REVIEW ON MEDICINAL PLANT: AEGLE MARMELOS (LINN) CORREA

¹*Saliya Parveen Gulam Rasool and ²Mohamed Hassan Dehghan

^{1,2}Department of Pharmaceutics, Y.B Chavan College of Pharmacy, Aurangabad, 431001.

*Corresponding Author: Saliya Parveen Gulam Rasool

Department of Pharmaceutics, Y.B Chavan College of Pharmacy, Aurangabad, 431001.

Article Received on 06/02/2022

Article Revised on 27/02/2022

Article Accepted on 20/03/2022

ABSTRACT

The plants are the good substitution for the medicines because of their less or no side effect and their ability to cure the problem from their root. The present study gives the complete profile of aegle marmelos belongs to family *Rutaceae*, commonly known as a bael in India. This review gives the detailed information about the phytochemistry and pharmacological activity of aegle marmelos. A number of biologically active compounds (Alkaloids, Terpenoids, Vitamins, Coumarins, Tannins, Carbohydrates, Flavonoids, Fatty Acids, and Essential Oils) isolated from various parts of aegle marmelos, which belongs to various chemical groups. This plant is having great prospective to cure the disease like diabetes, cholesterol, peptic ulcer, inflammation, diarrhea, and dysentery, anticancer, cardio protective, anti bacterial, anti fungal, radio protective, anti pyretic, analgesic, constipation, respiratory infection, antioxidant, hepatoprotective, wound healing and many more. Hence, this review may be a good reference for the researchers who are willing to commence further investigation about aegle marmelos.

KEYWORDS: Aegle marmelos, Ehanobotanical description, Phytochemistry, Pharmacological activity.

INTRODUCTION

The universal role of plants in the treatment of disease is exemplified by their employment in all the major system of medicine irrespective of the underlying philosophical premise. Plants have at one time supplied virtually all cultures with food, clothing, shelter and medicine. It is estimated that approximately 10 to 15 percent of roughly 300,000 species of higher plant, have a history of use in traditional medicine. In terms of both quantity and value of the medicinal plant exported India ranks second in the world. Plants are the very important for the human, because they possess several active constituents, which are the precursor for the synthesis of many drugs. Humans are considered as most developed among all living species on earth. They are adopting plants not only as an origin of food but also to delight various ailments of humankind since ancient age. Several plants or plant parts are used to heal a number of physical and mental disturbances and helps us to withstand successfully.

Aegle marmelos, "Fig 1" a plant of Indian origin having tremendous therapeutic potential, belongs to family Rutaceae. This plant is familiar with several names like Bael, Bengal quince, Golden apple, Wood apple, etc. Every part of plant such as fruit, seed, bark, leaves and root is used as an ingredient of several traditional formulations. Due to its curative properties, it is one of the most useful medicinal plants of India. The product obtained from bael, being highly therapeutic and is being popularized in India and international market. It is a subtropical plant, which grows in the dry forest of hilly and plain area and found in Bihar, Chhattisgarh, Uttar Pradesh, Uttarakhand, Jharkhand and Madhya Pradesh. Bael is a scared tree of Hindus as its leaves are offered to Lord Shiva for fulfillment of wishes. The tree is symbol of fertility.

It is cultivated as temple garden plant and the leaves of *Aegle marmelos* L. are use for praying Lord Shiva "Fig 2". Its fruits are use as food as well as traditional medicine "Fig 3".

The special focus of this review highlights the morphology, phytochemistry, traditional use and medicinal uses of *Aegle marmelos* for its further investigation and development of active constituents.



Fig 1: Aegle marmelos plant.



Fig 3: Aegle marmelos fruit.

TAXONOMICAL CLASSIFICATION

The detailed taxonomical classification of *Aegle* marmelos is given in Table 1.^[6,14,15]

Table 2: Vernacular names of Aegle marmelos.



Fig 2: Aegle marmelos leaves.

Table 1: Taxonomical classification of Aeglemarmelos.

| Sr. no. | KINGDOM | PLANTAE | | |
|---------|--------------------------------------|---|--|--|
| 1 | Subkingdom | Tracheobionta | | |
| 2 | Super division | Spermatophyta | | |
| 3 | Division | Magnoliophyta | | |
| 4 | Class | Magnoliopsida | | |
| 5 | Subclass | Rosidae | | |
| 6 | Order | Sapindales | | |
| 7 | Family | Rutaceae | | |
| 8 | Genus | Aegle | | |
| 9 | Species | Aegle marmelos | | |
| | 1 2 3 4 5 6 7 8 | 1Subkingdom2Super division3Division4Class5Subclass6Order7Family8Genus | | |

VERNACULAR NAMES OF AEGLE MARMELOS

Aegle marmelos is extensively distributed all over India and is acknowledged by various names at various places. The details of vernacular names are listed in Table $2.^{[6,13,14]}$

| | Sr. no. Different languages | | Names | | |
|---------------------------------|-----------------------------|--------------------|--|--|--|
| | 1 Bengali | | Bel, Shreefal | | |
| ľ | 2 Burmese | | Ohshit, Opesheet | | |
| Ī | 3 | English | Wood/Stone apple, Bengal Quince, Indian Quince | | |
| | 4 | French | Oranger du Malabar | | |
| | 5 | Indonesian | Mojo tree | | |
| | 6 | Javanese | Modjo | | |
| | 7 | Khmer | Banu | | |
| | 8 | Lao (Sino-Tibetan) | Toum | | |
| | 9 | Latin | Aegle marmelos | | |
| | 10 | Malay | Pokok Maja Batu | | |
| | 11 | Marathi | Kaveeth | | |
| | 12 | Nepali | Bel, Gudu | | |
| | 13 | Old Hindi | Sir Phal | | |
| | 14 | Sanskrit | Shreephal, Bilva, Bilwa | | |
| | 15 | Tamil | VilvaMaram, VilvaPazham | | |
| | 16 | Telugu | Maredu | | |
| | 17 | Thai | Mapin, Matum, Tum | | |
| | 18 | Urdu | Bel | | |
| 19 Vietnamese MbauNau, Trai Mam | | Vietnamese | MbauNau, Trai Mam | | |

www.ejpmr.com

HABITAT AND DISTRIBUTION

Aegle marmelos is a semitropical plant that flourishes at an approximate altitude of 1200 meter from sea level. It is mainly obtained in hill areas and dry forests. The tree has its origin from eastern ghat and central India. It is native to India and bael tree is usually available in the range of Himalaya to west Bengal, in central and south Asia. It grows around foot hill of Uttar Pradesh, Bihar, Chhattisgarh, Madhya Pradesh, Uttaranchal, Jharkhand, The Deccan Plateau, the East coast, Myanmar, srilanka.^[2,7,16,17,18]

BOTANICAL DESCRIPTION

Aegle marmelos is a slow-growing, medium sized tree, up to 12-15 m tall with short trunk, thick, soft, flaking bark, and spreading with spiny branches. A clear, gummy sap, resembling gum Arabic, exudes from wounded branches and hangs down in long strands, becoming gradually solid. It is sweet at first taste and then irritating to the throat. The full botanical description of Aegle marmelos is given in Table 3.^[6,14,19,20]

| Sr. no. | Plant part | Morphological characterization |
|---------|------------|---|
| 1 | Bark | The bark is brownish or grey in colour, contains a number of straight long spines. It contains gums, which often comes out from wounded branches and then becomes solid. These gums can be explained as a clear, gummy sap. It is sweet at first taste and then irritating to the throat. |
| 2 | Leaf | Its leaves are trifoliate, having round base and pointed tip. Young leaves are light green and matured leaves are dark green in colour |
| 3 | Flower | The flowers are greenish or yellowish in colour and bisexual in nature. Generally, it is visible with new leaves. |
| 4 | Fruit | The bael fruit has a hard-outer jacket and having a diameter of approximately 5 to 12 centimeters. It is green in unripe condition and changes to yellowish brown when ripen. It contains up to 20 orange pulp in the inside. |
| 5 | Seed | The seeds are small (nearly 1 cm in length), hard, flattened-oblong, bearing woolly hairs and each enclosed in adhesive sac |

Table 3: Botanical description of Aegle marmelos.

EHANOBOTANICAL DESCRIPTION

Aegle marmelos is one of the most useful Indian medicinal plants; it has numerous of use in day-to-day life. Each plant parts are used for preparation of several medicines. Among different parts, fruit is one of the important parts that can cure maximum number of diseases. Bael leaf extract is used to cure ophthalmia, ulcer and intestinal worms by twice-daily intake. Treatment of eye diseases requires poultice that are obtained from bael leaf. A mixture of boiled rice water and unripe fruit pulp cures vomiting during pregnancy by taking twice daily. Fruit is eaten during convalescence after diarrhea. The ripe fruit promotes digestion and is helpful in treating inflammation of rectum. Fine powder of unripe fruit showed significant use on intestinal parasites and effective against *Entamoeba histolytica* and *Ascaris lumbricoides*.

The decoction of root and sometimes the stem bark is useful in intermittent fever, also in hypochondriasis and palpitation of the heart. The detailed description is given in table 4.^[6,21-38]

| Sr. no. | Plant part | Ehanobotanical use | | |
|------------|---------------|--|--|--|
| 1 | Leaf | Abscess, backache, eye complaints, abdominal disorders, vomiting, cut and wounds, ulcer, dropsy, beriberi, weakness of heart, cholera, diarrhea, cardio tonic, blood sugar, injuries caused by animals, nervous disorders, hair tonic, acute bronchitis, child birth. Veterinary medicine for wounds, killing worms, fodder for sheep, goat and cattle, stimulation of respiration and contraction of denervosed nictitating membrane in anaesthetized cats. | | |
| 2 | Fruit | Astringent, diarrhea, gastric troubles, constipation, laxative, tonic, digestive, stomachic, dysentery, brain and heart tonic, ulcer, antiviral, intestinal parasites, gonorrhea, epilepsy. Toys, edible, jam, preserve. | | |
| 3 | Root | Dog bite, gastric troubles, heart disorders, intermittent fevers, antiamoebic, hypoglycemic, rheumatism. | | |
| 4 | Bark | Stomach disorder, intermittent fevers, heart disorder. | | |
| 5 | Seed | Febrifuge. | | |
| 6 | Flower | Expectorant, epilepsy. | | |
| 7 | Whole plant | Abdominal pain, abscess, astringent, backache, dog bite, breast pain, cholera, constipation, convulsions, cramp, diabetes, diarrhea, dysentery, fever, eye complaints, gastric trouble, abdominal disorders, jaundice, laxative, nausea, night fever, heart disorders, snakebite, stomach disorder, vomiting, tonic, cut and wounds. | | |
| 8 | Root, Bark | Fish poison. | | |
| 9 | Seed mucilage | Plaster for walls. | | |

Table 4: Ehanobotanical description of Aegle marmelos.

| 10 | Seed oil | Laxative. |
|----|----------------------------|--|
| 11 | Wood | Beads worn by low caste, special couches for rheumatic patients. |
| 12 | Gum around seed | To improve adhesive strength of water paints. |
| 13 | Unripe fruit rind, Bark | Yellow dye. |
| 14 | stem | Pestles of oil and sugar mills. |

PHYTOCHEMISTRY OF AEGLE MARMELOS

Extensive investigations has been carried out on different parts of A. marmelos and as a consequence, varied classes of compound viz., alkaloids, Coumarins, Terpenoids, fatty acids and amino acids have been isolated from its different parts. The details of chemical constituents obtained from Aegle marmelos are given in table 5.

| Sr. no. | Name | Compound | Plant part | Medicinal property and use | Reference |
|---------|------------|--|---------------------------|---|-----------------------|
| 1 | Alkaloids | Aegelenine Aegeline Aegelinosides A Aegelinosides B Dictamine Ethyl cinnamamide Ethyl cinnamate Fragrine Halfordinol | Fruits, leaves | Antidiabetic, antibacterial, anti-inflammatory, and anticancerous | [6,14,39,40,41,42,43] |
| 2 | Coumarins | Alloimperatorin Imperatorin Isoimperatorin Marmelide Marmelosin Marmesin Marmin Psoralen Umbelliferone Methyl ethrer Xanthotoxol Zanthotoxol | All parts | Antidiabetic,antioxidant, anti- inflammatory, and Anti analgesic | [6,14,39,42,44,45] |
| 3 | Terpenoids | Caryophyllene Cineol cis-Limonene oxide cis-Linalool oxide Cubedol Elemol Epi-cubebal Hexanylhexanoate Humulene Isosylvestrene Limonene Linalool Methyl perilate Myrcene P-cymene Terpinolene Valencene Caryophyllene Cineol cis-Limonene oxide cis-Linalool oxide Cubedol Elemol Epi-cubebal Hexanylhexanoate | Fruit,leaves, and bark | Anticancer | |

| Humulene | | | |
|--------------------|--|---|--|
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | Fruits | | [6,46] |
| | | | [0,40] |
| | icuves | | |
| | Fruits | Yellow dye for calico and silk | [6,14,47] |
| | | | [0,14,47] |
| | | | |
| | | | |
| | | Anti-inflammatory | [6,14,46,47] |
| | Fruits | | [0,14,40,47] |
| | | | |
| | | | |
| Rutin | | | |
| Flavone | | | [6,14,48] |
| Flavone-3-ols | | | [0,2.0,0] |
| flavone glycosides | | Antidiabetic | |
| Palmitic Acid | | | |
| Stearic Acid | | | |
| Oleic Acid | Seeds | | [6,46] |
| Linoleic acid | | | |
| Linolenic Acid | | | |
| Alpha-Pinene | | | |
| Beta-Myrcene | | | |
| Alpha-Phellandrene | | | |
| Isosylvestrone | | | |
| Delta-Carene | | | |
| Beta-Ocimene | Laguas | Antimicrobial,antifungal Insecticidal activity | [6,14,49] |
| Linalool | Leaves | | |
| Terpenolene | | | |
| Alpha-Cubebene | | | |
| Alpha-Terpineol | | | |
| Delta-Elemene | | | |
| | | | |
| | FlavoneFlavone-3-olsflavone glycosidesPalmitic AcidStearic AcidOleic AcidLinoleic acidLinolenic AcidAlpha-PineneBeta-MyrceneAlpha-PhellandreneIsosylvestroneDelta-CareneBeta-OcimeneLinaloolTerpenoleneAlpha-CubebeneAlpha-Terpineol | IsosylvestreneLimoneneLinaloolMethyl perilateMyrceneP-cymeneTerpinoleneValenceneThiaminRiboflavinNiacinAscorbic Acid4,7,8-trimethoxyfuro-quinolineGalactoseArabinoseUronic acidL-RhamnoseAralrinoseD-galacluronic AcidFlavoneFlavoneFlavoneFlavoneFlavoneflavone glycosidesInoleic acidLinoleic acidLinoleic AcidStearic AcidOleic AcidStearic AcidOleic AcidJapha-PineneBeta-MyrceneAlpha-PhellandreneIsosylvestroneDelta-CareneBeta-OcimeneLinaloolTerpenoleneAlpha-CubebeneAlpha-Terpineol | IsosylvestreneIsosylvestreneLimaloolIsosylvestreneLinaloolIsosylvestreneMethyl perilateIsosylvestreneMyrceneIsosylvestreneP-cymeneIsosylvestreneTerpinoleneIsosylvestreneValenceneIsosylvestreneThiaminFruits,RiboflavinIsosylvestreneAscorbic AcidIsosylvestrene4,7,8-trimethoxyfuro- quinolineIsosylvestreneGalactose ArabinoseFruits,IsosylvestreneFruitsVonci cacidFruitsUronic acidFruitsD-galacluronic AcidVound healingRutinAntiidepressent, Anticonvulsant, |

NUTRITIONAL VALUE

Physico-chemical studies have revealed that bael fruit is

rich in mineral and vitamins contents. Major components of nutritional importance are listed in Table 6. $^{[50]}$

Table 6: Nutrional value of Aegle marmelos (% or per 100gm).

| Sr. no. | Components | Value(%) |
|---------|-----------------|----------|
| 1 | Water(moisture) | 64.2 |
| 2 | Protein | 1.8 |
| 3 | Fat | 0.2 |
| 4 | Mineral | 1.5 |
| 5 | Fiber | 2.2 |
| 6 | Carbohydrate | 30.6 |
| 7 | Calcium | 0.09 |
| 8 | Phosphorus | 0.05 |
| 9 | Potassium | 0.6 |
| 10 | Iron | 0.3 |
| 11 | Vitamin A | 186 |

I

| 12 | Vitamin B1 | 0.01 |
|----|-----------------|------|
| 13 | Nicotinic acid | 0.9 |
| 14 | Riboflavin | 1.2 |
| 15 | Vitamin C | 0.01 |
| 16 | Calorific value | 129 |

REPORTED PHARMACOLOGICAL STUDIES Antioxidant activity

Antioxidant activity of Aegle marmelos plant is due to the presence of flavones, isoflavones, flavonoids, coumarin lignans, anthocvanin. catechins and isocatechins. Aegle marmelos is extensively reported to possess antioxidant activity against a variety of free radicals. The percentage of free radical inhibition was also high in unripe fruit than that of the ripe fruit. Methanol and aqueous extract of A. marmelos fruit pulp was screened for antioxidant activity by DPPH radical scavenging method, reducing power assay, nitric oxide scavenging assay, superoxide radical scavenging assay, ABTS radical scavenging assay and H2O2 radical scavenging assay. Both aqueous and alcoholic extract exhibited good antioxidant activity.^[41,51,52]

Antimicrobial Activity

The antimicrobial activity of leaves of Aegle marmelos was performed by agar well diffusion method. The aqueous, petroleum ether and ethanol extract of leaves of Aegle marmelos exhibited efficient antimicrobial activity against Escherichia coli, Streptococcus pneumonia, Salmonella typhi, Klebsiella pneumonia and Proteus vulgaris. The ethanolic extract shows activity against Penicillium chrysogenum and the petroleum ether and aqueous extract shows activity against Fusarium presence oxysporum.The of leaf constituents Cuminaldehyde and Eugenol may be responsible for antimicrobial activity. The antimicrobial activity against gram-negative strains was higher than that of gram positive strains.^[51,52,53]

Antifungal activity

The antifungal activity of leaves of *Aegle marmelos* was reported 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.*^[52]

Antidiarrheal Activity

The in vitro Antidiarrheal activity of dried fruit pulps of *Aegle marmelos* was reported. Antidiarrheal activity was performed by MIC method against the causative organisms of diarrhea. The ethanolic extract shows good activity against *Shigella boydii*, *S. sonnei and S. flexneri*, moderate against *S. dysenteriae*.^[52,54]

Anti-constipating effect

Aegle marmelos fruits are generally used to clean and tones up intestine. Most of the available ripe fruits are considered as a natural therapy of various kinds of laxatives. Regular intake of this fruit for two to three months results in evacuation of old accumulated fecal matter from bowels. It is generally taken in the form of 'sherbat', made by pulp of ripe fruit.^[3,6]

Antidiabetic activity

All the extracts of *Aegle marmelos* proved to be active against diabetic rabbits, however, among the various extracts, methanolic extract of leaves showed maximum anti diabetic effect. Methanolic extract (120 mg/kg,p.o.,) was administered to alloxan induced diabetic rats and on 12th day sugar levels was found to be reduced by 54%.^[6,55]

Antiproliferative activity

The stem bark of *Aegle marmelos* ethanolic extract was reported to produce antiproliferative activity against various human tumor cell lines. The results showed the inhibition of in vitro proliferation of human tumor cell lines, including the leukemic K562, T lymphoid Jurkat, Blymphoid Raji, erythroleukemic HEL, melanoma Colo38, and breast cancer MCF7 and MDAMB-231 cell lines.^[6,52]

Cytoprotective effect

This effect of the leaves of Aegle marmelos was reported in Cyprinus carpio (fresh water fish). Cyprinus carpio was exposed to heavy metals followed by the treatment with the dried powder of Aegle marmelos leaves. This Treatment resulted in cytoprotective effect by stabilization of plasma membrane and modulation of antioxidant enzyme system.^[52,56]

Hepatoprotective Effect

The study of Aegle Marmelos leaves extract on alcohol induced liver injury in albino rats and shows excellent hepatoprotective effects. Similarly, aqueous extract of bael fruit pulp and seeds are effective in the treatment and prevention of CCI4 induced hepatic toxicity.^[57]

Antifertility effect

The aqueous extracts of leaves of Aegle marmelos show antifertility effect in male Albino rats. The rats were administered with aqueous extracts (250 mg/kg body weight) for 45 days. This treatment resulted in reduction in the weights of testis, epididymes and seminal vesicle. The extract also resulted in reduction of testicular sperm count, epididymal sperm count and motility and abnormal sperm count.^[58]

Analgesic activity

The methanolic extract of Aegle marmelos leaves were reported for antinociceptive response using writhing and tail immersion test in mice. Maximum possible effects of methanolic extract (200 mg/kg p.o.) were more statistically significant when compared to other doses. It concludes that methanolic extract of Aegle marmelos leaves produces significant analgesic activity.^[59]

Antiarthritis activity

Aegle marmelos leaves were reported to be active against collagen induced arthritis in Wistar albino rats. Radiological and histopathological changes were also significantly reduced in methanol extract treated rats.^[60]

Contractile activity

The contractile activity of alcoholic extract of Aegle marmelos leaves were reported on guinea pig isolated ileum and tracheal chain due to its traditional use in treating asthma and related afflictions. Alcoholic extract of A. marmelos leaves 1 mg/ml and 2 mg/ml as a low and high dose respectively; it showed maximum relaxation of guinea pig ileum and tracheal chain due to the depression of H1 receptors.^[61]

Antihyperlipidemic activity

Aegle marmelos were evaluated in diet induced hyperlipidemic models of Wister albino rats at a dose of 125 and 250mg/kg dose. Aqueous extracts of fruits and seeds were applied to streptozotocin induced diabetic rats through oral administration significantly reduces tissue lipid profile and serum.^[62-63]

Counteracting Cardiotoxic effect

Alcoholic extract of aegle marmelos unripe fruit were found to perform cardioprotective effect in isoproterenol induced myocardial infarction. A very potent compound named as auraptene, is responsible for this activity.^[64]

Anticancer activity

The anticancer potential 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 extracts of Aegle marmelos were shows toxicity on all used assays.^[65]

Antiviral activity

Hydro alcoholic extract of aegle marmelos produces antiviral activity against Ranikhet disease virus. Interferon like activity against the same virus is also reported. Thus, aegle marmelos can be used as a better viricidal potential and may be exploited as a potent antiviral agent in near future.^[66]

Anti-ulcer activity

Pyranocoumarin isolated from the seeds of Aegle marmelos, and its oral administration showed significant protection against pylorus-ligated and aspirin-induced gastric ulcers in rats and cold restraint stress-induced gastric ulcers in rats and guinea pigs.^[67]

Antimalarial activity

A. marmelos root extract shows antimalarial activity against the parasite *Plasmodium falciparum* (K1,

multidrug resistant), using the method of Trager and Jensen. Quantitative assessment of in-vitro antimalarial activity was determined by means of the micro culture radioisotope technique. The IC50 or inhibitory concentration produced the concentration which showed in 50% decrease in parasite growth that was indicated by the in-vitro uptake of [3 H] – hypoxanthine by *P. falciparum*. Dihydro artemisinin were taken as standard compound (IC50 4.1 nmol L).^[68,69]

Anti-micro filarial activity

Methanolic extract of *Vitex nigundo L*. roots and leaves of *Vitex nigundo L*., *Ricinus communis L*. and *Aegle marmelos Corr* were tested for possible antifilarial effect against Brugia malayi microfilariae. Microfilariae were obtained by lavage of the peritoneal cavities of jirds with intraperitoneal filarial infection of 3 months or more duration. Out of all observed extracts, Vitex nigundo L. root extract and A. marmelos Corr. leaves extracts at 100 mg/ml concentration shows total loss of motality of microfilariae after 48 hours incubation.^[70]

Anticonvulsant activity

The anticonvulsant activity of ethanolic extract of *aegle marmelos* leaves on maximal electroshock (MES) and pentylenetetrazole (PTZ) in male mice were performed. The extracts were administered orally in mice at 100 and 200 mg/kg doses. At 200 mg/kg dose, the extract suppressed hind limb tonic extensions (HLTE) induced by MES and shows protector effect in PTZ-induced seizures. As ethanolic extract of *Aegle marmelos* leaves delayed the occurrence of MES and PTZ convulsions, it can be concluded that it interfere with gabanergoc mechanisms for producing anticonvulsant effect and it reveals presence of flavonoid that are attributed to their anticonvulsant action.^[71]

Antihistaminic activity

The effects of Skimmianine (obtained from roots of *Aegle marmelos*) on histamine release from rat, mast cells are tested. Two cell lines were used for this study namely, rat basophilic leukemia (RBL-2H3) and rat peritoneal mast cells (RPMCs). DNP24-BSA, thapsigargin, ionomycin, compound 48/80 were applied as inducers for histamine release from rat mast cell. Based upon the docking scores, Skimmianine highly inhibited histamine release by acting on histamine H1 receptor from RBL-2H3 cells induced by DNP24-BSA, thapsigargin and ionomycin.^[72]

Antidepressant and anxiolytic activity

Methanolic extract of *Aegle marmelos* leaves shows antidepressant and anxiolytic activities and its interaction with antidepressant and anxiolytic drugs using tail suspension test and elevated plus maze in mice were reported. The result were observed including time spent on, number of entries into, number of stretch attend postures and number of head dips in arms of elevated plus maze and immobility duration in tail suspension test. These activities are possibly due to increasing monoamines level at postsynaptic sites that has been confirmed by several other methods. From result, it can be concluded that methanolic extract of Aegle marmelos leaves shows potent anxiolytic and antidepressant activities and it enhances the antidepressant and anxiolytic activities of Imipramine and Fluoxetine.^[73]

Anti-stress and adaptogenic activity

Aqueous extract of Aegle marmelos were studied for anti-stress and adaptogenic activities by using Swimming endurance and post-swimming motor function test, Cold swimming endurance test and forced swim test in albino rats of either sex. When extracts were subjected to forced swim model for adaptogenic activity in rats, failed to show an increase in serum cholesterol and serum triglyceride level, but increase were not sustained on subsequent groups. It enhances swimming endurance time along with post motor function like rota rod falling time and spontaneous motor activity. These extract enhances cold swimming endurance time and could restrict the increase in the level of these markers during stress.^[74]

Radio protective effect

Radio protective effect of Aegle marmelos extract was studied by exposing to different doses of gammaradiation in mice and found that oral administration of extract resulted in an increase in radiation tolerance by 1.6 Gy. Again, study shows, the effects of plant extract on the peripheral blood and small intestine of Swiss albino mice. They exposed the animals to gamma radiation and data were collected against radiation-induced changes in the peripheral blood, spleen colony forming units, and intestinal mucosa, reported that Aegle marmelos extract significantly reduces the deleterious effect of radiation in intestine and bone marrow of mouse.^[75,76]

Wound healing activity

The effect of methanolic extract of Aegle marmelos seeds ointment and injection were observed by Excision wound models in male Wister rats. The wounds were treated topically with application of ointment till the wounds were completely healed.76 The wounds were monitored and measured on 0, 4, 8, 12, 16 and 20 post wounding day.

By following the method of Ehrlich and Hunt, Incision wound model were performed in male Wister rats. The wounds were treated with extract ointment daily for 10 days. Post 9th day, sutures were removed and wound was measured using tensiometer by the method of Lee.

In the excision model, the extract epithelializes faster and showed higher rate of contracting wounds as compared with control. The extract showed healing process as evidenced by increase tensile strength in incision model. The results were compared with standard drug nitrofurazone.^[77,78]

Anti thyroid Activity

Isolated, Scopoletin (7-hydroxy-6- methoxy coumarin) from Aegle marmelos leaves and its potential effect to regulate hyperthyroidism were investigated. It was observed that scopoletin (at 1.00 mg / kg, p.o. for 7 days) to levothyroxine treated animals, decreased serum thyroid hormones level. It was also proved that the scopoletin have superior therapeutic activity than the standard antithyroid drug, propylthiouracil.^[79]

Toxicity studies

The leaves of Aegle marmelos were studied for its acute and sub acute toxicity properties. The different extracts of the Aegle marmelos leaves were tested in Wistar albino rats for its LD50 values, acute and sub acute toxicity effects. The results revealed that LD50 value of the different extracts, ranging from 1300 mg to 1700 mg/kg body wt. During acute toxicity, dead animals usually presented with their hearts stopped in systolic standstill. There were no remarkable changes noticed in the histopathological studies after 50 mg/kg body wt (daily, 14 days).^[80]

FUTURE ASPECTS

Aegle marmelos contains a large number of phytoconstituents hence it can be used for the treatment of various disorders in human being. Most of the compounds have not properly been evaluated for the exploration of new lead molecule or pharmacophore. However, mechanisms of action of a few bioactive compounds have been identified so far. Thus, in the near future aegle marmelos could be further exploited as source of useful phytochemical compound and may play a very important role in modern system of medicines.

CONCLUSION

Aegle marmelos is one of the important plants with several medicinal and nutraceutical properties. It has several medicinal properties, which are used in traditional medicinal system and used to cure several diseases. In last few decades, Aegle marmelos is extensively studied for its medicinal properties by advanced scientific techniques and a variety of bioactive compounds have been isolated from the different part of plant and were analyzed pharmacologically. This review summarized its various botanical description, phytoconstituents and pharmacological activities i.e. antibacterial, antifungal, antiviral, antidiabetic, antimalarial, antioxidant etc. in detailed.

ACHKNOWLEGEDMENT

I am very thankful to my husband Mohammed Nabeel Ahmed for their support and having trust on me during the work of my review. In addition, a special thanks to my guide M.H Dehghan for the great cooperation throughout the writing of review. Also thankful to Y.B Chavan campus for providing the facilities to carry out this review.

REFERENCES

- 1. Evans William Charles, Pharmacognosy, 16th edition. Saunders Elsevier, Edinburgh, 2009; 3-4.
- 2. Barrett Marilyn, The Hand Book of Clinically Tested Herbal Remedies, 1st edition, CBS Publishers and Distributers, New Delhi, 2007; 3-6.
- Sharma PrabodhChander, Bhatia Vivek, et al, A Review on Bael Tree, Natural Product Radiance, 2007; 6(2): 171-178.
- Dhankhar Sandeep, Ruhil S, et al, Aegle marmelos Correa: A Potential Source of Phytomedicine. Journal of Medicinal plant Research 2011; 5(9): 1497-1507.
- Balunas MJ, Kinghorn AD. Drug Discovery from Medicinal Plants. Life Sciences, 2005; 78(5): 431-41.
- Kausik Bhar, Sumanta Mondal, Padilam Suresh, An Eye-Catching Review of Aegle marmelos L. (Golden Apple), Pharmacogn J., 2019; 11(2): 207-224
- Pushpendra K. Patel, et al,Aegle marmelos:A Review on its Medicinal Properties, Int. J. Pharm. Phytopharmacol. Res., 2012; 1(5): 332-341.
- Sharma GN, Dubey SK, Sharma P, Sati N. Medicinal Values of Bael (Aegle marmelos) (L) Corr: A Review. International Journal of Current Pharmaceutical Review and Research, 2007; 1(3): 2011.
- 9. Sharma VK. In: Wasteland Horticulture, APH Publishing Corporation, New Delhi, 1997; 40: 89.
- 10. Singh S. Standardization of processing technology of bael (Agele marmelos Correa). Thesis Doctor of Philosophy in Horticulture, College of Agriculture CCS, HAU, Hisar, 2000.
- 11. Jain SK, Sastry ARK. Threatened Plants in India. Calcutta: Botanical Survey of India, 1979.
- Ramveer Singh, Ajeet Singh, et al, Ethno-medicinal and Pharmacological activities of Aegle marmelos (Linn.) Corr: A review, The Pharma Innovation Journal, 2019; 8(6): 176-181.
- The Ayurvedic Pharmacopoeia of India, Government of India, Ministry of Health and Family Welfare, Department of Ayush, India, 1999; 1(1): 35-6.
- 14. Desai nilesh V et al, A review on aegle marmelos: A potential medicinal tree, International research journal of pharmacy, 2012; 3(8).
- 15. Nidhi S, Widhi D. History and Taxonomy of Aegle marmelos: A Review. International Journal of Pure and Applied Bioscience, 20.
- 16. Lambole Vijay B, Murti Krishna, *et al.*, Phytopharmacological Properties of Aegle marmelos as a Potential Medicinal Tree: An Overview. International journal of Pharmaceutical Review and Research, 2010; 5(2): 67-71.
- Behl PN, Srivastava G, Herbs useful in Dermatological Therapy, 2nd edition, CBS Publishers and Distributers, New Delhi, 2002; 17-19.

- 18. Joshi PV, Patil RH, et al, In Vitro Anti diarrhoeal Correa ex Roxb. DriedA mixture of boiled rice water and unripe fruit pulp cures vomiting during pregnancy by taking twice daily. Fruit Pulp. Natural Product Radiance, 2009; 8: 498-502.
- Lambole VB, Murti K, Kumar U, Sandipkumar PB, Gajera V. Phytopharmacological properties of Aegle marmelos as a potential medicinal tree. International Journal of Pharmaceutical Sciences Review and Research, 2010; 5(2): 67-72.
- 20. Vijay D. Havaldar, et al, A Systematic Review on Aegle marmelos (Bael), Research Journal of Pharmacognosy and Phytochemistry, January -March, 2020; 12(1).
- Dhankhar S, aegle marmelos(linn).correa; a source of phytomedicines, J Medi Plant Res., 2010; 5(9): 1497-1507.
- 22. Sukhdev AR. A selection of prime ayurvedic plant drugs-Ancient modern concordance. Anamaya publication, 2003; 55-58.
- 23. Rajadurai M. Comparative effect of aegel marmelos extract and alpha tocopherl on serum lipid, lipid peroxides and cardiac enzyme level in rats with isoproterenol induced myocardial infarction Sing Med J., 2005; 46(2): 78-81.
- 24. Kirtikar KR, Basu.B.D, indian medical plant, international book publication, 1995; 1: 499-502.
- 25. Robber J E, Tyler V E, Herbs of choice- The therapeutic use of phytomedicines, int J phrmsci, 2002; 3(2); 199-203.
- 26. Kala CP. Ethnobotany and ethnoconservation of A. marmelos (L.) Correa. Indian Journal of Traditional Knowledge. 2006;5(4):537-40.
- Chandra PK. Ethnobotany and ethnoconservation of Aegle marmelos (L.) Correa. Indian Journal of Traditional Knowledge, 2006; 5(4): 537-40.
- 28. Kala CP. Ethnobotany and ethnoconservation of A. marmelos (L.) Correa. Indian Journal of Traditional Knowledge, 2006; 5(4): 537-40.
- 29. Anonymous. The Wealth of India: Raw Materials Series. Publications and Information Directorate, New Delhi, 1989; 33-4.
- Parmar C, Kaushal MK. Wild Fruits of the sub-Himalayan Region, Kalyani Publishers, New Delhi, 1982; 136.
- Jain SK. Dictionary of Indian Folk Medicine and Ethno-botany. Deep Publications, New Delhi, 1991; 311.
- 32. Grieve M, Leyel CF. A Modern Herbal, Tiger Books International, London, 1992; 770.
- 33. Gaur RD. Flora of the district Garhwal North West Himalaya with ethnobotanical notes, TransMedia, Srinagar Garhwal, 1999; 811.
- Kaushik P, Dhiman AK. Medicinal Plants and Raw Drugs of India, Bishen Singh Mahendra Pal Singh, Dehradun, 1999; 623.
- 35. Veerappan AK, Srinivasan RD. Cardiotonic effect of A. marmelos Corr. on amphibian heart in-situ preparation. Proc 6th Internet World Congress for Biomedical Sciences. 2000.

- 36. Available from: <u>www.uclm.es/inabis2000/posters/files/133/index.ht</u> m
- George KV, Mohanan N, Nair SS. Ethnobotanical investigations of A. marmelos (Linn) Corr, in: Ethnobotany and Medicinal Plants of India and Nepal, by Singh V and Jain AP, Scientific Publishers, Jodhpur, 2003; 29-35.
- Anonymous, international cyber business services. 2000.www. holistic-online.com/herbal-med/-herbs/h 134.htm.
- 39. Chamila Kumari Pathirana et al, review article;Bael (Aegle marmelos L. Corre^a), a Medicinal Tree with Immense Economic Potentials, Hindawi Advances in Agriculture Volume 2020, Article ID 8814018, P ++13.
- 40. A. Shoeb, R. S. Kapil, and S. P. Popli, "Coumarins and Alkaloids of Aegle marmelos," Phytochemistry, 1973; 12: 2071-2072.
- S. Rajan, M. Gokila, P. Jency, P. Brindha, and R. H. Sujatha, "Antioxidant and phytochemical properties of aegle marmelos fruit pulp," International Journal of Current Pharmaceutical Research, 2011; 3: 65– 70.
- 42. V. B. Lambole, K. Murti, U. Kumar, B. P. Sandipkumar, and V. Gajera, "Phytopharmacological properties of Aegle marmelos as a potential medicinal tree: an overview," International Journal of Pharmaceutical Sciences Review and Research, 2010; 5: 67–72.
- A. Chatterjee, R. Sen, and G. D. Aegelinol, "Amonorlactonic constituent of Aegle marmelos," Phytochemistry, 1977; 17: 328-329.
- 44. T. Sarkar, M. Salauddin, and R. Chakraborty, "Indepth pharmacological and nutritional properties of bael (aegle marmelos): a critical review," Journal of Agriculture and Food Research, 2020; 2: 100081.
- 45. Bramhachari PV, Reddy YK. Phytochemical examination, Antioxidant and radical scavenging activity of A. marmelos (L.) Correa extracts. J Pharm Res., 2010; 3(12): 3023-5.
- 46. Kumar KPS, Umadevi M, Bhowmik D, Singh DM, Dutta AS. Recent trends in medicinal uses and health benefits of Indian traditional herbs Aegle marmelos. The Pharma Innovation, 2012; 1(4): 57-65.
- 47. Daniel M. Medicinal plants-chemistry and properties of medicinal plant. IBH publication, 2006; 147.
- Sivraj R, Balakrishnan A. Preliminary phytochemical analysis of Aegle marmelos. Int J Pharm Sci Res., 2011; 2(1): 146-50.
- 49. Nabaweya AI, Fatma SES, Magdy MDM, Mohamed AF, Nayera AMAW, Doaa AHD. Chemical composition, antimicrobial and antifungal activities of essential oils of the leaves of A. marmelos (L.) Correa growing in Egypt. Journal of Applied Pharmaceutical Science, 2015; 5(2): 001-5.
- 50. Prabodh chander shrma et al, a review on bael tree; natural product radiance, 2007; 6(02): 171-178

- 51. Sharmila S, Devi PAV. A review on: Aegle marmelos. Journal of Pharmacy Research, 2011; 4: 720-2.
- 52. Bhaskara Rao et al, A review on pharmacological and phytochemical properties of Aegle marmelos (L.) Corr. Serr. (Rutaceae); Asian Journal of Plant Science and Research, 2011; 1(2): 8-17
- 53. Duke JA. Handbook of Biologically Active Phytochemicals and Their Activities, CRC Press, 1992.
- 54. P.V. Joshi, R.H. Patil, V.L. Maheshwari, invitro anti diarrhoeal activity and toxicity profile of aegle marmelos;Natural Product Radiance, 2009; 8: 498-502.
- 55. Sabu MC, Kuttan R. Antidiabetic activity of Aegle marmelos and its relationship with its antioxidant properties. Indian J Physiol Pharmacol, 2004; 48(1): 81-8.
- 56. R. Vinodhini, M. Narayanan, Cytoprotective effect of Nelumbo nucifera and Aegle marmelos in Common Carp (Cyprinus carpio L.) exposed to heavy metals; International Journal of Integrative Biology, 2009; 7: 124-129.
- 57. Ganesh N. Sharma et al, Medicinal Values of Bael (Aegle marmelos) (L.) Corr.: A Review, IJCPR, February-April 2011; 2(1).
- 58. K. Sathiyaraj, A. Sivaraj, G. Madhumitha, P.V. Kumar, A.M. Saral, K. Devi, B.S. Kumar, Pharmacological aspects of Asian Natural Plant Aegle marmelos (L.) Correa Int. J. Curr. Pharm. Res., 2010; 2: 26-29.
- 59. Shankarananth V, Balakrishnan N, Suresh D, Sureshpandian G, Edwin E, Sheeja E. Analgesic activity of methanol extract of A. marmelos leaves. Fitoterapia, 2007; 78(3): 258-9.
- 60. Trivedi HP, Pathak NL, Gavaniya MG, Patel AK, Trivedi HD, Panchal NM. A. marmelos suppresses inflammation and cartilage destruction in collageninduced arthritic rat. International Journal of Pharmaceutical Research and Development, 2011; 3: 38-45.
- 61. Arul V, Miyazaki S, Dhananjayan R. Mechanisms of the contractile effect of the alcoholic extract of A. marmelos Corr. on isolated guines pig ileum and tracheal chain. Phytomedicine, 2004; 11(7-8): 679-83.
- 62. Kamalakkannan N, Prince PS. Hypoglycemic effect on water extracts of A. marmelos fruits in streptozotocin diabetic rats. Journal of Ethnopharmacology, 2003; 87(2-3): 207-10.
- 63. Narayanasamy R, Leelavinothan P. In-vivo and invitro antioxidant activities of coumarin on chemical induced hyperglycemic rats. International Journal of Pharmaceutical Sciences and Research, 2011; 2(4): 968-78.
- 64. Rajadurai M, Prince PS. Comparative effect of A. marmelos extract and alphatocopherol on serum lipid, lipid peroxides and cardiac enzyme levels in rats with isoproterenol – induced myocardial infarction. Singapore Med J., 2005; 46(2): 78-81.

- Jagetia GC, Venkatesh P, Baliga MS.; "Aegle marmelos (L.) Correa inhibits the proliferation of transplanted Ehrlich ascites carcinoma in mice", Biol Pharm Bull, 2005; 28(1): 58-64.
- Maity P, Hansda D, Bandyopadhyay U, Mishra DK. Biological activities of crude extracts of chemical constituents of Bael, A. marmelos (L) Corr. Indian Journal of Experimental Biology, 2009; 47(11): 849-61.
- 67. Goel R. K., Maiti R. N, Manickam M.and. Ray A. B. "Antiulcer activity of naturally occurring pyrano cumarin and isocoumarins and their effect on prostanoid synthesis using human colonic mucosa", Indian J Exp Biol., 1997; 35: 1080-83.
- ager W, Jensen JB. Human malaria parasites in continuous culture. Science, 1976; 193(4254): 673-5.
- Desjardins RE, Canfield CJ, Haynes JD, Chulay JD. Quantitative assessment of antimalarial activity in vitro by a semi-automated microdilution technique. Antimicrobial Agents and Chemotherapy, 1979; 16(6): 710-8.
- Sahara KS, Anandhraman V, Meshram VG, Meshram SU, Reddy MV, Tumane PM, et al. Antimicrofilarial activity of methanolic extract of Vitex nigundo and A. marmelos and their phytochemical analysis. Ind J Exp Biol., 2008; 46(2): 128-31.
- Sankari M, Chitra V, Silambujanaki P, Raju D. Anticonvulsant Activity of Ethanolic Extract of A. marmelos Leaves in Mice. Int J Pharm Tech Res., 2010; 2(1): 640-3.
- 72. Nugroho AE, Riyanto S. Effects of skimmianine, a quinoline alkaloid of A. marmelos Corra roots, on the histamine release from rat mast cells. J Bas App Sci., 2010; 6(2): 141-8.
- Kothari S, Minda M, Tonpay SD. Anxiolytic and Antidepressant activities of methanol extract of A. marmelos leaves in mice. Ind J Physiol Pharmacol, 2010; 54(4): 318-28.
- 74. Duraisami R, Mohite VA. Anti-stress, adaptogenic activity of standardized dried fruit extract of A. marmelos against diverse stressors. Asi J Pharm Clin Res., 2010; 3(4): 11-3.
- Jagetia, G C, and Venkatesh, P. "Radioprotection by oral administration of Aegle marmelos (L.) Correa in vivo." J. Environ. Pathol. Toxicol. Oncol., 2005; 24: 315-332.
- 76. Jagetia, G C, Venkatesh, P, Archana, P, Krishnanand, B R, and Baliga, M S., "Effects of Aegle marmelos (L.) Correa on the peripheral blood and small intestine of mice exposed to gamma radiation", J. Environ. Pathol. Toxicol. Oncol., 2006; 25: 611-624.
- Lee KH. Studies in the mechanism action of salicylates II, effect of vitamin A on wound healing retardation action of aspirin. J Pharmacol Sci., 1968; 57(7): 1238-40.
- Jaswanth A, Akilandeswari L, Manimaran V, Ruckmani S. Wound healing activity of Aegle marmelos. Ind J Pharm Sci., 2001; 63(1): 41-4.

- 79. Panda S, Kar A; "Evaluation of the antithyroid, antioxidative and antihyperglycemic activity of scopoletin from Aegle marmelos leaves in hyperthyroid rats", Phytother Res., 2006; 20(12): 1103-5.
- A. Veerappan, S. Miyazaki, M. Kadarkaraisamy, D. Ranganathan, "Acute and subacute toxicity studies of Aegle marmelos Corr., an Indian medicinal plant"; Phytomedicine, 2007; 14: 209-215.