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Review Article

An Eye-Catching Review of *Aegle marmelos* L. (Golden Apple)

Kausik Bhar[1]*, Sumanta Mondal[2], Padilam Suresh[3]

ABSTRACT

Introduction: Plants and their products are a major source for food and medicine that are highly beneficial for various animals and humans. This article focuses on complete profile of *Aegle marmelos* L. which belongs to the family *Rutaceae*, is commonly known as bael, widely available in several places in India. **Ethnobotany:** Traditional use of *A. marmelos* for various diseases includes abdominal disorders, ulcer, cholera, diarrhea, nerve disorders, gonorrhea, heart disorders, dog bite, jaundice, snake bite and many more. A number of biologically active compounds isolated from various parts of *A. marmelos* which belongs to various chemical groups. **Phytochemistry:** The isolated components belong to Alkaloids, Terpenoids, Vitamins, Coumarins, Tannins, Carbohydrates, Flavonoids, Fatty Acids, Essential Oils and some other miscellaneous compounds. **Pharmacological Activities:** The plant also possess various pharmacological activities such as Antioxidant, Antibacterial, Antifungal, Antidiarrheal, Antidiabetic, Antiproliferative, Cytoprotective, Hepatoprotective, Antifertility, Analgesic, Antiarthritis, Contractile, Antihyperlipidemic, Cardioprotective, Radioprotective, Anticancer, Antiviral, Antiulcer, Immunomodulatory and Wound Healing properties. **Conclusion:** Hence this review can be a good reference for researchers who are willing to undertake further investigation about *A. marmelos*.

Key words: *Aegle marmelos*, Ethnobotany, Pharmacological activities, Phytochemistry, Traditional use.

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INTRODUCTION

The journey of life for birds, animals and humans had started with utilization of plants or plant parts as food. Various plant parts like root, steam, leaf, flower and fruits are used by animal kingdom for survival of their lives. 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 mankind 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. Ancient literature such as Rigveda, Yajurveda, Atharvaveda, Charak Samhita and Sushrut Samhita also describes the use of plants for the treatment of various health problems.[1] By considering the importance of plants and their role as medicine, several researches are going on to find the active chemical constituents. Traditional uses of plants or plant parts are showing the direction to the use of plants for specific kind of disease or diseases. In last five decades, these plants have been extensively studied by advanced scientific techniques and reported for various medicinal properties viz, anticancer activity, antibacterial activity, antifungal activity, antidiabetic activity, antioxidant activity, hepatoprotective activity, haemolytic activity, larvicidal activity and anti-inflammatory activity etc.[2]

Aegle marmelos L. (Family: Rutaceae) [Figure 1] is a widely available plant in various places in India. This plant is familiar with sevaeal names like Bael, Bengal quince, Golden apple, Wood apple, etc. It is cultivated as temple garden plant and the leaves of *Aegle marmelos* L. are used for praying Lord Shiva [Figure 2]. Its fruits are used as food as well as traditional medicine [Figure 3]. This is an important medicinal plant having traditional and folk medicines and ethnomedicinal applications. For diarrhoea and dysentery treatment, bael fruit is having traditional application. This plant leaves are the causes of abortion or infertility in women.[3]

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

TAXONOMICAL CLASSIFICATION

The detailed taxonomical classification of *A. marmelos* is given in Table 1.[4]

VERNACULAR NAMES OF *AEGLE MARMELOS*

A. 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.[5]

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Figure 1: *Aegle marmelos* L. plant.

Figure 2: *Aegle marmelos* L. leaves.

Figure 3: *Aegle marmelos* L. fruits.

Table 1: Taxonomical classification of *Aegle marmelos* L.

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

Table 2: Vernacular names of *Aegle marmelos* L.

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

GEOGRAPHICAL DISTRIBUTION

A. marmelos is a semitropical plant that flourish at an approximate altitude of 1200 meter from sea level. It is mainly obtained in hill areas and dry forests. It is found almost all states in India like Himachal Pradesh, Andhra Pradesh, Bihar, Jammu and Kashmir, Kerala, Karnataka, Madhya Pradesh, Maharashtra, Punjab, Rajasthan, Uttar Pradesh, Tamil Nadu and West Bengal.[6] It is also cultivated in Nepal, Myanmar, Vietnam, Tibet, Ceylon, Laos, Cambodia, Malayasia, Sri Lanka, Bangladesh, Thailand, Indonesia, the dried areas of Java, Fiji and some parts of Philippine Islands.

BOTANICAL DESCRIPTION

A. marmelos belongs to the family Rutaceae. It is a slow growing medium to small size tree contains about 25 to 30 feet in height. The steam is soft, thick, a few spiny branches.[7] The full botanical description of *A. marmelos* is given in Table 3.

ETHANOBOTANICAL INFORMATION

According to various Indian Ayurveda practitioners and traditional herbal healers, several parts of *A. marmelos* are used for the treatment of a number of health hazards. Each and every 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. Various types of powder, paste, pills are used which are obtained from bael plant. In the preparation of dasamula, chyavanprash, etc., bael is an important ingredient. Due to its digestive and carminative properties, it is used to cure various diseases. Bael can be considered as an important medicine in Ayurveda for treating chronic diarrhea, dysentery, brain tonic, etc. A good combination of five parts of bael such as root, bark, leaf, flower and fruit can be highly considered as an effective agent for the treatment of certain mental disorders. Fruit powder of bael produces anti-proliferative and anti-cancer activity.[8]

A mixture of boiled rice water and unripe fruit pulp cures vomiting during pregnancy by taking twice daily.[9] Bael unripe fruit pulp mixed with milk and sugar cures urogenital disorders. For the treatment of dysentery and abscess, half roasted unripe pulp mixed with sugar is essential.[8]

Bael leaf extract is used to cure ophthalmia, ulcer and intestinal worms by twice daily intake.[10] Treatment of eye diseases requires poultice that are obtained from bael leaf.[11] Leaf juice is having a number of medicinal importance especially for controlling diabetes. Bael root decoction is given to patient suffering from fever and cold. Root and bark decoction is useful for treating fevers as well as heart disorders.[8] The detailed information is given in Table 4.

PHYTOCHEMISTRY

Several research works have been done to identify active chemical constituents from various parts of bael plant. Extensive investigations have been carried out on different parts of *A. marmelos* and as a consequence, varied classes of compound viz., alkaloids, coumarins, terpenoids, fatty acids and aminoacids have been isolated from its different parts. Notably, majority of reports on the isolation and compound characterizations have been reported by many Indian workers. The details of chemical constituents obtained from *A. marmelos* are given in Table 5.

Table 3: Botanical description of *Aegle marmelos* L.

Plant Part	Morphological characteristics
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.
Leaf	Its leaves are trifoliate, having round base and pointed tip. Young leaves are light green and matured leaves are dark green in colour.
Flower	The flowers are greenish or yellowish in colour and bisexual in nature. Generally, it is visible with new leaves.
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 upto 20 orange pulp in the inside.
Seed	The seeds are small (nearly 1 cm in length), hard, flattened-oblong, bearing woolly hairs and each enclosed in adhesive sac.

Table 4: Ethnobotanical information of *Aegle marmelos* L.

Plant part	Ethnobotanical uses
Leaf	Abscess, backache, eye complaints, abdominal disorders, vomiting, cut and wounds, ulcer, dropsy, beriberi, weakness of heart, cholera, diarrhoea, cardio tonic, blood sugar, injuries caused by animals, nervous disorders, hair tonic, acute bronchitis, child birth.[12,15,16,18,21,23] Veterinary medicine for wounds, killing worms, fodder for sheep, goat and cattle, stimulation of respiration and contraction of denervosed nictitating membrane in anaesthetised cats.[12,18,20,22]
Fruit	Astringent, diarrhoea, gastric troubles, constipation, laxative, tonic, digestive, stomachic, dysentery, brain and heart tonic, ulcer, antiviral, intestinal parasites, gonorrhoea, epilepsy.[12,16,17,18,21] Toys, edible, jam, preserve.[14,18,19]
Root	Dog bite, gastric troubles, heart disorders, intermittent fevers, antiamoebic, hypoglycaemic, rheumatism.[15,21]
Bark	Stomach disorder, intermittent fevers, heart disorder.[21,23]
Seed	Febrifuge.[12]
Flower	Expectorant, epilepsy.[16,17]
Whole plant	Abdominal pain, abscess, astringent, backache, dog bite, breast pain, cholera, constipation, convulsions, cramp, diabetes, diarrhoea, dysentery, fever, eye complaints, gastric trouble, abdominal disorders, jaundice, laxative, nausea, night fever, heart disorders, snakebite, stomach disorder, vomiting, tonic, cut and wounds.[12,13,15,16,17,18,21,23]
Root, Bark	Fish poison.[18]
Seed mucilage	Plaster for walls.[22]
Seed oil	Laxative.[17]
Wood	Beads worn by low caste, special couches for rheumatic patients.[14,19,22]
Gum around seed	To improve adhesive strength of water paints.[22]
Unripe fruit rind, Bark	Yellow dye.[19,22]
Stem	Pestles of oil and sugar mills.[19,22]

Table 5: Phyto-constituents isolated from *Aegle marmelos* L.

Isolated Chemical Compounds	Reference
Alkaloids	
Ethyl Cinnamate	24, 25
O-3,3-(di methylallyl) halfordinol	24, 25
N-2-methoxy-2-[4-(3',3'-dimethylallyloxy) phenyl] ethyl cinnamate	24, 25
N-2-ethoxy-2-ethyl cinnamid	32
Halfordino	36
Marmeline	36
Anhydromarmeline	35
Aegelinosides A	35
Aegelinosides B	35
Terpenoids	
α-Phellandrene	27
p-cymene	27
P-Menth-1-en-3,5-diol	27
Limonene	24, 26
α-Pinene	32
β-Myrcene	32
Isosylvestrene	32
δ-Carene	32
β -Ocimene	32
Vitamins	
Thiamin	32
Riboflavin	32
Niacin	32
Ascorbic Acid	32
Coumarins	
Marmelosin	28
Marmesin	28
Imperatorin	28
Marmin	28
Alloimperatorin	28
Methyl ether	28
Xanthotoxol	28
Scopoletin	28
Scoparone	28
Umbelliferone	28
Psoralen	28
Marmelide	28
Tannins	
4,7,8-trimethoxyfuro-quinoline	29
Carbohydrates	
Galactose	29, 30
Arabinose	29, 30
Uronic acid	29, 30
L-rhamnose	29, 30
Aralrinose	32
D-galacluronic Acid	32
Flavonoids	
Rutin	31
Flavone	31
Flavone-3-ols	31
Flavone glycosides	31
Fatty Acids	
Palmitic Acid	32
Stearic Acid	32
Oleic Acid	32
Linoleic acid	32
Linolenic Acid	32
Essential Oils	
Alpha-Pinene	38
Beta-Myrcene	38
Alpha-Phellandrene	38
Isosylvestrone	38
Delta-Carene	38
Beta-Ocimene	38
Trans-2-hydroxy cinnamic acid	38
Gama-Terpinene	38
Terpenolene	38
Linalool	38
3-Isothujanol	38
4-Terpineol	38
Thuj-3-en-10-al	38
Alpha-Terpineol	38
Delta-Elemene	38
Alpha-Cubebene	38
Gama-Elemene	38
Alpha-Humulene	38
Alpha-Terpinyl isobutyrate	38
Gama-Muurolene	38
Gama-Curcumene	38
Valencene	38
Beta-Selinene	38
Alpha-Muurolene	38
Beta-Bisabolene	38
Gama-Cadinene	38
Beta-Bisabolol	38
Miscellaneous	
Anthocyanins	32
Skimmianine	32
y-sitosterol	32
B- sitosterol	32
Hamycin	32
Oxalic Acid	32

Table 5: Cont'd.

Isolated Chemical Compounds	Reference
Carotene	32
Allo-imperatorin	32
Psoralin	32
Auraptine	32
Marmin	32
Umbelliferone	32
Lupeol	32
Dimethoxy Coumarin	32
Scopoletin	32
Lembamide	32
Marmesin	32
Skimmlamine	32
Luvangetin	33
Imperatorin	34
Xanthotoxin	34
Alpha-amyrin	37

PHARMACOLOGICAL ACTIVITIES

Antioxidant activity

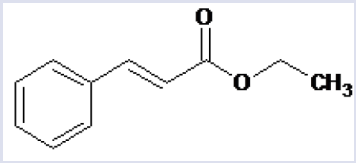
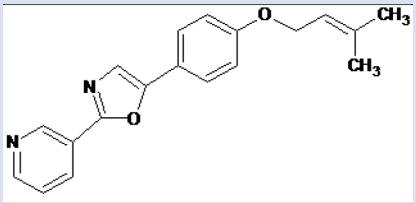
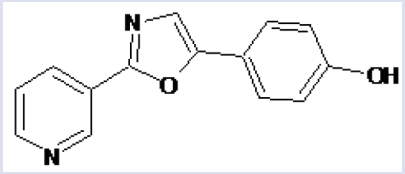
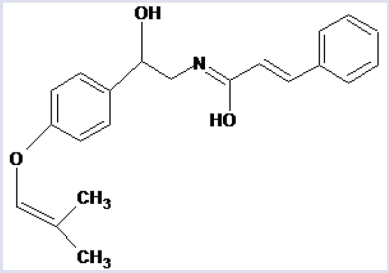
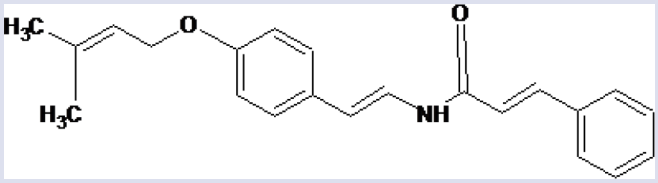
Screening of fruit pulp of *A. marmelos* methanolic and aqueous extract for antioxidant activity by DPPH radical scavenging method, reducing power assay, nitric oxide scavenging assay, superoxide radical scavenging assay, ABTS radical scavenging assay and H_2O_2 radical scavenging assay. Both aqueous and alcoholic extract exhibited good antioxidant activity.[39] The percentage of free radical inhibition was also high in unripe fruit than that of the ripe fruit.[40]

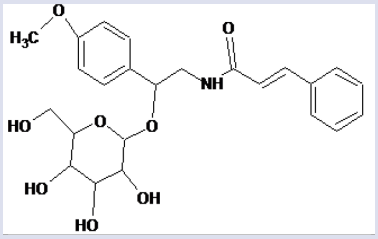
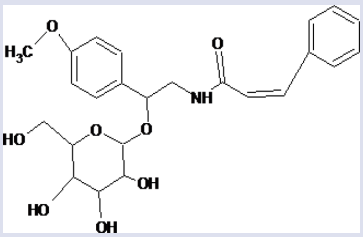
Antimicrobial activity

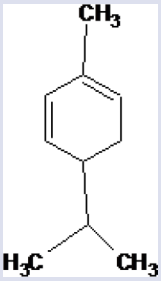
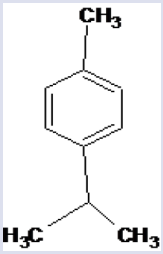
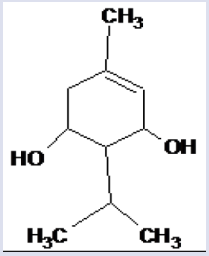
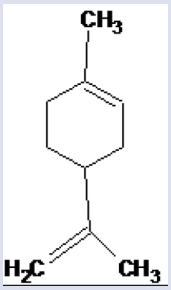
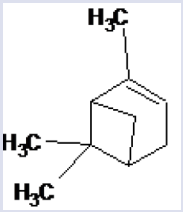
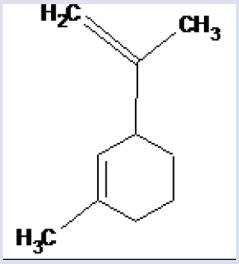
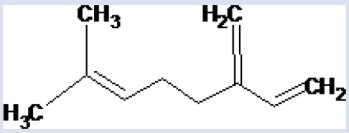
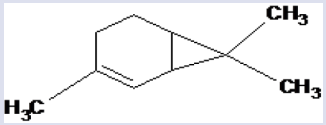
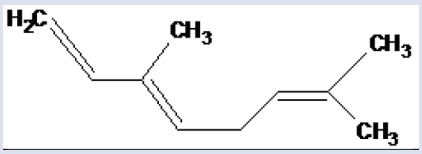
Antimicrobial activity was performed by using petroleum ether, ethanol and aqueous extract of *A. marmelos* leaves by following agar well diffusion method. These extracts proved to be effective against *Escherichia coli, Streptococcus pneumoniae, Salmonella typhi, Klebsiella pneumoniae and Proteus vulgaris*. The ethanolic extract shows activity against *Penicillium chrysogenum* and the petroleum ether and aqueous extract shows activity against *Fusarium oxysporum*.[41] The antimicrobial activity against gram-negative strains was higher than that of gram positive strains.[42] The presence of leaf constituents Cuminaldehyde and Eugenol may be responsible for antimicrobial activity.[43]

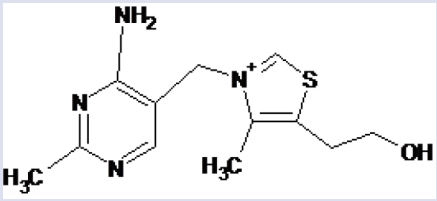
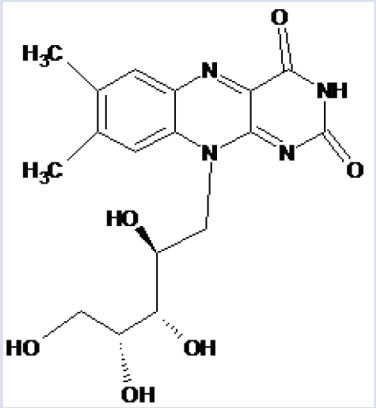
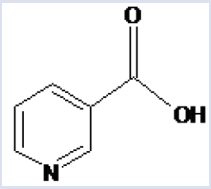
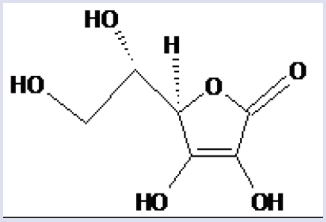
Antifungal activity

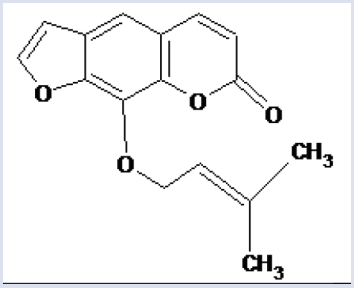
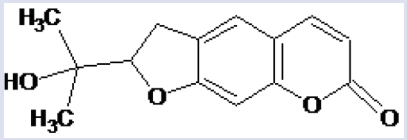
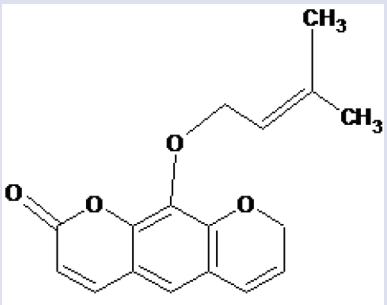
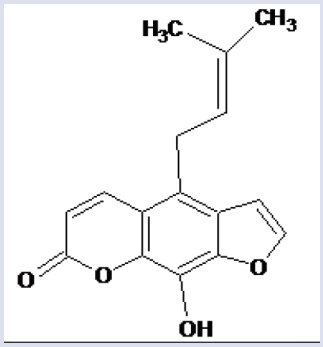
This activity was performed by using 21 days old culture of dermatophytic fungi with distilled water. The suspension was adjusted spectrophotometrically to an absorbance of 0.0600 at 450 nm. Susceptibility testing was performed by micro dilution method.[44] Potent antifungal activity was found when *A. marmelos* leaf extract was applied against *Trichophyton mentagrophytes*, *T. rubrum, Microsporum canis, M. gypseum, Epidermophyton floccosum*.[45]

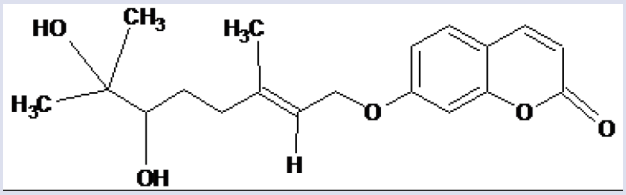
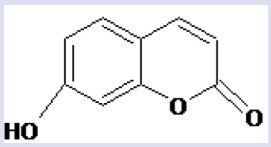
Alkaloids	
	
Ethyl Cinnamate	O-3,3-(di methylallyl) halfordinol
	
Halfordinol	Marmeline
	
Anhydromarmeline	

	
Aegelinosides A	Aegelinosides B

Terpenoids		
		
α-Phellandrene	p-cymene	p-Menth-1-en-3,5-diol
		
Limonene	α-Pinene	Isosylvestrene
		
β-Myrcene	δ-Carene	
		
β –Ocimene		

Vitamins	
	
Thiamin	Riboflavin
	
Niacin	Ascorbic Acid

Coumarins	
	
Marmelosin	Marmesin
	
Imperatorin	Alloimperatorin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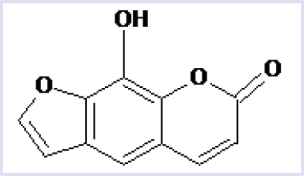	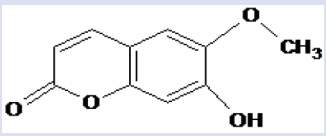
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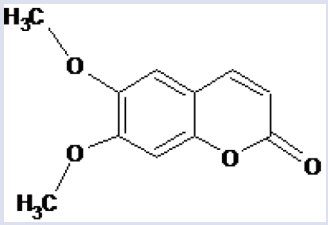
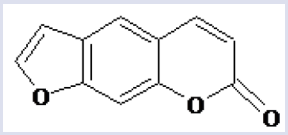
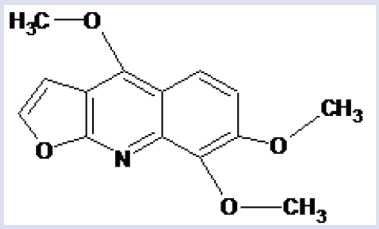
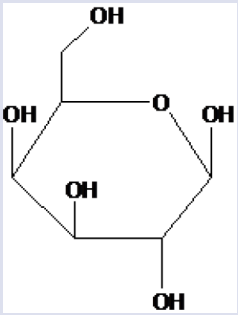
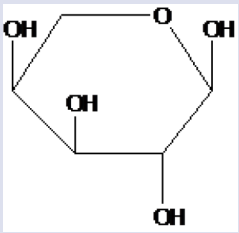
	
Scoparone	Psoralen

Tannins

4,7,8-trimethoxyfuro-quinoline

Carbohydrates	
	
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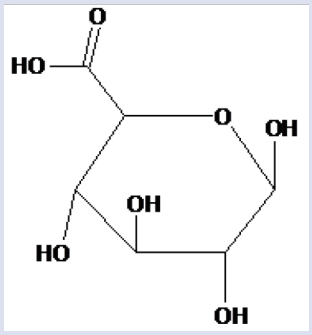
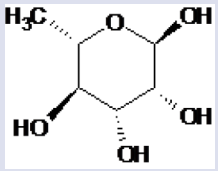
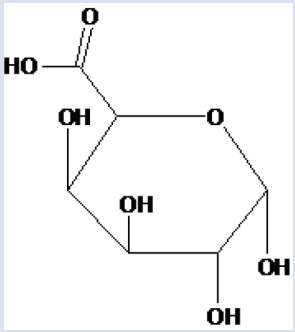
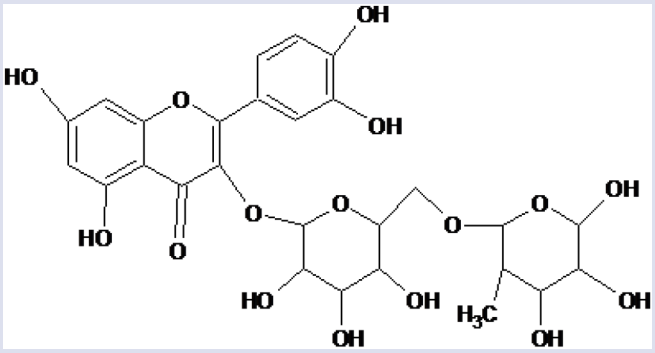
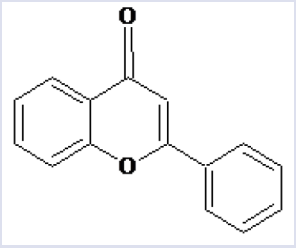
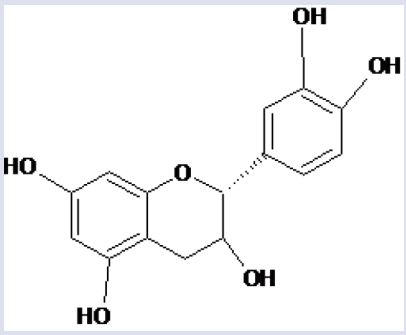
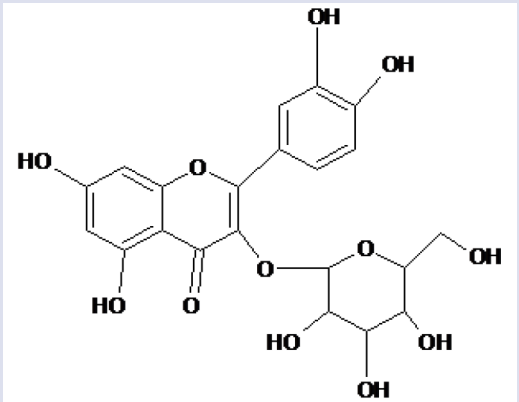
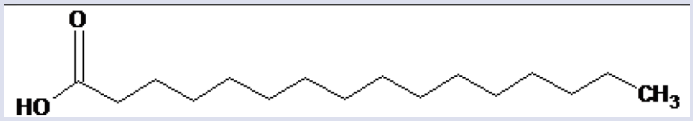
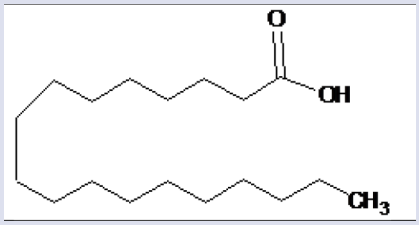
		
Uronic acid	L-rhamnose	D-galacturonic Acid

Flavonoids	
	
Rutin	Flavone
	
Flavan-3-ol	Flavone glycoside

Fatty Acids

Palmitic Acid

Stearic Acid

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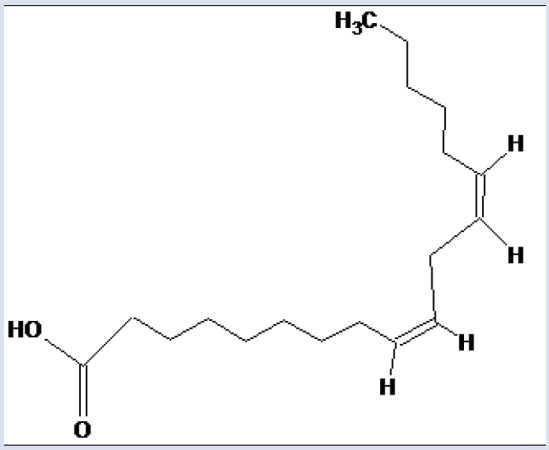
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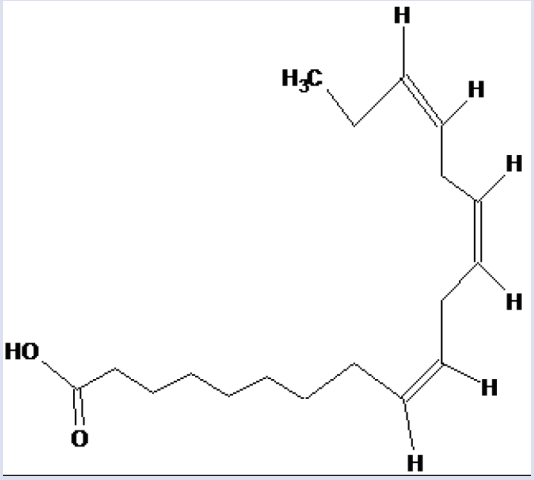
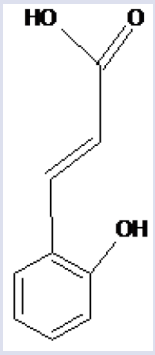
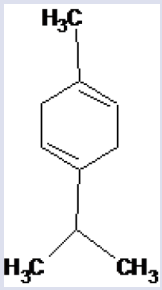
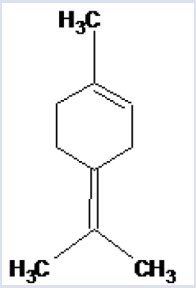
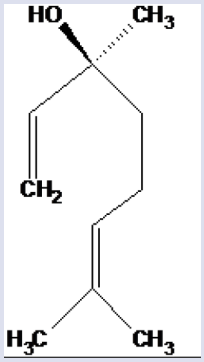
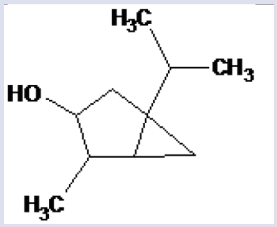
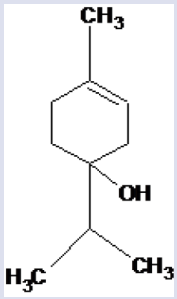
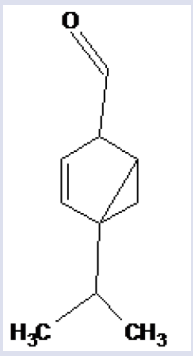
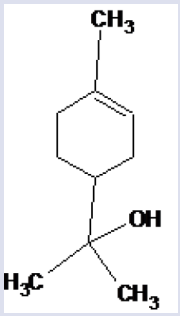
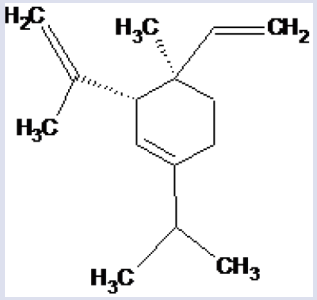
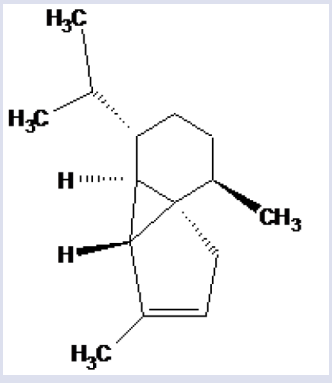
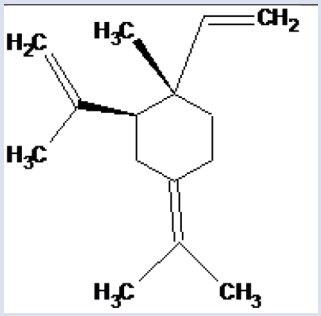
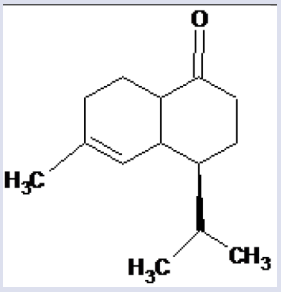
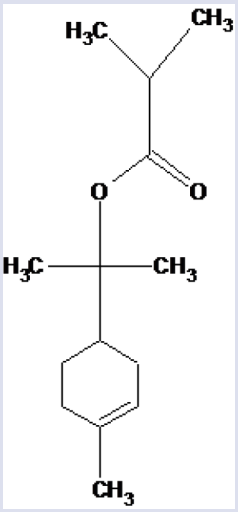
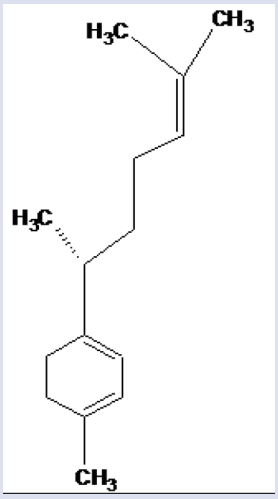

Linolenic Acid

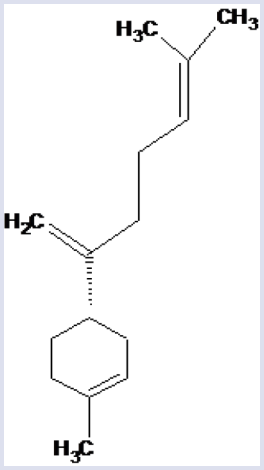
Essential Oils		
		
Trans-2-hydroxy cinnamic acid	Gama-Terpinene	Terpenolene
		
Linalool	3-Isothujanol	4-Terpineol
		
Thuj-3-en-10-al	Alpha-Terpineol	Delta-Elemene
		
Alpha-Cubebene	Gamma-Elemene	Gamma-Muurolene



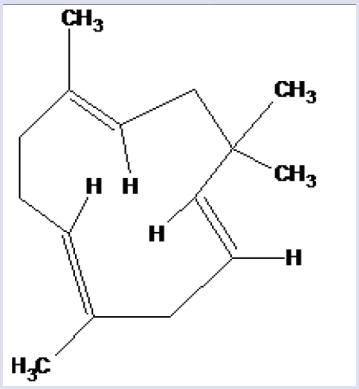
Alpha-Terpinyl isobutyrate



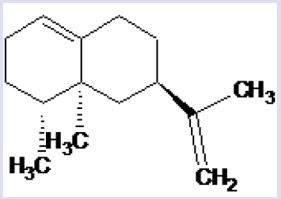
Gamma-Curcumene



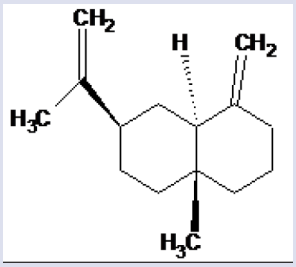
Beta-Bisabolene



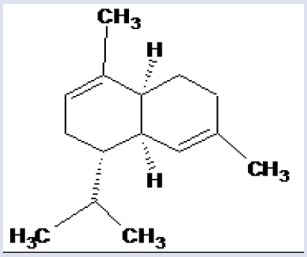
Alpha-Humulene



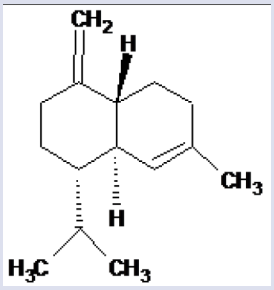
Valencene



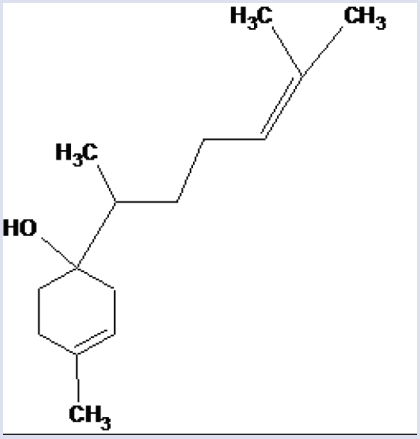
Beta-Selinene



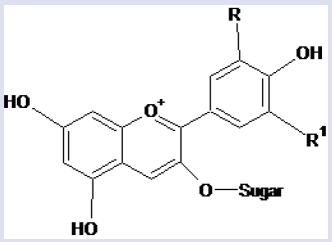
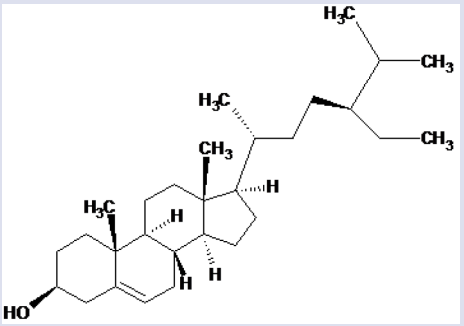
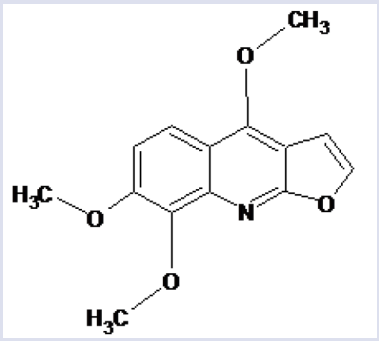
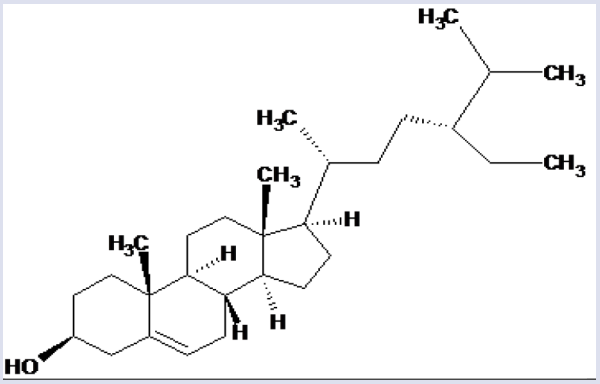
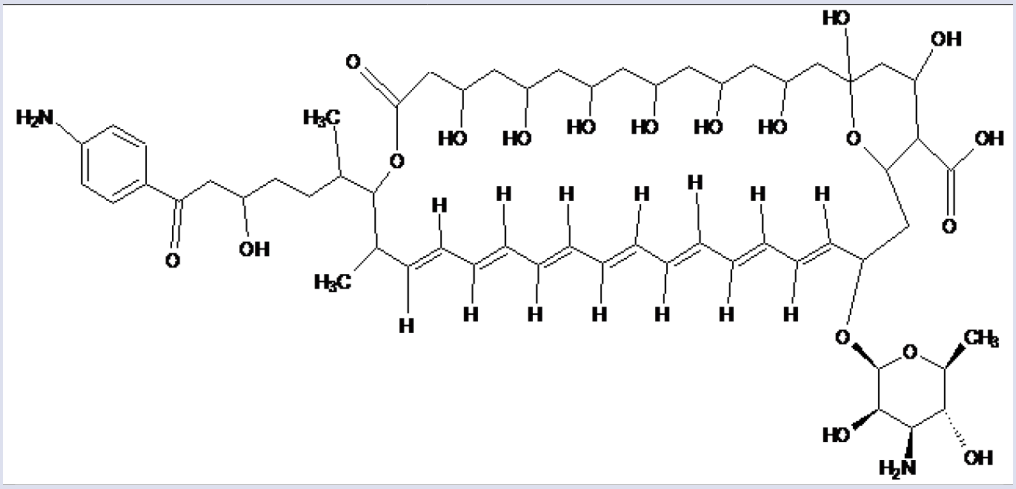
Alpha-Muurolene



Gamma-Cadinene



Beta-Bisabolol

+++Miscellaneous	
	
Anthocyanins	Gamma-sitosterol
	
Skimmianine	Beta- sitosterol
	
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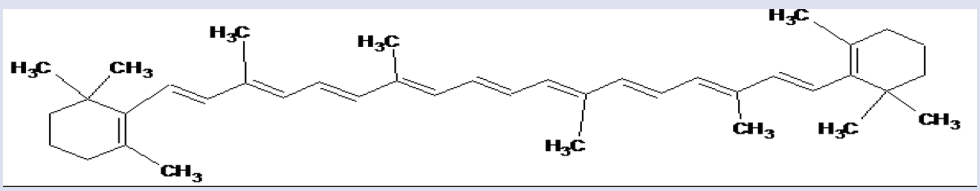
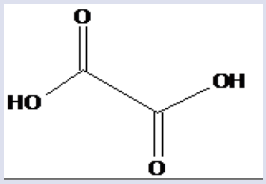
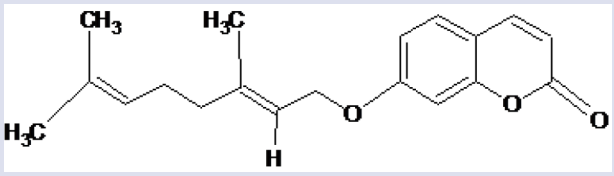
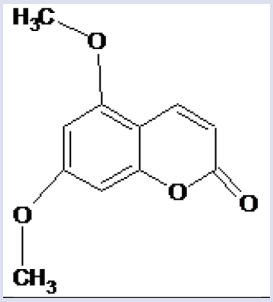
	
Carotene	



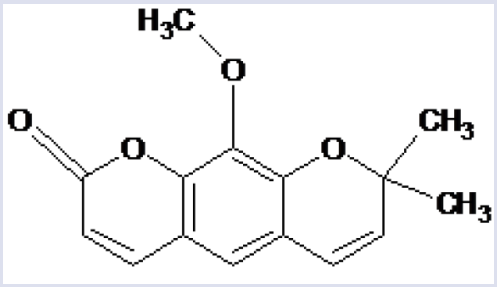
Oxalic Acid



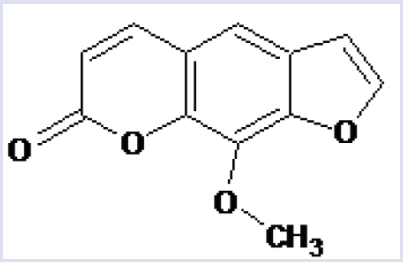
Auraptene



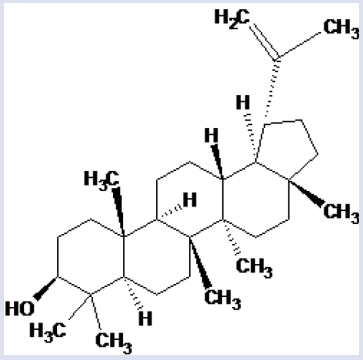
Dimethoxy Coumarin



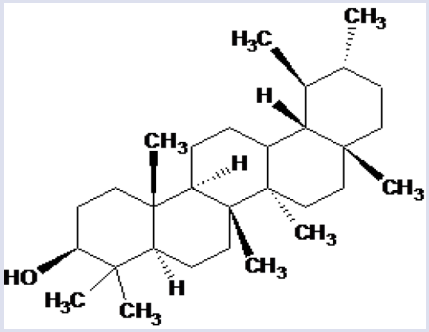
Luvangetin



Xanthotoxin



Lupeol



Alpha-amyrin

Anti-constipating effect

Most of the available ripe fruits are considered as a natural therapy of various kinds of laxatives. *A. marmelos* fruits are generally used to clean and tones up intestine. 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.[46]

Antidiarrheal activity

A. marmelos fruit is having wide use for controlling chronic diarrhea and dysentery. Due to astringent property of this fruit, the unripen bael is most prized as a means of halting diarrhea and dysentery, which are prevalent in India in summer months.[46-48] Antidiarrheal activity was performed against a few causative organisms of diarrhea by MIC method. The ethanolic extract showed good activity against *Shigella boydii, S. sonnei, S. flexneri, moderate against S. dysenteriae*.[49]

Antidiabetic activity

All extracts of *A. marmelos* proved to be active against diabetic rabbits, however, among the various extracts, methanolic extract of leaves showed maximum anti diabetic effect.[50] Methanolic extract (120 mg/kg,p.o.,) was administered to alloxan induced diabetic rats and on 12th day sugar levels were found to be reduced by 54%.[51]

Antiproliferative activity

A. marmelos steam bark ethanolic extract were reported to produce antiproliferative activity against various human tumor cell lines. Cells were grown in tissue culture flasks in complete growth medium in a carbon dioxide incubator. The cells are allowed to grow in carbon dioxide incubator for 24 hrs and then extracts were added in complete growth medium. These are incubated further 48 hrs. The result showed the inhibition of *in vitro* proliferation of human tumor cell lines, including the lukemic K562, T-lymphoid Jurkat, Blymphoid Raji, erythroleukemic HEL, melanoma Colo 38 and breast cancer MCF7 and MDAMB – 231 cell lines.[52]

Cytoprotective effect

This effect was reported for *Cyprinus carpio* or freshwater fish. Experimental fish were kept in sublethal concentration of metal ion for a period of 1, 8, 16 and 32 days. After 32 days, these fishes were fed with *Aegle marmelos* crude powder (500 mg/kg diet). Treatment resulted in cytoprotective effect by stabilization of plasma membrane and modulation of antioxidant enzyme system.[53]

Hepatoprotective effect

A. marmelos leaf produces hepatoprotective effect for liver injury in albino rats due to alcohol consumption. Rats are injected with bacterial suspension at a dose of 5x10^{6} CFU/0.1 ml through intraperitoneal route.

Then the animals were treated with *Aegle marmelos* alcoholic extract for 15 days in physiological saline at a concentration of 100 mg/kg of body weight. After 15 days, the animals were fasted for 12 hrs and then scarified under mild chloroform anesthesia. Bloods collected for serum separation and the organs are excised and washed in ice cold saline until homogenized. Biochemical parameters like SGOT, SGPT, alkaline phosphate,[54] total bilirubin[55] and protein[56] were analyzed. Estimation of blood glutathione performed using DTNB.[57] These albino rats were administered with 30% ethyl alcohol regularly for 40 days and then induced rats were fed plant leave powder for next 21 days. The experimental results indicated excellent hepatoprotective effect of the *A. marmelos* leaf.[58]

Antifertility effect

Methanolic leaf extract of *A. marmelos* at a dose of 200, 400 and 600 mg/kg, p.o., possess abnormal sperm count reduction with decrease in motility of sperm and it also affect the sexual behavior and epididymal sperm concentration for male rats.[59]

Analgesic activity

A. marmelos leaves methanol extract was reported for antinociceptive response using writhing and tail immersion test in mice. Maximum possible effect of methanolic extract (200 mg/kg p.o.) was more statistically significant when compared to other doses. It concludes that methanol extract of *A. marmelos* leaves produces significant analgesic activity.[60]

Antiarthritis activity

A. marmelos leaves were found to be active against collagen induced arthritis in Wistar albino rats.[61,62] Radiological and histopathological changes were also significantly reduced in methanol extract treated rats.[63]

Contractile activity

The contractile activity of *Aegle marmelos* leaves alcoholic extract was reported on guinea pig isolated ileum and tracheal chain due to its traditional use in treating asthma and related afflictions. *A. marmelos* leaves 1 mg/ml and 2 mg/ml alcoholic extract 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.[64]

Antihyperlipidemic activity

Aegle marmelos (Linn.) was evaluated in diet induced hyperlipidemic models of wister albino rats at a dose of 125 and 250mg/kg dose. Bael fruits and seeds aqueous extracts were applied to streptozotocin induced diabetic rats through oral administration significantly reduces tissue lipid profile and serum.[65-67]

Counteracting Cardiotoxic effect

Alcoholic extract of bael unripe fruit was found to perform cardioprotective effect in isoproterenol induced myocardial infarction. A very potent compound named as auraptene, is responsible for this activity.[68]

Radioprotective effect

Now-a-days radiotherapy is one of the most important therapies for curing cancer especially for those suffering from vital visceral malignancies. Although it is very useful all over the world, however it has some side effects. Radioprotective effect has been studied with the use of bael fruit hydroalcoholic extract in mice that are exposed to several doses of gamma radiation. Swiss albino male mice were administered 5, 10, 15, 20 or 40 mg/kg of *Aegle marmelos* extract intraperitoneally daily for 5 days before exposure to 10 Gy 60Co gamma-radiations. After 30 days of post radiation, maximum protections are reported by highest number of survivors.[69-71] Five consecutive dose of 15 mg/kg extract produces survival to 10 Gy radiation was observed.

Anticancer activity

A. marmelos extract tested by following sea urchin eggs assay, brine shrimp lethality assay and MTT assay method upon tumor cell lines. *A. marmelos* extract produces toxicity on all used assays.[69,72]

Antiviral activity

Virus is considered as a living substance inside host body and as a non-living outside the host body. It leads to seasonal outbreak and does not respond properly to most of the synthetic drugs. Hence the demand of natural bio-resources is increasing for overcoming this problem. Hydro alcoholic bael fruit extract produces antiviral activity against Ranikhet disease virus. Interferon like activity against the same virus is also reported. Thus bael fruit can be used as a better viricidal potential and may be exploited as a potent antiviral agent in near future.[69]

Anti-ulcer activity

Anti-ulcer activity was performed by preparing polyherbal formulation that was investigated by ethanol induced gastric ulcer model in wistar rats. The 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 500 mg/kg oral dose produces moderate inhibition of gastric lesions in ethanol induced ulcer model with respect to standard 20 mg/kg Omeprazole administration. The result shows that this polyherbal formulation might be useful in severe gastric ulcer. The formulation is proved to be non-toxic even at relatively high concentration.[73]

Immunosuppressant activity

Methanolic extract of *A. marmelos* fruit produces immunomodulatory activity by neutrophil adhesion test and carbon clearance assay. Wistar albino rats were pre-treated with extracts orally for 14 days. After the end of 14 days, blood samples were collected from retro-orbital plexus into heparinized vials and allow analyzing for DLC. After initial counts, blood samples were incubated with 80 mg nylon fibers/ml for 15 mins at 37°C. Then the samples were analyzed for TLC and DLC respectively to obtain neutrophil index of blood samples. Blood incubation with nylon fibers shows a decrease in neutrophils counts due to adhesion of neutrophils to the fibers.[74] 500 mg/kg extract produces an increase in adhesion of neutrophils and increase in phagocytic index in carbon clearance assay.[75]

Wound healing activity

Excision wound models in male Wister rats were used for observing the effect of methanolic extract of *A. marmelos* seeds ointment and injection. 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.

Incision wound model was performed in male wister rats by following the method of Ehrlich and Hunt.[77] 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.[78]

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.[79]

Antimalarial activity

Antimalarial activity of *A. marmelos* root extract was performed against the parasite *Plasmodium falciparum* (K_1, multidrug resistant), using the method of Trager and Jensen.[80] Quantotative assessment of *in-vitro* antimalarial activity was determined by means of the microculture radioisotope technique based on the method described by Desjardins *et al.*[81] The IC_{50} 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*. Dihydroartemisinin was taken as standard compound (IC_{50} 4.1 nmol L^{-1}).

Anti-microfilarial activity

Methanolic extract of *Vitex nigundo* L. roots and leaves of *Vitex nigundo* L., *Ricinus communis* L. and *A. 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. Among all observed extracts, *Vitex nigundo* L. root extract and *A. marmelos Corr.* leaves extracts at 100 mg/ml concentration produces total loss of motality of microfilariae after 48 hours incubation.[82]

Anticonvulsant activity

The anticonvulsant activity of ethanolic extract of *A. marmelos* leaves on maximal electroshock (MES) and pentylenetetrazole (PTZ) in male mice was performed. The extract was 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 *A. marmelos* leaves ethanolic extract delayed the occurence 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.[83]

Antidepressant and anxiolytic activity

Antidepressant and anxiolytic activities was also reported for *A. marmelos* leaves methanolic extract and its interaction with antidepressant and anxiolytic drugs using tail suspension test and elevated plus maze in mice was reported. The necessary outcome that were observed includes 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 post synaptic sites that has been confirmed by several other methods. From result, it can be concluded that methanolic extract of *A. marmelos* leaves shows potent anxiolytic and antidepressant activities and it enhances the antidepressant and anxiolytic activities of Imipramine and Fluoxetine.[84]

Hypolipidemic activity

Aqueous extract of *A. marmelos Corr*., leaves reported to be potent for lowering lipid level by using streptozotocin induced diabetic rats. The lipid profile parameters that were studied includes serum total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL) and very low-density lipoprotein (VLDL). Orally extracts are administered to STZ induced diabetic rats at increasing dose levels of 250, 350 and 450 mg/kg body weight. All these levels were observed significant reduction as compared to diabetic controlled rats. These results further suggested that *A. marmelos Corr.*, may be useful in the therapy and management of hyperlipidemia by reducing lipid levels.[85]

Antihistaminic activity

The effects of Skimmianine (chemical constituent from roots of *A. marmelos Corr.*) 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.[86]

Anti-stress and adaptogenic activity

Aqueous extract of *A. 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 was not sustained on subsequent groups. It increases swimming endurance time along with post motor function like rota rod falling time and spontaneous motor activity. These extract increases cold swimming endurance time and could restrict the increase in the level of these markers during stress.[87]

CONCLUSION

Several parts of *A. marmelos* have been reported as various traditional healers for treating various ailments of mankind. These contains Antioxidant, Antibacterial, Antifungal, Antidiarrheal, Antidiabetic, Antiproliferative, Cytoprotective, Hepatoprotective, Antifertility, Analgesic, Antiarthritis, Contractile, Antihyperlipidemic, Cardioprotective, Radioprotective, Anticancer, Antiviral, Anti-ulcer, Immunomodulatory and Wound Healing properties. A number of biologically active compounds isolated from various parts of *A. marmelos* which belongs to various chemical groups. The isolated components belong to Alkaloids, Terpenoids, Vitamins, Coumarins, Tannins, Carbohydrates, Flavonoids, Fatty Acids, Essential Oils and some other miscellaneous compounds. This review mainly focused on several phytochemical and pharmacological studies which have explained phytoconstituents and therapeutic potential of *A. marmelos*.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

***A. marmelos*:** *Aegle marmelos*; **DPPH:** 1,1-diphenyl-2-picryl hydrazyl; **ABTS:** 2,2'-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid; **H2O2:** Hydrogen Peroxide; **nm:** nanometer; ***T. rubrum*:** *Trichophyton rubrum*; ***M. gypseum*:** *Microsporum gypseum*; **MIC:** Minimum Inhibitory Concentration; ***S. sonnei*:** *Shigella sonnei*; ***S. flexneri*:** *Shigella flexneri*; ***S. dysenteriae*:** *Shigella dysenteriae*; **CFU:** Colony-Forming Unit; **SGOT:** Serum Glutamic-Oxaloacetic Transaminase; **SGPT:** Serum Glutamic Pyruvic Transaminase; **DTNB:** 5,5-dithio-bis-(2-nitrobenzoic acid); **MTT:** 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; **DLC:** Differential Leukocyte Count; **TLC:** Total Leukocyte Count; **IC50:** Half Maximal Inhibitory Concentration; **MES:** Maximal Electroshock; **PTZ:** Pentylenetetrazole; **HLTE:** Hind Limb Tonic Extensions; **TC:** Total Cholesterol; **TG:** Triglycerides; **LDL:** Low Density Lipoprotein; **HDL:** High Density Lipoprotein; **VLDL:** Very Low-Density Lipoprotein; **STZ:** Streptozotocin; **RBL-2H3:** Rat Basophilic Leukemia; **RPMCs:** Rat Peritoneal Mast Cells; **DNP24-BSA:** Dinitrophenylated Bovine Serum Albumin.

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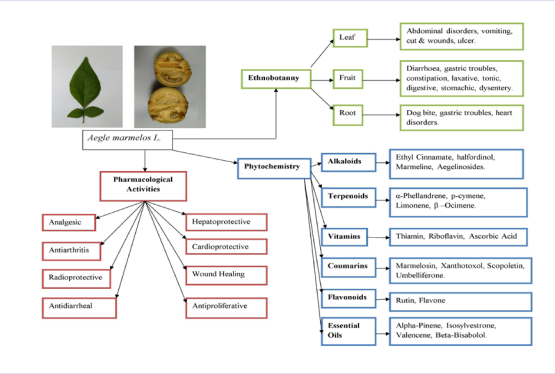
GRAPHICAL ABSTRACT



SUMMARY

- This review highlights phytochemical and pharmacological aspects of *Aegle marmelos* that may be helpful for future researches.
- Morphological Characters, Ethnobotanical uses, phytoconstituents present in *Aegle marmelos* helps researchers for their further proceedings.
- *Aegle marmelos* is a source of several chemical constituents like Alkaloids, Terpenoids, Vitamins, Coumarins, Tannins, Carbohydrates, Flavonoids, Fatty Acids, Essential Oils and other compounds.
- Golden Apple used in treatment of various diseases and ailments like Anti-oxidant, Antibacterial, Antifungal, Antidiarrheal, Antidiabetic, Antiproliferative, Cytoprotective, Hepatoprotective, Antifertility, Analgesic, Antiarthritis, Contractile, Antihyperlipidemic, Cardioprotective, Radioprotective, Anticancer, Antiviral, Anti-ulcer, Immunomodulatory and Wound Healing properties.

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