

Review Article

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Pharmacological Properties of *Aegle marmelos*: A Review

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ABSTRACT

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Medicinal plants are the base of traditional system of medicine and herbal industry for the development of new drug. The *A. marmelos* is also known as bael, wooden apple, belo and bilwa. The important phytochemicals isolated from various parts of the plant are alkaloids, cardiac glycoside, saponin, steroids, coumarines terpenoids, phenylpropenoids, tannins, polysaccharides and flavonoids. These phytochemical components are well known for their pharmacological and biological activity against certain chronic disease like cancer, cardiovascular disease, immunosuppressive disease and gastrointestinal disorder. The different parts of the plant extract possess pharmacological activities like anticonvulsant, antioxidant, antihyperglycemic, anxiolytic, antidepressant, antihistaminic, antimicrobial, hepato protective, analgesic, immuno modulatory, cardio protective and antithyroid activity. The present review article is focused to explore the different pharmacological activity of *A. marmelos*.

Introduction

Medicinal plants are potential source of phytochemicals valuable for novel drug discovery. Phytochemicals such as carotenoids, terpenoids, flavonoids, polyphenols, alkaloids, tannins, saponins, pigments, enzymes, minerals and vitamins, possess different kind of therapeutic effects like antimicrobial and antioxidant activity.

(Madhuri and Pandey, 2009). Most of the modern drugs are derived from natural sources; many of these isolations were based on the uses of the agents in traditional medicine (Cragg and Newman, 2001). In the ancient times, medicinal plants were used for control and prevention of health disorder and are continued to play a crucial role in the maintenance of human as well as animal health. Traditional medicines still enjoy

significant position in the modern drug industries due to the synergistic action with fewer side effects in the combination of herbal compounds. According to the World Health Organization plant extracts or their active constituents are used as folk medicine in traditional therapies of 80% of the world's population. Over 50% of all modern clinical drugs are of natural product origin (Kirbag *et al.*, 2009). In India, drugs of herbal preparations have been used in traditional system of medicines such as Unani and Ayurved since ancient times.

Aegle marmelos [L.] Correa is commonly known as wooden apple belongs to the Rutaceae family. The tree is considered under

the category of "fragrant" species. The *Aegle marmelos* is a small genus of three species distributed in tropical Asia and Africa. The tree of *A. marmelos* originates from Eastern ghats and central India and found mainly in foothills of Himalayas, Uttar Pradesh, Madhya Pradesh, Rajasthan, Chhattisgarh and Bihar. The leaves of *A. marmelos* are offered to Lord Shiva, whose worship cannot be completed without the leaves of this tree. It is also known as Shivadurme, the tree of Shiva. The value mentioned plant has also been found in ancient Indian scriptures like Yajurveda and Mahabharata (Asha and Krishan, 2016).

Table.1 Scientific classification and vernacular names of *Aegle marmelos* in India

Kingdom:	Plantae
Order:	Sapindales
Family:	Rutaceae
Subfamily:	Aurantioideae
Genus:	<i>Aegle</i>
Species:	<i>A. marmelos</i>
Nomenclature:	<i>Aegle marmelos</i> (L.) Corr. Serr.
Synonym:	Bel, Beli, Belgiri (Hindi) Bilva, shivdhruma, shivaphala, vilva (Sanskrit) Marredy (Malyalam) Belo (Oriya) Vilva marum, Vilvama (Tamil)

Chemical composition

Aegle marmelos having variety of classes of compound like alkaloids, cardiac glycoside, saponin, steroids, coumarines (marmelosin, marmesin, marmin, imperatorin, scopoletin), terpenoids, phenylpropenoids, tannins, polysaccharides and flavonoids. *Aegle marmelos* leaves contain γ -sitosterol, aegelin, lupeol, rutin, marmesinin, β -sitosterol, flavone, glycoside and phenylethyl cinnamamides. Shahidine, an alkaloid having oxazoline core has been isolated as a major

constituent from the fresh leaves of *Aegle marmelos* and it showed activity against a few Gram-positive bacteria (Asha and Krishan, 2016). New alkaloids from the leaves of *Aegle marmelos* were reported viz., halfordino, ethylcinnamamide and marmeline. Recently, series of phenylethyl cinnamides, which included new compounds named anhydromarmeline, aegelinosides A and B were isolated from *Aegle marmelos* leaves which are α -glucosidase inhibitors. α -Phellandrene which is terpenoid was found to be the common constituent of the essential oil

from leaves, twigs and fruits. α -Phellandrene (56%) and p-cymene (17%) were reported from leaf oil. Limonene (82.4%) was reported as the main constituent from bael leaves which are characteristic marker for identification of *Aegle marmelos* oil samples. There is approx. 9% tannin in the pulp of wild fruits in comparison to cultivated type. Tannin is also present in leaves as skimmianine also known as 4, 7, 8-trimethoxyfuro-quinoline. The phenylpropanoids included hydroxycoumarins, phenylpropenes and lignans. Aegeline, was initially claimed to be a new compound, was found to be identical to half ordinal, the basic constituent of halfordia scleroxyla (Neeraj and Johar, 2017). Rutin flavon, flavon glycosides and flavon-3-ols are the major flavonoids of *A. marmelos* leaves.

Therapeutic uses and pharmacology

Antihyperglycemic activity

The ethanolic extract of *Aegle marmelos* leaves possess antihyperglycemic activity when administered orally at 250 and 500 mg/kg to diabetic rats. A noticeable decrease in glucose absorption and inhibition of both α amylase and intestinal disaccharidase enzyme activity were observed due to inhibition of carbohydrate digestion and absorption, and improvement of insulin action to uptake glucose in peripheral tissue (Ansari *et al.*, 2017). Upadhya *et al.*, (2004) administered *Aegle marmelos* leaves extract @500 mg/kg to evaluate hypoglycaemic and antioxidant effect on diabetic rats. Male albino rats were randomly divided into three groups Group I, Group II and Group III, control, diabetic and diabetic rats with extract respectively administered with extract of *A. marmelos*. They found that decrease in blood glucose at the end of four weeks in group III animals compared with group II. According to Maqbool *et al.*, (2019) *A. marmelos* is effective as insulin in restoration of blood

glucose and body weight to normal levels. The recent study revealed that leaf juice of *A. marmelos* was effective in diabetes mellitus and possibly it was due to presence of bioactive components, aegelin 2, scopoletin and sitosterol in the leaves (Nigam and Nambiar, 2019).

Anti-inflammatory activity

Arul *et al.*, (2005) evaluated anti-inflammatory, antipyretic, and analgesic activities of different extracts of the leaves of *Aegle marmelos*. The extracts produced significant inhibition of the carragenin-induced paw edema and cotton pellet granuloma in rats. The leaves exhibited anti-inflammatory property due to presence of lupeol, skimmianine (Sharma and Dubey, 2016).

Anticonvulsant activity

The aqueous leaves extract of *A. marmelos* possess anticonvulsant activity against Pentylentetrazole induced seizures in mice. The anticonvulsant activity of aqueous leaves extract of *A. marmelos* was due to presence of Lupeollinoleate, Skimmianine, Eugenol which was identified by Liquid chromatography mass spectrometry (Puthillath, *et al.*, 2016). Ethanolic extract of leaves of *A. marmelos* reveals anticonvulsant activity due to presence of flavonoid and it interfere with GABAergic mechanism to exert their anticonvulsant activity (Patel *et al.*, 2012).

Antihistaminic activity

The study on rats exhibited that skimmianine, zeorin and Aegeline markedly inhibited the histamine release from rat leukemia cell line (RBL-2H3 cell) induced by DPN 24-BSA, thapsigargin and ionomycin (Nugroho, 2010 2011a, 2015; Patkar *et al.*, 2012). Marmin

also inhibit the histamine release and suppressed Ca^{2+} influx on RBL-2H3 cell line (Nugroho, 2011b).

Anxiolytic and antidepressant

The methanolic leaves extract of *A. marmelos* possess anxiolytic and antidepressant activity and it enhances anxiolytic and antidepressant activity of imipramine and fluoxetine (Kothari *et al.*, 2010).

Antioxidant activity

Antioxidants are having free radicals scavenging activity and capability of protecting the cells in oxidative stress. Antioxidant activity of these plants is due to the presence of flavones, isoflavones, flavonoids, anthocyanin, coumarin, lignans, catechins and isocatechins. *A. marmelos* is extensively reported to possess antioxidant activity against a variety of free radicals (Sekar *et al.*, 2011).

Ethanollic leaves extract of *A. marmelos* possess antioxidant activity due to present of flavonoids, alkaloids and terpenoids (Gupta *et al.*, 2015). Another study revealed that antioxidant activity of leaf extract of *A. marmelos* was due to present of high levels of total phenolic content (TPC) and total flavonoid content (TFC) in the extract (Kumar *et al.*, 2016).

Hepatoprotective activity

It was reported that leaves, seed and pulp of fruit of *A. marmelos* shows hepatoprotective activity (Asha and Krishan, 2016). The methanolic leaves extract of *Aegle marmelos* @500 mg/kg possess hepatoprotective activity against paracetamol induced hepatotoxicity in rats (Singh, 2013). According to Ramamurthy and Gowri, (2015) alcoholic extract of *Aegle marmelos* @100

mg /kg b.w. produced hepatoprotective activity against *Staphylococcus aureus* intoxicated rats.

Antimicrobial activity

It has been reported that *A. marmelos* traditionally used for the treatment of various infectious diseases to inhibit the broad range of pathogenic microorganisms. Meena *et al.*, (2016) evaluated antibacterial activity of leaves and fruit extract of *A. marmelos*. Inhibition zones of 11 mm and 9 mm were observed by using leaf and fruit extract against *Roultella planticola*. The plant extract produced maximum inhibition zone of (18mm) activity against fungal strains *viz. Penicillium chrysogenum* and minimum (7mm) against *Candida albicans*.

Analgesic activity

The methanolic leaves extract of *A. marmelos* at the dose of 200 and 300 mg/kg showed significant analgesic activity on acetic acid-induced writhing and tail flick test in mice (Shankarananth *et al.*, 2007).

Antifungal activity

According to study of Rana *et al.*, (1997) essential oil from *Aegle marmelos* leaves may interfere with the Ca^{2+} -dipicolonic acid metabolism pathway and possibly inhibit the spore formation at concentration of 500 ppm. Ethanolic, methanolic and water leaves extract of *A. marmelos* possesses antifungal activity against dermatophyte fungi Balakumar *et al.*, (2011)

Neuroprotective activity

Ethanollic leaves extract of *A. marmelos* exhibited neuroprotective effect against streptozocine induced cognitive impairment in male rats. The extract also showed

acetylcholinesterase (AChE) inhibitory activity in the brain. The inhibition of AChE improves the symptoms of cognitive deficit by elevating the levels of acetylcholine (Raheja *et al.*, 2019).

Anti-ulcer activity

Methanolic extract of unripe fruit of *Aegle marmelos* reduced gastric ulceration and prevent the oxidative stress caused by *Helicobacter pylori*-Lipopolysaccharide in rats (Ramakrishna *et al.*, 2015). Gastro protective effect of extract was due to the presence of luvangetin which lowers oxidative stress in the gastro duodenal mucosa (Asha and Krishan, 2016). Some other study suggested that ripe fruit of *A. marmelos* protect gastric mucosa in NSAID induced ulceration in rats by its antisecretory and cytoprotective property (Singh and Guha, 2012). Methanolic and aqueous fruit seed extract of *A. marmelos* exhibited antiulcer activity due to presence of quercetin compound (Sharma *et al.*, 2011).

Antiviral activity

The ethanolic Bael fruit extract have shown antiviral activity against virus of Ranikhet disease. Bael fruit contain marmilide which is the most effective viricidal agent which interferes with early events of replicating cycle (Maity *et al.*, 2009)

Anti-cancer activity

Research proved that extracts from *Aegle marmelos* are able to inhibit the *in vitro* proliferation of human tumor cells, erythroleukemic HEL, melanoma colo38, MDAMB- 231 and breast cancer MCF7 cell lines (Lampronti *et al.*, 2003). The ethanolic leaf extract of *A. marmelos* showed greater antiproliferative activity against colon, breast carcinoma and leukaemia cell line (Bhatti *et*

al., 2013). Anticancer activity was due to leaves and fruit of bael which contain lupeol, eugenol, citral, and marmelin skimmianine (Asha and Krishan, 2016). It has been observed that ethanolic leaves extract of *A. marmelos* showed antiproliferative activity against ascites tumor in swiss albino mice (Chockalingam *et al.*, 2012). Gupta *et al.*, (2016) reported that the hydromethanolic *A. marmelos* bark extract has antitumor and antioxidant potential against 7, 12-dimethylbenzanthracene (DMBA) induced skin papillomagenesis in swiss albino mice.

Immunomodulatory activity

It was observed that methanolic leaves extract of *A. marmelos* stimulate cell mediated and antibody mediated immune responses in rats (Choubey *et al.*, 2010) but low dose of methanolic extract of *Aegle marmelos* was found to be most effective in cell mediated immune response, whereas, high dose was best effective in humoral immunity (Govinda and Asdaq, 2011).

Antithyroid activity

A. marmelos leaves extract decreased thyroid hormone level. It was due to presence of scopoletin which have more dominant therapeutic activity than propylthiouracil drug (Sharma *et al.*, 2011).

Other activities

Aqueous leaves extract of *A. marmelos* exhibited cardioprotective effect against isoproterenol induced myocardial infarction in rats (Ramachandra *et al.*, 2012) the cardio protective activity is due to the presence of aurapten as potent compound. Bael fruit is the most effective remedy for prevention of diarrhea (Brijesh *et al.*, 2009). It has been reported that antidiarrhoeal activity was due to presence of tannins (Miranda *et al.*, 1993)

and flavonoids (Di Carlo, 1993) that inhibit intestinal motility. Hydroalcoholic fruit extract of *A. marmelos* produced radioprotective effect against gamma radiations in mice and it was due to phenolics and flavonoids present in fruits of *A. marmelos* (Jagetia *et al.*, 2004). The β -sitosterol and rutin were reported to possess hypocholesterolemic effect and the rutin was identified in the alcoholic leaves extract of *A. marmelos* (Porchelvan and Venkatakrishnamurali, 2014).

Toxicology

According to Veerappan *et al.*, (2007) intraperitoneal administration of the leaves extract of *A. marmelos* at doses of 50, 70, 90 and 100 mg/kg body weight for 14 consecutive days to male and female wistar rats did not induce any short term toxicity. It was observed that the extract of leaves of *A. marmelos* have a high margin of drug safety (Rana *et al.*, 1997). Another study revealed that the *A. marmelos* was non-toxic up to a dose of 1750 mg/kg body weight and LD₅₀ of extract was 2250 mg/kg, i.p in mice (Jagetia *et al.*, 2005). Porchelvan and Porchelvan and Venkatakrishnamurali, (2014) reported that chronic administration of leaf powder of *Aegle marmelos* was non-toxic up to dose of 2000 mg/ kg b. w. in rats.

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