A critical review on phytochemical and medicinal properties of Aegle marmelos and Adhatoda vasica

Abstract

It has been established that up to 25% of the drugs prescribed in conventional medicines are allied directly or indirectly to natural substances mostly of plant origin. Hence, during the last few decades there has been an increasing interest in the study of medicinal plants and their long-established use in different countries. However, today it is compulsory to afford scientific testimony as to whether it is reasonable to use a plant or its active principles. As far as contemporary drugs are concerned they must be further characterized after their pharmacological screening by studying the pharmacokinetic and pharmacodynamic properties, including toxicity. Therefore the present communication constitutes a review on the medicinal properties, ethnomedicinal uses, phytochemistry, pharmacological activities, pharmacokinetic and toxicity of an Indian medicinal plant, Justicia adhatoda. A wide range of phytochemical constituents have been isolated from J. adhatoda which possesses activities like antitussive, abortifacient, antimicrobial, cardiovascular protection, anticholinesterase, anti-inflammatory and other important activities. Aegle marmelos family Rutaceae is an alleged ayurvedic medicinal tree commonly known as the bael. It is a medium sized tree growing throughout the forest of India of altitude 1200 meter. It is found all over India, from sub-Himalayan forest, Bengal, central and south India. It is considered to be a holy tree in India. Various parts of this plant such as leaves, roots, seed, bark and fruit, possess anti-microfilarial, antifungal, immunomodulatory, anti-proliferative, wound healing, antifungal, analgesic, anti-inflammatory, antipyretic, hypoglycaemic, antidiyslipidemic, anti-fertility, and insecticidal activity. Various phytopharmacological evaluations have been reported in this writing for the important potential of the Aegle marmelos.

Introduction

Plants have played a critical role in maintaining human health and civilizing the quality of human life for thousands of years. The use of plants as medicines is as old as human civilization itself and out of about 258,650 species of higher plants reported from the world; more than 10% are used to cure ailings communities (Shinwari, 2010). Many of the existing medicinal system such as Ayurveda, Unani, Homeopathy, Naturopathy, Siddha and other alternative medicinal system have been utilizing plants as effective medicines to cure many harmful diseases (Prasad et al., 2011). The world health organization (WHO) has estimated that 80% of the earth’s inhabitant relied on traditional medicine for their primary health care needs and most of these therapies involved the use of plant extract or their active compounds (Bruneton, 1995). Justicia adhatoda (L.) Nees (family Acanthaceae) is a shrub widespread throughout the tropical regions of Southeast Asia (Chakrabarty and Brantner, 2001). The name J. adhatoda (L.) Nees and Adhatoda zeylanica Medic are used synonymously. It is commonly known as Vasaka or Malabar nut. It is a perennial, evergreen and highly branched shrub (1.0 m to 2.5 mm height) with unpleasant smell and bitter taste (Patel and Venkata-Krishna-Bhatt, 1984). It has opposite ascending branches with white, pink or purple flowers (Patel and Venkata-Krishna-Bhatt, 1984). It is a highly valuable Ayurvedic medicinal plant used to treat cold, cough, asthma and tuberculosis (Sharma et al., 1992). Its main action is expectorant and antispasmodic (bronchodilator) (Karthikeyan et al., 2009). Moreover the importance of Vasaka plant in the treatment of respiratory disorders can be understood from the ancient Indian saying, “No man suffering from phthisis need despair as long as the Vasaka plant exists” (Dymock et al., 1893). Thus the frequent use of J. adhatoda has resulted in its inclusion in the WHO manual “The Use of Traditional Medicine in Primary Health Care” which is intended for health workers in South-East Asia to keep them informed of the restorative utility of their surrounding flora (WHO, 1990). The major alkaloids of the plant, vasicine and vasicinone, have been found to be biologically active.

Plant Description

Bael (Aegle Marmelos (Linn), family Rutaceae, is also known as Bale fruit tree, is a moderate sized, slender, aromatic tree, 6.0 -
7.5 m in height, and 90 to 120 cm in girth, with a somewhat fluted bole of 3.0-4.5 meter growing wild throughout the deciduous forests of India, ascending to an altitude of 1200 meter in the western Himalayas and also occurring in Andaman island. This is generally considered as sacred tree by the Hindus, as its leaves are offered to Lord Shiva during worship. According to Hindu mythology, the tree is another form of Lord Kailashnath. Leaves, fruit, stem and roots of this tree at all stages of maturity are used as ethno medicine against various human ailments. \textit{A. marmelos} is a subtropical plant and found in India, Ceylon, China, Nepal, Sri Lanka, Myanmar, Pakistan, Bangladesh, Nepal, Vietnam, Laos, Cambodia, Thailand, Indonesia, Malaysia, Tibet, Sri Lanka, Java, Philippines and Fiji. In India it found in Sub-Himalayan tracts from Jhelum eastwards to West Bengal, in Central and South India. It found almost in all the states of India. \textit{A. marmelos} is known by different names in different parts of world.

\textit{Justicia adhatoda}

\textbf{Medicinal properties:} \textit{J. adhatoda} is a well known plant drug in Ayurvedic and Unani medicines (Claeson et al., 2000). It is used by Ayurvedic physicians and possesses some medicinal properties. It has been used for the treatment of various diseases and disorders, particularly for the respiratory tract ailments. Therefore, it is a primary herb of the Ayurvedic system used in the treatment of cough, bronchitis, asthma and symptoms of common cold (Karthikeyan et al., 2009). The source of the drug ‘Vasaka’ is well known in the indigenous system of medicine for its beneficial effects, particularly in bronchitis (Kumar et al., 2005). Similarly Bisolven, a branded drug containing Vasaka as an ingredient is used to clear the airways by decreasing the mucus secretions and opening the passages (Racle, 1976). There are various herbal formulations accessible for the treatment of various kinds of respiratory disorders, such as, Kanjang, an oral solution with a fixed combination of standardized extracts of \textit{Echinacea purpurea}, \textit{J. adhatoda} and \textit{Eleutherococcus senticosus} has been used in the relief of symptoms allied with the common cold (coughing and irritability of the throat), with a well established medical use comprising 50 million human daily doses (Narimanian et al., 2005). The major efficacy of this solution is mainly due to the presence of Vasaka. Other constituents of Kanjang have been exposed to have antistress effects, which might be occasioned partly by an endocrine and partly by an immunomodulatory mechanism of action. This plant is a source of Vitamin C and has medicinal uses, mainly antispasmodic, fever reducer, anti-inflammatory, anti-bleeding, bronchodilator, anti-diabetic, disinfectant, anti-jaundice and oxtocyte (Maurya and Singh, 2010). It is antiperiodic, astringent, diuretic, purgative and is also used as an expectorant in addition to liquefy sputum (Salalamp et al., 1996). The leaves, flowers and roots of this plant used in herbal drugs against tubercular activities (Barry et al., 1955), cancer (Pandey, 2002) and possessed anti-helminthic properties (Ayyanar and Ignacimuthu, 2008). The leaf juice is stated to cure diarrhea, dysentery and glandular tumor (Ayyanar and Ignacimuthu, 2008). Similarly in Homeopathy, the plant has been used in the treatment of cold, cough, pneumonia, fever, jaundice, catarrh, whooping cough and asthma (Asolkar et al., 1992).

\textbf{Ethnomedical uses:} All the parts of \textit{J. adhatoda} has been used for their curative effects from ancient times (Atal, 1980). It has been used in Ayurvedic system of medicine for the treatment of various ailments of respiratory tract in both children and adults. Various parts of the plant are used in Indian traditional medicine for the treatment of asthma, joint pain, lumber pain, sprains, cold, cough, eczema, malaria, rheumatism, swelling and venereal diseases (Jain, 1991). \textit{J. adhatoda} has also been used by the European medical practitioners. The fluid extract and tincture were used in England as an Antispasmodic, Expectorant and febrifuge. It was said to be beneficial in intermittent, typhus fever and Diphtheria (Wren, 1932). In Germany, the leaves are used as an expectorant and spasmylic agent (Madaus, 1938). In Sweden \textit{J. adhatoda} is classified as a natural remedy and some preparations against cough containing an extract of Vasaka are accessible (Farnhol, 1998). The ethnomedicinal uses of various parts of \textit{J. adhatoda} are along these lines.

\textbf{Whole plant:} The whole plant is used as an ingredient of numerous popular formulations including cough syrup used in combination with Ginger (\textit{Zingiber officinale}) and Tulsi (\textit{Ocimum sanctum}) where it exerts its action as an expectorant and antispasmodic (Atal, 1980). The plant is used for treatment of excessive phlegm and menorrhagia in Sri Lanka (Kirtikar and Basu, 1975). It is also used for the treatment of bleeding piles (Ahmad et al., 2009), impotence and sexual disorders (Pushpangadan et al., 1995).

\textbf{Leaves:} A yogic practice is to chew the leaf buds alone or with a little ginger root, to clear the respiratory passages in preparation for the vigorous breathing exercises. The various preparation of leaves are used for curing bleeding, haemorrhage, skin diseases, wounds, headache and leprosy in Southeast Asia (Adnan et al., 2010; Atta-Ur-Rahman et al., 1986; Roberts, 1931). The bruised fresh leaves are used for snake-bites in India and Sri Lanka (Roberts, 1931). Usually, yellow leaves are exploited for cough (Lal and Yadav, 1883) and smoke from leaves is used for asthma (Shah and Joshi, 1971). The plant leaves are used for checking postpartum haemorrhage and urinary trouble (Pushpangadan et al., 1995). It is found that 70% of the pregnant women in the Gora village of Lucknow (Uttar Pradesh, India) use the leaves of \textit{J. adhatoda} to induce abortion (Nath et al., 1997). Moreover, it is observed that the Neterhat people in Bihar (India) used a decoction of the leaves to stimulate and heal before and after delivery (Jain et al., 1994). The leaf powder boiled in sesame oil is used to stop bleeding, earaches as well as pus from ears (Reddy et al., 1989) and jaundice (Reddy et al., 1988).

Decoction and ash of leaves are used for bronchial complaints such as asthma, tuberculosis (Jain and Puri, 1984), antipyretic (Jain, 1965) and relieve acidity. The leaves are toxic to ‘all forms of lower life’ and have insecticidal effects (Agrawal et al., 1986). It was also used for stomach catarrh with constipation, gout, urinary stone (Madaus, 1938) and warmed leaves used externally for rheumatic pains and dislocation of joint (Rao and Jamir, 1982).
Moreover, the preparation of leaves in spirit is used for curing the wealthy persons suffering from certain humors in Myanmar (Kirtikar and Basu, 1975).

**Root:** The extract of roots of *J. adhatoda* is commonly used by rural population against diabetes, cough and certain liver disorders (Bhat et al., 1978). The paste, powder and decoction of root is used for curing tuberculosis, diphtheria, malarial fever, leucorrhoea and eye diseases in Southeast Asia (Dymock et al., 1890; Kirtikar and Basu, 1975). The paste of roots mixed with sugar and used for treatment of acute nightfall in Sitapur District, Uttar Pradesh, India (Siddiqui and Hussain, 1993). Moreover, the macerated roots of *J. adhatoda* are applied on the pubic region and vagina to help parturition (Pathak, 1970) and it facilitates the expulsion of foetus (Iyengar, 1994). The root decoction is also used for gonorrhea (Siddiqui and Hussain, 1993).

**Flower:** The fresh flowers are used for ophthalmia and various preparations of flowers are used for treatment of cold, phthisis, asthma, bronchitis, cough, antispasmodic, fever and gonorrhoea in South-East Asia (Dymock et al., 1890; Kirtikar and Basu, 1975; Atta-Ur-Rahman et al., 1986). The flowers are also used as antiseptic to improve blood circulation and hectic heat of blood (Kirtikar and Basu, 1975; Atta-Ur-Rahman et al., 1986; Dymock et al., 1890).

**Fruit:** The fruit of *J. adhatoda* are used for curing cold, antispasmodic, bronchitis, Jaundice (Kirtikar and Basu, 1975), Diarrhoea, Dysentery, Fever and as laxative (Roberts, 1931; Kirtikar and Basu, 1975; Atta-Ur-Rahman et al., 1986).

**Phytochemistry:** The chemical compounds found in *J. adhatoda* plant includes essential oils, fats, resins, sugar, gum, amino acids, proteins and vitamins ‘C’ etc (Bhat et al., 1978). The phytochemical analysis show that phenols, tannins, alkaloids, anthraquinone, saponins, flavonoids and reducing sugars were found in the leaves of *J. adhatoda* (Pathak, 1970). But the pharmacologically most studied chemical component in *J. adhatoda* is a bitter quinazoline alkaloid, vasicine (1, 2, 3, 9-tetrahydropyrole [2, 1-b] quinoxolin-3-ol, C11H12N2O) which is present in the leaves, roots and flowers.

It can be synthesized by addition of 2-aminoenzyaminone to the vicinyl vicinal trycarylon reagent which leads to the short synthesis of Vasicine (Wasserman and Kuo, 1991). Besides vasicine, the leaves contain several alkaloids (Vasicinone, Vasicinol, Adhatodine, Adhatonine, Adhvasinone, Anisotine and Hydroxypeganine), betaine, steroids and alkanes (Lahiri and Prahdan, 1964; Chowdhury and Bhattacharyya, 1987). Vasicine is metabolized to vasicinone and analysis of *J. adhatoda* leaf extract showed that it contained 0.85% vasicine and 0.027% vasicinone. The absolute stereochemistry of (-)-Vasicine and (+)-Vasicinone have been shown to be the 3S configuration on the basis of X-ray analysis of the alkaloid hydrobromides. Similarly, Vasicinol and Vasicinolone which have been interrelated should also have the 3S configuration (Joshi et al., 1996). The novel alkaloid isolated and characterized as 1, 2, 3, 9-tetrahydro- 5-methoxypyrrolic [2, 1-b] quinoxolin-3-ol (Chowdhury and Bhattacharyya, 1987). The roots also contain alkaloids (vasical, vasicinoline, vasicinone and adhatonine), a steroid (daucosterol), carbohydrates and alkanes. In the flowers triterpenes (á-amyrin), flavonoids (Apigenin, Astragalin, Kaempferol, Quercetin, Vitexin) and alkanes have been found (Haq et al., 1967).

**Pharmacology:** The major phytochemical active compounds like vasicine and vasicinone which are isolated from water and alcoholic extracts of vasaka exert effective pharmacological actions.

**Antitussive:** The extracts of *J. adhatoda* were shown to comprise a good antitussive activity in anaesthetized rabbits and guinea pigs as well as in unaesthetized guinea pigs. Because Vasicine showed the bronchodilatory activity both in vitro and in vivo. Although, Vasicinone the main metabolite of Vasicine, which is also present in *J. adhatoda* extracts, showed bronchoconstriction in vivo. The two alkaloids in combination showed a bronchodilatory activity both in vitro and in vivo (Atal, 1980). It may be due to the presence of the specific site of action of Vasicinone and Vasicine (major alkaloids) which suppress coughing by its action on its neuronal system in the medulla (Dhuley, 1999). Intravenously, it was (1/20 -1/40) as active as codeine on mechanically and electrically induced coughing in rabbits and guinea pigs.

**Abortifacient:** Vasicine was found to have uterotonic activity in different species including human beings. It was shown that the effect was influenced by the priming degree of the uterus by estrogens. Vasicine initiated rhythmic contractions of human myometrial strips from both non-pregnant and pregnant uterus with the effect which was comparable with that of oxytocin and mathergin (Atal, 1980). In a study conducted on rats, rabbits, hamsters and guinea pigs, it was found that vasicine has uterotic and abortifacient effects possibly by enhancing the synthesis and release of prostaglandins. In this study dose dependent effect was observed with effective doses ranging between 2.5 to 10 mg/kg. However, administration of estradiol dipropionate potentiated the abortifacient effect in guinea pigs whereas treatment with aspirin inhibited the abortifacient activity due to inhibition of release of prostaglandins (Chandoke, 1982).

**Antimicrobial activity:** The water extract was shown to be active against microbial flora isolated from patients with gingivitis (Patel and Venkata-Krishna-Bhatt, 1984). The alcoholic extract of leaves and roots showed antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*, whereas water extract showed activity against *S. aureus* only (George et al., 1947). The crude ethanolic extract of the leaves exhibited antimicrobial activity against *Staphylococcus epidermidis, Bacillus subtilis, Proteus vulgaris* and *Candida albicans* (Karthikeyan et al., 2009). Moreover the methanolic extract of *J. adhatoda* exhibited positive antimicrobial activity for *P. aeruginosa, S. aureus* and *B. subtilis* while *E. coli* was not effectively inhibited by extracts of tested plant (Shiwari et al., 2009). While the extract of plant showed minimum inhibition in the growth of fungi, *Microsporum gypseum, Chrysosporium tropicum* and *Trichophyton terrestrae* (Quershi et al., 1997).

**Antituberculosis activity:** *Mycobacterium tuberculosis* was found to be inhibited by benzyl amine, ambroxol, bromhexine (semi synthetic derivatives of vasicine) due to their mucolytic action. As these compounds are concentrated in macrophages they might exert a clinically useful effects on intracellular tuberle bacillci by enhancement of lysozyme level in bronchial secretions and levels of rifampicin in...
lung tissue and sputum. Therefore these compounds are being active as adjunctive for therapy of tuberculosis (John and Snell, 1996).

**Cardioprotective activity:** In combination of vasicine and vasicinone significant reduction in cardial depressant effects was observed. No effect was shown by vasicinone (DI-form), however L-form was found to be weakly effective stimulating cardiac muscles (Atal, 1980).

**Anticholinesterase activity:** Vasicinone obtained from the roots, produced transient hypotension in cats, contraction of isolated intestine and depression of isolated heart in guinea pigs, thus showing good anticholine anteresterase activity (Lahiri and Prahdan, 1964).

**Anti-inflammatory activity:** The methanolic extract of *J. adhatoda* was evaluated for anti-inflammatory activity by the modified hen’s egg choriogallantoic membrane test. The alkaloid fraction showed potent activity at a dose of 50 lg/pellet (Chakrabarty and Brantner, 2001).

**Other activities:** The essential oil from the leaves of *J. adhatoda* showed smooth muscle relaxant activity in the isolated guinea-pig tracheal chain (Cruz et al., 1979). Methanolic extract from the plant has been shown to possess anti-allergic activity in guinea pig at doses of 6 mg per animal (Muller et al., 1993). The ethanolic extracts from the leaves showed hypoglycaemic activity after oral administration in rats and rabbits (Modak and Rao, 1966; Dhar et al., 1966). Leaf showed significant hepatoprotective effect at doses of 50 to 100 mg/Kg on liver damage induced by D-galactosamine in rats (Bhattacharyya et al., 2005). The radiomodulatory influence of ethanolic extract of leaves was studied against radiation-induced hematological alterations in peripheral blood of swiss albino mice. A significant increase in serum alkaline phosphatase activity and decrease in acid phosphatase activity was observed in irradiated animals during the entire period of study (Kumar et al., 2005). It exerts antioxidant effect against lipid peroxide and xanthine oxidase induced oxidation (Jahangir et al., 2006). Leaf powder of this plant showed considerable anticyelarring activity in experimental rats in ethanol induced ulceration model (Shrivastava et al., 2006). The rate of healing was found to be higher in the plant extract treated wounds in buffaloes as compared to pancreatic tissue extracts (Zama et al., 1985). The decoction of leaves activated the trypsin enzyme hence stimulated the digestion process (Vijaya and Vasudevan, 1994).

**Pharmacokinetics:** The studies on absorption and distribution of vasicine in mice after intravenous, intramuscular and subcutaneous administration show similar results as these reported in rats (Zutsch et al., 1980). Vasicine (20 mg/kg) given intramuscularly was well absorbed reaching a maximum concentration of about 56 lg/ml in blood in both pregnant and non-pregnant rats and about 10 lg/ml in amniotic fluid (Atal, 1980). After intravenous injection in rats and mice high concentration of vasicine were found in the uterus within 5 min and the peak level was achieved after 10 min. The half-life was after intravenous, 5 to 7 min, 1.5 and 2 h intramuscular and subcutaneous administration respectively. It is reported that vasicine and its metabolites are mainly excreted in the urine. On intravenous and intramuscular administration about 55% of excreted product in the first 18 and 22 h respectively, was vasicine, while an oral administration about 18% of the excreted product was vasicine during the first 24 h (Atal, 1980). After oral administration, very low concentration was found in the uterus. Vasicine is metabolized in the liver to vasicinone and other metabolites which contribute to the first pass effects and which is an important way of elimination of Vasicine.

**Toxicity:** In a screening study of anti-fertility activity of *J. adhatoda*, after administration of extract of leaves either in mice or in rats, no effects on the pregnancy were recorded (Bhaduri et al., 1968). But the animals treated with about 100 mg/kg of different *J. adhatoda* extracts did not show any implantation sites (Prakash et al., 1985). The effect of *J. adhatoda* spissum leaf extract on early gestation was studied. There was no effect on the maternal body weight or any other parameter recorded in the form of statistically significant differences between the treated and control animals. Analysis of *J. adhatoda* leaf extract showed that it contained the vasicine ranges from 0.0541 to 1.105% (Bhaduri et al., 1968). So the toxicology study of vasicine has been performed separately. No remarkable adverse effects were recorded in any species Dhankhar et al., 625 (Atal, 1980). The general toxicity after repeated oral administration of vasicine daily for 6 month has been studied in rats and monkeys (Pahwa et al., 1987). Observations, clinical chemistry and histopathology of the major organs were performed in both the species. Moreover, autopsy and histopathological examination of major organs did not reveal any abnormalities. In rats vasicine (5 and 10 mg/kg body weight) was administered intraperitoneally to groups of ten animals at various interval of pregnancy. On 1 to 7 days pregnancy, no antimplantation effect but an abortifacient effect was observed after 7 days pregnancy (Atal, 1980). The teratogenic studies in vasicine were performed in rats and rabbits (Atal, 1980). Except for occasional pregnancy wastage seen at a dose of 2.5 mg/Kg but partial wastage at higher doses of vasicine did not exhibit any teratogenic effects or any other adverse effects in any of pups of the first or second germination (Atal, 1980). Vasicine has been tried in a preliminary human study being conducted for interruption of mid-trimester pregnancy by intraamniotic instillation of the drug. 

**Aegle marmelos**

Traditional use of *Aegle marmelos*: *A. marmelos* is extensively described in the Vedic literature for the treatment of various diseases. *A. marmelos* is traditionally used to treat jaundice, constipation, chronic diarrhea, dysentery, stomachache, stomachic, fever, asthma, inflammations, febrile delirium, acute bronchitis, snakebite, abdominal discomfort, acidity, burning sensation, epilepsy, indigestion, leprosy, myalgia, smallpox, spermatorrhea, leucoderma, eye disorders, ulcers, mental illnesses, nausea, sores, swelling, thirst, thyroid disorders, tumors, ulcers and upper respiratory tract infection.

**Phytochemical composition of *Aegle marmelos***: Different organic extracts of the leaves of *A. marmelos* have been reported to possess alkaloids, cardiac glycosides, terpenoids, saponins,
tannins, flavonoids and steroids. Aegle marmelos fruit pulp reported for the availability of steroids, terpenoids, flavonoids, phenolic compounds, lignin, fat and oil, inulin, proteins, carbohydrates, alkaloids, cardiac glycosides and flavonoids.

**Nutritional value of Aegle marmelos:** The fruit of A. marmelos possess high nutritional value. The fruit is used to make juice, jam, sirup, jelly, toffee and other products. The pulp is reported to contain water, sugars, protein, fiber, fat, calcium, phosphorus, potassium, iron, minerals and vitamins (Vitamin A, Vitamin B1, Vitamin C and Riboflavin). The leaves and the shoot of the plant are used as green vegetable in Indonesia.

**Pharmacological studies:** A. marmelos is one of the most widely used medicinal and neutricuitical plant in the family Rutaceae. In recent history this plants is reported for various medicinal properties. **Antioxidant Activity:** Antioxidants are the compounds with free radicals scavenging activity and capable of protecting the cells from free radical mediated oxidative stress. The antioxidant compounds can be derived from natural sources such as plants. 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.

Antioxidant activity of the fruit of A. marmelos was reported. Antioxidant activity and freeradical scavenging activity of the ripe and unripe fruit of Aegle marmelos was compared. Results indicate that the enzymatic antioxidants increased in ripe fruit when compared to unripe fruit extract (except glutathione peroxidase). 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 \( \text{H}_2\text{O}_2 \) radical scavenging assay.

Both aqueous and alcoholic extract exhibited good antioxidant activity. The antioxidant activity of the fruit of A. marmelos was reported. The aqueous extract of A. marmelos fruit was screened for antioxidant activity by the DPPH radical scavenging. The extract showed efficient antioxidant activity.

**Antimicrobial activity:** A. marmelos has been traditionally used for the treatment of various infectious diseases and been extensible reported to inhibit the broad range of pathogenic microorganisms. Many *in vitro* studies proved the antimicrobial potential of A. marmelos extracts towards the pathogenic microorganisms including bacteria and fungi. The antimicrobial activity of the leaves of A. marmelos was performed by agar well diffusion method. The aqueous, petroleum ether and ethanol extract of the leaves of Aegle marmelos exhibited efficient antimicrobial activity 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*. The antimicrobial activity of the leaves of Aegle marmelos was reported. The antimicrobial activity was checked by disc diffusion method. The petroleum ether extract of leaves was checked against multi resistant strains of *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Salmonella typhi, Proteus vulgaris, Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. The antimicrobial activity against gram-negative strains was higher than that of gram positive strains. The antifungal activity of the 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*.

The antifungal and antibacterial activity of the fruit of A. marmelos was reported. The antimicrobial activity was performed by tube dilution MIC method. The decoction of the fruit showed activity against *Aspergillus niger, Aspergillus fumigatus, Candida albicans* and *Staphylococcus aureus* and the MIC results for the above respective organisms was 19.5 \( \mu \text{g/ml} \), 39 \( \mu \text{g/ml} \), 625 \( \mu \text{g/ml} \) and 1.25 mg/ml. The antibacterial activity of the leaves, fruits and barks of Aegle marmelos was reported. The antimicrobial activity of chloroform, methanol and water was performed by disc diffusion method. The antimicrobial activity was checked against *Bacillus subtilis, Staphylococcus aureus, Klebsiella pneumoniae, Proteus mirabilis, Escherichia coli, Salmonella paratyphi A* and *Salmonella paratyphi B*. The methanol extract showed significantly high activity against above mentioned bacteria than that of the other extracts.

The antibacterial activity of the leaves of Aegle marmelos was reported. The antibacterial activity of the different extracts was evaluated by agar well diffusion method. The hexane, cold methanol, hot methanol and ciprofloxacin extracts showed high antibacterial activity against *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris, Micrococcus luteus, Enterococcus faecalis* and *Streptococcus faecalis*. **Cytoprotective effect:** The cytoprotective effect of the leaves of Aegle marmelos was reported in *Cyprinus carpio* (freshwater fish) exposed to heavy metals. *C. carpio* was exposed to heavy metals followed by the treatment with the dried powder of Aegle marmelos leaves. Treatment resulted in cytoprotective effect by stabilization of plasma membrane and modulation of antioxidant enzyme system. **Hepatoprotective effect:** The hepatoprotective effect of the leaves of A. marmelos and were reported in alcohol induced liver injury in Albino rats. The rats were administered with 30% ethyl alcohol for a period of 40 days. The induced rats were fed with leaves of A. marmelos for 21 days. The TBARS values of healthy, alcohol intoxicated and herbal drug treated animals were 123.35, 235.68 and 141.85 \( \text{ig/g tissue} \) respectively. This indicates the excellent hepatoprotective effect of the leaves of A. marmelos. **Antifertility effect:** The antifertility effect of the aqueous extracts of leaves of Aegle marmelos was reported in male Albino rats. The rats were administered with aqueous extracts (250 mg/kg body weight) of leaves of Aegle marmelos for 45 days. 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. **Insect controlling properties:** Essential oil from the leaves of A. marmelos was reported for showing insecticidal activity against four stored grain insect pests included *Callosobruchus chinensis*.
was evaluated for hypoglycemic and antioxidant effect by Upadhya Sunderam al Marmelos activity on acetic acid-induced writhing and tail flick test in mice. The dose level of 200 and 300 mg/kg showed significant analgesic castaneum administration of methanolic extract of Aegle marmelos was reported for insect repellent activity against Sitophilous oryzae and Tribolium castaneum. However Aegle marmelos essential oils didn’t showed 100% repellent activity against the test insects.

**Analgesic activity:** Leaves of A. marmelos were reported to possess analgesic activity. Methanol extract of leaves of A. marmelos was screened for analgesic activity by Acetic acid-induced writhing test in Swiss mice. The results indicated that methanol extract significantly reduced the writhing induced by acetic acid in tail flick test methanol extract (200 and 300 mg/kg body weight).

**Chemical constituents:** Various phytoconstituents have been isolated from the various parts of Aegle marmelos.

**Traditional uses of bael tree parts for medicinal purposes:** The different parts of Bael are used for various therapeutic purposes, such as for treatment of Asthma, Anaemia, Fractures, Healing of Wounds, Swollen Joints, High Blood Pressure, Jaundice, Diarrhoea Healthy Mind and Brain Typhoid Troubles during Pregnancy. Aegle marmelos has been used as a herbal medicine for the management of diabetes mellitus in Ayurvedic, Unani and Siddha systems of medicine in India, Bangladesh and Sri Lanka. Flowers are useful in diarrhea, excessive thirst, vomiting and eye disorders and it is advisable as diet in eruptive boils.

**Various proved therapeutic values of Aegle marmelos:**

**Wound healing activity:** Effect of topical and intraperitoneal administration of methanolic extract of Aegle marmelos ointment and injection was studied respectively on two types of wound models in rats, the excision and the incision wound model. Both the injection and the ointment of the methanolic extract of Aegle marmelos produced a significant response in both of the wound type tested. In the excision model the extract treated wounds were found to epithelialize faster and the rate of wound contraction was higher, as compared to control wounds. The extract facilitated the healing process as evidenced by increase in the tensile strength in the incision model. The results were also comparable to those of a standard drug nitrofurazone.

**Analgesic:** The methanol extract of leaves of Aegle marmelos at a dose level of 200 and 300 mg/kg showed significant analgesic activity on acetic acid-induced writhing and tail flick test in mice.

**Anti-diabetic activity:** Aqueous extract of Aegle marmelos leaves, was evaluated for hypoglycemic and antioxidant effect by Upadhyya et al (2004), by using alloxan induced diabetes in male albino rats and proposed AML may be useful in the long-term management of diabetes. Similarly, the anti hyperlipidaemic activity of aqueous extract of Aegle marmelos fruits was demonstrated by Marinzene et al (2005), using the streptozotocine induced diabetic wistar rats. Sunderam et al, (2009) worked on alcoholic extract of Aegle Marmelos, Momordica Charantia and Eugenia Jambolana separately; against Streptozotocine induced diabetic rats and confirmed their protective activity against laboratory induced cell necrosis, Whereas, Kuttan and Sabu (2004) studied on leaf extract of Aegle Marmelos on Alloxane induced diabetes and reported that used extract was enough capable to reduce oxidative stress by scavenging lipid peroxidation and enhancing certain Anti-oxidant levels which causes lowering of elevated blood glucose level. Beside of all above cited work, Hema and Lalithakumari (1999) had presented a tremendous results of Aegle Marmelos and documented its hypoglycemic action along with other pharmacological actions on molecular level.

**Hepatoprotective activity:** Singanan et al, (2007) worked on Aegle Marmelos leaf extract on alcohol induced liver injury in albino rats and presented data of excellent hepatoprotective effects. Similarly, Rammik (2008), also demonstrated that aqueous extract of bael fruit pulp and seeds are effective in the treatment and prevention of CCI4 induced hepatic toxicity.

**Antimicrobial Activity:** Maheshwari et al, (2009) studied on ethonic extract of dried fruit pulp of Aegle marmelos against various intestinal pathogens i.e. Shigella boydii, S. sonnei and S. Flexneri and proposed that certain phytochemicals including Phenols, Tannins and Flavonoids were effective against all. It was also confirmed by Kaur et al, (2009) by getting treat E. coli with Aegle marmelos fruit extract. In consonance, Citarasu et al, (2003) also experimented Aegle marmelos on certain pathogenic bacteria like Salmonella typhi, Pseudomonas aeruginosa, Aeromonas hydrophyla and Vibrio sp., and concluded its positive bactericidal effects.

The literature survey revealed that J. adhatoda has been widely studied for its pharmacological activities and regarded as Universal Panacea in Ayurvedic medicines and finds its position as a versatile plant having a wide spectrum of medicinal activities. It can be concluded that J. adhatoda is an important source of many pharmacologically and medicinally important chemicals such as Vasicine, Vasicinone, Vasicoline and other various useful minor alkaloids. There is not sufficient scientifically valid evidence to state that J. adhatoda extract could be potentially harmful to human beings. As the global scenario is now changing towards the use of non toxic plant products, development of modern drugs from vasaka should be emphasized. It is also clear that much needs to be discovered, both as to the active ingredients and their biological effects. Furthermore, the information summarized here is intended to serve as a reference tool to researchers in the field of ethnopharmacology of J. adhatoda. Numerous pharmacological studies have been conducted on different parts of Aegle marmelos. The present literature supports the potential of Aegle marmelos as a medicinal tree. It is quite evident from this review that Aegle marmelos contains a number of phytoconstituents which reveals its uses for various therapeutic purposes. The Plant or its individual parts can be used for the treatment of various disorders in human being such as, diabetes, liver toxicity, fungal infection, microbial infection, inflammation, pyrexia and to relieve pain. Still, more research can be done to investigate the unexplored and unexploited potential of this plant and to investigate the mechanism of actions with other therapeutic activities.
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References


