



REVIEW ARTICLE

AZIMA TETRACANTHA: A TREASURE TO BE HUNTED

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ABSTRACT

Traditional medicine has a long history of serving people all over the world. India is without doubt an herbal hub. Medicinal plants that are native to India and their use in various traditional systems of medicine are indeed awe-inspiring. The ethnobotany and ubiquitous plants provide a rich resource for Natural drug research and development. In recent years, the use of traditional medicine information on plant research received considerable interest. The medicinal plants contain several phytochemicals such as vitamins, carotenoids, terpenoids, flavonoids, polyphenols, alkaloids, tannins, saponins, enzymes, minerals etc. These phytochemicals possess antioxidant activities, which, prevent or can be used in the treatment of many diseases, including cancer. Several medicinal plants all over the world, including India, which are being used traditionally for the prevention and treatment of cancer. The present paper is a comprehensive review of a medicinal shrub, *Azima tetracantha* Lam. plant belonging to the family of Salvadoraceae and its various medicinal values.

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INTRODUCTION

Medicinal plants are still major parts of traditional medicinal systems in developing countries. Many infectious diseases are known to be treated with herbal remedies throughout the history of mankind. Even today plant materials continue to play a major role in primary health care as therapeutic remedies in many developing countries (Sukanya *et al.*, 2009). Medicinal plants which form the backbone of traditional medicine have in the last few decades been the subject of very intense pharmacological studies. This has been brought about by the acknowledgement of the value of medicinal plants as potential source of new compounds of therapeutic value and as source of new compounds in drug development. In many parts of the world medicinal plants are used for antibacterial, antifungal and antiviral activities. Plant derived drugs serve as prototypes to develop more effective and less toxic medicines. Tribal medicine has not been studied extensively (Zakaria, 1989). *Azima tetracantha* Lam. (Family: Salvadoraceae) locally known as "*Mulsangu*", is a rambling spinous shrub flowering throughout the year found in Peninsular India, West Bengal, Orissa, African Countries and extends through Arabia to tropical Asia. The common names of the plant are Uppimullu, Mulchangan, Needle bush, Yasanku and Kundali in Ayurvedic medicine. The leaves of the plant are elliptical in shape and are rigid, pale green colored. The flowers are small, greenish white (or) yellow colored, unisexual in axillary fascicles. The berries are white in colour; usually one seeded and edible. *Azima tetracantha* root bark is used in muscular rheumatism, while the leaf juice is used for

treating tooth and ear ache. In East Africa the powdered roots of *Azima tetracantha* Lam. are applied directly to snake bites and an infusion is taken orally as a treatment. In India and Sri Lanka the root, root bark and leaves are added to food as a remedy for rheumatism. It is planted as live fence in Bangalore (India). In Malaysia pickled leaves are used as an appetizer and against colds. The plant is promoted as an ornamental in the United States.

Several medicinal properties are attributed to this plant in the Indian system of medicine and included in the check list of traded medicinal plants. The ethno botanical survey reveals the usage of this plant as a unique folk medicine by the adivasis (tribal) (Hebbar *et al.*, 2004; Mohamed Al-Fatimi *et al.*, 2007; Vikneshwaran *et al.*, 2008; Ignacimuthu *et al.*, 2008). The root, root bark and leaves are administered with food as a remedy for rheumatism (Chopra *et al.*, 1956; Kirtikar *et al.*, 1984). It is a powerful diuretic given in rheumatism, dropsy, dyspepsia and chronic diarrhea and as a stimulant tonic after confinement (Nadkarni, 1976). The leaves are found to contain azimine, azcarpine, carpine and isorhamnitine-3-O-rutinoside etc., (Rall *et al.*, 1967; Williams & Nagarajan, 1988, Bennet *et al.*, 2004). Friedelin, lupeol, glutinol and β -sitosterol were isolated from the petroleum ether extract of the leaves of *A. tetracantha* (Rao & Prasada Rao, 1978). The seeds of this plant have been found to possess novel fatty acids along with other fatty acids (Daulatabad *et al.*, 1991). Antimicrobial activity was also reported for this plant (Siva *et al.*, 2008). *A. tetracantha* leaf powder was assessed for its anti-inflammatory activity (Ismail *et al.*, 1997). The benzene, chloroform and

aqueous extract of leaves of *A. tetraacantha* were screened for analgesic activity in mice using hot plate method (Nandgude *et al.*, 2007). The ethanolic leaf extract of *Azima tetraacantha* Lam. was investigated for hypoglycemic and hypolipidemic activity in alloxan-induced diabetic albino rats (Begum *et al.*, 2009).

Antibacterial activity of phytochemicals of *Azima tetraacantha* Lam

Antibacterial activity of phytochemical separation from alkaloids, flavonoids and sterol were tested against *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *E.coli* (Gowthami *et al.*, 2012). The sterols compound exhibited maximum zone of inhibition against *Bacillus subtilis* (25mm), and *Pseudomonas aeruginosa* (24mm). The alkaloid compound showed minimum zone of inhibition was observed in *Bacillus subtilis* (12mm) and *Pseudomonas aeruginosa* (12mm). Maximum zone of inhibition was observed in sterols compound when compared with alkaloids and flavonoids.

The reports of the study performed by Gayathri G *et al* in 2011 revealed that methanolic extract of *A.tetraacantha* leaves possess greater antimicrobial activity than CE. The test extracts showed percent inhibition in a concentration dependent manner against the test organisms such as *S.aureus*, *P. vulgaris* etc. The study designed by Duraipandiyar *et al.*, in 2011 evaluated the antifungal activity of *Azima tetraacantha* extracts and isolated compound (friedelin) against fungi. Antifungal activity was carried out using broth microdilution method and fractions were collected using (silica gel) column chromatography. The antifungal activity of *Azima tetraacantha* crude extracts and isolated compound (friedelin) were evaluated using the micro dilution method. Hexane extract showed some antifungal activity. The compound also exhibited antifungal activity against tested fungi. The results suggested that Friedelin is a strong antifungal agent.

The antimicrobial activity of leaves of the medicinal plant *Azima tetraacantha* collected from the regions of Ambalathara, Kerala, South India was checked against the clinical pathogens by agar well diffusion method by Hema *et al.*, 2012. *Azima* showed highest antimicrobial activity on ethanolic extracts. Antimicrobial activities of five solvent extracts (ethanol, methanol, acetone, chloroform and distilled water) were tested against seven clinical pathogens such as *Staphylococcus aureus* (Pus), *Klebsiella* sp. (Sputum), *Escherichia coli* (Urine), *Pseudomonas* sp. (Pus), *Enterococci* sp. (Urine), *Serratia* sp. (Sputum) and *Proteus* sp. (Sputum). Among the five solvents tested, ethanolic extracts of *Azima* showed higher significant activity against the pathogenic organisms such as *Proteus* sp. (Sputum), *Serratia* sp. (Sputum), *Pseudomonas* sp. (Pus) followed by *Escherichia coli* (Urine), *Staphylococcus aureus* (Pus) and *Klebsiella* sp. (Sputum)

Anti-inflammatory, analgesic and antipyretic effects of friedelin isolated from *Azima tetraacantha* Lam

The effects of friedelin on inflammation were studied by using carrageenan-induced hind paw oedema, croton oil-induced ear oedema, acetic acid-induced vascular permeability, cotton pellet-induced granuloma and adjuvant-induced arthritis. The analgesic effect of friedelin was evaluated using the acetic acid-induced abdominal constriction response, formalin-induced paw licking response and the hot-plate test. The antipyretic effect of friedelin was evaluated using the yeast-

induced hyperthermia test in rats (Paulrayer *et al.*, 2011). In the acute phase of inflammation, maximum inhibitions were noted with friedelin in carrageenan-induced paw oedema and croton oil-induced ear oedema. Administration of friedelin significantly decreased the formation of granuloma tissue. Friedelin also produced significant analgesic activity in the acetic acid-induced abdominal constriction response and formalin-induced paw licking response. Treatment with friedelin showed a significant dose-dependent reduction in pyrexia in rats. Abeer Y. Ibrahim *et al.*, 2011 carried out a study to reveal the Anti-inflammatory effect of *Salvadora persica*. In this study, the Anti-inflammatory effect of aqueous alcoholic crude extract and ethyl acetate extract of miswak sticks (*Salvadora persica* L.) was investigated in carrageenan induced rat paw oedema in respect to immunological parameters. Administration of aqueous alcoholic extract and ethyl acetate extract (100 mg/ml) significantly reduced the oedema thickness in a time dependent manner, the inhibition percentage of inflammation was 17% for crude extract and 27% for ethyl acetate extract. Also the two extracts reduced secretion of inflammatory mediators, interleukin-1 β (IL-1 β), IL-6, tumor necrosis factor- α (TNF- α) and transforming growth factor- β 1 (TGF- β 1) in serum. The ethyl acetate extract shows potent activity. The results of the study made by Nargis Begum T *et al* in 2011 suggest that the ethanolic leaf extract of *A. tetraacantha* in doses of 100 and 200 mg/kg, significantly reduce the temperature of pyretic rats as revealed from the observation that the average percentage of antipyretic activity increased with the concentration of the extracts (200mg/Kg) compared with the control.

Antioxidant and free radical scavenging activities of *Azima tetraacantha* Lam leaf extracts

Phenolic compounds are typical active oxygen scavengers in plants and are known to contribute directly to antioxidant action. The results indicate a high concentration of polyphenols in the leaves of *A. tetraacantha*. The hydroxyl groups of the phenolic compounds confer the scavenging ability of the plant (Yildirim *et al*, 2000). The decrease in absorbance of DPPH radical is due to its reduction by different antioxidants, which in turn indicates the free radical scavenging property of the leaves of *A. tetraacantha*. The studies conducted by Sriwardhana *et al.* (2003) reported a high correlation between DPPH radical scavenging potential and total phenolic content. The reducing capacity of a compound may also serve as a significant indicator of its potential antioxidant activity (Sreekanth *et al*, 2003, Leskovar *et al.*, 2004). In a study done by Gayathri G *et al* in 2011, the reducing capacity increased with increasing concentration of the plant extract. This shows that the antioxidant compounds can react with free radical to convert them to more stable products and thereby terminate radical chain reactions. *A. tetraacantha* leaves were proved to be good source of natural phenolic compounds. The methanolic extract of the *A. tetraacantha* leaves showed better free radical capacity against different reactive oxygen /nitrogen species, among other extracts although with different efficiencies. The high content of antioxidants like phenolic compounds, flavonoids and vitamins found in these extracts, may impart health benefits by combating the free radicals in synergistic manner along with other compounds and thus constitute part of the basis for the ethno pharmacological claim. (Thendral *et al.*, 2010).

According to Maruthi T Ekbote *et al.*, in 2010, the ethanolic extract of *A. tetraacantha* leaves exhibited a significant antioxidant effect showing increased levels of enzymatic and non-enzymatic parameters, viz. catalase, GSH, total thiols and decreased level of malondialdehyde.

Antinephrotoxic potential of *Azima tetraacantha*Lam

The biochemical markers of nephrotoxicity are urea, creatinine and GGT. Their levels are significantly elevated in nephrotoxic condition due to metal induced damage to nephrons. In nephrotoxicity, the serum urea and creatinine accumulates because the rate of serum urea and creatinine production exceeds the rate of clearance due to defects in the glomerular filtration rate. The results of the study done by Manikandaselvi *et al* in 2012 shows the significant elevation in the levels of urea, GGT and creatinine in ferrous sulphate induced group compared to control. After treatment with herbal drug viz, *Azima tetraacantha*Lam. there was a significant decrease in the levels near to normal compared to ferrous sulphate induced group.

Antiulcer Activity of *Azima tetraacantha*Lam

EEAT showed significant dose-dependent ulcer protective effect against cold restraint stress and aspirin plus pylorus ligation induced gastric ulcers. The gastro duodenal ulcer protecting effect of EEAT may be due to its predominant effect on the mucosal defensive factors rather than offensive factors.(Muthusamy *et al.*,2009)

Hepatoprotective activities of *Azima tetraacantha*Lam

Reports documented by Nargis *et al.*, 2011 reveals that the rats treated with ethanolic extract of *A. tetraacantha* showed a significant reduction in all the five-biochemical parameters of liver damage (AST, ALT, ALP, ACP and total bilirubin) elevated by carbon tetrachloride. Ethanolic leaf extract treatment of *A. tetraacantha* showed more significant reduction of AST, ALT, ALP, ACP and total bilirubin. Results recorded by Arthika *et al.*, 2011 shows that the EEAT reduced the hepatotoxin intoxication induced elevated biochemical parameters and decrease the protein synthesis and accumulation of triglycerides leading to fatty liver. Reduction of raised bilirubin level suggests the stability of the biliary function during the hepatic injury with paracetamol. Treatment with EEAT significantly reversed it, indicating that the phytoconstituents present in this extraction have hepatoprotective potential.

A study done by Maruthi T Ekbote *et al.*, 2010 provides scientific evidence on the correlative effects of hepatoprotective activities of *Azima tetraacantha*Lam. They induced hepatotoxicity by altering liver microsomal membranes in experimental animals by CCl₄administration. The chloroform and ethanol extracts of *A. tetraacantha* reduced the hepatotoxin intoxication induced elevated biochemical parameters and decrease the protein synthesis. Another work done by Balakrishnan *et al.*, 2012 reported that in the liver sections of the rats treated with EEAT root bark extract for 7 days, the normal cellular architecture was retained there by further confirming the potent hepatoprotective effect of EEAT root bark. The ethanol (50%) extract of *Azima tetraacantha*Lam. (EEAT) root bark afforded significant protection against CCl₄ induced hepatocellular injury.

Hypoglycemic and antihyperlipidemic activity of *Azima tetraacantha*Lam

The ethanolic leaf extract of *Azima tetraacantha*Lam. was investigated by Nargis *et al.*, 2009 for hypoglycemic and hypolipidemic activity in alloxan-induced diabetic albino rats. The ethanolic leaf extract of *Azima tetraacantha* produced significant reduction in plasma glucose and also had beneficial effects on the lipid profile in alloxan-induced diabetic rats at the end of the treatment period.

CONCLUSION

Science has long acknowledged the value of healing substances found in nature, such as digitalis, aspirin, penicillin, insulin, steroids, etc. There has been a resurgence of interest, both scientifically and popularly, in the utilization of natural approaches. No doubt, the valuable medicinal shrub, *Azima tetraacantha* will be a treasure and will top the list of patent hunters. Further research is needed to explore the active compounds present in the shrub and the molecular mechanism of those active compounds.

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