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Review Article

PHARMACOGNOSY OF *AZIMA TETRACANTHA* LAM.: A REVIEW

Sundaresan Nandhini[1]*, Ramalingam Radha[2]

*[1]PG Scholar, Department of Pharmacognosy, College of Pharmacy, Madras Medical College, Chennai, India.

[2]Professor & Head of the Department, Department of Pharmacognosy, College of Pharmacy, Madras Medical College, Chennai, India.

ABSTRACT

Plants have played a central role in the prevention and treatment of diseases since prehistoric times. In recent years, there has been growing interest in the study of medicinal plants and their extensive use in different countries. However, today it is essential to pay for the scientific proof as to whether it is rational to use a plant or its active principles. Hence the present communication constitutes a review with adequate information on the medicinal properties, ethno medicinal uses, phytochemistry, and pharmacological activities of an Indian medicinal plant, *Azima tetracantha* Lam belonging to the family of Salvadoraceae. A wide range of phytochemical constituents have been isolated from *A. tetracantha* Lam which possesses activities like as stimulant, expectorant, antispasmodic, analgesic, anti-inflammatory, anti-ulcer, anti-diarrhoeal, anti-microbial, hepatoprotective, nephroprotective, hypoglycemic and hyperlipidemic activities. Hence, extracts of *Azima tetracantha* could form one of the best options for developing novel natural medicine.

KEYWORDS: *Azima tetracantha* Lam, Salvadoraceae, Sung-ilai, Azimine etc.

INTRODUCTION

In India treating specific ailments by the use of the different parts of several medicinal plants has been in vogue from ancient times. The indigenous system of medicines namely Ayurvedic, Siddha and Unani has been in subsistence for several centuries. Some drugs from Ayurveda approaching modern diseases, have already reached the market place[1]. It is estimated that nearly 70000 plant species have been used for medicinal purposes. India recognizes more than 2500 plant species having medicinal value, Sri Lanka around 1400 and Nepal around 700[2]. About 40% of doctors' especially in India and in China have reverted to increasing use of indigenous drugs and natural medicines[3,4]. The World Health Organization (WHO) estimates that about 80% of the populations living in the developing countries rely almost exclusively on traditional medicines for their primary health care needs.

Azima tetracantha Lam (Family: Salvadoraceae) plays a major role in the medicinal properties. The plant parts of *Azima tetracantha* such as roots, leaves, fruits and stems are used traditionally to treat various ailments and possesses activities like stimulant, expectorant, antispasmodic, analgesic, anti-inflammatory, anti-ulcer, anti-diarrhoeal, anti-microbial, hepatoprotective, nephroprotective, hypoglycemic and hyperlipidemic activities[5]. This review provides the botany, morphological character, geographical distribution, medicinal values, physicochemical characters, phytochemical characters and pharmacological activities of *Azima tetracantha*.

Synonyms

Synonyms of *Azima tetracantha* includes *Monetia barlerioides* L'Herit., *Azima nova* J. F. Gmel., *Kandena spinosa* Rafin., *Monetia angustifolia* Boj. Ex A. DC., *Monetia tetracantha* (Lam.) Salisb. It is also called as "kundali" in Ayurveda, "mulchangan" in Siddha[6].

Scientific Classification[7]

The scientific classification of *A. tetracantha* is demonstrated as follows:

Kingdom: Plantae, Phylum: Tracheophyta, Class: Magnoliopsida, Order: Capparales, Family: Salvadoraceae, Genus: Azima, Species: *Azima tetracantha* lam.

Vernacular Names[8]

The vernacular names of *A. tetracantha* are described as follows:

Sanskrit: Kundali, Hindi: Kanta- gur-kamai, Malayalam: Essanku, Sankukuppi, English: Bee sting bush, Fire thorn, Needle bush, Tamil: Sung-ilai, Ichanka

Description[9]

Azima tetracantha is a perennial shrub growing upto 3m in hot, dry riverine scrub, particularly on alluvial or saline soil. The plant is dioecious, erect shrub with (1–)2 spines 0.5–5 cm long in each leaf axil, sometimes scandent with stems up to 8 m long; branchlets are terete or quadrangular, glabrous to densely hairy. 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. Fruits are globular, white shiny. Seeds are compressed, circular. It occurs naturally in central, eastern and southern Africa as well as in the Indian Ocean Islands, and extends through Arabia to tropical Asia.

Chemical Constituents[10]

Table1: The chemical constituents present in *Azima tetracantha*

Class	Chemical Constituents
Glucosinolates and glucosinolate derived compounds	3- indolylmethylglucosinolate N- hydroxyl- 3- indolylmethyl- glucosinolate N- methoxy- 3- indolylmethyl- glucosinolate Neoascorbigen
Dimeric piperidine alkaloids	Azimine Azcarpaine Carpaine

Medicinal Importance of *A. tetracantha*

Azima tetracantha is a potent diuretic to treat rheumatism, dropsy, dyspepsia, chronic diarrhorea; it is used as stimulant tonic after child birth. *A. tetracantha* is used to treat cough, phthisis, asthma, small pox and diarrhorea. Rheumatism has been cured by its leaves, root and root bark[5].

Traditional Uses

Traditionally, root used as diuretic. In Siddha, root is used in the treatment for dropsy and rheumatism. Leaves are used as stimulant, expectorant and antispasmodic. It is also used in cough and asthma. Bark is used as antiperiodic, astringent and expectorant. In western India, juice of the leaves is applied as ear drops against earache and crushed leaves are placed on painful teeth. In India and Sri Lanka the root, root bark and leaves were administered with food as a remedy for rheumatism, dropsy, dyspepsia, chronic diarrhea and is considered as stimulant tonic and given to pubertal women immediately after confinement[11,12]. Locally, the traditional healers from Tirunelveli district of Tamilnadu use the root bark (paste with buttermilk) as potent remedy for jaundice.

MACROSCOPIC CHARACTERS[13]

Table 2: Preliminary macroscopical characters of *Azima tetracantha*

Azima tetracantha		Characters
Leaf structures	Nature	Decussately opposite
	Shape	Blade elliptical-oblong to ovate-oblong or orbicular
	Dimensions	1.5–5.5 cm × 0.5–4.5 cm
	Stipules	Absent/ rudimentary
	Leaf margin	Simple and entire
	Leaf apex	Mucronate
	Leaf base	Pinnately veined with one pair of lateral veins
Flower structures	Petals shape	Linear oblong to oblong
	Length	2- 4 mm
	Lobes	Triangular
	Male flowers	Stamens inserted at the base
	Female flowers	Staminoids and superior ovary
Fruit structures	Nature	Globose berry
	Dimension	0.5- 1cm diameter

MICROSCOPIC CHARACTERS[13]

Table 3: Microscopical characters of *Azima tetracantha*

Azima tetracantha		Characters
Leaf structures	Transverse section	Dorsiventral nature
	Midrib	Flat and hemispherical
	Cuticle	Thin, rectangular and prominent
	Vascular bundle	Single and abaxial arc shaped phloem
	Sclerenchyma	Absent
	Lamina	230mm thick
	Trichomes	Absent
	Abaxial epidermis	Stomatiferrous
	Epidermal tissues	Stomata and epidermal cells
	Stomata	Anisocytic

	Petiole (basal and upper part)	1.15µm diameter, circular
Stem structures	Young stem	1.5mm thick, consists of a distinct continuous epidermis, cortex, vascular cylinder and pith
	Epidermal cells	Squarish or rectangular
	Cuticle	Thick
	Stomata	Frequently seen
	Cortex	150mm width, consists of chlorenchyma and parenchyma
	Pith	Wide, homogenous and parenchymatous.
	Vascular cylinder	29 discrete vascular bundles
Root bark structures	Periderm	No deep fissures and contains homogenous phellan cells
	Pseudocortex	Inner to the periderm, is a wide parenchymatous zone
	Secondary phloem	It consists of Collapsed and Non- collapsed phloem

PHARMACOLOGICAL ACTIVITIES

Antimicrobial activity of *Azima tetracantha* Lam

Antimicrobial activity of different extracts of *Azima tetracantha* root was carried out by Vinoth and Manivasagaperumal, in 2015 against human pathogenic bacterial and fungal strains using disc diffusion method. The study concluded that methanolic root extract of *Azima tetracantha* had a potential antimicrobial activity against all the microorganisms tested[14]. The *invitro* antimicrobial activity of *Azima tetracantha* leaves was studied by Vinoth *et al*., in 2014 against various human bacterial and fungal pathogens using disc diffusion method. Phytochemical analysis of *Azima tetracantha* leaf extracts revealed that the extracts justify the presence of secondary metabolites and their liability for the activity[15]. Antibacterial activity of phytocompound separation from alkaloids, flavonoids and sterol were tested against *Staphylococcus aureus, Bacillus subtilis, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *E.coli* by Gowthami *et al*., in 2012. The sterols compound exhibited maximum activity when compared with alkaloids and flavonoids[16]. The antimicrobial potential of leaves of *Azima tetracantha* was checked against the clinical pathogens by Hema *et al*., in 2012 using agar well diffusion method. 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 solvent extracts tested, ethanolic extracts of *Azima* showed superior activity against the pathogenic organisms[17]. The study based on the evaluation of the antifungal activity of *Azima tetracantha* extracts and isolated compound (friedelin) against fungi was carried out by Duraipandiyan *et al*., in 2010 using the micro dilution method. The study concluded that extracts have antifungal activity and strongly suggests that isolated compound friedelin as an antifungal agent[18]. The study designed by Maruthi *et al.,* in 2010 evaluated the anthelmintic and antimicrobial activities of *Azima tetracantha*. The results revealed that, alcoholic extract was found to possess antibacterial and antifungal activities while chloroform extract showed only antibacterial activity[19].

Antioxidant and free radical scavenging activities of *Azima tetracantha* Lam

Phenolic compounds are classic active oxygen scavengers in plants and are acknowledged to contribute directly to antioxidant action. The hydroxyl groups of the phenolic compounds confer the scavenging ability of the plant (Yildrim)[20]. The different extracts of *A. tetracantha* root were studied for antioxidant potential by Vinoth *et al.,* in 2015 by using different *invitro* assays such as inhibition of DPPH, ABTS, hydroxyl radical and superoxide anions. The total phenolic contents and ferric reducing antioxidant power of the extracts were also determined by using standard phytochemical reaction methods. The results revealed that the different extracts of *A. tetracantha* root showed a good dose dependent free radical scavenging activity in all the models. Ferric reducing antioxidant power was found to be increased with increase in extracts concentrations[21]. Muthuswamy et al., in 2012 performed an antioxidant study of methanol and ethyl acetate leaf extract of *Azima tetracantha* Lam. The study designed against the inhibition of the LPO, DPPH, superoxide anion, hydroxyl radical. The result indicated that the ethyl acetate extract posses moderate activity when compared with that of the standards[22]. In an antioxidant study of leaf extracts of *Azima tetracantha* Lam done by Gayathri G *et al.,* in 2011, the reducing capacity improved with the increasing concentration of the extract. This showed that the antioxidant compounds can react with free radical to convert them to more stable products and thereby terminate radical chain reactions. The report concluded that the leaves of *A. tetracantha* were proved to be good source of natural phenolic compounds[23]. The study designed by Thendral Hepsibha *et al.,* in 2010 evaluated antioxidant and free radical scavenging activities of *Azima tetracantha*. Lam. leaf extracts. The result suggested that the methanolic extract of the *A. tetracantha* leaves showed better free radical capacity against different reactive oxygen /nitrogen species, among other extracts although with different efficiencies. The study concluded that 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[24].

Anti- inflammatory, Analgesic and Antipyretic effects from *Azima tetracantha* Lam

The study designed by Antonisamy *et al*., in 2011 evaluated the anti-inflammatory, analgesic and anti-pyretic effects of friedelin. 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. In the acute phase of inflammation, maximum inhibitions were prominent with friedelin in carrageenan-induced paw oedema and croton oil-induced ear oedema. Administration of friedelin notably decreased the formation of granuloma tissue. Friedelin also produced considerable analgesic activity in the acetic acid-induced abdominal constriction response and formalin-induced paw licking response. Treatment with friedelin showed a noteworthy dose-dependent reduction in pyrexia in rats[25]. The anti-inflammatory activity of *Salacia oblonga* root bark powder and *Azima tetracantha* leaf powder was assayed in male albino rats using carrageenan-induced rat paw oedema (acute inflammation) and cotton pellet granuloma (chronic inflammation) methods by Syed Ismail *et al.,* in 1997. The study concluded that both the crude drugs were optimally active at a dose of 1000 mg/kg. In the cotton pellet granuloma assay, both the crude drugs were able to suppress the transudative, exudative and proliferative components of chronic inflammation[26].

Antinephrotoxic potential of *Azima tetracantha* Lam

The biochemical markers of nephrotoxicity are urea, creatinine and GGT. Their levels are significantly elevated in nephrotoxic situation 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 filteration rate. The study designed by Konda et al., in 2015 evaluated the nephroprotective effect of root extract of *Azima tetracantha* in glycerol-induced acute renal failure in Wistar albino rats. The study report suggested that there was a considerable improvement in biochemical parameters and histopathological changes when compared with glycerol treated group. The antioxidant activity of the root extract of *A. tetracantha* was tested *invitro* and *invivo*. Both *invitro* and *invivo* assays showed significant antioxidant activity and due to this, the nephroprotective effect of *A. tetracantha* in glycerol-induced acute renal failure was estabilished[6]. The results of the study done by Manikandaselvi *et al.,* in 2012 indicated the significant elevation in the levels of urea, GGT and creatinine in ferrous sulphate induced group compared to control. After treatment with *Azima tetracantha* Lam there was a significant decrease in the levels near to normal compared to ferrous sulphate induced group. The study concluded that the nephroprotection could be attained due to its antioxidant and free radical scavenging activity[27].

Hepatoprotective activities of *Azima tetracantha* Lam

Hepatotoxicity induced in albino rats by ferrous sulphate and their hepatoprotective effect was studied by using aqueous extracts of *Azima tetracantha* by Soumya and Nagarajan in 2014. Aqueous extracts of *Azima tetracantha* showed a significant reduction in all the biochemical parameters of liver damage glucose, protein, bilirubin, cholesterol, ALP, SOD, CAT, Vitamin E, TBARS, Albumin and globulin elevated by ferrous sulphate[28]. Antioxidant, free radical scavenging and liver protective effects of friedelin isolated from *Azima tetracantha* Lam leaves were performed by Sunil *et al.,* in 2013. The report in the study indicated that friedelin restored the levels of SGOT, SGPT, LDH, SOD, catalase (CAT), reduced glutathione (GSH) and glutathione peroxidase (GPx) and showed liver protection, comparable to the standard silymarin[29]. A study report by Sambasivam et al., in 2013 on hepatoprotective potential of *Azima tetracantha* and *Tribulus terrestris* on ferrous sulfate-induced toxicity in rat revealed that the hydroalcoholic extract of leaf powder of *Azima tetracantha* and the fruit powder of *Tribulus terrestris* retrieved the liver parameters to usual level and possesses significant hepatoprotective activity[30]. A study done by Balakrishnan *et al*., in 2012 reported that the ethanol (50%) extract of *Azima tetracantha* Lam. (EEAT) root bark afforded significant protection against carbon tetrachloride (CCl4) induced hepatocellular injury. The report also revealed that the normal liver cellular architecture was retained when the liver sections of the rats treated with EEAT root bark extract for 7 days there by further confirming the intoxicating hepatoprotective effect of EEAT root bark[31]. Reports documented by Nargis *et al*., in 2011 revealed that the rats treated with ethanolic extract of *A. tetracantha* showed a significant reduction in all the five-biochemical parameters of liver damage (AST, ALT, ALP, ACP and total bilirubin) elevated by carbon tetrachloride[32].

Antiulcer Activity of *Azima tetracantha* Lam

Antonisamy *et al.,* in 2015 recorded the protective effects of friedelin isolated from *Azima tetracantha* Lam against ethanol-induced gastric ulcer in rats. The result from the study showed that the friedelin isolated from the hexane extract of leaves of *Azima tetracantha* protected from ethanol caused severe gastric damage and suggested that friedelin could be a new effective natural gastroprotective tool against gastric ulcer[33]. EEAT showed notable dose-dependent ulcer protective effect against cold restraint stress and aspirin plus pylorus ligation induced gastric ulcers on the study performed by Muthusamy et al., in 2009. The conclusion of the study stated that the gastro duodenal ulcer protecting effect of EEAT may be due to its predominant effect on the mucosal defensive factors rather than offensive factors[34].

PHYTOCHEMISTRY

The preliminary phytochemical screening carried out on various extracts of *A. tetracantha* revealed the presence of phytoconstituents such as alkaloids, flavonoids, glycosides, steroids, carbohydrates, tannins, proteins and aminoacids. Other compounds such as friedelin, lupeol, glutinol and β- sitosterol have also been reported in *A. tetracantha.*

Physicochemical analysis[13]

The physicochemical characters such as organoleptic characters, fluorescence and the percentage of total ash, acid-insoluble ash, water-soluble ash and alkalinity of water soluble ash values of the powdered stem bark of *A.tetracantha* were evaluated.

Organoleptic characters of *A.tetracantha* stem bark powder

Colour: Pale brownish yellow

Appearance: Coarse powder

Odour: No characteristic odour

Taste: No characteristic taste

Table 4: Determination of consistency of *A. tetracantha* stem bark powder

Treatment	Observation
Powder treated with water	Non-sticky
Powder shaken with water	Honey comb like froth
Powder treated with 5% aqueous sodium	hydroxide Pale yellow
Powder treated with 60% aqueous sulphuric acid	Reddish brown
Powder pressed between filter paper for 24 hours	No oil stain

Table 5: Fluorescence characteristics of *A.tetracantha* stem bark powder

Treatment	Day light	UV light	
		254nm	365nm
Powder	Pale-brownish yellow	Pale green	Brown
Powder + 1N NaOH (aqueous)	Pale yellow	Pale yellow	Black
Powder + 1N NaOH (alcoholic)	Orange	Yellowish green	Black
Powder + 1N Hydrochloric acid	Pale yellow	Black	Black
Powder + 50% Sulphuric acid	Reddish brown	Dark brown	Black
Powder + 50% Nitric acid	Orange	Yellowish green	Black
Powder + Picric acid	Yellow	Green	Black
Powder + Acetic acid	Brown	No visible colour	Black
Powder + Ferric chloride	Orange	Green	Black
Powder +Con. Nitric acid	Brown	Green	Black
Powder + Nitric acid + Ammonia	Reddish orange with precipitate	Green	Black

Table 6: Ash values of *A.tetracantha* stem bark powder

Physicochemical Constants	Values
Total ash	21.625%
Water soluble ash	13.945%
Alkalinity of water soluble ash	1.73ml
Acid insoluble ash	0.665%

Phytochemical test[22]

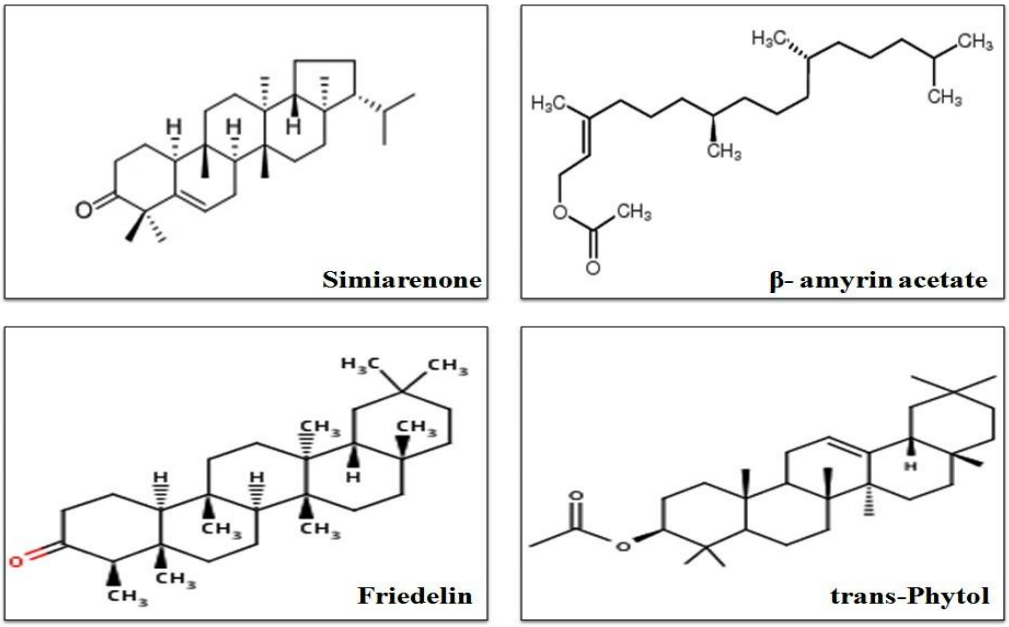
Table 7: Preliminary phytochemical test of various extracts of *A. tetracantha*.

Phytochemical Test	Pet. Ether extract	Ethylacetate Extract	Methanol Extract
Alkaloids	-	+	+
Carbohydrates	-	-	-
Glycosides	-	-	-
Protein & Aminoacids	-	-	-
Flavonoids	+	+	+
Tannins	-	-	-
Steriods	+	+	+
Oil	+	+	+

Phytochemical structures[35]

The phytochemical constituents with their structures present in *A. tetracantha* are given in Fig. 1:

Fig. 1: The phytochemical constituents with their structures present in *A. tetracantha*[35]



CONCLUSION

The information summarized here is well-intentioned to serve as a reference tool to researchers in the field of ethanopharmacology of *Azima tetracantha*. Based upon the literature survey, it can be concluded that *Azima tetracantha* has been widely studied for its pharmacological activities. Science has always acknowledged the value of healing substances found in nature, such as digitalis, aspirin, penicillin, insulin, steroids etc. There is no doubt that valuable medicinal shrub, *Azima tetracantha* will be a treasure and will top the list of treasure hunters. Further research is needed to explore the unclaimed therapeutic effect of active compounds present in the shrub and the plausible molecular mechanisms of those active compounds.

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***Address for correspondence**
Nandhini Sundaresan
PG Scholar
Department of Pharmacognosy,
College of Pharmacy, Madras Medical College, Chennai-600003, Tamil Nadu, India.
Email: nandypharma1787@gmail.com
Mobile: +91 9566035357