Keywords: Chinaberry, Traditional medicinal plant; Antioxidant; Pharmacological activities; Active compounds

ABSTRACT

Plants being the prime source of medication since time immemorial have been consumed as a source of nutrition as well as therapy against different ailments and diseases. Medicinal plants are a major source of raw material for the traditional systems like Ayurveda, Siddha & Unani. Even the modern system of medicine has more than 25 percent of drugs in use, which is either plant-based or plant-derived. Although several trees possess various medicinal properties, it has been ignored by indigenous & modern system of medicine *Melia azedarach* L. (Family: Meliaceae). For Chinaberry (*Melia azedarach* L.), one of the important medicinal plants from the *Meliaceae* family, medicinal properties by traditional practitioners are being quoted for every plant part. Extracts of fruits, seeds, leaves of *M. azedarach* have shown many characteristics of medicinal and pesticide activities against several pathogenic and pest organisms respectively. Pharmacological investigations verify different health maintenance activities of *M. azedarach* viz. anti-nephrolithiasis, hepatoprotective, antibacterial, anti-parasitic, antiulcer, anthelmintic, antioxidant, and antipyretic action. There is also considerable literature available related to its chemistry. The present review presents an up-to-date literature survey of the ethnomedicinal, phytochemical and pharmacological account of *Melia azedarach* L.
INTRODUCTION:

*Melia azedarach* commonly known as bread tree has been investigated extensively by many workers about its potential activity as a pesticide and medicinal plant. This paper is a comprehensive literature review of the potentiality of using *M. azedarach* for pesticidal and medicinal purposes *Melia azedarach*, known by such common names as the chinaberry tree, China tree, China neem tree, pride of India, Indian lilac, lelah, paraiso, syringa, white cedar, umbrella tree, bead tree, and Cape lilac, is a deciduous tree in the Meliaceae (mahogany) family.\(^1\)\(^-\)\(^3\) *M. azedarach* produces purple, 5-petaled flowers in spring. The fruit of *M. azedarach* is hard, yellow to yellow-green, 0.4–0.8 in (1–2 cm) diameter berries or drupes on stalks. Native to Southeast Asia and northern Australia, the plant was introduced to the United States in the mid-1800s as an ornamental tree. *M. azedarach* contains multiple limonoid tetrano triterpenes, such as meliatoxins A1, A2, and A3; meliatoxins function as neurotoxins. These chemicals are found in the highest concentrations in the fruit but also can be found in the bark, leaves, and flowers.\(^4\)\(^-\)\(^9\) Various studies have described poisonings in animals caused by *M. azedarach* ingestion.\(^3\), \(^10\), \(^11\) However, the literature on adverse human exposures to the plant is limited. Adverse clinical effects reported in humans primarily involve 4 organ systems: gastrointestinal (i.e., nausea, vomiting, and abdominal pain), cardiovascular (i.e., dysrhythmia, tachycardia, and hypotension), respiratory (i.e., cyanosis, dyspnea, and respiratory depression), and neurologic (i.e., blurred vision, numbness, headache, weakness, ataxia, agitation, and seizures).\(^3\), \(^12\) The objective of this investigation was to characterize *M. azedarach* ingestions reported to Texas poison centers. According to the Early Detection and Distribution Mapping System, *M. azedarach* can be found in 122 of the 254 Texas countries.\(^1\),\(^13\)

**Common names of *M. azedarach***:

(Germany) *Cinarorno*, (Brazil); *Ku /ian* (China); giant paradise (Argentina), syringa tree (South Africa).\(^{14-17}\)

**Taxonomy of *M. azedarach*:** \(^{18}\)

**Scientific name:** *Melia Azedarach* Linn.

**Standard trade name:** White Cedar (WC)

**Subdivision:** Angiospermae

**Class:** Dicotyledonae

**Subclass:** Polygonae

**Series:** Disciflorae

**Order:** Geraniales

**Family:** Meliaceae

**Genus:** Azedarach

**Species:** Melia

**Botanical description:**

*Melia azedarach* is a small to medium deciduous tree attaining a height up to 45 m tall; bole fluted below when old, up to 30-60 (max. 120) cm in diameter, with a spreading crown and sparsely branched limbs. It is grown as an ornamental avenue tree and sometimes as a shade tree in coffee and tea plantation. The tree is hardy and drought-resistant and is found grown widely in the sub-Himalayan region up to 2000 m above sea level.\(^{19}\)

The plant regenerates freely from seeds during rain under natural conditions. It can also be artificially propagated by direct sowing, transplanting seedlings from a nursery, or by cutting and root suckers. The bark is smooth, greenish-brown when young, turning grey and fissured with age. Leaves are alternate, 20-40 cm long, bipinnate, or occasionally tripinnate. Leaflets 3-11, serrate, dark green on the upper surface and paler underneath. They produce a pungent odour when crushed. The inflorescence is a long, axillary panicle up to 20 cm long. Flowers are purple and fragrant, numerous on slender stalks, white to lilac; sepals 5-lobed, 1 cm long; pentamerous, each petal 5-lobed. 9 cm long petals 5-lobed, 0.9 cm long, pubescent; staminal...
tube deep purple-blue brown.0.6 cm long. Fruit or berries are small, yellow drupe, nearly round, about 15 mm in diameter, smooth and hard as a stone, containing 4 to 5 black seeds. Seed is oblongoid, 3.5 mm x 1.6 mm, smooth, brown, and surrounded by pulp. 20,21

An attractive ornamental and shade tree with high lateral branching. Hardy and drought resistant. Ferny foliage turning yellow in autumn. Leaves are dark green on the upper surface and paler underneath. They emit a pungent smell when crushed. Flowers are purple and fragrant. Fruits or berries are yellow, nearly round, smooth and so hard as a stone, containing 4 to 5 black seeds.

**Distribution:** *Melia azedarach* Linn. is native to tropical Asia. It is widespread and naturalized in most of the tropics and subtropical countries. It was introduced and naturalized in the Philippines, United States of America, Brazil, Argentine, many African countries, and many Arab countries. 17

**Reported Activity**

**Cytotoxic activities of the extracts:**

The cytotoxic activities were determined for hexane, chloroform, and ethyl acetate fractions of the extract. Brine shrimp eggs were used to determine the cytotoxic activities. All three tested fractions showed significant cytotoxic effects on brine shrimp. It was found that for these fractions, with the increase in concentration from 30 to 100 mg/mL, the cytotoxic activities were enhanced many folds.22

**Antiviral potential:**

Medicine, a peptide isolated from leaves of *M. azedarach* inhibited the multiplication of foot and mouth disease virus. It also exhibited antiviral activity against the herpes simplex virus when an aqueous extract of chinaberry was made and examined on *Vesicular stomatitis* (VSV), polio, and herpes simplex (HSV) viruses in cell culture. The purified extracts from leaves of (MA) which contains meliacaprin inhibited VSV and HSVI multiplication in vitro when added after infection with no cytotoxic effect.

In the field of veterinary medicine, the larvicidal and ovicidal activity of (MA) extracts on the helminthus *Haemonchus contortus* was reported. Both leaves and seed extracts revealed the presence of triterpenoids and steroids, and both also presented alkaloids and condensed
tannins. Compounds present in leaves are different from these in seeds since the former inhibits mainly egg hatching and the later, larval development.

**Antibacterial potential:**

The antibacterial potential of *M. azedarach* L. was tested using crude leaf extracts against human pathogenic bacterial strains. Various bacterial pathogenic were subjected to extracts (using Petrol, Benzene, Ethyl acetate, Methanol, Aqueous, Chloramphenicol). The bacterial strains were *Bassillus subtilis*, *Proteus mirabilis*, *Shigella flexeneri*, *Sh. dysenteriae*, *Plesiomonas shigellides*, and *Staphylococcus aureus*. Ethyl acetate was the most effective extract followed by the methanolic fraction that inhibits the growth of all tested pathogens.

*Melia azedarach* flower extracts were prepared and used to treat bacterial skin disease in children. The methanolic extract of flowers was used to make a cream preparation. An activity comparison of the prepared cream and the skin drug, neomycin was made. The diameter of the infected area (mm²) before and after the two weeks treatment. The results showed that (MA) cream was a significantly potent cure in several cases. (MA) flowers extract showed its potential in curing rabbits suffering from a skin infection produced by *Staphylococcus aureus*. The healing effects were found comparable to the known drug neomycin.

The crude extract (CEx) from leaves and stem barks of *M. azedarach* in chloroform, petroleum ether, acetate ethyl, butanol, and aqueous fractions was evaluated using seven different concentrations. Disk diffusion and minimum inhibitory concentration assays were used to evaluate the antibacterial activity. 0.12% chlorhexidine was used as a positive control. The CEx and the petroleum ether fraction from *M. azedarach* showed significant antibacterial activity against *S. mutans*, confirming it's antibiotic potential.

**Fungicidal Potential:**

The activity of ethanolic leaf, seed, and fruit extracts from (MA) in controlling plant and human pathogenic fungi such as *Aspergillus flavus*, *Fusarium moniliform*, *Microsporum canis*, and *Candida albicans* has been reported. In other studies, a serial agar dilution method was utilized in proving the fungistatic activity of hexanic and ethanolic extracts from fruit, seed kernels, and leaves of (MA) against *A. flavus*, *Diaporthe phaseolorum var. meraidionales*, *Fusarium oxysporum*, *F. solani*, *F. vertiliiodes*, and *Schlerotina sclerotiorum*. Three compounds were isolated from crude extracts and identified as, vanillin, hydroxyl -3-
methoxcinnamaldehyde, and (+-) pinoresinol.\textsuperscript{26} In a subsequent research effort, the seeds of ripe fruits from \textit{M. azedarach} L. were utilized to isolate the active compound Scopoletin, a hydroxyl coumaramin\textsuperscript{25}, and the subsequent testing of its antifungal synergistic effect. Results revealed a good antifungal activity of the isolated compounds when tested against \textit{F. verticilloides} as well as its synergistic effect when it was combined with two conventional fungicides mancozab or carboxin. A summary of various pesticidal activities along with pests targeted, plant parts utilized. The antibacterial potential of \textit{M. azedarach} L. has been tested using crude leaf extracts against human pathogenic bacterial strains.\textsuperscript{27} Various bacterial pathogenic were subjected to extracts (using Petrol, Benzene, Ethyl acetate, Methanol, Aqueous, Chloramphenicol). The bacterial strains were \textit{Basillus subtilis, Proteus mirabilis, Shigella flexeneri, Sh. dysenteriae, Plesiomonas shigellides}, and \textit{Staphylococcus aureus}. Ethyl acetate was the most effective extract followed by a methanolic fraction that inhibits the growth of all tested pathogens.

The activity of ethanolic leaf, seed, and fruit extracts from (MA) in controlling plant and human pathogenic fungi such as \textit{Aspergillus flavus, Fusarium moniliform, Microsporum canis}, and \textit{Candida albicans} has been reported.

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\textbf{Insecticidal, Acaricidal, and Rodenticidal Activities:}

The Meliaceae plant family is known to contain a variety of compounds, which show insecticidal, antifeedant, growth-regulating, and development modifying properties.\textsuperscript{28} Effects of \textit{M. azedarach} extracts of various parts of the plant on many pests have been already reported.\textsuperscript{26,29} An extensive work conducted by Wondscheer, j., and coworkers (2004) on larvicidal action of \textit{M. azedarach} against the dengue mosquito \textit{A. aegypti} in Brazil. Results showed the Potentiality of (MA) in controlling this insect via its larval stage. In a parallel manner to the previously mentioned investigation(s), the larvicidal and oviposition deterrent effects of fruit and leaf extracts from \textit{M. azedarach} on \textit{Aedes aegypti} (Diptera: Culicidae)
were investigated. A comparison tests of kernels of ripe fruits from *M. azedarach* and *A. indica* against larvae of dengue fever vector were carried out. The overall results indicated the superiority of *A. indica* over *M. azedarach* in insecticidal activity, but the LC(s) of the former fall within the confidence interval of the latter. More work on the same vector *A. aegypti* was conducted by various investigators (Omena 2007). The newest research work by Coria proved that ethanolic leaf extract of *M. azedarach* is a strong larvicide on *A. aegypti*, and all tested larvae died before pupation, and significantly delayed development time, in addition to its inhibition ability of oviposition by the vector females. In comparison with leaf extract the fruit extract showed much weaker effects. The efficacy of leaves and seeds methanolic extracts against the malarial vector *Anopheles stephensi* under laboratory conditions. This cooperative work of two groups, one from India and the other one from South Korea, proved that both extracts showed strong larvicidal, pupicidal, adulticidal, antiovipositional activity, and biting deterrenncy, though seed extract exerted higher bioactivity than leaves extract at all doses tested. In their conclusion investigator expressed optimism regarding the potentiality of *M. azedarach* in controlling the insect effectively and less expensively than available chemical pesticides, yet call for the need to study the mode of action of the biopesticide under field conditions.

Many triterpenoids present in plants of the Meliaceae family are described as showing insecticidal activity. Bohnenstengal *et al.* reported the isolation of three meliacarpin derivatives from *M. azedarach* leaves. The activity of meliacarpin derivatives was tested on larvae of the polyphagous pest insect *Spodoptera littoralis* by incorporating it into an artificial diet to larvae in a chronic feeding bioassay. Results indicated a comparable insecticidal activity to the well-known lipo pesticide azadirachtin found in neem trees. The crude ethanolic seed extract of Brazilian *M. azedarach* showed both phago inhibitory and anti molting activities to the hemophagous insect *Rhodnius prolixus*, one of the vectors of chagas disease. The efficacy of ripe fruit extracts of *M. azedarach* L. was evaluated against the tick *Boophilus microplus* (Acari: Ixodidae). Organic solvent extracts were prepared and tested on larvae and engorged females by immersion. Hexane-Chloroform extracts of ripe fruit showed good efficacy on larvae mortality, and to less level of efficacy in the case of female adults. The investigation came up with a conclusion implying that crude extract of *M. azedarach* fruits was as effective as azadirachtin of neem tree in inhibiting the oviposition and embryogenesis of *B. microplus* as it has been observed by some investigators. The other interesting observation stated by Borges *et al.* is that most of the fruit extract activity was...
seen in the polar and intermediate polarity solvents which could be attributed to components structurally related to steroids and terpenoids.

The phytochemistry analysis of *M. azedarach* ethanol extracts, revealed the presence of triterpenoids and steroids, respectively, and both seeds and leaves also presented alkaloids and condensed tannins. These compounds can inhibit the development of insect feeding and also they display ovicidal activity in insects.  

Meliacarpin was found first in *M. azedarach* extracts and later in *A. Indica*. Meliantiol showed strong antifeedant properties against the desert locust, *S. gregaria* (Kraus *et al* 1981), and meliartenin inhibited larval feeding of *E. panuelate* and *S. eridania* (Carpinella *et al* 2002). The seed oil of *M. azedarach* acted as a strong oviposition deterrent for rice gall midge, *Orseolia oryzae*, and a feeding deterrent for oriental army warm, *Mythimna a separata* (Chiu *et al*.1984). Fruit extracts of both *M. Azedarach* and *A. Azadirachta* showed a feeding deterrent effect against the larvae of *Plutella xylostella* at higher doses and also against a variety of insect species belonging to three orders including Coleoptera, Lepidoptera, and Orthoptera (Carpinella *et al* 2003). Seed oil sprays were also effective against citrus red mite, *Panonychus citri*, and the orange spiny whitefly, *Aleurocanthus spiniferus* but was not harmful to several predatory mites such as *Amblyseius spp*. The rodenticidal potentiality of both neem and chinaberry trees was investigated. Seed extracts of both plants proved to be effective in inhibiting folliculogenos is in albino rats. Polar extract (MeOH) and non-polar extract (Hexane) were used in this investigation. The results revealed the significant activity of both extracts from both plants in reducing the number of normal single-layered follicles in the rat. This preliminary experiment could lead to further studies to find a suitable rodenticide that is ecologically safe and biologically active. Reports on using flowers of *M. azedarach* and flowers and leaves as an abortifacient in East Africa and Saudia Arabia have been recorded. In rats, 50 % ethanolic extract of stem bark of the same plant was found to be devoid of anti - implantation activity.

A more recent report on utilizing leaf extract of *M. azedarach* (MA) showed that it is inactive as a pregnancy interceptive. On the other hand it was found that chloroform extract of (MA) roots showed significant contraceptive activity.

The antifertility of extracts from (MA) and *ferula assafoetida* was investigated by measuring changes in activities of key enzymes of carbohydrate metabolism in rat uterus on day 7 of pregnancy. It was observed that on day 7 of pregnancy one key enzyme of the glycolytic
pathway (Phosphofructokinase) was significantly reduced in the uteri of treated rats as compared to controls. Hexosemonophosphate pathway also appeared to be sensitive to treatment with the plant extracts and showed an inhibitory effect on the enzyme activities of glucose-6-phosphate dehydrogenase. Oxidative energy metabolism through the TCA cycle was maximally affected by the treatment. Investigators concluded that plants lacking phytoestrogens may intercept pregnancy by their ability to disrupt energy metabolism in rat uterus during implantation, especially the oxidative pathway.

*M. azedarach* Antidiarrhoeal activity:

The bark of Antidiarrhoeal, *M. azedarach* deobstruent, diuretic (Joy et al., 1998) reduces rheumatic pain, used in fever to relieve thirst, nausea, vomiting and general debility, loss of appetite, stomach ache. Bark decoction is used as a remedy for fever aches and pains, bark paste is used to treat piles, used as a lotion on ulcers, syphilitic.

Asthmatic Activity:

The stem of the *M. azedarach* plant shows the activity for the treatment of asthmatic patients for the treatment of the disease.

Antidiabetic Effect of Extracts of *Melia azedarach*:

The extracts of *Melia azedarach* give therapeutic value in type-2 diabetes mellitus and related complications thus supporting their traditional uses in the Indian traditional system of medicine. It has been previously observed that isolated compounds from *Melia azedarach* leaves and fruits showed potent antidiabetic activity. Ethanol extract prepared from *Melia azedarach* leaves and fruits showed 40.7 and 55.9% inhibition of PTP-1B enzyme at 10 μg/ml concentration. Furthermore, chloroform fraction of fruits and butanol fraction of leaves were found to inhibit PTP-1B enzyme by 50.2% and 65.5% at the same 10 μg/ml concentration, respectively.

All prepared extracts and fractions were evaluated for their *in vitro* as well as *in vivo* hypoglycaemic activities via inhibition of PTP-1B enzyme activity, stimulation of glucose uptake by C2C12 as well as improvement in blood glucose profile in STZ induced Sprague-Dawley rats as compared to the standard metformin, a hypoglycaemic drug to validate their effect. Uses of medicinal plants for the treatment of various ailments have their own merits and demerits. Diabetes being a metabolic disorder bears a lot of complications if it is not
properly managed. Unavailability of suitable antidiabetic agents and side effects associated with synthetic drug regimes prompt us to search out newer antidiabetic agents from natural resources. *Melia azedarach* twigs extract possess strong *in-vitro* as well as *in-vivo* antidiabetic effects which may be responsible for their hypoglycemic property. Furthermore, pharmacological and chemical investigations are under process to find out the active constituents responsible for the antidiabetic activity and to elucidate its mode of action. The barks of *M. azedarach* including a new compound and a natural tirucallane-type triterpenoid. Among them, compounds 10, 13, 19, 21, 32, 35, 36, and 39 were isolated from Meliaceae for the first time. Among the tested compounds, five tirucallane-type triterpenoids (7, 9, 10, 12, and 13) showed significant inhibitory activities against PTP1B, which might be attributed to the antidiabetic potential of *M. azedarach*. The results presented valuable new information in the chemistry of the genus Melia and reports on interesting and significant PTP1B activity relevant to the solution against diabetes.49-51

**In vitro acaricidal effect of Melia azedarach embryoated eggs and engorged nymphs:**

The extracts and petroleum ether extracts of the plants have great potential to be developed as a novel acaricidal for controlling eggs and nymphs of *H. Dromedarii*. The ethanolic and petroleum ether extracts of the ripen fruits of *M. azedarach* revealed oviacial efficacy against the camel tick *H. dromedarii*. The Malformation was observed in larvae hatched from eggs treated with the lowest concentrations of all the tested extracts. The major active constituent of Azadirachta and *Melia* is azadirachtin that causes negative effects on the development of insects.52, 53

**Anticancer activity:**

The anticancer property of methanolic extract on aerial parts of *A.indica* and *M. azaderach* that inhibited MCF cell lines at different concentrations (50, 100, 150, 200μg/ml). IC50 values of solvent extract of aerial parts of *A. indica* and *M. azaderach* were 165.5629 and 280.8989 μg/ml respectively. 200 μg/ml of the methanolic extract of *A. indica* revealed the highest percentage of inhibition of 65.5% and the lowest viability activity of 60.4%. In comparison to these methanolic extracts of *M. azedarach* showed the highest percentage of inhibition of 47.05% in 200 μg/ml of plant extract and the lowest viability activity of 68%. In our study, IC50 value and percentage of inhibition of the methanolic extracts of *A. indica* showed high cytotoxic activity than *M. azedarach*. The presence of phytochemicals such as steroids, alkaloids, phenols, flavonoids, saponins, tannins, anthraquinone, and amino acids in
A. indica and M. azedarach extracts. Methanolic extracts of A. indica showed high activity against K. pneumonia, whereas, M. azedarach was found to be active against S. aureus. The medicinal plants, Azadirachta indica A. Juss and Melia azedarach Linn can be effectively utilized as a natural medicine to treat various bacterial infections. Also, these two medicinal plants can be effectively used as anticancer agents.

The rhizosphere microbiome of Melia azedarach during removal of benzo(a)pyrene from cadmium co-contaminated soil:

Benzo(a)pyrene (BaP) is a highly persistent biohazard polyaromatic hydrocarbon and is often reported to be present in soils co-contaminated with heavy metals. The present study explains the rhizodegradation of BaP using bacterial consortium in the rhizosphere of Melia azedarach, along with a change in taxonomical and functional properties of the rhizosphere microbiome. The relative abundance of the most dominant phylum Proteobacteria was 2% higher with BaP, while in the presence of both BaP and Cd, its abundance was 2.2% lower. Functional metagenome analysis also revealed the shifting of microbial community and functional gene abundance in the favor of xenobiotic compound degradation upon augmentation of bacterial consortium. Interestingly, upon the addition of BaP the range of functional abundance for genes of PAH degradation (0.165e0.19%), was found to be decreasing. However, augmentation of a bacterial consortium led to an increase in its abundance including genes for degradation of benzoate (0.55e0.64%), toluene (0.2e0.22%), naphthalene (0.25e0.295%) irrespective of the addition of BaP and Cd. Moreover, under greenhouse conditions, the application of the M. azedarach-bacterial consortium enhanced the degradation of BaP in the rhizosphere (88%) after 60 days, significantly higher than degradation in bulk soil (68.22%). The analysis also showed an increase in degradation of BaP by 15% with plant-native microbe association than in bulk soil. Therefore, the association of the M. azedarach bacterial consortium enhanced the degradation of BaP in soil along with the taxonomical and functional attributes of the rhizosphere microbiome.

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