ISSN 2349-7203

IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH

An official Publication of Human Journals

HUMAN

Human Journals

Review Article

September 2021 Vol.:22, Issue:2

A Comprehensive Review on Traditional, Phytochemical, and Pharmacological Activity of *Melia azedarach*

ISSN 2349-7203

IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH

An official Publication of Human Journals

HUMAN

Ashish[1], Amit Chaudhary[1]*, Hans Raj[1], Kapil Kumar Verma[2], Kalpana Thakur, Abhishek Chaudhary

[1] School of Pharmacy, Abhilashi University, Chail Chowk, Mandi, Himachal Pradesh-175028 India.

[2]Minerva College of Pharmacy, Indora, Kangra, Himachal Pradesh-176402 India.

Submitted: 19 August 2021

Accepted: 25 August 2021

Published: 30 September 2021

HUMAN JOURNALS

www.ijppr.humanjournals.com

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* :

Bakain, Ramyaka, *Drek*, Dharek, Karmuka, Keshamushti, Khammaga, Ghoranim, Kalo neem, Bakan Limado, Bakai Nimbu, Neem, *Taruka vepa, Malaivernba, Karin vernbu, Serna veppu, Arbevu, Hutchu*, Bakana Nimb, *(*India); Persian lilac, Lilac, Chinaberry, Paradise tree, White cedar, Umbrella tree, Bead tree, Syringa., Hoop tree, China tree, Pride of India (England), *Lilas des indes, Lilas de chine, Lilas de perse, Paraiso, Margoiser*, (France); *Lelaila, Aleli, Pasilla, Violeta,* (Singapore) *Mindi kechil, Persischer zedrachbaurn,* (Malayasia) Chiwesischer holunder, *Poteronosterbaurn, Paradiesbaurn, Persischer fleider,* (Germany) *Cinarnorno*, (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 *m*g/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 *Basillus 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.[23, 24]

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.[25] 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. vertllioides*, and *Schlerotina sclerotiorum*. Three compounds were isolated from crude extracts and identified as, vanillin, hydroxyl -3-

methoxcinnamaldehyde, and (+-) pinoresinol.[26] In a subsequent research effort, the seeds of ripe fruits from *M. azedarach* L. were utilized to isolate the active compound Scopoletin, a hydroxyl coumaramin[25,] and the subsequent testing of its antifungal synergistic effect. Results revealed a good antifungal activity of the isolated compounds when tested against *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 M. azedarach L. has been tested using crude leaf extracts against human pathogenic bacterial strains.[27] Various bacterial pathogenic were subjected to extracts (using Petrol, Benzene, Ethyl acetate, Methanol, Aqueous, Chloramphenicol). The bacterial strains were *Basillus subtilis, Proteus mirabilis, Shigella flexeneri, Sh. dysenteriae, Plesiomonas shigellides, and 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 *Aspergillus flavus*, *Fusarium moniliform*, *Microsporum canis*, and *Candida albicans* has been reported.

Three compounds were isolated from crude extracts and identified as vanillin, hydroxyl -3-methoxcinnamaldehyde, and (+-) pinoresinol. In a subsequent research effort, the seeds of ripe fruits from *M.azedarach* L. were utilized to isolate the active compound Scopoletin, a hydroxyl coumarin, and the subsequent testing of its antifungal synergistic effect. Results revealed a good antifungal activity of the isolated compounds when tested against *F. verticilloides* as well as its synergistic effect when it was combined with two conventional fungicides mancozab or carboxin.

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.[28] Effects of M.azedarch extracts of various parts of the plant on many pests have been already reported.[26,29] An extensive work conducted by Wondscheer, j., and coworkers (2004) on larvicidal action of *M. azedarach* against the dengue mosquito *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 larvicidial and oviposition detterent effects of fruit and leaf extracts from *M. azedarach* on *Aedes aegypti* (Diptera: Culicidae) were investigated. A comp rison tests of kernels of ripe fruits from *M. azedarach* and *A.indica* against tlarvae 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.[30] 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.[31] 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 deterrency, 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. azedrach* 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 Bazilian *M. azedarach* showed both phago inhibitory and anti molting activities to the hemophagous insect *Rhodnius prolixus*, one of the vectors of chagas disease.[32] 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.[33] 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.[34]

Meliacarpin was found first in *M. azedarach* extracts and later in *A. Indica*.[35] 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, *Mythimn 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[36] 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*.[37] 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.[38] 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*[39] and flowers and leaves[40] 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.[41]

A more recent report on utilizing leave extract of *M. azedarach* (MA) showed that it is inactive as a pregnancy interceptive.[42] 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.[43]

***M.azedarach* Antidiarrhoeal activity:**

The bark of Antidiarrhoeal, ***M.azedarach*** deobstruent, diuretic(Joy *et al.*,1998) rheumatic pain, used in fever to relieve thirst, nausea, vomiting and general debility, loss of appetite, stomachache.[44] Bark decoction is used as a remedy for fever aches and pains,[45] Bark paste is used to treat piles, used as a lotion on ulcers, syphilitic.[46-48]

Asthmatic Activity:

The stem of the M. azedarach plant shows the activity for the treatment of asthmatic patients for the treatment of the disease.[47, 48]

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 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 embryonated 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 ovicidal 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.[54]

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. azedarachbacterial consortium enhanced the degradation of BaP in soil along with the taxonomical and functional attributes of the rhizosphere microbiome.[55]

REFERENCES:

1. Early Detection and Distribution Mapping System (EDDMapS). Chinaberry, Melia azedarach L. The University of Georgia – Center for Invasive Species and Ecosystem Health. Available at: https://www.eddmaps.org/species/subject.cfm?sub=3049. Accessed April 24, 2017.

2. Forrester MB, Layton GM, Varney SM. Melia azedarach ingestions reported to Texas poison centers. The Journal of emergency medicine. 2020 Apr 1;58(4):e179-84

3. Phua DH, Tsai WJ, Ger J, Deng JF, Yang CC. Human Melia azedarach poisoning. Clinical Toxicology. 2008 Jan 1;46(10):1067-70.

4. Huang RC, Tadera K, Yagi F, Minami Y, Okamura H, Iwagawa T, Nakatani M. Limonoids from Melia azedarach. Phytochemistry. 1996 Oct 1;43(3):581-3.
5. Takeya K, Qiao ZS, Hirobe C, Itokawa H. Cytotoxic azadirachtin-type limonoids from Melia azedarach. Phytochemistry. 1996 Jun 1;42(3):709-12.
6. Ahn JW, Choi SU, Lee CO. Cytotoxic limonoids from Melia azedarach var. japonica. Phytochemistry. 1994 Aug 1;36(6):1493-6.
7. Nakatani M, Huang RC, Okamura H, Naoki H, Iwagawa T. Limonoid antifeedants from Chinese Melia azedarach. Phytochemistry. 1994 May 1;36(1):39-41.
8. Guo X, LaW, Zhang S,Wu A,Wang Z. Ku lain pi. In: Guo X, ed. A dictionary of poisonous chinese herbal medicines. Tianjin, China: Tianjin Scientific Translation Publishing Company; 1991:296.
9.Oelrichs PB, Hill MW, Vallely PJ, MacLeod JK, Molinski TF. Toxic tetranortriterpenes of the fruit of Melia azedarach. Phytochemistry. 1983 Jan 1;22(2):531-4.
10. Ferreiro D, Orozco JP, Mirón C, Real T, Hernández-Moreno D, Soler F, Pérez-López M. Chinaberry tree (Melia azedarach) poisoning in dog: a case report. Topics in companion animal medicine. 2010 Feb 1;25(1):64-7.
11. Hare WR, Schutzman H, Lee BR, Knight MW. Chinaberry poisoning in two dogs. Journal of the American Veterinary Medical Association. 1997 Jun 1;210(11):1638-40.
12. Kiat TK. Melia azedarach poisoning. Singapore Med J. 1969 Mar 1;10(1).
13. Bina S, Javadi I, Iravani O. Evaluation of the Repellency Effect of Neem (Melia azedarach) Plant Extracts Based on the Mittler & Dadd Method. Journal of Agricultural Chemistry and Environment. 2017 Nov 8;6(04):165.
14. Kumar R, Singh R, Meera PS, Kalidhar SB. Chemical components and insecticidal properties of Bakain (Melia azedarach L.)–A review. Agricultural Reviews. 2003;24(2):101-15.
15. Yogendr B, Kalpana P, Rawat MS, Sunil J, Sampada U. Antiulcer activity of Melia azedarach Linn in aspirin induced and pylorus ligated rats. Journal of Pharmacy Research. 2009;2(9):1456-9.
16. Lungu L, Popa CV, Morris J, Savoiu M. Evaluation of phytotoxic activity of Melia azedarach L. extracts on Lactuca sativa L. Romanian Biotechnological Letters. 2011 Mar 1;16(2):6089-95.
17. Sharma D, Paul Y. Preliminary and pharmacological profile of Melia azedarach L.: An overview. Journal of Applied Pharmaceutical Science. 2013 Dec;3(12):133-8.
18. Joy PP, Thomas J, Mathew S, Skaria PB. Medicinal plants, kerala agricultural university. Aromatic and medicinal plants research station. 1998:4-6.
19. Seth MK. Trees and their economic importance. The Botanical Review. 2003 Oct;69(4):321-76.
20. Sultana S, Khan MA, Ahmad M, Bano A, Zafar M, Shinwari ZK. Authentication of herbal medicine neem (Azadirachta indica A. Juss.) by using taxonomic and pharmacognostic techniques. Pakistan Journal of Botany. 2011 Dec 1;43(SI):141-50.
21. Al-Rubae AY. The potential uses of Melia azedarach L. as pesticidal and medicinal plant, review. American-Eurasian Journal of Sustainable Agriculture. 2009;3(2):185-94.
22. Zahoor M, Ahmed M, Naz S, Ayaz M. Cytotoxic, antibacterial and antioxidant activities of extracts of the bark of Melia azedarach (China Berry). Natural product research. 2015 Jun 18;29(12):1170-2.
23. Della Bona A, Nedel F. Evaluation of Melia azedarach extracts against Streptococcus mutans. Journal of medicinal food. 2015 Feb 1;18(2):259-63.
24. Mishra G, Jawla S, Srivastava V. Medicinal Chemistry & Analysis.
25. Carpinella MC, Ferrayoli CG, Palacios SM. Antifungal synergistic effect of scopoletin, a hydroxycoumarin isolated from Melia azedarach L. fruits. Journal of Agricultural and Food Chemistry. 2005 Apr 20;53(8):2922-7.
26. Carpinella MC, Defago MT, Valladares G, Palacios SM. Antifeedant and insecticide properties of a limonoid from Melia azedarach (Meliaceae) with potential use for pest management. Journal of Agricultural and Food Chemistry. 2003 Jan 15;51(2):369-74.
27. Khan AV, Khan AA, Shukla I. In vitro antibacterial potential of Melia azedarach crude leaf extracts against some human pathogenic bacterial strains. Ethnobotanical Leaflets. 2008;2008(1):53.
28. Nugroho BW, Edrada RA, Wray V, Witte L, Bringmann G, Gehling M, Proksch P. An insecticidal rocaglamide derivatives and related compounds from Aglaia odorata (Meliaceae). Phytochemistry. 1999 Jun 1;51(3):367-76.

29. Saxena RC, Epino PB, Tu CW, Puma BC. Neem, chinaberry and custard apple: antifeedant and insecticidal effects of seed oils on leafhopper and planthopper pests of rice. Schriftenreihe der Gesellschaft fur Technische Zusammenarbeit. 1984.
30. Coria C, Almiron W, Valladares G, Carpinella C, Ludueña F, Defago M, Palacios S. Larvicide and oviposition deterrent effects of fruit and leaf extracts from Melia azedarach L. on Aedes aegypti (L.)(Diptera: Culicidae). Bioresource Technology. 2008 May 1;99(8):3066-70.
31. Nathan SS, Sehoon K. Effects of Melia azedarach L. extract on the teak defoliator Hyblaea puera Cramer (Lepidoptera: Hyblaeidae). Crop protection. 2006 Mar 1;25(3):287-91.
32.Kelecom A, Carbal MM, Garcia ES. A new euphane tritrpine from the Melia azedarach. J. Braz. Chem. Soc. 1996;7:1-4.
33.Borges LM, Ferri PH, Silva WJ, Silva WC, Silva JG. In vitro efficacy of extracts of Melia azedarach against the tick Boophilus microplus. Medical and Veterinary entomology. 2003 Jun;17(2):228-31.
34.Su M, Mulla MS. Activity and biological effects of neem products against arthropods of medical and veterinary importance. J. Am. Mosq. Control Assoc. 1999;15:133-52.
35.Krous W. Azadirachtin and other triterpenoids. The neem tree Azadirachta indica A. Juss and other meliaceous plants. 1995:36-88.
36. Charleston DS, Kfir R, Vet LE, Dicke M. Behavioural responses of diamondback moth Plutella xylostella (Lepidoptera: Plutellidae) to extracts derived from Melia azedarach and Azadirachta indica. Bulletin of entomological research. 2005 Oct;95(5):457-65.
37. Chiu SF. Recent advances in research on botanical insecticides in China.
38. Roop JK, Dhaliwal PK, Guraya SS. Extracts of Azadirachta indica and Melia azedarach seeds inhibit folliculogenesis in albino rats. Brazilian journal of medical and biological research. 2005;38:943-7.
39. Pandey G. Medicinal plants of Himalaya. Sri Satguru Publications; 1995.
40. Khalil AM, Ashy MA, Tawfik ni, eltawil b. Constituents of local plants. 3. Constituents of various parts of the melia-azedarach l plant. Pharmazie. 1979 Jan 1;34(2):106-8.
41. Bhakuni DS, Dhar ML, Dhar MM, Dhawan BN, Mehrotra BN. Screening of Indian plants for biological activity: Part II.
42. Keshri G, Lakshmi V, Singh MM. Pregnancy interceptive activity of Melia azedarach Linn. in adult female Sprague-Dawley rats. Contraception. 2003 Oct 1;68(4):303-6.
43. Al-Rubae AY. The potential uses of Melia azedarach L. as pesticidal and medicinal plant, review. American-Eurasian Journal of Sustainable Agriculture. 2009;3(2):185-94.
44. Rahmatullah M, Khatun MA, Morshed N, Neogi PK, Khan SU, Hossan MS, Mahal MJ, Jahan R. A randomized survey of medicinal plants used by folk medicinal healers of Sylhet Division, Bangladesh. Advances in Natural and Applied Sciences. 2010 Jan 1;4(1):52-62.
45. Kokwaro JO. Medicinal plants of east Africa. University of Nairobi press; 2009.
46.Breyer-Brandwijk MG. The Medicinal and Poisonous Plants of Southern and Eastern Africa being an Account of their Medicinal and other Uses, Chemical Composition, Pharmacological Effects and Toxicology in Man and Animal. The Medicinal and Poisonous Plants of Southern and Eastern Africa being an Account of their Medicinal and other Uses, Chemical Composition, Pharmacological Effects and Toxicology in Man and Animal.. 1962(Edn 2).
47.Sen A, Batra A, Rao DV. Pivotal role of plant growth regulators in clonal propogation of Melia azedarach L. Int. J. Pharm. Sci. Rev. Res. 2010;5(2):43-9.
48. Sharma D, Paul Y. Preliminary and pharmacological profile of Melia azedarach L.: An overview. Journal of Applied Pharmaceutical Science. 2013 Dec;3(12):133-8.
49. Zhang SN, Huang L, Ma RJ, Yang MF, Wei BF, Song HZ, Wang HS, Tan QG. Chemical constituents from the barks of Melia azedarach and their PTP1B inhibitory activity. Natural product research. 2020 Feb 20:1-6.
50.Chowtivannakul P, Srichaikul B, Talubmook C. Antidiabetic and antioxidant activities of seed extract from Leucaena leucocephala (Lam.) de Wit. Agriculture and Natural Resources. 2016 Sep 1;50(5):357-61.
51. Khan MF, Rawat AK, Khatoon S, Hussain MK, Mishra A, Negi DS. In vitro and in vivo antidiabetic effect of extracts of Melia azedarach, Zanthoxylum alatum, and Tanacetum nubigenum. Integrative medicine research. 2018 Jun 1;7(2):176-83.

52. Su M, Mulla MS. Activity and biological effects of neem products against arthropods of medical and veterinary importance. J. Am. Mosq. Control Assoc. 1999;15:133-52.
53. Abdel-Ghany HS, Fahmy MM, Abuowarda MM, Abdel-Shafy S, El-Khateeb RM, Hoballah EM. In vitro acaricidal effect of Melia azedarach and Artemisia herba-alba extracts on Hyalomma dromedarii (Acari: Ixodidae): embryonated eggs and engorged nymphs. Journal of Parasitic Diseases. 2019 Dec;43(4):696-710.
54. Malar TJ, Antonyswamy J, Vijayaraghavan P, Kim YO, Al-Ghamdi AA, Elshikh MS, Hatamleh AA, Al-Dosary MA, Na SW, Kim HJ. In-vitro phytochemical and pharmacological bio-efficacy studies on Azadirachta indica A. Juss and Melia azedarach Linn for anticancer activity. Saudi journal of biological sciences. 2020 Feb 1;27(2):682-8.
55. Kotoky R, Pandey P. Difference in the rhizosphere microbiome of Melia azedarach during removal of benzo (a) pyrene from cadmium co-contaminated soil. Chemosphere. 2020 Nov 1;258:127175.