Pharmacological potentials of *Melia azedarach* L. - A review

Azam M. M.¹, Mamun-Or-Rashid A. N. M.¹, Towfique N. M.¹, Sen M. K.^{1*}, Nasrin. S²

¹Department of Biotechnology and Genetic Engineering, Faculty of Applied Science and Technology, Islamic University, Kushtia-7003, Bangladesh

²Scientific Officer, Plant Biotechnology Division, National Institute of Biotechnology, Savar, Dhaka, Bangladesh

Email address:

Monokeshsen@yahoo.com (Sen M. K.)

To cite this article:

Azam M. M., Mamun-Or-Rashid A. N. M., Towfique N. M., Sen M. K., Nasrin. S. Pharmacological Potentials of *Melia Azedarach* L. - A Review. *American Journal of BioScience*. Vol. 1, No. 2, 2013, pp. 44-49. doi: 10.11648/j.ajbio.20130102.13

Abstract: Medicinal plants are widely used by the traditional medicinal practitioners to cure different diseases due to their world-wide availability and fewer side effects. *Melia azedarach* L. (Ghoda Neem locally) belongs to the family Meliaceae, is a highly significant medicinal plant found almost everywhere in Bangladesh. Traditionally, different parts such as leaf, flower, seed, fruit, and young branches of have been used for the treatment of malaria, diabetes, purgative, cough, skin disease, and so on. Experimental and clinical studies prove that it has antioxidant, antimicrobial, anti-inflammatory, cardioprotective, analgesic, anticancer, antiulcer, antipyretic, antiplasmodial and male contraceptive properties. For the last few decades or so, extensive research work has been done to prove its biological activities and pharmacology of its extracts. The present compendium review will focus on is traditional uses and pharmaceutical activities found on different scientific research and reports. This review also includes reports on phytochemistry, taxonomy, morphology, monographs, distribution and toxic effects of *M. azedarach*.

Keywords: *Melia Azedarach*, Traditional Uses, Pharmaceutical Activities, Phytochemistry

1. Introduction

The herbal medicines occupy distinct position right from the primitive period to present day. The ethnobotanical pharmacology is as old as man himself. Novel approaches to the development of new antimicrobials remain an important area of research. In recent years, multiple drug/chemical resistance in both human and plant pathogenic microorganisms has developed due to indiscriminate use of commercial antibiotics commonly applied in the treatment of infectious diseases [1]. This situation has led scientists to search for new antimicrobials from various sources, including medicinal plants [1-2]. To date, nearly 25 to 45% of modern prescriptions contain plant derived lead molecules as a basic source in drug formulations [3].

M. azedarach, is a species of deciduous tree in the mahogany family, Meliaceae, that is an evergreen tree, cultivated in various parts of the Indian subcontinents. Neem has a long history of use in the traditional medical systems of India (Ayurvedic, Unani-Tibb). Leaves have been used as a natural insecticide to keep with stored food,

but must not be eaten as they are highly poisonous. A diluted infusion of leaves and trees has been used in the past to induce uterus relaxation [4]. Extracts from neem leaf, seed, and bark possess a wide spectrum of antibacterial action [5, 1]. Recently, the antibacterial activity of neem seed oil was assessed *in vitro* against 14 strains of pathogenic bacteria [5, 1].

The US Academy of Sciences currently gives very high importance to the Neem tree. The United Nations declared Neem as the “Tree of the 21st Century”. Neem is now widely used in USA in pharmacy, health, beauty, pet care, pesticides and insecticides, and agriculture. Its derivatives are being exported in several industrialized countries including EU. With a lifetime value of up to \$25,000 from pharmaceuticals alone, the neem has much to offer people in Africa’s drylands including food, medicine, timber and shade [6].

Bangladesh being a tropical country is blessed with vast natural resources and ancient knowledge for its judicious utilization. However, in order to make these remedies acceptable to modern medicine, there is a need to scientifically evaluate them, to identify the active principles and to understand the mechanism of action. However, this

study was designed to assess the pharmacological activity of *M. azedarach* by scientific evidences.

1.1. Taxonomy of *M. azedarach*

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Sapindales
Family	Meliaceae
Genus	Melia
Species	<i>M. azedarach</i>
Binomial name	<i>Melia azedarach</i> L.

1.2. Plant Parts Used

Leaf, flower, seed, oil, root, young branches, fruit and bark.

1.3. Monograph

Bengali name: Ghoda Neem.
Common name: Chinaberry tree, Texas umbrella,
Scientific name: *Melia azedarach*
Family: Meliaceae.
Duration: Perennial.
Growth habit: Multi-branched tree.
Bangladesh nativity: Native.

1.4. Morphology

M. azedarach L. is a small to medium sized deciduous tree. It grows to a height of 5 to 15m tall and 30 to 60cm in diameter. The plant is characterized by the presence of a spreading, dense and dark green crown. Its bark is dark brown in color, relatively smooth, and fissured. The leaves are alternate, leaflets are short stalked and thin, hairless, dark green and relatively pale. Flowers are white with purple stripes and are characterized by the presence of a typical fragrance. Fruits or berries are yellow, round, smooth, and fleshy. Dried fruits are hard with 4 to 5 seeds [3].

1.5. Tree Propagation and Keeping

With an extensive and deep root system, the neem can grow also in marginal and leached soils, up to an altitude of 1500 m. The tree requires annual rainfall from 500 to 1150 mm; it tolerates drought but cannot withstand water-logged areas and poorly drained soils. Neem is propagated from seeds or cuttings. Young seeds germinate readily in 14 to 21 days at 19 to 22° C. The neem tree will grow in full sun to partial shade, better in a well-drained soil mix. The tree

grows well in pots and its size is easily controlled by pruning. Even though very drought tolerant in nature, it is more sensible when still in pots. Trees in pots should be watered regularly and the soil should dry slightly before watering again. The plants can be fertilized monthly to increase growth speed. Watering should be reduced and fertilization avoided during cold months. All repotting and pruning should be done at this time [6].

1.6. Distribution

It is native in Pakistan, India, Indochina, Southeast Asia and Australia. It is widespread and naturalized in most of the tropics and subtropical countries [3]. The genus *Melia* includes four other species, occurring from Southeast Asia to northern Australia.

2. Phytochemistry

The chemical composition of *M. azedarach* is highly complex. Its main chemical composition is a blend of 3 to 4 related main compounds and over 20 others present in smaller amounts but use full as well. These compounds are mainly triterpenes with the most effective being the limonoids abundant in its oil. At least nine limonoids are effective in inhibiting insect growth, especially some of the most deadly varieties found in human health and agriculture worldwide. Of these limonoids, azadirachtin has been found to be the main ingredient for fighting insects and pests, being up to 90% effective in most instances. It repels and disrupts the life cycle, however does not kill immediately, but is nonetheless one of the most effective growth and feeding deterrents ever examined. Meliantriol is another feeding inhibitor which prevents locusts damages, and therefore has been used traditionally for crop protection. Also nimbin and nimbidin are found in neem, they have anti-viral and anti-fungal properties useful to humans and animals. Gedunin, a minor limonoid, is effective in treating malaria through leaves infusion [6].

3. Folk Remedies and Traditional Uses

A rich heritage of knowledge on preventive and curative medicines was available in ancient scholastic work Ayurveda (Indian traditional system of medicine) and so on. Neem extracts are used in Ayurvedic remedies for common colds, headaches, stomach disorders, inflammation, diabetes, various forms of poisoning and malaria. Various traditional uses of the *M. azedarach* are mentioned in Table 1.

Table 1. Folk remedies and traditional uses of *M. azedarach*

Parts used	Uses	Method	References
Leaf	Leprosy, scrofula, anthelmintic, antilithic, diuretic, deobstruent, resolvent, insecticidal, burns, malaria, gingivitis, piles, pyrexia, chicken pox, smallpox and warts, remove toxins, purify blood and prevent damage caused by free radicals, mosquito coils	Fresh extract	[7, 8, 9, 10, 3, 6]

Root	Resolvent, deobstruent, antiseptics, antimicrobial and inflammatory diseases	---	[7, 8, 9, 3, 6]
Seed	Rheumatism, anthelmintic, antileprotic, antipoisonous, mosquito coils	---	[7, 8, 9, 3, 6]
Seed oil	Antiseptic for sores and ulcers, rheumatism and skin diseases such as ringworm and scabies, malaria fever and leprosy, antibacterial, central nervous system depressant, mild analgesic, aromatherapy	---	[7, 8, 9, 3, 6]
Fruit	Insecticidal, diabetes, purgative, antihemorrhoidal and anthelmintic	Powdered dust	[7, 8, 9, 3, 6]
Wood and bark	Insecticidal	Crude extract	[7, 8, 9, 3]
Stem bark	Anticancerous, antispasmodic, antiviral, gonorrhea, tiredness, cough, fever, loss of appetite, worm infestations, wound, vomiting, skin diseases and excessive thirst.	---	[7, 8, 9, 10, 3, 6]
Flower	Cough, astringent, anthelmintic and non toxic	---	[6]
Young branch	Tooth diseases	Brushing	[11]

4. Pharmacology

During the last two decades, *M. azedarach* has demonstrated various pre-clinical activities in animal models in vitro testing. Most important findings are shown in Table 2.

Table 2. Pharmacological activities of *M. azedarach*

Disease	Extract	Plant parts	References
Malaria	Leaf decoction/ triterpenoids and Limonoids	Leaf and seed	[12-17]
Inhibit Inflammation	Gallic acid and epicatechin	---	[13-16]
Antifungal activities	Neem oil, leaf extracts, methanolic extract, ethanolic extracts	Fruit and seed	[18, 19, 20, 16, 21, 22]
Eczema	Neem oil	Leaf	[23-24]
Leprosy	Neem oil	Leaf	[23, 3, 24]
Blood purification	---	Bark, leaf and ripe fruit	[23-25]
Remedy for intestinal worms	---	Bark, leaf and ripe fruit	[12]
Antiplasmodial activity	Triterpenoids and limonoids	Seed	[5]
Antibacterial	Methanol extracts, ethanol extract, crude leave, flower and fruit-seed extracts	Leaf, seed and bark	[5, 3, 22, 26]
Headache	Nim sakam	Leaf	[27]
Chickenpox	Paste of green neem leaf, Nim sakam,	Leaf	[27]
Continuous fever during pregnancy	Nim sakam	Leaf	[27]
Burns	Fresh leaf extract is applied externally	Leaf	[10, 3]
Gonorrhea	Stem bark infusion 30-50 ml is administered orally twice a day	---	[10, 3]
Piles	Leaf extract 5 ml is administered orally thrice a day	Leaf	[10, 3, 28]
Gingivitis	Fresh leaf extract is used as mouth wash	Leaf	[10, 3]
Pyrexia	Leaf extract 5-10 ml is administered orally twice a day for 7 days	Leaf	[10, 3]
Tuberculosis	Nim sakam	Leaf	[3, 27]
Pimples	---	---	[29]
Scrofula	---	Leaf	[3]
Anthelmintic	---	Leaf	[3]
Antilithic	---	Leaf	[3]
Diuretic	---	Leaf	[3]
Deobstruent	---	Leaf	[3]
Rheumatism	Neem Oil	Seed	[30, 3, 31]
Paroxysmal fever	Bark decoction	Bark	[32-33]
Skin disease	Bark decoction	Bark	[32-33]

Splenomegaly	Stem exudate	Stem	[32-33]
Antiparasitic activity	Drupe extract	---	[34-35]
Gangrene	Leaf	Leaf	[23-24]
Heal chronic wounds	Leaf	Leaf	[23-24]
Antiheperglycemic	Leaf	Leaf	[23-24]
Ringworm	Leaf	Leaf	[29, 36, 23, 24]
Acne	Leaf	Leaf	[37, 23, 16, 24]
Anticancer Agent	Leaf	Leaf	[23-24]
Hepato-renal protective activity	Leaf	Leaf	[23-24]
Hypolipidemic effects	Leaf	Leaf	[23-24]
Antihepatotoxic activities	Ethanol extract	---	[38]
Antioxidant	Ethanol extract	---	[30, 38, 39]
Stomachache	---	---	[38]
Uterine illnesses	---	---	[38]
Cystitis	---	---	[38]
Diuretic and febrifuge	---	---	[38]
Anti-helminthic	---	---	[38, 40]
Cytotoxic activities	---	---	[38, 40]
Antiviral activities	---	---	[40, 38]
Anti-dysenteric activities	---	---	[30-31]
Cold, cough and fever	---	Bark	[28]
Traumatic injury	---	---	[30-31]
Acaricidal	---	---	[41, 16]
Anti-fertility	---	---	[13, 15, 16]
Nematicidal	---	---	[42, 16]
Kausa/Sores	Nim sukum, Nim chal	Bark and leaf	[27]
Antidiabetic	Neem oil	Seed	[43, 30, 31]
Nausea	---	---	[44-45]
Vomiting	---	---	[44-45]
Dandruff	---	---	[29, 36]
Antifeedant activity	---	---	[46, 16]

5. Male Contraceptive Potentiality

It has been reported that sperm motility of rats showed a significant difference for those receiving *M. azedarach* (50mg/kg and 150mg/kg doses) compared to that of the controls. Daily sperm production (DSP) showed a significant reduction for those on *M. azedarach* with 150mg/kg doses in comparison to the control group ($p < 0.05$). The results also demonstrated a significant reduction in fertility rate by 50 and 150mg/kg doses ($p < 0.01$) compared to the controls that means *M. azedarach* is able to decrease fertility indices. So it requires being studied more extensively and introduced more widely to the world for having male contraceptive potentials [47].

6. Toxicity

Fruits are poisonous to humans if eaten in large quantity. The first symptoms of poisoning appear a few hours after ingestion. They may include loss of appetite, vomiting, constipation or diarrhea, bloody faeces, stomach pain, pulmonary congestion, cardiac arrest, rigidity, lack of coordination and general weakness. Death may take place after about 24 hours. Like in relatives, tetranortriterpenoids constitute an important toxic principle. These are chemically related to azadirachtin, the primary insecticidal compound in the commercially important neem oil. These compounds are probably related to the wood and seed's resistance to pest infestation, and may be to the unattractiveness of the flowers to animals [4].

7. Conclusion

The neem can contribute to solve some of the major problems of health and food production. The scientific

information of this plant confirms all the ancient claims, including safety for mammals and environment. Its bioactivity spectrum against harmful organisms is increasing. So, it can be concluded that *M. azedarach* is a traditionally and clinically proved medicinal plant for both its application and efficacy. Keeping the various health benefits in view, investigations are highly required to purify the *M. azedarach* components in an economical way and their characterization in term of chemical nature and mood of action in molecular level. Almost certainly, such natural components might prove to be potentially beneficial but comparatively less toxic than present day drugs.

Acknowledgement

The authors would like to thank the Department of Biotechnology and Genetic Engineering for conducting this review.

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