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Neem (*Azadirachta Indica*): A Potential Medicinal Plant

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ABSTRACT: In traditional medicine most of the diseases have been treated by administration of plant or plant product. Neem (*Azadirachta indica* A. Juss) is the most useful traditional medicinal plant in Bangladesh. Each part of the neem tree has some medicinal property. During the last five decades, apart from the chemistry of the neem compounds considerable progress has been achieved regarding the biological activity and medicinal applications of neem. It is now considered as a valuable source of unique natural products for development of medicines against various diseases and also for the development of industrial products. This review gives a bird's eye view mainly on the biological activities of the neem and some of their compounds isolated, pharmacological actions of the neem extracts, clinical studies and plausible medicinal applications of neem along with their safety evaluation.

KEYWORDS: Traditional medicine, Medicinal property, Biological activity, Pharmacological action, *Azadirachta indica*.

I. INTRODUCTION

Neem is a fast growing evergreen popular plant commonly found in India, Bangladesh, America, Africa, Pakistan, Nepal etc. it has been used in ayurvedic medicine since 4000 years. It is called 'arista' in Sanskrit meaning perfect, complete and imperishable[22]. It is also called reliever of sickness and sorborog nibaroni. It is mostly grows in Southeast Asia, West Africa and America including Mexico. The importance of the neem tree has been recognized by the US National Academy of Sciences, which published a report in 1992 entitled 'Neem - a tree for solving global problems'. The Sanskrit name 'nimba' comes from the term 'nimbat swasthyam dadati' which means 'to give good health'. The benefits of neem are listed in ancient documents 'Charak-Samhita' and 'Susruta-Samhita', which form the foundation of the Indian system of natural treatment, Ayurveda. It is commonly called 'Indian lilac' or 'Margosa' and belongs to the family Meliaceae. The Persian name of neem is 'Azad- Darakth- E- Hind' which means 'Free tree of India'. Neem is considered to be a part of India's genetic diversity. Neem tree is the most researched tree in the world and is said to be the most promising tree of 21st century. It has great potential in the fields of pest management, environment protection and medicine. Neem is a natural source of insecticides, pesticides and agrochemicals.[23]

II. TAXONOMICAL CLASSIFICATION

Order:	Rutales
Suborder:	Rutinae
Family:	Meliaceae
Subfamily:	Melioideae
Genus:	<i>Azadirachta</i>
Specie:	<i>Indica</i>
Latin:	<i>Azadirachta indica</i> [2]

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III. BOTANICAL DESCRIPTION

Plant Appearance

It is a tree 40-50 feet or higher, with a straight trunk and long spreading branches forming a broad round crown; it has rough dark brown bark with wide longitudinal fissures separated by flat ridges. The leaves are compound, imparipinnate, each comprising 5-15 leaflets[11]. The compound leaves are themselves alternating with one another. It bears many flowered panicles, mostly in the leaf axils. The seel are ovate and about one cm long with sweet scented white oblanciolate petals. It produces yellow drupes that are ellipsoid and glabrous, 12-20 mm long. Fruits are green, turning yellow on ripening, aromatic with garlic like odor. Fresh leaves and flowers come in March-April. Fruits mature between April and August depending upon locality.

Geographical Distribution

Dinajpur, Jaypurhut, Kurigram, Bogra, Gaibandha, Rajshahi, Mymensing, Habigonj, Moulovibazar, Pabna, Kushtia, Noakhali, Sylhet, Jhalakathi, Potuakhali, Feni, Jessore, Chittagong, Dhaka, Comilla are the districts where neem plant grows available in Bangladesh. In urban areas they also have found in few numbers. A native to east India and Burma, it grows in much of south East Asia and West Africa, and more recently Caribbean and south and Central America. In India it occurs naturally in Siwalik Hills, dry forests of Andhra Pradesh, Tamil Nadu and Karnataka to an altitude of approximately 700 m. It is cultivated and frequently naturalized throughout the drier regions of tropical and subtropical India, Pakistan, Sri Lanka, Thailand and Indonesia. It is also grown and often naturalized in Peninsular Malaysia, Singapore, Philippines, Australia, Saudi Arabia, Tropical Africa, the Caribbean, Central and South America.[11][23]

Cultivation Collection of Neem

Neem is a large tree growing about 25 m in height with semi-straight to straight trunk, 3 m in girth and spreading branches forming a broad crown. A neem tree normally starts fruiting after 3-5 years. In about 10 years it becomes fully productive. From the tenth year onwards it can produce up to 50 Kg of fruits annually. The plant is reported to live up to two centuries. The tree has adaptability to a wide range of climatic, topographic and edaphic factors. It grows well in dry, stony shallow soils and even on soils having hard calcareous or clay pan at a shallow depth[23]. Neem tree requires little water and plenty of sunlight. The tree grows naturally in areas where the rainfall is in the range of 450 to 1200 mm. However, it has been introduced successfully even in areas where the rainfall is as low as 150 to 250 mm. Neem grows on altitudes up to 1500 m. It can grow well in wide temperature range of 00C to 490C.

III. AYURVEDIC APPLICATION

In ayurvedic text neem has been regarded as the 'sarva roga nivarini' as it keeps all the diseases at bay. Since ages neem has been used to cure almost all kinds of diseases and also taken to maintain a healthy life. Every part of neem such as bark, seed oil, leaf, roots has ayurvedic properties and hence used in therapeutic preparations. Neem has been an inherent part of ayurveda since ages; its blood purification property made it a favourite natural ingredient, as a remedy for skin ailments and curing diabetes. It was also used to cure prevalent diseases like malaria and other insect bites. Neem twigs were used as a cheap and healthy oral care. Neem finds mention in almost all ayurveda texts.[4][10]

IV. UNANI MEDICINE

Neem is popularly known as 'Yavan Priya' meaning the beloved of muslims. It has for long been used in the traditional unani system of medicine for its beneficial properties. All parts of neem i.e. the roots, stem, leaves, fruits, bark and seeds have therapeutic value.[4][10]

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Table 1: Compounds of Neem[5][10]

Neem compound	Source	Biological activity
Nimbidin		Anti-inflammatory Antipyretic Hypoglycaemic Antigastric ulcer Spermicidal Antifungal Antibacterial
Sodium nimbidate		Anti-inflammatory
Nimbin	Seed oil	Spermicidal
Nimbolide	Seed oil	Antibacterial Antimalarial
Gedunin	Seed oil	Antifungal Antimalarial
Azadirachtin	seed	antimalarial
Mahmoodin	Seed oil	antibacterial
Gallic acid (epicatechin) and catechin	bark	Anti-inflammatory and immunomodulatory
Margolone , margolonone and isomargolonone	bark	Anti bacterial
Cyclic trisulphide and cyclic tetrasulphide II.	Leaf	Anti fungal
Polysaccharides I.		Anti inflammatory
Polysaccharides GIa, GIb	bark	Anti tumor
Polysaccharides GIIa, GIIIa	bark	Anti inflammatory
NB-II peptidoglycan	bark	immunomodulatory

V. PHARMACOLOGICAL ACTION

Antibacterial Activity

The petroleum ether, methanol and aqueous extracts of the leaves of *Azadirachta indica* (Meliaceae), bulbs of *Allium cepa* (Liliaceae) and methanol extract of gel of *Aloe vera* (Liliaceae) were screened for their anti-microbial activity using the cup plate agar diffusion method. They were tested against six bacteria; two Gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and four Gram-negative bacteria (*Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and *Salmonella typhi*). The susceptibility of the microorganisms to the extracts of these plants was compared

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with each other and with selected antibiotics. The methanol extract of *Azadirachta indica* exhibited pronounced activity against *Bacillus subtilis*. [11]

Anti fungal activity

Extracts of neem leaf, neem oil and seed kernels are effective against certain human fungi, including *Trichophyton*, *Epidermophyton*, *Microsporum*, *Trichosporon*, *Geotricum* and *Candida*. High antimycotic activity with extracts of different parts of neem has already been reported. [5]

Anti helminthic Activity

Products such as fresh leaves, seeds, bark act as antihelmintic for eco small ruminants which rear primarily on grazing land and tree leaves. These cause a high occurrence of helminthic diseases and protozoan diseases along with these things are also mend to manage pediculosis and tick infestations. [9]

Anti oxidant activity

Extracts from young flowers and leaves have strong antioxidant potential. An indicator of oxidative stress, malondialdehyde (MDA), was reduced by 46.0% and 50.6% for flower- and leaf-based extracts, respectively, prompting the recommendation to use neem as a vegetable bitter tonic to promote good health. [11]

Anti-inflammatory, Antipyretic and Analgesic activities

The chloroform extract of stem bark is effective against carrageenin-induced paw oedema in rat and mouse ear inflammation. Inflammatory stomatitis in children is cured by the bark extract. Antipyretic activity has been reported in neem oil. A methanol extract of the leaves exerts antipyretic effect in male rabbits. The plant also possesses analgesic activity mediated through opioid receptors in laboratory animals. Anti-inflammatory and antipyretic activities in various extracts have been reviewed. [4]

Anti diabetic evaluation

The pharmacological hypoglycemic action of *Azadirachta indica* has examined in diabetic rats. After treatment for 24 hrs, *Azadirachta indica* 250mg/kg (single dose study) reduced glucose (18%), cholesterol (15%), triglycerides (32%), urea (13%), creatinine (23%), and lipids (15%). Multiple dose study for 15 days also reduced creatinine, urea, lipids, triglycerides and glucose. In a glucose tolerance test in diabetic rats with neem extract 250 mg/kg demonstrated glucose levels were significantly less compared to the control group. *Azadirachta indica* significantly reduce glucose levels at 15th day in diabetic rats. [11]

Immuno stimulant activity

The aqueous extract of neem bark possesses anticomplement activity, acting both on the alternative as well as the classical pathway of complement activation in human serum. Recently, an aqueous extract of stem bark has been shown to enhance the immune response of Balb-c mice to sheep red blood cells in vivo. [5] The aqueous extract of leaf also possesses potent immunostimulant activity as evidenced by both humoral and cell-mediated responses. Leaf extract at 100 mg/kg after three weeks of oral administration causes higher IgM and IgG levels along with increased titer of antiovalbumin antibody. Neem oil has been shown to possess immunostimulant activity by selectively activating the cell-mediated immune mechanisms to elicit an enhanced response to subsequent mitogenic or antigenic challenge.

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Antiulcer effect

Neem leaf aqueous effect in rats exposed to restraint – cold stress or ethanol orally by preventing mucus depletion and mast cell degranulation. An aqueous extract of neem bark has been shown from our laboratory to possess highly potent antacid secretory and antiulcer activity and the bioactive compound has been attributed to a glycoside.[4]

Anti fertility effect

Neem oil proved spermicidal against rhesus monkey and human spermatozoa in vitro. In vivo studies showed that intravaginal application of neem oil prior to coitus can prevent pregnancy. Antifertility effect of neem oil has also been studied and suggested to be a novel method of contraception. Oral administration of aqueous extract of neem leaf also shows antifertility effect in mice. Purified neem seed extract (Praneem) has also been demonstrated to abrogate pregnancy in both baboons and bonnet monkeys, when administered orally. From the hexane extract of neem seed, an active fraction containing six components has been found to completely abrogate pregnancy in rodents when given orally up to a concentration of 10%, with no apparent side effect. The effect is possibly due to activation of cell-mediated immune reaction.[5] The mechanism of action of neem oil appears to be non-hormonal, probably mediated through its spermicidal effect and may have less side effects than steroidal contraceptives.

Anti malarial activity

Neem seed and leaf extracts are effective against malarial parasites. Components of the alcoholic extracts of leaves and seeds are effective against both chloroquin-resistant and sensitive strains of malarial parasite. Recently, neem seed extract and its purified fractions have been shown to inhibit growth and development of asexual and sexual stages of drug-sensitive and resistant strains of the human malarial parasite *P. falciparum*. [5][23]

Hepato protective activity

The aqueous extract of neem leaf was found to offer protection against paracetamol induced liver necrosis in rats.[5] The elevated levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma glutamyl transpeptidase (GGT) indicative of liver damage, were found to be significantly reduced on administration of the neem leaf aqueous extract.

Antiviral activity

Aqueous leaf extract offers antiviral activity against Vaccinia virus, Chikungemya and measles virus in vitro. The antiviral and virucidal effects of the methanolic extract of neem leaves (NCL-11) have recently been demonstrated against group-B Coxsackie viruses. NCL-11 inhibits plaque formation in different antigenic types of Coxsackie virus B at a concentration of 1 mg/ml at 96 h in vitro. Further studies indicated that NCL-11 is most effective in Coxsackie virus B-4 as a virucidal agent, in addition to its interference at the early events of its replication.[5]

CNS Activity

Varying degrees of central nervous system (CNS) depressant activity in mice was observed with the leaf extract. Fractions of acetone extract of leaf showed significant CNS depressant activity. Leaf extract up to a dose of 200 mg/kg body weight produces significant anxiolytic activity in rats. The crude ethanolic extract of stem bark and root bark showed hypotensive, spasmolytic and diuretic activities.[5]

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Anti-dental caries

A neem-extract dental gel significantly reduced plaque and bacteria (*Streptococcus mutans* and *Lactobacilli* species were tested) over the control group that used commercially available mouthwash containing the germicide chlorhexidine gluconate (0.2% w/v). In preliminary findings, neem inhibited *Streptococcus mutans* (bacterium causing tooth decay) and reversed incipient carious lesions (that is primary dental caries).[11][23]

Anti-HIV/AIDS

In HIV/AIDS patients, a 12-week oral administration of acetone water neem leaf extract (IRAB) had a significant influence in vivo on CD4 cells (which HIV reduces) without any adverse effects in the patients[11]. Of the 60 patients who completed treatment, 50 were completely laboratory-test compliant. The mean levels of CD4 cells increased by 159% in 50 patients, which is a major increase; the number of HIV/AIDS pathologies decreased from the 120 baseline to 5; and significant increases were experienced in body weight (12%), hemoglobin concentration (24%), and lymphocyte differential count (24%). IRAB is recommended as part of an HIV/AIDS drug treatment program.

Skin Disorders

Neem can treat many skin disorders, including scabies and lice; in a paste combination with *Curcuma longa* (turmeric), neem was used to treat scabies in 814 people—97% of them were cured within 3 to 15 days of application, and no adverse reactions were observed.[11][23]

Wound Healing Effect

Numerous plants/their constituents play an important role in the wound healing effect. A study was made to evaluate the wound healing activity of the extracts of leaves of *A. indica* and *T. cordifolia* using excision and incision wound models in Sprague Dawley rats and results revealed that extract of both plants significantly promoted the wound healing activity in both excision and incision wound models.[2]

VII. CONCLUSION

The above collected information regarding the use of *Azadirachta indica* in world is matched with available literature. Recent years, ethno-botanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. It is best classical approach in the search of new molecules for management of various diseases. Thorough screening of literature available on *Azadirachta indica* depicted the fact that it is a popular remedy among the various ethnic groups, Unani, Ayurvedic and traditional practitioners for treatment of ailments. Researchers are exploring the therapeutic potential of this plant as it has more therapeutic properties which are not known.

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