

NEEM: A BOON IN MEDICAL AND DENTAL THERAPIES: A REVIEW

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ABSTRACT

In traditional medicine, most of the diseases have been treated by administration of plant or plant product. Neem, the versatile medicinal plant is the unique source of various compounds. It is considered as a valuable source of unique natural products for the development of medicines against various diseases and also for the development of industrial products. Neem, an elegant medicinal plant was found to be the source of various bioactive compounds of medicinal and cosmetic importance. Each part of the neem tree has some medicinal property. 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, and plausible medicinal and dental applications.

Keywords: Alternative therapy, Dentistry, Neem, *Azadirachta indica*.

INTRODUCTION

Name of medicinal plant: *Azadirachta indica*

Family: Meliaceae

Common name: Indian: Holy tree, Indian lilac tree

Hindi: Neem, Nim

Sanskrit: Nimba[1]

Neem, a tropical tree in the Indian sub-continent[2] has been used for its medicinal properties in the Ayurvedic medicine for more than 4000 years. Plant parts have compounds which demonstrate potential in the fields of medicine, post-management, environment protection. The native source of eco-friendly agrochemical, insecticides, and pesticides is the neem [3]. It is part of India's rich genetic diversity [4]. In the world, there were many researches done on this tree and it is considered to be a reliable tree of the 21st century. Neem is adaptable to a far-range of topographic, edaphic factors, and climate. It flourishes very well in stony, dry, shallow soils and also on soils having hard clay pan, at a shallow depth. It requires plenty of sunlight and little water [4]. Within the range of 450-1200 mm rainfall neem tree grows well in these areas. However, where the rainfall is as low as 150-250 mm neem trees has been introduced even in these areas. Neem grows on altitudes up to 1500 m [5,6]. In wide, temperature range of 0-49°C neem trees were grown [7]. Poorly drained soils and water-logged areas cannot combat by neem trees. A suitable pH range lies in between 4 and 10 for the growth of neem tree. Acidic soils have been neutralized in a unique way with the property of calcium mining of neem tree [7].

Biologically active principles obscured from the tree include: Valassin, azadirachtin, gedunin, salanin, meliacin, nimbin, and all other derivatives of the principles. Meliacin is the bitter principles of neem seed oil and for the distinctive odor of the oil tignic acid (5-methyl-2-butanic acid) is responsible [8-10]. These compounds associated to natural products called limonoids (triterpenoids). Active principles are highly soluble in organic solvents such as alcohols, hydrocarbons, esters, and ketones and slightly hydrophilic but more lipophilic [11].

Recently, it is grown in Caribbean and south and Central America and it mainly grown in east India and Burma but it also grown in most of West Africa and south East Asia. It grows naturally in India in dry forests of Andhra Pradesh, Karnataka and Tamil Nadu, Siwalik Hills, to the height of 700 m approximately. It is grown throughout the drier regions of subtropical and tropical India, Sri Lanka, Pakistan, Indonesia, and Thailand. It is also cultivated in Australia, Peninsular Malaysia,

Tropical Africa, Singapore, Saudi Arabia, Central and South America, the Caribbean, Philippines [12].

CONSTITUENTS

The chemical constituents consist of various biologically active compounds that can be derived from the neem tree, including steroids, triterpenoids, alkaloids, carotenoids, ketones, flavonoids, and phenolic compounds biologically more active compound is azadirachtin, which is actually a mixture of seven isomeric compounds named as azadirachtin A-G and azadirachtin E is the most effective one [13]. Other compounds that have a biological activity are salannin, volatile oils, meliantriol and nimbin [14].

Commercially available as:

- Mouth washes [15]
- Neem oils
- Soaps [1]
- Creams [1]
- Shampoo [1].

From the ancient times, different parts of tree have been used for their medicinal properties as described for fruit, bark and leaf. Extracts of leaf and bark and neem oil have been traditionally used for their therapeutic effect to control intestinal helminthiasis, respiratory disorders, constipation, leprosy and also to promote general health. It is also evident for its use in the treatment of chronic syphilitic sores, indolent ulcer, and rheumatism. To control different skin infections neem, oil has been found to be useful. Root, bark, fruit flower and leaf have a combined effect in curing burning sensations, phthisis, itching, blood morbidity, skin ulcers, and biliary afflictions (Table 1).

MEDICAL AND DENTAL IMPLICATIONS

Immunostimulant activity

Anti-complement activity is possessed by the aqueous extract of neem bark which acts on human serum by activating both the classical as well as the alternative pathway of the complement system. Nowadays, immune response of Balb-C mice to sheep red blood cells *in vivo* is enhanced by the aqueous extract of stem bark. Immunostimulant activity is procured by the aqueous extract of the leaf which is evident by cell-mediate and humoral responses. Higher immunoglobulin M (IgM) and IgG levels in association with anti-ovalbumin antibody which increases in titer which is provoked by the oral administration

Table 1: A few medicinal uses of neem [16]

Part	Medicinal use
Bark	Analgesic, alternative and curative of fever
Flower	Bile suppression, elimination of intestinal worms and phlegm
Seed pulp	Intestinal worms and leprosy
Fruit	Relieves piles, intestinal worms, epistaxis, urinary disorder, eye problem, phlegm, diabetes, wounds and leprosy
Leaf	Eye problem, leprosy, intestinal worms, epistaxis, anorexia, skin ulcers, biliousness
Oil	Intestinal worms and leprosy
Gum	Effective against skin diseases like ring - Worms, scabies, wounds and ulcers
Twig	Relieves cough, piles, phantom tumor; asthma, spermatorrhea, intestinal worms, diabetes, obstinate urinary disorder
Root, bark, leaf, flower and fruit together	Blood morbidity, itching, biliary afflictions, burning sensation, skin ulcer and leprosy

of leaf extract at 100 mg/kg after 3 weeks. Mitogenic or antigenic challenge response is enhanced by elicitation due to cell-mediated immune mechanism which is selectively activated by the activity of immunostimulant which is procured by the neem oil.

Anti-malarial activity

Malarial parasites are effectively killed by the neem seed and leaf extracts. Both chloroquin-sensitive and resistant strains of malarial parasite are affected by the constituents of alcoholic extracts of neem leaves and seeds. Nowadays, growth and development of both sexual and asexual stages of *Plasmodium falciparum* a malarial parasite strain is inhibited by the seed extract of neem and their purified fractions.

Anti-fungal activity

Human fungi, including *Epidermophyton*, *Geotrichum*, *Trichosporon*, *Trichophyton*, *Candida*, and *Microsporium*, are effectively inhibited by extracts of neem oil, seed kernels, and neem leaf. It has been reported earlier that different parts of neem extracts have high antimycotic activity.

Anti-bacterial activity

Gram-positive and Gram-negative microorganisms that include streptomycin and *Mycobacterium tuberculosis* resistant strains which are inhibited by the antibacterial activity of seeds oil, bark oil, and leaves oil. *In vitro* study, oil from the leaves, seeds and bark inhibits *Klebsiella pneumoniae*, *Mycobacterium pyogenes*, *M. tuberculosis*, and *Vibrio cholerae*. *Streptococcus mutans* and *Streptococcus faecalis* are effectively inhibited by the antimicrobial property of neem extracts. From neem oil a new vaginal contraceptive (NIM-76) exhibits inhibitory effect on the growth of diverse pathogens including fungi, virus, and bacteria. Nowadays, *in vitro* study against 14 strains of pathogenic bacteria was evaluated by the antibacterial activity of neem seed oil.

Antiviral activity

In vitro study, on Measles virus, Vaccinia virus and Chikungunya inhibited by the antiviral activity offered by the aqueous leaf extract. Group-B coxsackieviruses have been inhibited by the virucidal and antiviral effect of neem leave methanolic extract (NCL-11). *In vitro* study NCL-11 also hinders plaque formation in various antigenic types of coxsackievirus B at a concentration of 1 mg/ml at 96 hrs. Further studies demonstrated that NCL-11 is more potent in coxsackievirus B-4 as a virucidal agent, and it also interferes at the early event of its replication.

Anti-carcinogenic activity

Oral squamous cell carcinoma induced by 7,12-dimethylbenz[a]anthracene is suppressed by aqueous neem leaf extracts is exhibited by decreased occurrence of neoplasm. The chemopreventive effect in the oral mucosa may be exerted by neem by modulation of glutathione

and its metabolizing enzymes. Aqueous neem leaf extract exerts its protective effect in N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) (a carcinogenic material)-induced oxidative stress has also been showed by the decreased formation of lipid peroxides and exalted level of antioxidants and detoxifying enzymes in the stomach, a primary target organ for MNNG as well as in the liver and in circulation [16].

Anti-oxidant

Extracts from young flowers and leaves have strong antioxidant potential. An indicator of oxidative stress, malondialdehyde, 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.

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. 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 are 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 [14].

Anti-inflammatory, anti-pyretic and analgesic activities

Carrageenan-induced paw edema in rat and mouse ear inflammation is effectively suppressed by chloroform extract of stem bark. Bark extract is effective against inflammatory stomatitis in children. Neem oil has effective anti-pyretic activity. Analgesic activity mediated through opioid receptors in laboratory animals is also reported in the plant. Anti-pyretic and anti-inflammatory activities in various extracts have been reviewed [16].

Anti-ulcer

Neem bark extract reduced human gastric acid hypersecretion, and gastroesophageal and gastroduodenal ulcers. After 10 weeks, the duodenal ulcers were nearly fully healed; after 6 weeks, one case of esophageal ulcer and gastric ulcer were fully healed.

Anti-dental caries

A neem-extract dental gel significantly reduced plaque and bacteria (*S. 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 *S. mutans* (bacterium causing tooth decay) and reversed incipient carious lesions (that is, primary dental caries) [14].

A. indica also known as neem is used as a perfect tool for maintaining healthy periodontium in India and South Asia since 1000 of years. Neem has antiseptic, insecticidal, antiulcer, astringent, and for medicinal properties. Neem leaves are used for curing of gingivitis and periodontitis. The anti-inflammatory action of neem is exhibited by inhibiting prostaglandin E and 5 HT and reducing the inflammation. "Azadiachtin" explains antibacterial action by destroying the bacterial cell wall and inhibiting the growth of bacteria via the breakdown of cell wall disturbing the osmotic pressure which leads to cell death [15].

CONCLUSION

Neem, the multipurpose medicinal plant is the unique source of different compounds. 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 the management of various diseases. Immense research should be undertaken for a better economic and therapeutic utilization of the neem and its products.

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