

# Medicinal and Therapeutical Potential of Neem (*Azadirachta indica*): A Review

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**Abstract-** *Azadirachta indica* is a fast growing, evergreen tree found commonly in India, Africa and America. Neem is one of the most useful traditional medicinal plant in India. It is a highly esteemed tree with several beneficial properties and applications, especially known for its incredible therapeutic and ethnomedicinal values for mankind. It has been used in different medicinal systems: Ayurveda, unani, homeopathic medicine, therefore considered as cynosure of modern medicine. Neem has been used as the traditional medicine since a long time. The main focus of research on Neem has been on the insecticidal properties but in recent years investigations have expanded to the medicinal utilizations as well. A large number of studies have been published on the medicinal properties of Neem and Neem extracts, covering a wide range of indications and ailments. The present paper reviews the medicinal and therapeutical aspects of Neem.

**Index Terms-** *Azadirachta indica*, isoprenoids, antifertility, insect repellent, anti- bacterial.

## I. INTRODUCTION

In human society from time immemorial medicinal plants have played an important role in prevention and control of diseases. Neem, a native of Indian subcontinent is a highly esteemed tree for the people in the region. In India, it occurs naturally in shivalik hills, dry forests of Andhra Pradesh, TamilNadu and Karnataka upto an altitude of 700 m. It is cultivated and frequently naturalized throughout the drier regions of tropical and sub-tropical India. The plant is considered sacred and is used by the Hindus in several ceremonies, rituals and in worship of new year day [1]. Neem is an evergreen tree, cultivated in various parts of India. Each and every part of the tree has been used as traditional medicine for house-hold remedy against various human ailments from antiquity [2-7].

The Neem tree has been described as *A. indica* as early as 1830 by De Jussieu and its taxonomic position is as follows:

Order	Rutales
Suborder	Rutinae
Family	Meliaceae (mahogany family)
Subfamily	Melioideae
Tribe	Melieae
Genus	<i>Azadirachta</i>
Species	<i>indica</i>

The genus *Azadirachta* A. Juss which comprises three species of Indo-Malayan origin has been characterized in detail [8,9].

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 advancement of Neem research has earlier been documented [10,11]. Neem has found to contain a vast array of biologically active compounds, which are chemically diverse and have got an enormous therapeutic potential. Not only this, many reviews have already appeared from time to time on its constituents in general [12-14]. A huge number of compounds have been isolated from different parts of Neem and several reviews have also been published on the chemistry and structural diversity of these compounds. [6,7,15-21]. The compounds have been divided into two major classes: isoprenoids and others [20]. The isoprenoids include diterpenoids and triterpenoids containing protomeliacins, limonoids, azadirone and its derivatives, gedunin and its derivatives, vilasinin type of compounds and Csecomeliacins such as nimbin, salanin and azadirachtin. The nonisoprenoids include proteins (amino acids) and carbohydrates (polysaccharides), sulphurous compounds, polyphenolics such as flavonoids and their glycosides, dihydrochalcone, coumarin and tannins, aliphatic compounds, etc. The details of the chemistry of various compounds falling under these groups have already been reviewed [19,20]. Role of few significant compounds whose bioactivity has been studied is presented here. Thus the current review attempts to highlight some of the common uses of compounds derived from Neem which could potentially be developed as therapeutics, reversible contraceptive and insect repellent.

## II. THERAPEUTIC USES OF NEEM COMPOUNDS

Each part of the Neem tree has some medicinal property and is thus commercially exploitable. Several pharmacological activities and medicinal applications of various parts of Neem are well known. Although a large number of compounds have been isolated from various parts, a few have been studied for biological activity as shown in Table 1. Nimbidin, a major crude bitter principle extracted from the oil of seed kernels of *A. indica* demonstrated several biological activities. From this crude principle some tetranortriterpenes, including nimbin, nimbinin, nimbidinin, nimbolide and nimbidic acid have been isolated [12,20]. Nimbidin and sodium nimbidate possess significant dose-dependent anti-inflammatory activity against carrageenin induced acute paw oedema in rats and formalin-induced arthritis [21,22]. Antipyretic activity has also been

reported and confirmed in nimbidin[23]. Oral administration of nimbidin demonstrated significant hypoglycaemic effect in fasting rabbits[24]. A significant antiulcer effect was observed with nimbidin in preventing acetylsalicylic acid, indomethacin, stress or serotonin-induced gastric lesions as well as histamine or cysteamine-induced duodenal ulcers[25,26]. Nimbidin can also suppress basal as well as histamine and carbachol-stimulated gastric acid output and may act as an antihistamine by blocking H<sub>2</sub> receptors, thereby helping as an antiulcer agent [27]. The

spermicidal activity of nimbidin and nimbin was reported in rats and human as early as 1959 [ 28, 29].

Nimbidin also demonstrated antifungal activity by inhibiting the growth of *Tinea rubrum*[30]. *In vitro*, it can completely inhibit the growth of *Mycobacterium tuberculosis* and was also found to be bactericidal[20]. Diuretic activity was also reported for sodium nimbidinate in dogs [31]. Nimbolide has been shown to exert antimalarial activity by inhibiting the growth of *Plasmodium falciparum*[32,33]. Nimbolide also shows antibacterial activity against *S. aureus* and *S. coagulase* [34].

**Table-1: Some bioactive compounds from Neem.**

S.No	Compound name	Source	Biological activity	Reference
1.	Nimbin	Seed oil	spermicidal	22
2.	Nimbidin	Seed oil	Antipyretic Hypoglycaemic Antiarthritic Antifungal Antibacterial Diuretic Anti-inflammatory	23 24 25 26 26 27 28
3.	Azadirachtin	Seed oil	Antimalarial	29
4.	Mahmoodin	Seed oil	Antibacterial	20
5.	Gedunin	Seed oil	Antimalarial Antifungal	31 30
6.	Sodium nimbidate		Anti-inflammatory	28,25
7.	Gallic acid,(-)epicatechin and catechin	Bark	Anti-inflammatory Immunomodulatory	32
8.	Margolone, Margolonone and isomargolonone	Bark	Antibacterial	33
9.	Cyclic trisulphide and cyclic tetrasulphide	Leaf	Antifungal	34
10.	Polysachharides		Anti-inflammatory	35
11.	Polysachharides G1A,G1B	Bark	Antitumour	36
12.	Polysachharides G2A,G3A	Bark	Anti-inflammatory	37
13.	NB-2 Peptidoglycan	Bark	Immunomodulatory	38,39
14.	Nimbolide	Seed oil	Antimalarial, Antibacterial	31,40

### III. ANTIFERTILITY ACTIVITY OF NEEM

Neem has long been documented to have antifertility in males [41,42]. Oral administration of ethanolic extracts of Neem to adult male lice at 0.5mg, 1.0 mg or 2.0 mg. per kg body weight for 6 weeks interfered with sperm DNA and caused chromosome strand breakage, spindle disturbances and deregulation of genes responsible for sperm morphology. A linear decrease in the percentage of sperm motility was observed with various concentrations (1-50 mg per 1 million sperm) of Neem leaf extract, with motility falling to absolute zero within 20 seconds of exposure to 3 mg dose [43]. The aqueous leaf extract of Neem when administered to male mice at a dose of 200 mg per kg for 28 days damaged the seminiferous tubules, resulting in the slackening of germinal epithelium, degeneration of germ cells and dearrangement of germ cell types [44]. Neem leaf powder when given to Rats for 48 days reduced motility and

density of sperm and caused structural changes of Leydig cells and Seminiferous tubules. [45].

### IV. ANTIBACTERIAL ACTIVITY OF NEEM

The susceptibility of the microorganisms to the extracts of Neem leaves was compared with certain specific antibiotics. The methanol extract of *Azadirachta indica* exhibited pronounced activity against *Bacillus subtilis* (28 mm)[46]. Neem oil preparations have been found effective against a wide spectrum of bacteria viz., *B. cerus*, *B. pumilus*, *S. aureus*, *M. tuberculosis*, *E. coli*, *P. vulgaris*, *S. typhi*, *K. pneumoniae*, *S. dysenteriae*, *Enterococcus faecalis*, *Streptococcus mutans*, *Streptococcus salivarius*, *Streptococcus mitis*, *Streptococcus sanguis* and even *Streptomycin* resistant strains[47-53]. *Azadirachta indica* leaves possessed good anti bacterial activity, confirming the great potential of bioactive compounds and is

useful for rationalizing the use of this plant in primary health care [54]. Neem oil also has definite antiplaque activity [55]. Neem leaf extract can inhibit the formation of biofilm in *Pseudomonas aeruginosa* [56].

#### V. ANTIMALARIAL ACTIVITY OF NEEM ACTIVITY

The antimalarial activities of the tablet suspension of the bark and leaf of *Azadirachta indica* were evaluated on *Plasmodium yoelli nigeriensis* infected mice. The tablet suspensions exhibited high prophylactic, mode-rate suppressive and a very minimal curative schizonticidal effect. The tablet suspensions from the leaf and bark at a concentration of 800 mg/kg and chloroquine at a concentration of 62.5 mg/kg body weight produced average percentage (%) parasitaemia of 79.6%, 68.2% and 99.5% for leaf, bark and chloroquine, respectively, in chemosuppression. Also in the prophylactic treatment, the tablet suspensions at 800 mg/kg and pyrimethamine at a concentration of 0.35 mg/kg gave an average parasitaemia reduction of 75.3%, 65.6% and 98.3% for the leaf, bark and pyrimethamine, respectively. There was a clear indication of moderate beneficial effect[57]. Extracts of Neem are effective against a variety of protozoal pathogen like *Plasmodium spp.*[58]

An active ingredient iroquin A isolated from Neem leaves is toxic to causative strains of malaria [59,60]. *In vitro* experiments have demonstrated cent-percent mortality within 72 h even in a ratio of 1:20,000.

#### VI. ANTI-ULCER ACTIVITY OF NEEM

Inhibition of acid secretion was confirmed by inhibition of H<sup>+</sup> K<sup>+</sup> ATPase activity, while blockade of oxidative damage of gastric mucosa was evident from blocking of lipid peroxidation and scavenging of endogenous hydroxyl radical (OH). Furthermore, they compared the bark extract with known antiulcer drugs ranitidine and omeprazole in the PL and the stress ulcer models and found that the extract was almost equipotent to the standard drugs. The bark extract exhibited more anti-oxidant activity than a variety of known anti-oxidants. There has also been reported an antiulcer effect of Neem leaf extract and the prevention of mucus depletion and mast cell degranulation as possible mechanism.[61]. Neem extracts give significant protection from discomfort and speed the healing of gastric and duodenal lesions [62].

#### VII. INSECT REPELLENT

Azadirachtin is a powerful insect antifeedant that disrupts metamorphosis in moth larvae at extremely low concentrations[63]. A number of studies have shown that Neem compounds are more effective insect repellent than the widely used synthetic chemical known as N,N,-diethyl -m-toluamide, a suspected carcinogen. Neem oil affects the efficacy of commercially available insecticides[64]. Neem seed extracts are effective against both asexual and sexual stages of chloroquin-resistant as well as sensitive strains of malarial parasites *P.falciparum*. Seed extract have inhibited growth and development of the human malarial parasitic agent. Neem extract

was found to have some neuronal protective effect in malaria positive cases[65] and thus mitigate the inflammation of central nervous system.[66] Azadirachtin present in Neem can be used as a potential agent for controlling *Argulus*, a common ectoparasite of ornamental fish[67].

#### AIDS

The National Institutes of Health reports Neem extracts killed the AIDS virus and patents have been awarded for these extracts as an AIDS treatment [68].

#### Periodontal disease

German researchers have proven Neem extracts prevent tooth decay and periodontal disease [69,70] leading to good oral health[71]. Neem leaf extract has a antimicrobial effect on *Enterococcus faecalis* and *Candida albicans*. Therefore, it can be a potential endodontic irrigant [72].

#### VIII. CONCLUSION

Considering the significance of Neem tree in the field of ethnomedicinal science, work must be carried out to exploit the therapeutic utility of this plant to combat diseases. Attention must be given on the development of modern drugs after thorough investigations on the bioactivity, mechanism of action, pharmacotherapeutics, toxicity and similar aspects of chemical constituents of Neem extract. There is still a lot of scope in this field for better utilization of this wonder plant.

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