



## Review Paper

# Neem (*Azadirachta indica* A. Juss) - A Nature's Drugstore: An overview

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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 India. 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, *azadirachta indica*, pharmacological action, biological activity.

## Introduction

*Azadirachta indica* commonly known as neem, is native of India and naturalized in most of tropical and subtropical countries are of great medicinal value and distributed widespread in the world. The chemical constituents contain many biologically active compounds that can be extracted from neem, including alkaloids, flavonoids, triterpenoids, phenolic compounds, carotenoids, steroids and ketones, biologically most active compound is azadirachtin, it is actually a mixture of seven isomeric compounds labelled as azadirachtin A-G and azadirachtin E is more effective<sup>1</sup>. Other compounds that have a biological activity are salannin, volatile oils, meliantriol and nimbin<sup>2</sup>. 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<sup>3</sup>.

**Taxonomical classification**<sup>4</sup>: The taxonomic classification of neem is as follows: Kingdom : Plantae, Order: Rutales, Suborder: Rutinae, Family: Meliaceae, Subfamily : Melioideae, Tribe : Melieae, Genus : *Azadirachta*, Species: *indica*,

**Vernacular names**<sup>5</sup>: Bengali: Nim, Nimgachh, Gujarati: Danujhada, Limbado, Limbra, Limdo, Hindi : Nim, Nimb, Sanskrit : Arista, Nimba, Nimbah, Picumarda, English : Indian Lilac, Margosa tree, Neem tree, Kannada: Bemu, Bevinamara, Bivu, Kaybevu, Punjabi : Bakam, Drekh, Nim.

**Distribution:** 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<sup>5</sup>.

**Botanical description:** 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. The compound leaves are themselves alternating with one another. It bears many flowered panicles, mostly in the leaf axils. The sepal are ovate and about one cm long with sweet scented white oblanceolate 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 odour. Fresh leaves and flowers come in March-April. Fruits mature between April and August depending upon locality<sup>5-6</sup>.

**Phytochemistry:** Biologically active principles isolated from different parts of the plant include: Azadirachtin, meliacin, gedunin, nimbidin, nimbolides, salannin, nimbin, valassin, meliacin forms the bitter principles of *Neem* oil, the seed also contain tignic acid responsible for the distinctive odour of the oil<sup>7</sup>. Neem kernels contain 30-50 % of oil mainly used by the soap, pesticide and pharmaceutical industries and contain many active ingredients which are together called triterpene or limnoids<sup>8</sup>. The four best limnoids compounds are: Azadirachtin,

Salannin, Meliantriol, and Nimbin. Limonoids contain insecticidal and pesticidal activity<sup>9</sup>.

**Pharmacological actions:** Abortifacient, analgesic, anthelmintic, antibacterial, antiyeast, antiulcer, antifertility, antifilarial, antifungal, antihyperglycemic, anti-inflammatory, antiviral, antimalarial, diuretic, antinematodal, antipyretic, antispasmodic, insecticidal, antispermatogenic, antitumor, hypercholesteremic, hypoglycaemic, immunomodulator<sup>5-6</sup>.

**Medicinal use:** All parts of the tree have been used medicinally for centuries. It has been used in Ayurvedic medicine for more than 4000 years due to its medicinal properties. The earliest Sanskrit medical writings refer to the benefits of Neem's fruits, seeds, oil, leaves, roots and bark. Each has been used in the Indian Ayurvedic and Unani medicine, and is now being used in pharmaceutical and cosmetics industries<sup>10</sup>.

**Advantages of various Neem parts**<sup>10</sup>: Neem oil: useful for pest control, cosmetics, medicines, etc.

**Neem seed cake:** Natural fertilizer and insecticide.

**Neem leaves:** useful for chickenpox, increase immunity of the body, reduce fever caused by malaria, treating various foot fungi, useful against termites, used in curing neuromuscular pains.

**Neem bark and roots:** control fleas and ticks on pets, fights against skin infections such as acne, psoriasis, scabies, eczema, etc, treats diabetes, AIDS, cancer, heart disease, herpes, allergies, ulcers, hepatitis and several other diseases.

**Health and Personal Care products:** Neem personal care products derived from seed, oil and leaf include; Skin care - including eczema cream, antiseptic cream, and nail care; hair care - shampoo, and hair oils; oral hygiene - toothpaste and neem twigs; therapeutic - loose Neem leaves - tea, vegetarian capsules, powders; household products - soaps, insect repellent (spray and lotion), and candles.

**Therapeutic uses:** Hot water extract of the bark is taken orally by the adult female as a tonic and emmenagogue. Anthraquinone fraction of dried flower, fruit and leaf is taken orally for leprosy. Hot water extract of the flower and leaf is taken orally as an anti-hysterical remedy, and used externally to treat wound. The dried flower is taken orally for diabetes. Hot water extract of dried fruit is used for piles and externally for skin disease and ulcers. Hot water extract of the entire plant is used as anthelmintic, an insecticide and purgative. Juices of bark of *Andrographis puniculata*, *Azadirachta indica*, *Tinospora cardifolia*, are taken orally as a treatment for filariasis. The hot water extract is also taken for fever, diabetes, and as a tonic, refrigerant, anthelmintic. Fruit leaf and root, ground and mixed with dried ginger and "Triphala" is taken orally with lukewarm water to treat common fever<sup>6</sup>. Leaves due to insecticidal properties are kept with woollen and other cloths for long time. Leaf juice is given in gonorrhoea and leucorrhoea. Leaves

applied as poultice to relieve boils, their infusion is used as antiseptic wash to promote the healing of wound and ulcers. A paste of leaves is used to treat wounds, ring worms, eczema and ulcers. Bathing with *Neem* leaves is beneficial for itching and other skin diseases. Leaf juice is used as nasal drop to treat worm infestation in nose. Steam inhalation of bark is useful in inflammation of throat. Decoction can cure intermittent fever, general debility convalescent, and loss of appetite after fever<sup>11</sup>. Infusion of flower is given in dyspepsia and general debility<sup>12</sup>. The tender twigs of the tree are used as tooth brush which is believed to keep the body system healthy, the breath and mouth clean and sweet<sup>13,14</sup>. Seed oil is used in leprosy, syphilis, eczema, chronic ulcer<sup>11,13</sup>.

## Scientific Reports

**Larvicidal Activity:** Aqueous extracts of four plants were tested for larvicidal properties laboratory reared larvae were exposed to 1, 2, 3, 4 and 5 ppm concentrations of the extracts of *Azadirachta indica* A Juss, *Gymnema sylvestre*, *Nerium indicum* mill and *Datura metel* L. respectively in Zoology research laboratory of D.A-V Degree College, Kanpur, India. Result showed that the *Azadirachta indica* elicited 70-99% mortality, followed by *G. sylvestre* 44-89%, *N. indicum* 41-74% and *D. metel* elicited 19-54% mortality to larvae. The extracts of *A. indica* and *G. sylvestre* were found to be significantly effective in controlling *Culex larvae*<sup>15</sup>.

**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 with each other and with selected antibiotics. The methanol extract of *Azadirachta indica* exhibited pronounced activity against *Bacillus subtilis* (28 mm)<sup>16</sup>.

**Antidiabetic 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<sup>16</sup>.

**Antioxidant:** 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<sup>17</sup>.

**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<sup>18</sup>.

**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 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<sup>19</sup>.

**Antiulcer:** Neem bark extract reduced human gastric acid hypersecretion, and gastro-esophageal 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<sup>20</sup>.

**Antimalarial 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 that moderate beneficial effect<sup>21</sup>.

**Anti-tumour Effect:** A study on *Azadirachta indica* has revealed a chemopreventive capability by regressing the hepatocarcinogenesis induced by diethyl Nitrosamine (DEN) / 2 Acetylaminofluorene (AAF) carcinogens on Sprague- Dawly rats<sup>22</sup>.

**Antifertility effect:** Neem and seed extracts administered orally at the beginning of the post-implantation stage resulted in pregnancy termination in rodents and primates, without any permanent effects. The mechanism of action is not fully understood<sup>23</sup>. Praneem (licensed to Panacea Biotec, India) is a

poly herbal vaginal tablet that has proven to be effective in immobilizing sperm<sup>24, 25</sup>.

**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)<sup>26</sup>. In preliminary findings, neem inhibited *Streptococcus mutans* (bacterium causing tooth decay) and reversed incipient carious lesions (that is, primary dental caries)<sup>27</sup>.

**Antihypertensive and antihypercholesteremic effect:-** Administration of aqueous extract of neem along with DOCA salt prevented the development of hypertension in rats<sup>28</sup>. Administration of the mature leaf extract decreased serum cholesterol significantly without changing serum protein, protein urea and uric acid level in rats<sup>29, 30</sup>.

## 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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**Abbreviations:** Adrien-Henri de Jussieu - A. Juss, Acquired immunodeficiency syndrome-AIDS, Cluster of differentiation 4 -CD4, Human immunodeficiency virus - HIV, Linnaeus - L., Milligram - mg, Millilitre - ml, Kilogram -kg, Hours- h, Malondialdehyde - MD, Acetone water neem extract- IRAB, Diethyl nitrosamine -DEN, Acetylaminofluorene - AAE, Weight - w, Volume - v, Deoxycorticosterone Acetate - DOCA

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