

Exploring the Therapeutic Wonders of Neem: A Natural Remedy for Modern Ailments

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ABSTRACT:

The Himalayan region is home to the medicinal herb neem (*Azadirachta indica*) and thrives in tropical and semi-tropical regions. A member of the Meliaceae family, neem (*Azadirachta indica*) is known for its abundance of antioxidants, which contribute to its health-promoting properties. Throughout the world, Chinese, Ayurvedic, and Unani remedies have made extensive use of it to treat and prevent a wide range of illnesses, particularly in the Indian Subcontinent. These chemical constituents, which include azadirachtin, cyclic trisulphide, gedunin, nimbin, nimbolide, mahmoodin and others, have anti-gastric-ulcer, anti-pyretic, anti-arthritic, anti-inflammatory, anti-bacterial, anti-malarial, spermicidal, anti-fungal, antitumor properties and immunomodulatory. Neem leaves have long been used in medicine to treat a wide range of conditions, including liver issues, eye difficulties, nose bleeding, and appetite loss. It is also used as an alternative medicine, an analgesic, and a treatment for urinary tract disorders and fevers. It is also used to treat a variety of medical conditions, including biliary disorders, diabetes, asthma, cough, phantom tumors, and blood morbidity. People from many countries have traditionally used different parts of the plant to treat a variety of illnesses, including anorexia, leprosy, epistaxis, intestinal worm elimination, eye problems, skin ulcers, ringworms biliousness, wounds, burning sensations, and itching.

INTRODUCTION

A precious gift from nature, neem is an all-powerful tree. Neem's Latin name, *Azadirachta indica*, comes from the Persian. i-Hind signifies "of Indian origin," dirakht means "tree," and azad means "free." It therefore properly translates to "the free tree of India".[1] Neem belongs to the Meliaceae family of mahogany trees. It grows in tropical and semi-tropical areas and is indigenous to India and Burma. It is one of two species in the genus *Azadirachta*. [2] Neem (*Azadirachta indica* A. Juss) is perhaps the most advantageous traditional medicinal herb in India. The neem tree can be exploited for profit because all of its parts—seeds, leaves, gum blossoms, oil, and bark are widely used for various reasons and have some therapeutic benefit. [3] The neem tree was brought to Australia, South East Asia, East and sub-Saharan Africa, At least 30 nations in Asia, Africa, Central and South America, Europe, Malaysia, China, South Asia, and Southeast Asia have adopted neem since 1997. [4] Neem trees have yielded a number of bioactive substances with pharmacological potential that are often referred to as "metabolites." Primary metabolites, which include protein, fatty substances, glucose, or sugar derivatives, and secondary metabolites, which include triterpenes, are the two categories of metabolites. The latter are most frequently utilized in medicine [5]. Other substances include catechins, which have been detected in trace levels, nimbins, flavonoids, and saponins. Alkaloids, limonoids, tannins, terpenoids, sterols and glycoproteins are additional compounds. [6] Anti-plasmodial, anti-trypanosomal, anti-oxidant, anti-inflammatory, anti-cancer, anti-bacterial, anti-viral, larvicidal, and fungicidal, among other biological and pharmacological properties, have been ascribed to various plant components and extracts. [7] They also have anti-implantation, immunomodulating, molluscicidal, nematocidal, immune-contraceptive, insecticidal, anti-feedant, spermicidal, ant-helminthic, anti-diabetic, anti-ulcer, and insect repellent properties. [8] Neem is recognized to have anti-malarial properties due to its anti-plasmodial action. Additionally, it is used to treat conditions like cancer, gastro intestinal, diabetes, atherosclerosis, leprosy, smallpox, infections, hair problems, urinary tract illnesses, and hypertension. [9] Neem has also been a part of many medical items from ancient times. Neem extracts are now a necessary ingredient in toothpaste, but neem twigs were once used to clean teeth. It has been known since 1803 that this plant can help ward off fever and mosquitoes. It is

currently a component of goods such as moisturizers, astringents, night creams, body and hand lotions, cream cleansers, hair shampoos, and conditioners. The leaves of neem plants are used to treat chicken pox, and the oil that is collected from the seeds is used in medications, cosmetics, and pest control products.[10]

1.1 Plant profile



Figure 1: leaves, flower, fruit and bark of neem tree.

1.2 Scientific Names [11][12]

Botanical name	Azadirachta Indica
Domain	Eukaryote
Kingdom	Plant
Subkingdom	Vascular Plant
Division	Mangoliophyta
Class	Magnoliopsida
Subclass	Asteridea
Suborder	Rutales
Order	Rutales
Family	Mahogany
Subfamily	Melioideae
Tribe	Melieae
Genus	Azadirachta
Species	Indica

1.3 Vernacular Names[14][15][16]

Ayurveda	Arishta, Arishtaphala, Nimba, Nimbaka, Pichumarda, Tiktaka
Bengali	Nim, Nimb
Canarese	Bevu, Bemu, Bevina, Nimba
Deccan	Nim
English	Indian Lilac, Margosa tree
French	Lilas de chine, Azadirac de l'Inde
German	Gemeiner, Zedrach,
Hindi	Balnimb, Nimb, Nim, Ninb, Nimgachh,
Malayalam	Arytikta, Aryaveppu, Veppu, Vepa,

Marathi	Balantanimba, Limbachajhada, Limba, Nimbay
Punjab	Bakam, Nim, Drekh, Bukhain
Tamil	Arulundi, Vembu, Vepa, Veppan, Veppu, Vempu
Telugu	Nimbamu, Vepa, Yapa, Vemu
Urdu	Neem

1.4 Geographical Description [17]

Azadirachta indica is a tropical evergreen with a wide range of uses, commonly referred to as the Indian lilac or neem tree. The tree, which is indigenous to India and Burma, has been introduced to South America, Africa, the Middle East, and Australia. Originally from tropical and semitropical areas, Azadirachta indica was domesticated in Asia. The drought-tolerant neem tree, which thrives in sandy, well-drained soil, is now common throughout India and Indonesia.

1.5 Botanical Description [2][18][19][20]

Neem grows up to 20–23 m tall and trunk is straight and has a diameter around 4-5 ft. The leaves are compound, imparipinnate, with each comprising 5–15 leaflets. Its fruits are green in color which turns golden yellow on ripening in the months of June–August.

Tree: The neem tree (*Azadirachta indica*) is a tropical evergreen that branches off from mahogany and grows up to twenty feet in three years. It grows well in regions that receive as little as 18 inches of annual rainfall and flourishes in hot climates of up to 120 degrees Fahrenheit. It has been said that they can live up to 200 years.

Leaves: Slightly yellowish-green, compound, alternating, rachis 15–25 cm long, 0.1 cm thick; acute, opposite, lanceolate, exstipulate, serrate, leaflets with oblique bases, 7–8.5 cm long and 1.0–1.7 cm wide, with an indistinct odor and a harsh taste.

Stem bark: The outside of the bark is cracked, rough, and rusty-grey; the inside is laminated, foliaceous, yellowish, fibrous and fractured. the smell is distinctive; and the taste is bitter. The thickness of the bark varies greatly depending on the age.

Flower, fruits, and seeds: In early July, the tree is frequently blanketed in sweet-looking blossoms. Usually drooping panicles up to 25 cm long, the fragrant and white blooms are arranged axillary. Its olive-sized fruit that is semi-sweet. There is a lot of oil in the seed, which has amazing medicinal and botanical qualities. Using a juicer to press the kernels makes it simple to extract the oil.

1.6 Traditional uses of the azadirachta indica plant

Unani, Siddha, and Ayurveda: regarded as a foundational herb. The tree's leaves, bark, roots, blossoms, seeds, oil, and gum are all used. In Ayurveda, it is categorized according to qualities like Sheet Virya (cooling potency) and Tikta (bitter). [21]

In India: Neem leaves are traditionally put in bunches at entrances to ward off illnesses, chicken pox and bad luck. Internally administered leaf or bark decoctions are used as an antipyretic and have long been used to treat malaria. External treatments for ringworm, psoriasis, eczema, acne, scabies, and leprosy sometimes involve the use of leaf paste, oil, or bark decoctions. [22][23][24][25]

Unani : The best blood-purifying drugs are said to be the root's leaves and bark. There are skin conditions, fever, malaria, and general health tonics that are frequently based on locally modified Ayurvedic or traditional Chinese medicine concepts. [26][27]

Burma: In addition to producing neem oil, which is sold locally for the production of soap and candles, the factory uses neem to control peanut and vegetable pests.[27]

Indonesia : It has recently been discovered that seeds with a high concentration of active chemicals are incredibly efficient against insects. In conventional agricultural systems, its application as a biopesticide is acknowledged and occasionally used. [28][29]

Malaysia : Neem leaves are used to treat fungal infection, , rashes, wounds, and infections and chewing sticks are widely used for oral hygiene [30]

Africa : Known locally as "Dogonyaro" (Nigeria) or by similar names, leaves and bark are widely used in several African nations to treat fever and malaria symptoms , taken as a general health tonic. In Africa, this is among the most common applications.[31]

2. Chemical constituents of *Azadirachta indica*

More than 300 different phytochemicals have been found in *Azadirachta indica*. Plant components differ greatly in concentration and distribution. Neem contains a variety of ingredients in different plant portions, including nimbosterol, quercetin, azadirachtin, and many liminoids. A variety of chemicals, including as nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol, and other amino acids, as well as nimbolin and a number of other components, are found in leaves. [32]

2.2 Major Chemical constituents in different part of *Azadirachta indica* [33]

Leaf	nimbosterol, Quercetin, nimbin, nimbolin
Bark	Nimbidin, nimbosterol, margosine, nimbin.
Flower	Nimbosterol, melicitrin, gallic acid, kaempferol,
Seed	Azadirachtin, azadiradione, vepinin, nimbin, fraxinellone, vilasinin,

2.3 Biological Activity and Neem compound [34]

Anti-inflammatory	Nimbidin, sodium nimbidate, gallic acid, catechin, polysachharides
Antipyretic, diuretic, anti-gastric ulcer, , hypoglycemic	Nimbidin
Antifungal	Nimbidin, gedunin, cyclic trisulfide
Antibacterial	Nimbidin, margolone, margolonone, isomargolonone, nimbolide, mahmoodin
Spermicidal	Nimbin, nimbidin
Anti-malarial	Nimbolidfe, gedunin, azadirachtin
Antitumor	Polysaccharides
Immunomodulatory	NB-II peptoglycan, gallic acid, epicatechin, catechin,

2.4 Structure of chemical constituents:

1. Nimbolin [C₃₉H₄₆O₈]

One of the main limonoid components of *Azadirachta indica*, or neem, is nimbolide. It has been observed that nimbolide has strong antiproliferative effects on a variety of cancer cell lines. By modifying kinase-driven oncogenic signaling networks, nimbolide inhibits the development of cancer hallmarks like inflammation, invasion, angiogenesis, metastasis, prolonged proliferation, and apoptosis evasion.[35] Nimbolide also showed antifibrotic and anti-inflammatory properties by significantly causing the regression of pre-existing inflammation-driven fibrosis. The ability of nimbolide to reduce the amounts of LOXL2, a collagen cross-linker that is aberrantly produced in scleroderma, is another noteworthy discovery of this study. For the first time, study shows that nimbolide is a strong antifibrotic drug that can be employed as a pharmaceutical intervention for the treatment of scleroderma, even though more mechanistic research is needed. [36]

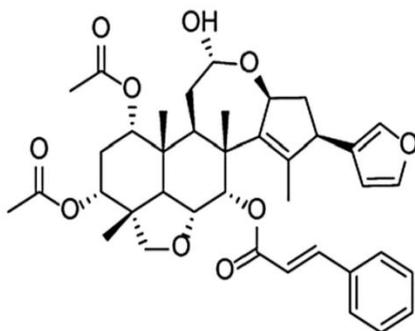


Fig. 2 Nimbolin

2. Nimbin [C₃₉H₄₆O₈]

The primary limonoid found in neem, or *Azadirachta indica*, is nimbin. The bitter components of neem and neem oil contain these additional important triterpenoids. Significant anti-inflammatory action has been shown by nimbin, which in certain trials is on par with common medications like phenylbutazone. *Azadirachta indica* bark extract's (NBE) antiviral effectiveness against m-CoV-RSA59 and SARS-CoV-2 infections was evaluated. [37] Additionally, nimbidin exhibits anti-arthritic and anti-inflammatory qualities, reduces fever, lowers blood sugar, and has antihistaminic properties. Nimbidin's broad-spectrum antibacterial action against a variety of Gram-positive and Gram-negative bacteria, as well as its antifungal qualities, make it especially noteworthy. [21]

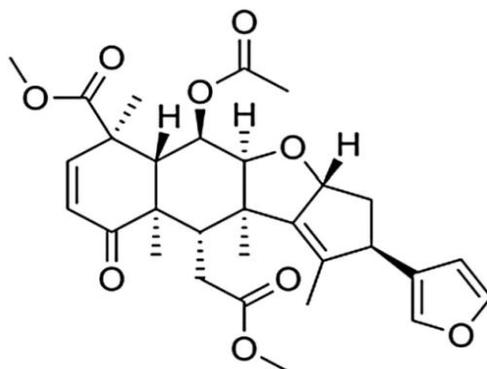


Fig. 3 Nimbin

3. Azadiradione [C₃₀H₃₆O₉]

Azadiradione (AZD), a bioactive agent isolated from *Azadiractaindica*. This neem chemical, which is mostly present in seeds, is the most researched and important from a commercial standpoint and give anti-nociceptive and anti-inflammatory activities. [38] It also exhibits activity against some bacteria, fungi, and nematodes, however this is frequently less noticeable than its insecticidal effects. [39]

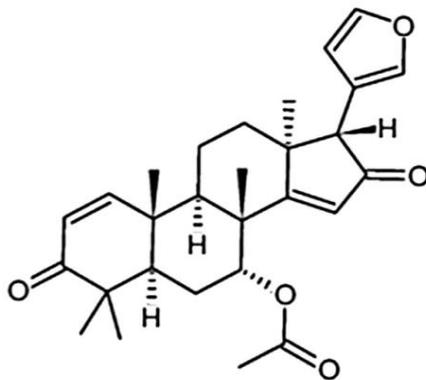


Fig.4 Azadiradione

4. Quercetin [C₁₅H₁₀O₇]

Quercetin, along with other flavonoids like kaempferol and myricetin, has been identified in various parts of the Neem like leaves, bark, flower, seeds. quercetin, a valuable bioactive flavonoid that plays a major role in its antibacterial, anti-inflammatory, antidiabetic, antioxidant, and anticancer effects. [40]

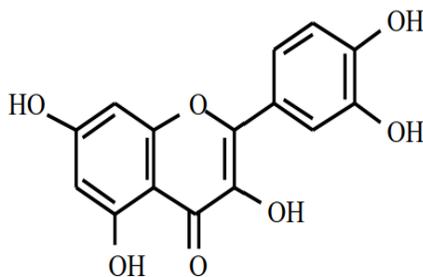


Fig.5 Quercetin

3. Pharmacological activity of *Azadirachta indica*



Fig. 6 Activity of *Azadirachta indica*

1. Anti-Inflammatory activity: Numerous plant extracts include phytochemicals that reduce inflammation. Neem extracts derived from various sections have anti-inflammatory properties. Azadiradione, a phytochemical, and the fruit peel of *A. indica* are excellent anti-inflammatory drugs. [41]

2. Anti-microbial activity: Neem has 35 biologically active chemicals, which give it strong antimicrobial properties. People in India used to keep neem leaves on their beds, books, and cabinets to keep bugs away. Neem juice from the leaves and twigs are also used for a tonic and to clean teeth. The neem tree's fruits and bark have yielded several strong medicinal substances, including triterpenoids and limnoods. Neem extracts and their various components are crucial in inhibiting a variety of microorganisms, including bacteria, fungus, and viruses. [42] The antibacterial properties of *Azadirachta indica*'s methanol and hexane chloroform extracts were tested against *Escherichia coli*, *Klebsiella pneumonia*, *Proteus vulgaris*, *Bacillus subtilis*, *Streptococcus faecalis*, *Micrococcus luteus* and *Enterococcus faecalis*. Hexane extracts shown minimal antibacterial action, chloroform was found to be moderately effective, and methanol extract was found to be the most effective. [43]

3. Anti-cancer activity: The flavonoid found in neem plants exhibits anti-cancer cell proliferation properties. A high flavonoid intake may reduce the possibility of cancer. [44] *A. indica* oil contains limonoids that are effective against 7, 12 Dimethylbenz (a) anthracene's mutagenesis effects. [45]

4. Anti-Hypolipidemic activity: *Azadirachta indica* leaf extract showed strong hypolipidemic effects. After four weeks of anthergenic diet, the impact of leaf extract on serum and liver lipid parameters specifically, cholesterol, total lipids, phospholipids, and triglycerides—was investigated in rats. [46]

5. Anti-plasmodial activity: The aqueous leaf extract of *Azadirachta indica* showed strong antiplasmodial effects in *Plasmodium berghei*-infected BALB/c mice, with notable activity observed at doses of 50 mg/kg and 100 mg/kg compared to the untreated control group. [47]

6. Anti-hypertensive activity: Co-treatment with an aqueous extract of *Azadirachta indica* (neem) and deoxycorticosterone acetate (DOCA) salt was found to effectively inhibit the onset of hypertension in experimental rat models. This suggests a potential antihypertensive role for neem in salt-induced hypertension. [48]

7. Anti-oxidant activity: Extracts from young flowers and leaves of neem demonstrated strong antioxidant activity, significantly lowering malondialdehyde (MDA) levels by 46.0% and 50.6%, respectively—an indication of reduced oxidative stress—supporting its recommendation as a bitter vegetable tonic for enhancing overall health. [49]

8. Anti-diabetic activity: Neem leaf extract contains alkaloids that aid in the regeneration of the pancreatic islets and the restoration of insulin secretion. It was also shown that saponins and tannins had hypoglycemic properties. Because they significantly reduces diastolic blood pressure and blood sugar, the terpenoids in the plants are very heart-healthy. In order to treat peripheral neuropathy, anthraquinones are commonly utilized because they have been demonstrated to lower blood glucose levels. The study found that feeding different doses of aqueous neem leaf extract at specific times (25, 48.4, 93.5, 180.9, and 350 mg/kg) to diabetic mice (alloxan-induced) decreases their blood glucose levels. The plant extract was comparable to glibenclamide, the standard drug, in both procedures and at all dosages. [50]

9. Anti-ulcer activity: One of the most prevalent acute stomach lesions is stress-induced ulceration. In this regard, we have looked into how Neem crude extract affects stomach ulcers brought on by stress. To create stress, mice were driven to undergo a forced swim test. After that, they received different dosages of crude extract of Neem (E25, E50, and E75 mg per kg, b.w.). [51]

10. Anti-fertility activity: The findings indicate that testosterone concentration is impacted by neem leaf extract. Testosterone levels decreased in male rats that received daily intraperitoneal dosages of neem leaf at 50, 100, and 150 mg/kg of weight of body for 15 days. The findings also demonstrated that the extract from neem leaves had an impact on FSH levels. FSH levels decreased when male rats were given neem leaf extract daily for 15 days at doses of 50, 100, and 150 mg/kg of body weight. [52] Furthermore, male rats administered 200 mg/kg body weight of neem leaf extract for 28 days similarly had a drop in testosterone levels. According to other research, neem leaf extracts consumption results in histological alterations in the anterior pituitary and a drop in luteinizing hormone (LH) levels. [53]

11. Neuroprotective activity: There were different levels of central nervous system (CNS) depressing activity in mice when the leaf extract was administered. Leaf acetone extract fractions exhibited strong central nervous system depressive effects. In rats, a dose of 200 mg/kg body weight of leaf extract results in notable anxiolytic action. [54]

Conclusion

In conclusion, *Azadirachta indica*, commonly known as the Neem, demonstrates significant pharmacological potential due to its diverse bioactive compounds. Research indicates that extracts from various parts of the plant exhibit promising activities, including anti-microbial, anti-fungal, anti-viral, anti-gastric-ulcer, anti-pyretic, anti-arthritic anti-inflammatory and anti-cancer properties. Additionally, *Azadirachta indica* has shown efficacy in managing various diseases, such as anti-feedant, spermicidal, ant-helminthic, cancer, diabetes, hypertension, and microbial infections. Further studies are warranted to elucidate the mechanisms of action of its bioactive components and to explore its potential therapeutic applications in clinical settings.

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