



**IN-DEPTH REVIEW ON TAXONOMY, PHYTOCHEMISTRY, TRADITIONAL USES  
AND PHARMACOLOGICAL SIGNIFICANCE OF AZADIRACHTA INDICA PLANT**

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**ABSTRACT**

Azadirachta indica, or neem, is a plant whose therapeutic virtues have made it popular around the world in recent years. Neem is a contemporary medical marvel that has been utilized widely in Ayurvedic, Unani, and Homoeopathic treatment. Neem is a lovely evergreen tree with wide leaves that may reach heights of 30 meters and widths of 2.5 meters. Its normally straight trunk has a diameter of 30 to 80 cm. Its outspread branches create a circular crown with up to 20 meters wide deep green foliage and fragrant honey blooms. Azadirachtin is a common starting point for the synthesis of biopesticides, but it also has additional qualities that have been identified, the most notable of which are its antimalarial and anticancer effects. There are several different techniques for extracting azadirachtin, such as solvent extraction at high or low temperatures and solid-liquid extraction. Alcohol-based solvents are favored for isolating azadirachtin from plant components because they are linked to greater extraction yields. Extracts must usually be cleaned up before they can be further purified. Neem seeds have yielded the greatest quantities of azadirachtin; nonetheless, there is a significant fluctuation in concentration values across batches. Therefore, regular techniques for azadirachtin identification and quantification must be established in addition to extraction processes. This study aims to discuss the pharmacological relevance, phytochemistry, taxonomy, and traditional usage of the Azadirachta indica species.

**KEYWORDS:** Epicatechin, Anti-oxidant, Azadirachta indica, Anticarcinogenic, Anti-diabetic.

**INTRODUCTION**

Neem, or Azadirachta indica, is a plant that belongs to the Meliaceae family and has long been used for its therapeutic qualities. The tree is native to tropical and semitropical regions of the world, and its many parts—seeds, leaves, flowers, and bark—are widely utilized for a variety of uses. From the various plant sections, many phytochemicals, including quercetin and azadirachtin, and liminoids, including nimbin, nimbinin, and nimbidin, have been purified. Additionally, a variety of substances

like nimbanene, 6desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, nhexacosanol, nimbiol, and numerous other kinds of chemicals are present in the leaves.<sup>[1,3]</sup> Since ancient times, neem tree extracts have been widely utilized in health management due to its numerous health-promoting qualities.<sup>[4]</sup>

The neem tree is residence to Sithala, the goddess of chicken pox, according to Hindu mythology. Drinking neem tea helps lower fever and headaches. Intestinal

issues are treated using its flowers. Neem bark has analgesic properties and helps treat malaria-related high fever. Neem leaves can also be used to treat skin conditions. India has a strong belief that neem is a universally effective medicine (Biswas et al., 2002).<sup>[5]</sup> Herbs such as harida (*Currucuma longa*), amrita (*Tinospora cordifolia*), punarnava (*Boerhavia diffusa*), neem (*Azadirachta indica*), and tulsi (*Oscimum sanctum*) work as natural anti-microbial agents and may be employed in combination to treat anthrax in animals.<sup>[6]</sup> Centre for Traditional Medicine and Research (CTMR), Chennai, India revealed the medicinal uses of different parts viz., fruits, seeds, leaves, roots, bark etc., of neem trees.

Previous research has shown that neem leaf crude extract has strong hypoglycemia and hypolipemic properties in

addition to hepatoprotective and hypertensive properties. Through the activation and inactivation of distinct cell signaling pathways, the various sections of the tree and the derived oils demonstrate a function in the control of tumors. In 7,12-dimethylbenz (a) anthracene (DMBA)-induced cancer cells, ethanolic neem leaf extract (NLE) has been shown to inhibit Bcl-2 and mutant p53 expression while increasing the activity of proapoptotic genes such as caspase 3 and caspase 8.<sup>[7,8]</sup>

#### SYNONYMS<sup>[9]</sup>

- *Azadirachta indica* var. *minor* Valetton
- *Azadirachta indica* var. *siamensis* Valetton
- *Azadirachta indica* subsp. *vartakii* Kothari, Londhe & N.P. Singh
- *Melia azadirachta* L.
- *Melia indica* (A. Juss.) Brandis.

#### VERNACULAR NAMES<sup>[10,11]</sup>

Hindi	Nim, Nimb, Nimgachh, Balnimb, Ninb
English	Margosa tree, Indian Lilac
Sanskrit	Arishta, Ravipriya, Vranashodhakari, Nimba, Prabhadra, Arkapadapa, hhardana, Kitaka, Malaka, Shita, Subhadra, Yavaneshta
Urdu	Neem
Tamil	Vepa, Veppu, Vembu, Veppan, Arulundi, Vempu
Telgu	Vepa, Kondavepa, Turakavepa, Nimbamu, Vemu, Yapa
Punjab	Bakam, Nim, Bukhain, Drekh, Mahanim
Bengali	Nim, Nimb, Nimgachh
Burma	Tamabin, Ta-mar bin, Kamakha, Bawtamaka, Kamaka, Thamaka, Thin, Thinborotamakha
French	Lilas de chine, Margosier
Gujrati	Limba, Danujhada, Kohumba, Limbado, Limbra
Malayalam	<i>Nimbam, Rajaveppu</i>
German	Grossblaettiger, Zedrach

#### TAXONOMICAL CLASSIFICATION<sup>[12]</sup>

<b>Kingdom</b>	<b>Plantae</b>
Order	Rutales
Suborder	Rutinae
Family	Meliaceae
Subfamily	Melioideae
Tribe	Melieae
Genus	<i>Azadirachta</i>
Species	<i>Indica</i>

#### MACROSCOPICAL CHARACTERISTICS<sup>[13,17]</sup>

##### 1. Leaves

- i. They are imparipinnate, alternate, exstipulate, 3-6 cm long on long slender petioles; leaflets 7-17; alternate or opposite, very shortly stalked, 1-1.5 cm long.
- ii. Apex: ovate-lanceolate, attenuate
- iii. Base: Unequal
- iv. Colour: Smooth and dark green.
- v. Odour: typical.
- vi. Taste: Bitter.

##### 2. Fruits

- i. Shape: Ovoid, bluntly pointed, smooth drupe.

- ii. Colour: Green (Young and unripe); Yellow to brown (Mature and ripe).
- iii. Very scanty pulp and hard bony endocarp.
- iv. Solitary with a thick Testa and embryo with foliaceous cotyledons in the axis of scanty endocarp.

##### 3. Seed Oil

- i. Colour: Yellow to brown.
- ii. Taste: Bitter.
- iii. Odour: Garlic.

**MICROSCOPIC CHARACTERISTICS<sup>[18,19]</sup>****4.1. Leaf Midrib**

4-5 layer of collenchyma present below the pidermis. Parenchymatous cells consist of rosette crystals of calcium oxalate. Non lignified fibre strand surrounded the phloem.

**4.2. Lamina**

Lamina typically consist of thin walls with a dorsiventral structure and an epidermal layer on both sides of the surface. Neem (*Azadirachta indica*) has anomocytic stomata on its lower surface. The stomatal index is 13.0-14.5 on the bottom surface and 8.0-11.5 on the top surface.

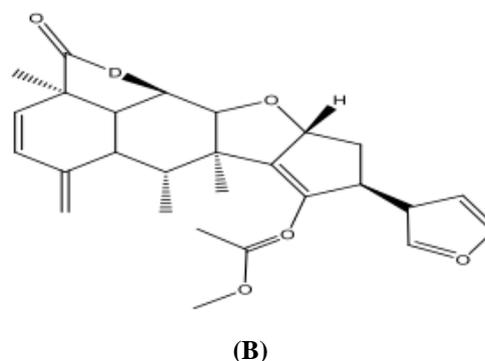
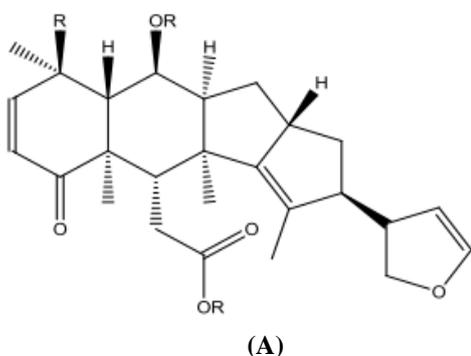
**GEOGRAPHICAL DISTRIBUTION**

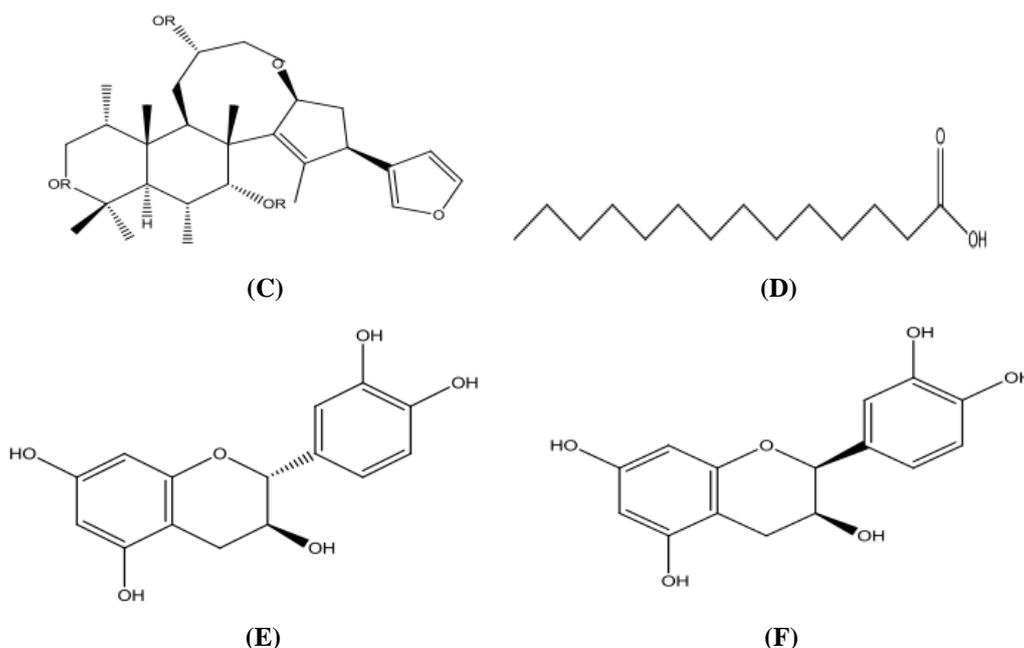
The *Azadirachta indica* tree grows in the Swalik Hills. It is mostly grown in Tamil Nadu, Andhra Pradesh, and Karnataka's arid forests.<sup>[20]</sup> Neem, or *Azadirachta Indica*, is a tree that grows wild in the Irawali valley and is farmed west of the Sutlej. *Azadirachta A. Juss.*, which is

found in the Indian subcontinent, and *Azadirachta excels*, which is found in the Phillipines and Indonesia, are the two species of *Azadirachta*. About 25 million trees have been planted throughout India, with 5.5% of those trees being grown in Karnataka. This places the state in third place, behind Tamilnadu in first place and Karnataka U.P. in second place with 55.7% and 17.8% of neem growth, respectively. The following states in India, together with the Andaman and Nicobar islands, have neem trees: Andhra Pradesh, Delhi, Assam, Gujarat, Haryana, Kerala, Himachal Pradesh, Madhya Pradesh, Meghalaya, Maharashtra, Orissa, Punjab, West Bengal.<sup>[21]</sup> India is the world leader in the production of neem seeds, with an annual production of over 4,42,300 tons. The tree has been discovered in no fewer than 78 nations throughout the globe. It is estimated that 16.6 million neem trees are planted in India. According to current research, neem trees are cultivated in around 72 nations across the globe, as well as in continents such as Africa, Asia, Australia, Central America, and South America.<sup>[16]</sup>

**PHYTOCHEMICAL PROFILE**

Part	Constituent
Leaves <sup>[22]</sup>	i. Nimbin, 6- desacetylnimbinene. ii. Nimbinene, Nimbandiol, nimbolide. iii. Quercetin, $\beta$ -sitosterol. iv. Ascorbic acid, n-hexacosanol, nonacosane and amino acid.
Fruits <sup>[9]</sup>	i. Gedunin. ii. 7-deacetoxy-7 $\alpha$ - hydroxygedunin. iii. Azadiredione, azadirone, nimbiol. iv. 17-epiazadiradione.
Seeds <sup>[23]</sup>	i. Tetranortriterpenoids; 1, 2-diepoxyazadiradione. ii. 7-acetylneotrichilenone, 7-desacetyl-7-benzoylgedunin iii. Azadirachtin.
4. Oils <sup>[24]</sup>	i. Fatty acid:- Myristic acid, palmitic acid, stearic acid, oleic acid and linoleic acid. ii. Glycerides:- Oleopalmitostearin, oleodistearin, odiolein and linoleodiolein. iii. Bitter principle:- Nimbidin, nimbidinin, Nimbin, nimbinin and nimbidol. <sup>[7]</sup>





Structure (A) Nimbin (B) Nimbolide (C) Nimbilin (D) Palmitic acid (E) Catechin (F) Epicatechin.

### TRADITIONAL AND CURRENT USES

The neem tree is beneficial in almost every aspect, and its antibacterial and antifungal qualities are the basis for many of its therapeutic and cosmetic applications. Neem is frequently found in dandruff shampoos as well as in soaps and lotions for skin ailments including psoriasis, acne, and athlete's foot.<sup>[11]</sup> In rural regions, young twigs are used as simple toothbrushes, and it is also a component of various toothpastes and mouthwashes, particularly in the Indian subcontinent.<sup>[25]</sup> Traditional diabetic treatments have long used neem leaves, and some clinical research indicates that neem may help regulate blood sugar levels. Pregnant women should avoid consuming neem oil, bark, or leaves since it may result in miscarriage.<sup>[26]</sup>

The oil that is obtained from seeds is the basis for several industrial pesticide products, including as dusts, granules, and concentrates, and may be used directly as an insect and mite repellent, insecticide, and fungicide. Azadirachtin, the main active component in insecticides, functions as a feeding inhibitor and disrupts the hormones responsible for insect molting, preventing larvae from maturing into adults as intended. Neem oil reduces pest fecundity by inhibiting mating and reproductive behaviors, which can kill soft-bodied insects on contact. Neem oil is used as a fungicide to treat blight, mildew, rust, black spot, anthracnose, and scab. Neem oil degrades rapidly when exposed to UV light, thus repeated applications are frequently required. Neem-based insecticides are often used in organic farming applications because of their low toxicity to animals.<sup>[27,29]</sup>

### PHARMACOLOGICAL SIGNIFICANCE

#### 1. Antimicrobial Activity

The purpose of the study was to ascertain neem leaf extract's antibacterial effectiveness. The neem leaf alcoholic extract, which exhibits antibacterial activity in comparison to a gentamycin standard. The highest level of inhibition on *Bacillus pumillus*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* is demonstrated by the neem alcoholic extract. Neem extract activity was also discovered to be beneficial in preventing the growth of the carcinogenic bacteria *S. sobrinus*.<sup>[30,31]</sup>

#### 2. Anticarcinogenic Activity

Reduced incidence of neoplasm is evidence that neem leaf aqueous extract efficiently inhibits oral squamous cell carcinoma produced by 7, 12-dimethylbenz [a] anthracene (DMBA).<sup>[32]</sup> The chemopreventive action of neem on the oral mucosa may be mediated through the regulation of glutathione and the enzymes that metabolize it. It has also been shown that neem leaf extract protects against oxidative stress caused by N-methyl-N<sup>o</sup>-nitro-N-nitrosoguanidine (MNNG), a carcinogenic material, by reducing the production of lipid peroxides and raising antioxidant and detoxifying enzyme levels in the stomach, which is the main organ for MNNG, as well as in the liver and blood.<sup>[33]</sup>

#### 3. Anti-Diabetic Activity

The medication is administered for 21 days using an aqueous methanol extract of *B. spectabilis* and an *Azadirachta indica* chloroform extract. Its ability to bring fasting glucose levels back to normal suggests that it has antihyperglycemic properties.<sup>[34]</sup>

#### 4. Analgesic and Antipyretic Activity

Rats were given an aqueous neem leaf extract (400 mg/kg body weight) one hour before to the

intraperitoneal injection of formalin and once daily for seven days to compare its anti-inflammatory effects with that of dexamethasone (0.75 mg).<sup>[35]</sup> After 3, 6 hours, on day 3, 7 after formalin injection, the percentage of inhibition of paw edema in the case of neem was 28, 40, 45, and 58%, respectively, while in the case of dexamethasone, the percentage was 43, 58, 61, 65%. In every instance, the decrease was statistically significant ( $p < 0.001$ ). The results of this study indicate that dexamethasone has a greater anti-inflammatory impact than neem extract.<sup>[36]</sup>

### 5. Antimalarial Activity

Research has revealed that neem has antimalarial properties. The effects of neem seed extracts on the human malaria parasite *Plasmodium falciparum* were examined, and the findings were quite noteworthy.<sup>[37]</sup> The fact that neem constituents impacted parasites that had previously been discovered to be resistant to traditional antimalarial drugs (chloroquine, pyrimethamine) and had an anti-plasmodial effect is noteworthy; this suggests a different mode of action.<sup>27</sup> As a result, the neem seed fractions work against parasite stages that cause the clinical presentation as well as those that carry on spreading malaria. The limonoids were extracted from fresh neem leaves and shown to have antimalarial properties against the strain of *P. falciparum* that is resistant to chloroquine.<sup>[38]</sup>

### 6. Wound-healing Activity

The traditional medicine has long recognized the ability of neem leaves to heal wounds. In one study, the benefits of neem oil on chronic, nonhealing wounds were investigated. The findings revealed that, after 8 weeks of therapy, almost 44% of patients had 50% wound healing.<sup>[39]</sup> A notable decrease in the largest diameter wounds was noted in a different study that examined the wound-healing properties of neem leaf aqueous extract.<sup>[17]</sup> According to research, neem leaf aqueous extracts' ability to heal wounds is thought to function biochemically through neovascularization and an inflammatory response.<sup>[39]</sup>

### 7. Anti-inflammatory Activity

The purpose of the study was to examine the anti-inflammatory properties of lawsonia inner mis (henna) and azadirachta indica individual extracts in vitro while utilizing the same solvent in combination.<sup>[13]</sup> When compared to diclofenac sodium, the ethanolic extract of *Azadirachta indica* has anti-inflammatory properties. Diclofenac sodium at 50, 100, and 200  $\mu\text{g/ml}$  inhibits protein denaturation in percentage terms as well as in terms of membrane stabilizing ethanolic extract. It prevents 57.3% of protein denaturation and exhibits 46.62% membrane stabilization. At a concentration of 200  $\mu\text{g/ml}$ , the ethanolic extract of henna exhibits 53.75% inhibition of protein denaturation and 39.89% protection membrane stabilization; at concentrations higher than 200  $\mu\text{g/ml}$ , membrane stabilization increases and protein denaturation decreases.

The ethanolic extract of henna and neem when combine for study of anti-inflammatory activity it shows at the concentration of 200  $\mu\text{g/ml}$  it shows increase in the anti-inflammatory activity.<sup>[40]</sup>

### 8. Hepatoprotective Activity

Administering aqueous neem leaf extract was shown to be beneficial for rats whose liver necrosis was caused by paracetamol. The elevated levels of blood aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transpeptidase (GGT) indicative of liver damage were found to be significantly reduced with administration of the neem leaf aqueous extract.<sup>[41]</sup>

### 9. Antioxidant Activity

The leaves, bark, roots, seeds, and flowers of neem trees all play a function in managing illness by regulating different biological activity. An analysis of the antioxidant activity of many extracts made from different neem tree sections was done. The findings imply that leaf, flower, and stem bark extracts have strong antioxidant properties.<sup>[11]</sup> It was also discovered in another investigation that ethanolic extracts of flowers and seed oil had superior free radical scavenging capabilities.<sup>[42]</sup>

### 10. Anti-ulcer Activity

Rats administered either ethanol or cold stress for two hours were used to test the antiulcer properties of neem tree leaf aqueous extracts. The extracts were given as single- or five-dose pretreatment regimens at 10, 40, or 160 mg leaf/kg body weight. Neem lowered ethanol-induced stomach mucosal damage and, in rats exposed to stress, the severity of gastric ulcers in a dose-dependent manner.<sup>[43,45]</sup>

### 11. Anti-Dental Caries Activity

Comparing a Neem extract dental gel to a control group that used commercial mouthwash containing the germicidal Chlorhex-idin gluconate (0.2%)w/v, the dental gel dramatically reduced plaque and bacteria (including strainococcus mutations) and *Lactobacilli* species.<sup>[46,9,47]</sup>

### 12. Insecticidal Activity

In Sudan, the seeds of *Azadirachta indica* exhibit noteworthy results as an insecticide when applied at the ideal dosage for vegetable pest management. Neem seeds are used to extract oil, which may be stored at room temperature. The oil is also used to combat test insects, such as *Trogloclerma granarium* larvae, and the results indicate that the oil is effective against these insects.<sup>[48]</sup>

### 13. Anti -Stress Activity

Small amounts of neem leaf extract have a calming effect that lowers tension and anxiety.<sup>[49]</sup>

### 14. Hypolipidemic Activity

*Azadirachta indica* leaf extract had notable hypolipidemic effects. Rats given an anti-herogenic diet

for four weeks were used to study the impact of leaf extract on blood and liver lipid markers, such as cholesterol, total lipids, phospholipids, and triglycerides.<sup>[50]</sup>

### 15. Neuroprotective Activity

In animal models, standardized neem extract has also been shown to exhibit neuroprotective properties. Allodynia, hyperalgesia, motor coordination, and motor nerve conduction velocity were decreased in the peripheral neuropathy animal models, however these behavioral alterations were greatly mitigated by continuous administration of this extract. Furthermore, in animal models, the neem extract dramatically decreased the amplified effects of oxidative and nitrosative stress, inflammatory mediators, and mRNA expression of Bax and iNOS.<sup>[51]</sup>

### 16. Anti -Vitiligo Activity

It is thought that vitiligo is an auto immune condition that results in color loss in some skin areas. the dosage of four grams of neem leaves, preferably eaten before each meal, three times a day. Applying neem oil to the afflicted regions helps to reverse the discoloration.<sup>[52]</sup>

### 17. Cardioprotective effect

Neem tree extract is widely known for its cardioprotective qualities as a folk remedy. To that end, most hemodynamic, biochemical, and histological parameters are markedly restored by *A. indica* extract administered at a dosage of 250–1000 mg/kg. The study also found that, in comparison to vitamin E, neem extract has equipotent cardioprotective properties.<sup>[53]</sup>

### 18. Diuretic Activity

The crude ethanolic extract from the root and stem bark demonstrated diuretic, spasmolytic, and hypotensive effects. Sodium nimbinate, the chemical component, has been found to be a potent diuretic in dogs. The main focus of the medication was the renal tubules, where it caused the reabsorption of water and electrolytes by delaying the excretion of phenolsulfonphthalein. It was shown that an increased oral dose had effective results. A clinical trial was conducted on nine patients with anasarca and congestive heart failure to investigate the diuretic effects of sodium nimbinate. Of these, eight individuals clearly responded with diuretics.<sup>[54]</sup>

### 19. Antifertility potential

An investigation of the effects of neem flower alcohol extract on the estrous cycle, ovulation, fertility, and fetal morphology was conducted using rat models. The study's findings unequivocally demonstrated that 80% of the rats' altered estrous cycles included a noticeably longer diestrus phase. In the morning of estrus, this extract reduced the quantity of ova shedding in a statistically significant way. In addition, neem oil administered intravenously blocked spermatogenesis without influencing the generation of testosterone.<sup>[55,56]</sup>

## CONCLUSION

One of the most significant sources of medicinal materials is plants. From ancient times to the present, medicinal plants have been extensively studied for their potential to improve human health and enable individuals to deal with challenging and uncomfortable circumstances. The fight against the occurrence of infectious diseases like malaria, HIV/AIDS, and chronic illnesses like cancer, cardiovascular disease, and age-related degenerative diseases is one of the main objectives of the Millennium Development Goals (MDGs). Secondary metabolites, which are valuable for therapeutic purposes and may be used as drug candidates, are abundant in medicinal plants. The use of plant extracts as medicinal agents is gaining popularity.

Neem, or *Azadirachta indica*, has been used for a variety of purposes since ancient times. Numerous phytochemical, experimental, and clinical studies have been conducted on it. Studies in the lab have shown that it has the following effects: anti-inflammatory, antileishmanial, antimalarial, antimicrobial, antinociceptive, anti-plasmodial, antipyretic, antitumor, antiulcer, antiviral, CNS depressant, hepatoprotective, hypoglycemic, hypolipidemic, larvicidal, nematicidal, and spermicidal. The majority of traditional medicine's claims have been validated by scientific research. However, in order to establish *Azadirachta indica* as a standard medicine, further thorough clinical study is important to examine the entire therapeutic potential of diverse sections of the plant.

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