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NEEM (*AZADIRACHTA INDICA*) AS A MEDICINAL PLANT: PHARMACOLOGICAL INSIGHTS AND THERAPEUTIC POTENTIAL

Dr. Kuldeep Saini[1*], Ms. Minata[2], Dr. Arvind Kumar[3], Mr. Anurag Kumar[4], Mr. Zuber Ahamad[5], Himanshu Goyal[6]

[1]Associate Professor, Department of Pharmaceutical Chemistry, S.D. College of Pharmacy and Vocational Studies, Muzaffarnagar, 251001, Uttar Pradesh, India.
[2]Assistant Professor, Department of Pharmaceutics, S.D. College of Pharmacy and Vocational Studies, Muzaffarnagar, 251001, Uttar Pradesh, India.
[3]Professor, Department of Pharmaceutical Chemistry, S.D. College of Pharmacy and Vocational Studies, Muzaffarnagar, 251001, Uttar Pradesh, India.
[4]Assistant Professor, Department of Pharmaceutical Chemistry, S.D. College of Pharmacy and Vocational Studies, Muzaffarnagar, 251001, Uttar Pradesh, India.
[5]Assistant Professor, Department of Pharmaceutics, S.D. College of Pharmacy and Vocational Studies, Muzaffarnagar, 251001, Uttar Pradesh, India.
[6]Student, S.D. College of Pharmacy and Vocational Studies, Muzaffarnagar, 251001, Uttar Pradesh, India.

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***Corresponding Author**

Dr. Kuldeep Saini

Associate Professor, Department of Pharmaceutical Chemistry, S.D. College of Pharmacy and Vocational Studies, Muzaffarnagar, 251001, Uttar Pradesh, India.

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ABSTRACT

Neem (*Azadirachta indica*) is a well-known medicinal plant that has been widely used in traditional medicine for centuries. In recent years, extensive pharmacological studies have been conducted to scientifically validate its therapeutic potential. Various parts of the neem plant, including leaves, bark, seeds, and oil, contain bioactive compounds such as azadirachtin, nimbidin, nimbolide, and flavonoids, which contribute to its diverse biological activities. Experimental and preclinical studies have demonstrated that neem exhibits significant antimicrobial, anti-inflammatory, antioxidant, antidiabetic, immunomodulatory, hepatoprotective, gastroprotective, and anticancer properties. These pharmacological effects are primarily mediated through mechanisms involving inhibition of inflammatory mediators, modulation of immune responses, regulation of oxidative stress, and induction of apoptosis in abnormal cells. The present review summarizes and highlights the major pharmacological activities of *Azadirachta indica*, emphasizing its potential as a natural source for the development of safe and effective therapeutic agents.

KEYWORDS: Neem; *Azadirachta indica*; Pharmacological activities; Antimicrobial; Anti-inflammatory; Antioxidant; Medicinal plant.

INTRODUCTION

Medicinal plants have played a vital role in the development of human healthcare systems since ancient times. A large proportion of the world's population, particularly in developing countries, continues to rely on plant-based medicines for primary healthcare needs. In recent decades, there has been renewed global interest in herbal drugs due to their perceived safety, cost-effectiveness, cultural acceptability, and therapeutic efficacy. Among the numerous medicinal plants explored for pharmacological potential, neem (*Azadirachta indica* A. Juss.) occupies a prominent position due to its wide range of biological and therapeutic activities.

Neem is a fast-growing evergreen tree belonging to the family Meliaceae and is native to the Indian subcontinent. It is widely distributed in tropical and subtropical regions of Asia, Africa, and parts of the Americas. Neem has been extensively used in traditional systems of medicine such as Ayurveda, Siddha, Unani, and folk medicine for the treatment of various ailments including infections, inflammation, diabetes, skin disorders, and gastrointestinal diseases. Almost all parts of the neem tree—leaves, bark, flowers, fruits, seeds, and oil—have been reported to possess medicinal properties, making it one of the most versatile medicinal plants known.

The therapeutic importance of neem is attributed to its rich phytochemical composition. Phytochemical investigations have revealed the presence of numerous biologically active compounds such as limonoids, flavonoids, alkaloids, tannins, glycosides, and steroids. Among these, azadirachtin, nimbidin, nimbolide, salannin, and quercetin are considered major bioactive constituents responsible for neem's pharmacological actions. These compounds have been shown to exert multiple effects at the molecular and cellular levels, supporting the traditional claims of neem's medicinal value.

From a pharmacological perspective, neem has attracted considerable scientific attention due to its broad spectrum of biological activities. Experimental studies have demonstrated that neem exhibits antimicrobial activity against a wide range of pathogenic bacteria, fungi, and viruses. This antimicrobial potential is particularly important in the context of increasing resistance to conventional antibiotics. Neem extracts have been reported to inhibit microbial growth by disrupting cell membranes, inhibiting enzyme activity, and interfering with nucleic acid synthesis.

Inflammation is a key underlying factor in many chronic diseases, and neem has been extensively studied for its anti-inflammatory properties. Neem-derived compounds have been shown to suppress inflammatory mediators such as prostaglandins, nitric oxide, and cytokines. These effects contribute to its usefulness in inflammatory conditions such as arthritis, dermatitis, and wound healing. In addition, neem exhibits strong antioxidant activity, which plays a crucial role in neutralizing free radicals and reducing oxidative stress. Oxidative stress is implicated in the pathogenesis of various disorders including cancer, diabetes, cardiovascular diseases, and neurodegenerative conditions.

Neem has also demonstrated significant antidiabetic activity in preclinical studies. Extracts of neem leaves have been reported to lower blood glucose levels, improve insulin sensitivity, and protect pancreatic β-cells from oxidative damage. These findings suggest that neem may be beneficial in the management of diabetes mellitus and its associated complications. Furthermore, neem's immunomodulatory properties enable it to regulate immune responses by enhancing macrophage activity, modulating cytokine production, and improving overall immune function.

Fig. 1: Neem Plant and oil.

Composition and Natural Origin

Neem (*Azadirachta indica* A. Juss.) is a naturally occurring medicinal plant belonging to the family Meliaceae. It is indigenous to the Indian subcontinent and has been cultivated for centuries in tropical and subtropical regions due to its remarkable medicinal value. The plant is well adapted to diverse climatic conditions and is commonly found in India, Bangladesh, Sri Lanka, Southeast Asia, and parts of Africa. Neem has long been regarded as a "village pharmacy" because of the wide range of therapeutic applications associated with its various parts.

From a natural origin perspective, neem is a rich reservoir of bioactive phytochemicals. Almost every part of the plant, including leaves, bark, seeds, fruits, flowers, roots, and oil, contributes to its pharmacological potential. These plant parts contain a complex mixture of secondary metabolites that are responsible for neem's biological activities. The diversity of these compounds explains the broad spectrum of pharmacological effects observed in experimental and traditional uses.

Chemically, neem is characterized by the presence of limonoids, which are considered its most important bioactive constituents. Limonoids such as azadirachtin, nimbolide, salannin, nimbin, and nimbidin are predominantly found in neem seeds and bark. Among these, azadirachtin is one of the most extensively studied compounds and is known for its significant biological activity. Nimbidin, isolated mainly from neem seed oil, has been associated with anti-inflammatory, antimicrobial, and antioxidant effects.

Neem leaves are particularly rich in flavonoids, phenolic compounds, tannins, and glycosides. Flavonoids such as quercetin and kaempferol contribute to neem's antioxidant and anti-inflammatory properties. Phenolic compounds present in the leaves and bark play a crucial role in scavenging free radicals and protecting cells from

oxidative damage. Tannins and alkaloids further enhance the antimicrobial and astringent properties of the plant.

Neem bark contains polysaccharides, sterols, and additional limonoids that exhibit immunomodulatory and anti-inflammatory activities. The bark has traditionally been used for treating fever, pain, and inflammatory disorders, which aligns with its phytochemical composition. Neem seed oil, obtained by cold pressing or solvent extraction, is another important natural product that contains fatty acids along with bioactive limonoids, contributing to its therapeutic usefulness.

The natural origin of neem-based compounds provides a significant advantage in pharmacological applications. These compounds are biodegradable, generally exhibit low toxicity at therapeutic doses, and act through multiple biological pathways. Unlike synthetic drugs that often target a single mechanism, neem phytochemicals exert synergistic effects, enhancing their therapeutic potential while reducing the risk of adverse effects.

In summary, the pharmacological importance of neem is deeply rooted in its natural origin and rich chemical composition. The presence of diverse bioactive compounds across different parts of the plant forms the basis for its wide-ranging biological activities. This complex phytochemical profile makes *Azadirachta indica* a valuable natural source for the development of novel and effective pharmacological agents.

Table 1: Taxonomical Description of *Azadirachta indica*.

Category	Description
Kingdom	Plantae
Division/Phylum	Magnoliophyta (Angiosperms)
Class	Magnoliopsida (Dicotyledons)
Order	Sapindales
Family	Meliaceae
Genus	Azadirachta
Species	Azadirachta indica
Common Name	Neem, Indian Lilac
Plant Type	Evergreen tree
Height	15–20 m on average
Leaves	Pinnate, 20–40 cm long, leaflets 7–17, lanceolate
Flowers	Small, white, fragrant, in axillary panicles
Fruit	Drupe, ovoid, 1.5–2.5 cm, yellow when ripe
Bark	Rough, grey-brown, fissured
Habitat	Tropical and subtropical regions, well-drained soils

Different parts of neem and uses

Leaves: Neem leaves are pinnate with 7–17 leaflets. They contain compounds like nimbin, nimbidin, and azadirachtin, which give them strong antibacterial, antifungal, and antiviral properties. They are used to treat skin disorders like acne, eczema, and wounds. Fresh leaves are also used as a natural pesticide in agriculture.

Fig. 2: Leaves of Azadirachta Indica.

Bark: The neem tree has rough, greyish-brown bark containing bitter compounds that have medicinal properties. It is traditionally used to reduce fever, treat malaria, and aid digestion. The bark extract is also applied externally for skin problems.

Seeds: Neem seeds contain oil (neem oil) that is rich in azadirachtin, making it an effective insect repellent and pesticide. The oil is used in cosmetics, hair care products, and traditional medicine for its anti-inflammatory and antimicrobial effects.

Fruits/Pulp: Neem fruits are small, yellow drupes. Their pulp is sometimes used to extract oil or prepare medicinal remedies. The fruit also has pesticidal properties and is used in folk medicine.

Fig. 3: Fruits part of Azadirachta Indica.

Flowers: Small, fragrant, white flowers of neem are edible and used in certain traditional dishes. They also have medicinal properties, such as boosting immunity and aiding digestion.

Fig. 4: Flowers part of Azadirachta Indica.

Twigs: Neem twigs are often used as natural toothbrushes (called "datun") because of their antibacterial properties. They help in maintaining oral hygiene and preventing gum disease.

Fig. 5: Twigs part of Azadirachta Indica.

Pharmacological Activities of Neem (*Azadirachta indica*)

1. Antimicrobial Activity

Neem exhibits broad-spectrum antimicrobial activity against bacteria, fungi, and viruses. Extracts obtained from neem leaves, bark, seeds, and oil have shown inhibitory effects against both Gram-positive and Gram-negative bacterial strains. The antimicrobial action is mainly attributed to bioactive compounds such as nimbidin, nimbolide, azadirachtin, and quercetin. These compounds disrupt microbial cell wall integrity, interfere with protein synthesis, and inhibit essential enzymatic functions, leading to suppression of microbial growth. Neem has also demonstrated antifungal activity against dermatophytes and opportunistic fungi, making it useful in the management of skin and systemic infections.

2. Anti-inflammatory Activity

Neem possesses significant anti-inflammatory properties, which have been confirmed in several experimental

models. Neem extracts reduce inflammation by inhibiting the synthesis and release of inflammatory mediators such as prostaglandins, leukotrienes, nitric oxide, and pro-inflammatory cytokines. Nimbidin, isolated from neem seed oil, plays a major role in suppressing both acute and chronic inflammatory responses. These properties support the traditional use of neem in conditions such as arthritis, wounds, and inflammatory skin disorders.

3. Antioxidant Activity

Oxidative stress is a major contributing factor in the development of various chronic diseases. Neem demonstrates strong antioxidant activity due to the presence of flavonoids, polyphenols, and carotenoids. Neem leaf and bark extracts scavenge free radicals, inhibit lipid peroxidation, and enhance endogenous antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. By reducing oxidative damage at the cellular level, neem contributes to tissue protection and disease prevention.

4. Antidiabetic Activity

Neem has shown promising antidiabetic effects in preclinical studies. Administration of neem leaf extracts has been associated with significant reductions in blood glucose levels. The antidiabetic activity of neem is attributed to improved insulin sensitivity, enhanced glucose uptake by peripheral tissues, and protection of pancreatic β-cells from oxidative stress. Neem also helps regulate lipid metabolism, thereby reducing complications associated with diabetes mellitus.

5. Immunomodulatory Activity

Neem exhibits immunomodulatory properties by influencing both innate and adaptive immune responses. Studies have shown that neem extracts stimulate macrophage and lymphocyte activity, enhance antibody production, and regulate cytokine secretion. Neem polysaccharides and limonoids contribute to these effects by modulating immune cell signaling pathways. This immunoregulatory action makes neem potentially useful in managing immune-related disorders and infections.

6. Anticancer Activity

The anticancer potential of neem has been extensively investigated in recent years. Neem constituents such as nimbolide and azadirachtin have demonstrated the ability to inhibit tumor cell proliferation, induce programmed cell death (apoptosis), and suppress angiogenesis. These effects are mediated through the modulation of cell cycle regulators, activation of apoptotic pathways, and reduction of oxidative stress. Neem has shown activity against various cancer cell lines, suggesting its potential role as a complementary therapeutic agent.

7. Hepatoprotective Activity

Neem exhibits protective effects against liver damage caused by toxins and oxidative stress. Experimental studies have shown that neem extracts normalize liver enzyme levels and prevent histopathological changes in hepatic tissue. The hepatoprotective activity is largely attributed to antioxidant and membrane-stabilizing properties, which help preserve liver function and structure.

8. Gastroprotective Activity

Neem has demonstrated gastroprotective effects in experimental ulcer models. Neem extracts reduce gastric acid secretion, increase mucus production, and enhance mucosal defense mechanisms. Nimbidin plays a key role in protecting the gastric lining from injury caused by stress, alcohol, and non-steroidal anti-inflammatory drugs. These findings support the traditional use of neem in gastrointestinal disorders.

9. Wound Healing Activity

Neem promotes wound healing by enhancing collagen synthesis, increasing tensile strength, and reducing microbial contamination at the wound site. Its anti-inflammatory and antimicrobial properties contribute to faster tissue repair and regeneration. Neem extracts have been shown to accelerate wound contraction and epithelialization in experimental models.

10. Neuroprotective Activity

Recent studies suggest that neem possesses neuroprotective effects due to its antioxidant and anti-inflammatory properties. Neem extracts may protect neuronal cells from oxidative damage and neuroinflammation, indicating potential benefits in neurodegenerative conditions. Although further research is required, preliminary findings are promising.

11. Antiviral Activity

Neem has demonstrated antiviral activity against several enveloped and non-enveloped viruses in experimental studies. Neem leaf and bark extracts interfere with viral adsorption, penetration, and replication within host cells. Bioactive constituents such as nimbolide and flavonoids are believed to inhibit viral protein synthesis and block virus-host cell interactions. These properties support the traditional use of neem in viral infections and immune-related conditions.

12. Antimalarial Activity

Neem has been reported to possess antimalarial properties, particularly against *Plasmodium* species. Neem leaf and bark extracts have shown inhibitory effects on parasite growth in experimental models. The antimalarial activity is attributed to limonoids and quassinoid-like compounds that interfere with parasite metabolism and replication, suggesting neem as a potential source for antimalarial drug development.

13. Analgesic Activity

Neem exhibits analgesic or pain-relieving effects in various experimental pain models. The analgesic activity is closely linked to its anti-inflammatory properties, as neem suppresses the release of pain-inducing mediators

such as prostaglandins and bradykinin. These effects validate the traditional use of neem in managing pain associated with inflammation and injury.

14. Antipyretic Activity

Neem has shown significant antipyretic (fever-reducing) activity in experimental studies. Neem bark and leaf extracts reduce elevated body temperature by inhibiting the synthesis of pyrogenic substances and inflammatory mediators in the hypothalamus. This pharmacological effect supports its traditional application in febrile conditions.

15. Antifertility Activity

Neem has been studied for its antifertility and contraceptive properties. Neem seed oil and extracts have demonstrated spermicidal activity and the ability to inhibit implantation in experimental models. These effects are believed to result from hormonal modulation and direct action on reproductive cells. Due to these properties, neem has been explored as a potential natural contraceptive agent.

16. Antiulcer Activity

Neem exhibits antiulcer activity by reducing gastric acid secretion and enhancing the protective mucus layer of the stomach. Neem extracts also reduce oxidative damage and inflammation in gastric tissues. These combined actions help prevent ulcer formation and promote healing of existing ulcers.

17. Antihyperlipidemic Activity

Neem has shown lipid-lowering effects in experimental studies. Neem leaf extracts reduce total cholesterol, triglycerides, and low-density lipoprotein levels while improving high-density lipoprotein levels. This activity is associated with improved lipid metabolism and antioxidant action, suggesting potential benefits in cardiovascular health.

18. Anthelmintic Activity

Neem has demonstrated anthelmintic activity against intestinal parasites. Neem extracts impair the energy metabolism of helminths, leading to paralysis and death of the parasites. This activity supports the traditional use of neem in treating parasitic infections.

19. Antiallergic Activity

Neem exhibits antiallergic properties by inhibiting histamine release and reducing allergic inflammation. Neem extracts stabilize mast cells and suppress immune hypersensitivity reactions. These effects indicate potential usefulness in allergic disorders such as asthma and dermatitis.

20. Nephroprotective Activity

Neem has shown nephroprotective effects in experimental models of kidney damage. Neem extracts reduce oxidative stress, inflammation, and tissue injury in renal tissues. The protective effects are attributed to antioxidant and anti-inflammatory mechanisms that help preserve kidney function.

Advantages of Neem (*Azadirachta indica*)

1. **Wide Pharmacological Spectrum**
   - Exhibits antimicrobial, anti-inflammatory, antioxidant, antidiabetic, immunomodulatory, anticancer, hepatoprotective, gastroprotective, antiviral, and antimalarial activities.

2. **Natural Origin & Rich Phytochemicals**
   - Contains limonoids, flavonoids, nimbidin, nimbolide, and polyphenols.
   - Multi-target mechanisms provide synergistic therapeutic effects.

3. **Safety Profile**
   - Generally safe at therapeutic doses.
   - Biodegradable and environmentally friendly.

4. **Cost-Effective & Accessible**
   - Widely available in tropical and subtropical regions.
   - Supports sustainable herbal medicine.

5. **Low Risk of Resistance**
   - Multi-compound composition reduces likelihood of microbial resistance.

Disadvantages of Neem (*Azadirachta indica*)

1. **Slow Therapeutic Action**
   - Effects are gradual; not suitable for acute or emergency conditions.

2. **Variability in Composition**
   - Phytochemical concentrations vary with plant part, location, season, and extraction method.

3. **Potential Toxicity**
   - High doses, especially neem oil, may cause toxicity, particularly in children.

4. **Limited Clinical Evidence**
   - Most studies are in vitro or in animals; human clinical trials are limited.

5. **Drug Interactions**
   - Can interact with antidiabetic, immunosuppressive, and anticoagulant medications, altering efficacy.

6. **Standardization Challenges**
   - Lack of uniform formulations and dosage guidelines due to natural variability.

CONCLUSION

Neem (*Azadirachta indica*) is a highly versatile medicinal plant with a rich history of use in traditional medicine systems. Modern pharmacological studies have confirmed its broad spectrum of biological activities, including antimicrobial, anti-inflammatory, antioxidant, antidiabetic, immunomodulatory, anticancer,

hepatoprotective, gastroprotective, antiviral, and neuroprotective effects. The diverse therapeutic potential of neem is largely attributed to its complex mixture of bioactive compounds, such as limonoids, flavonoids, nimbidin, and nimbolide, which act through multiple molecular and cellular mechanisms.

The advantages of neem include its natural origin, multi-targeted pharmacological effects, relatively low toxicity at therapeutic doses, accessibility, cost-effectiveness, and low potential for inducing microbial resistance. However, limitations such as variability in chemical composition, slow therapeutic action, limited clinical trials in humans, potential toxicity at high doses, and possible drug interactions highlight the need for careful usage and standardization.

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