

REVIEW ARTICLE

## PHARMACOLOGICAL POTENTIAL OF *AZADIRACHTA INDICA* LEAF EXTRACT IN DERMATOPHYTE INFECTIONS: A REVIEW

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**ABSTRACT:** Dermatophyte infections are superficial fungal infections that affect keratin-rich tissues such as the skin, hair, and nails, and are primarily caused by dermatophyte species including *Trichophyton*, *Microsporum*, and *Epidermophyton*. These infections, commonly referred to as ringworm, athlete's foot, and jock itch, are highly prevalent worldwide, particularly in tropical and subtropical regions, and are often associated with itching, inflammation, and recurrent infections. Conventional antifungal therapies are widely used for treatment; however, their prolonged use may lead to adverse effects, drug resistance, high treatment costs, and reduced patient compliance. These limitations have increased the demand for safer, cost-effective, and plant-based therapeutic alternatives for the management of dermatophyte infections. *Azadirachta indica* (Neem) is a well-known medicinal plant widely used in traditional systems of medicine for the treatment of various skin diseases and infections. Neem leaves are rich in bioactive phytochemicals such as nimbidin, nimbin, azadirachtin, nimbolide, quercetin, flavonoids, tannins, and terpenoids, which contribute to its multiple pharmacological activities. Scientific studies have reported that neem leaf extract possesses significant antifungal activity against dermatophytes, along with anti-inflammatory, antioxidant, and antimicrobial properties that help in reducing fungal growth, inflammation, and oxidative stress, thereby promoting skin healing and infection control. Furthermore, neem-based topical formulations such as gels, creams, and ointments have shown enhanced therapeutic efficacy in dermatological applications. However, further studies on extract standardization, toxicity evaluation, and clinical trials are required to establish its therapeutic potential.

**Keywords:** *Azadirachta indica*, Neem, Dermatophytes, Antifungal activity, Skin infections, Medicinal plant

## I. INTRODUCTION

Dermatophyte infections, also known as dermatophytosis or tinea infections, are the superficial fungal infections that occur in keratinized structures like skin, hair and nails. These fungi are some of the most widespread fungi in the world especially in the tropical and subtropical areas where heat and humidity are conducive to the growth of fungi [1]. Itch, redness, inflammation, scaling, and ring-shaped skin lesions are common features of dermatophyte infections, which have a tremendous impact on the quality of life of the affected patients because they cause discomfort and recurrent infections. Poor hygiene, overcrowding, immunocompromised conditions, and the use of immunosuppressive drugs have led to the prevalence of dermatophytosis in recent years [2].

Dermatophyte infections are mainly caused by three genera of fungi: *Trichophyton*, *Microsporum*, and *Epidermophyton*. The most common causal organisms in humans are *Trichophyton rubrum* and *Trichophyton mentagrophytes*. They can invade the keratinized tissues by producing the Keratinase enzymes, which break down Keratin and enable the fungi to colonise the skin, hair, and nails resulting in infection [3].

Though there are a number of synthetic antifungal drugs like azoles, allylamines and griseofulvin that can be used to treat dermatophyte infections, their long-term use is linked to a number of limitations including development of drug resistance, side effects, high cost and reoccurrence of infection. Such problems have attracted the attention of growing interest in herbal medicines as alternative therapeutic agents because of their safety, low cost, and various pharmacological effects [4].

*Azadirachta indica* (Neem), a member of the family Meliaceae, is a popular medicinal plant that has been highly used in traditional systems of medicine like Ayurveda in the treatment of several skin diseases and infections. Neem leaves contain abundant bioactive phytochemicals that have antifungal, anti-inflammatory, antioxidant, and antimicrobial properties; flavonoids, tannins, terpenoids, and limonoids [5].

This review seeks to offer an extensive overview of phytochemical composition, antifungal, pharmacological, and formulation strategies of the *Azadirachta indica* leaf extract in the treatment of dermatophyte infections [6].

## 2. Literature Search Methodology

A comprehensive literature search was carried out to collect relevant scientific information related to the pharmacological potential of *Azadirachta indica* leaf extract in dermatophyte infections. Various electronic scientific databases were used to gather published research and review articles. The major databases searched included PubMed, Google Scholar, ScienceDirect, and SpringerLink. The literature search focused on studies related to antifungal activity, phytochemical composition, pharmacological activities, and dermatological applications of *Azadirachta indica* leaves [7].

Different keywords and combinations of keywords were used during the literature search to obtain relevant articles. The main keywords used included “*Azadirachta indica*,” “Neem leaf extract,” “Dermatophytes,” “Antifungal activity,” “Skin infection,” “Herbal antifungal,” and “Medicinal plants in dermatology.” Boolean operators such as AND and OR were used to refine the search and obtain more specific and relevant results. Reference lists of selected articles were also screened manually to identify additional relevant studies [8].

The inclusion criteria for selecting articles included studies related to phytochemical analysis of neem leaves, *in vitro* antifungal studies against dermatophytes, *in vivo* pharmacological studies, anti-inflammatory and antioxidant studies, and formulation-based studies such as gels, creams, and ointments containing neem extract. Both original research articles and review articles published in English were included [9]. The exclusion criteria included studies not related to dermatophyte infections, studies conducted on other parts of the plant (except leaves), articles with insufficient experimental data, duplicate publications, and non-English articles. The collected literature was carefully screened, analyzed, and organized systematically to prepare this review [10].

## 3. Botanical Description and Ethnomedicinal Uses

### Botanical Classification

Neem or *Azadirachta indica* is a significant medicinal tree of the family Meliaceae. It is also common in tropical and subtropical areas particularly within India, Pakistan, Bangladesh and other South Asian nations. Neem is a rapidly growing evergreen tree and is of great use both in medicine, farming, and pharmaceutical. It is usually referred to as Neem in English, Nimba in Sanskrit and Neem in Hindi. The medicinal value of almost all the parts of the plant such as leaves, bark, seeds and oil is valuable; however, the leaves are mostly utilized in curing skin diseases and infections (Fig. 1; Table 1) [11].

### Morphology of Neem Leaves

The leaves of the neem are compound, imparipinnate and alternately positioned on the branches. The leaves contain multiple leaflets which make each leaf. The leaflets are

lanceolate in form and have serrated or toothed edges and sharp ends. These are dark green leaflets that have a smooth surface, a pronounced midrib and lateral veins. The neem leaf has an average length of between 20 to 40 cm, with an average length of each leaflet being between 3 and 8 cm. The presence of several bioactive compounds makes neem leaves have a characteristic bitter taste. The primary component of dermatological preparations is the use of the leaves due to the antifungal, anti-inflammatory, and antimicrobial effects [12].

### Traditional Uses in Skin Diseases

The application of neem leaves in the treatment of different skin diseases has a long history dating back centuries, including ringworm, eczema, acne, psoriasis, scabies, wounds, ulcers and other fungal infections. Fresh neem leaves are traditionally ground into a paste and applied to fungal infected skin to alleviate fungal infection, inflammation and itching. The decoction of the neem leaves is also applied to the affected areas to wash them and prevent the growth of microbes and ensure faster healing. Neem leaves are also boiled in water and people take bath in these waters in many rural regions to treat the skin infection and to ensure that the skin is hygienic [13].

### Use in Ayurveda and Folk Medicine

*Azadirachta indica*, commonly referred to as Nimba in Ayurveda, is regarded as one of the most valuable medicinal plants in skin diseases and purifying the blood. In Ayurvedic literature, neem is said to be antibacterial, antifungal, anti-inflammatory and detoxifying. Ayurvedic preparations based on neem are usually applied to treat skin infections, itch, inflammation and wounds. Neem is used in folk medicine as a paste, powder, juice, decoction and oil in the treatment of several dermatological problems. The popularity of neem in treating skin diseases has prompted a greater scientific curiosity in assessing its pharmacological potential especially in antifungal action against dermatophytes [14].

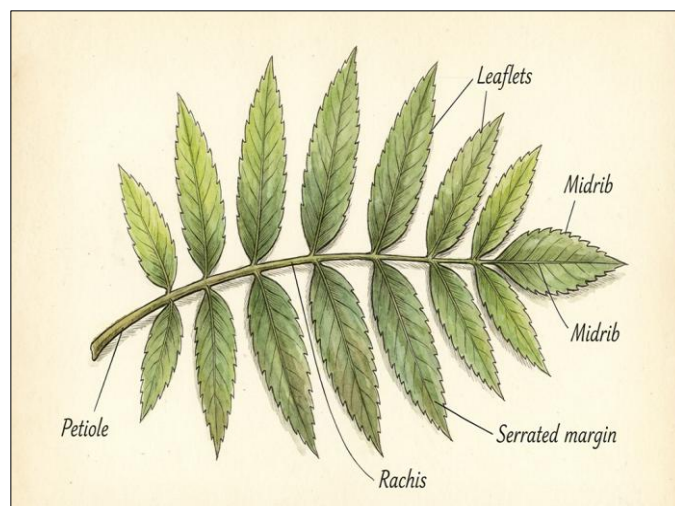


Figure 1: Botanical Morphology of *Azadirachta indica* Leaf [15]

**Table 1: Taxonomical Classification and Ethnomedicinal Uses of *Azadirachta indica* [16]**

S. No.	Parameter	Description
1	Kingdom	Plantae
2	Division	Magnoliophyta
3	Class	Magnoliopsida
4	Order	Sapindales
5	Family	Meliaceae
6	Genus	Azadirachta
7	Species	Azadirachta indica
8	Common Name	Neem
9	Plant Parts Used	Leaves, Bark, Seeds, Oil
10	Traditional Uses	Ringworm, eczema, acne, psoriasis
11	Medicinal Properties	Antifungal, antibacterial, anti-inflammatory, antioxidant
12	System of Medicine	Ayurveda, Unani, Folk medicine

#### 4. Phytochemical Profile of *Azadirachta indica* Leaves

*Azadirachta indica* (Neem) leaves are rich sources of various bioactive phytochemicals that make it a rich source of pharmacological activities especially antifungal, anti-inflammatory, antioxidant and antimicrobial activities. The phytochemical content can be different according to the geographical area, the mode of extraction and the solvent employed, but the neem leaves are always characterized by a complex of secondary metabolites that cause the therapeutic properties [17].

##### 4.1 Preliminary Phytochemical Screening

Preliminary phytochemical screening of neem leaf extracts (aqueous, ethanolic, methanolic, and chloroform extracts) has revealed the presence of several important classes of secondary metabolites (Table 2) [18].

**Flavonoids:** Flavonoids such as quercetin are abundantly present in neem leaves and are known for their strong antioxidant and anti-inflammatory properties. They play a significant role in neutralizing free radicals and reducing oxidative stress associated with skin infections [19].

**Tannins:** Tannins are polyphenolic compounds that exhibit astringent and antimicrobial properties. They help in protein precipitation, forming a protective layer over the skin and preventing microbial invasion [20].

**Alkaloids:** Alkaloids present in neem leaves contribute to antimicrobial and pharmacological activities. They may interfere with microbial metabolism and growth, thereby aiding in infection control [21].

**Saponins:** Saponins possess surfactant properties and exhibit antimicrobial and immune-modulatory effects. They help in enhancing skin permeability and may facilitate better absorption of active compounds [22].

**Terpenoids:** Terpenoids are one of the major classes of compounds in neem leaves and are responsible for antifungal and anti-inflammatory activities. They play a crucial role in disrupting fungal cell membranes [23].

**Glycosides:** Glycosides contribute to various pharmacological effects, including antimicrobial and antioxidant activities, and may enhance the overall therapeutic efficacy of neem extracts [24].

#### 4.2 Major Bioactive Compounds

Neem leaves contain several key bioactive constituents that are directly responsible for their pharmacological properties.

**Nimbidin:** Nimbidin is one of the major active compounds isolated from neem and is known for its potent anti-inflammatory and antifungal activities [25].

**Nimbin:** Nimbin exhibits antimicrobial and antifungal properties and contributes to the overall therapeutic effect of neem in skin infections [26].

**Azadirachtin:** Azadirachtin is a well-known limonoid primarily recognized for its insecticidal activity, but it also exhibits antimicrobial properties [27].

**Quercetin:** Quercetin is a flavonoid with strong antioxidant and anti-inflammatory effects. It plays a vital role in reducing oxidative stress and inflammation in infected skin [28].

**Gedunin:** Gedunin is a limonoid compound with reported antifungal and anti-inflammatory properties, contributing to neem's therapeutic action [29].

**Nimbolide:** Nimbolide is a bioactive terpenoid known for its antimicrobial, antifungal, and anti-inflammatory effects, making it important in dermatological applications [30].

#### 4.3 Analytical Techniques

Various analytical techniques have been employed for the identification, separation, and characterization of phytochemicals present in neem leaves.

**Thin Layer Chromatography (TLC):** TLC is commonly used for preliminary separation and identification of phytochemical constituents in neem leaf extracts.

**High Performance Thin Layer Chromatography (HPTLC):** HPTLC provides more accurate and reproducible results and is widely used for fingerprint profiling of neem extracts.

**High Performance Liquid Chromatography (HPLC):** HPLC is used for the quantitative estimation and precise identification of individual bioactive compounds such as quercetin and nimbidin [31].

**Gas Chromatography–Mass Spectrometry (GC-MS):** GC-MS is an advanced analytical technique used to identify volatile and semi-volatile compounds, providing detailed information about the chemical composition of neem leaf extracts [32].

**Table 2: Major Phytochemicals Present in Neem Leaves (*Azadirachta indica*) [33]**

S. No.	Phytochemical	Chemical Class	Plant Part	Pharmacological Activity
1	Nimbidin	Terpenoid	Leaves	Anti-inflammatory, Antifungal
2	Nimbin	Terpenoid	Leaves	Antimicrobial, Antifungal
3	Azadirachtin	Limonoid	Leaves	Antimicrobial, Insecticidal
4	Nimbolide	Terpenoid	Leaves	Antifungal, Anti-inflammatory
5	Gedunin	Limonoid	Leaves	Antifungal, Anti-inflammatory
6	Quercetin	Flavonoid	Leaves	Antioxidant, Anti-inflammatory
7	Tannins	Polyphenol	Leaves	Astringent, Antimicrobial
8	Saponins	Glycoside	Leaves	Antimicrobial, Immunomodulatory
9	Alkaloids	Alkaloid	Leaves	Antimicrobial
10	Flavonoids	Polyphenol	Leaves	Antioxidant
11	Terpenoids	Terpenoid	Leaves	Antifungal
12	Glycosides	Glycoside	Leaves	Antimicrobial

## 5. Antifungal Activity Against Dermatophytes

The *Azadirachta indica* leaf extract has been widely used as an antifungal against dermatophytes which are the major causal agents of the skin, hair and nail superficial fungal infections. Neem leaves also harbor bioactive compounds of nimbidin, nimbolide, gedunin and quercetin, which have excellent antifungal effects. Different in vitro experiments have shown that neem leaf extracts made in methanol, ethanol and water have significant dermatophytes inhibitory effects. The antifungal effect of the neem can be explained primarily by the possibility to interfere with the structure of fungal cells, prevent fungal growth, and the infection spread. Neem extracts do not only prevent fungal growth, but also inflammation and healing of infected skin [34].

### 5.1 Dermatophyte Species Affected

Neem leaf extract has shown antifungal activity against several dermatophyte species responsible for common fungal infections in humans.

**Trichophyton rubrum:** The most prevalent causative agent of dermatophytosis is *Trichophyton rubrum* which causes infections like tinea corporis, tinea pedis and tinea unguium.

The extract of the Neem leaf has demonstrated great antifungal properties in relation to this organism, since it inhibits the growth of fungi and the germination of their spores [35].

**Trichophyton mentagrophytes:** This species infects skin, hair and nails, especially athlete feet and ringworm. Various antifungal studies have shown Neem extract to be a strong inhibitor of *T. mentagrotres* [36].

**Microsporum gypseum:** *Microsporum gypseum* is a dermatophyte that is a soil organism that infects the skin of humans and animals. Neem leaf extract, has been found to have moderate to high antifungal activity against this species [37].

**Epidermophyton floccosum:** This dermatophyte mainly infects the skin and nails and causes conditions such as tinea cruris and tinea pedis. Neem extract has been reported to inhibit the growth of *E. floccosum* by affecting fungal cell membrane integrity.

### 5.2 Mechanism of Antifungal Action

The antifungal activity of *Azadirachta indica* leaf extract is due to multiple mechanisms, which make it effective against dermatophytes (Table 3).

**Cell Wall Damage:** Neem phytochemicals disrupt the fungal cell wall structure, leading to leakage of cellular contents and fungal cell death.

**Inhibition of Ergosterol Synthesis:** Neem compounds inhibit the synthesis of ergosterol, an essential component of the fungal cell membrane. This leads to membrane damage and inhibition of fungal growth.

**Protein Synthesis Inhibition:** Some bioactive compounds present in neem interfere with fungal protein synthesis, thereby preventing fungal growth and reproduction.

**Reactive Oxygen Species (ROS) Generation:** Neem extract induces the production of reactive oxygen species within fungal cells, causing oxidative stress and damage to cellular components, leading to fungal cell death [38].

**Table 3: Antifungal Activity of Neem Leaf Extract Against Dermatophytes [39]**

S. No.	Neem Extract Type	Dermatophyte Species	Method Used	Concentration	Result	Reference
1	Ethanollic leaf extract	<i>Trichophyton rubrum</i>	Agar well diffusion	50 mg/ml	Strong inhibition	In vitro study
2	Methanollic leaf extract	<i>Trichophyton mentagrophytes</i>	MIC method	25 mg/ml	Significant inhibition	Antifungal study
3	Aqueous leaf extract	<i>Microsporum gypseum</i>	Disc diffusion	100 mg/ml	Moderate inhibition	Experimental study
4	Hydroalcoholic extract	<i>Epidermophyton floccosum</i>	MIC method	50 mg/ml	Strong inhibition	Pharmacological study
5	Ethanollic extract	<i>Trichophyton rubrum</i>	Disc diffusion	75 mg/ml	High antifungal activity	In vitro study
6	Methanollic extract	<i>Microsporum gypseum</i>	Agar diffusion	50 mg/ml	Moderate activity	Research report
7	Aqueous extract	<i>Trichophyton mentagrophytes</i>	MIC	100 mg/ml	Moderate inhibition	Experimental study
8	Chloroform extract	<i>Epidermophyton floccosum</i>	Disc diffusion	25 mg/ml	Mild inhibition	Laboratory study
9	Methanollic extract	<i>Trichophyton rubrum</i>	MIC	20 mg/ml	Strong inhibition	Antifungal assay
10	Ethanollic extract	<i>Microsporum canis</i>	Agar diffusion	50 mg/ml	Moderate inhibition	In vitro study
11	Hydroalcoholic extract	<i>Trichophyton mentagrophytes</i>	Disc diffusion	75 mg/ml	Strong inhibition	Pharmacology study
12	Neem leaf oil extract	<i>Epidermophyton floccosum</i>	MIC	30 mg/ml	Significant inhibition	Experimental study

## 6. Anti-inflammatory and Antioxidant Activity

The *Azadirachta indica* leaf extract has great anti-inflammatory and antioxidant properties which are important in the treatment of dermatophyte infections. Dermatophyte infections not only result in the development of fungus on the skin, but also cause inflammation, erythema, itch, and oxidative stress at the point of infection. Neem leaf extract can be used to minimize these symptoms by various pharmacological processes [40].

### Reduction of Skin Inflammation

Neem leaf extract has bioactive substances like nimbidin, nimbolide, quercetin, and flavonoids that have a high anti-inflammatory activity. These substances are used to ease redness, swelling, itching, and irritation of fungal skin infections. The anti-inflammatory effect of neem can be attributed to the inhibition of inflammatory mediators like prostaglandins and histamine which cause inflammation and itch to the affected skin [41].

### Inhibition of Cytokines

Neem leaf extract has been reported to inhibit the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-1 (IL-1), and interleukin-6 (IL-6). The release of these cytokines occurs in the case of fungal infections and helps to increase inflammation and tissue damage. Neem prevents the destruction of the skin tissue by suppressing these cytokines and thus inflammation [42].

### Free Radical Scavenging Activity

Reactive oxygen species (ROS) are generated on the site of infection during dermatophyte infection and this leads to oxidative stress and slows skin healing. The leaves of neem have flavonoid, tannin, and phenolic compounds, which are antioxidants and free radical scavengers. This antioxidant effect defends against oxidative damage to skin cells, as well as enhancing healing [43].

### Role in Skin Healing

Neem leaf extract has combined anti-inflammatory and antioxidant effects, which aid in healing the skin. Neem increases fibroblast, collagen formation, and tissue regeneration, which play key roles in repairing skin damages. It also assists in decreasing infection, inflammation and oxidative stress at the same time thereby hastening the healing process in dermatophyte infections [44].

## 7. Mechanism of Action in Dermatophyte Infection

*Azadirachta indica* leaf extract has a multifactorial pharmacological action that makes it effective as a therapeutic agent against dermatophytic infections. Neem does not work via any one mechanism; rather, it exhibits antifungal, anti-inflammatory, antioxidant, and skin protective properties in combination, rendering it an efficient natural therapy against dermatophyte infections (Fig. 2) [45].

## Antifungal Action

The neem leaf extract also has a high antifungal activity against dermatophytes like Trichophyton, Microsporum and Epidermophyton. The bioactive substances found in neem, including nimbidin, nimbolide, gedunin, and azadirachtin, interfere with the integrity of the cell wall and cell membrane in fungi. These substances prevent the production of ergosterol, a vital constituent of fungal cell membrane. The ergosterol blockage causes the membrane to become permeable, resulting in cellular content leakage; and death of the fungal cells. Neem also prevents the germination and growth of fungus spores as well as mycelial growth and thus prevents infection spreading [46].

## Anti-inflammatory Action

Dermatophyte infections cause inflammation characterized by redness, itching, swelling, and irritation. Neem leaf extract reduces inflammation by inhibiting inflammatory mediators such as prostaglandins, histamine, and pro-inflammatory cytokines including TNF- $\alpha$ , IL-1, and IL-6. This helps in reducing skin irritation and inflammation associated with fungal infections [47].

## Antioxidant Action

During fungal infection, reactive oxygen species (ROS) are generated, which cause oxidative stress and damage to skin cells. Neem leaves contain flavonoids, tannins, and phenolic compounds that act as antioxidants and neutralize free radicals. This antioxidant activity protects skin cells from oxidative damage and supports the healing process [48].

## Skin Protection and Healing

Neem helps in skin recovery through collagen synthesis, proliferation of fibroblasts and tissue regeneration. It also develops a protective barrier on the skin, which inhibits secondary microbial infection. The neem leaf extract has antifungal, anti-inflammatory and antioxidant properties that contribute to the reduction of infection, inflammation and oxidative stress, therefore leading to the healing of the dermatophyte infected skin faster [49].

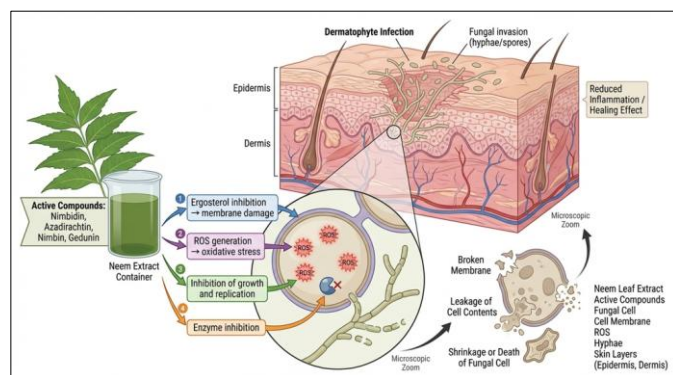


Figure 2: Mechanism of Antifungal Action of Neem Leaf Extract in Dermatophyte Infection [50]

## 8. Safety and Toxicity Studies

The safety evaluation of *Azadirachta indica* leaf extract is an important aspect in the development of topical formulations for the treatment of dermatophyte infections. Though neem has a long history of traditional usage in skin diseases, scientific research has also been done to determine the toxicity and safety profile of neem [51].

### Acute Toxicity

In acute toxicity tests of neem leaf extracts, it has been found that it is relatively safe at therapeutic levels. They have been reported in experimental studies done on animal models that the neem leaf extract does not elicit any significant effects of toxicity when taken in moderate doses. The LD 50 of neem leaf extract has been reported to be quite high which means that it has low toxicity. The vast majority of studies have demonstrated that neem leaf extract can be safely applied topically and is not associated with systemic toxicity in case of external use [52].

### Skin Irritation Test

Topical formulations with neem extract are tested by skin irritation to determine the safety of these products. The tests are typically done on the skin of animals or human subjects to see whether there is any redness, swelling, itching or irritation. In most studies, formulations of neem leaf extract (gels, creams and ointments) have demonstrated little or no skin irritation confirming that neem is safe when used topically in fungus skin treatment [53].

### Safe Concentration for Topical Use

The research indicates that neem leaf extract is safe and efficacious as a topical formulation at a certain range of concentration. It is generally believed that neem extracts of 2-10 percent in creams, gels and ointments are safe and effective as antifungal and anti-inflammatory agents. Concentrations exceeding this limit can occasionally result in mild irritation of the skin in sensitive individuals, hence it needs to be properly formulated and standardized [54]. In sum, neem leaf extract demonstrates a favorable safety profile with low toxicity and low skin irritation and is well tolerated hence making it an ideal choice in topical therapy of dermatophyte infections.

## 9. Future Perspectives

Although *Azadirachta indica* leaf extract has shown promising pharmacological activities against dermatophyte infections, several research gaps still exist that need to be addressed in order to establish neem as a clinically effective antifungal agent. Future research should focus on clinical validation, extract standardization, advanced drug delivery systems, and formulation development [55].

### Need for Clinical Trials

Most of the studies on neem leaf extract have been conducted using *in vitro* antifungal assays and *in vivo* animal models.

However, well-designed clinical trials in human subjects are still limited. Therefore, future research should focus on randomized controlled clinical trials to evaluate the safety, efficacy, dosage, and duration of treatment of neem-based formulations in dermatophyte infections. Clinical studies will help in establishing neem as an evidence-based herbal antifungal agent [56].

### Standardization of Extract

One of the major challenges in herbal medicine is the lack of extract standardization. The phytochemical composition of neem leaves may vary depending on geographical location, harvesting time, and extraction method. Therefore, future studies should focus on standardization of neem leaf extract based on marker compounds such as nimbidin, azadirachtin, and quercetin. Standardization will ensure consistent quality, safety, and therapeutic efficacy of neem-based formulations [57].

### Development of Topical Formulations

Future research should also focus on the development of effective topical formulations such as gels, creams, ointments, and transdermal delivery systems containing neem leaf extract. These formulations can improve drug penetration, increase contact time with infected skin, and enhance therapeutic efficacy [58].

### Nano-formulations Research

Nanotechnology-based drug delivery systems such as nanoemulsions, nanoparticles, liposomes, and nanogels represent a promising approach for improving the antifungal activity of neem leaf extract. Nanoformulations can enhance drug stability, solubility, skin penetration, and controlled drug release, thereby improving the overall therapeutic effectiveness in dermatophyte infections.

Overall, future research should focus on clinical validation, extract standardization, advanced formulations, and nanotechnology-based delivery systems to fully explore the therapeutic potential of neem in dermatophyte infections [59].

## Conclusion

*Azadirachta indica* (Neem) leaf extract has demonstrated significant pharmacological potential in the management of dermatophyte infections due to its broad spectrum of bioactive phytochemicals and multifactorial mechanism of action. Neem leaves contain important phytoconstituents such as nimbidin, nimbin, azadirachtin, nimbolide, quercetin, flavonoids, tannins, and terpenoids, which are responsible for its antifungal, anti-inflammatory, antioxidant, and antimicrobial activities. These bioactive compounds act by inhibiting fungal growth, damaging fungal cell membranes, reducing inflammation, scavenging free radicals, and promoting skin healing.

The antifungal activity of neem leaf extract against dermatophytes such as *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Microsporum gypseum*, and *Epidermophyton floccosum* has been reported in various in vitro and in vivo studies. In addition to its antifungal activity, neem also plays an important role in reducing skin inflammation, oxidative stress, and tissue damage associated with dermatophyte infections. The presence of multiple pharmacological activities in a single plant makes neem a promising natural therapeutic agent for the treatment of dermatophytosis.

Furthermore, neem leaf extract has shown good potential in topical formulations such as creams, gels, ointments, and nanoformulations, which improve its therapeutic effectiveness in skin infections. Neem is also considered relatively safe for topical use with minimal toxicity and skin irritation.

However, despite promising experimental evidence, further research is required for the standardization of neem extracts, detailed toxicity studies, and well-designed clinical trials to confirm its safety and efficacy in humans. Therefore, *Azadirachta indica* can be considered a promising natural antifungal agent for dermatophyte infections, but future clinical research is necessary to establish its role in modern dermatological therapy.

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**CONFLICT OF INTEREST:** Nil

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