

# A Review on Herbal Antifungal Agents: A Natural Approach to Combating Fungal Infections

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## Abstract

**Background:** Fungal infections represent a major global health concern, affecting millions of individuals and contributing substantially to morbidity and healthcare burden. The emergence of antifungal resistance, toxicity, drug interactions, and therapeutic failures has increased the need for safer and more effective treatment strategies.

**Objective:** This review aims to provide a structured overview of the antifungal potential of medicinal plants and plant-derived products as alternative or complementary approaches for managing fungal infections, with particular emphasis on their phytochemical constituents, mechanisms of action, and therapeutic prospects.

**Methods:** Relevant scientific evidence concerning herbal antifungal agents was reviewed, focusing on plants including *Curcuma longa* L., *Aloe barbadensis* Miller, *Azadirachta indica*, *Allium sativum*, *Cocos nucifera*, *Ficus racemosa*, *Argemone mexicana*, *Smilax zeylanica*, *Sonchus asper*, *Lantana camara*, *Moringa oleifera*, and *Bauhinia vahlii*. Their reported activity against clinically important fungal genera, including *Candida*, *Aspergillus*, *Trichophyton*, *Epidermophyton*, *Microsporum*, and *Malassezia*, was considered.

**Results:** Herbal antifungal agents demonstrate promising activity through multiple mechanisms, including disruption of fungal cell membranes, inhibition of ergosterol biosynthesis, interference with adhesion and biofilm formation, modulation of oxidative stress, and enhancement of host immune responses. Their diverse phytochemical profiles may provide opportunities for overcoming resistance associated with conventional antifungal therapy.

**Conclusion:** Despite encouraging preclinical evidence, limitations related to standardization, bioavailability, pharmacokinetics, toxicity evaluation, formulation, and regulatory approval remain. Future research should prioritize well-designed clinical studies, standardized extracts, advanced delivery systems, and mechanistic investigations. Integrating validated herbal antifungal agents with conventional therapy may provide sustainable and potentially effective strategies for managing resistant fungal infections.

## Introduction

Herbal medicine is one of the oldest healing traditions, with roots going back thousands of years. It has played a key role in treating various diseases, including skin infections. Ancient civilizations like the Egyptians, Chinese, Indians, and Greeks recorded the medicinal uses of plants for treating infections, wounds, and inflammatory conditions. Systems such as Ayurveda, Unani, Traditional Chinese Medicine (TCM), and Homeopathy have

used herbal remedies to manage infectious and inflammatory diseases. The growing issue of antimicrobial resistance, side effects from synthetic drugs, and limited access to healthcare in many areas have led to renewed interest in plant-based medicines for treating skin infections, including those caused by bacteria, viruses, fungi, and parasites<sup>1</sup>. Skin infections pose a major global health challenge, affecting millions of people each year. They can lead

to a wide range of clinical symptoms, from mild irritation to serious systemic complications. The causes of these infections vary and include bacteria, viruses, fungi, and parasites, each with unique mechanisms of disease. Understanding the causes of skin infections is essential for developing effective treatments and preventive measures.

Bacterial skin infections are among the most common dermatological issues, mainly caused by Gram-positive bacteria like *Staphylococcus aureus* and *Streptococcus pyogenes*. Impetigo is a highly contagious bacterial infection that commonly affects children and shows up as honey-colored crusted lesions. Cellulitis is a deeper bacterial infection that causes pain, warmth, swelling, and redness, while necrotizing fasciitis is a fast-spreading soft tissue infection that needs immediate medical attention due to its potential to cause life-threatening complications. Various risk factors contribute to bacterial skin infections, including poor hygiene, skin trauma, immunosuppression, and crowded living conditions<sup>2</sup>. Viral skin infections, caused by members of the Herpesviridae, Papillomaviridae, and Poxviridae families, manifest in diverse clinical forms, ranging from acute infections to chronic recurrences. Herpes simplex virus (HSV) infections produce painful vesicular lesions, with HSV-1 primarily affecting the oral mucosa and HSV-2 causing genital herpes. Varicella-zoster virus (VZV) is responsible for chickenpox in primary infections and shingles upon reactivation. Other viral skin infections, such as those caused by human papillomavirus (HPV), result in various types of warts, while molluscum contagiosum, a poxvirus infection, produces dome-shaped papules<sup>3</sup>. Among infectious skin diseases, fungal infections have gained global significance, affecting millions of individuals and accounting for a substantial proportion of dermatological conditions. These infections, collectively referred to as dermatomycoses, are primarily caused by dermatophytes, yeasts, and non-dermatophyte molds. *Dermatophytes*, such as *Trichophyton*,

*Microsporum*, and *Epidermophyton*, invade keratinized tissues, leading to tinea infections affecting various body sites, including tinea pedis (athlete's foot), tinea corporis (ringworm), and tinea capitis (scalp ringworm). Transmission occurs through direct contact with infected individuals, animals, or contaminated surfaces, with warm and humid conditions favoring fungal proliferation. Yeasts, particularly *Candida albicans* and *Malassezia* species, also play a significant role in fungal skin diseases. Candidiasis occurs due to the overgrowth of *Candida* species, leading to erythematous, macerated plaques in moist skin folds, whereas *Malassezia* infections, such as pityriasis versicolor and seborrheic dermatitis, result in hypopigmented or hyperpigmented lesions and flaky, inflamed patches on the skin<sup>4</sup>. Non-dermatophyte molds (NDMs), including *Aspergillus*, *Fusarium*, and *Scopulariopsis*, are increasingly recognized as emerging fungal pathogens, particularly in onychomycosis (fungal nail infections) and cutaneous fungal infections in immunocompromised patients<sup>5</sup>. The epidemiology of fungal skin infections highlights their global significance, with an estimated 750 million cases annually. In 2017, fungal infections accounted for 10.09% of all skin diseases globally, with a prevalence rate affecting 20–25% of the population. Certain regions, particularly tropical and subtropical climates, report incidence rates as high as 40–60% due to favorable environmental conditions for fungal growth. In India alone, over 57 million individuals are affected by serious fungal infections, with dermatophytosis prevalence ranging from 6.09% to 61.5%, depending on regional variations<sup>6</sup>. The rising cases of antifungal resistance present a significant challenge for effective treatment. Drug-resistant strains of *Candida*, *Aspergillus*, and dermatophytes are becoming serious public health issues. This resistance comes from the inappropriate use of antifungals, biofilm formation, and the natural genetic changes in fungi. There is an urgent need for alternative treatment options<sup>7</sup>. Because of these issues, herbal medicine is

gaining attention as both an alternative and a complementary treatment for fungal infections. Traditional herbal remedies contain various bioactive compounds, such as phenolics, flavonoids, alkaloids, tannins, and essential oils. These compounds can fight fungi, bacteria, and help the immune system. Some popular herbal antifungal agents include aloe vera, lemongrass oil, coconut oil, apple cider vinegar, garlic, turmeric, tea tree oil, green tea, neem, and baking soda. Aloe vera has phenolic compounds, salicylic acid, and sulfur that strongly combat *Candida* species. Lemongrass oil, which is high in quercetin and citral, shows powerful antifungal effects against dermatophytes and yeasts. Coconut oil contains lauric, capric, and caprylic acids, which break down fungal cell membranes, making it helpful in treating fungal acne and dermatophytosis. Apple cider vinegar helps balance skin pH, preventing fungal overgrowth. Garlic, with its allicin content, has broad antifungal activity and disrupts fungal biofilms. Turmeric, containing curcumin, works as a strong antifungal and anti-inflammatory agent, often mixed with honey or coconut oil. Tea tree oil, which has terpinen-4-ol, is effective against *Candida* and dermatophytes. Neem (*Azadirachta indica*), with its nimbin and azadirachtin, stops the formation of fungal biofilms, making it useful for chronic infections<sup>7</sup>.

Despite the hopeful therapeutic effects of herbal antifungal agents, there are still challenges regarding standardization, bioavailability, and large-scale clinical testing. Research shows that plant-based antifungals can work just as well as synthetic ones while causing fewer side effects and reducing resistance. However, more standardization, improved drug delivery methods, and pharmacokinetic studies are needed to make the most of these treatments.

### **Methodology**

A systematic literature review was conducted to evaluate the antifungal properties of selected medicinal herbs. Various reputable scientific

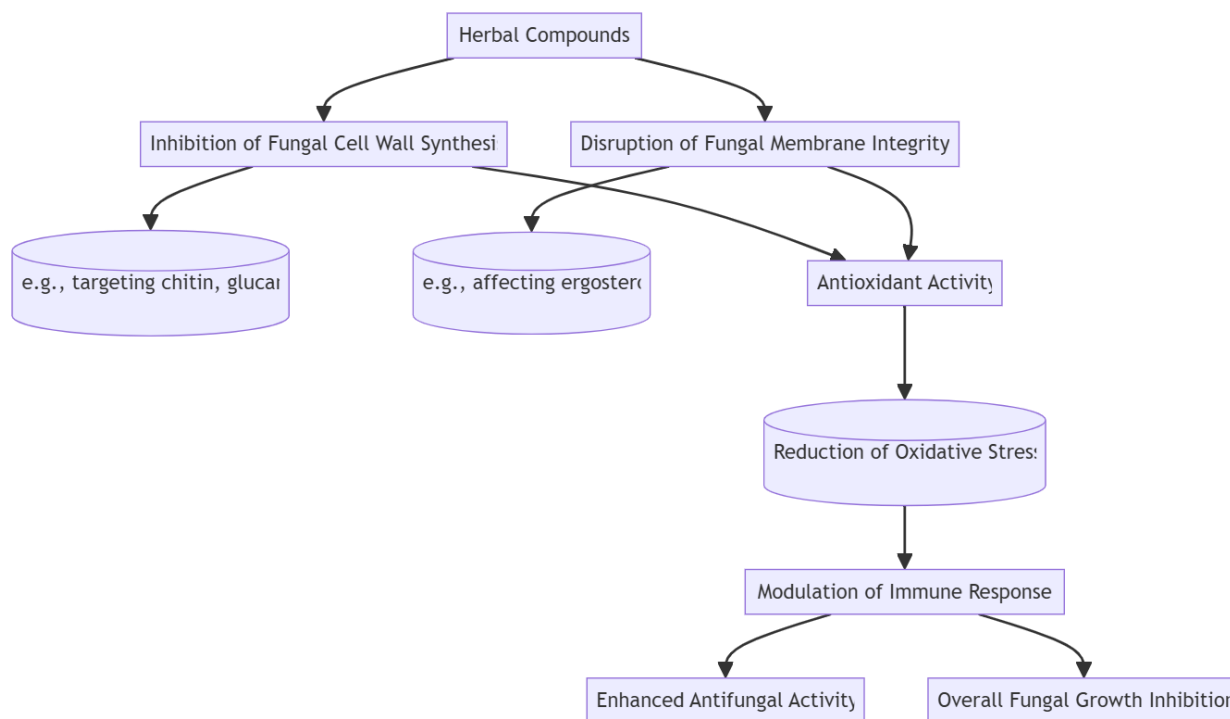
databases were utilized, including Wikipedia, Google Scholar, PubMed, Napralert, MAPACSIR, ScienceDirect, Nature, Elsevier, ResearchGate, Scopus, IMPD, MPD, Springer, Springer Nature, and IntechOpen. These databases provided a comprehensive collection of peer-reviewed studies, review articles, clinical trials, and meta-analyses related to the antifungal efficacy of herbal compounds. The inclusion criteria focused on studies published in peer-reviewed journals that investigated the phytochemical constituents, antifungal mechanisms, and traditional uses of medicinal plants. Only articles that provided scientific validation through in vitro, in vivo, and clinical studies were considered. Studies that lacked empirical data or did not meet methodological rigor were excluded.

### **Mechanism of action**

Herbal compounds have antifungal effects through several mechanisms. They mainly work by blocking fungal cell wall synthesis, damaging fungal membrane integrity, and affecting oxidative stress and immune response. One major way is by inhibiting fungal cell wall synthesis. Herbal compounds target essential components such as chitin and glucan, which are key parts of fungal cell walls. By interfering with these components, herbal extracts weaken the cell wall, leading to cell rupture and death. Another important mechanism is the disruption of membrane integrity. This often involves targeting ergosterol, a key sterol in fungal membranes. Many plant-derived compounds, like essential oils and alkaloids, either change ergosterol synthesis or directly disrupt membrane stability. This causes increased permeability and results in fungal cell death. Besides these direct antifungal actions, herbal compounds also show antioxidant properties. This is important for fighting fungi. Oxidative stress significantly affects fungal survival, and herbal antioxidants reduce oxidative damage by neutralizing reactive oxygen species (ROS). Lowering oxidative stress helps modulate immune

responses, enabling the body to better defend against fungal infections<sup>8-11</sup>. By improving the immune response, these herbal compounds enhance antifungal activity and act as general inhibitors of fungal growth. The combined effects of disrupting cell walls, destabilizing membranes, reducing

oxidative stress, and modulating immune responses make herbal medicine a promising option for treating fungal infections. These diverse mechanisms emphasize the potential of plant-based antifungal agents in creating effective and sustainable treatments for resistant fungal strains.



**Fig. 01: Mechanisms of Antifungal Action of Herbal Compounds**

### Some potential antifungal plants

#### **1. Turmeric (*Curcuma longa* L.)**

Turmeric (*Curcuma longa* L.) is a herb from the Zingiberaceae family that grows in South Asia. It has been used in traditional medicine for centuries. The plant is famous for its bright yellow rhizome, which serves as both a spice and a healing agent in several traditional medical systems, especially Ayurveda, Traditional Chinese Medicine (TCM), and Siddha medicine. Turmeric has been used to treat skin infections, wounds, and inflammation. Its healing properties come from its phytochemicals, including curcumin, turmerones, and other curcuminoids.

These compounds provide antifungal, antimicrobial, and anti-inflammatory benefits.

In addition to its antifungal mechanisms, curcumin has strong antioxidant properties, which enhance its healing potential. By lowering oxidative stress and modifying immune responses, turmeric helps the body fight fungal infections more effectively. Its anti-inflammatory properties also ease symptoms like redness, itching, and swelling that often accompany fungal infections. This makes turmeric an effective antifungal agent and a helpful remedy for skin irritation caused by fungi.

Clinical studies have looked into turmeric's effectiveness in treating fungal infections through both in vitro and in vivo research. Evidence shows that using turmeric extracts, curcumin gels, and essential oils can significantly improve symptoms of fungal infections. Research on Candida infections reveals that curcumin can halt fungal growth and biofilm formation. This positions it as a promising alternative or complementary treatment to standard antifungal drugs. Furthermore, clinical trials suggest that turmeric-based forms may speed up healing in lesions infected with fungi.

Overall, turmeric (*Curcuma longa* L.) offers a natural, effective, and easily accessible antifungal remedy with various ways of working, including disrupting cell membranes, blocking ergosterol, and reducing oxidative stress. Its traditional applications and modern research validate its potential as a holistic antifungal treatment. As resistance to conventional antifungal drugs continues to grow, turmeric emerges as a notable plant-based antifungal agent that provides therapeutic benefits with minimal side effects. Future studies and clinical trials will further confirm its effectiveness and refine its formulations for broader medicinal use.<sup>12-22</sup>

## 2. **Aloe Vera (*Aloe barbadensis* Miller)**

Aloe vera (*Aloe barbadensis* Miller) is a succulent plant from the Asphodelaceae family. It is well-known for its healing properties and has been extensively used in traditional medicine for centuries. Native to North Africa and the Arabian Peninsula, this plant is now grown around the world due to its therapeutic applications, especially in skin care and wound healing. Aloe vera has been used for skin infections, burns, and inflammation, making it a versatile natural remedy. Its healing properties come from a rich mix of phytochemicals, including aloin, anthraquinones, polysaccharides, flavonoids, and sterols. These compounds contribute to its

antimicrobial, antifungal, and anti-inflammatory effects.

Scientific studies have shown Aloe vera's antifungal effectiveness, particularly against Candida species, which cause oral thrush, vaginal candidiasis, and systemic fungal infections. Research suggests that the antifungal effects of Aloe vera primarily stem from its anthraquinones and polysaccharides. These compounds work through various mechanisms to stop fungal growth. One significant action involves boosting the immune response. This enhancement helps the body fight off fungal infections by increasing macrophage activity and producing cytokines. This immune modulation allows the body to control fungal growth and prevent it from returning. Aloe vera also directly acts against fungi by stopping cell growth, disrupting cell membranes, and hindering essential metabolic processes.

Aloe vera's polysaccharides, especially acemannan, play an important role in healing wounds and regenerating skin. This makes it especially valuable for treating dermatophytic infections, including ringworm, athlete's foot, and tinea infections. These polysaccharides promote fibroblast growth, collagen production, and tissue repair, speeding up healing for fungal-infected wounds. Additionally, aloe vera's anti-inflammatory properties help reduce symptoms like redness, itching, and swelling that commonly occur with fungal infections<sup>23-33</sup>.

## 3. **Neem (*Azadirachta indica* A. Juss.)**

Neem (*Azadirachta indica* A. Juss.) is a fast-growing tree in the Meliaceae family. It has a long history of use in traditional medicine, especially in Ayurveda, for treating various ailments, including skin and systemic infections. This tree, native to the Indian subcontinent, is known for its quick growth, unique pinnate leaves, and clusters of small, fragrant flowers. Neem's healing properties come from its rich mix of phytochemicals, including azadirachtin, nimbin,

limonoids, and other bioactive compounds. These elements provide neem with diverse medicinal benefits, making it important in traditional healthcare.

Neem is traditionally used to address many health issues. In Ayurvedic medicine, it has served to treat skin infections, wounds, fevers, and other systemic diseases. Its role in managing skin conditions stands out, as traditional healers use neem preparations to tackle fungal, bacterial, and parasitic skin infections. Using neem for systemic infections indicates its potential to fight internal infections and bolster the body's defenses. This wide array of traditional uses underscores neem's versatility and importance in healthcare practices. Scientific evidence supports neem's antifungal activity, especially against common pathogens like *Candida* and *Aspergillus* species. Numerous lab studies show neem can halt the growth of these fungi, suggesting it might serve as a natural antifungal agent. These studies reveal that neem extracts and isolated compounds can effectively stop the growth and spread of these fungi in controlled environments. The observed antifungal activity supports the traditional use of neem for treating fungal infections.

Clinical studies have confirmed neem's effectiveness in treating fungal infections affecting the skin and nails. Using neem-based formulations topically has shown promising results in managing dermatophytosis, candidiasis, and other fungal skin infections. Neem oil and leaf extracts are incorporated into creams, ointments, and other topical preparations for treating these conditions. Studies have also looked into neem for nail fungal infections, with some evidence indicating it can reduce fungal growth and improve nail appearance. However, more extensive, randomized controlled trials are necessary to fully assess neem's efficacy and safety for various fungal infections in humans. Despite the need for more research, existing

evidence, along with its long-standing traditional use, suggests that neem has considerable potential as a natural antifungal agent for topical applications.<sup>34-47</sup>

#### 4. Garlic (*Allium sativum* L.)

Garlic (*Allium sativum*), a bulbous plant from the Amaryllidaceae family, has long been used in traditional medicine for its wide-ranging antimicrobial properties. It originates from Central Asia but is grown globally due to its culinary and medicinal importance. Garlic contains bioactive sulfur compounds such as allicin, ajoene, diallyl sulfides, and thiosulfates. These compounds provide antifungal, antibacterial, antiviral, and anti-inflammatory benefits. They have been studied for their potential against fungal infections, especially *Candida* species, dermatophytes (like *Trichophyton* and *Microsporum*), and *Aspergillus fumigatus*.

The antifungal effects of garlic are mainly linked to allicin, which forms when garlic is crushed or chopped. Allicin affects fungi by breaking down their cell membranes, stopping ergosterol production, and interfering with protein synthesis. Ergosterol is vital for fungal cell membranes, and its disruption increases permeability, leading to leaks of cell contents and eventual death. Additionally, ajoene, another powerful compound in garlic, inhibits fungal growth by targeting mitochondrial functions and oxidative stress pathways.

Research has confirmed garlic's strong antifungal capabilities against *Candida albicans*, a common opportunistic fungal pathogen. In vitro studies have shown that garlic extracts significantly lower fungal viability, biofilm formation, and hyphal growth, key factors in *Candida* infections. Additionally, garlic has been shown to work well with standard antifungal medications like fluconazole and amphotericin B, suggesting it could be a valuable supplement

for treating drug-resistant fungal infections. In clinical settings, garlic has been explored as an alternative or complementary treatment for fungal infections of the skin, nails, and mucous membranes. A study evaluating garlic extract gel in patients with vaginal candidiasis found that it was equally effective as clotrimazole in reducing symptoms such as itching, burning, and discharge. Another study highlighted the efficacy of garlic mouth rinses in reducing oral *Candida* colonization in immunocompromised patients, further supporting its potential use in oral health and systemic fungal infections<sup>48-57</sup>.

### 5. Coconut Oil (*Cocos nucifera* L.)

Coconut oil (*Cocos nucifera* L.), derived from the fruit of the coconut palm tree in the Arecaceae family, has been widely used in traditional medicine for its antifungal, antimicrobial, and skin-nourishing properties. Indigenous cultures have long utilized coconut oil as a natural remedy for fungal infections, skin conditions, and overall health maintenance<sup>55</sup>. Rich in medium-chain fatty acids (MCFAs), including lauric acid, capric acid, and caprylic acid, coconut oil exerts potent antifungal activity, particularly against *Candida albicans* and *Malassezia* species, which are common causes of fungal infections in humans<sup>58</sup>.

The antifungal mechanism of coconut oil is primarily linked to its fatty acid composition, with lauric acid being the most active component. Lauric acid converts into monolaurin through enzymatic processes. Monolaurin can disrupt fungal cell membranes, which increases permeability and leads to cell death<sup>59</sup>. Capric and caprylic acids also inhibit fungal growth by affecting lipid metabolism, energy production, and membrane integrity<sup>60</sup>. These effects weaken the cell structure of fungi, making them more susceptible to host immune responses and antifungal treatments.

Research has shown that coconut oil is effective against fungi. Coconut oil had strong fungicidal

action against *Candida albicans*, decreasing its capacity to colonize and create biofilms<sup>61</sup>. This is important because *Candida* infections, like oral thrush, vaginal candidiasis, and systemic candidiasis, often resist typical antifungal drugs such as fluconazole. The ability of coconut oil to prevent biofilm formation suggests it could serve as a natural alternative or additional treatment for fungal infections<sup>62-64</sup>. Clinical studies support using coconut oil for skin conditions. Coconut oil as effective as ketoconazole cream for treating fungal dermatitis, while also providing hydration and reducing inflammation<sup>65</sup>. Another study focused on neonatal fungal infections demonstrated that coconut oil safely reduced fungal colonization in preterm infants, showing its gentle and non-toxic properties<sup>66</sup>.

### 6. *Ficus racemosa* L.

*Ficus racemosa* L., also known as cluster fig or Indian fig, is a deciduous tree in the Moraceae family. It's found in tropical and subtropical areas, such as India, Southeast Asia, and Australia. This tree is recognized in traditional medicine practices like Ayurveda, Unani, and Siddha for treating skin infections, ulcers, diabetes, and inflammatory issues. Various parts of the tree, including the bark, leaves, fruits, and latex, provide medicinal benefits, especially for their antimicrobial and antifungal effects. The phytochemical makeup of *Ficus racemosa* is crucial for its antifungal activity. It contains flavonoids, tannins, coumarins, phenolics, and alkaloids known for their antimicrobial effects. Flavonoids, in particular, demonstrate strong antifungal properties by disrupting fungal enzymes and preventing spore germination. Tannins attach to fungal proteins and enzymes, which disturbs metabolism and cell wall production. Coumarins also inhibit fungal growth and reproduction. Although there are still few clinical studies on the antifungal effectiveness of *Ficus racemosa*, some reports show promising results. One study found that applying *Ficus racemosa* extracts topically reduced symptoms like itching, redness, and

scaling in fungal skin infections, suggesting its potential as an alternative treatment for dermatophytosis. Ethnobotanical surveys have highlighted its traditional use for treating fungal infections, further indicating its relevance in folk medicine<sup>67-71</sup>.

## 7. *Argemone mexicana* L.

*Argemone mexicana* L., known as Mexican poppy, is a spiny annual herb in the Papaveraceae family. It originates from Mexico and Central America, and it has spread to tropical and subtropical regions worldwide, including India, Africa, and the Caribbean. This plant has been widely used in traditional medicine to treat various conditions, especially skin diseases, infections, wounds, and inflammation<sup>72-74</sup>. The action mechanism of *Argemone mexicana* against fungi is tied to its alkaloids. Berberine and sanguinarine interfere with the synthesis of fungal nucleic acids, resulting in DNA damage that hinders fungal replication<sup>75</sup>. These alkaloids also target fungal enzymes and proteins, disrupting metabolic pathways and lowering fungal viability. Research suggests that berberine can block fungal efflux pumps, making it harder for fungi to resist antifungal treatments<sup>76</sup>. Several studies have looked into *Argemone mexicana*'s potential for antifungal therapy. One study found that topical application of *Argemone mexicana* extracts significantly lowered skin fungal infections, showing effects similar to conventional antifungal drugs<sup>77</sup>. Another study found that combining extracts with standard antifungal medications improved fungal eradication and reduced drug resistance. However, more detailed clinical trials are needed to validate its therapeutic effectiveness, optimal dosage, and safety for human use.<sup>78</sup>

## 8. *Smilax zeylanica* L.

*Smilax zeylanica* L., known as Indian Sarsaparilla, is a climbing vine in the Smilacaceae family. It is found in India, Sri

Lanka, Southeast Asia, and other tropical regions, thriving in moist, shaded areas. Traditionally, *Smilax zeylanica* has been used in Ayurvedic and folk medicine to address skin infections, inflammation, and microbial diseases<sup>79</sup>. The plant has attracted scientific interest due to its rich phytochemical composition and broad antimicrobial activities, especially against fungal pathogens.

The mechanism of action of *Smilax zeylanica* against fungal pathogens is linked to its ability to modulate fungal stress response pathways. Research suggests that the saponins present in the plant disrupt fungal membrane integrity, leading to leakage of essential cellular components and eventual fungal death<sup>81</sup>. Additionally, flavonoids and glycosides interfere with fungal oxidative stress mechanisms, inhibiting fungal growth and proliferation. Some studies indicate that *Smilax zeylanica* also inhibits fungal enzyme activity, preventing fungi from adhering to host tissues and forming biofilms, which are critical for fungal pathogenicity<sup>82</sup>. Several clinical studies have explored the potential of *Smilax zeylanica* in antifungal therapy. One study observed that a topical formulation containing *Smilax zeylanica* extract significantly reduced symptoms of dermatophytosis, with improvements in skin lesions, itching, and inflammation. Another study demonstrated that oral administration of *Smilax zeylanica* extract enhanced immune responses, helping the body combat fungal infections more effectively. Moreover, research suggests that combining *Smilax zeylanica* extracts with conventional antifungal drugs can enhance fungal eradication rates and reduce resistance development<sup>83</sup>.

## 9. *Sonchus asper*

*Sonchus asper* (spiny/prickly sow-thistle; taxon: *Sonchus asper* (L.) Hill) is an annual or biennial herb with milky latex, belonging to the daisy family Asteraceae. This weed is found all over the world and is native to Europe, Africa,

and Asia. It is now common across India and many other regions. In English, it is known as spiny or prickly sow-thistle. In India, it has various names: Dudhi, Dodak, and Titlia in Hindi; Oosithagarai in Tamil; Ratrinta in Telugu; and Varapputhannel in Malayalam. In traditional medicine, *S. asper* is used to treat wounds, burns, scabies, and various respiratory, kidney, and metabolic problems. The most studied antifungal properties come from methanolic extracts. Leaf extracts inhibit *Candida albicans* and *Aspergillus flavus* in lab tests. Methanol extracts from the roots or aerial parts reduce the growth of plant-pathogenic fungi like *Rhizoctonia solani* and *Botrytis cinerea*; these effects often depend on the dose. The main parts used are the leaves for topical and ethnomedicinal applications, with methanol extracts showing greater effectiveness than aqueous ones. Roots are also used in antifungal tests. In agar-diffusion and MIC assays, root methanol fractions have shown fungistatic and fungicidal effects against the plant pathogen *Rhizoctonia solani*. Potential active compounds identified by GC-MS include benzoic-acid derivatives and 13-cis-retinoic acid. Fungal skin diseases impact about 20 to 25% of the global population, with India having a significant burden and a shifting range of dermatophytes. This situation raises interest in plant-based remedies, although there is still a lack of clinical trials involving *S. asper* for treating skin fungal infections in humans<sup>84</sup>.

#### 10. **Lantana camara L.**

*Lantana camara* L. (Verbenaceae) is a perennial, bushy shrub often used as an ornamental hedge. It is commonly known as lantana, wild sage, shrub verbena, and Spanish flag. In India, it is referred to as nagaouri in Odia, raimuniya/rai in Hindi, ghaneri/tantani in Marathi, unnichedi in Tamil, and pulikampa in Telugu, among others. This plant is native to the American

tropics, including Central and South America and the Caribbean. It has become a widespread invasive weed in Africa, Asia (including India), Australia, and the Pacific. Ethnobotanically, lantana leaves are used externally for skin issues, wounds, scabies, leprosy, and for ulcers and respiratory problems. In terms of biological validation, methanol and ethanol extracts of the leaves—and sometimes the flowers show antifungal activity against *Aspergillus niger*, *A. flavus*, dermatophytes, and other fungi. Broader screening, including GC-MS-guided fractions, supports its antimicrobial and antioxidant properties. For antifungal testing, methanol or ethanol extracts from leaves (and flowers) are the most commonly reported. Some studies also test its effectiveness against plant pathogens, such as *Colletotrichum gloeosporioides*. In public health, superficial mycoses affect about 20 to 25% of the world's population, with increasing resistance in dermatophytes, particularly *Trichophyton rubrum* and *T. mentagrophytes/T. indotineae*. This has led to interest in plant-based treatments. In Ayurveda, *L. camara* is not a traditional staple; the peer-reviewed literature documents experimental topical gels and emulgels using its leaf extract for wound care. However, marketed, peer-reviewed Ayurvedic formulations that identify lantana as a primary ingredient are limited. Most use is in folk and ethnodermatological practices rather than formal Ayurvedic medicine<sup>85</sup>.

#### 11. **Bauhinia vahlii**

*Bauhinia vahlii*, often recognized as *Phanera vahlii*, is commonly known as Maloo creeper, Camel's foot creeper, or Mahul bel. It is a large woody climber, or liana, from the Fabaceae family, specifically the subfamily Caesalpinioideae. This plant is native to

northern and central India and grows over trees using tendrils. It has large, bilobed leaves that resemble a camel's hoof, produces white to yellow flowers, and bears long pods with edible seeds. Other names for this plant include *Bauhinia vahlii* Wight & Arn. The genus has been reclassified by many authors into *Phanera*. In India, it is known by various local names such as Mahul in Hindi, Siali in Odia, and Sandal in Marathi. The actual names can vary by region. *Bauhinia vahlii* is typically wild-harvested from tropical moist and dry deciduous forests, although it can sometimes be cultivated from seeds in similar environments. It native or wild throughout India, Nepal, and surrounding areas. In terms of morphology and microscopy, the leaves have 11 to 15 nerves, are deeply heart-shaped, and are split into two lobes. Key features of the roots include concentric rings of stone cells in the secondary tissues and high starch content in the secondary phloem. These characteristics help verify the quality of the crude drug. When it comes to ethnobotany and claimed uses, local tribes roast or cook the seeds for food. They traditionally use parts of the plant, including the bark, leaves, and stem, for treating wounds, skin issues, inflammation, diabetes, and for fiber and tannins. In Ayurveda, the root of *B. vahlii* is recognized as a source for the traditional medicine "Murva," which is used in treatments for skin diseases and metabolic disorders. However, the identity of Murva has caused historical debate since various species might be used regionally. Biological validation focuses on antifungal properties. In vitro studies have shown that extracts from the roots, stems, and leaves in ethanol, ethyl-acetate, and methanol exhibit antifungal activity. Root extracts, including hexane, ethyl-acetate, and methanol, inhibited *Candida albicans* and some bacteria in agar tests. Ethanol extracts from leaves and stems

also showed inhibition against *C. albicans* and *Aspergillus niger*, with leaf extracts often proving more effective than stem extracts. These antifungal properties are generally linked to the flavonoids, tannins, and terpenoids present in those extracts. Additionally, studies on animals and *in vitro* indicate that *B. vahlii* has antidiabetic, anti-inflammatory, and antioxidant effects. The authenticated root extract shows antidiabetic activity in specific models. For antifungal testing, the common parts and solvents used include roots with hexane, ethyl-acetate, or methanol and leaves and stems with ethanol. Test organisms are usually *Candida albicans* and *Aspergillus niger*, with some research also targeting plant pathogens, such as *Sclerotinia* species, in related *Bauhinia* plants. In the context of epidemiology, antifungals are crucial because superficial fungal infections affect approximately 20 to 25% of the global population. There has been a noticeable increase and challenges in treating these infections, especially in South Asia in recent years. This situation has sparked interest in safe botanical options for topical or adjunct therapies. Regarding Ayurvedic formulations and the market, instead of a single branded item, *B. vahlii* root is mentioned in both academic and pharmacognostic literature as a potential source for the Ayurveda drug "Murva." This drug is featured in several traditional formulations<sup>86</sup>.

## 12. *Moringa oleifera*

*Moringa oleifera* is a fast-growing deciduous tree belonging to the Moringaceae family. It is native to northern India and is widely cultivated in tropical and subtropical regions. Known as the Sajana in Odia, Sahjan in Hindi, drumstick tree in English, and Murungai in Tamil, it thrives in well-drained

sandy or loamy soils under full sunlight. It can also tolerate drought conditions.

It typically grows to a height of 10 to 12 meters and features tripinnate leaves and slender seed pods. A microscopic look reveals many chloroplasts, stomata, and vascular bundles. The tree is rich in phytochemicals, including vitamins A, B-complex, C, and E, as well as minerals like calcium and iron, along with flavonoids, phenolic acids, alkaloids, glucosinolates, saponins, sterols, and isothiocyanates. Profiling of leaf extracts using GC-MS and LC-MS has identified compounds such as quercetin, kaempferol, and 6-decenoic acid (Z) (19.87%), indicating a significant presence of phenolic and flavonoid compounds. Quantitative data on phytochemicals shows that the fruit contains alkaloids, flavonoids, and steroids that are effective against *Candida albicans*. The tannin levels in the roots and seeds range from approximately 65 to 109 mg/100 g, while alkaloid content varies from about 1.9% to 4.0%. This highlights its strong bioactive profile. Traditionally, *M. oleifera* has been used to treat skin ailments basically fungal problems, promote wound healing, fight infections, and manage inflammatory

disorders. Modern studies support its antifungal, anti-inflammatory, antioxidant, and wound-healing benefits. In vitro antifungal tests show that *M. oleifera* is active against dermatophytes, including *Trichophyton* spp., *Epidermophyton*, *Microsporum*, basically *Aspergillus flavus*. The essential oil from the plant contains 44 identifiable compounds identified by GC-MS. Leaf extracts achieved 99% inhibition of *Botrytis cinerea*, with a minimum inhibitory concentration (MIC) of 5 mg/mL. This was confirmed through GC-MS (e.g., 6-decenoic acid) and LC-MS (flavones, quercetin, kaempferol), which caused structural damage to the fungal mycelia. Additionally, proteins derived from Moringa, such as Mo-CBP3 and Mo-CBP4, exhibit both fungistatic and fungicidal effects against *Fusarium* spp., *Candida*, and *Trichophyton* by disrupting cell walls and increasing reactive oxygen species (ROS). Moringa seed oil also shows strong inhibition against *Malassezia furfur*, a fungus involved in seborrheic dermatitis, with zones reaching approximately 26 mm, MIC at 2.5%, and minimum fungicidal concentration (MFC) at 5%. It is widely used in cosmetics and cosmeceuticals for its photoprotective, moisturizing, anti-aging, and skin-lightening effects<sup>87</sup>.

**Table 01: Overview of Major Fungal Skin Diseases: Causes, Symptoms, and Treatment**

| Sl. No | Diseases | Causative agent | Etiology / Transmission | Symptoms | Synthetic drug(s) (dose, route, local/systemic) |
|--------|----------|-----------------|-------------------------|----------|-------------------------------------------------|
| .      |          |                 |                         |          |                                                 |

|    |                                                  |                                                                                    |                                                                                   |                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                   |
|----|--------------------------------------------------|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 01 | Tinea corporis / cruris (ringworm, body / groin) | Dermatophytes ( <i>Trichophyton</i> , <i>Microsporum</i> , <i>Epidermophyton</i> ) | Direct contact with infected people, animals, or surfaces; humid or covered skin. | <ul style="list-style-type: none"> <li>• <b>Early:</b> small, red, scaly, itchy patch with central clearing.</li> <li>• <b>Late:</b> larger annular plaque, severe itching, secondary bacterial infection</li> </ul> | Topical terbinafine cream, apply once daily for 1 to 2 weeks. Alternatively, take oral terbinafine 250 mg once daily for 2 weeks for extensive disease.                                                                                           |
| 02 | Tinea pedis (athlete's foot)                     | Dermatophytes ( <i>T. rubrum</i> , <i>T. interdigitale</i> )                       | Moist occlusive footwear, communal floors                                         | <ul style="list-style-type: none"> <li>• <b>Early:</b> interdigital maceration or vesicles</li> <li>• <b>Late:</b> chronic scaling, fissures, secondary cellulitis</li> </ul>                                        | Topical allylamines or azoles include terbinafine cream, which should be applied twice daily for 1 to 4 weeks. If the condition does not improve or is widespread, use systemic terbinafine at a dose of 250 mg taken by mouth daily for 2 weeks. |
| 03 | Tinea capitis (scalp ringworm)                   | Dermatophytes ( <i>Microsporum</i> , <i>Trichophyton</i> species)                  | Person-to-person, shared hair items; common in children                           | <ul style="list-style-type: none"> <li>• <b>Early:</b> scaly scalp patches, pruritus, broken hairs</li> <li>• <b>Late:</b> extensive alopecia, kerion (inflamed boggy mass), scarring</li> </ul>                     | Systemic treatment is required: use microsize griseofulvin at 20 to 25 mg/kg/day for children for 6 to 8+ weeks, or use oral terbinafine based on weight according to the guidelines. Topicals alone are not enough.                              |
| 04 | Onychomycosis (nail fungal infection)            | Dermatophytes (often <i>T. rubrum</i> ), also yeasts/molds                         | Traumatic nail, communal showers, chronic tinea pedis                             | <ul style="list-style-type: none"> <li>• <b>Early:</b> subungual debris, discoloration, lifting of nail</li> <li>• <b>Late:</b> thickened, dystrophic, painful nails, secondary infection</li> </ul>                 | Systemic first-line treatment is terbinafine 250 mg taken by mouth daily for 6 weeks for fingernails or 12 weeks for toenails. There are also topical options like ciclopirox and efinaconazole, but these take longer to work.                   |
| 05 | Cutaneous candidiasis / intertrigo               | <i>Candida</i> spp. (e.g., <i>C. albicans</i> )                                    | Overgrowth in warm, moist skin folds, antibiotic use, diabetes                    | <ul style="list-style-type: none"> <li>• <b>Early:</b> erythematous macerated patches, itching/burning</li> </ul>                                                                                                    | Topical nystatin powder or cream or azoles (clotrimazole or miconazole) twice a day. For extensive disease, use fluconazole 100 to 150 mg                                                                                                         |

|    |                                                            |                                                                        |                                                                                         |                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                  |
|----|------------------------------------------------------------|------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                            |                                                                        |                                                                                         | <ul style="list-style-type: none"> <li>• <b>Late:</b> satellite pustules, erosions, fissuring, secondary bacterial infection</li> </ul>                                                                 | by mouth weekly or 50 to 100 mg by mouth daily for 1 to 2 weeks (systemic).                                                                                                                                                                                                                      |
| 06 | Pityriasis (Tinea) versicolor                              | <i>Malassezia</i> spp. (yeast)                                         | Normal skin flora overgrowth in hot, humid climates; oily skin                          | <ul style="list-style-type: none"> <li>• <b>Early:</b> Fine, scaly hypopigmented or hyperpigmented macules (trunk)</li> <li>• <b>Late:</b> confluent patches with persistent pigment changes</li> </ul> | Topical selenium sulfide or ketoconazole shampoo should be applied to lesions for short courses. Alternatively, use systemic itraconazole 200 mg by mouth daily for 7 days or fluconazole 300 mg by mouth weekly for 2 weeks for extensive or recurrent disease.                                 |
| 07 | Cutaneous aspergillosis (rare; often in immunocompromised) | <i>Aspergillus</i> spp. (e.g., <i>A. fumigatus</i> , <i>A. niger</i> ) | Traumatic inoculation, burns, contaminated devices; secondary from disseminated disease | <ul style="list-style-type: none"> <li>• <b>Early:</b> erythematous papules/nodules or pustules</li> <li>• <b>Late:</b> necrotic ulcers, black eschars, deep tissue invasion</li> </ul>                 | Systemic antifungals for invasive disease include voriconazole, which is preferred for invasive aspergillosis, or itraconazole. Dose regimens vary by drug and severity, guided by infectious disease specialists, ophthalmologists, or dermatologists. Surgical debridement is often necessary. |

### Comparative Analysis of Herbal Antifungals against Conventional Drugs

Fungal infections pose a significant health challenge globally, ranging from superficial skin and nail infections to life-threatening systemic diseases. While synthetic antifungal drugs, particularly azoles, have been the cornerstone of treatment for decades,

the emergence of widespread antifungal resistance, coupled with concerns about drug toxicity and limited efficacy in recurrent infections, has spurred the exploration of alternative and complementary therapies. Among these, plant-based, or herbal, antifungals have garnered considerable attention due to their diverse mechanisms of action and potential for fewer side effects. This analysis delves into a comparative examination of herbal antifungals against conventional drugs, including azoles,

polyphenol-based antifungals, and combination therapies.

### 1. Azoles vs. Herbal Antifungals:

Azoles, including fluconazole, ketoconazole, and clotrimazole, function by inhibiting ergosterol biosynthesis, a crucial component of the fungal cell membrane. By targeting lanosterol 14 $\alpha$ -demethylase, these drugs disrupt membrane integrity, leading to fungal cell death. While initially effective, the prolonged and often indiscriminate use of azoles has resulted in the rapid development of resistance, particularly in *Candida* species. Mechanisms of resistance include mutations in the target enzyme, increased efflux pump activity (pumping the drug out of the cell), and biofilm formation. This resistance greatly limits the clinical use of azoles. It often leads to treatment failure and forces the use of more toxic and expensive second-line antifungal agents<sup>9-11</sup>.

Herbal antifungals, however, often use multiple action mechanisms to target various aspects of fungal physiology. This approach can make it harder for fungi to develop resistance. Some notable examples include:

- **Turmeric (*Curcuma longa*):** Curcumin, the active compound in turmeric, exhibits antifungal activity by disrupting fungal cell membranes, interfering with cell signaling pathways, and inhibiting biofilm formation. They also have strong anti-inflammatory and antioxidant properties that can help the body fight fungal infections.
- **Neem (*Azadirachta indica*):** Neem extracts, which are rich in azadirachtin and other bioactive compounds, show antifungal activity through various mechanisms. These include disrupting fungal cell membranes, inhibiting biofilm formation, and interfering with fungal adhesion to host tissues. Neem also has immune-modulating effects that improve the host's immune response to infection.
- **Garlic (*Allium sativum*):** Allicin, the compound that gives garlic its distinctive odor, has broad-

spectrum antimicrobial activity, including antifungal effects. It disrupts fungal cell membranes, inhibits essential enzymes, and interferes with fungal growth and reproduction.

- **Other Examples:** Many other herbs also show antifungal potential. *Ficus racemosa*, *Argemone mexicana*, *Smilax zeylanica*, *Sonchus asper*, *Lantana camara*, *Moringa oleifera*, and *Bauhinia vahlii* (kaempferol, rutin) contain flavonoids and polyphenols that disrupt how fungi adapt to stress, bind to fungal proteins, and modulate the host's immune response. Unlike azoles, which mainly target a single enzyme, herbal antifungals often attack multiple pathways, reducing the chances of resistance development. Furthermore, the immunomodulatory effects of many herbal extracts can synergize with their direct antifungal activity, boosting the host's ability to clear the infection.

### 2. Polyphenol-Based Antifungals vs. Herbal Compounds:

Polyphenols, a diverse group of plant-derived compounds, including flavonoids, tannins, and phenolic acids, have demonstrated significant antimicrobial properties, including antifungal activity. Synthetic or semi-synthetic polyphenol-based drugs, such as resveratrol, catechins (from green tea), and quercetin, have shown promise in preclinical studies. These compounds often target fungal stress response pathways, disrupting their ability to adapt to adverse conditions and survive<sup>11</sup>.

Herbal extracts are rich sources of polyphenols, often containing a wider array of these compounds than single-molecule polyphenol drugs. This broader spectrum of polyphenols may contribute to a more diverse range of antifungal actions. For example:

- **Flavonoids:** These compounds, abundant in *Smilax zeylanica* and *Bauhinia vahlii*, can disrupt fungal cell membranes, inhibit essential enzymes, and interfere with fungal stress adaptation mechanisms and also block efflux pumps.

- **Tannins:** Found in *Ficus racemosa*, tannins can bind to fungal proteins, disrupting their function and inhibiting biofilm formation. They can also interfere with fungal cell wall synthesis.

- **Berberine:** Extracted from plants like *Argemone mexicana*, berberine exhibits antifungal activity by inhibiting fungal DNA replication and interfering with cell division. While synthetic polyphenol drugs provide targeted antifungal activity, herbal extracts offer a complex mix of these compounds. This complexity can lead to synergistic effects and a broader range of action.

### 3. Combined Azole and Polyphenol Therapy vs. Herbal Therapy:

Recognizing the limits of single-agent therapy and the rising problem of antifungal resistance, researchers have looked into combining azoles with other antifungal agents, including polyphenols. Several studies have shown encouraging results with these combinations:

- **Fluconazole + Curcumin:** Combining fluconazole with curcumin has been shown to enhance fungal membrane disruption and reduce fluconazole resistance in *Candida albicans*. Curcumin's ability to disrupt efflux pump activity can raise the intracellular concentration of fluconazole, making it more effective.
- **Ketoconazole + Quercetin:** This combination has shown better antifungal effectiveness against dermatophytes while lowering the toxicity linked to ketoconazole. Quercetin may enhance the antifungal activity of ketoconazole while reducing its side effects.
- **Itraconazole + EGCG (from green tea):** Combining itraconazole with EGCG has been found to improve antifungal penetration and disrupt biofilms. EGCG can prevent

biofilm formation, making fungi more vulnerable to itraconazole<sup>87-90</sup>.

These combination therapies aim to use the synergistic effects of different antifungal agents to enhance effectiveness and fight resistance. However, herbal antifungals often inherently have this combined approach in their complex phytochemical makeup. Neem, turmeric, and coconut oil, for instance, show multiple antifungal mechanisms, such as disrupting membranes, modulating immunity, and reducing oxidative stress. This natural multi-targeting ability of herbal extracts may provide an edge over synthetic drug combinations. It lowers the risk of resistance development and minimizes the chances of drug-drug interactions and added toxicity<sup>91-97</sup>.

### Challenges and Future Directions

The rise in drug-resistant fungal infections makes it necessary to explore alternative treatment options. Herbal antifungals have emerged as promising candidates. However, several significant challenges prevent their widespread use in mainstream medicine. One major challenge is standardization. Unlike synthetic drugs, herbal extracts are complex mixtures of bioactive compounds, and their concentrations can vary due to factors like species, climate, soil conditions, and extraction methods. This variability makes it difficult to determine dosages, conduct clinical research, and obtain regulatory approval, which limits their use in treatment. Furthermore, poor bioavailability and stability of many herbal compounds, such as curcumin (turmeric) and allicin (garlic), decrease their effectiveness. Better drug delivery systems, including Nano encapsulation and liposomal formulations, could improve absorption and efficacy. Another important limitation is the lack of large-scale clinical trials. Although in vitro and in vivo studies support antifungal activity, few randomized controlled trials have compared herbal antifungals to standard treatments. Without this evidence, medical professionals are reluctant to

recommend herbal therapies, and regulatory agencies have difficulty approving them. Additionally, regulatory barriers differ across countries, with herbal medicines often treated as supplements instead of pharmaceuticals, leading to inconsistent quality control. Future efforts should focus on standardized cultivation, improved extraction methods, and better analytical techniques (such as HPLC and mass spectrometry) to ensure consistent therapeutic effects. Nanotechnology approaches can boost bioavailability, while large-scale clinical trials are essential to confirm safety and efficacy. Investigating combinations of herbal compounds and pairing them with synthetic antifungals could improve effectiveness and limit resistance<sup>98-100</sup>. Addressing these challenges could make herbal antifungals safe, cost-effective, and sustainable alternatives to traditional treatments. This would offer hope in the battle against resistant fungal infections and enhance global healthcare outcomes.

## **Conclusion**

Fungal infections create a major challenge for public health. The growing resistance to standard antifungal drugs increases the need for new treatment options. Herbal antifungal agents from plants like Turmeric, Aloe Vera, Neem, Garlic, Coconut Oil, *Ficus racemosa*, *Argemone mexicana*, *Smilax zeylanica*, *Sonchus asper*, *Lantana camara*, *Moringa oleifera* and *Bauhinia vahlii* have shown strong antifungal effects against various fungal pathogens. These plant-based treatments work in several ways. They can disrupt fungal cell membranes, block ergosterol production, prevent fungal adhesion and biofilm formation, reduce oxidative stress, and boost immune responses. Despite the robust scientific support for these herbal agents, several challenges limit their broader use in clinics. Issues with standardization, difficulties with bioavailability, and

the absence of large-scale clinical trials are significant hurdles that must be overcome. Developing new drug delivery methods, like nano-formulations and enhanced extracts, could help increase the stability and absorption of these natural compounds. Additionally, combining traditional knowledge with modern drug research can lead to the creation of effective antifungal formulations that have fewer side effects.

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