Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Forensic and Community Medicine

Journal homepage: www.ijfcm.org

Review Article

A harnessing herbal oils for fungal infections: From superficial to systemic challenges

Anand Singh Chouhan[1], Vinay Jain[1*], Vinita Kushwah[2], Jogendra Kushwah[2], Poonam Yadav[2]

[1]Shri Ram College of Pharmacy, Banmore, Madhya Pradesh, India
[2]Shivnath Singh College, Gwalior, Madhya Pradesh, India

Abstract

Fungal infections, or mycoses, pose a significant global health challenge, ranging from superficial skin conditions to life-threatening systemic diseases. The increasing prevalence of these infections is driven by factors such as rising immunosuppressive conditions and environmental changes. Current antifungal treatments face limitations, including drug resistance and toxicity, underscoring the urgent need for novel therapeutic strategies. This review explores fungal infections comprehensively, discussing their types, etiology, mechanisms of pathogenesis, and the challenges posed by antifungal resistance.
Herbal oils, derived from plants such as neem, coconut, and lavender, hold promise as alternative or adjunct therapies due to their potent antifungal properties and mechanisms of action. However, integrating these oils into clinical practice is not without challenges, particularly in standardization and clinical validation. This review emphasizes the potential of combining traditional remedies with modern medicine to address fungal diseases effectively. Future directions include advancing research on herbal formulations and overcoming hurdles to develop innovative therapeutic strategies that mitigate the growing burden of fungal infections.

Keywords: Fungal infections, Antifungal resistance, Herbal oils, Neem oil, Coconut oil, Lavender oil, Alternative therapies, Pathogenesis, Clinical validation, Bioactive compounds.

Received: 13-11-2024; **Accepted:** 18-12-2024; **Available Online**: 18-03-2025

1. Introduction

Fungal activity refers to the biological processes carried out by fungi, which are a diverse group of eukaryotic organisms that play crucial roles in ecosystems, industries, and human health. Fungi contribute to nutrient cycling by decomposing organic matter, forming symbiotic associations with plants, and participating in various ecological functions.[1] However, some fungi are pathogenic and can cause infections in humans, animals, and plants, leading to significant health and economic challenges.[2]

The image depicted as **Figure 1** provides a detailed visual representation of fungal infections, highlighting the characteristic manifestations on human tissue. It illustrates the typical lesions caused by various fungal pathogens, ranging from superficial dermatophytic infections to more invasive forms like candidiasis or aspergillosis.[14,22] Such visuals are instrumental in understanding the morphological features of these infections, aiding in their diagnosis and differentiation from other skin conditions. This figure underscores the diversity in clinical presentations, emphasizing the importance of accurate identification and timely therapeutic interventions.

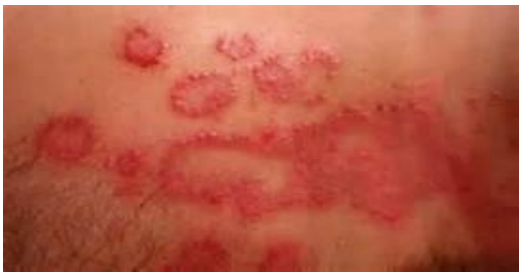

Figure 1: Fungal infection phase on skin

*Corresponding author: Vinay Jain
Email: chouhananand61@gmail.com

https://doi.org/10.18231/j.ijfcm.2025.003

Pathogenic fungi such as *Candida albicans*, *Aspergillusfumigatus*, and *Cryptococcus neoformans* are responsible for a range of infections, particularly in immunocompromised individuals. These infections, known as mycoses, can be superficial, such as dermatophytosis, or systemic, such as invasive aspergillosis, which often leads to high morbidity and mortality rates.[3,4] The severity of fungal infections is exacerbated by the emergence of drug-resistant strains and the limited arsenal of effective antifungal agents.[5]

In addition to their pathogenic roles, fungi have significant industrial and pharmaceutical applications. They are sources of antibiotics (e.g., penicillin), immunosuppressants (e.g., cyclosporine), and bioactive compounds used in medicine and agriculture.[6] Moreover, fungal enzymes, such as cellulases and amylases, are widely utilized in biotechnological processes.[7]

Understanding fungal activity, including their metabolic pathways and mechanisms of interaction with hosts, is critical for developing novel antifungal agents and enhancing their industrial utility. Research into fungal genomics and metabolomics has opened new avenues for exploiting fungi in diverse fields while addressing the challenges posed by fungal pathogens.[8,9]

Advancements in antifungal therapies, such as combination treatments and nanotechnology-based delivery systems, have shown promise in overcoming resistance and enhancing efficacy. Additionally, exploring natural products and plant-based compounds for antifungal activity has gained attention as a sustainable approach to managing fungal infections.

Fungal infections pose a significant challenge to human health, especially among immunocompromised individuals such as those with HIV/AIDS, cancer patients undergoing chemotherapy, and organ transplant recipients. Fungi, as eukaryotic organisms, share several cellular mechanisms with humans, which makes targeting fungal cells without affecting host cells a challenge. This difficulty has driven the evolution of antifungal treatments over the years, leading to more targeted and safer therapies. Illustrates the visible effects of fungal infection on human skin. The lesions depicted are indicative of fungal invasion, characterized by redness, scaling, inflammation, or discoloration depending on the type of fungal pathogen involved. This figure highlights the localized impact of dermatophytic fungi, which often target keratinized tissues such as the skin, hair, and nails. The visual representation underscores the importance of recognizing such presentations for early diagnosis and the prevention of further spread or complications.[12]

2. Historical of Antifungal Infection

The history of antifungal treatments dates back to ancient times, where herbal remedies were often used to treat superficial fungal infections. Traditional medicine systems such as Ayurveda, Traditional Chinese Medicine, and ancient Egyptian practices utilized plant extracts for skin and nail infections. However, the formal understanding of fungal infections and their specific treatment began in the 19th century with the advent of microbiology.[31]

1. 19th century discoveries: In the 1800s, scientists like Anton de Bary and Robert Koch made significant contributions to understanding fungal pathogens, identifying the roles of fungi in diseases such as dermatophytosis. The discovery of fungal pathogens paved the way for the need to develop specific antifungal agents.[31,32]
2. Introduction of iodine and topical agents: The use of iodine, sulfur compounds, and topical agents like salicylic acid for the treatment of fungal infections became common in the late 19th and early 20th centuries.[36] These agents, though effective for superficial infections, lacked systemic efficacy.
3. Breakthrough with antibiotics and the first systemic antifungals: The discovery of antibiotics in the mid-20th century led to a revolution in the treatment of microbial infections, including fungi. In 1950, the discovery of the first systemic antifungal agent, *amphotericin B*, marked a turning point in antifungal therapy.
    a. Amphotericin B: The first systemic antifungal agent: Amphotericin B, derived from *Streptomyces nodosus*, was introduced in the 1950s and became the gold standard for treating severe systemic mycoses, including cryptococcal meningitis, histoplasmosis, and aspergillosis. Despite its potency, amphotericin B has significant nephrotoxicity, leading to the development of lipid formulations that reduce its adverse effects.
    b. Introduction of Azoles in the 1960s: The 1960s and 1970s saw the introduction of the azole class of antifungals, with clotrimazole and miconazole being among the first. These drugs, working by inhibiting the fungal enzyme *lanosterol 14-alpha-demethylase*, hinder ergosterol synthesis, which is essential for fungal cell membrane integrity. The azole class brought a safer alternative for treating systemic and superficial infections compared to amphotericin B.
4. Evolution of antifungal classes**:** The late 20th century witnessed the development of several new classes of antifungal drugs, each targeting different aspects of fungal cell physiology.
    a. Triazoles: The second generation of azoles, known as triazoles (e.g., fluconazole, itraconazole, voriconazole), offered improved safety profiles and efficacy. Fluconazole, introduced in the late 1980s, became a cornerstone for the treatment of *Candida* infections due to its ability to achieve high concentrations in the cerebrospinal fluid, making it effective against fungal meningitis. Voriconazole further expanded the antifungal

arsenal with its activity against *Aspergillus* species.

b. Echinocandins: Echinocandins (e.g., caspofungin, micafungin, anidulafungin) represent a newer class of antifungals that inhibit the synthesis of *β-(1,3)-D-glucan*, a critical component of the fungal cell wall. Introduced in the early 2000s, they are particularly effective against invasive candidiasis and provide an alternative for azole-resistant infections. Echinocandins have a favorable safety profile but limited oral bioavailability, restricting their use to intravenous administration.

Fungal infections, or mycoses, can affect various parts of the human body and range in severity from superficial, localized infections to systemic infections that can be life-threatening. The classification of fungal infections is based on the depth of the infection and the type of fungi involved. Here's a detailed overview of the types of fungal infections:

2.1. Superficial mycoses

Superficial fungal infections are limited to the outermost layers of the skin, hair, and nails. They are usually not life-threatening and primarily cause cosmetic concerns. They are more common in tropical climates.

2.1.1. Examples

1. *Tineaversicolor (Pityriasisversicolor)*: Caused by the *Malassezia* species, it leads to discolored patches on the skin, usually on the chest, back, and upper arms.
2. *Tineanigra*: A rare infection caused by *Hortaeawerneckii*, characterized by dark patches on the palms or soles.
3. *White piedra and black piedra*: These are infections of the hair shaft caused by fungi like *Trichosporon* (white piedra) and *Piedraiahortae* (black piedra).

2.1.2. Symptoms

1. Discolored patches or spots on the skin.
2. Mild itching or scaling.
3. Cosmetic changes to the hair shaft.

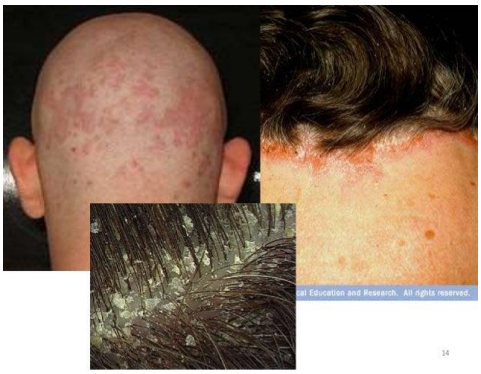

Figure 2: Superficial and cutaneous fungal infection

Presented as **Figure 2** demonstrates the clinical manifestations of superficial and cutaneous fungal infections on human skin. These infections, often caused by dermatophytes, Candida species, or Malassezia, are restricted to the outer layers of the skin, hair, and nails. The figure highlights common symptoms such as erythema, scaling, itching, and occasional vesicle formation. Such visual evidence is critical for identifying the characteristic patterns of superficial fungal infections, such as ringworm (tinea), athlete's foot, or candidiasis. This depiction underscores the necessity for prompt clinical evaluation and targeted antifungal therapy to manage these conditions effectively.[8,9]

2.2. Cutaneous mycoses (Dermatophytoses)

Cutaneous fungal infections affect the keratinized tissues such as the skin, hair, and nails. These infections are often caused by dermatophytes, a group of fungi that can digest keratin.

2.2.1. Examples

1. *Tineapedis (Athlete's Foot)*: A common infection of the feet caused by *Trichophyton*, *Epidermophyton*, or *Microsporum* species. It leads to itching, scaling, and cracking of the skin between the toes.
2. *Tineacorporis (Ringworm)*: Appears as ring-shaped, red, scaly patches on the body. It can occur on the arms, legs, and trunk.
3. *Tineacruris (Jock Itch)*: Affects the groin area, causing itching, redness, and scaling.
4. *Tineacapitis*: Affects the scalp, leading to hair loss and scaly patches.
5. *Onychomycosis (Tineaunguium)*: Infection of the nails, leading to thickening, discoloration, and brittleness.

2.2.2. Symptoms

1. Itching, redness, and scaling of the affected areas.
2. Circular or ring-like patterns on the skin.
3. Thickened and discolored nails.

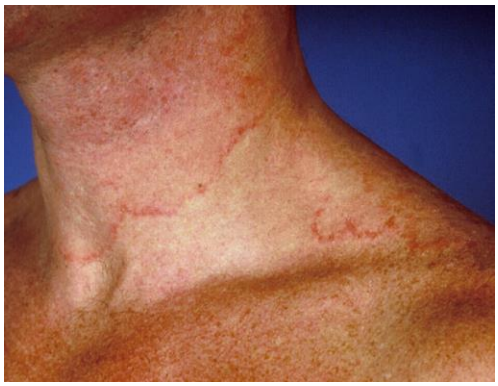

Figure 3: Cutaneous mycoses (Dermatophytoses)

Figure 3 illustrates the clinical presentation of cutaneous mycoses, a type of fungal infection that primarily affects the keratinized layers of the skin, hair, and nails. These infections, caused by dermatophytes such as *Trichophyton*, *Microsporum*, or *Epidermophyton* species, often lead to symptoms like redness, scaling, cracking, and itching.[20] The

figure showcases the hallmark signs of cutaneous mycoses, which may include annular lesions with central clearing or thickened, discolored nails in onychomycosis. This visual aids in understanding the pathophysiology and progression of fungal infections that extend beyond superficial layers, emphasizing the importance of early and effective treatment to prevent further complications.[24]

2.3. Subcutaneous mycoses

Subcutaneous fungal infections occur when fungi enter the skin or subcutaneous tissue through a wound or trauma. These infections are typically chronic and can cause significant localized damage if not treated.

2.3.1. Examples

1. *Sporotrichosis*: Also known as "rose gardener's disease," it is caused by *Sporothrixschenckii*. It typically starts as a small nodule at the site of injury (often from handling soil or plants) and can spread along the lymphatic vessels.
2. *Chromoblastomycosis*: A chronic infection caused by dematiaceous (pigmented) fungi such as *Fonsecaea*, *Phialophora*, and *Cladophialophora*. It presents as verrucous (warty) skin lesions.

2.3.2. Symptoms

1. Development of nodules or ulcers at the site of inoculation.
2. Formation of pus-filled lesions or abscesses.
3. Chronic swelling and fibrosis of the affected area.

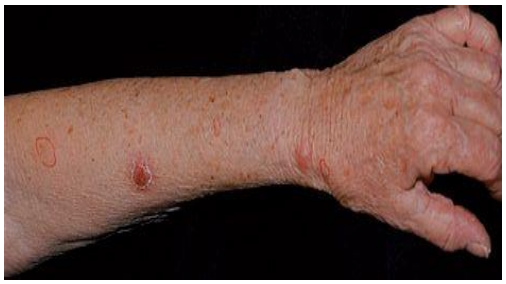

Figure 4: Subcutaneous mycoses

Figure 4 depicts the clinical manifestations of subcutaneous mycoses, a deeper fungal infection involving the dermis, subcutaneous tissues, and sometimes the underlying muscles and bones. These infections often arise following traumatic implantation of fungal spores into the skin. Common pathogens include *Sporothrixschenckii* (causing sporotrichosis), dematiaceous fungi (causing chromoblastomycosis), and *Madurella* species (causing mycetoma). The image highlights characteristic signs such as nodular lesions, ulceration, and localized swelling. Such visual representations are crucial in understanding the chronic nature and progressive tissue damage associated with subcutaneous mycoses, underscoring the need for precise diagnosis and prolonged antifungal or surgical management.[12,13]

2.4. Systemic mycoses (Endemic Mycoses)

Systemic fungal infections can affect internal organs and are usually caused by fungi that are capable of surviving and proliferating at body temperature. These infections often begin in the lungs after inhalation of fungal spores and can disseminate throughout the body. Systemic mycoses are more serious and can be life-threatening, especially in immunocompromised individuals.

2.4.1. Examples

1. *Histoplasmosis*: Caused by *Histoplasmacapsulatum*, it is found in soil contaminated with bird or bat droppings. It primarily affects the lungs, leading to respiratory symptoms.
2. *Blastomycosis*: Caused by *Blastomycesdermatitidis*, it is prevalent in North America and can cause lung infections that may disseminate to the skin and bones.
3. *Coccidioidomycosis (Valley Fever)*: Caused by *Coccidioidesimmitis* and *Coccidioidesposadasii*, it is endemic to arid regions of the Americas. It can cause flu-like symptoms and, in severe cases, spread to other organs like the bones, skin, and central nervous system.
4. *Paracoccidioidomycosis*: Caused by *Paracoccidioidesbrasiliensis*, this infection is endemic in South America and can cause chronic lung infections and mucosal lesions.

2.4.2. Symptoms

1. Flu-like symptoms such as fever, cough, and fatigue.
2. Dissemination to other organs can cause symptoms related to the affected areas, such as skin lesions or bone pain.[35]
3. Chronic infections can mimic tuberculosis or other chronic respiratory diseases.

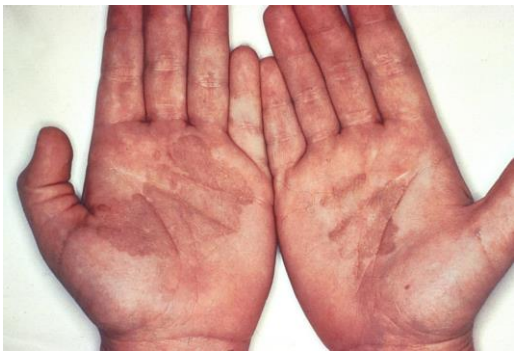

Figure 5: Systemic mycoses (Endemic Mycoses)

Systemic mycoses are severe fungal infections that affect internal organs and tissues, posing a significant threat to immunocompromised individuals. These infections are often caused by opportunistic fungi such as *Aspergillus*, *Candida*, and *Cryptococcus* species. The impact of delayed diagnosis is profound, leading to increased mortality rates due to the rapid progression of the disease and the often limited treatment window. Early and accurate diagnosis, coupled with timely intervention, is critical to improving patient

outcomes in cases of systemic mycoses. The pathological manifestations of systemic mycoses showing in **Figure 5**, also known as endemic mycoses, which involve deep-seated infections affecting multiple organ systems. These infections are typically caused by dimorphic fungi such as *Histoplasmacapsulatum*, *Blastomycesdermatitidis*, *Coccidioidesimmitis*, and *Paracoccidioidesbrasiliensis.*[25] The figure highlights the disseminated nature of the infection, with signs of granuloma formation, tissue necrosis, or pulmonary involvement, depending on the fungal species and host immune status. Systemic mycoses primarily affect immunocompromised individuals or those exposed to endemic fungal regions. This visual underscores the clinical severity and diagnostic complexity of systemic fungal infections, emphasizing the need for timely antifungal treatment and supportive care.

2.5. Opportunistic mycoses

Opportunistic fungal infections occur primarily in individuals with weakened immune systems, such as those with HIV/AIDS, cancer, or those taking immunosuppressive drugs. These infections can be severe and difficult to treat due to the patient's compromised immune response.

2.5.1. Examples

1. *Candidiasis*: Caused by *Candida* species, especially *Candida albicans*, it can range from superficial infections like oral thrush and vaginal yeast infections to systemic infections (candidemia) in immunocompromised patients.
2. *Aspergillosis*: Caused by *Aspergillus* species, it commonly affects the lungs but can spread to the sinuses, brain, and other organs. Invasive aspergillosis is a major concern in patients with weakened immune systems.
3. *Cryptococcosis*: Caused by *Cryptococcus neoformans* and *Cryptococcus gattii*, this infection often affects the lungs and can spread to the brain, leading to cryptococcal meningitis in immunocompromised patients.
4. *Mucormycosis*: Caused by fungi from the order *Mucorales* (e.g., *Rhizopus*), it is a rapidly progressing infection that affects the sinuses, brain, and lungs. It is particularly dangerous in patients with uncontrolled diabetes or those receiving corticosteroid therapy.

2.5.2. Symptoms

1. Symptoms vary widely depending on the organ affected but often include fever, cough, chest pain, headache, and neurological symptoms.
2. Skin lesions, abscesses, or tissue necrosis can occur with cutaneous or disseminated forms.
3. Mucormycosis often presents with tissue destruction in the affected area, like black eschar in the nasal cavity or palate.

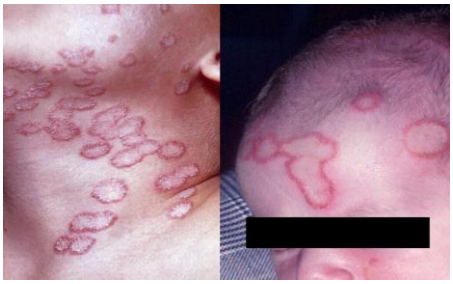

Figure 6: Opportunistic mycoses

Demonstrates the clinical presentation of opportunistic mycoses, a category of fungal infections that predominantly affect Show in **Figure 6** immunocompromised individuals. Common causative agents include *Candida* species (causing candidiasis), *Aspergillus* species (causing aspergillosis), *Cryptococcus neoformans* (causing cryptococcosis), and *Mucorales* (causing mucormycosis). The image highlights the diverse manifestations of opportunistic mycoses, such as mucosal involvement, pulmonary lesions, or invasive dissemination to vital organs. These infections often arise in patients with underlying conditions like HIV/AIDS, diabetes, malignancies, or those receiving immunosuppressive therapy. The figure emphasizes the critical importance of early recognition, laboratory diagnosis, and aggressive antifungal treatment to mitigate high morbidity and mortality associated with these infections.

3. Emerging Fungal Infections

Emerging fungal pathogens have become a growing concern, especially with the rise of antifungal resistance and climate change contributing to the spread of certain fungi to new regions.

3.1. Examples

1. *Candida auris*: This is a multidrug-resistant *Candida* species that has emerged as a global health threat. It can cause bloodstream infections with a high mortality rate and is resistant to many common antifungals.
2. *Fusariosis*: Caused by *Fusarium* species, it affects immunocompromised patients and can present as keratitis, sinus infections, or disseminated disease.
3. *Scedosporiosis*: Caused by *Scedosporium* species, these infections can be difficult to treat due to intrinsic resistance to many antifungals and often occur in patients with lung disease or after near-drowning incidents.

3.2. Challenges

1. Multidrug resistance makes treatment difficult.
2. The ability of some fungi to survive at higher temperatures raises concerns about their adaptation to human hosts.

Figure 7: Emerging fungal infections

3.3. Pathophysiology of fungal infection

Fungal infections, or mycoses, arise when pathogenic fungi breach host defenses and establish infection in tissues. The pathophysiology of fungal infections is complex and involves several stages, including fungal adhesion, invasion, immune evasion, and tissue damage. These infections can be superficial, affecting in **Figure 7** the skin and mucous membranes, or systemic, invading deeper tissues and organs, particularly in immunocompromised individuals.[10]

1. *Adhesion and colonization:* The pathogenesis begins with the adherence of fungal cells to host tissues. Fungi utilize adhesins, specialized surface proteins, to attach to host cells and extracellular matrix components like fibronectin and laminin.[11] For example, Candida albicans uses adhesins such as Als proteins to colonize mucosal surfaces.
2. Invasion and tissue damage: After adhesion, fungi invade host tissues either by enzymatic degradation or by morphogenesis. Many pathogenic fungi secrete hydrolytic enzymes, such as proteases and phospholipases, to break down host cell barriers and facilitate invasion.[12] Dimorphic fungi like *C. albicans* undergo a morphological switch between yeast and hyphal forms, enhancing their invasive potential.[13]
3. Immune evasion: Fungi employ various strategies to evade the host immune response. They can mask their surface antigens, produce immune-modulatory molecules, and suppress the production of pro-inflammatory cytokines. For instance, Cryptococcus neoformans produces a polysaccharide capsule that inhibits phagocytosis. Similarly, Aspergillusfumigatus releases gliotoxin, which suppresses immune cell functions.[14]
4. Host immune response: The immune system plays a critical role in controlling fungal infections. Innate immunity, particularly through pattern recognition receptors like Toll-like receptors (TLRs) and C-type lectin receptors (CLRs), recognizes fungal components such as β-glucans and chitin.[15] However, when the immune system is compromised due to conditions like HIV/AIDS or immunosuppressive therapies, the risk of systemic fungal infections increases significantly.
5. Tissue damage and disease manifestation: Fungal infections often cause tissue damage through direct invasion and the release of fungal toxins. For example, aflatoxins produced by *Aspergillusflavus* are hepatotoxic and carcinogenic. The inflammatory response of the host also contributes to tissue damage, leading to symptoms such as redness, swelling, and necrosis.[16]
6. Chronic and systemic infections: In systemic infections, fungi like *Candida* and *Aspergillus* spread via the bloodstream, causing sepsis and organ failure. The persistence of fungal infections can lead to chronic conditions, characterized by granuloma formation and fibrosis.[17]
7. Advances in understanding pathophysiology: Recent research highlights the role of fungal biofilms in infection persistence and resistance to antifungal treatments. Biofilms, complex communities of fungal cells embedded in an extracellular matrix, protect fungi from immune attacks and drug penetration, complicating treatment outcomes.[18]

3.4. Etiology of fungal infections

The etiology of fungal infections encompasses a wide variety of factors, including environmental exposure, host-related conditions, and fungal virulence traits. These infections can be caused by opportunistic or primary pathogenic fungi, depending on the host's immune status and the pathogen's characteristics.[17]

3.4.1. Environmental factors

Environmental exposure to fungal spores is a major cause of fungal infections. Fungi are ubiquitous in nature, with soil, decaying vegetation, and water serving as primary reservoirs. Species like Aspergillus and Cryptococcus are commonly found in soil, while Candida is part of the normal human microbiota but can become pathogenic under certain conditions.[18]

3.4.2. Opportunistic pathogens

Opportunistic fungal infections arise in immunocompromised individuals, such as those undergoing chemotherapy, organ transplants, or HIV/AIDS patients. Common opportunistic pathogens include *Candida albicans*, *Aspergillusfumigatus*, and *Cryptococcus neoformans*. These fungi exploit weakened immune defenses, leading to systemic infections.[19] The environmental mechanism of fungal infection, highlighting the process by which fungi from natural habitats invade human hosts. Many fungal pathogens, such as *Aspergillus*, *Histoplasma*, and *Coccidioides*, originate in soil, decaying vegetation, bird droppings, or other organic matter. The figure demonstrates key pathways of exposure, including inhalation of fungal spores, direct contact with contaminated surfaces, or traumatic implantation of fungal elements into the skin.[23] This mechanism underscores the role of environmental factors, such as spore density, climate, and human activities, in the epidemiology of fungal infections. The image emphasizes the transition from environmental saprophytism to human pathogenicity, influenced by host susceptibility and immune response. This depiction is crucial in understanding preventive measures and the ecological context of fungal diseases.

Table 1: Comparative pathophysiology of major fungal pathogens: Adhesion, invasion, immune evasion, and tissue damage mechanisms

Pathogen	Adhesion Mechanisms	Invasion Mechanisms	Immune Evasion Strategies	Tissue Damage Mechanisms
Candida spp.	Adhesins (e.g., Als proteins, Hwp1) bind to host epithelial and endothelial cells.[37]	Hyphal formation allows penetration into tissues.	Produces enzymes (e.g., secreted aspartyl proteases) to degrade host defenses; shields with biofilms.[44]	Secretes hydrolytic enzymes (e.g., proteases, lipases) causing tissue destruction.[39]
Aspergillus spp.	Surface proteins (e.g., AspF2) mediate binding to epithelial cells and extracellular matrix (ECM).[43]	Hyphal growth and production of enzymes (e.g., proteases) degrade host barriers.[41]	Produces gliotoxin, which inhibits immune cell activation and induces apoptosis.[41]	Hyphal growth mechanically disrupts tissues; secretes mycotoxins.
Cryptococcus spp.	Capsule components bind to host cells and ECM.[40]	Produces urease to cross the blood-brain barrier (BBB).	Capsule resists phagocytosis; melanin production neutralizes oxidative stress.	Produces laccase and enzymes, leading to tissue necrosis.
Histoplasmacapsulatum	Binds to macrophages via surface receptors (e.g., HSP60).	Survives within macrophages and disseminates through the bloodstream.[45]	Modifies phagosome to avoid fusion with lysosomes; suppresses immune response.	Causes granulomatous inflammation and tissue destruction.
Pneumocystis jirovecii	Glycoprotein-rich surface binds to alveolar epithelial cells.	Lacks active tissue invasion but adheres tightly to alveoli, causing inflammation.	Evades immune response by altering surface glycoproteins; produces extracellular vesicles.[38]	Induces inflammation, leading to alveolar damage.

Table 1 provides a comparative analysis of the key pathophysiological mechanisms employed by major fungal pathogens, including *Candida*, *Aspergillus*, *Cryptococcus*, *Histoplasma*, and *Pneumocystis*. It highlights their distinct strategies for adhesion, invasion, immune evasion, and tissue damage, which contribute to their virulence and pathogenicity. Understanding these mechanisms is crucial for developing targeted antifungal therapies and mitigating the challenges of resistance and disease progression. This comparison underscores the complexity of fungal infections and the need for comprehensive therapeutic approaches.

3.4.3. Opportunistic pathogens

Opportunistic fungal infections arise in immunocompromised individuals, such as those undergoing chemotherapy, organ transplants, or HIV/AIDS patients. Common opportunistic pathogens include *Candida albicans*, *Aspergillusfumigatus*, and *Cryptococcus neoformans*. These fungi exploit weakened immune defenses, leading to systemic infections.[19] The environmental mechanism of fungal infection, highlighting **Figure 8** the process by which fungi from natural habitats invade human hosts. Many fungal pathogens, such as *Aspergillus*, *Histoplasma*, and *Coccidioides*, originate in soil, decaying vegetation, bird droppings, or other organic matter. The figure demonstrates key pathways of exposure, including inhalation of fungal spores, direct contact with contaminated surfaces, or traumatic implantation of fungal elements into the skin.[23] This mechanism underscores the role of environmental factors, such as spore density, climate, and human activities, in the epidemiology of fungal infections. The image emphasizes the transition from environmental saprophytism to human pathogenicity, influenced by host susceptibility and immune response. This depiction is crucial in understanding preventive measures and the ecological context of fungal diseases.[26]

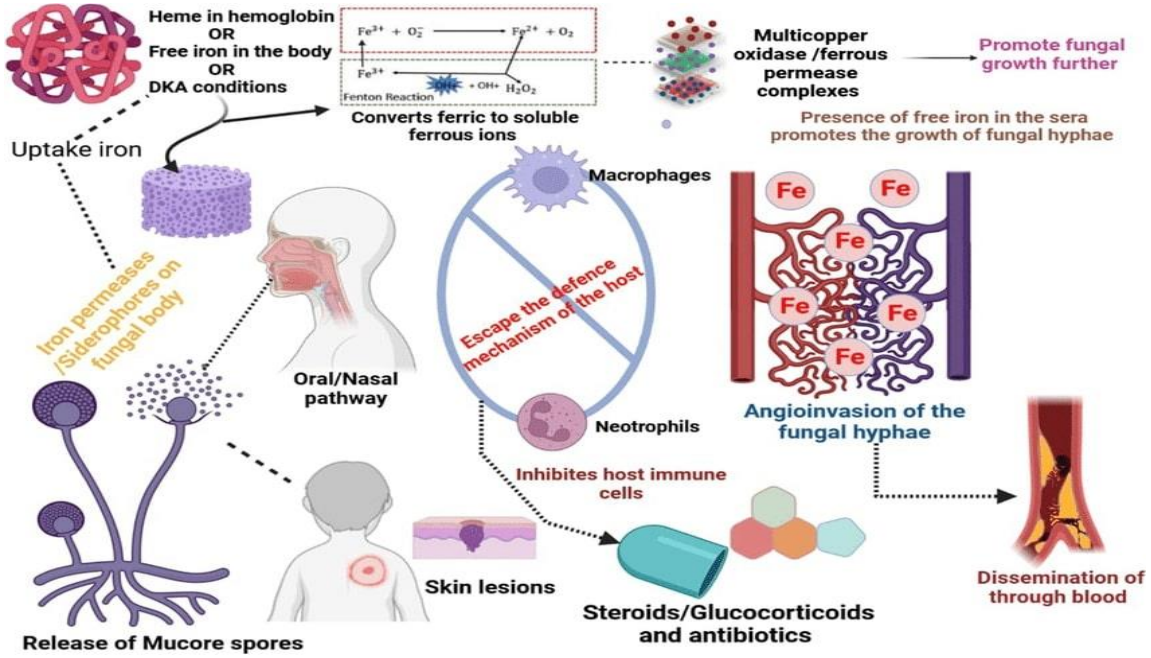

Figure 8: Mechanism of infection environmental

3.4.4. Primary pathogenic fungi

Primary pathogenic fungi can infect healthy individuals and are often endemic to specific geographic regions. Examples include *Histoplasmacapsulatum*, *Blastomycesdermatitidis*, and *Coccidioidesimmitis*, which are known to cause respiratory and systemic infections through inhalation of fungal spores.[20]

3.4.5. Host-related factors

Several host-related factors increase susceptibility to fungal infections. These include underlying diseases like diabetes mellitus, prolonged antibiotic use, and the use of immunosuppressive drugs. Disruption of the skin or mucosal barriers through trauma or medical devices such as catheters also predisposes individuals to fungal infections.[21]

3.4.6. Fungal virulence factors

Fungal pathogens possess specific virulence factors that enable them to invade and survive within the host. These include the ability to form biofilms, produce hydrolytic enzymes, and evade the immune response. For instance, Candida albicans can switch between yeast and hyphal forms, enhancing its pathogenicity.[22]

3.4.7. Climate and geographic influence

The distribution of fungal infections is influenced by climatic and geographic factors. Tropical and subtropical regions, with warm and humid climates, are hotspots for fungal diseases. For example, *Histoplasma* infections are prevalent in the Ohio and Mississippi River valleys in the United States.[23]

3.4.8. Advances in understanding etiology

Recent studies emphasize the role of microbiota imbalance (dysbiosis) in fungal infections, particularly in conditions like candidiasis. Dysbiosis leads to the overgrowth of pathogenic fungi, disrupting the microbial community's balance.[24] Additionally, genetic predispositions, such as mutations in immune-related genes, have been linked to increased susceptibility to fungal diseases.[25]

3.5. Treatments for fungal infections

The treatment of fungal infections involves antifungal agents, which can be broadly categorized into systemic and topical therapies. The choice of treatment depends on the type of fungal infection, its severity, and the patient's overall health condition. Recently, natural and herbal therapies have gained attention due to their reduced side effects and emerging resistance to synthetic antifungal agents.[27]

3.5.1. Conventional antifungal agents

1. Polyenes: Polyenes, such as Amphotericin B, bind to ergosterol in fungal cell membranes, causing membrane disruption and cell death. Although highly effective, Amphotericin B is associated with significant nephrotoxicity.
2. Azoles: Azoles, including fluconazole, itraconazole, and voriconazole, inhibit the synthesis of ergosterol, a critical component of fungal cell membranes. These are widely used for treating systemic and superficial infections.
3. Echinocandins: Echinocandins, such as caspofungin and micafungin, inhibit β-glucan synthase, disrupting fungal cell wall integrity. They are effective against *Candida* and *Aspergillus* species but are less active against other fungi.

4. Allylami: Allylamines like terbinafine target squaleneepoxidase, an enzyme essential for ergosterol synthesis. They are particularly effective in treating dermatophytic infections.[28]
5. Flucytosine: Flucytosine, a pyrimidine analog, inhibits fungal DNA and RNA synthesis. It is often used in combination with Amphotericin B for treating cryptococcal meningitis.[29]

3.5.2. Adjunctive therapies

Adjunctive therapies, such as surgical debridement and immune modulation, may be necessary in severe cases. For example, granulocyte colony-stimulating factors (G-CSF) can enhance host defenses in immunocompromised patients.[30]

3.6. Herbal treatments for fungal infections

Herbal therapies have gained attention as an alternative or complementary treatment for fungal infections. Essential oils, in particular, possess antifungal properties due to their bioactive compounds, which target fungal membranes and enzymes.

1. Tea tree oil (Melaleucaalternifolia): Tea tree oil exhibits strong antifungal activity against dermatophytes, Candida species, and Malassezia spp. Terpinen-4-ol, the main active component, disrupts fungal cell membranes and inhibits ergosterol synthesis.[31]
2. Lavender oil (Lavandulaangustifolia): Lavender oil is effective against a range of fungal pathogens, including *Candida albicans* and *Aspergillus* spp. It contains linalool and linalyl acetate, which interfere with fungal cell membrane integrity and inhibit spore germination.[32]
3. Neem oil (Azadirachtaindica): Neem oil contains bioactive compounds like azadirachtin and nimbidin, which exhibit antifungal properties. Neem oil has been shown to inhibit the growth of dermatophytes and *Candida* species by targeting fungal enzymes.[33]
4. Coconut Oil (Cocosnucifera): Coconut oil is rich in medium-chain fatty acids like lauric acid, which exhibit antifungal activity. It disrupts fungal cell membranes and has been found effective in treating skin infections caused by *Candida* and dermatophytes.
5. Clove Oil (Syzygiumaromaticum): Clove oil, rich in eugenol, has demonstrated antifungal activity against *Candida albicans* and *Aspergillus* spp. Eugenol disrupts fungal membranes and inhibits enzyme activity, leading to cell death.
6. Oregano Oil (Origanumvulgare): Oregano oil contains carvacrol and thymol, which exhibit broad-spectrum antifungal activity. These compounds inhibit fungal growth by disrupting the membrane potential and causing oxidative stress.[34]
7. Eucalyptus Oil (Eucalyptus globulus): Eucalyptus oil has shown antifungal activity against *Candida albicans* and dermatophytes. Its primary component, 1, 8-cineole, disrupts fungal cell membranes and inhibits growth.
8. Thyme Oil (Thymus vulgaris): Thyme oil contains thymol and carvacrol, which exhibit strong antifungal activity. These compounds disrupt fungal cell membranes and inhibit enzyme activity, making thyme oil effective against a range of fungal pathogens.

4. Discussion

Fungal infections present a pressing global health issue, exacerbated by the increasing prevalence of immunosuppressive states and environmental changes. The growing challenge of antifungal resistance further complicates treatment strategies, underscoring the urgent need for alternative approaches. Conventional antifungal therapies, while effective, are often constrained by side effects, resistance, and high costs, particularly in resource-limited settings. Exploration of herbal oils, such as those derived from neem, coconut, and lavender, offers a promising alternative. These oils possess significant antifungal properties due to their bioactive compounds, including terpenes, phenols, and flavonoids, which disrupt fungal cell membranes and inhibit fungal growth. Integrating such natural remedies into therapeutic regimens could address some of the challenges posed by antifungal resistance while improving accessibility and affordability. However, despite the promising results demonstrated in in vitro studies, clinical trials validating the efficacy and safety of herbal oils remain limited. To establish their clinical applicability, future research should prioritize rigorous methodologies, such as double-blind, placebo-controlled randomized trials, to evaluate their therapeutic potential under standardized conditions. Additionally, studies focusing on dose optimization, long-term safety, pharmacokinetics, and efficacy against various fungal pathogens are essential. Comparative studies involving conventional antifungal drugs could further elucidate the relative advantages of herbal oils in diverse clinical scenarios. By bridging the gap between traditional remedies and modern medicine through robust scientific validation, herbal oils can emerge as a viable component of integrated antifungal treatment strategies, particularly in settings where conventional therapies face significant limitations.

5. Conclusion

Fungal infections, particularly those caused by antifungal-resistant strains, remain a significant global health challenge. While herbal oils such as neem, coconut, and lavender demonstrate promising antifungal properties, their clinical applicability requires further validation. Rigorous methodologies, including double-blind, placebo-controlled randomized trials, are essential to establish their efficacy, safety, and potential as adjunct or alternative therapies.

Addressing challenges such as standardization, variability in efficacy, and long-term safety will be critical to

integrating these natural remedies into mainstream antifungal treatment regimens. By combining traditional knowledge with modern scientific approaches, herbal oils could play a pivotal role in mitigating the global burden of fungal infections, particularly in resource-constrained settings.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Hawksworth DL, Lücking R. Fungal diversity revisited: 2.2 to 3.8 million species. *Microbiol Spectr.* 2017;5(4):1-17.
2. Brown D, Denning DW, Gow NAR, Levitz SM, Netea MG, White TC. Hidden killers: Human fungal infections. *Sci Transl Med*. 2012;4(165):165rv13.
3. Perfect JR, Bicanic T. Cryptococcosis diagnosis and treatment: what do we know now. *Fungal Genet Biol*. 2014;78:49–54.
4. Bongomin F, Gago S, Oladele RO, Denning DW. Global and multi-national prevalence of fungal diseases: Estimate precision. *J Fungi*. 2017;3(4):57.
5. Wiederhold NP. Antifungal resistance: Current trends and future strategies to combat. *Infect Drug Resist*. 2017:10:249–59
6. Demain AL, Sanchez S. Microbial drug discovery: 80 years of progress. *J Antibiot (Tokyo).* 2009;62(1):5–16.
7. Gupta VK, Kubicek CP, Berrin JG, Wilson DW, Couturier M, Berlin A, et al. Fungal enzymes for bio-products from sustainable and waste biomass. *Trends Biochem Sci.* 2016;41(7):633–45.
8. Brakhage AA. Regulation of fungal secondary metabolism. *Nat Rev Microbiol.* 2013;11(1):21–32.
9. Keller NP. Fungal secondary metabolism: Regulation, function, and drug discovery. *Nat Rev Microbiol.* 2019;17(3):167–80.
10. Calderone RA, Fonzi WA. Virulence factors of *Candida albicans*. *Trends Microbiol.* 2001;9(7):327–35.
11. Verstrepen KJ, Klis FM. Flocculation, adhesion, and biofilm formation in yeasts. *Mol Microbiol.* 2006;60(1):5-15.
12. Monod M, Capoccia S, Léchenne B, Zaugg C, Holdom M, Jousson O. Secreted proteases from pathogenic fungi. *Int J Med Microbiol.* 2002;292(5-6):405–19.
13. Sudbery PE. Growth of Candida albicans hyphae. *Nat Rev Microbiol.* 2011;9(10):737–48.
14. Kwon-Chung KJ, Sugui JA. What do we know about the role of gliotoxin in the pathobiology of *Aspergillus fumigatus*? *Med Mycol*. 2008;47(Suppl 1):S97–S103.
15. Romani L. Immunity to fungal infections. *Nat Rev Immunol.* 2011;11(4):275–88.
16. Amaike S, Keller NP. Aspergillus flavus. *Annu Rev Phytopathol.* 2011;49:107–33.
17. Lorenz MC. Host-microbe interactions: fungi. *Curr Opin Microbiol.* 2010;13(4):389–91.
18. Fanning S, Mitchell AP. Fungal biofilms. *PLoS Pathog.* 2012;8(4):e1002585.
19. Andes D, Nett J, Oschel P, Albrecht R, Marchillo K, Pitula A. Development and characterization of an in vivo central venous catheter Candida albicans biofilm model. *Infect Immun*. 2004;72(10):6023–31.
20. Chandra J, Kuhn DM, Mukherjee PK, Hoyer LL, McCormick T, Ghannoum MA. Biofilm formation by the fungal pathogen Candida albicans: Development, architecture, and drug resistance. *J Bacteriol.* 2001;183(18):5385–94.
21. Nett JE, Andes DR. Fungal biofilms: in vivo models for discovery of anti-biofilm drugs. *Microbiol Spectr*. 2015;3(3):E30.
22. Perfect JR. The impact of the host on fungal infections. *Am J Med.* 2012;125(1 Suppl):S39–51.
23. Casadevall A, Pirofski LA. The damage-response framework of microbial pathogenesis. *Nat Rev Microbiol.* 2003;1:17–24.
24. Denning DW, Bromley MJ. How to bolster the antifungal pipeline. *Science.* 2015;347(6229):1414–6.
25. Kauffman CA. Endemic mycoses: Blastomycosis, histoplasmosis, and sporotrichosis. *Infect Dis Clin North Am*. 2006;20(3):645–62.
26. Lionakis MS, Netea MG. Candida and host determinants of susceptibility to invasive candidiasis. *PLoS Pathog.* 2013;9(1):e1003079.
27. Mayer FL, Wilson D, Hube B. Candida albicans pathogenicity mechanisms. *Virulence*. 2013;4(2):119–28.
28. Gow NAR, Netea MG, Munro CA, Ferwerda G, Bates S, Mora-Montes HM, et al. Immune recognition of Candida albicans beta-glucan by dectin-1. *J Infect Dis*. 2007;196(10):1565–71.
29. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. *Clin Microbiol Rev.* 2007;20(1):133–63.
30. Groll AH, Gea-Banacloche JC, Glasmacher A, Just-Nuebling G, Maschmeyer G, Walsh TJ. Clinical pharmacology of antifungal compounds. *Infect Dis Clin North Am*. 2003;17(1):159–91.
31. Ghannoum MA, Rice LB. Antifungal agents: mode of action, mechanisms of resistance, and correlation of these mechanisms with bacterial resistance. *Clin Microbiol Rev*. 1999 Oct;12(4):501–17.
32. Denning DW. Echinocandin antifungal drugs. *Lancet.* 2003;362(9390):1142–51.
33. Ryder NS. Terbinafine: mode of action and properties of the squalene epoxidase inhibition. *Br J Dermatol*. 1992;126 Suppl 39:2–7.
34. Carson CF, Riley TV. Antimicrobial activity of the major components of the essential oil of Melaleuca alternifolia. *J Appl Bacteriol*. 1995;78(3):264–9.
35. Ogbolu DO, Oni AA, Daini OA, Oloko AP. In vitro antimicrobial properties of coconut oil on Candida species in Ibadan, Nigeria. *J Med Food*. 2007;10(2):384–7.
36. Bakkali F, Averbeck S, Averbeck D, Idaomar M. Biological effects of essential oils--a review. *Food Chem Toxicol*. 2008;46(2):446–75.
37. Naglik JR, Moyes DL, Wächtler B, Hube B. Candida albicans interactions with epithelial cells and mucosal immunity. *Microbes Infect*. 2011;13(12-13):963–76.
38. Gow NAR, Yadav B. Microbe Profile: Candida albicans: a shape-changing, opportunistic pathogenic fungus of humans. *Microbiology (Reading).* 2017;163(8):1145–7.
39. Calderone RA, Fonzi WA. Virulence factors of Candida albicans. *Trends Microbiol.* 2001;9(7):327–35.
40. Naglik JR, Challacombe SJ, Hube B. Candida albicans secreted aspartyl proteinases in virulence and pathogenesis. *Microbiol Mol Biol Rev*. 2003;67(3):400–28.
41. Latgé JP. Aspergillus fumigatus and aspergillosis. *Clin Microbiol Rev*. 1999;12(2):310–50.
42. Dagenais TRT, Keller NP. Pathogenesis of *Aspergillus fumigatus* in Invasive Aspergillosis. *Clin Microbiol Rev.* 2009;22(3):447–65.
43. Sugui JA, Pardo J, Chang YC, Zarember KA, Nardone G, Galvez EM, et al. Gliotoxin is a virulence factor of Aspergillus fumigatus: gliP deletion attenuates virulence in mice immunosuppressed with hydrocortisone. *Eukaryot Cell*. 2007;6(9):1562–9.
44. Kwon-Chung KJ, Sugui JA. *Aspergillus fumigatus*—What Makes the Species a Ubiquitous Human Fungal Pathogen? *PLoS Pathog.* 2013;9(12):e1003743.
45. Kozel TR, Wickes BL. Fungal diagnostics. *Cold Spring Harb Perspect Med*. 2014;4(4):a019299.

Cite this article: Chouhan AS, Jain V, Kushwah V, Kushwah J, Yadav P. Harnessing herbal oils for fungal infections: From superficial to systemic challenges. *Indian J Forensic Community Med*. 2025;12(1):9–18.