CURRENT PERSPECTIVES ON FUNGAL INFECTIONS: PATHOGENESIS, DIAGNOSIS AND HERBAL TREATMENT

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Abstract. Fungal infections, or mycoses, pose a significant global health concern affecting humans, animals, and plants. These infections can manifest as superficial, subcutaneous, or systemic, with millions of serious cases reported annually, resulting in substantial mortality rates worldwide. The rise in fungal infections is attributed to various factors, including social and medical advancements facilitating their spread. The pathogenesis of fungal infections involves complex interactions between fungal pathogens and the host's immune system. Fungi adhere to, invade, and evade immune responses, leading to tissue damage and disease progression. Compromised immunity, moist environments, and certain medications contribute to fungal infection development. Diagnosing fungal infections, particularly invasive ones, remains challenging. Conventional methods like histopathology and culture have limited sensitivity, prompting the development of newer techniques such as molecular and immunological assays to improve accuracy and timeliness. Herbal approaches to fungal infection treatment have gained attention due to limitations of conventional antifungal medications, including drug resistance. Traditional medicine has long utilized plant extracts for their medicinal properties, with research suggesting their potential efficacy against fungal infections. In summary, understanding pathogenesis, improving diagnostic methods, and exploring herbal treatment options are crucial for effectively managing fungal infections and addressing the challenges they pose in healthcare.
Keywords: *superficial, subcutaneous, histopathology, immunological assay*

Introduction

Fungal infections, commonly referred to as mycoses, are illnesses resulting from fungal pathogens that have the potential to impact a variety of tissues and organs in humans, animals, and plants (Groll et al., 2014). Presently, mycoses are being recognized more and more as a significant global health issue. There is a growing awareness of the considerable influence fungal pathogens have on plant and animal health. Indeed, a recent study highlighted the noteworthy and concerning effects of these pathogens on species extinction, food security, and ecosystem disruptions (Fisher et al., 2012). There are three primary categories of fungal infections: superficial, subcutaneous and systemic mycoses (*Figure 1*) (Hay, 2006), and this categorization helps in comprehending the varied expressions of fungal pathogens and outlining how they affect different tissues and organs in the human body (Brown et al., 2012). Various subclasses of fungal infections exist. Annually, over 150 million cases of severe fungal infections occur worldwide, resulting in approximately 1.7 million deaths each year. These numbers are on the rise due to various social and medical advancements in recent decades that have facilitated the spread of fungal infections (Kainz et al., 2020). Although the general occurrence of fungal infections is relatively minimal, there is a

discernible rise in the prevalence of persistent and recurrent fungal illnesses induced by both genuine and opportunistic pathogens. This pattern has been noted worldwide in both humans and animals over recent decades (Fisher et al., 2012). The contemporary way of living has broadened the scope of contact with fungi (Khan and Karuppayil, 2012). Evaluating the worldwide influence and dissemination patterns of fungal illnesses is essential. This comprehension allows us to pinpoint effective prevention strategies, develop dependable diagnostic techniques, and establish successful treatments (Vallabhaneni et al., 2016).

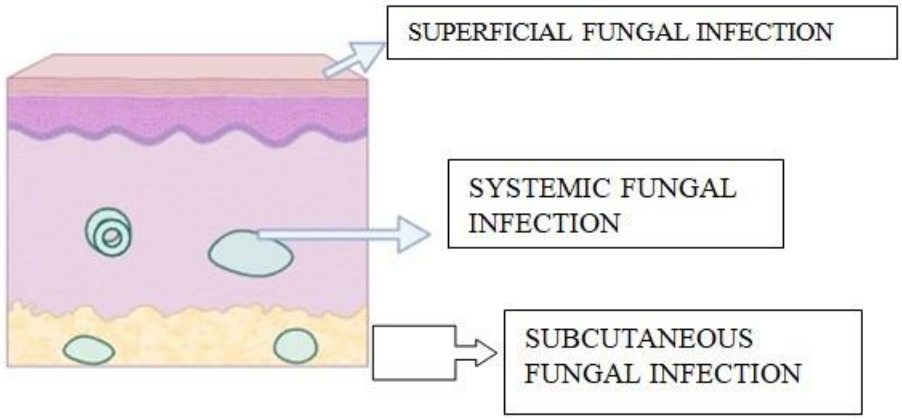

Figure 1. *Types of fungal infection.*

Discussion

A robust immune system is vital for protecting healthy individuals against fungal diseases, which can impact both those in good health and those with serious illnesses. Out of 1.5 million fungal species, only around three hundred can cause diseases in humans, and only a small number affect those who are healthy (Köhler et al., 2015). Despite the increase in fungal diseases, the limited availability of drugs and the emergence of drug resistance restrict treatment options (Polvi et al., 2015). The targeted therapeutic strategy relies on comprehension of the pathogenesis of fungal infections (Juvvadi et al., 2017). The emergence of fungal infections involves a complex interplay between the host's immune response and the virulence traits displayed by the fungi. Fungal pathogens typically bind to host tissues through adhesion molecules. For instance, Candida species utilize adhesins for binding to epithelial cells {Adhesion and Colonization} (Odds, 1988). Fungal hyphae or yeast forms can invade host tissues. Factors like hyphal formation and the secretion of enzymes, such as proteases and lipases, contribute to tissue penetration {Tissue Invasion} (Gow and Hube, 2012). Some Fungi have evolved mechanisms to evade the host immune system, such as the ability to switch between different morphological forms, antigenic variation, and the inhibition of phagocytosis {Immune Evasion} (Brown et al., 2012). The host response involves both innate and adaptive immunity. Phagocytic cells, such as macrophages and neutrophils, play a crucial role in clearing fungal infections Host immune response) (Romani, 2011). Dysregulation of the immune response can lead to immunopathology, contributing to the severity of fungal infections {immunopathology} (Lionakis and Netea, 2013). The main cause of fungal infections is the result of compromised immunity, Moist environments, compromised skin barriers, and certain medications can also contribute to

fungal infection development (Reddy et al., 2022). Additionally, several other causes for fungal infections related to human are there in which fungi can infect several major site of the body (*Figure 2*).

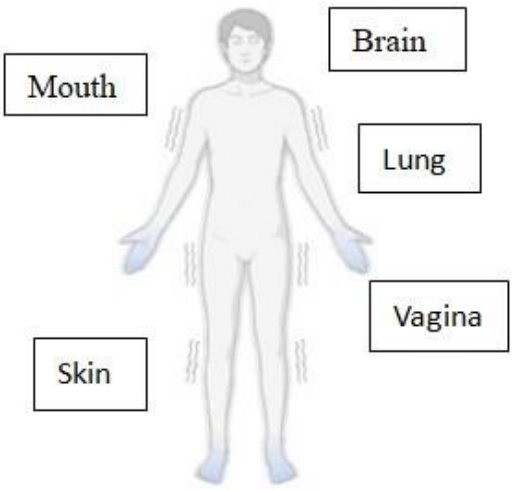

Figure 2. *Major site of fungal infection.*

The prevalence of invasive fungal infections has seen a significant rise in the last two decades (Alexander, 2002). When identifying fungal infections, doctors encounter a challenge when the patient has a weakened immune system. In such cases, many types of fungi can cause harm. Additionally, existing diagnostic methods may not always provide a conclusive diagnosis (Stevens, 2002). The current occurrence of invasive fungal infections varies, with rates ranging from 15% to 25% among bone marrow transplant recipients and from 5% to 42% in solid organ transplant recipients Given that Candida and Aspergillus contribute to over 80% of all fungal cases in both bone marrow and solid organ transplantation, this discourse will concentrate on advancements in diagnostic technology for detecting invasive candidiasis, aspergillosis and others (Viscoli and Castagnola, 1999; Paya, 1993). The EORTC (European Organization for Research and Treatment of Cancer)/Invasive Fungal Infections Cooperative Group and the MSG-ERC (Mycoses Study Group Education & Research Consortium) jointly devised definitions that encompass the diagnostic aspects of fungal infections at the clinical level. These definitions have proven highly beneficial for researchers engaged in epidemiological studies and diagnostic assays (Mendonca et al., 2022). There are various methods available for identifying pathogenic fungi, ranging from conventional fungal cultures to PCR-based techniques (De Pauw et al., 2008). Accurate diagnosis necessitates the identification of pathogenic fungi through histopathological or culture methods from sterile sites. To establish a probable or possible diagnosis, three variables must be assessed: (a) host factors, which pertain to the patient's susceptibility to fungal infection and involve the evaluation of various parameters such as recent neutropenia history, receipt of allogeneic stem cell transplant, prolonged corticosteroid use, immunosuppressive therapy, and inherent immunodeficiency; (ii) clinical signs and symptoms associated with the fungal infection, considering manifestations like tracheobronchitis, sinonasal infection, and central nervous system infection; and (iii) mycological evidence, supported by a positive result from a diagnostic test, whether conventional, molecular, or imaging (Mendonca et al., 2022; Donnelly et al., 2020).

Invasive fungal infection is marked by elevated rates of illness and death. Despite the increasing occurrence of these infections, their diagnosis, prevention, and treatment remain challenging (Talaviya and Majmudar, 2012). Despite the continuous emergence of novel and potent synthetic medications in the market, medicinal plants, rooted in the historical foundation of healthcare, offer an economical and accessible alternative applicable to a range of pathologies. This is especially notable in developing countries (Ashcroft and Li Wan Po, 1999). People are looking for new ways to fight fungal infections. Instead of just making artificial medicines, they are also paying a lot of attention to natural substances that can kill fungi. This focus on natural products is making people search for different treatments (Kathiravan et al., 2012). For an extended period, individuals have employed alternative, complementary, and homemade therapies. Researchers have investigated plants with medicinal qualities to determine the practicality, sustainability, and affordability of utilizing natural drugs derived from these plants (Orafidiya et al., 2002).

Immune response to fungal infection

The immune system developed in response to the selective pressure exerted by infectious microorganisms. Consequently, all multicellular organisms have evolved diverse defence mechanisms capable of activation during infections. These mechanisms aim to safeguard the host organism by eliminating invading microbes and neutralizing their virulence factors (Medzhitov and Janeway, 1997). The body's defence mechanisms against fungi are diverse, spanning from basic safeguards that emerged in the early stages of multicellular organism evolution (innate immunity) to more advanced adaptive responses triggered specifically in the presence of infection and disease (adaptive immunity). The initial line of defence through innate mechanisms involves the presence of physical barriers that act as a separation between the organism and its environment. These barriers include the skin and mucous membranes found in the respiratory, gastrointestinal, and Genito-urinary tracts. Both the skin and mucous membranes serve as physical obstacles, equipped with antimicrobial substances on their surfaces, with some produced by the epithelial and endothelial cells. Additionally, they host a commensal microflora consisting of saprophytic microorganisms, which hinders the colonization of pathogenic microorganisms (Blanco and Garcia, 2008). Candida strains, particularly Candida albicans, commonly inhabit the skin and specific mucous membranes but typically infiltrate these areas only in specific situations. The risk of both local and systemic candidiasis rises when physical disruptions, such as burns, surgical wounds, and the insertion of intravenous catheters or other catheters, compromise these protective barriers (Bross et al., 1989). White blood cells called neutrophils, monocytes, polymorphonuclear cells and natural killer cells are the key defenders that protect the body from yeast infections. Phagocytes present in target organs during an infection try to eliminate or harm fungi. More active cells, like neutrophils and monocytes, are brought to infection sites through inflammatory signals like cytokines, chemokines, and complement components. Fungi are harmed or killed through the production and release of reactive oxygen intermediates and antimicrobial peptides. The choice between intracellular or extracellular antifungal methods depends on the infecting species, morphotype, and exposure route (Shoham and Levitz, 2005). Macrophages, which are antigen-presenting cells (APC), seize control of the fungi and initiate various processes. The tissue-resident macrophages function as effector cells, producing cytokines and chemokines that trigger additional immune cell responses.

Additionally, their role is crucial in the formation of granulomas (Heninger et al., 2006) and Dendritic cells, acting as antigen-presenting cells (APCs), undergo antigen processing upon fungal identification. They then transport these antigens to T cells, guiding their differentiation into various T-helper (Th) subsets, including Th1, Th2, and Th17 cells (Netea et al., 2004).

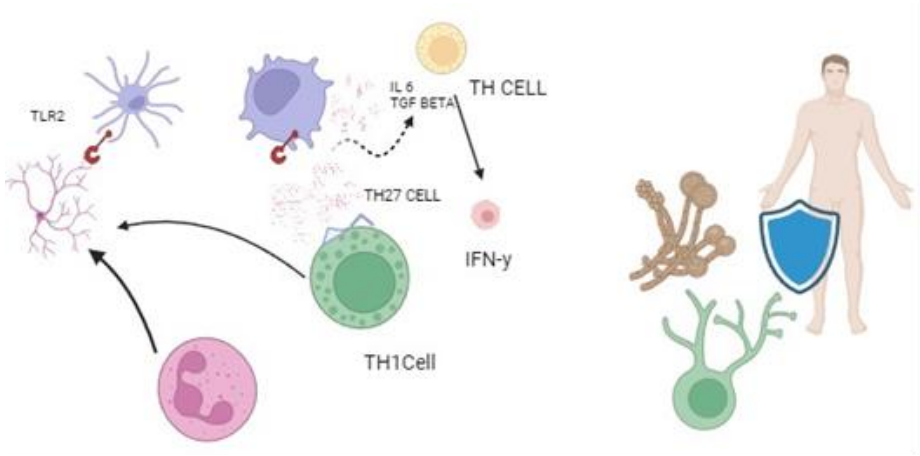

Figure 3. *Immunity against fungus.*

The discussion in the field of medical mycology has centred on how our immune system combats fungal infections. Two primary concepts emerged: cell-mediated immunity (CMI), where specific immune cells defend against fungi, and humoral immunity (HI), which entails antibodies. Demonstrating the protective role of antibodies was challenging, but evidence consistently indicated the vital contribution of immune cells. Numerous studies and instances of heightened susceptibility in individuals with immune cell deficiencies supported this idea. Furthermore, the formation of granulomas in tissues was frequently identified as a crucial factor in managing these infections (Polonelli et al., 2000). While some studies hinted at the potential involvement of antibodies in protection, the uncertainty surrounding humoral immunity (HI) persisted due to inconsistent findings. The overall consensus was that cell-mediated immunity (CMI) played a significant role, whereas humoral immunity had minimal or no apparent role (Blanco and Garcia, 2008; Casadevall, 1995).

Pathogenesis

The progression of fungal infections encompasses a complex process with various mechanisms and pathways. While generally maintaining a symbiotic relationship with hosts, fungi possess the ability to induce mucosal infections in individuals with robust immune systems and systemic or life-threatening infections in those with compromised immune functions (Ruiz-Moyano et al., 2024). Disease-causing fungi can be classified into two primary types: primary pathogens and opportunistic pathogens. The former usually come from the environment and infect individuals who have either been exposed to a significant quantity of the fungus or lack immune protection against it. Opportunistic pathogens take advantage of weakened or immunocompromised hosts to cause infection. They may derive from an environmental source (e.g., Cryptococcus neoformans and Aspergillus fumigatus) or exist harmoniously in the bodies of healthy organisms (such as Candida species). The understanding of fungal pathogenesis is not as comprehensive as that of bacterial pathogens. Unlike bacteria, only a small number

of fungi are considered as professional pathogens (Van Burik and Magee, 2001). Initially, fungal spores or hyphae colonize host tissues through mechanisms such as inhalation, direct contact, or compromised skin barriers. Adhesion to host cells follows, facilitated by specific fungal surface proteins interacting with host receptors. Subsequent invasion occurs as fungi penetrate tissues either mechanically or through the secretion of enzymes that degrade host barriers. Fungi then employ various strategies to evade host immune defences, including modulation of immune signalling pathways, inhibition of phagocytosis, and morphological switching to evade recognition. The resulting host immune response, characterized by the release of inflammatory mediators, contributes to tissue damage and pathology. Ultimately, tissue damage arises from the direct actions of fungal enzymes, toxins, and metabolic byproducts, as well as from the collateral effects of the host immune response. The specific mechanisms of pathogenesis can vary depending on the fungal species involved and the host's immune status. Factors such as immunosuppression, underlying medical conditions, and antibiotic use can predispose individuals to mycoses. A comprehensive understanding of fungal pathogenesis is crucial for the development of effective diagnostic and therapeutic strategies.

Diagnosis

Identifying fungal infections, particularly those that are invasive, remains challenging. Conventional diagnostic approaches like histopathology, microscopy, and culture, though regarded as reliable standards, exhibit limited sensitivity. This highlights the necessity for advancing new methods to detect fungal pathogens effectively (Willinger, 2019). The initial procedures involve cultivating fungi in either plates or liquid mediums, followed by susceptibility testing to determine minimum inhibitory concentrations (MICs) and breakpoints for the appropriate administration of antifungal medications. Although these methods are still widely used, they postpone the initiation of treatment and adversely impact patient outcomes in terms of recovery or survival. Additionally, their precision is inferior when compared to newer techniques such as molecular and immunological assays (Vanzolini and Magnani, 2024). One of the primary challenges in precise diagnosis lies in acquiring tissue for histopathological examination. Invasive methods like biopsies might not be suitable for numerous neutropenic patients suspected of having invasive aspergillosis (IA) due to increased bleeding risk linked to thrombocytopenia. Even if accessible, relying solely on histopathology may not provide comprehensive results since various fungal species can exhibit similar histopathological characteristics. However, employing specific fluorescent-antibody staining techniques under particular research or institutional protocols could enhance the identification of a particular fungus (Perfect, 2013). Generally various process has been utilized for the diagnosis of the fungal infection.

Direct examination and histopathological examination

Histopathological examination plays a crucial role in diagnosis of fungal infection especially when combined with clinical history and other laboratory test. Histopathological examination or direct examination of clinical specimens utilizes fungal stains like Periodic Acid Schiff (PAS) and Grocott Methenamine Silver (GMS) to offer indications of fungal infection presence (Douglas et al., 2023). Nevertheless, the precision of diagnostic identification at the genus or species level is below 80% (Sangoi

et al., 2009). Histopathology offers significant advantages including speed, cost-effectiveness, and the ability to provisionally identify the infecting fungus while demonstrating tissue reactions. However, without special techniques like immunofluorescence or unique fungal structures such as spherules, definitively identifying the species of the causative agent through histopathology is challenging. Nonetheless, it typically furnishes crucial information before fungal isolation in a mycology laboratory. Moreover, histopathology remains the sole method to diagnose infections caused by L. loboi or Rhinosporidium seeberi (Gupta et al., 2009). Nevertheless, misidentifications are possible, even in yeast infections, such as confusing Histoplasma capsulatum with Nakaseomyces (formerly Candida) glabratus. It's crucial to correlate histopathological findings with microbiological results (Shah and Hazen, 2013).

Culture

Cultures are experiments employing a receptacle along with a medium capable of fostering the proliferation of microorganisms such as fungi and bacteria. The primary diagnostic method for invasive candidiasis (IC) is culture, especially from sterile body sites like blood, peritoneal fluid, and pleural fluid. However, blood cultures have low sensitivity, detecting only around half of IC cases according to various autopsy studies. Nearly all (95%) Candida-positive blood cultures typically show positivity within 96 hours, though the time varies depending on the Candida species; for instance, C. glabrata tends to grow slower compared to C. albicans (McCarty et al., 2021). Culture can be conducted in either Petri dishes or large test tubes. Petri dishes offer the benefit of a greater surface area but are more susceptible to dehydration. On the other hand, large test tubes are safer to handle and less prone to drying out. Fungal cultures are typically grown at 25°C–30°C and 37°C due to pathogen preferences. Colony traits are observed, followed by slide mounts in lactophenol cotton blue stain for morphological examination. Dimorphic species are considered for molds showing rapid growth or cobweb-like mycelium (Bosshard, 2016). Moreover, these cultures frequently require 2 to 3 days for results to materialize, meaning clinicians lack real-time information. Mold cultures derived from respiratory tract samples are notably less sensitive, even in confirmed cases of invasive disease and cultures obtained from the upper respiratory tracts frequently indicate colonization rather than invasive illness. Additionally, given the widespread presence of certain filamentous fungi, cultures are susceptible to inadvertent contamination by environmental conidia/spores (Sabino and Wiederhold, 2022).

Nucleic acid detection

In the last ten years, significant strides have been made to establish standardized PCR diagnostics for invasive fungal diseases (IFD), especially invasive aspergillosis (IA), through initiatives like the Fungal PCR Initiative. These endeavors have led to the inclusion of Aspergillus and Pneumocystis PCR in the second revision of the European Organization for Research and Treatment of Cancer and Mycoses Study Group Education and Research Consortium (EORTC/MSGERC) definitions for categorizing IFD. Like any test, it's crucial to grasp the testing methods and how they're impacted by factors such as the types of patients, their health status, clinical and risk factors, and the likelihood of infection. This understanding is essential for using fungal PCR tests

effectively (White et al., 2022). Although PCR provides sensitive detection of specific fungal DNA in tissue samples, there's a risk of overly selective amplification. Next-generation sequencing platforms offer a broader perspective on microbial DNA within a tissue sample. Nevertheless, preliminary findings indicate that host DNA and various microbes in the sample could hinder the identification of the actual causative agents (Frickmann et al., 2019). To effectively utilize this promising technology, it may be necessary to selectively remove background DNA and enrich the pathogen. Vigilant monitoring is essential to prevent fungal contamination, and molecular findings should be considered alongside histopathological results (White et al., 2020).

Immunodiagnostic assay

Fungal disease diagnosis includes various methods: traditional culture, histopathology, molecular techniques, and immunodiagnostic assays like CF, ID, EIA, and LFA. These modern assays provide quick and accurate results, with LFAs being particularly convenient as they don't require refrigeration and can be done bedside. Factors like infection origin, medical history, symptom timing, and site help choose the appropriate test (Caceres et al., 2020). The ID assay utilizes a solid-phase method derived from the liquid tube agglutination assay. In this technique, equal concentrations of solubilized antigen and antibody are mixed, resulting in the formation of a visible precipitate termed a "latticework" complex, indicating a positive outcome (Lindsley et al., 2006). CF assays rely on the functionality of the traditional complement pathway. Essentially, patient serum is treated to deactivate natural human complement factors and then combined and allowed to react with antigens derived from the specific infectious agent being investigated. LFA are immunochromatographic assays that utilize the capillary flow of a specimen across a porous membrane divided into three main sections: a sample application pad, a conjugate pad, and a reaction area. In summary, the patient's specimen is applied to the sample pad and moves towards the conjugate region. Depending on the target substance being analysed, the conjugate pad contains lyophilized antibodies or antigens linked to a reporter label. If the target substance is present, it binds to the labeled conjugate, and this complex travels to the reaction pad. The reaction pad contains immobilized secondary antibodies or antigens, as well as a control antibody specific to the labeled reporter molecule. The presence of visible bands indicates the concentration of detector particles; the presence of a control band alone confirms the validity of the test, indicating the absence of the target substance in the specimen (Caceres et al., 2020; Ramanan et al., 2017).

Herbal approach towards the treatment

Three categories of fungi are responsible for human illnesses-thread-like structures, individual cells known as yeasts, and dimorphic fungi displaying attributes of both. Fungal ailments typically persist over time, often necessitating extended treatment and pose specific threats to individuals with compromised immune systems. Traditional medicine has utilized various plant extracts to treat fungal infections over time (Martin and Ernst, 2004). There are many antifungal treatments used in clinics, categorized into five main groups: azoles, allylamines, echinocandins, griseofulvin, and flucytosine. This highlights the urgent need for finding new antifungal medications. Research into the phytochemistry of various plants suggests that plant-derived compounds could offer better medicinal options compared to synthetic drugs. The use of plants as medicine

dates back to ancient times, and traditional remedies based on medicinal plants have been used for centuries. Thus, one method for discovering antimicrobial treatments involves testing plant extracts (Kaushik and Agarwal, 2019). So this section detailing comprehensive details about various plants that have been scientifically validated for their antifungal properties (*Table 1*).

Table 1. *List of different plant having antifungal efficiency.*

Plant name (species)	Family	Parts used	Test species	Reference
Asphodelus luteus	Liliaceae	Whole plant	*Trichophyton violaceum*	Ali-Shtayeh and Abu Ghdeib (1999)
Anagallis arvensis	Primulaceae	Whole plant		
Capparis spinosa	Capparidaceae	Root, fruit, flower		
Cassia fistula L.	*Caesalpinaceae*	Root bark (acetone extract)	*Trichophyton mentagrophytes,*	Vaijayanthimala et al. (2004)
Cassia occidentali	Caesalpinaceae	Leaf (ethanolic extract)		
Coffea arabica	Rubiaceae	Seed (ethanolic extract)	*Trichophyton rubrum*	
Curcuma longa L	Zingiberaceae	Rhizome (ethanolic extract)		
Piper regnellii	Piperaceae	Leaves (hydrocholic extract)	*Trichophyton mentagrophytes* *Trichophyton rubrum* *Microsporum canis* *Microsporum gypseum*	Koroishi et al. (2008)
Ocimum gratissimum	Labiatae	*Leaves* (hexane extract)	*Trichophyton mentagrophytes* *Trichophyton rubrum* *Microsporum canis* *Microsporum gypseum*	Silva et al. (2005)
Juniperus oxycedrus	Cupressaceae	leaves	*Candida albicans* *Candida glabrata*	Cavaleiro et al. (2006)
Cassia occidentalis	Leguminosae	Leaves (Ethanolic extract)	*Aspergillus clavatus* *Candida albicans*	Davariya and Vala (2011)
Mitracarpus villosus	Rubiaceae	Leaves (Ethanolic extract)	*Trichophyton rubrum, Microsporum gypseum, Candida albicans*	Irobi and Daramola (1993)
Juniperus oxycedrus	Cupressaceae	Leaves	*Candida albicans* *Candida glabrata* *Candida tropicalis* *Candida krusei*	Cavaleiro et al. (2006)
Fragaria virginiana	Rosaceae	Leaves	*Candida albicans*	Webster et al. (2008)
Epilobium angustifolium	Onagraceae	Root	*Candida glabrata*	
Potentilla simplex	Rosaceae	Stems, leaves	*Candida krusei*	
Bauhinia manca	Fabaceae	Stem	*Botrytis Claoiceps* *Coprinus* *Rhizoctonia* *Saprolegnia cinerea*	Achenbach et al. (1988)
Bougainvillea glabra	Nyctaginaceae	Stem, leaves, flowers, fruits	*Coccidioides immitis*	Alanís-Garza et al. (2007)
Salvia texana	Lamiaceae	Stem, leaves, flowers, fruits	*Aspergillus fumigatus*	
Clematis drummondii	Ranunculaceae			
Clematis drummondii	Ranunculaceae	Stem, leaves, flowers, fruits	*Coccidioides immitis* *Aspergillus fumigatus* *Candida albicans*	
Arrabidaea brachypoda	Bignoniaceae	Leaves	*Cladosporium sphaerospermum*	Alcerito et al. (2002)
Centaurea granatensis	Asteraceae	Leaves, Stem, flowers	*Cunninghamella echinulata*	Barrero et al. (2000)
Melia azedarach	Meliaceae	Fruit	*Fusarium verticillioides*	Carpinella et al. (2005)

Mammea longifolia	Clusiaceae	Root	*Fusarium oxysporum*	Deng and Nicholson (2005)
Pinus radiata	Pinaceae	Root	*Dothistroma pini*	Franich et al. (1983)
Berberis heterophylla	Berberidaceae	Stem, leaves	*Trichophyton mentagrophytes* *Trichophyton rubrum* *Epidermophyton floccosum*	Freile et al. (2006)
Euphorbia characias	Euphorbiaceae	Stem	*Candida albicans*	Giordani et al. (2001)
Glycosmis cyunocarpa	Rutaceae	Leaves	*Cladosporium cladosporioides*	Greger et al. (1992)
Lycium chinense	Solanaceae	Root	*Saccharomyces cerevisiae* *Trichosporon beigelii*	Lee et al. (2004)
Camptotheca acuminata	Nyssaceae	Leaves	*Alternaria alternata* *Epicoccum nigrum* *Pestalotia guepinii*	Li et al. (2005)
Celastrus hypoleucus	Celastraceae	Root	*Rhizoctonia solani* *Glomerella cingulata* *Erysiphe graminis*	Luo et al. (2005)
Rubia tinctorum *Rhamnus frangula*	Rubiaceae Rhamnaceae	Roots Bark	*Trichoderma viride* *Aspergillus niger* *Alternaria alternata*	Manojlovic et al. (2005)
Combretum woodii *Combretum moggii* *Combretum petrophilum* *Combretum nelsonii*	Combretaceae Combretaceae Combretaceae Combretaceae	Leaves Leaves Leaves Leaves	*Candida albicans*, *Cryptococcus neoformans* *Aspergillus fumigatus* *Microsporum canis* *Sporothrix schenckii*	Masoko et al. (2007)
Artemisia absinthium *Rumex obtusifolius* *Taraxacum officinale* *Plantago lanceolata* *Malva sylvestris*	Asteraceae Polygonaceae Asteraceae Plantaginaceae Malvaceae	Leaves Leaves Leaves Leaves Leaves	*Penicillium expansum*	Parveen et al. (2014)
Cumin cyminum	Apiaceae	Seed	*Alternaria burnsii*	Jagani et al. (2023)
Allium sativum	Amaryllidaceae	Bulb	*Fusarium oxysporium*	Omer et al. (2023)
Ocimum basilicum	Lamiaceae	Leaves		
Moringa peregrina	Moringaceae	Leaves	*Candida kruzei*	De Pauw (2011)

Conclusion

The document provides an overview of fungal infections, focusing on their pathogenesis, diagnosis, and herbal treatment approaches. Fungal infections, also known as mycoses, are increasingly recognized as a significant global health concern affecting humans, animals, and plants. These infections can be superficial, subcutaneous, or systemic, with over 150 million serious cases reported annually, resulting in approximately 1.7 million deaths worldwide. The rise in fungal infections is attributed to factors such as social and medical advancements, which facilitate their spread. The pathogenesis of fungal infections involves complex interactions between fungal pathogens and the host's immune system. Fungi adhere to host tissues, invade them, and evade immune responses, leading to tissue damage and disease progression. Factors such as compromised immunity, moist environments, and certain medications contribute to fungal infection development. Diagnosing fungal infections, especially

invasive ones, remains challenging. Conventional methods like histopathology and culture have limited sensitivity, necessitating the development of newer techniques such as molecular and immunological assays. These advancements aim to improve the accuracy and timeliness of diagnosis. Herbal approaches to fungal infection treatment have gained attention due to the limitations of conventional antifungal medications, including drug resistance. Traditional medicine has long utilized plant extracts for their medicinal properties, and research into plant-derived compounds offers promising alternatives to synthetic drugs. The phytochemistry of various plants suggests their potential efficacy against fungal infections, highlighting the importance of exploring natural remedies in modern healthcare. In summary, understanding the pathogenesis, improving diagnostic methods, and exploring herbal treatment options are crucial for effectively managing fungal infections and addressing the challenges posed by these pathogens in healthcare.

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Conflict of interest

The authors confirm that there is no conflict of interest involve with any parties in this research study.

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