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OVERVIEW ON ANTIFUNGAL EFFICACY OF OCIMUM SPECIES: A REVIEW OF TRADITIONAL USE, MECHANISM OF ACTION, AND POTENTIAL AS ALTERNATIVE THERAPEUTICS

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ABSTRACT

Human skin serves as a physical barrier, but occasionally fungi can infect it. If this happens on the third layer of the skin, the infection gets worse. To treat fungal infections, antifungal creams, liquids, or sprays based on azole derivatives are available; however, these formulations exhibit a range of adverse effects at the application site. Herbal extracts and other essential oils have demonstrated potent antifungal activity in recent years. In Ayurvedic medicine, Tulsi scientifically referred known as Ocimum sanctum Linn., is a common medicinal herb. Many fungal infection treated with it due to its antibacterial qualities. We have included a current summary of the Tulsi plant's anti-infective qualities in this review, with an emphasis on its antibacterial and antifungal activities.[1]

KEYWORDS: Human skin, Tulsi, fungal infection.

INTRODUCTION

The most prevalent organisms implicated in systemic and topical fungal infections are species of Candida. Of all the candidal species, Candida albicans is recognized as the most prevalent and virulent. Although there are many antifungal medications, new pathogen strains become resistant to them. Plant-based medications can serve as an alternate treatment to stop this resistance. Both urban and rural Indian cultures frequently use herbal remedies. According to recent research, some herbs contain active compounds that work against particular diseases.

Native to the Indian subcontinent

Ocimum sanctum, often known as Tulsi, is widely esteemed aromatic herb with both culinary and medicinal

significance, classified under the family Lamiaceae. It has been employed in traditional Ayurvedic formulation for more than three millennia. The fungicidal activity of Tulsi is due to the action of secondary Metabolites that are present in Tulsi, including alkaloids, glycosides, saponins, tannins, ascorbic acids, eugenol and several other metabolites.[2]

FUNGAL INFECTION

Systemic infections caused by yeasts or molds growing in deep-seated tissues are known as systemic mycosis. Systemic mycosis are associated with elevated morbidity and mortality rates than superficial fungal infections, making them deadly conditions. The most prevalent invasive infections that have been found are caused by species of Aspergillus, Pneumocystis, Cryptococcus, Candida, and others. Furthermore, endemic fungal species such as Blastomyces, Histoplasma, Paracoccidioides, and Coccidioides have also been linked to serious systemic infections in patients with weakened immune systems. Organ transplant recipients, hematologic patients in need of stem cell transplantation, AIDS patients, diabetics, burn patients, patients with neoplastic diseases, patients receiving long-term immunosuppressive therapy, and people with chronic respiratory conditions are among the groups at risk of developing an opportunistic mycotic infection.[3]

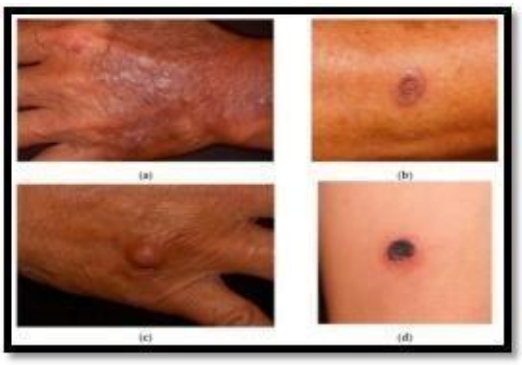
TYPES OF FUNGAL INFECTION

1. SUPERFICIAL FUNGAL INFECTION

Fungal infections that are superficial Your skin, nails, and mucous membranes (such as your mouth, throat, or vagina) are all impacted by superficial fungal infections. The following are instances of superficial fungal infections:

- **Ringworm**: Ringworm is caused by dermatophytes, a class of fungi that feed on the cells of the skin, hair, and nails. Dermatophytes are capable of infecting various keratinized tissues,including the hands(tinea mannum),scalp(tinea capitis),groin and inner thighs(tinea cruris),and the facial region involving hair follicles(tinea barbae),among other sites.
- **Candidiasis:** Candida (most often Candida albicans) is responsible for candidiasis, a mycotic infection involving the skin and mucous membranes (mucocutaneous). These include esophageal candidiasis, vulvovaginal candidiasis, oral thrush, some forms of diaper rash, and candidal intertrigo.

2. SUBCUTANEOUS FUNGAL INFECTION



If a fungus enters into a tissue injury, generally from an injury sustained while handling plants (such as a thorn scratch), you may develop a fungal infection beneath the epidermis (subcutaneous). They result in skin problems like rashes and ulceration. Tropical and subtropical geographical regions of have higher rates of subcutaneous fungal infections. Among the examples are:

- **Rose gardener's disease, or sporotrichomichosi**: The sporotrichosis is caused by the sporothrix fungus. Sporotrichosis can also affect other regions of your body, such as your lungs.
- **Mycosis chromoblastosis**: Chromatoblastomycosis can be caused by a wide variety of fungus. Chronic (longlasting) skin infections may result from it.

3. DEEP FUNGAL INFECTION

Deep fungal infections can occur in organs other than the cutaneous and systemic sites such as the, brain, blood, lungs, or urinary tract. Certain infections are opportunistic, which means that they often only infect those with compromised immune systems. Invasive or deep fungal diseases include:

- **Histoplasmosis**: The etiological agent of histoplasmosis, Histoplasma, can invade the central nervous system, lungs, or other bodily regions. It is frequently seen in the lowlands of the Mississippi and Ohio rivers
- **Aspergillosis**: The mold that causes aspergillosis, Aspergillus, is associated with several lung illnesses, such as chronic pulmonary aspergillosis and allergic bronchopulmonary aspergillosis (ABPA). It may potentially develop into a fungal ball (aspergilloma) or infect other areas of your body.[4]

SYNTHETIC ANTIFUNGAL AGENTS

1. Polyenes

a. Amphotericine

b. Nystatin

2. Azoles

a. Ketoconazole

b. Miconazole

c. Clotrimazole

d. Itraconazole

3. Allylamines

a. Terbinafine

b. Naftifine

4. Echinocandins

a. Caspofungin

b. Micafungin

5. Antibiotics

a. Griseofulvin

ADVERSE EFFECT OF SYNTHETIC ANTIFUNGAL AGENT:

1. NYSTATIN

Drug	Clinical Indication	Topical Use And Major Adverse Effect
Nystatin	Treatment of muco-cutaneous fungal infection, particularly candidiasis.	Effectivefor localized lesions; rare but serious risk of Stevens-Johnson syndrome[6]

2. AZOLES

esult in diarrhea, vomiting, nausea, and abdominal pain. All azoles can cause hepatotoxicity, which includes increased liver function tests, hepatitis, cholestasis, and/or fulminant liver failure. Every azole medication has distinct side effects as well:

KETOCONAZOLE

Drug	Clinical Indication	Major Adverse Effects
Ketoconazole	Systemicand topical management offungal infection.	Orthostatic, Hypotension, Thrombocytopenia, Dermatitis.

FLUCONAZOLE

Drug	Clinical Indication	Major Adverse Effect
Fluconazole	Broadly used for muco- cutaneous and systemic fungal infection, including candidiasis and cryptococcosis.	Headache, dizziness, hepatotoxicity

ITRACONAZOLE[7]

Drug	Clinical Indication	Major Adverse Effects
Itraconazole	Treatment of systemic and mucocutaneous fungal infection, including aspergillosis.	Headache, fatigue, hepatotoxicity

3. ALLYLAMINE

Drug	Clinical Indication	Major Adverse Effects
Allylamine	Management of dermatophytoses including tinea corporis.	Fatigue, taste disturbance, headache

4. ECHINOCANDINS[8]

1. ANIDULAFUNGIN

Drug	Clinical Indication	Major Adverse Effects
Anidulafungin	Treatment of invasive and esophageal candidiasis.	Hypotension, headache, hepatotoxicity.

2. CASPOFUNGIN

Drug	Clinical Indication	Major Adverse Effects
Caspofungin	Treatment of invasive candidiasis, refractory invasive aspergillosis.	Chills, hypokalemia, fever, headache

3. MICAFUNGIN[9]

Drug	Clinical Indication	Major Adverse Effect
Micafungin	Tretment of candidemia, invasive candidiasis.	Anemia, thrombocytopenia, fever, headache.

5. GRISEOFULVIN[10]

Drug	Clinical Indication	Major Adverse Effect
Griseofulvin	Tretment of dermatophytoses, including tinea corporis.	Dizziness, photosensitivity, fatigue, headache

MEDICINAL PLANT AS ASOURCE OF NEW ANTIFUNGAL

In both industrialized and developing nations, medicinal plants have long been utilized to cure a variety of illnesses.[10,11] Because of the numerous advantages of using medicinal plants, including lower costs and fewer side effects, they have also garnered a lot of interest in recent years.[12,13] It has additionally been thought that using plant-based products to combat bacterial, fungal, and parasite illnesses is a beneficial strategy.[14,15] Furthermore, by identifying the active chemicals of the plants, specific steps can be performed to create medications.Some plants have already been demonstrated to possess antifungal properties against fungal infections, including tulsi, ginger, Narcissus tazetta, Myrtus communis, dill, cilantro, garlic, onions, henna, oak, and black beans. Among the antifungal or other therapeutic microbially active substances present in these plants include flavonoids, alkaloids, tannins, citronellol, geraniol, thymoquinone, and phenolic compounds.[16,17]

RELEVANCE OF OCIMUM SANCTUM IN ANTIFUGAL ACTIVITY:

The active ingredients of sacred basil (Ocimum sanctum) comprises a diverse range of bioactive constituents, including alkaloids, enzymatic compounds, and various inorganic elements. The fungitoxicity of Ocimum sanctum against fungal pathogens was studied to assess the plant's resistance to fungal infections. All four forms of Ocimum sanctum leaf extract—crude (10%), powdered (10%), boiled (10%), and ethanol (1%), were found to significantly inhibit the growth of the test fungus, which included Rhizoctonia solani, R. bataticola, Phoma sorghina, Colletotrichum gloeosporioides, Fusarium oxysporum f.sp. pallidoroseum, F. oxysporum f.sp. ciceri, Sclerotium rolfsii, Sclerotinia sclerotiorum, Alternaria solani, and A. alternata. None of the forms, nevertheless, were able to totally stop any of the test fungi from growing.

Recent research indicates that tulsi has antibacterial, antiviral, and antifungal qualities that enable it to fight against a range of microbes that make people sick. Tulasi has also been shown to boost immunity against viral threats by enhancing immune responses in both stressed and unstressed animals as well as healthy humans. Phytphytochemical studies have identified compound such as eugenol, methyl chavicol, linalool, ursolic acid, and rosamaric acid many of which exhibit documented antimicrobial and antifunal activity. These compounds are belived to target fungal membranes, inhibit ergosterol biosynthesis, disrupt biofilms and induce oxidative stress in fungal cells.[18,19,20]

Antifungal Mechanism Exhibited By Ocimum Sactum

1. Disruption of Cell Membrane Integrity

The volatile oil of *O. sanctum* contains fat-soluble compounds such as eugenol and linalool that can enter fungal cell membranes. This disrupts the membrane, making it more permeable and causing leakage of essential cellular contents like ions and nucleotides, ultimately leading to cell death. This effect has been observed in *Candida* species, including *C. albicans* and *C. tropicalis.*

2. Inhibition of Ergosterol Biosynthesis

Eugenol, a major component of *O. sanctum* essential oil, interferes with the production of ergosterol, an important component of fungal cell membranes. This disruption weakens the membrane, affecting its function and integrity, and inhibits fungal growth. Studies have reported this effect in *Candida* species.

3. Production of Reactive Oxygen Species (ROS)

Bioactive compounds in *O. sanctum* essential oil can stimulate the production of reactive oxygen species (ROS) inside fungal cells. ROS cause oxidative damage to lipids, proteins, and DNA, which can lead to fungal cell death. This mechanism contributes significantly to the fungicidal efficacy of *O. sanctum*.[21]

BOTANICAL PROFILE OF OCIMUM SANCTUM

TAXONOMY

Class: Magnoliopsida Kindgdom Plant: Genus Ocimum Species: Ocimum basilicum Order: Lamiales

Family: Lamiaceae

Division: Magnoliophyta.[22]

BOTANICAL DIVERSITY OF GENUS OCIMUM (TULSI):

1 .Ocimum gratissimum L / (Vana Tulsi)

Botanical Description[23]

Common Name	Family	Genus	Species	Plant Type	Stem Characteristics	Leaf Characteristics	Height
Alfalfa, Basil, Basilclove	Lamiaceae	Ocimum	O. Gratissimum	Fragrant, herbaceous plant	Upright, branching, roundquadrangular; lignified at basal region.	Opposite, slender leaves with marginal serration	1-3cm tall

TAXONOMY

Taxonomy The Lamiaceae family of plants are mostly categorized as herbs, spices, and other aromatic varieties. There are 7200 species of vines, shrubs, and trees in the Lamiaceae family, which includes 236 genera worldwide.[24]

Antifungal Activity of Ocimum Gratissimum

Many researchers have reported the antifungal properties of *Ocimum gratissimum*. According to Lemos et al. (2005), the chloroformic fraction of the plant inhibited 92% of *Cryptococcus neoformans* isolates at a concentration value of 62.5 µg/mL, while eugenol, one of its main components, inhibited 16% of the isolates at 0.9 µg/mL. Mohr et al. (2017) found that the volatile oil extracted from *O. gratissimum* (0.312–40 mg/mL) effectively suppressed the proliferation of *Fusarium oxysporum* f. sp. *lycopersici* and *Rhizoctonia solani*.[25]

Nakamura et al. (2004) studied the in vivo fungicidal efficacy of *O. gratissimum* essential oil on various *Candida* species. The results showed that the extract exhibited fungicidal activity against *Candida albicans*, *Candida krusei*, *Candida parapsilosis*, and *Candida tropicalis*. The treated fungal cells showed inhibited bud development and noticeable changes within cell wall and internal structures. These results suggest that *O.*

gratissimum essential oil may serve as a potential herbal treatment for fungal infections and a natural antifungal agent for environmental use.[26]

Furthermore, Silva et al. (2005) reported that the extract obtained from leaves of *O. gratissimum* contains bioactive compounds that show strong in vitro activity against dermatophytes. Overall, these studies confirm the significant antifungal potential of *O. gratissimum*.[27]

2. Ocimum Americanum

Botanical Profile

Common Names	Family	Genus	Species	Plant Type	Stem Characteristics	Leaf Characteristics	Height
Hoary basil, Lemon basil	Lamiaceae	Ocimum	O.americanum	Aromatic, herbaceous plant	Erect, branched, quadrangular stem	Opposite, lanceolate to ovate leaves; finely serrated margins	3090cm tall

Taxonomy

Several studies have reported that *Ocimum americanum* L. has strongantifungal activity**,** mainly due to its essential oils and phenolic compounds. The essential oil derived from its leaves contains important bioactive components such as eugenol, thymol, linalool, camphor, 1, 8-cineole, and geraniol, which are responsible for its wide range of antifungal effects.[29]

Antifungal Activity of Ocimum Americanmum

Both the essential oil and solvent extracts of *O. americanum* have been found to suppress the proliferation of several pathogenic fungi, including *Candida albicans*, *Aspergillus niger*, *Fusarium oxysporum*, *Rhizoctonia solani*, and *Trichophyton mentagrophytes* (Prasad et al., 2012; Oyedeji et al., 2009). The antifungal action of the plant is mainly associated with damage to the cytoplasmic membrane of fungi**,** leakage of cell contents**,** and **i**nhibition of spore germination and hyphal growth (Orafidiya & Oyedele, 1993).[30,31]

a. Ocimum Tenuiflorum/Krishna Tulsi

Botanical Profile[32]

Common Names	Family	Genus	Species	Plant Type	Stem Characteristic	Leaf Characteristics	Height
Tulsi, Holy Basil	Lamiaceae	Ocimum	*O.tenuiflorum* (*O.sanctum*)	Aromatic, perennial herb	Erect, branched, quadrangular stem; slightly hairy	Opposite, simple, ovate leaves with serrated margins; green or purple varieties	30–60 cm tall

Taxonomy

The scientific name for Krishna Tulsi is Ocimum tenuiflorum L. (also referred to as Ocimum sanctum L.), and it is a member of the Lamiaceae family. Of the more than 150 members of the genus Ocimum, which are mostly found in

tropical and subtropical areas, it is considered one of the most significant species. Krishna Tulsi's distinctive leaves and stems exhibiting deep purple pigmentatio, potent perfume, and high concentration of essential oils make it easy to differentiate it from other types like Rama Tulsi (O. gratissimum).[33]

Antifungal Activity of Ocimum Tenuiflorum

Studies on clinically isolated dermatophyte fungi have shown that both alcoholic along with water based extract of *Ocimum tenuiflorum* exhibit strong antifungal activity. The plant contains several bioactive compounds, including flavonoids, alkaloids, and essential oils, which are responsible for its antimicrobial properties. Important metabolites such as eugenol, estragole, ursolic acid, and ferulic acid are well known for their ability to fight microbial infections.[34]

4. Ocimum Basilicum

Botanical Profile[35]

Common Names	Family	*Genus*	Species	Plant Type	Stem Characteristics	Leaf Characteristics	Height
Sweet basil, Common basil	Lamiaceae	Ocimum	O. basilicum	Aromatic, annual herb	Erect, soft, branched, quadrangular stem	Opposite, simple, broad ovate leaves; smooth or slightly toothed margins	30–90 cm tall

Taxonomy

Ocimum basilicum (sweet basil) is an erect, aromatic annual herb that grows 30–90 cm tall. The stems are square-shaped and sometimes slightly purplish. The leaves are opposite, bright green, and range from oval to lance-shaped, with smooth or slightly toothed edges. They contain essential oil glands that give the plant its strong aroma. Flowers are small, tubular, white to pale pink, and grow in clusters at the tips of stems. The plant has shallow, fibrous roots and prefers well-drained soil. Its essential oils are rich in bioactive constituents including eugenol, linalool, and methyl chavicol.[36]

Antifungal Activity of Ocimum Basilicum

Ocimum basilicum (sweet basil) is known for its antifungal activity, mainly due to its essential oils and bioactive compounds such as eugenol, linalool, and methyl chavicol. It has exhibited activity against various pathogenic fungi, including *Candida albicans*, *Aspergillus niger*, *Fusarium* species, and dermatophytes like *Trichophyton* species.[37]

CONCLUSION

Fungal infections, from mild skin infections to serious invasive diseases, are a growing health problem worldwide because of their high risk and the increasing resistance of fungi to existing antifungal drugs. Current synthetic antifungal agents like azoles, polyenes, echinocandins, and allylamines are widely used, but their side effects and reduced effectiveness over time make new alternatives necessary. Medicinal plants, especially Ocimum sanctum (Tulsi) and other Ocimum species, have shown strong fungicidal activity resulting from natural compounds such as eugenol, linalool, methyl chavicol, and ursolic acid. These compounds act by damaging fungal cell membranes, blocking ergosterol production, and creating oxidative stress in fungal cells. Such findings suggest that Tulsi and related plants could be developed as safer and effective antifungal treatments in the future.[38,39,40]

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