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A COMPREHENSIVE REVIEW ON HERBAL APPROACHES FOR MANAGING ONYCHOMYCOSIS

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Onychomycosis; Fungal infections; Herbal formulations; Medicinal plants; Antifungal activity; Nail lacquer; Essential oils; Dermatophytes; Drug delivery systems; Phytochemicals

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ABSTRACT

Fungal infections are increasingly prevalent worldwide, affecting the skin, hair, nails, and in severe cases, internal organs. Among these, onychomycosis is a chronic and common nail disorder primarily caused by dermatophytes such as *Trichophyton rubrum* and *Trichophyton mentagrophytes*, along with yeasts and non-dermatophyte molds. The condition is characterized by nail discoloration, thickening, and onycholysis, significantly impacting patient quality of life. Conventional antifungal therapies, although effective, are often associated with limitations such as systemic side effects, poor patient compliance, long treatment duration, and emerging drug resistance. In recent years, medicinal plants and herbal formulations have gained considerable attention as alternative antifungal therapies due to their safety, cost-effectiveness, and multitarget mechanisms of action. Various plant-derived bioactive compounds, including flavonoids, phenolics, tannins, terpenes, and essential oils, have demonstrated significant antifungal activity against dermatophytes, yeasts, and non-dermatophyte molds. Additionally, novel herbal drug delivery systems such as creams, gels, ointments, nail lacquers, and transdermal patches have shown promising results in improving drug penetration, stability, and therapeutic efficacy. This review highlights the pathogenesis, classification, and clinical manifestations of onychomycosis, along with the potential of herbal agents and advanced formulation approaches in its management. Furthermore, it discusses the advantages, limitations, and future perspectives of herbal antifungal therapies, emphasizing their role as safer and effective alternatives to conventional treatments.

INTRODUCTION

Fungal infections are diseases caused by fungi, which are ubiquitous microorganisms present in air, soil, water, and on living organisms. These infections may be superficial, involving the skin, hair, and nails, or systemic, affecting internal organs and the bloodstream. Although fungal infections can occur in healthy individuals, immunocompromised patients are at significantly higher risk. Common superficial infections include athlete's foot, ringworm, and candidiasis, which spread through direct contact or inhalation of fungal spores [1].

Dermatophytes and yeasts are the primary causative agents of most fungal infections. Dermatophytes, particularly *Trichophyton rubrum* and *Trichophyton mentagrophytes*, are responsible for the majority of skin and nail infections, whereas yeasts of the genus *Candida*, especially *Candida albicans*, cause mucocutaneous and systemic infections. Dermatophyte infections account for more than 90% of superficial fungal cases [2].

Onychomycosis is a chronic fungal infection of the nail characterized by discoloration, thickening, and onycholysis of the nail plate. It predominantly affects toenails and may involve the nail bed, matrix, and plate. The condition is mainly caused by dermatophytes, although non-dermatophyte molds and yeasts may also be implicated. Approximately 90% of toenail and 75% of fingernail infections are attributed to dermatophytes. The global prevalence of onychomycosis is estimated to be around 5%, while in India it ranges from 0.5% to 5%, with higher incidence observed in the elderly population. In contrast, pediatric cases are relatively rare, affecting about 0.5–2.6% of children, often associated with trauma or environmental exposure [3].

Accurate diagnosis of onychomycosis is essential for effective management. In addition to their protective and aesthetic roles, human nails serve as a potential route for localized drug delivery, especially in nail disorders such as psoriasis and onychomycosis. Topical drug delivery systems, including nail lacquers and other formulations, have gained importance for targeted therapy.

In recent years, there has been growing interest in the use of medicinal plants and herbal formulations as alternatives to conventional antifungal agents. Herbal products are generally considered safer, cost-effective, and associated with fewer adverse effects. Numerous plant extracts have demonstrated significant antifungal activity against dermatophytes, non-dermatophyte molds, and yeasts, highlighting their potential in the management of fungal infections [4].

Types of Fungal Infections

1. **Superficial Fungal Infections:**These affect the outermost layers of the skin, hair, and nails. Examples include tinea infections such as ringworm (***tinea corporis***), athlete's foot (***tinea pedis***), and nail infections (***tinea unguium*** or onychomycosis).
2. **Subcutaneous Fungal Infections:**These occur when fungi enter through cuts or wounds, affecting deeper layers of the skin and subcutaneous tissue. Examples include chromoblastomycosis and mycetoma.
3. **Systemic (Deep) Fungal Infections:**These involve internal organs such as the lungs or bloodstream and are often severe. Examples include blastomycosis and coccidioidomycosis.
4. **Opportunistic Fungal Infections:**These occur primarily in immunocompromised individuals. Common examples include candidiasis (***Candida albicans***) and aspergillosis (***Aspergillus*** species) [5].

Onychomycosis

The term ***onychomycosis*** is derived from the Greek words ***"onyx"*** (nail) and ***"mykes"*** (fungus). It is a chronic fungal infection of the nails characterized by discoloration, thickening, and onycholysis of the nail plate. The condition

most commonly affects toenails, although fingernails may also be involved. Infection can extend to any component of the nail unit, including the nail plate, nail bed, and nail matrix.

Onychomycosis is caused by dermatophytes, yeasts, and non-dermatophyte molds (NDMs). Dermatophytes, particularly ***Trichophyton rubrum*** and ***Trichophyton interdigitale***, are the most common causative agents. Other organisms such as ***Epidermophyton floccosum***, ***Microsporum gypseum***, and ***Candida albicans*** may also contribute. NDMs, including species of ***Aspergillus***, ***Scopulariopsis***, ***Alternaria***, ***Acremonium***, and ***Fusarium***, account for approximately 2–25% of cases. However, the clinical diagnosis of NDM-associated onychomycosis is often difficult due to its similarity to dermatophytic infections.

Onychomycosis is a widespread and persistent condition, affecting approximately 10–30% of the global population. Clinically, it presents with nail discoloration, thickening, brittleness, and distortion, which may lead to discomfort and reduced quality of life. The prevalence increases with age and is higher in individuals with predisposing factors such as diabetes, immunosuppression, or nail trauma [6].

Historically, treatment involved surgical removal of the infected nail, which was painful and invasive. Currently, management primarily includes antifungal therapy administered either topically (e.g., creams, gels, and nail lacquers) or systemically. Oral antifungal agents are absorbed into systemic circulation and diffuse into the nail plate, while topical formulations provide localized drug delivery with reduced systemic side effects [7].

Anatomy of Normal nail:

The nail unit is a specialized structure located on the dorsal aspect of the distal fingers and toes, serving important protective and sensory functions. It is composed of epithelial and connective tissue components. The nail plate consists of compact keratinized layers interspersed with small amounts of water and lipids, which contribute to its flexibility and smooth, glossy appearance. Structurally, the nail unit comprises four main epithelial components: the nail matrix, nail bed, hyponychium, and eponychium. In addition to protection, the nail enhances tactile sensation by providing counter-pressure to the fingertip, thereby improving sensory perception [8].

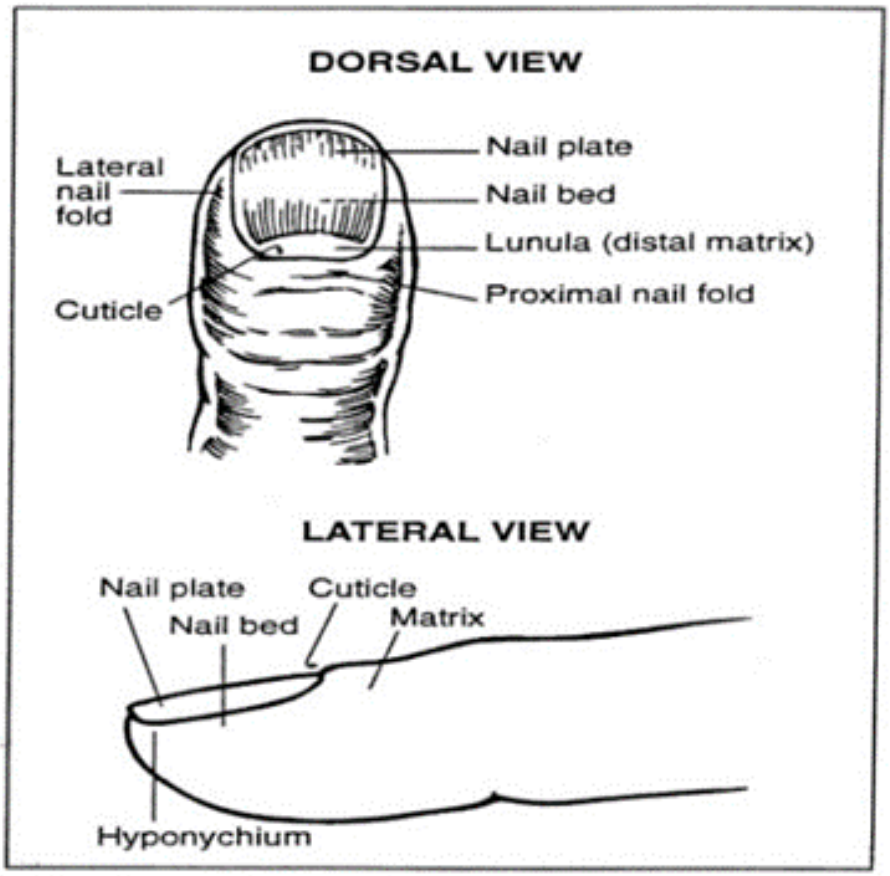


Fig. 1: Structure of the nail unit

Types of onychomycosis:

Fig.2. Types of onychomycosis

Pathogenesis

Onychomycosis is primarily acquired through direct contact of the nail unit with dermatophytes, non-dermatophyte molds, or yeasts. The nail apparatus is particularly susceptible to infection due to its limited cell-mediated immunity. Fungal pathogens produce enzymes with proteolytic, keratinolytic, and lipolytic activities, which facilitate degradation of the nail plate keratin and promote fungal invasion. Disruption of the natural protective barriers further increases the risk of infection. The site and pattern of fungal invasion determine the various clinical subtypes of onychomycosis. Additionally, the ability of fungi to form biofilms contributes to their persistence, enhances resistance to antifungal therapies, and complicates treatment outcomes [9].

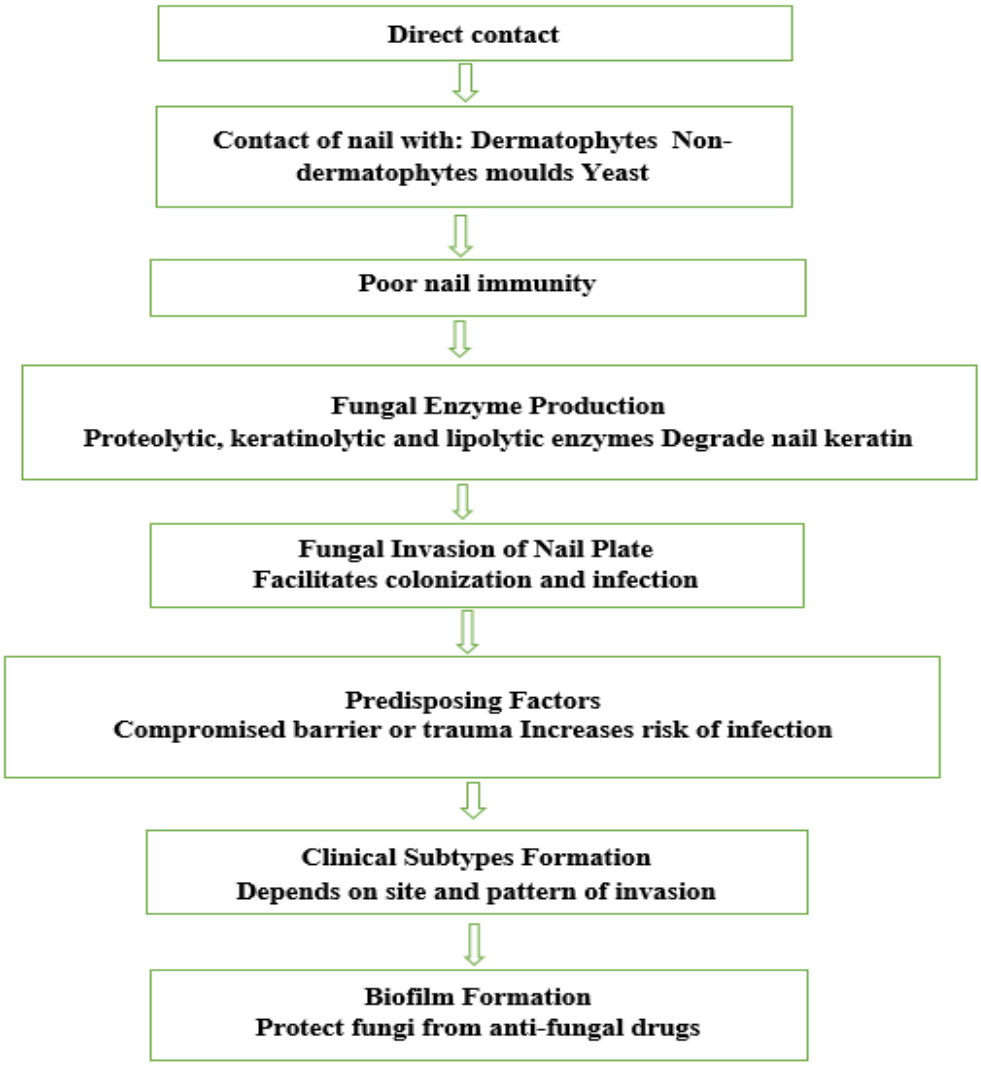


Fig.3.Pathogenesis

Clinical Types of Onychomycosis

Distal Lateral Subungual Onychomycosis (DLSO): The most common form of onychomycosis, typically initiating at the hyponychium and spreading to the nail bed and plate. It is characterized by subungual hyperkeratosis, onycholysis, and nail thickening. ***Trichophyton rubrum*** is the predominant

causative agent. Toenails are more frequently affected and are often associated with tinea pedis, whereas fingernail involvement may be linked to tinea manuum.

Endonyx Onychomycosis (EO):A less common type confined to the nail plate, usually caused by ***Trichophyton soudanense***. It presents as milky-white discoloration with lamellar splitting, ridging, and pitting, without subungual hyperkeratosis or onycholysis. Nail thickness and surface remain largely unaffected.

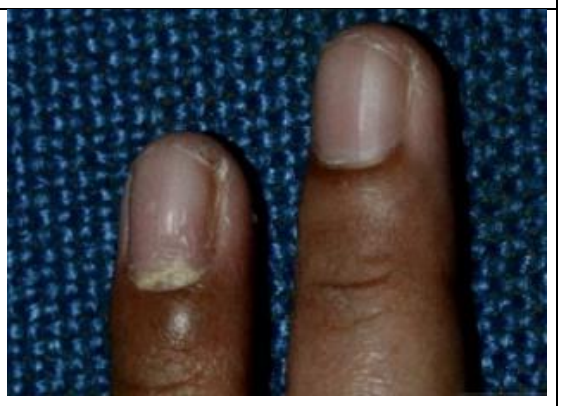
Superficial White Onychomycosis (SWO):A relatively rare form characterized by superficial white patches on the nail plate, predominantly affecting toenails. It is commonly caused by ***Trichophyton mentagrophytes***, while fingernail involvement in immunocompromised patients (e.g., HIV) is often associated with ***T. rubrum***.

Proximal Subungual Onychomycosis (PSO): Typically caused by ***Trichophyton rubrum***, this form begins at the proximal nail fold and spreads distally to involve the nail matrix and plate. It presents with leukonychia, proximal onycholysis, and subungual hyperkeratosis. It is more frequently observed in immunocompromised individuals and may involve multiple nails.

Total Dystrophic Onychomycosis (TDO): Represents the end stage of the disease, involving complete destruction of the nail plate, bed, and matrix. Nails become thickened, brittle, and crumbly. It may occur as a primary condition (e.g., chronic mucocutaneous candidiasis) or as a progression of other clinical forms of onychomycosis [10].

Clinical manifestations:

Clinical manifestations	**Diagram**
Dermatophytoma presenting as a linear, yellow, band on the nail plate of the right big toe in a patient with distal lateral subungual onychomycosis	
Onychomycosis in a patient with coexisting tinea pedis.	

Distal lateral subungual onychomycosis: yellowish discoloration and onycholysis.	
White superficial onychomycosis	
Proximal subungual onychomycosis	

Medicinal plants and herbal products have gained considerable attention as alternative therapies for fungal infections due to their safety, affordability, and wide availability. Plant-derived secondary metabolites play a crucial role in antifungal activity and serve as potential sources for novel therapeutic agents. The development of antifungal drugs is particularly challenging because fungal cells possess a rigid cell wall composed of chitin and β-glucans, which limits drug penetration.

Numerous studies have reported the antifungal efficacy of plant extracts and essential oils against dermatophytes, non-dermatophyte molds (NDMs), and yeasts. Medicinal plants are rich in diverse phytochemicals such as phenolic acids, flavonoids, tannins, terpenes, essential oils, allicin, and alliin, which exhibit significant biological activity. These compounds are derived from various plant parts, including leaves, flowers, seeds, bark, roots, and fruits.

Traditionally, medicinal plants have been widely used for the treatment of nail and skin infections across different cultures. In recent years, extensive research has focused on isolating and characterizing antifungal

compounds from plant sources. These bioactive constituents function as natural defense mechanisms in plants and offer promising opportunities for the development of effective and safer antifungal therapies in modern healthcare systems [11].

Plant (Common Name)	Key Constituents	Part Used	Extraction Method	Uses	Ref
Azadirachta indica (Neem)	Nimbin, Azadirachtin	Bark, leaves, seeds	Solvent extraction / Soxhlet	Skin fungal infections, candidiasis	12
Curcuma longa (Turmeric)	Curcuminoids	Rhizomes	Solvent extraction	Wound healing, antifungal	13
Aloe barbadensis (Aloe vera)	Aloin, Emodin	Leaf gel	Gel extraction, homogenization	Skin infections, cosmetics	14
Lonicera japonica	Flavonoids, phenolics	Flower buds	Alcoholic extraction	*Candida*, *Aspergillus* infections	15
Zingiber officinale (Ginger)	Gingerol, shogaols	Rhizomes	Steam distillation	Antifungal, preservation	16
Salvia officinalis (Sage)	Essential oils	Leaves	Steam/Soxhlet extraction	Oral candidiasis	17
Allium sativum (Garlic)	Allicin	Bulb	Solvent extraction	Candidiasis (oral, vaginal)	18
Syzygium aromaticum (Clove)	Eugenol	Flower buds	Steam distillation	Skin & mucosal fungal infections	19
Cuminum cyminum (Cumin)	Cuminaldehyde	Seeds	Solvent extraction	Antifungal activity	20
Lippia alba	Citral, linalool	Leaves	Steam distillation	Skin and nail infections	21
Acorus calamus (Sweet flag)	β-asarone	Rhizomes	Steam distillation	Skin fungal infections	22
Melaleuca alternifolia (Tea tree)	Terpinen-4-ol	Leaves	Steam distillation	Nail, scalp infections	23
Heracleum	Furanocoumarins	Aerial parts	Steam/solvent	Wound infections	24

maximum			extraction		
Artemisia frigida	Terpenes	Leaves, stems	Steam distillation	Traditional skin infection treatment	25
Alnus viridis	Tannins, flavonoids	Bark, leaves	Solvent extraction	*Candida* inhibition	26
Euphorbia hirta	Flavonoids, saponins	Aerial parts	Solvent extraction	Onychomycosis	27
Schinus molle	Essential oils	Leaves, fruits	Steam distillation	Antifungal (agriculture)	28
Ocimum sanctum (Tulsi)	Eugenol	Leaves	Steam distillation	Ringworm, skin infections	29
Swertia chirayita	Xanthones	Roots, aerial parts	Solvent extraction	Skin infections, wounds	30
Baccharis trimera	Flavonoids	Leaves	Solvent extraction	Folk antifungal use	31
Solidago gigantea	Phenolics	Aerial parts	Ethanol extraction	Skin, throat infections	32
Betula alleghaniensis	Phenolics, tannins	Bark, leaves	Ethanol extraction	Candidiasis	33
Ajania tibetica	Camphor	Aerial parts	Steam distillation	Traditional wound care	34
Psidium guajava (Guava)	Flavonoids, tannins	Leaves, bark	Solvent extraction	Antimicrobial, antifungal	35
Origanum vulgare (Oregano)	Phenolics, essential oils	Leaves	Steam/solvent extraction	Natural antifungal preservative	36

Novel Herbal Formulations

The present review highlights five novel herbal dosage forms herbal creams, gels, ointments, nail lacquers, and transdermal patches as promising approaches for the development of effective, safe, and natural antifungal therapies. These formulations offer advantages such as targeted delivery, improved patient compliance, and reduced systemic side effects.

Among these, medicated nail lacquers have emerged as an innovative system for the treatment of onychomycosis. Originally developed for cosmetic purposes, nail lacquers have been adapted to deliver antifungal agents directly to the infected nail. They form a polymeric film over the nail plate, enabling sustained drug release and localized action with minimal systemic absorption. The effectiveness of nail lacquers depends on key formulation parameters such as adhesion, drying time, non-volatile content, water resistance, and drug permeability. Film-forming polymers like

nitrocellulose ensure prolonged drug retention, while penetration enhancers facilitate drug diffusion across the nail plate. Herbal nail lacquers, incorporating plant-derived antifungal agents, are gaining attention as safer alternatives to synthetic formulations [37]

In addition, essential oil-based nanoemulsions (EO-NEs) represent a rapidly advancing area in herbal drug delivery. Essential oils are volatile plant-derived compounds with well-documented antifungal, anti-inflammatory, antioxidant, and therapeutic properties. Formulation into nanoemulsions enhances their stability, solubility, and bioavailability, thereby improving therapeutic efficacy. EO-NEs also exhibit preservative properties, contributing to extended shelf life. Recent developments in formulation and characterization of these systems highlight their significant potential in pharmaceutical and nutraceutical applications, particularly in antifungal therapy [38].

Type	Key Ingredients	Evaluation Parameters	Conclusion	Ref
Herbal Cream	*Azadirachta indica*, *Nelumbo nucifera*, Neem, Turmeric, Tulsi, Aloe vera	pH, spreadability, consistency, zone of inhibition	Exhibited significant antifungal activity against *Candida albicans* with good spreadability, non-greasy nature, and acceptable pH (~6–6.5).	39,40
Herbal Gel	Aloe vera, Betel leaf, *Origanum vulgare*, *Syzygium aromaticum* oils	pH, viscosity, spreadability, MIC, inhibition zone	Showed strong antifungal activity with good physicochemical properties and stability; comparable to standard antifungal agents.	41,42
Herbal Ointment	Neem, Tea tree oil, Garlic, Turmeric, Clove oil	pH, viscosity, homogeneity, MIC, patch test	Demonstrated good physicochemical characteristics and notable antifungal activity; promising natural alternative.	43.44
Herbal Nail Lacquer	Neem, Tulsi, Betel, *Psidium guajava*, *Cissus quadrangularis*	Drying time, adhesion, film thickness, permeation, inhibition zone	Showed effective transungual delivery, good film properties, and strong antifungal activity comparable to marketed products.	45,46
Herbal Patches	CMC, Guar gum, Olea europaea extract	pH, folding endurance, in vitro release	Provided sustained drug release with improved bioavailability; suitable for antifungal wound applications.	47-51

Advantages of Herbal Formulations

Multitarget Mechanism: Herbal formulations often exhibit a multitarget mode of action due to the presence of diverse bioactive compounds. This enables them to act on multiple biological pathways, making them effective against multifactorial diseases and complex infections. Such a mechanism also reduces the likelihood of

drug resistance, as pathogens find it more difficult to adapt to multiple simultaneous targets. Additionally, synergistic interactions among phytoconstituents can enhance therapeutic efficacy while potentially minimizing adverse effects compared to combination therapy with multiple synthetic drugs. Furthermore, the development of multitarget herbal formulations may be more cost-effective than producing multiple single-target drugs [52]

Safety and Reduced Systemic Side Effects: Herbal formulations are generally considered safer and are associated with fewer systemic side effects due to their natural origin and localized action. They provide an expanded antifungal arsenal with diverse mechanisms of action. Many plant-derived compounds exhibit strong antifungal activity, particularly against ***Candida*** species and other pathogenic fungi. Their biocompatibility and lower toxicity make them suitable for long-term use, especially in topical applications [53].

Challenges and Limitations

Despite their advantages, herbal formulations face several limitations. Many herbal extracts are chemically unstable and sensitive to environmental factors such as light, heat, oxygen, moisture, and pH variations, which can lead to degradation and reduced efficacy. Additionally, poor solubility and low permeability of several phytoconstituents limit their bioavailability and therapeutic effectiveness. Compounds such as resveratrol, curcumin, and naringenin exhibit limited aqueous and lipid solubility, restricting their ability to reach target sites. These challenges necessitate the development of advanced drug delivery systems to enhance stability, solubility, and bioavailability of herbal actives [54].

Future Perspectives

Nail lacquers, traditionally used for cosmetic purposes, have evolved into promising drug delivery systems for nail disorders such as onychomycosis. Unlike conventional topical formulations (e.g., creams and lotions), which are easily removed and show limited nail penetration, medicated nail lacquers form a persistent film over the nail surface, enabling sustained drug release and improved therapeutic efficacy.

The limitations of conventional antifungal therapies including toxicity, resistance, and cost have driven the search for safer and more effective alternatives. Herbal products, either as isolated phytoconstituents or standardized plant extracts, offer significant potential as lead compounds for novel antifungal drug development. Moreover, combining herbal agents with synthetic drugs may enhance efficacy, reduce required dosages, and minimize adverse effects. Future research should focus on optimizing such combination therapies and developing advanced delivery systems to improve the clinical utility of herbal antifungal formulations [55, 56].

CONCLUSION

Onychomycosis is a persistent and widespread fungal infection that poses significant therapeutic challenges due to its chronic nature, high recurrence rate, and limitations associated with conventional antifungal treatments. The emergence of drug resistance, systemic toxicity, and prolonged treatment duration necessitates the development of safer and more effective therapeutic alternatives.

Herbal formulations have demonstrated considerable potential in the management of fungal infections due to their diverse bioactive constituents, multitarget mechanisms, and favorable safety profiles. Various medicinal plants and their phytochemicals have shown significant antifungal activity against dermatophytes, yeasts, and non-dermatophyte molds. Moreover, the development of novel drug delivery systems such as herbal creams, gels, ointments, nail lacquers, and transdermal patches has enhanced the therapeutic

effectiveness by improving drug penetration, stability, and patient compliance.

Despite these advantages, challenges such as poor solubility, low bioavailability, and stability issues of herbal compounds remain. Therefore, future research should focus on advanced delivery systems, nanoformulations, and combination therapies to overcome these limitations. Overall, herbal antifungal formulations represent a promising, safe, and cost-effective approach for the treatment of onychomycosis and other fungal infections, with significant potential for future clinical applications.

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