RESEARCH PAPER

Topical Nanocarriers for the Management of Superficial Candidiasis - A Review

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ABSTRACT

Background

Candida infections are among the most common fungal diseases in humans, primarily caused by Candida albicans, with an increasing prevalence of non-albicans species such as C. glabrata, C. tropicalis, C. krusei, and multidrug-resistant C. auris. Superficial candidiasis affects the skin and mucosal tissues, particularly in immunocompromised and high-risk individuals. Although topical antifungal therapy is preferred due to targeted delivery and reduced systemic effects, conventional formulations are limited by poor solubility, insufficient tissue penetration, short residence time, and frequent recurrence.

Objective

To overcome the limitations of conventional therapies, nanotechnology-based topical delivery systems have been developed. Nanoscale carriers such as liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and nanoemulsions enhance antifungal therapy by improving drug solubility, tissue penetration, retention time, and overall therapeutic effectiveness at the target site.

Methodology

Nanocarrier-based topical systems offer clear advantages over conventional formulations by enhancing drug permeation, solubility, and stability. Their nanoscale structure enables improved penetration through keratinized tissues and provides controlled, sustained drug release, which may reduce dosing frequency and recurrence. Lipid-based nanoparticles such as SLNs and NLCs further protect unstable antifungal agents and improve local retention, thereby increasing therapeutic efficacy and patient compliance, especially in high-risk populations.

Conclusion

Superficial candidiasis remains a major clinical issue, particularly in high-risk populations. While topical antifungal therapy is preferred, conventional formulations are limited in effectiveness. Nanotechnology-based systems such as liposomes, SLNs, NLCs, and nanoemulsions improve solubility, tissue penetration, and sustained release, offering enhanced antifungal efficacy and reduced recurrence, and supporting the need for further clinical research.

Keywords: Candidiasis; topical antifungal therapy; nanotechnology; lipid nanoparticles; nanoemulsions; drug delivery.

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INTRODUCTION

Candidiasis comprises a spectrum of infections caused by yeasts of the genus Candida, which normally exist as commensals on human skin and mucosal surfaces. Under physiological conditions, these organisms remain harmless; however, disruption of host immunity or local microenvironmental balance can trigger their transition to pathogenic forms. Key predisposing factors include immunosuppression (e.g., HIV infection, chemotherapy, organ transplantation), diabetes mellitus, pregnancy, prolonged use of broad-spectrum antibiotics, hormonal therapy, and persistent moisture or occlusion [1].

Although Candida albicans continues to be the most frequently isolated pathogen, the incidence of non-albicans Candida species has risen markedly over the past two decades. This epidemiological shift is clinically significant because many non-albicans species exhibit reduced susceptibility or intrinsic resistance to commonly used azole antifungals [2]. In

particular, Candida auris has emerged globally as a major concern due to multidrug resistance and persistence on skin and medical surfaces.

Superficial candidiasis commonly presents as vulvovaginal candidiasis, oral thrush, angular cheilitis, intertrigo, diaper dermatitis, onychomycosis, and fungal keratitis. Vulvovaginal candidiasis affects nearly 75% of women at least once in their lifetime, with recurrent disease occurring in approximately 5–8%. Although rarely life-threatening, these infections cause significant discomfort, psychological burden, reduced quality of life, and healthcare costs [3].

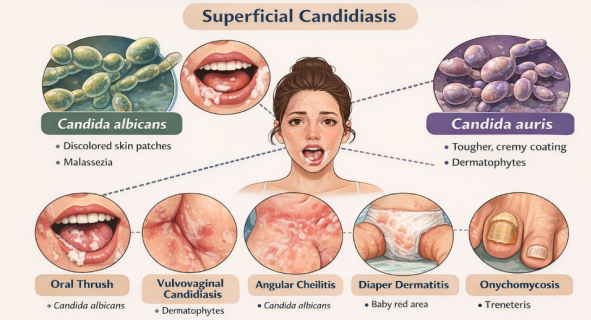

Figure 1: Common Superficial candidiasis infection

Topical antifungal therapy is generally preferred for superficial infections because it enables localized drug delivery while limiting systemic toxicity [4]. Nevertheless, treatment failures and recurrences remain frequent, underscoring the need for improved topical delivery strategies

LIMITATIONS OF CONVENTIONAL TOPICAL ANTIFUNGAL THERAPY

Traditional topical antifungal dosage forms such as creams, ointments, gels, lotions, sprays, powders, and vaginal suppositories primarily contain azoles, polyenes, or allylamines [5]. Despite their widespread use, several physicochemical and biological barriers limit their effectiveness.

A major limitation is the poor aqueous solubility of many antifungal drugs, particularly azoles and polyenes, which restricts drug loading and local bioavailability. To compensate, formulations often require high levels of surfactants or solvents, increasing the risk of irritation and sensitization [6].

The stratum corneum presents another formidable barrier, especially in chronic or hyperkeratotic infections, resulting in insufficient drug levels in deeper epidermal layers. Moreover, conventional topical preparations typically exhibit short residence time due to removal by washing, sweating, friction, or vaginal secretions, necessitating frequent dosing and reducing patient adherence.

MECHANISTIC RATIONALE FOR NANOFORMULATIONS IN TOPICAL CANDIDIASIS

Nanotechnology-based topical drug delivery systems offer multiple mechanistic advantages over conventional formulations. Encapsulation of antifungal agents within lipidic or polymeric nanocarriers significantly enhances apparent solubility and allows higher local drug concentrations at the site of infection [7].

The nanoscale size of these carriers improves interaction with biological membranes and facilitates penetration through intercellular lipid pathways and hair follicles to [8].

Sustained and controlled release from nanoformulations prolongs local drug exposure, reduces dosing frequency, and improves patient compliance [9]. Importantly, certain nanoformulations possess intrinsic antifungal properties. Nanoemulsions, essential oil-based systems, and metallic nanoparticles can disrupt fungal cell membranes, enhancing drug access to sessile cells [10].

Furthermore, surface modification of nanocarriers with mucoadhesive polymers such as chitosan or hyaluronic acid increases adhesion to mucosal surfaces, improving residence time and therapeutic efficacy in vaginal and oral candidiasis [11]. These mechanistic advantages provide a strong scientific basis for the development of nano-enabled topical antifungal therapies.

Table 1: Topical Nanoformulation Platforms for treatment of Candidiasis [12-15]

Nanoformulations	Key Features	Typical Antifungals
Liposomes	Phospholipid vesicles; biocompatible; enhance skin deposition	Amphotericin B, clotrimazole
Niosomes	Non-ionic surfactant vesicles: stable and cost-effective	Ketoconazole, fluconazole
Transfersomes	Ultra-deformable vesicles; deep skin penetration	Terbinafine
Ethosomes	High ethanol content;	Econazole, clotrimazole

Nanoformulations	Key Features	Typical Antifungals
	improved permeation	
Solid Lipid Nanoparticles (SLN)	Controlled release; occlusive effect	Miconazole
Nanostructured Lipid Carriers (NLC)	Higher drug loading than SLN	Ketoconazole
Nanoemulsions	High solubilization of lipophilic drugs	Amphotericin B
Polymeric nanoparticles/micelles	Sustained release; stability	Fluconazole
Metal nanoparticles (AgNPs, AuNPs)	Intrinsic antifungal activity	Silver nanoparticles

FORMULATION DESIGN CONSIDERATIONS FOR TOPICAL ANTIFUNGAL NANOFORMULATIONS

Rational design of topical nanoformulations requires careful consideration of multiple interdependent parameters to ensure efficacy, safety, and translational feasibility.

a) Drug selection and compatibility

The choice of antifungal agent should be guided by the spectrum of activity, potency against *Candida* species, and physicochemical compatibility with the carrier system. Azoles remain the most widely used drugs; however, increasing resistance necessitates exploration of combination strategies or alternative agents [16].

b) Carrier selection based on target tissue

The carrier type should be matched to the infection site. For vulvovaginal and oral candidiasis, mucoadhesive systems such as chitosan-coated nanoparticles or NLC-based gels are preferred to maximize residence time [17]. For cutaneous candidiasis, SLNs, NLCs, transfersomes, and nanoemulsions with strong skin penetration capability are more appropriate.

c) Particle size and surface properties

Particle sizes below 200 nm generally enhance penetration and stability, while surface charge influences interaction with skin and mucosal tissues. Positively charged systems (e.g., chitosan-coated nanoparticles) improve mucoadhesion but may increase cytotoxicity if not optimized [18].

d) Release kinetics

An optimal balance between initial burst release (for rapid fungicidal action) and sustained release (to prevent regrowth) is essential. Lipid composition, polymer molecular weight, and surfactant concentration are key determinants of release behavior [19].

e) Excipient safety and scalability

All excipients should be pharmacopeial grade and non-irritant at dermatological concentrations. Manufacturing methods such as high-pressure homogenization and microfluidization are preferred due to scalability and reproducibility under GMP conditions [20].

Table 2: Comprehensive table summarizing key research reports on nanocarrier systems used with antifungal drugs

Nanocarrier Type	Antifungal Drug	Target Microorganism(s)	Application / Use	Reference
Liposomes	Amphotericin B	*Trichophyton interdigitale*, *T. rubrum* dermatophytes	Topical dermatophytosis; improved MIC and reduced resistance compared to free drug	[21]
SLNs	Miconazole	*Candida*, *dermatophytes*	High encapsulation, improved antifungal efficacy	[22]
SLNs / Nanostructured Lipid Carriers (NLCs)	Voriconazole	*Candida albicans*, other fungal pathogens	Controlled release systems for ocular delivery & vaginal/systemic use	[23]
Nanoemulsion	Amphotericin B	Various pathogenic fungi	Topical delivery with enhanced	[24]

Nanocarrier Type	Antifungal Drug	Target Microorganism(s)	Application / Use	Reference
			skin permeation vs conventional gel	
Polymeric Nanoparticles	Voriconazole, other azoles (review)	Invasive fungal infections	Enhanced stability, targeted delivery & reduced systemic side effects	[25]
Cyclodextrin-based Nanocarriers	Multiple azoles	Broad spectrum fungi	Improved solubility & bioavailability across delivery routes	[26]
Ethosomes / Transfersomes	Terbinafine / other antifungals	Dermatophytes	Topical nano-vesicular carriers for better skin penetration	[27]

CONCLUSION

Topical nanoformulations represent a transformative approach to the management of candidiasis by addressing the key limitations of conventional antifungal therapy. Lipid-based and polymeric nanocarriers enhance solubility, penetration, and retention, offering clear advantages over traditional formulations. While preclinical evidence is compelling, successful clinical translation will depend on standardized evaluation, comprehensive safety profiling, scalable manufacturing, and well-designed clinical trials. Given the rising burden of antifungal resistance and recurrent infections, nano-enabled topical antifungal therapy is poised to become a high-impact area in translational pharmaceutical research.

Superficial candidiasis remains a significant clinical challenge, particularly in immunocompromised and high-risk populations. Although topical antifungal therapy is the standard approach due to localized delivery and reduced systemic toxicity, conventional formulations are hindered by poor solubility, limited tissue penetration, short residence time, and high recurrence rates. Nanotechnology-based topical delivery systems, including liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), nanoemulsions, and polymeric nanoparticles, offer substantial advantages over conventional therapies. These nanoscale carriers enhance drug solubility, penetration through keratinized tissues, retention time, and provide controlled and sustained drug release, thereby improving therapeutic efficacy, reducing dosing frequency, and minimizing recurrence. The mechanistic benefits of nanoformulations—enhanced membrane interaction, deeper tissue penetration, sustained drug exposure, and potential intrinsic antifungal activity—support their growing role in the management of superficial candidiasis. Future research should focus on clinical translation, optimization of carrier design, safety profiling, and addressing emerging resistance patterns among non-albicans Candida species, including multidrug-resistant *Candida auris*.

CONFLICT OF INTEREST

The authors declare no conflict of interest

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AUTHOR CONTRIBUTION

Naini Krishna Rao contributed to the literature collection, conceptualization, drafting, and organization of the manuscript. Swapna. S assisted with manuscript review, editing, and validation. All authors have read and approved the final version of the manuscript

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