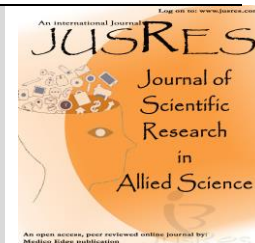




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The Science Behind Antifungal Creams: What Ingredients Actually Matter

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ABSTRACT

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Topical antifungal creams represent the first-line treatment for superficial fungal infections, offering targeted therapy with reduced systemic side effects. This review examines the active pharmaceutical ingredients that determine therapeutic efficacy, their mechanisms of action, and recent advances in formulation science. Seven major classes of topical antifungals are currently used, each with distinct mechanisms targeting fungal cell membrane synthesis or integrity. Clinical studies demonstrate significant efficacy differences between drug classes, with allylamines showing superior cure rates compared to azoles in certain indications. Novel delivery systems including nanoparticles, liposomes, and solid lipid nanoparticles are emerging to enhance skin penetration and therapeutic outcomes. Understanding the molecular basis of antifungal action and formulation science is essential for optimizing treatment selection and developing next-generation topical therapies.

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INTRODUCTION

Fungal skin infections affect over 1 billion people worldwide, making them among the most common dermatological conditions globally. Fungal skin infections are the most common global issue for skin health, with topical antifungal therapy usually preferred because of targeted therapy and fewer side effects. The treatment landscape has evolved significantly since the introduction of the first synthetic antifungals, with modern formulations offering enhanced efficacy, improved patient compliance, and reduced treatment duration.

While most fungi do not play a significant role in human disease, there are several hundred fungi that do, resulting in fungal infection or disease ranging from common benign infections like 'jock itch' to serious, life-threatening infections. Topical antifungal

creams serve as the cornerstone of treatment for superficial mycoses, including dermatophytosis (tinea infections), cutaneous candidiasis, and pityriasis versicolor.

The success of topical antifungal therapy depends on multiple factors: the active pharmaceutical ingredient's intrinsic potency, its mechanism of action, formulation characteristics that affect skin penetration, and the specific pathogen involved. This review provides a comprehensive analysis of the science underlying antifungal cream efficacy, examining both established agents and emerging formulation technologies.

CLASSIFICATION AND MECHANISMS OF ANTIFUNGAL AGENTS

Azole Antifungals

Azoles are a class of antifungals that block the production of ergosterol, a structural fat that makes up the walls of fungi. The lack of

ergosterol causes fungi to weaken, collapse, and die. This class includes imidazoles (clotrimazole, miconazole, ketoconazole) and triazoles (fluconazole), which represent the most widely used topical antifungals.

The mechanism involves inhibition of 14 α -demethylase (CYP51), a cytochrome P450 enzyme crucial for ergosterol biosynthesis. Topical miconazole, a synthetic imidazole, is a fungistatic agent that is highly efficacious (>90%) in tinea infection with better side effect profile. Clotrimazole remains one of the most prescribed agents due to its broad spectrum activity and established safety profile.

Allylamine Antifungals

Allylamines are a class of antifungals that block the integration of a fat called squalene into ergosterol. The accumulation of squalene is toxic to fungi, killing the cells directly. Allylamines are a new type of antifungal drug that is highly selective for the fungal enzyme but has a minimal effect on humans.

Terbinafine and naftifine are the primary members of this class. They work by inhibiting the enzyme squalene-epoxidase, which converts squalene to lanosterol, the raw material for producing ergosterol in fungal cells. This fungicidal action often results in faster cure rates compared to azoles.

OTHER ANTIFUNGAL CLASSES

Naphthalenes work similarly to allylamines, blocking squalene integration into ergosterol.

Polyenes directly disrupt ergosterol structure in fungal walls. Benzylamines are a type of antifungal that blocks the replication of fungal DNA, while hydroxypyridinones disrupt iron essential to the survival of fungal cells.

Ciclopirox olamine represents a unique mechanism. It works by causing depletion of important substrates such as amino acids and/or ions within fungal cells, resulting in the inhibition of transport of these substances across fungal cell membranes and disrupts the synthesis of DNA, RNA and proteins.

COMPARATIVE EFFICACY AND CLINICAL PERFORMANCE

Clinical Trial Evidence

Clinical studies demonstrate that a one week course of terbinafine 1% cream is more effective in the treatment of tinea pedis than a four week course of clotrimazole 1% cream, both in terms of mycological cure and effective treatment. Specific cure rates showed mycological cure rates of 93.5% for terbinafine and 73.1% for clotrimazole at week four, and 97.2% for terbinafine and 83.7% for clotrimazole at week six.

Meta-Analysis Findings

A systematic review evidenced the superiority of antifungal drugs compared to placebo, regardless of the dermatomycosis under evaluation, with odds ratio values ranging from 2.05 to 67.53. Allylamines were better than azoles only for the outcome of sustained cure.

In comparative studies of topical terbinafine and miconazole, both agents demonstrated effectiveness, with topical cream being 80% efficacious for localized tinea corporis, pedis, cruris, and pityriasis versicolor.

FORMULATION SCIENCE AND DRUG DELIVERY

TRADITIONAL FORMULATIONS

Conventional antifungal creams rely on standard emulsion technology with active ingredients dispersed in oil-in-water or water-in-oil bases. The choice of base affects drug release, skin penetration, and patient acceptability. Factors influencing formulation performance include:

- Vehicle composition and pH
- Presence of penetration enhancers
- Drug particle size and crystalline form
- Stability and compatibility with excipients

ADVANCED DELIVERY SYSTEMS

NANOPARTICLE FORMULATIONS

Recent work demonstrates that the combination of nanometal with antifungal drugs increases antifungal activity. Silver nanoparticles change membrane permeability and enhance drug penetration, eventually leading to cell death. These systems offer dual mechanisms: intrinsic antimicrobial

activity of the nanoparticle and enhanced drug delivery.

Liposomal Systems

Liposomal gel of ketoconazole shows higher drug retention in the skin compared to gel and cream formulations due to their ability to alter the biodistribution profile of entrapped drug. Liposomes can be designed with different surface properties to optimize skin penetration and target specific tissue layers.

Solid Lipid Nanoparticles (SLNs)

SLNs offer increased drug loading, improved skin penetration and reduced drug leakage of topically applied anti-fungal drugs. Both

SLNs and NLCs protect the encapsulated drug against photo degradation and have comparable antifungal activity to marketed products.

Penetration Enhancement Strategies

The topical therapy of nail diseases is limited by the low permeability of drugs through the nail plate. To increase drug penetration, the integrity of the nail plate must be compromised to enhance ungual drug permeation. Co-delivery with acetylcysteine statistically significantly prolonged the mean residence time of oxiconazole in nail layers and increased retention of the drug.

Table 1: Classification and Mechanisms of Major Antifungal Classes in Topical Creams

Antifungal Class	Representative Agents	Mechanism of Action	Target Site	Activity Type
Azoles (Imidazoles)	Clotrimazole, Miconazole, Ketoconazole	Inhibition of 14 α -demethylase (CYP51)	Ergosterol biosynthesis pathway	Fungistatic
Azoles (Triazoles)	Fluconazole	Inhibition of 14 α -demethylase (CYP51)	Ergosterol biosynthesis pathway	Fungistatic
Allylamines	Terbinafine, Naftifine	Inhibition of squalene epoxidase	Early ergosterol synthesis	Fungicidal
Naphthalenes	Tolnaftate	Squalene epoxidase inhibition	Early ergosterol synthesis	Fungicidal
Polyenes	Nystatin	Direct binding to ergosterol	Fungal cell membrane	Fungicidal
Ciclopirox	Ciclopirox olamine	Metal ion chelation, membrane disruption	Multiple cellular targets	Fungicidal
Benzylamines	Butenafine	DNA replication inhibition	Fungal genetic material	Fungicidal

Table 2: Comparative Efficacy Data of Common Topical Antifungal Agents

Agent	Concentration	Treatment Duration	Mycological Cure Rate (%)	Clinical Efficacy (%)	Common Indications
Terbinafine	1%	1-2 weeks	93.5-97.2	89.7	Tinea pedis, cruris, corporis
Clotrimazole	1%	2-4 weeks	73.1-83.7	58.7-73.1	Candidiasis, dermatophytosis
Miconazole	2%	2-4 weeks	>90	80-90	Tinea infections, candidiasis
Ketoconazole	2%	2-3 weeks	75-85	70-80	Seborrheic

					dermatitis, tinea
Naftifine	1%	2-4 weeks	85-90	75-85	Dermatophytosis
Fluconazole	Oral/topical	Variable	85-95	80-90	Candidiasis (systemic)
Ciclopirox	0.77%	2-4 weeks	70-80	65-75	Tinea, seborrheic dermatitis

Data compiled from multiple clinical studies and meta-analyses

FACTORS AFFECTING TREATMENT SUCCESS

Patient-Related Factors

Treatment success depends on proper application technique, adherence to prescribed duration, and continuation beyond symptom resolution. Most conditions take up to four weeks to resolve, and patients must be educated about the importance of completing the full treatment course.

Pathogen-Specific Considerations

Different fungal species exhibit varying susceptibility to antifungal agents. Tolnaftate is effective in inhibiting the growth of dermatophytes such as *Epidermophyton* and *Microsporum*, but the drug has no use against candida or bacteria infections. This highlights the importance of proper diagnosis and agent selection.

Resistance Patterns

WHO released the fungal priority pathogens list (FPPL) in November 2022, cataloguing the 19 fungi that represent the greatest threat to public health, considering unmet research and development needs. While resistance in superficial mycoses remains relatively uncommon, appropriate antifungal stewardship is essential.

FUTURE DIRECTIONS AND EMERGING TECHNOLOGIES

Novel Drug Delivery Systems

Biodegradable polymer microneedles consisting of polyglycolic acid coated with voriconazole show superior antifungal activity, with piezoelectric inkjet printing technology successfully used to load miconazole onto polymeric microneedles.

Combination Therapies

Novel formulations combining traditional antifungals with penetration enhancers or antimicrobial nanoparticles are entering

clinical development, potentially offering synergistic effects.

Personalized Medicine Approaches

Future developments may include genetic testing to predict treatment response and customized formulations based on individual skin characteristics and infection patterns.

CONCLUSION

The efficacy of topical antifungal creams depends on a complex interplay of active ingredient selection, formulation science, and patient factors. Allylamines demonstrate superior sustained cure rates compared to azoles, particularly for dermatophyte infections, while azoles remain effective first-line treatments for many superficial mycoses.

Recent advances in nanotechnology and drug delivery systems offer promising approaches to enhance skin penetration and therapeutic outcomes. The development of novel formulations incorporating nanoparticles, liposomes, and penetration enhancers represents the next frontier in topical antifungal therapy.

Clinicians should consider the specific pathogen, infection site, patient compliance factors, and comparative efficacy data when selecting antifungal treatments. As our understanding of fungal pathogenesis and drug delivery mechanisms continues to evolve, the future holds promise for more effective, faster-acting, and patient-friendly topical antifungal therapies.

The science behind antifungal creams extends far beyond the active ingredient alone – successful treatment requires optimization of the entire drug delivery system to ensure adequate penetration to the infection site while maintaining safety and tolerability.

REFERENCES

1. Boehm A, et al. Topical antifungal agents: mechanisms and clinical applications. *StatPearls*. 2025.
2. Poojary SA. Topical antifungals: a review and their role in current management of dermatophytoses. *Clin Dermatol Rev*. 2017;1(Suppl 1):S24-S29.
3. Jana S, Gayen S, Kumari R, et al. Mechanism of action of antifungal agents. *How Synthetic Drugs Work*. 2023;1(1):431-445.
4. Evans EG, et al. Comparison of terbinafine and clotrimazole in treating tinea pedis. *Br J Dermatol*. 1993;129(4):429-434.
5. Crawford F, Hollis S. Topical treatments for fungal infections of the skin and nails of the foot. *Cochrane Database Syst Rev*. 2007;(3):CD001434.
6. Rotta I, et al. Efficacy of topical antifungal drugs in different dermatomycoses: a systematic review with meta-analysis. *Rev Assoc Med Bras*. 2012;58(3):308-318.
7. Greer DL. Successful treatment of tinea cruris with topical terbinafine. *Clin Exp Dermatol*. 1989;14(2):117-119.
8. Sharma A, et al. Efficacy and tolerability of sertaconazole nitrate 2% cream vs miconazole 1% cream. *Indian J Dermatol*. 2011;56(5):523-526.
9. Leenutaphong V, Niumpradit N, Tangwiwat S. Comparison of 1 week terbinafine cream vs 4 weeks miconazole cream in patients with tinea pedis. *J Med Assoc Thai*. 1999;82(10):1006-1010.
10. Korting HC, Rychlik R, Pfeil B. Comparative efficacy and safety of topical antifungal treatments. **Dtsch Med Wochensh*