World Journal of Pharmaceutical Science and Research

www.wjpsronline.com

Review Article

ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 11
Page: 62-68

HYDROGEL-BASED TOPICAL ANTIFUNGAL DRUG DELIVERY SYSTEMS

Ummehani Kallawala*, Dharmik Patel, Sayur Asani, Dax Mardiya, Parth Mori, Krisha Bhatt

Krishna School of Pharmacy & Research, A Constituent School of Drs. Kiran & Pallavi Patel Global University, Varnama, Vadodara, Gujarat, India.

Article Received: 09 September 2026 | | ***Article Revised: 30 September 2026*** | | ***Article Accepted: 20 October 2026***

***Corresponding Author: Ummehani Kallawala**
Krishna School of Pharmacy & Research, A Constituent School of Drs. Kiran & Pallavi Patel Global University, Varnama, Vadodara, Gujarat, India. **DOI:** https://doi.org/10.5281/zenodo.23798916

How to cite this Article: Ummehani Kallawala, Dharmik Patel, Sayur Asani, Dax Mardiya, Parth Mori, Krisha Bhatt (2026) HYDROGEL-BASED TOPICAL ANTIFUNGAL DRUG DELIVERY SYSTEMS. World Journal of Pharmaceutical Science and Research, 5(11), 62-68.

Copyright © 2026 Ummehani Kallawala | World Journal of Pharmaceutical Science and Research.
This work is licensed under creative Commons Attribution-NonCommercial 4.0 International license (CC BY-NC 4.0).

ABSTRACT

Fungal infections span superficial skin conditions to life-threatening systemic diseases, especially in immunocompromised patients. Conventional antifungals often suffer from poor aqueous solubility, limited skin retention, systemic toxicity, and rising resistance. To address these limitations, this study focuses on the formulation and evaluation of an antifungal hydrogel for topical delivery. Hydrogels are three-dimensional, cross-linked polymeric networks that retain significant water, offering improved drug residence time, controlled release, enhanced patient acceptability, and localized therapeutic action. The proposed hydrogel employs Carbopol as the gelling polymer, with propylene glycol and glycerine serving as humectants and permeation enhancers, while purified water acts as the aqueous vehicle for the active pharmaceutical ingredient. This system aims to increase topical drug retention, provide sustained release, reduce dosing frequency, and ultimately improve therapeutic outcomes in localized fungal infections. Such a formulation could be particularly valuable for cutaneous and mucocutaneous candidiasis, dermatophytosis, and other superficial mycoses requiring targeted, non-systemic therapy.

KEYWORDS: Antifungal hydrogel; Topical drug delivery; Carbopol; Controlled release; Skin retention; Permeation enhancement; Propylene glycol; Glycerine; Superficial fungal infections; Cutaneous candidiasis; Dermatophytosis; Localized therapy.

INTRODUCTION

Fungi are eukaryotic organisms. Pathogenic fungi can cause infections ranging from mild cutaneous conditions to diseases such as cryptococcal meningitis. Mycoses are classified as local (superficial, cutaneous, subcutaneous) or systemic (deep, bloodborne). The acquisition of fungal infection can occur through either an exogenous

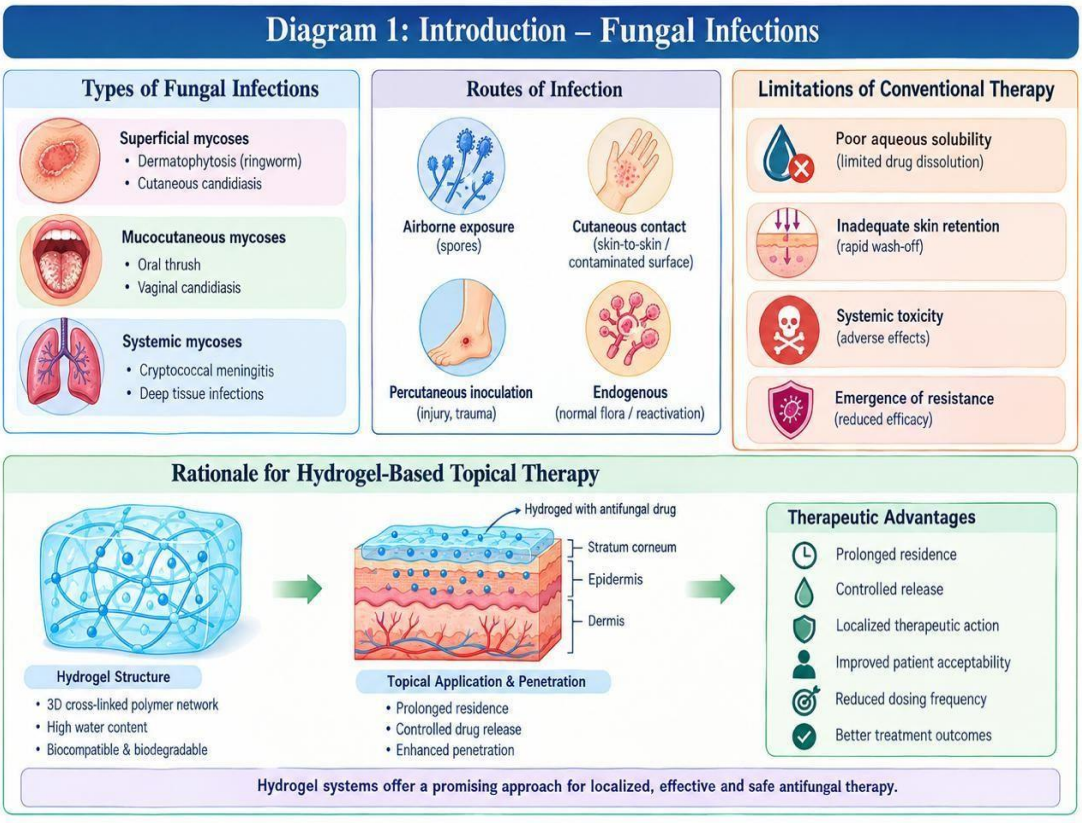
(airborne/inhalation, cutaneous exposure, or percutaneous inoculation) or an endogenous process (normal flora or reactivation of an existing infection). The virulence of the organism is classified as either a primary infection (a disease arising in a healthy host) or an opportunistic infection (a disease arising in human hosts with a compromised immune system or other defenses).

Hydrogels are three-dimensional, hydrophilic polymer networks that are physically or chemically cross-linked and capable of absorbing large amounts of water. Their water-retaining ability results from hydrophilic functional groups, while cross-links prevent dissolution. Important properties include swelling, elasticity, flexibility, softness, biocompatibility, biodegradability, and responsiveness to pH, temperature, and ionic strength.

Hydrogels are widely used in drug delivery because they can protect drugs, prolong residence at the absorption site, and provide controlled or stimuli-responsive release. Their tissue-like texture and high water content also make them useful in biosensors, contact lenses, artificial skin, prosthetic materials, wound dressings, tissue engineering, and mucosal drug delivery. Mucoadhesive hydrogels can interact with glycoproteins in mucosaltissues through hydrogen bonding, particularly when they contain hydroxyl and carboxyl groups.

Although conventional creams and gels are clinically useful, topical formulation performance is not determined by potency alone. The vehicle controls residence time, release rate, spreading, hydration of the stratum corneum and fraction of drug available at the target site. Hydrogels are three-dimensional polymeric networks with high water content that can provide a non-greasy, cosmetically acceptable platform for topical delivery.

Topical antifungal therapy remains the preferred treatment for localized fungal infections because it delivers the drug directly to the infected tissues while minimizing systemic exposure and adverse effects.



MATERIAL AND METHOD

1. Hydrogels as antifungal drug delivery vehicles

Conventional topical and systemic antifungal therapies are often limited by poor drug penetrability, systemic toxicity, and the emergence of drug resistance, which has driven interest in polymeric hydrogel and nanogel platforms as delivery vehicles. These 3-dimensional crosslinked hydrophilic polymer networks can enhance drug solubility, stability, and localized delivery. Their high water content, tunable mesh size, and biocompatibility make them attractive for cutaneous, mucosal, and ocular fungal infections.[1,5,10]

2. Preparation methods (cross-linking techniques)

Hydrogels can be prepared using several cross-linking approaches:

- Physical cross-linking -via hydrogen bonding, hydrophobic interactions, electrostatic attraction, chain entanglement, freeze-thaw cycles, ionic interactions, and complex coacervation.
- Chemical cross-linking - using covalent cross-linkers such as glutaraldehyde, epichlorohydrin, and adipic acid dihydrazide.
- Grafting polymerization - monomers are polymerized onto an existing polymer backbone.
- Radiation cross-linking - high-energy radiation generates free radicals without added chemical cross-linkers.
- Heat-induced aggregation -heating promotes polymer/protein aggregation and gel formation. Physical hydrogels are generally reversible and prepared under mild conditions, whereas chemical hydrogels are more stable, mechanically stronger, and typically irreversible.[3]

3. General laboratory-scale preparation procedure

Based on the methods reported across the reviewed studies, a representative procedure is:

1. Disperse the accurately weighed gelling agent (Carbopol) in purified water and allow it to soak/hydrate for 12–24 h with intermittent stirring.
2. Separately dissolve the antifungal drug in a small quantity of ethanol or a suitable co-solvent, and disperse the preservatives (methyl and propyl paraben) into the aqueous/polymer phase with gentle heating if required.
3. Incorporate the drug solution into the hydrated polymer dispersion with continuous stirring; add glycerine (humectant) slowly with continuous mixing.
4. Neutralize the dispersion drop-wise with triethanolamine under slow, continuous stirring until a smooth, transparent gel of the desired consistency is obtained.2
5. Store the gel in a clean, airtight container and allow it to equilibrate for 24 h before evaluation.

The overall procedure was similar across the reviewed studies; the main variable was usually the concentration of the gelling agent, adjusted within the reported range across trial batches to identify the most suitable formulation.[2,7]

A miconazole nitrate hydrogel study compared Carbopol grades 934P, 971P, and 974P, using FT-IR to confirm drug–polymer compatibility and evaluating pH, viscosity, and percentage swelling index.[7]

An aloe vera-based hydrogel was prepared by homogenizing Carbopol 934, then blending in aloe vera extract, propylene glycol 400, glycerin, and methyl paraben, followed by neutralization with triethanolamine to obtain a uniform gel.[2]

4. Polymers used

- Chitosan and hyaluronic acid — biodegradable, mucoadhesive natural polymers well suited to antifungal and ophthalmic gels, offering controlled drug release and wound-healing support.
- HPMC (hydroxypropyl methylcellulose) — a semisynthetic cellulose derivative providing water solubility and swelling capacity.
- PLGA — enables tunable, sustained release when formulated into nanoparticles.
- Combining these polymers can provide hybrid systems with enhanced residence time, biocompatibility, and prolonged therapeutic action for topical and ocular use.

More recently, nanogels (crosslinked hydrophilic networks generally reported in the nanoscale range) have extended this polymer toolkit. Their tunable particle size, stimuli responsiveness, high drug-loading capacity, and biocompatibility can improve permeation across biological barriers and enable controlled release at the infection site. Vitamin E TPGS-based nanogels, for example, have been reported to improve dermal delivery of amphotericin B, with increased skin deposition and antifungal activity compared with conventional formulations.[1,8,9]

5. Common antifungal agents in hydrogel delivery

Drug	Formulation approach
Terbinafine hydrochloride	Formulated in Carbopol, Natrosol, or chitosan gels for topical delivery against fungal pathogens.
Miconazole nitrate	Broad-spectrum imidazole incorporated into Carbopol-based hydrogel networks for localized cutaneous application.
Ketoconazole	Solubility and antifungal activity can be enhanced using dendrimer–hydrogel composites.
Amphotericin B	Investigated in polymeric and nanogel-based matrices for topical or mucosal delivery.
Itraconazole	Itraconazole-loaded solid lipid nanoparticle-bearing hydrogels have been investigated for sustained dermal delivery against dermatophytes.
Voriconazole	Thermosensitive in-situ gels using poloxamers and cellulose derivatives have been investigated for fungal keratitis, providing site-specific ocular delivery.

Examples of these approaches are reported in studies of terbinafine hydrogels, miconazole nitrate hydrogels, ketoconazole–dendrimer hydrogels, and voriconazole thermosensitive insitu gels.[5,7,6,11,12]

6. Drug release mechanisms

- Diffusion-controlled -the most common mechanism; drug diffusion through the hydrated polymer network may be described using Fickian or empirical models.
- Chemically controlled - release is driven by reactions within the delivery matrix, including hydrolytic or enzymatic cleavage of polymer chains or reversible/irreversible polymerdrug interactions; mechanisms may involve surface erosion or bulk degradation.
- Swelling-controlled -occurs when drug diffusion is closely related to hydrogel swelling and movement of the interface between swollen and unswollen regions. These mechanisms are commonly distinguished experimentally by fitting in-vitro diffusion data to zero-order, first-order, Higuchi, and Korsmeyer–Peppas kinetic models.[3,10]

7. Advantages and disadvantages of antifungal hydrogels

Advantages

- High water content provides flexibility and can improve compatibility with biological tissues.
- Good transparency and ease of modification.
- Biocompatibility and biodegradability can be achieved depending on the polymer system.
- Controlled or sustained release of therapeutic agents can be designed.
- Stimuli-responsive systems can respond to pH, temperature, or other environmental changes.
- Hydrogels can provide a soothing topical application and prolonged residence at the application site.

Disadvantages

- Some hydrogel systems have relatively high formulation or manufacturing costs.
- Purely physical gels may have lower mechanical strength.
- Sterilization can be challenging for some polymer systems.
- Some formulations may be non-adherent or may show deposition/dehydration-re
- Some formulations may be non-adherent or may show deposition/dehydration-related issues in specialized applications such as contact lenses.

The balance between mechanical properties, stability, adhesion, and drug-release performance depends strongly on polymer type and cross-linking method.[1,3,10] 8. Evaluation parameters After preparation, hydrogels are generally subjected to physicochemical, drug-release, microbiological, and safety tests. The principal variables reported across formulation studies include the type and concentration of the gelling agent, which influence viscosity, spreadability, swelling, gel strength, and drug release.[2,5,7,8]

8. Evaluation parameters

After preparation, hydrogels are generally subjected to physicochemical, drug-release, microbiological, and safety tests. The principal variables reported across formulation studies include the type and concentration of the gelling agent, which influence viscosity, spreadability, swelling, gel strength, and drug release.[2,5,7,8]

Parameter	Common method / instrument	Reported/typical interpretation
Physical appearance and homogeneity	Visual inspection against light	Clear/translucent and free from visible aggregates
Ph	Digital pH meter	Formulation-dependent; commonly adjusted to a skin-compatible range
Viscosity	Brookfield viscometer or rheometer	Generally increases with increasing polymer concentration
Spreadability	Spread between glass slides under a fixed load	Generally decreases as polymer concentration increases
Gel strength	Time or force required for a weighted probe to penetrate a defined depth	Generally increases with increasing polymer concentration
Drug content	UV–visible spectrophotometric or chromatographic assay after suitable dilution	Commonly assessed against labelled claim
In-vitro diffusion/release	Franz diffusion cell with suitable membrane	Data may be fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models
Antifungal activity	Cup-plate/agar-well diffusion or microdilution	Zone of inhibition or MIC/MFC, as appropriate
Skin irritation	Validated erythema/edema assessment where ethically justified	Used to assess topical tolerability
Stability	Accelerated/long-term storage under defined temperature and humidity conditions	Monitor changes in appearance, pH, viscosity, and drug content

RESULT AND DISCUSSION

A consistent formulation trend is that increasing gelling-polymer concentration generally increases viscosity and gel strength, while spreadability and drug diffusion may decrease. This inverse relationship means that formulators must balance rheological and mechanical performance against therapeutic release goals when selecting an appropriate gelling-agent concentration. A formulation that is too dilute may provide inadequate viscosity andresidence time, whereas excessive polymer concentration may impede drug diffusion and spreadability.[2,5,7] Recent work is moving from conventional polymer hydrogels toward nanogel and stimuliresponsive systems, including thermosensitive and pH-responsive platforms. These approaches aim to combine the water-retentive and biocompatible characteristics of hydrogels with improved drug loading, permeation, and controlled release. Nevertheless, toxicity, long-term stability, reproducibility, scale-up, and regulatory translation remain important considerations.[8,9,10,11,12]

CONCLUSION

Fungal infections continue to represent an important healthcare challenge worldwide. Although numerous antifungal drugs are available, conventional topical formulations often suffer from poor aqueous solubility, inadequate skin penetration, limited residence time, and reduced therapeutic effectiveness.

Nanocarrier-based drug delivery systems, including liposomes, microemulsions, transfersomes, transethosomes, nanoparticles, and thermosensitive in situ gels, have demonstrated remarkable potential to overcome these limitations. These advanced delivery systems improve drug solubility, enhance penetration through biological barriers, provide sustained drug release, increase local drug concentration, reduce systemic toxicity, and improve patient compliance.

The five studies reviewed consistently demonstrated superior physicochemical properties, enhanced drug permeation, improved antifungal activity, and better therapeutic performance compared with conventional formulations. These findings strongly support the continued development of nanotechnology-based topical antifungal drug delivery systems. Although several challenges remain regarding large-scale manufacturing, long-term stability, and regulatory approval, continued research and clinical evaluation are expected to facilitate the successful translation of these innovative formulations into routine clinical practice.

Overall, nanocarrier-based antifungal formulations represent a promising future direction in pharmaceutical drug delivery and have the potential to significantly improve the management of superficial and localized fungal infections.

ACKNOWLEDGEMENT

The authors sincerely express their gratitude to their respected teachers, mentors, and colleagues for their valuable guidance, constructive suggestions, and continuous encouragement during the preparation of this review article entitled ―Recent Advances in Nanocarrier-Based Topical Antifungal Drug Delivery Systems.‖ The authors are also thankful to their institution for providing the necessary academic facilities, resources, and support required for the completion of this work. The authors gratefully acknowledge all those who contributed directly or indirectly to the successful completion of this review article.

REFERENCES

1. El-Badry M, Fetih G, Shakeel F. Comparative topical delivery of antifungal drug croconazole using liposome and micro-emulsion-based gel formulations. Drug Deliv, 2014; 21(1): 34-43.
2. Asghar Z, Jamshaid T, Sajid-ur-Rehman M, et al. Novel transethosomal gel containing miconazole nitrate: Development, characterization, and enhanced antifungal activity. Pharmaceutics, 2023; 15: 2537.
3. Farooq M, Usman F, Zaib S, et al. Fabrication and evaluation of voriconazole-loaded transethosomal gel for enhanced antifungal and antileishmanial activity. Molecules, 2022; 27: 3347.
4. Cheng Z, Kandekar U, Ma X, et al. Optimizing fluconazole-embedded transfersomal gel for enhanced antifungal activity and compatibility studies. Front Pharmacol, 2024; 15: 1353791.
5. Chaiwut C, Tadtong S, Akachaipaibul P, et al. Thermosensitive in situ ophthalmic gel for effective local delivery and antifungal activity of ketoconazole nanoparticles. Gels, 2025; 11: 13.
6. Bee N, Dubey N, Sahu R, Choudhary B. A Comprehensive Review on Hydrogel. Int J Pharm Sci, 2024; 2(10): 583–594.
7. Patil S, Patil S, Joshi V. Formulation and Evaluation of Hydrogel. Int J Pharm Sci, 2025; 3(5): 2494–2499.
8. Kesharwani P, Bisht A, Alexander A, Dave V, Sharma S. Biomedical applications of hydrogels in drug delivery system: An update. J Drug Deliv Sci Technol, 2021; 66: 102914. 9. Bhagwat AR, Singh S, Belwalkar S, Kaple P. Hydrogel: From Preparation to Applications – A Review on Key Properties and Formulation Techniques. Int J Creative Res Thoughts, 2025; 13(4): c882–c895.
9. Çelebi N, Ermiş S, Özkan S. Development of topical hydrogels of terbinafine hydrochloride and evaluation of their antifungal activity. Drug Dev Ind Pharm, 2015; 41(4): 631–639.
10. Winnicka K, Wroblewska M, Wieczorek P, Sacha PT, Tryniszewska E. Hydrogel of Ketoconazole and PAMAM Dendrimers: Formulation and Antifungal Activity. Molecules, 2012; 17(4): 4612–4624..
11. Bhattacharya S, Paul B, Roy Biswas G. Development and Evaluation of Hydrogel of an Anti-Fungal Drug. Int J Pharm Pharm Sci, 2023; 15(10): 29–33.
12. Kale M, Sheikh AA, Sagrule SA, Biyani KR. Formulation and Evaluation of Nanogel Based Antifungal Drug Delivery Systems. World J Pharm Sci Res, 2026; 5(4): 539–546.
13. Kale M, Sheikh A, Sagrule S, Biyani K. Nanogel-Based Antifungal Drug Delivery Systems: Advances in Design, Characterization, Therapeutic Applications, and Future Directions. Int J Sci R Tech, 2026; 3(4): 485–494.
14. Teng Y, Li S, Tang H, Tao X. Medical Applications of Hydrogels in Skin Infections: A Review. Infect Drug Resist, 2023; 16: 391–401.
15. Üstündağ Okur N, Yozgatlı V, Okur ME, Yoltaş A, Siafaka PI. Improving therapeutic efficacy of voriconazole against fungal keratitis: Thermo-sensitive in situ gels as ophthalmic drug carriers. J Drug Deliv Sci Technol, 2019; 49: 323–333.
16. Sampathi S, Maddukuri S, Ramavath R, Dodoala S, Kuchana V. Modified cyclodextrinbased thermosensitive in situ gel for voriconazole ocular delivery against fungal keratitis. Int J Appl Pharm, 2024; 16(1): 150–160.
17. Ankita Kemdarne*, Hrushikesh Joshi, A Comprehensive Review on Hydrogel, Int. J. of Pharm. Sci., 2026; 4(7): 2974-2986.