

NANOEMULGEL TECHNOLOGY IN TOPICAL ANTIFUNGAL THERAPY: CURRENT PERSPECTIVES AND APPLICATIONS***Ankit Kumar Pal, Vipul Singh, Dr. Sanjay Kumar Kushwaha**

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ABSTRACT

Fungal skin infections are among the most prevalent dermatological disorders worldwide, affecting millions of individuals and significantly reducing quality of life. Conventional topical antifungal formulations such as creams, ointments, and lotions often exhibit limitations including poor drug solubility, inadequate skin permeation, limited retention at the site of infection, frequent dosing requirements, and reduced patient compliance. These challenges have encouraged the development of advanced topical drug delivery systems capable of improving therapeutic efficacy and enhancing localized drug action. Nanoemulgel technology has emerged as a promising approach in topical antifungal therapy by combining the advantages of nanoemulsions and gel-based systems into a single multifunctional formulation. Nanoemulgels consist of nanosized oil droplets dispersed within a gel matrix, which

enhances drug solubilization, stability, spreadability, and skin permeation. The nanoscale droplet size provides a large surface area that facilitates improved penetration through the stratum corneum and prolonged retention of antifungal agents at the target site. Various antifungal drugs including ketoconazole, clotrimazole, itraconazole, fluconazole, terbinafine, and luliconazole have demonstrated enhanced therapeutic performance when incorporated into nanoemulgel systems. This review highlights the composition, preparation methods, characterization parameters, mechanisms of enhanced drug delivery, and therapeutic applications of nanoemulgels in antifungal therapy. In addition, recent advances, comparative advantages over conventional topical systems, safety considerations, formulation challenges,

and future perspectives are discussed. Overall, nanoemulgels represent an innovative and effective platform for topical antifungal delivery with significant potential to improve treatment outcomes, patient adherence, and the management of superficial fungal infections in modern dermatological practice.

1. INTRODUCTION

Fungal infections represent a major global healthcare concern due to their increasing prevalence, recurrent nature, and associated morbidity. Superficial fungal infections affecting the skin, hair, and nails are among the most common dermatological disorders worldwide and are primarily caused by dermatophytes, yeasts, and molds.^[1] Conditions such as candidiasis, dermatophytosis, tinea infections, and pityriasis versicolor significantly affect patient quality of life, particularly in tropical and humid regions where fungal growth is favored. Topical antifungal therapy remains the preferred treatment approach for superficial fungal infections because it enables localized drug delivery directly at the site of infection while minimizing systemic adverse effects. Commonly used antifungal agents include azoles, allylamines, polyenes, and echinocandins, which act by disrupting fungal cell membrane synthesis or function.^[2] Despite the widespread use of topical antifungal formulations such as creams, ointments, gels, and lotions, conventional delivery systems exhibit several limitations that compromise therapeutic efficacy. Poor aqueous solubility of many antifungal drugs, inadequate skin penetration, limited drug retention at the target site, frequent dosing requirements, and instability of active pharmaceutical ingredients often result in suboptimal clinical outcomes.^[3] Additionally, traditional topical formulations may cause skin irritation, greasiness, poor spreadability, and reduced patient compliance. The barrier function of the stratum corneum further restricts drug permeation, particularly for lipophilic antifungal compounds with high molecular weight. These limitations have encouraged the development of advanced drug delivery systems capable of enhancing topical bioavailability and improving therapeutic performance.^[4] In recent years, nanoemulgel technology has emerged as a promising and innovative platform for topical antifungal drug delivery. Nanoemulgels are hybrid formulations that combine the advantages of nanoemulsions and gels into a single system. Nanoemulsions are thermodynamically or kinetically stable colloidal dispersions composed of oil, water, surfactants, and co-surfactants with droplet sizes typically ranging from 20–200 nm. Incorporation of nanoemulsions into gel matrices improves formulation viscosity, spreadability, stability, and patient acceptability.^[5] Due to their nanosized droplets and large surface area, nanoemulgels enhance drug solubilization, skin permeation, and

localized drug retention. Furthermore, they provide controlled drug release, reduced irritation potential, and improved antifungal activity compared with conventional formulations. Nanoemulgels have shown significant potential for delivering poorly water-soluble antifungal agents such as itraconazole, ketoconazole, clotrimazole, fluconazole, and terbinafine.^[6] The growing interest in nanotechnology-based topical delivery systems has accelerated research on antifungal nanoemulgels for improved therapeutic outcomes. Various formulation strategies involving natural oils, penetration enhancers, bio adhesive polymers, and optimized surfactant systems have been investigated to enhance antifungal efficacy and stability. Several preclinical and clinical studies have demonstrated superior permeation characteristics, prolonged drug release, enhanced patient compliance, and increased antifungal effectiveness of nanoemulgel formulations.^[6] The present review aims to provide a comprehensive overview of nanoemulgel technology in topical antifungal therapy. The review discusses the pathophysiology of fungal infections, challenges associated with conventional topical antifungal formulations, formulation principles of nanoemulgels, methods of preparation, characterization parameters, mechanisms of enhanced skin delivery, and recent advances in antifungal nanoemulgel research. In addition, the review highlights current applications, therapeutic advantages, safety considerations, regulatory aspects, and future perspectives of nanoemulgel-based antifungal systems in modern dermatological therapy.^[7]

2. Nanoemulgel Systems: Composition and Functional Characteristics

Nanoemulgels are advanced semisolid drug delivery systems formed by incorporating nanoemulsions into a gel matrix to combine the advantages of both nanoscale emulsified systems and conventional topical gels.^[8] These hybrid formulations have gained considerable attention in topical antifungal therapy because of their ability to improve drug solubility, skin permeation, stability, and patient compliance. Nanoemulgels are particularly suitable for lipophilic antifungal drugs that exhibit poor aqueous solubility and limited bioavailability when administered through conventional topical formulations.^[9]

Structure and Components of Nanoemulgels

Nanoemulgels generally consist of two integrated phases: a nanoemulsion system and a gel base. The nanoemulsion phase is composed of oil droplets dispersed within an aqueous medium and stabilized by surfactants and co-surfactants.^[10] These droplets typically range from 20 to 200 nm in diameter, providing a large interfacial surface area for enhanced drug

solubilization and absorption. The nanoemulsion is subsequently incorporated into a suitable hydrogel matrix to obtain a semisolid formulation with improved viscosity and topical applicability.^[11] Structurally, nanoemulgels may exist as oil-in-water (O/W) or water-in-oil (W/O) systems depending on the physicochemical properties of the drug and intended therapeutic application.^[12] Oil-in-water nanoemulgels are most commonly employed for topical antifungal delivery because they provide better patient acceptability, non-greasy texture, ease of washing, and enhanced drug release. The gel matrix helps maintain prolonged residence time at the application site while preventing rapid runoff from the skin surface.^[3] The functional performance of nanoemulgels depends greatly on the appropriate selection and optimization of formulation components. Each component contributes to formulation stability, drug loading capacity, skin permeation, and therapeutic efficacy.^[13]

Oils, Surfactants, Co-surfactants, and Gelling Agents

The oil phase serves as the primary carrier for lipophilic antifungal drugs and significantly influences drug solubilization and permeation behavior. Both natural and synthetic oils are utilized in nanoemulgel formulations. Commonly used oils include olive oil, clove oil, eucalyptus oil, castor oil, oleic acid, isopropyl myristate, medium-chain triglycerides, and sesame oil. Certain essential oils also possess intrinsic antifungal and penetration-enhancing properties, thereby contributing synergistically to therapeutic activity.^[14] Surfactants play a crucial role in reducing interfacial tension between the oil and aqueous phases, leading to the formation of stable nanosized droplets. Nonionic surfactants are preferred in topical formulations because of their lower toxicity and better skin compatibility. Frequently used surfactants include Tween 20, Tween 80, Span 20, Span 80, Cremophor RH40, and Labra sol. The concentration and hydrophilic-lipophilic balance (HLB) value of surfactants strongly affect nanoemulsion stability and droplet size distribution.^[15] Co-surfactants are incorporated to further reduce interfacial tension and improve flexibility of the interfacial film. They facilitate spontaneous nanoemulsion formation and enhance formulation stability. Common co-surfactants include ethanol, propylene glycol, polyethylene glycol, Transductal P, and isopropyl alcohol. In addition to stabilizing the nanoemulsion system, some co-surfactants also function as permeation enhancers.^[16] The gel phase is prepared using hydrophilic polymers that provide suitable consistency, spreadability, and bio adhesive properties. Frequently employed gelling agents include Carbopol 934, Carbopol 940, hydroxypropyl methylcellulose (HPMC): xanthan gum, sodium carboxymethyl cellulose, and poloxamers. These polymers improve viscosity and physical stability while ensuring ease of application

and prolonged retention on the skin surface. Neutralizing agents such as triethanolamine are often added to adjust pH and facilitate gel formation.^[17]

Advantages of Nanoemulgel-Based Delivery

Nanoemulgel systems offer several advantages over conventional topical formulations, making them highly promising for antifungal therapy. One of the major benefits is enhanced solubilization of poorly water-soluble antifungal drugs, which improves drug loading and bioavailability. The nanosized droplets provide a large surface area that facilitates intimate contact with the skin and enhances drug penetration through the stratum corneum.^[18] Nanoemulgels exhibit improved physical stability compared with traditional emulsions because their small droplet size reduces creaming, coalescence, and phase separation. The incorporation of nanoemulsions into gel matrices further stabilizes the system and improves viscosity, thereby enhancing patient convenience and application characteristics.^[19] Another significant advantage is controlled and sustained drug release, which helps maintain therapeutic drug concentrations for extended durations and reduces dosing frequency. Nanoemulgels also demonstrate superior spreadability, non-greasy texture, ease of removal, and better aesthetic appeal compared with ointments and creams. These properties contribute to improved patient adherence to treatment.^[20] Additionally, nanoemulgels may reduce local irritation and systemic side effects due to localized drug targeting and reduced systemic absorption. Enhanced permeation and retention of antifungal drugs at the site of infection can improve therapeutic efficacy against resistant or recurrent fungal infections.^[14]

Mechanisms of Enhanced Skin Permeation and Drug Release

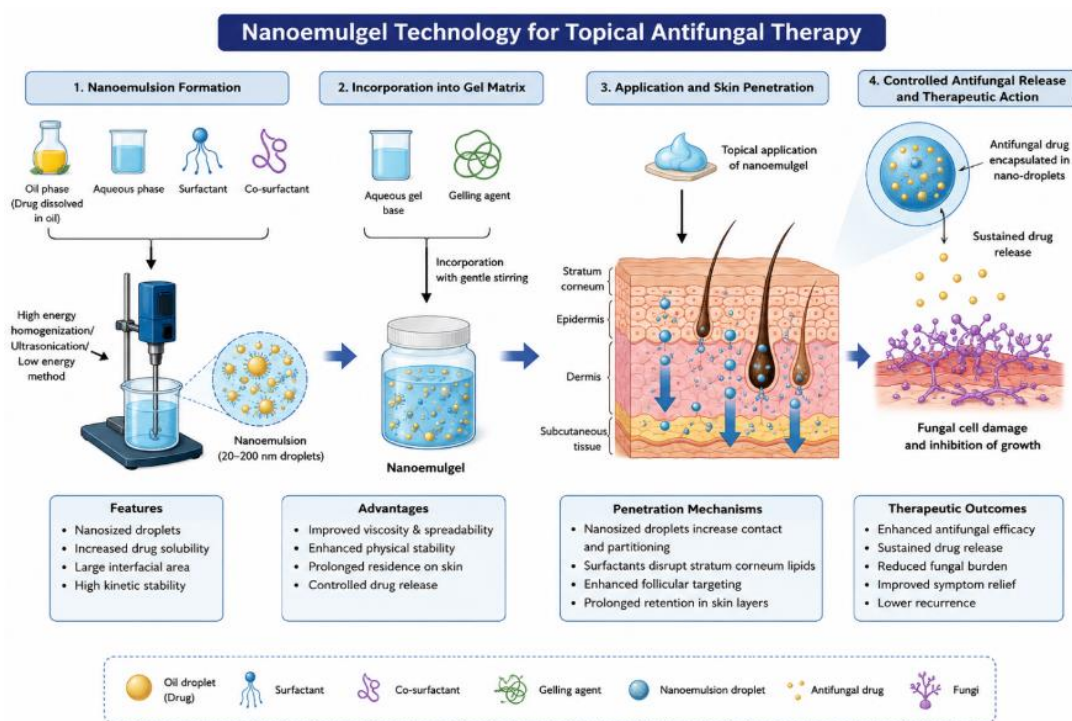
The improved performance of nanoemulgels in topical antifungal delivery is attributed to multiple mechanisms that facilitate enhanced skin permeation and drug release. The nanosized droplets possess a high surface area and close contact with the stratum corneum, promoting efficient drug partitioning into the skin layers. Smaller droplets can penetrate more effectively through intercellular lipid pathways and hair follicles.^[21]

Surfactants and co-surfactants present in the formulation act as penetration enhancers by disrupting the highly ordered lipid structure of the stratum corneum. This disruption temporarily increases skin permeability and facilitates drug diffusion into deeper skin layers. Certain oils such as oleic acid and essential oils further enhance permeation by fluidizing skin lipids.^[22]

Nanoemulgels also improve drug thermodynamic activity due to the solubilized state of the drug within the oil droplets. This creates a concentration gradient that drives passive diffusion across the skin barrier. The gel matrix prolongs contact time between the formulation and skin surface, allowing sustained drug release and increased drug retention at the target site.^[23]

In addition, follicular targeting plays an important role in nanoemulgel-mediated delivery. Nano-sized droplets may accumulate within hair follicles and sebaceous glands, serving as reservoirs for prolonged drug release. This mechanism is particularly beneficial in treating fungal infections involving hair follicles and deeper skin structures.^[14]

Overall, the synergistic combination of nanoscale emulsification and gel-based delivery enables nanoemulgels to overcome the limitations of conventional topical formulations and achieve enhanced antifungal therapeutic outcomes.^[6]



3. Formulation and Characterization of Nanoemulgels

The development of nanoemulgels for topical antifungal therapy involves systematic formulation design and extensive physicochemical characterization to ensure stability, safety, and therapeutic effectiveness. The formulation process generally includes preparation of a stable nanoemulsion system followed by its incorporation into a suitable gel matrix. Various formulation variables such as oil phase composition, surfactant concentration, droplet size,

and polymer selection significantly influence the performance of the final nanoemulgel system.^[24]

Methods of Nanoemulsion Preparation

Nanoemulsions are prepared using either high-energy or low-energy emulsification techniques depending on the formulation requirements, equipment availability, and physicochemical properties of the drug. The primary objective of nanoemulsion preparation is to produce stable nanosized droplets with uniform size distribution and high drug-loading efficiency.^[25]

High-energy methods utilize external mechanical energy to reduce droplet size and generate kinetically stable nanoemulsions. Commonly employed techniques include high-pressure homogenization, ultrasonication, microfluidization, and high-speed stirring. In high-pressure homogenization, the coarse emulsion is passed through a narrow gap under high pressure, resulting in intense turbulence and droplet disruption.^[26] Ultrasonication employs acoustic cavitation generated by ultrasonic waves to break larger droplets into nanosized particles. These techniques are widely used because they produce nanoemulsions with narrow particle size distribution and improved physical stability.^[27]

Low-energy methods rely on the physicochemical properties of formulation components and spontaneous emulsification processes. These methods include phase inversion temperature, phase inversion composition, and self-nano emulsification techniques. In spontaneous emulsification, the oil phase containing drug, surfactant, and co-surfactant is mixed with the aqueous phase under gentle stirring, resulting in formation of nanosized droplets without significant external energy input. Low-energy methods are advantageous because they are cost-effective, simple, and suitable for thermolabile drugs.^[28]

Selection of the appropriate preparation method depends on factors such as desired droplet size, formulation stability, industrial scalability, and sensitivity of antifungal agents. Optimized formulation variables are essential to achieve enhanced drug solubilization, permeation, and therapeutic performance.^[29]

Conversion of Nanoemulsion into Nanoemulgel

After preparation of the nanoemulsion, it is incorporated into a gel base to obtain a nanoemulgel formulation suitable for topical application. The gel matrix improves

formulation viscosity, spreadability, skin retention, and patient acceptability. The conversion process typically involves dispersing a suitable gelling agent in purified water under continuous stirring until complete hydration occurs.^[30]

Commonly used gelling polymers include Carbopol 934, Carbopol 940, hydroxypropyl methylcellulose (HPMC); xanthan gum, sodium alginate, and poloxamers. The prepared gel base is neutralized using agents such as triethanolamine or sodium hydroxide to achieve appropriate consistency and pH. Subsequently, the optimized nanoemulsion is slowly incorporated into the gel matrix with continuous stirring to ensure homogeneous distribution.^[31]

The final nanoemulgel should exhibit desirable rheological properties, physical stability, and smooth texture without phase separation or aggregation. Appropriate optimization of gel viscosity is important because excessive viscosity may hinder drug release, whereas very low viscosity may reduce skin retention and application convenience.^[32]

Physicochemical Characterization

Comprehensive physicochemical characterization of nanoemulgels is essential to evaluate formulation quality, stability, and therapeutic potential. Various analytical parameters are assessed to ensure reproducibility and optimal topical performance.^[12]

Particle Size and Polydispersity Index

Particle size is one of the most critical parameters affecting drug permeation, stability, and release characteristics of nanoemulgels. The nanosized droplets provide a larger surface area that enhances skin interaction and drug absorption. Particle size is generally measured using dynamic light scattering (DLS) techniques.^[12]

An ideal nanoemulsion system should possess droplet sizes typically below 200 nm with narrow size distribution. Smaller droplet size improves formulation stability and facilitates efficient permeation through the stratum corneum. The polydispersity index (PDI) indicates uniformity of particle size distribution within the formulation. A lower PDI value, generally below 0.3, reflects homogeneous droplet distribution and better physical stability.^[33]

Zeta potential is also frequently evaluated to determine surface charge and predict colloidal stability. Higher absolute zeta potential values indicate reduced aggregation tendency due to electrostatic repulsion between droplets.^[34]

Viscosity and pH

Viscosity is an important rheological parameter that influences spreadability, extrudability, and retention time of nanoemulgels on the skin surface. Appropriate viscosity ensures easy application and prolonged contact with infected skin areas. Rheological behavior is commonly assessed using viscometers or rheometers at different shear rates.^[35]

Most nanoemulgels exhibit pseudoplastic or shear-thinning behavior, which is advantageous for topical application because viscosity decreases during spreading and recovers afterward. Excessively high viscosity may retard drug release, while low viscosity can reduce formulation stability and residence time.^[36]

The pH of nanoemulgels should be compatible with the physiological pH of the skin, generally ranging between 5 and 7, to minimize irritation and maintain skin integrity. pH measurements are carried out using digital pH meters after formulation equilibration.^[37]

Drug Content and Entrapment Efficiency

Drug content analysis is performed to determine the amount of antifungal drug uniformly incorporated within the formulation. Uniform drug distribution is essential for dose accuracy and therapeutic consistency. Drug content is usually quantified using analytical techniques such as UV-visible spectrophotometry or high-performance liquid chromatography (HPLC).^[38]

Entrapment efficiency refers to the percentage of drug successfully encapsulated within the nanoemulsion droplets relative to the total amount of drug used during formulation. High entrapment efficiency is desirable because it improves drug stability and sustained release characteristics. Entrapment efficiency is influenced by factors such as oil composition, surfactant concentration, and drug lipophilicity.^[39]

Stability and Release Studies

Stability studies are conducted to evaluate the physical, chemical, and microbiological stability of nanoemulgels during storage. Parameters such as appearance, phase separation, particle size, viscosity, pH, and drug content are monitored under different temperature and humidity conditions. Centrifugation studies, heating-cooling cycles, freeze-thaw tests, and accelerated stability studies are commonly performed to predict long-term stability.^[40]

In vitro drug release studies are essential to assess the release kinetics and diffusion behavior of antifungal agents from nanoemulgels. These studies are generally carried out using Franz diffusion cells with synthetic or biological membranes. Nanoemulgels typically exhibit sustained and controlled drug release profiles due to the combined effects of nanosized droplets and gel matrix diffusion barriers.^[41]

Ex vivo permeation studies using animal or human skin models are also employed to evaluate skin penetration and drug retention. Such studies help establish the enhanced permeation capability of nanoemulgels compared with conventional topical formulations.^[8]

Overall, formulation optimization and comprehensive characterization play a crucial role in the successful development of nanoemulgels for effective topical antifungal therapy.^[14]

4. Applications of Nanoemulgels in Topical Antifungal Therapy

Nanoemulgel-based drug delivery systems have emerged as highly promising platforms for the treatment of superficial fungal infections due to their superior permeation characteristics, enhanced drug retention, and improved therapeutic efficacy.^[6] The incorporation of antifungal agents into nanoemulgel systems enables efficient delivery across the skin barrier while maintaining prolonged residence time at the infected site. These systems have been extensively investigated for the topical administration of various antifungal drugs including clotrimazole, ketoconazole, fluconazole, itraconazole, terbinafine, luliconazole, and miconazole.^[3]

The increasing prevalence of dermatophytid infections, candidiasis, and other superficial mycoses has created a demand for advanced topical delivery systems capable of overcoming the limitations of conventional creams and ointments. Nanoemulgels provide localized drug targeting, enhanced patient compliance, and sustained therapeutic activity, making them suitable candidates for modern antifungal therapy.^[9]

Nanoemulgels for Dermal Fungal Infections

Nanoemulgels have demonstrated considerable effectiveness in the management of a wide range of dermal fungal infections affecting the skin, nails, and mucosal surfaces. Common fungal conditions treated using nanoemulgel systems include tinea corporis, tinea pedis, tinea cruris, candidiasis, pityriasis versicolor, and onychomycosis. These infections are primarily

caused by dermatophytes such as *Trichophyton*, *Microsporum*, and *Epidermophyton* species, along with opportunistic fungi including *Candida albicans*.^[42]

Several antifungal drugs possess poor aqueous solubility and limited skin penetration, which restrict their therapeutic effectiveness in conventional topical dosage forms. Nanoemulgels enhance the solubilization of these lipophilic drugs within the oil phase, thereby improving their availability at the target site. The nanosized droplets facilitate closer interaction with the skin surface and promote effective penetration into deeper epidermal layers where fungal pathogens reside.^[43]

Nanoemulgel formulations containing ketoconazole, clotrimazole, terbinafine, and itraconazole have shown enhanced antifungal activity against various fungal strains in experimental studies. Essential oils incorporated into nanoemulgels, such as clove oil, tea tree oil, eucalyptus oil, and peppermint oil, may provide additional antifungal and anti-inflammatory effects through synergistic mechanisms. These multifunctional systems not only eradicate fungal pathogens but also alleviate associated symptoms such as itching, redness, scaling, and inflammation.^[44]

Furthermore, nanoemulgels have shown potential in improving the management of chronic and recurrent fungal infections by maintaining prolonged drug concentrations within the skin layers. Sustained drug release and localized retention reduce the frequency of application and improve treatment adherence among patients.^[3]

Improved Skin Retention and Permeation

One of the most significant advantages of nanoemulgels is their ability to enhance skin permeation and drug retention compared with traditional topical formulations. The stratum corneum acts as the primary barrier limiting penetration of many antifungal agents. Nanoemulgels overcome this barrier through multiple physicochemical mechanisms.^[14]

The small droplet size of nanoemulsions provides a large interfacial surface area that increases drug contact with the skin surface and facilitates diffusion through intercellular lipid pathways. Surfactants and co-surfactants present in the formulation disrupt the highly organized lipid arrangement of the stratum corneum, temporarily increasing skin permeability and enabling enhanced drug transport.^[45]

Lipophilic oils and penetration enhancers further improve dermal delivery by fluidizing skin lipids and increasing partitioning of the drug into skin tissues. The gel matrix prolongs contact time between the formulation and skin surface, preventing rapid removal and allowing sustained release of the antifungal drug over extended periods.^[46]

Nanoemulgels also exhibit improved follicular targeting, where nanosized droplets accumulate within hair follicles and sebaceous glands, acting as drug reservoirs for prolonged antifungal action. This mechanism is especially beneficial for fungal infections involving hair-bearing areas and deeper skin structures.^[3]

Enhanced skin retention minimizes systemic absorption and reduces the risk of systemic side effects associated with oral antifungal therapy. As a result, nanoemulgels provide efficient localized treatment with improved safety profiles and reduced drug wastage.^[9]

In Vitro, Ex Vivo, and In Vivo Evaluation Studies

Extensive in vitro, ex vivo, and in vivo investigations have been conducted to evaluate the therapeutic performance of antifungal nanoemulgels. These studies provide critical information regarding drug release behavior, permeation characteristics, antifungal activity, and clinical effectiveness.^[47]

In vitro drug release studies commonly utilize Franz diffusion cells to examine the release kinetics of antifungal agents from nanoemulgel formulations. Most studies report sustained and controlled drug release profiles compared with conventional creams and gels. Enhanced release rates are attributed to improved drug solubilization within the nanoemulsion system and increased surface area of nanosized droplets.^[48]

Ex vivo permeation studies are generally performed using excised animal or human skin models to evaluate transdermal diffusion and skin retention. Nanoemulgels consistently demonstrate higher permeation flux, increased drug deposition within skin layers, and improved retention time compared with marketed topical products. These findings confirm the ability of nanoemulgels to enhance localized drug delivery.^[8]

In vitro antifungal activity is commonly assessed using agar diffusion methods, minimum inhibitory concentration (MIC) studies, and zone of inhibition analysis against fungal strains such as *Candida albicans* and *Trichophyton rubrum*. Nanoemulgel formulations frequently

exhibit superior antifungal efficacy due to enhanced drug penetration and sustained release behavior.^[14]

In vivo studies conducted on animal models and clinical subjects further support the therapeutic advantages of nanoemulgels. These studies have demonstrated faster recovery, reduced fungal burden, improved symptom relief, and lower recurrence rates compared with conventional topical systems. Histopathological analysis often confirms reduced inflammation and restoration of normal skin architecture following treatment with antifungal nanoemulgels.^[14]

Skin irritation and sensitivity studies are also performed to evaluate formulation safety. Most nanoemulgels exhibit minimal irritation because of their non-greasy nature, controlled drug release, and reduced use of harsh solvents.^[49]

Comparative Advantages over Conventional Topical Systems

Nanoemulgels possess several comparative advantages over traditional topical formulations such as creams, ointments, lotions, and gels. Conventional topical systems often suffer from poor drug solubility, inadequate permeation, instability, greasiness, and frequent dosing requirements. In contrast, nanoemulgels offer enhanced physicochemical stability and improved therapeutic efficiency.^[50]

The nanoscale droplet size significantly improves solubilization of hydrophobic antifungal drugs, resulting in enhanced bioavailability and faster onset of action. Controlled and sustained drug release from nanoemulgels maintains therapeutic concentrations for longer durations, thereby reducing dosing frequency and improving patient compliance.^[14]

Unlike ointments, nanoemulgels are non-greasy, easily spreadable, aesthetically acceptable, and washable, making them more convenient for routine use. Their bio adhesive gel structure ensures prolonged residence time on the skin while minimizing formulation runoff.^[8]

Nanoemulgels also demonstrate superior penetration into deeper skin layers and hair follicles, leading to improved treatment outcomes in stubborn and recurrent fungal infections. Reduced systemic absorption lowers the risk of adverse effects commonly associated with systemic antifungal therapy.^[6]

Additionally, nanoemulgels can accommodate multifunctional excipients such as essential oils, herbal extracts, and permeation enhancers, enabling synergistic therapeutic effects. These properties collectively make nanoemulgels highly effective and patient-friendly alternatives to conventional topical antifungal formulations.^[6]

Overall, the application of nanoemulgel technology represents a significant advancement in topical antifungal therapy, offering improved drug delivery, enhanced therapeutic efficacy, better patient adherence, and promising potential for future dermatological applications.^[51]

5. Challenges, Future Perspectives, and Conclusion

Despite the promising therapeutic advantages of nanoemulgels in topical antifungal delivery, several scientific, technological, and regulatory challenges remain associated with their large-scale development and clinical translation.^[51] Although numerous laboratory-scale studies have demonstrated improved drug permeation, stability, and antifungal efficacy, only limited nanoemulgel formulations have progressed toward commercial application. Addressing formulation complexities, long-term safety concerns, and regulatory requirements is essential for successful industrial and clinical implementation of nanoemulgel-based topical therapies.^[48]

Limitations in Formulation Development and Scale-Up

One of the major challenges in nanoemulgel development is the selection and optimization of suitable formulation components. The physicochemical properties of oils, surfactants, co-surfactants, and gelling agents significantly influence nanoemulsion stability, droplet size, viscosity, drug release, and skin permeation. Improper optimization may lead to phase separation, droplet aggregation, instability, or reduced therapeutic efficacy during storage.^[11]

The high concentration of surfactants required for nanoemulsion stabilization may sometimes cause skin irritation, toxicity, or hypersensitivity reactions, especially during prolonged use. Maintaining a balance between formulation stability and biocompatibility remains a critical challenge in topical nanoemulgel design.^[52]

Another limitation involves the physical and chemical stability of nanoemulgels under varying environmental conditions. Factors such as temperature fluctuations, pH changes, oxidation, and microbial contamination may affect formulation integrity and shelf life. Long-

term stability studies are therefore essential to ensure product reliability and therapeutic consistency.^[53]

Scale-up and industrial manufacturing of nanoemulgels also present significant technical challenges. Reproducibility of nanosized droplets and maintenance of uniform particle distribution during large-scale production require sophisticated equipment and strict process control. High-energy preparation methods such as ultrasonication and high-pressure homogenization may increase manufacturing costs and energy consumption. Furthermore, batch-to-batch variation can affect product quality and regulatory approval.^[54]

The incorporation of poorly water-soluble antifungal drugs into nanoemulgels may also face limitations related to drug loading capacity and crystallization during storage. Ensuring consistent drug entrapment and controlled release behavior remains a key area of formulation research.^[55]

Safety and Regulatory Considerations

Although nanoemulgels are generally considered safe for topical administration, comprehensive safety evaluation is necessary because nanoscale systems may interact differently with biological tissues compared with conventional formulations. The small droplet size and enhanced permeation ability raise concerns regarding potential systemic absorption, skin irritation, immunogenicity, and long-term toxicity.^[56]

Certain surfactants, penetration enhancers, and synthetic excipients used in nanoemulgel formulations may disrupt skin barrier integrity or cause allergic reactions in sensitive individuals. Therefore, biocompatibility and dermatological safety testing are essential before clinical application. Repeated-dose toxicity studies, skin sensitization assessments, and histopathological evaluations are commonly required to establish formulation safety.^[57]

Regulatory approval of nanotechnology-based drug delivery systems remains complex due to the absence of universally harmonized guidelines specific to nanoformulations. Regulatory agencies require detailed characterization of particle size distribution, zeta potential, formulation stability, excipient safety, and manufacturing reproducibility. Standardization of analytical methods and quality control procedures is still evolving in the field of nanomedicine.^[58]

In addition, regulatory authorities often require extensive preclinical and clinical data to demonstrate therapeutic superiority, safety, and quality consistency over conventional dosage forms. These requirements may increase development time and overall production costs. Consequently, the translation of nanoemulgel formulations from research laboratories to commercial pharmaceutical products remains relatively limited.^[48]

Future Trends in Nanoemulgel-Mediated Topical Therapy

The future of nanoemulgel-mediated antifungal therapy appears highly promising due to continuous advancements in nanotechnology, polymer science, and dermatological drug delivery systems. Emerging formulation strategies are focused on improving targeting efficiency, therapeutic performance, patient convenience, and long-term safety.^{[3], [59]} One important future trend involves the use of multifunctional nanoemulgels containing natural bioactive compounds, herbal extracts, and essential oils with intrinsic antifungal, anti-inflammatory, and antioxidant properties. Such systems may provide synergistic therapeutic effects while reducing dependence on synthetic antifungal drugs.^[14] Stimuli-responsive and smart nanoemulgel systems are also gaining considerable attention. These formulations can respond to environmental triggers such as pH, temperature, enzymes, or fungal metabolites to achieve site-specific and controlled drug release. Smart delivery systems may improve therapeutic precision and reduce unnecessary drug exposure.^[60] Advances in polymer engineering and nanocarrier design may further enhance skin targeting and follicular delivery of antifungal agents. Incorporation of biodegradable, biocompatible, and mucoadhesive polymers can improve formulation safety and retention characteristics. Lipid-based hybrid systems, nanoemulsion-loaded hydrogels, and nanostructured carriers are expected to expand the scope of topical antifungal therapy.^[3] Artificial intelligence and computational modeling are increasingly being explored for optimization of nanoemulgel formulations and prediction of stability, permeation, and release kinetics. These technologies may accelerate formulation development and reduce experimental workload.^[14] Future clinical research should focus on large-scale human trials, long-term safety studies, and comparative evaluations with marketed antifungal products. Development of cost-effective manufacturing processes and establishment of standardized regulatory frameworks will also be essential for broader commercialization and clinical acceptance of nanoemulgel-based therapies.^[48]

CONCLUSION

Nanoemulgel technology represents a significant advancement in topical antifungal drug delivery by combining the advantages of nanoemulsions and gel-based systems into a single multifunctional platform. These systems effectively address many limitations associated with conventional topical formulations, including poor drug solubility, inadequate skin permeation, limited retention, and low patient compliance. The nanosized droplets of nanoemulgels enhance drug solubilization, permeation, and localized retention within infected skin tissues, resulting in improved therapeutic efficacy against superficial fungal infections. In addition, nanoemulgels provide sustained drug release, better spreadability, non-greasy texture, and enhanced patient acceptability. Numerous *in vitro*, *ex vivo*, and *in vivo* studies have demonstrated the superior antifungal performance of nanoemulgels compared with traditional creams, ointments, and gels. Despite their considerable potential, challenges related to formulation optimization, large-scale manufacturing, long-term stability, safety evaluation, and regulatory approval continue to limit widespread commercialization. Continued research and technological innovation are therefore required to overcome these barriers and establish standardized approaches for nanoemulgel development. Overall, nanoemulgels hold substantial promise as next-generation topical delivery systems for antifungal therapy. With ongoing advancements in nanotechnology and pharmaceutical sciences, nanoemulgel-mediated topical treatments are expected to play an increasingly important role in improving the management of fungal skin infections and enhancing patient outcomes in modern dermatological practice.

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