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Expert Opinion Article

Griseofulvin-Loaded Microemulsion Gel For Topical Antifungal Therapy: A Review Of Formulation, Optimization And Evaluation

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Abstract

Objective: To explore the formulation and potential of griseofulvin-loaded microemulsion gels (microemulgels) as an advanced topical delivery system to overcome the limitations of conventional griseofulvin therapy.

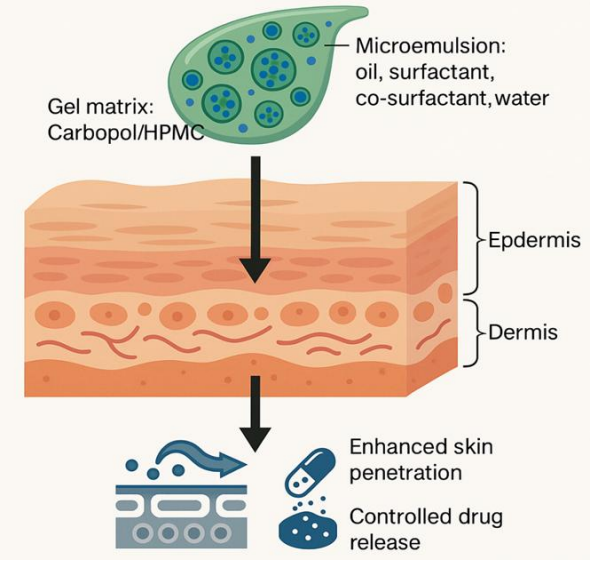
Significance of Review: Griseofulvin is a lipophilic antifungal agent with poor water solubility and inconsistent oral bioavailability, requiring high doses and long treatment durations. Conventional topical therapies fail due to poor skin penetration. Microemulsion-based gels offer a promising alternative by enhancing solubility, skin permeation, and local therapeutic concentration with fewer systemic side effects.

Key Findings: Microemulsions, composed of oil, water, surfactant, and co-surfactant, form thermodynamically stable systems with droplet sizes below 100 nm. When integrated into gel matrices, they offer improved viscosity, spreadability, and controlled drug release. Studies from 2015 to 2025 have optimized component selection (e.g., oleic acid, Tween 80, ethanol), pseudo-ternary phase diagrams, and characterization parameters such as droplet size, zeta potential, pH, viscosity, and drug content. Gel incorporation with agents like Carbopol or HPMC yields stable formulations with sustained release profiles. In vitro and ex vivo evaluations demonstrate superior skin permeation and antifungal activity over traditional creams.

Conclusion: Griseofulvin-loaded microemulsion gels represent a novel and effective strategy for topical antifungal therapy, overcoming solubility and penetration challenges. Continued development, including safety evaluation and scale-up validation, could establish these systems as viable commercial alternatives for dermatophytic infections.

Keywords : Griseofulvin , Microemulsion gel , Topical drug delivery , Solubility enhancement , Skin permeation , Antifungal agent

Graphical Abstract



1. Introduction

The distribution of drugs via the skin has long been recognized as a non-invasive and patient-compliant route of administration, affording benefits such as avoidance of hepatic first-pass metabolism, better drug localization, and decreased systemic adverse

effects. However, efficient topical and transdermal drug administration is considerably hampered by the stratum corneum the outermost layer of the skin which serves as a strong barrier to the penetration of most pharmacological substances, particularly those with low water solubility. To overcome this obstacle, innovative drug delivery methods have been developed to increase the movement of active pharmaceutical ingredients (APIs) across the epidermal barrier. Among them, microemulsion-based delivery technologies have emerged as potential carriers, notably for lipophilic drugs[1]. . A microemulsion is a transparent, isotropic, and thermodynamically stable dispersion of oil and water stabilised by surfactants and cosurfactants[2]. Small droplets (<100 nm) provide a significant surface area for medication release. Incorporating microemulsions into a semi-solid gel creates a "microemulgel" that combines the penetration-enhancing characteristics of microemulsions with the spreadability and controlled release of gels[3]. This structure is particularly promising for lipophilic antifungal drugs.

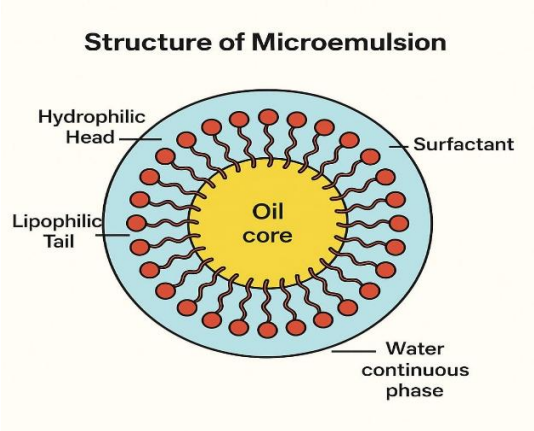


Figure 1 : The figure Shows the structure of microemulsion (O/W) type

In recent years, a number of studies have revealed the potential of microemulsion-based delivery methods to boost the topical bioavailability of griseofulvin. By refining the choices of oils, surfactants, and cosurfactants, and adjusting the physicochemical features of the formulation, researchers have been able to considerably increase the skin penetration and antifungal activity of griseofulvin-loaded microemulgels. These formulations not only promote continuous medication release but also increase patient adherence owing to their simple administration and good aesthetic characteristics.
Griseofulvin, a classic antifungal drug (BCS Class II), exhibits this requirement since it has extremely poor water solubility and unpredictable gastrointestinal absorption.Furthermore, traditional oral medicine is linked with a wide range of side effects and drug interactions. The study's goal was to develop a topical preparation of griseofulvin that would deliver the drug locally at a therapeutically effective concentration[4]. A topical microemulsion gel might deliver the drug directly to dermatophyte-infected skin, enhancing local concentration while minimising systemic exposure. This study looks at the rationale, methodology, and results for developing griseofulvin-loaded microemulsion gels, with a focus on contemporary research (2015-2025). This article aims to offer a complete overview of the recent advancements in the development and characterisation of griseofulvin-loaded microemulsion gels. This article aims to offer a complete overview of the recent advancements in the development and characterisation of griseofulvin-loaded microemulsion gels.

2. Background of griseofulvin

Griseofulvin, developed from Penicillium griseofulvum, is a fungistatic substance suggested for dermatophyte infections (*tinea capitis, onychomycosis*). It accomplishes its action by binding fungal tubulin and inhibiting mitotic spindle function[5]. Griseofulvin is poorly absorbed after an oral intake. Micronized (*Grifulvin V*) and ultramicronized (*Gris-PEG*) preparations are used to increase absorption. For micronized formulations, a peak serum concentration is attained at roughly 4 h after an oral dosage. Absorption is greatly boosted with dietary fat consumption, which adds to the variability of the bioavailability. Formulations that were micronised and ultramicrosized have been developed to improve absorption. Skin, hair, and nails are keratinised tissues where the substance preferentially accumulates. It is found in large concentrations in the stratum corneum and hair shafts[4]. However, long treatment periods (6–12 weeks) and high dosages are sometimes necessary to achieve optimal tissue levels via oral dosing, which raises concerns about toxicity (e.g. hepatic,

haematologic consequences) and compliance[6,7]. Due to insufficient penetration into hair shafts, topical treatment using traditional griseofulvin formulations has generally failed to heal deep follicular infections or tinea capitis. Nonetheless, there is interest in topical griseofulvin to reduce systemic side effects. Nimni et al. found that an optimised topical formulation attained significantly greater and more sustained drug concentrations in rat skin compared to oral administration[8]. Aggarwal et al. developed a carbopol gel incorporating griseofulvin, vitamin E-TPGS, and ethanol to improve cutaneous distribution; this gel demonstrated increased penetration and effectiveness in skin models. These results indicate that suitably designed topical devices may enhance the efficacy of griseofulvin while minimising systemic exposure[9,10].

3. Rationale for microemulsion based delivery

Topical and transdermal drug delivery methods offer various advantages over traditional oral or parenteral routes, such as localized therapy, avoidance of hepatic first-pass metabolism, and enhanced patient compliance. However, the greatest challenge in successful cutaneous medication administration resides in the skin's powerful barrier function, notably the stratum corneum. This outermost layer is formed of keratinized cells embedded in a lipid matrix, which restricts the permeability of most hydrophilic and high-molecular-weight substances. The difficulty is exacerbated when developing medications such as griseofulvin, which exhibit poor water solubility and reduced bioavailability upon oral administration.

Microemulsions offer various advantages for delivering hydrophobic medicines like griseofulvin through the skin.

1) Their nanometric droplet size considerably enhances drug surface area and interaction with the skin, allowing partitioning into the lipid matrix of the stratum corneum[11].
2) The substantial solubilization capacity of the oil/surfactant mixture can drastically improve the apparent solubility of griseofulvin, resulting to higher thermodynamic activity and pushing flux into the skin[1].
3) The formulation's surfactants and cosurfactants (such as polysorbates and glycols) facilitate penetration by opening intercellular channels and fluidizing stratum corneum lipids[12].
4) According to studies, topical antifungal microemulsions (such as miconazole and amphotericin B) can boost skin penetration by a factor of many when compared to traditional creams[13].

Aggarwal et al. developed a microemulsion of griseofulvin (5% oleic acid, 40% Tween-80/ethanol) with ~12 nm droplets and high solubilisation of griseofulvin. This formulation cured fungal infections in guinea pigs in 7 days and achieved 3-7× higher skin penetration than aqueous or cream formulations[14,15].

Furthermore, when microemulsions are mixed into a gel foundation to generate microemulgels, they gain higher viscosity, better spreadability, and longer retention on the skin surface, ensuring continuous drug release and improved therapeutic activity. These characteristics make microemulsion-based gels ideal for administering griseofulvin topically in the treatment of dermatophytic infections, where localised, non-systemic therapy is both efficacious and patient-friendly[16,17]. Despite their advantages, pure microemulsions are frequently low-viscosity liquids, making them difficult to apply and keep on the skin. Converting them into gels ("microemulgels") addresses this issue[2].The polymeric gel matrix (e.g. Carbopol, HPMC) enhances viscosity and provides a sustained-release depot, while conserving the nano-structure[3]. A microemulgel thus combines the penetrating advantages of the microemulsion with the patient-friendly features of a gel: it is readily spreadable, non-greasy, and can give controlled release of the drug. Overall, microemulgel systems appear promising for boosting the dermal and transdermal distribution of griseofulvin, thereby improving therapy of cutaneous fungal infections[13].

4. Components of Microemulsion

The right selection and optimisation of each of the microemulsion system's constituent parts the oil phase, surfactant, co-surfactant, and aqueous phase are important to its successful formulation[18]. Each ingredient contributes in a unique and complementary way to assure the final formulation's physicochemical stability, medicine solubilisation capacity, and efficient skin penetration[19]. Depending on their concentration ratios, interfacial tensions, and miscibility characteristics, these elements spontaneously assemble into a structured colloidal dispersion, giving birth to the thermodynamic stability and nanoscale droplet size of microemulsions[20]. The physicochemical features of griseofulvin, particularly its poor aqueous solubility and lipophilic character, must be taken into account in choosing each component for a microemulsion gel loaded with griseofulvin[21].

Component	Function	Example
Oil Phase	Solubilizes lipophilic drug	Isopropyl myristate, Oleic acid, Capryol 90, Labrafac PG

Surfactant	Lowers interfacial tension	Tween 80, Span 20, Cremophor RH40, Labrasol
Co-surfactant	Increases flexibility of interface	PEG 400, Propylene glycol, Transcutol P, Ethanol
Aqueous Phase	Continuous phase	Distilled water, PBS, Normal saline
Active Drug	Therapeutic agent	Griseofulvin, Luliconazole, Fluconazole, Diclofenac

• **Oil Phase :** The oil must dissolve a high amount of griseofulvin. Common choices include fatty acids (oleic acid) or esters (isopropyl myristate)[15]. Oleic acid is frequently used due to its excellent solubilization of lipophilic drugs and inherent penetration-enhancing effect on skin lipids.For instance, after screening oil solvents, Aggarwal et al. chose oleic acid because it had a high solubility of griseofulvin. If alternative oils, such as vegetable oils or medium-chain triglycerides, dissolve the drug efficiently, they may be employed. Additionally, the oil should typically not irritate the skin[22].Oleic acid, for example, is not only a good solvent for lipophilic drugs but also acts as a permeation enhancer by disrupting the lipid architecture of the stratum corneum. Isopropyl myristate, on the other hand, has excellent spreading properties and is widely used for its ability to enhance skin permeation. Selection of the appropriate oil phase is typically guided by solubility studies, where the solubility of griseofulvin is determined in various oils, and the one showing the highest solubility is selected.

• **Surfactants :** Amphiphilic molecules known as surfactants help to create stable, transparent microemulsions by lowering the interfacial tension between the water and oil phases[19]. They help maintain the system's thermodynamic stability by stabilising the scattered phase droplets and avoiding coalescence. Because they are less likely to cause toxicity and irritation than ionic surfactants, non-ionic surfactants are favoured in pharmaceutical formulations[23]. Polysorbates (e.g., Tween 20, Tween 80), sorbitan esters (e.g., Span 20, Span 80), and polyoxyl castor oil derivatives (e.g., Cremophor EL, RH40) are often used surfactants in microemulsion systems. Because of its high hydrophilic-lipophilic balance (HLB) value, which promotes the development of oil-in-water (O/W) systems that are ideal for moisturising the skin, Tween 80 is especially preferred in topical treatments[20]. The capacity of the surfactant to solubilise the medication, keep droplet size within the nanometre range (usually 10–200 nm), and encourage skin penetration all play a role in the choosing. The surfactant should also be non-toxic, biocompatible, and able to create a stable interfacial layer surrounding the oil droplets[24].For microemulsions, Tween-20 or Tween-80 are often used due to their strong emulsification power and skin safety profile. You may also use other surfactants, such as Cremophor EL or Labrasol. The decision is based on creating a microemulsion zone in the phase diagram and optimising oil solubilisation.

• **Co-Surfactants :** Co-surfactants are tiny amphiphilic molecules that function in concert with surfactants to further lower interfacial tension and increase the flexibility of the interfacial layer. This flexibility is important to stabilize microemulsions across a greater range of component concentrations. Co-surfactants also serve a key function in decreasing the needed concentration of the principal surfactant, which may assist prevent possible skin irritation.
Commonly utilised co-surfactants include short-chain alcohols (ethanol, propylene glycol, isopropanol), glycols (polyethylene glycol, Transcutol P), and other hydrophilic solvents[25]. Ethanol is extensively utilised owing to its dual action as a co-surfactant and a penetration enhancer; it disturbs the lipid structure of the stratum corneum, permitting deeper drug permeability fig 1. Propylene glycol is also a popular option for its humectant characteristics and compatibility with a broad variety of surfactants and oils[26].The selection and ratio of co-surfactant to surfactant are commonly optimized using pseudoternary phase diagrams to determine the area of microemulsion production. Glycols (propylene glycol, Transcutol®), medium-chain alcohols, or short-chain alcohols (ethanol, isopropanol) aid in increasing flexibility and fluidizing the interface. They aid in the drug's dissolution and permit the development of a bigger microemulsion zone[23]. Ethanol was used by Aggarwal et al. as a cosurfactant.Propylene glycol is widely employed as a co-surfactant/solvent, since it is also a permeation enhancer[27]. Transcutol® (diethylene glycol monoethyl ether) is another powerful cosurfactant that may boost medication solubility in the formulation. The surfactant:cosurfactant ratio (Smix) is tuned (typically 1:1 or 2:1) to generate a stable microemulsion.

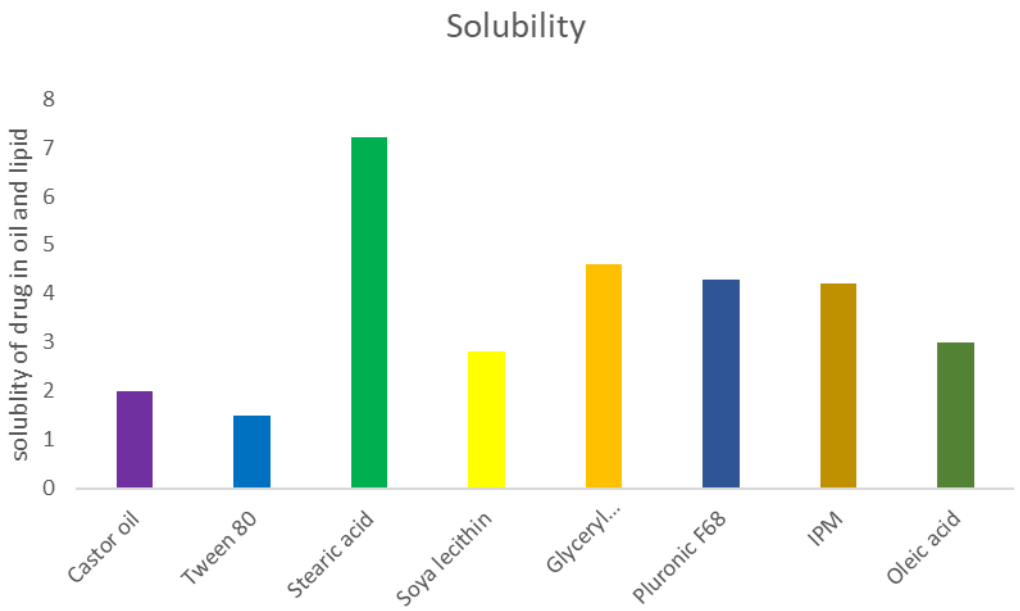


Figure 2: The figure Shows the Screening of solubility of griseofulvin in different solid lipid and surfactant

• **Aqueous Phase:** The aqueous phase normally consists of pure water, which may be modified with buffers or preservatives depending on the needs of the formulation[28]. The amount of the aqueous phase impacts the curvature of the surfactant layer and consequently the kind of microemulsion formed O/W (oil-in-water), W/O (water-in-oil), or bicontinuous. For topical treatments, O/W systems are frequently favoured owing to their positive sensory qualities, ease of spreadability, and superior hydration benefits[18]. The aqueous phase may also act as the vehicle for other excipients such as viscosity enhancers, preservatives (e.g., methylparaben, benzalkonium chloride), and stabilizers, depending on the final dosage form[29]. Typically purified water is used. The proportion of water is adjusted during formulation. Some formulations include water-miscible solvents (e.g. PEG400, ethanol in water) to aid solubilization. The water content and phase behavior is mapped in pseudoternary diagrams[30].

5. Pseudo ternary phase diagram in preparation of Microemulsion

A ternary phase diagram is a graphic representation of three- component systems (oil, water, Smix{surfactant, cosurfactant mixture}) that is shown as a triangle diagram with each side corre sponding to a separate binary system. These phases are presented in the sequence in which they formed. This triangle determines not only the phase behavior and emulsion type, but also the characteristics, and stability of the emulsion. The ternary phase diagram illustrates possible phases and their equilibrium based on the composition of a three-component mixture at constant temperature and pressure. The apex of the triangles represents the pure component, also known as 100%, and it steadily falls until it reaches 0% when it reaches another apex whereanother component is also 100%.

Pseudo ternary phase diagram can be either created by oil titration method or by water titration method.

• **In oil titration method**, Smix is first prepared and mixed uniformly with water and then oil is added dropwise to the mixture.

• **In water titration method**, Smix is first mixed with oil and then water is added dropwise into the mixture . The physicochemical characteristics of the resulting emulsions, such as transparency, stability and globule size are assessed. The area spanned by these ratio points on the phase diagram represents the range of microemulsion existence.

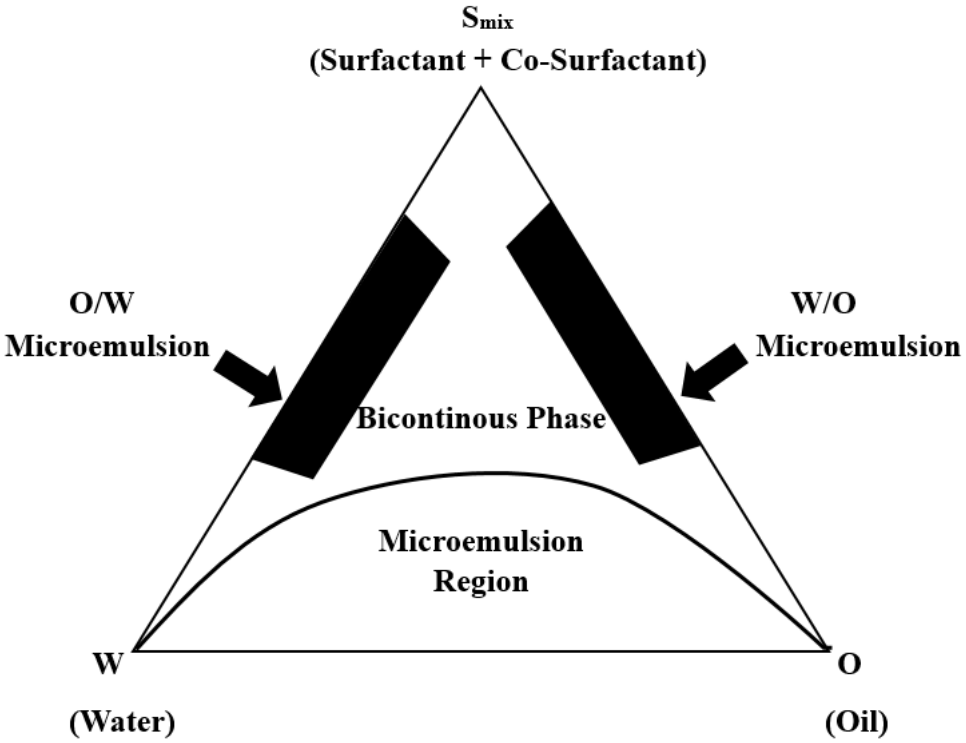


Figure 3: The figure Shows the pseudo ternary phase diagram

6. Formulation technique

Microemulsions develop spontaneously when oil, surfactant/cosurfactant combination (Smix) and water are combined in the right proportions[2]. The formulation procedure generally involves: (1) screening solvents for optimal drug solubility; (2) creating pseudoternary phase diagrams; and (3) choosing an optimum composition[31]. Oil and surfactant/cosurfactant are mixed, and water is titrated dropwise until a clear, isotropic mixture forms, marking the microemulsion region[32]. Pseudo-ternary phase diagrams (oil–Smix–water) are presented for different surfactant:cosurfactant ratios to determine the biggest microemulsion existence area.Formulation optimization can also employ design of experiments[33]. For example, Sabale and Vora used a 3^2 factorial design varying oil and Smix ratios to maximize transparency, minimize droplet size, and optimize release.Central composite design or mixture design may be employed to concurrently examine oil, surfactant, and aqueous fractions. In reality, one may establish a medication concentration (e.g. 0.2%–1% w/w griseofulvin) and look for the oil/Smix/water proportions that form a stable, clear system[34]. Sonication or light heating may be employed to help mixing, but real microemulsions need no high-energy input they should develop spontaneously at ambient temperature if correctly designed[35].

After selecting an optimum microemulsion, the gel phase (e.g. Carbopol) is generated separately (typically by swelling the polymer in water or the microemulsion)[36]. The microemulsion is subsequently absorbed into the gel basis by gradual mixing, frequently with a neutralization phase (e.g. triethanolamine for Carbopol) to obtain required pH[37]. For instance, Modani et al. produced Carbopol-934 gel and then dispersed their nadifloxacin microemulsion into it[38]. The outcome is a thixotropic microemulgel that preserves nanoemulsion droplets inside a semi-solid matrix. Throughout formulation, drug loading and homogeneity are verified; the finished gel should contain the desired drug content[39].

The formulation of griseofulvin-loaded microemulsion gel requires a methodical approach comprising solubility investigations, microemulsion creation utilising pseudoternary phase diagrams, optimization of formulation components, and lastly, inclusion into a suitable gel foundation for topical treatment. The procedure starts with solubility screening of griseofulvin in different oils, surfactants, and co-surfactants to find the excipients that display greatest drug solubilization potential. Since griseofulvin is a weakly water-soluble medication, solubilizing it adequately inside the oil phase is critical for guaranteeing therapeutic effectiveness. Oils such as isopropyl myristate, oleic acid, and caprylic/capric triglycerides are widely investigated owing to their dual function as solubilizers and skin permeability enhancers. Once the proper oil, surfactant, and co-surfactant are discovered, pseudoternary phase diagrams are created to establish the ideal concentration ranges that result in

the generation of microemulsions. These diagrams are created by titrating a combination of oil, surfactant, and co-surfactant (Smix) with the aqueous phase while keeping a stable Smix ratio. The generated plots aid to identify the microemulsion zone and assist in determining the appropriate formulation with maximum clarity, stability, and smallest droplet size.

After determining the ideal microemulsion composition, griseofulvin is dissolved in the specified oil phase, followed by the addition of surfactant and co-surfactant with gentle stirring. The aqueous phase is progressively introduced dropwise with continuous mixing to allow spontaneous emulsification and creation of a clear, low-viscosity microemulsion system. The formulation is normally allowed to equilibrate at ambient temperature for several hours to ensure full production and stability of the microemulsion[40]. Droplet size and polydispersity index (PDI) are commonly assessed using dynamic light scattering to validate nanoscale dispersion, which is crucial for good skin penetration and consistent medication release (Shakeel et al., 2009). Zeta potential analysis is also undertaken to measure physical stability. Once the microemulsion is perfected, it is turned into a gel using an appropriate gelling agent to boost its viscosity and topical application. Carbopol 934, xanthan gum, or hydroxypropyl methylcellulose (HPMC) are often utilised as gelling agents because to their biocompatibility, ability to keep pH within the skin-friendly range, and desirable rheological qualities[41]. The gel base is prepared by dispersing the polymer in distilled water under constant agitation, followed by neutralization (in the case of Carbopol) with triethanolamine to attain the desired gel consistency[42]. The preformed microemulsion is then incorporated into the gel base under slow, continuous stirring to ensure uniform distribution without disrupting the droplet architecture[43]. The final formulation, termed a microemulsion gel or microemulgel, exhibits improved viscosity, controlled drug release, and better adherence to the skin surface compared to liquid microemulsions alone (Nanda et al., 2011). This approach not only improves the therapeutic profile of griseofulvin but also enhances patient compliance by providing a non-greasy, stable, and easily spreadable topical formulation. Thus, the careful execution of formulation techniques, from solubility enhancement to gel incorporation, is pivotal in the successful development of griseofulvin microemulsion gels for effective topical antifungal therapy[44].

7. Characterization Parameter

Droplet Size and PDI: Dynamic light scattering (DLS) is used to assess the mean droplet diameter and the polydispersity index (PDI). A homogenous microemulsion is suggested by a low PDI (<0.3) and a small mean size (typically <100–200 nm). Aggarwal et al., for instance, employed PDI 0.109 to produce a mean size of roughly 12 nm. Miconazole microemulsion droplets, approximately 87 nm in size, were reported by Phechkrajang et al. Smaller droplets are more stable; instability is evidenced by a droplet's size growing over time (by Ostwald ripening). Nanodroplet morphology may be checked and droplet shape may be viewed using electron microscopy (TEM/SEM)[45].

Zeta potential (surface charge): it is evaluated to determine electrostatic stability. Nonionic surfactant-based microemulsions generally have near-neutral zeta (as in Aggarwal's –0.14 mV so steric stabilization (from surfactant layer) is necessary. Zeta values >|30| mV (positive or negative) generally indicate strong charge stability. A low absolute zeta shows the formulation depends on steric barriers. This parameter is examined during stability investigations; considerable change may suggest aggregation[46].

pH : Topical microemulsions should have a skin-friendly pH of about 5.5. Following sample dilution, a calibrated pH meter is used to evaluate it. Aggarwal's microemulsion contains pH. After gel inclusion (especially with Carbopol), adjust pH to ~5-6 using neutraliser. Deviations from skin pH might cause irritation, hence pH is a crucial check. ~6.5 was judged skin-compatible[47].

Viscosity : The viscosity of the microemulsion (and microemulgel) is determined using a viscometer or rheometer. Pure microemulsions have minimal viscosity; adding gel polymer significantly enhances viscosity[48]. Rheological profiling (flow curves) is done. Typically, microemulgels exhibit non-Newtonian shear-thinning behaviour (viscosity decreases with shear), which is beneficial for application. Viscosity also influences release rate; greater viscosity may delay release[49].

Uniformity and loading : It is validated by assaying griseofulvin content (e.g. UV spectrophotometry or HPLC). A known volume of the formulation is diluted/dissolved and evaluated. Drug content should meet label claim (typically >95%) and should be homogeneous across samples[50]. Content homogeneity is crucial to achieve dosage accuracy in each application. n water-continuous (O/W) microemulsions, conductivity is comparatively high; in oil-continuous (W/O), it is low. A typical O/W microemulgel formulation (with water as continuous phase) would demonstrate substantial conductivity (10–100 μS/cm)T.his test also tests for inversion with dilution: an O/W microemulsion will remain conductive when diluted with water[51]. Measuring electrical conductivity can identify O/W vs W/O microemulsions. Other characterizations include refractive index (for isotropy) and resilience (e.g.

diluting 10× in water to test whether it remains clear)[52].

For a topical product, particle size, PDI, zeta, pH, viscosity, and drug content are the essential parameters. These characteristics suggest a correctly produced and stable microemulsion which is important before moving to gel integration and subsequent testing.

8. Evaluation of microemulsion gel

Comprehensive evaluation of the final griseofulvin microemulgel includes physical and performance tests:

- **Spreadability:** Assessed by placing a fixed amount of gel between glass plates under a standard weight and measuring the time or diameter of spread. Good spreadability indicates ease of topical application. For instance, Modi *et al.* measured the diameter of gel spread by 50 g weight after a set time. Spreadability values (e.g., ~10–20 g·cm/s) are reported.
- **Extrudability:** For products in tubes, the force or weight required to extrude gel from a tube is measured. A good microemulgel should be easily extrudable under slight thumb pressure[48].
- **Rheology:** Viscosity and flow behavior are determined with a viscometer or rheometer. Microemulgels typically show pseudoplastic (shear-thinning) flow. For example, Modi *et al.* reported viscosity and thixotropy for their HPMC microemulsion gel. Rheograms should show high viscosity at low shear (for retention) and lower viscosity at high shear (for spreadability)[45].
- **Drug Release (In Vitro):** Using Franz diffusion cells with synthetic membranes or dialysis (to measure drug diffusing out of gel into receptor medium). The cumulative amount of griseofulvin released over time is plotted. Microemulsion gels usually show faster release than conventional gels or creams, due to high drug solubilization. Aggarwal's microemulsion showed much higher release than a cream. Modi *et al.* found their nadifloxacin microemulgel released ~90% of drug in 24 h, significantly more than a control cream .
- **Skin Permeation (Ex Vivo):** Franz cell studies using excised animal (porcine or rat) or human cadaver skin as membrane. The flux (μg/cm^2·h) and cumulative permeation are determined. Griseofulvin microemulgels have shown multiple-fold higher permeation than suspension or cream. For example, [46†L303-L312] reported 3–7× enhancement. In vitro antifungal tests can correlate release with efficacy.
- **Antifungal Activity:** In vitro microbiological assays (e.g. disk diffusion or broth dilution) compare the antifungal effect of microemulsion gel vs conventional. Enhanced activity has been reported for microemulgel formulations (due to increased drug delivery)
- **Stability Studies:** Physical and chemical stability are tested under accelerated conditions (e.g. 40°C/75% RH for 3–6 months). Key measures: droplet size, PDI, pH, viscosity, and drug content over time. The microemulsion should not separate or crystallize drug. Aggarwal's optimized GF microemulsion was stable at 4°C, 25°C, and 40°C for 6 months. Shelat's terbinafine microemulsion gel retained >90% drug content after 3 months at 40°C. Additionally, freeze–thaw cycles and centrifugation tests can be done. Lack of phase change or precipitation indicates good stability.
- **Skin Irritation/Safety:** In vivo or in vitro tests (e.g. on guinea pig or reconstituted human epidermis) assess potential irritation. Most published GF microemulsion gels (and others) report being non-sensitizing and well tolerated. However, high surfactant content is a concern, so skin safety is carefully evaluated.Overall, evaluation ensures the microemulgel has appropriate rheological properties and delivers drug effectively to/through the skin while remaining stable.

9. Challenges and Limitation

Despite promise, several challenges exist in developing griseofulvin microemulsion gels.

1. Microemulsions often require high concentrations of surfactants/cosurfactants (up to 30–50% of formulation). Such high surfactant levels may cause skin irritation or disruption of skin barrier.
2. Microemulsions are inherently low-viscosity; while gelling agents help, maintaining a balance between viscosity and drug release is tricky. Overly stiff gels may slow release too much; too fluid may not retain well. Optimization is needed so that the gel remains on skin without impeding diffusion.
3. Stability can be a limitation. Microemulsions can undergo phase inversion or drug precipitation under stress. For example, ethanol or PG (commonly used cosurfactants) may slowly evaporate, altering composition. Thus, formulations must be robust (e.g. droplet size and PDI remain unchanged over time). Aggarwal's formulation was stable for 6 months at 4–40°C.but each new formulation must be similarly tested.
4. Manufacturing scale-up can be complex: precise mixing and quality control of microemulsions can be more challenging than conventional semisolids. Additionally, incorporating drug at high load in a reproducible way requires good processing protocols.
5. Specific to griseofulvin, limitations include its intrinsic pharmacology: as a fungistatic agent, it requires sustained exposure and may not cure infections as quickly as fungicidal drugs (like terbinafine). Also, griseofulvin can be phototoxic

and has many drug interactions systemically; while systemic absorption is reduced topically, dermal phototoxicity would need evaluation. Finally, patient acceptance is a factor: microemulgel formulations must be non-greasy and cosmetically appealing to ensure adherence.

10.Conclusion

The exploration and optimization of griseofulvin-loaded microemulsion gels underscore a transformative advancement in topical antifungal therapy. By leveraging the unique physicochemical properties of microemulsions—namely, their thermodynamic stability, nano-sized droplets, and high drug solubilization capacity—researchers have successfully addressed the primary limitations of conventional griseofulvin delivery. Incorporation into a gel matrix further refines these systems, yielding formulations that are easy to apply, non-greasy, and capable of sustained drug release. Critical formulation parameters include careful selection of oil phases (e.g., oleic acid or isopropyl myristate) to maximize griseofulvin solubility, nonionic surfactants (such as Tween 80) for low-irritation emulsification, and co-surfactants (e.g., ethanol or propylene glycol) to modulate interfacial flexibility and penetration enhancement. Pseudoternary phase diagrams guide the identification of optimal oil–surfactant–co-surfactant–water ratios, ensuring the formation of clear, low-viscosity microemulsions. Characterization studies consistently demonstrate droplet sizes below 100 nm with low polydispersity indices, near-neutral zeta potentials, skin-compatible pH values, and rheological profiles suited for topical application. After gel incorporation, microemulgels exhibit pseudoplastic shear-thinning behavior conducive to skin retention and drug diffusion. In vitro and ex-vivo evaluations reveal significantly higher permeation flux and cumulative drug release compared to traditional cream or suspension vehicles, translating to improved antifungal activity in preclinical models. Stability assessments confirm that appropriately formulated microemulgels remain phase-stable and retain drug content under accelerated storage conditions, although attention must be paid to potential co-surfactant evaporation and droplet coalescence over time. Remaining challenges include mitigating high surfactant concentrations that may cause irritation, balancing viscosity for optimal release versus retention, and ensuring robust scale-up processes for manufacturing. Future research should emphasize long-term safety evaluations, exploration of alternative biocompatible excipients to reduce surfactant load, and clinical investigations to confirm therapeutic superiority. Overall, griseofulvin-loaded microemulsion gels hold considerable promise for enhancing local drug concentration, minimizing systemic exposure, and improving patient adherence in the management of dermatophytic infections.

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