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Potency of Micro-Gels in Effective Management of Fungal Infection Diseases

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Abstract

Microemulgel has vast application treating and preventing skin infection for better absorption and reducing toxicity. Microemulgel offer new alternation for the design that can be against fungal infection. Microemulgel formulation increase the efficacy, diffusion, permeation of drug and give optimum result. Microemulgel combination of both gel and mcroemulsion so it increases patient compliance. In this review we provide a broad overview on the uses of microemulgel in fight against fungal infection we have analyzed some research on microemulgel as a potential step for fungal treatment. We also give a brief summary of research that has been done and novel development show promise for the further growth of microemulgel in the pharmaceutical field.

Keywords: *Microemulgel, Co-surfactant, Greaseless, Bioavailability, Amphophilic.*

1. Introduction

The created formulations are known as microemulgels when both micro-emulsion and gel are employed in combination dosage forms. These formulations include the benefits of both emulgel and micro-emulsion. Drugs that are both hydrophilic and hydrophobic are included in dosage formulations.[1] They offer a significant surface area for medication absorption, and the oil part boosts drug permeability and bioavailability.[3] Additionally, adding micro-emulsion to gel increases its stability. Moving on to micro-emulsions, microemulgels are elegant and simple to wash when necessary.[2]

Hoar and Schulman et al, developed the idea of a microemulsion in the 1940s. A microemulsion is a mixture of liquids that is optically isotropic and thermodynamically stable.[3] It contains water, oil, and amphophilic. The vehicle that enhances the administration, effectiveness, and bioavailability of many medications is the micro-emulsion.[4] A microemulsion is a transparent, thermodynamically stable dispersion of two immiscible liquids that contains oil and water and is stabilised by molecules of surfactant through the formation of an interfacial layer.[5]

Figure 1: Development of Microemulgel Formulation

A kinetically stable liquid dispersion of an aqueous phase, a lipid phase, and a surfactant is referred to as a microemulsion.[6] The size of the dispersed particles ranges from 5 to 200 nm, and there is very little oil/water interfacial surface tension. Because of their small (less than 25%) globule size, microemulsions are transparent.[7] The microemulsion cannot be formed without a significant amount of energy input. A co-surfactant is frequently used in addition to the surfactant, the lipid phase, and the aqueous phase.[8]

Emulgel:

Emulgel is the dosage form, created when emulsion and gel are used together. It is an emulsion and gel mix, as the name would imply. As a result, it has lately been employed as a means of delivering different medications to the skin for topical and systemic effects.[9] In reality, an old emulsion becomes an emulgel when a gelling ingredient is present in the water phase. Lipophilic medications are encapsulated using the direct method (oil in water), whereas hydrophilic pharmaceuticals are encapsulated using the reverse system (water in oil).[10]

Emulsions are readily cleaned when necessary and offer a certain level of elegance. Additionally, they have a strong capacity for skin penetration. Emulgels used topically have a number of desired qualities, including thixotropy, grease lessness, ease of application and removal, emollience, non-staining, water solubility, a longer shelf life, bio-friendliness, transparency, and a pleasing look.[11] Gels are a more recent type of dosage forms that are produced by trapping significant volumes of aqueous or hydroalcoholic liquid in a web of colloidal solid particles.[20] These particles may be inorganic, like aluminum salts, or organic polymers that can be either natural or manufactured.[12]

Compared to the ointment or cream basis, they feature a larger aqueous component that allows for increased drug solubility and facile migration of the drug via a vehicle that is virtually a liquid.[13] These offer greater usability and patient acceptance. Despite the fact that gels have numerous benefits, hydrophobic medication delivery is a significant drawback. Emulgels are created and utilized to get over this restriction so that even a hydrophobic medicinal moiety can benefit from the special qualities of gels.[14]

Drugs are delivered to the skin via emulsions made of water and oil, as well as oil in water. It is important to understand the variables that affect percutaneous absorption while using topical medications.[15] Molecules can enter the skin through the intact stratum corneum, sweat ducts, or sebaceous follicles, respectively.[16] More than 99% of the entire skin surface that may be used for percutaneous medication absorption is on the surface of the stratum corneum. For percutaneous absorption, passage through this outermost layer is the rate-limiting stage.[17]

The establishment of a concentration gradient, which provides the force for drug movement across the skin, drug release from the vehicle (partition coefficient), and drug diffusion across the layers of skin (diffusion coefficient) are the main steps in percutaneous absorption.[18] Low molecular mass (600 Da), good solubility in oil and water, and a high partition coefficient are all desirable properties of topical medications. Water soluble ions and polar molecules cannot pass through intact stratum corneum, with the exception of very minute particles.[19]

The barrier function of the skin can be altered using topical formulations. For instance, topical antibiotics and antibacterials help a compromised barrier ward off infection, sunscreens and the horny layer shield the viable tissues from ultraviolet radiation, and emollient preparations restore the pliability of a desiccated horny layer.[20] The necessity and effectiveness of the selected preservative must be proven to the satisfaction of the competent authority during the creation of semi-solid preparations for cutaneous application whose composition includes an antimicrobial preservative.[21]

In Efficacy of Antimicrobial Preservation, an appropriate test procedure and criteria for evaluating the formulation's preservative qualities are given. To assure sterility, prevent the admission of impurities and the growth of microorganisms, and ensure sterility, sterile semi-solid formulations are made for cutaneous application.[22] The active ingredient in the preparation, the formulation in which it is included, the container and closure utilized, or other factors might increase or decrease an antimicrobial preservative's effectiveness.[23]

Topical preparations must be microbiological in quality and must pass a sterility test. Total viable aerobic count (aerobic bacteria + fungus) per gramme shouldn't exceed 102 microorganisms. It should include no more than 101 enterobacteria, a limited number of other gram-negative bacteria per gramme, and be entirely free of Staphylococcus aureus and Pseudomonas aeruginosa.[24]

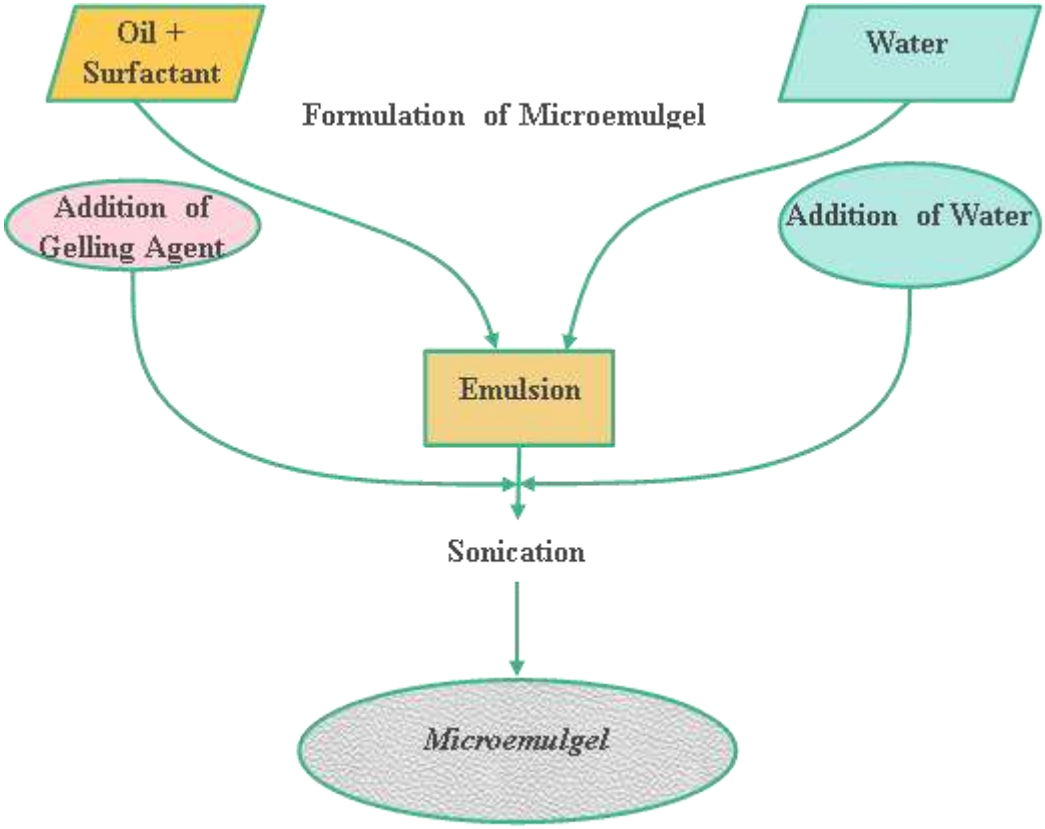

Figure 2: Basic steps in preparation of emulgel[25]

Recent Advancement in Micro-emulgel Based Formulations

Microemulgel based drug delivery system have made a remarkable difference in the bioavailability of drugs, especially anti-fungal agents, owing to their physical, chemical characteristic & biological attributes.[25] Innovative microemulgel formulation have become essential for better diffusion of drug & bioavailability enhancement. Consequently, the relevance of promising microemulgel strategies for fungal infection has become necessary.[26]

Table 1: Some recent research of microemulgels for fungal infections

Title	Author	Year	Result	Inferences	Ref.
Optimization of Microemulgel for Tizanidine Hydrochloride	Swati Jagdale et al.	2019	Isopropyl myristate was used as the oil, tween 80 as the surfactant, and transcutol P as the cosurfactant to create the microemulsion. With a Smix ratio of 1:1, the largest clear microemulsion zone was discovered. For batch B1, the FE-SEM revealed globules with a size of 28 m, and the microemulsion's high stability was indicated by its zeta potential of -1.27 mV. The most effective batch was F6, which displayed 92% drug release in under 8 hours.	The results showed tizanidine hydrochloride microemulgel formulation is a potential method for transdermal drug administration that will solve the issues with medication associated with first pass metabolism.	27
Microemulgel formulation of Kepok banana peel extract (Musa paradisiaca L) as an antioxidant	F F Sriarumtias et al.	2019	It can be established that formula 2 is the formula that best satisfies pharmaceutical criteria among emulgel preparations using methanol extract of	Results revieled that, using the methanolic banana peel extract in the emulgel did not cause skin irritation.	28

			Kepok banana peel (Musa paradisiaca L) and different quantities of 1XIC50, 2XIC50, and 3XIC50 employed as antioxidants.		
Formulation, Development and Evaluation of Etoricoxib Nanosize Microemulsion Based Gel for Topical Drug Delivery	Vania Rachael Fonseca et al.	2019	To prevent problems with oral administration, to make etoricoxib more soluble, and to enhance skin permeability, a microemulsion-based gel for topical delivery of the drug was developed in the foregoing study. After 8 hours, the improved formulations revealed a 57.8% drug release. The formulation's stability was also discovered. Etoricoxib microemulgel can be utilised to improve percutaneous delivery and provide a prolonged effect of medication release.	The study showed that the gel formulation based on microemulsions may be used to increase etoricoxib's solubility and skin permeability.	29
Formulation and Evaluation of Microemulsion Based Luliconazole Gel for Topical Delivery	Panchaxari Mallappa Dandagi et al.	2020	In the current research, an effort has been made to develop and assess luliconazole gel based on a microemulsion for its improved solubility and permeability for antifungal activity by employing poly unsaturated fatty acids like linseed oil. As a gelling agent, sodium alginate, a semi-synthetic polymer, was utilised. The globule size of the microemulsion was measured using Nanotrac. E1 and E4 were chosen as optimised microemulsions with 273.7 nm and 189.6 nm and PDI of 0.632 and 0.197 based on the measured MA, that is, surface area distribution of globules and polydispersity index.	Scientists suggest that Conventional dosage forms such as creams, ointments etc exhibit drawbacks like problem in stability, stickiness, poor absorption as well as permeation mainly in case of large molecule. To overcome this isuue, the origination of emulgel came into existence which basically focus on the delivery of hydrophobic drugs. The present research concluded that preparation and evaluation of microemulsion based luliconazole gel for its enhanced solubility and permeability for better antifungal activity.	30
Formulation and Evaluation of Topical Microemulgel Containing Terbinafine Hydrochloride	Zingade Sarika G.1 et al.	2021	Terbinafine hydrochloride is an FDA-approved antifungal medication used to treat fungal infections on the skin & has several advantages over simple traditional formulations, including simplicity of administration, increased residence duration at the application site, consistent drug release	The study revealed that terbinafine hydrochloride, a medication with limited bioavailability, is better suited to micro-emulgel formulation. The results revealed that microemulgel may achieve the maximal drug release after 24 hours (94.50%). The invention of the terbinafine	31

			with improved bioavailability, superior thermodynamic stability, and excellent transdermal permeability. Carbopol 940 and HPMC is used as a gelling agent, oleic acid as an oil, parabens as a preservative, and tween 20 as an emulgent and penetration enhancer.	hydrochloride micro-emulgel formulation was considerably more favourable than the current dosage forms since the medication is lipophilic in nature and difficult to enter through moist skin. Although the micro-emulgel formulation can permeate drugs, further research is needed to evaluate its therapeutic effectiveness.	
Development and optimisation of biopharmaceutical properties of a new microemulgel of cannabidiol for locally-acting dermatological delivery	Giulia Vanti et al.	2021	The ME-gel was made from a ME that contained 1% w/w CBD and was loaded with 20% Solutol HS 15, 9% Transcutol P, 5% Isopropyl Myristate, and 66% water. Due to CBD-ME's weak viscosity, it was jellified using Sepigel 305, which gave the formulation stability, shine, and an almost immediate rise in viscosity. The resulting microemulgel had a nice, creamy, gel-like consistency and was non-Newtonian pseudoplastic semisolid in formulation, like the majority of gels mentioned in the literature for topical administration.	This study showd that a novel CBD-based microemulgel (CBD-MEgel), which has been created and characterised for the treatment of inflammatory and pruritic skin problems as well as eczema and other cutaneous illnesses. Studies on the release and permeation of CBD formulations in microemulgels using skin-PAMPA and rabbit ear skin demonstrated regulated release and absorption qualities, leading to satisfactory retention in the skin layers without the need for transdermal administration.	32
Formulation, Development and Characterization of Ibuprofen Microemulgel for Arthritis	Muhammad Hammad Tariq Bhatti et al.	2022	The solubilization of the medicine, ibuprofen, provided by the developed micro emulsion system before it was transformed into emulgel is useful in boosting the bioavailability of the drug. The emulgel's particle size indicated that it was in the micro emulsion range and that it would be well absorbed when applied topically to skin. Ibuprofen interactions with carbopol and other chemicals used to prepare the microemulsion were studied using comprehensive Fourier Transform spectroscopy. F1 was chosen as the top formulation out of all of them since it had the greatest drug release percentage, at 94.6 percent.	The first emulgel was the best formulation in the current investigation in terms of all factors and attributes. The created micro emulgel demonstrated the highest level of system stability and drug solubility. The produced emulgel may be a cost-effective formulation since it reduces topical dosage and frequency while also having the maximum bioavailability (94%) of any formulation. The mechanism created for loading ibuprofen, or emulgel, is stable and compatible with the medication, as shown by all of the results. The emulgel helps treat sports injuries and arthritis by quickly relieving pain and encouraging patient compliance.	33

Design, Optimization and Evaluation of Microemulgel Containing Antifungal Drugs	Rajappa Margret Chandira et al.	2022	To increase medication absorption and bioavailability, the current study developed a microemulsion gel formulation of salicylic acid and benzoic acid. Many formulations produced microemulgel formulations have a medication concentration of 85 to 96%. Salicylic acid and benzoic acid were produced at various quantities (2, 4, 6, 8 and 10 g/ml) and examined using the appropriate media and UV at 230 nm and 210 nm.	This study suggests that Benzoic and salicylic acid microemulgels better for the treatment of fungal infections were designed, optimised, and evaluated for stays in the skin for a longer period, allowing for more effective absorption and absorption into the bloodstream. Carbopol 934 and HPMC k 15m were used as gelling agents, oil as a preservative, and emulsifying agent as a penetration enhancer in the research to create benzoic and salicylic acid microemulgels.	34
Development of Phyto cosmeceutical Microemulgel Containing Flaxseed Extract and Its In Vitro and In Vivo characterization	Rabia Tasneem et al.	2022	The most acceptable components that were readily accessible, together with an ethanolic extract of flaxseed, were chosen to effectively synthesise a stable microemulgel. It has to be professionally evaluated on various skin conditions including eczema and psoriasis	Studies on the release of bioactive components demonstrated the controlled release properties of the microemulgel containing flaxseed extract. Results of in vivo experiments shown that the active formulation restored the skin's erythema, melanin, sebum level, hydration, and elasticity after any UV-related flaws.	35

4. Conclusion

Currently available conventional antifungal drug therapy suffers from severe limitation such as bio distribution, insufficient targeting by the therapy agents, poor bioavailability, poor solubility, low therapeutic indices. Combined with microemulgel formulation would be a better option for fungal infection, providing that all the setback and clarifications are dealt with. The microemulsion-based gel was, produced have a high potential for the delivery of the medication through the transdermal route for fungal infection disease.

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