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A SYSTEMATIC REVIEW: NOVEL APPROACH ENHANCING ANTIFUNGAL DRUG FOR TOPICAL ROUTE

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ABSTRACT

Microemulsion, provide a new angle against fungal infections. These paper analyses the possibility of using these adaptable formulations to provide antifungal medications directly to the skin, we examine the special qualities of microemulsion and their capacity to: Breach the Barriers: Their minuscule size allows for deeper penetration into the epidermis, avoiding the skin's natural resistance, the stratum corneum. Microemulsion composition allows for exact targeting of particular fungal strains and skin diseases, providing a customized therapeutic strategy. This review highlights the benefits of microemulsion based antifungal formulations over traditional ones by critically analyse the most recent research in this area. Studied several antifungal medications that have been used and the formulation techniques, and the difficulties that remain in this emerging sector. Microemulsion technology offers hope for a more successful and patient-friendly future by redefining the landscape of topical antifungal therapy with its special combination of features.

Keywords: Microemulsions, Antifungal drugs, Topical delivery, Skin penetration, Controlled release, Targeted therapy.

INTRODUCTION

Topical delivery system represents an approach for the treatment of localized disorders where composition is given topically to locations such as the skin, eyes, nose, and vagina. When a medication is given topically, it avoids the liver's hepatic first pass metabolism, alteration in gastric pH and variations in plasma levels that often occur when a drug is taken orally. The following are some additional benefits connected to the topical medication administration system: Adherence and acceptance of patients, Application comfort and ease of use, A non-invasive, painless method, Enhancement of the bioavailability of drugs, An improved pharmacological and physiological response, Little exposure of the medicine to non-infectious tissue or locations and little systemic effects[1].

Most traditional topical formulations aim to provide the medication for a localized effect instead of a systemic one. Conventional treatments are suggested to target the skin's outer layer. The application of ointments or creams is a prerequisite for conventional topical skin care. When applied topically, drugs from these formulations partition to form an extremely concentrated layer of active substance that is quickly absorbed. Furthermore, issues like stickiness and greasiness with topical medications can occasionally lead to a patient's noncompliance with treatment. Because of the limited delivery system efficiency, these vehicles need a significant amount of active drugs in order to exist therapeutically efficacious.

Additionally, it could cause harmful reactions like rashes and hypersensitivity responses. Unmanaged evaporation of the active substance and an unpleasant odour are two other disadvantages. These devices frequently administer in an indiscriminate manner, and skin penetration varies greatly. For a medicine to be effective, it must meet two requirements: it must travel a considerable distance to the scene of the incident, and it must remain there in a focused manner suitable for a predetermined amount of time. Although the skin is the organ at the outermost and without difficulty accessible for medication administration, this does not imply that the drug's route to the site of action is straightforward.

Drugs have been used with penetration enhancers, such as dimethyl sulfoxide or propylene glycol leads, to improve drug penetration through the layers of the skin. The use of penetration enhancers speeds up the rate of transport across the epidermal barrier, but because the drug's blood level is raised, it also increases side effects. Research raises concerns about the safety of using penetration enhancers

for topical drug delivery due to reports of irritative or even toxic side effects [2].

Since its initial publication by Schulman over seven decades ago, while studying water-in-cresol microemulsions stabilized with soap/oleate and pentanol, microemulsions have been studied and applied. Years later, similar systemswhere water and oil are trapped in a homogenous phase that is transparent, isotropic, thermodynamically stable, and usually has low viscosity—were dubbed microemulsions. An isotropic, thermodynamically stable dispersion consisting of water, oil, and surfactant(s) with a dispersed domain diameter that can range from 1 to 100 nm, often between 10 and 50 nm is a microemulsion according to IUPAC [3].

Avoiding salivary metabolism, intestinal metabolism, and first pass metabolism in the liver. These systems able to self-administered by patients because to their ease of use. Drug input can be immediately stopped in an emergency by removing the medication delivery mechanism at any point during therapy. There is little inter- and intra-subject diversity because practically all humans have the same biological and structural makeup of skin. It is appropriate to deliver drugs that cause gastric discomfort and absorption through the skin. For medications with short biological half-lives, which would usually require frequent dosage, continuous, non-invasive infusion is possible. Better patient compliance is the result of less frequent dosing. It is possible to prevent therapeutic failures brought on by dose inconsistencies with traditional therapy. Compared to oral sustained drug delivery systems, the release lasts longer. Transdermal methods can be useful in situations when it is not desirable to maintain the medication concentration within the bio phase. Compared to traditional therapy, a smaller daily dosage of the medication is needed. The length of the drug's action is prolonged and predictable due to its controlled release [4].

Antifungal Drug

In order to treat superficial fungal infections, topical antifungal medications and/or oral medications may be used. In order to escape being removed from the skin surface by desquamation, fungi frequently infect the outer layer of the skin and then spread into the stratum corneum (SC). Creams, lotions, and sprays containing pharmacologic agents that are applied to the skin's surface can easily permeate the SC and kill fungus or at minimum prevent them from growing or dividing. Therefore, topical treatments are effective in clearing the skin of topical yeasts and fungus. Because topical dermatophytosis therapy tends to have little serum absorption, topical therapy is a more appealing treatment option for localized infections than oral drugs in terms of safety. The majority of side effects from topical medication administration is mild and temporary skin responses at the location of application; however, oral antifungal treatment can cause significant toxicity in liver, uncommon grievous skin reactions like Stevens-Johnson illness, as well as potential incompatibility between drugs as a result of cytochrome P450 system metabolism [5].

Different type of antifungal agents

Nystatin (nys)

It is a polyene antibiotic having fungicidal and fungistatic properties that is helpful in the management of cutaneous Candida infections. Its restricted solubility in aqueous solutions, which results in low absorption and bioavailability, limits its application. The molecular structure of the substance is revealed through the existence of a wide ring made of lactones that contains numerous dual bonds. The non-selective nystatin aggregates that arise in aqueous media have the ability to damage the cell membranes of fungi and mammals, resulting in poisoning and death of the hosting cell. It is therefore suggested that the administration of nystatin in an unaggregated form could enhance its therapeutic index [6].

Clotrimazole

Plempel, a chief mycologist at Bayer AG (Germany), created clotrimazole, the first imidazole topical antifungal, in the late 1960s.

One imidazole derivative with a wide range of antimycotic action is clotrimazole. Similar to other azoles, it functions by preventing 14-a demethylase from functioning, which stops the production of ergosterol from fungus and increases the cell membrane’s permeability. Clotrimazole may also disrupt the formation of membrane phospholipids, speed up significant intracellular ion outflow, damage cellular

nucleic acids, and prevent endogenous respiration. Cell growth and division eventually come to an end [7].

Econazole Nitrate

Commercial forms of econazole nitrate (EN) include lotion, powder, 1% ointment, 150 milligram vaginal pill,1% cream and solution. These delivery systems are ineffective as delivery systems; therefore, large active concentration of drugs must be included for successful medication. Consequently, a delivery system is required to increase the size of time a vital molecule is found on the skin while reducing amount of time it penetrates the body. Since the skin metabolizes EN slowly, regulating the drug's release will increase formulation efficacy and reduce application frequency [8].

Nitrate of miconazole

An antifungal drug with a wide spectrum, miconazole nitrate, can be difficult to formulate for topical use. Despite being is a salt of nitrate with an approximate octanol- water partition value of 6.25 and is insoluble in water, indicating that the nitrate salt is lipophilic. Miconazole nitrate's poor skin penetration, which is most likely caused by a low concentration of aqueous driving on the surface of the skin on the skin, makes topical application of the medication problematic for treating cutaneous illnesses and leaves potential for topical delivery system performance improvement. Among the previously documented methods for achieving miconazole nitrate are standard liposomes, ethosomes, niosomes, and microemulsions[9].

Itraconazole

Itraconazole an azole antifungal drug, is commonly used for clinical treatment of some deadly fungal illness. Itraconazole works by obstructing the production of ergosterol, a crucial part of the membrane of fungi cells. In a system with an aqueous buffer solution at pH 8.1 and n-octanol, the log partition coefficient of Itraconazole is 5.66, indicating the drug's hydrophobicity. Itraconazole pKa value is 3.7, making it base weak that is largely insoluble in water. With less toxicity than amphotericin B, it has proven to be useful in the management and avoidance of aspergillus infections, suggesting higher therapeutic index. Unfortunately, patients who are neutropenic have relatively low levels of Itraconazole bioavailability, and patients undergoing antineoplastic therapy frequently have insufficient plasma concentrations. Topical drug distribution would work better for these patients and presents a variety of potential for successful pharmacological therapy for fungal infections [10].

Voriconazole

There are oral and intravenous versions of voriconazole available. Topical voriconazole, when combined with systemic voriconazole, has been suggested as a novel and possible treatment for keratitis in recent clinical investigations. For the treatment of cutaneous aspergillosis, along with antifungal systemic drugs, 1% Voriconazole solution was given topically as an adjuvant treatment. Purpose of this work was to introduce insoluble voriconazole into a topical microemulsion (ME) system. The in vitro evaluation and optimization of the systems were conducted by examining the impact of varying ME component types and ratios on the physical and rheological characteristics. The effectiveness of employing this approach to enhance voriconazole topical or transdermal distribution was evaluated through an in vitro permeability study, which also examined the impact of two permeation enhancers. Additionally, the chosen ME's microbiological activity was examined against a strain of Candida albicans [11].

Ketoconazole

KTZ has extremely low solubility properties in typical solvents like alcohol and water. It can only be purchased as commercial suspension form as a semisolid aqueous shampoo and cream made of water for topical treatment. Due to the discrete particles' ineffective skin penetration, the cream has a low bioavailability of KTZ. Therefore, in order to treat infectious conditions that are vulnerable to infection, a vehicle with an appropriate concentration of KTZ must be applied directly to the skin[12].

Fluconazole

Fluconazole pharmacokinetic characteristics set it apart from other azole derivatives because it has two triazole rings, which reduce its lipophilicity and decrease its affinity for

proteins. After being applied to the skin, fluconazole diffuses and quickly and widely builds up in the stratum corneum. The skin has higher concentration of fluconazole than the serum does, and Stratum corneum eliminates it much more slowly than the serum or plasma do. For the majority of dermatophytes, in comparison to the minimal inhibitory concentration skin has noticeably higher concentration. Because of an interaction between fluconazole and keratin, fluconazole has a high affinity for the SC, which has been linked to its extended skin retention [13].

Terbinafine

Early in the 1990s, the lipophilic antifungal medication terbinafine (TBF) was first approved in order to treat fungal infections.TBF an allylamine having molecular weight 291.4 g/mol, the chemical formula C21H25N, and a logarithmic partition coefficient (LogP) of 6.0 for octanol/water. The chemical functions by preventing squalene epoxidase from participating in production of ergosterol by fungi, necessary ingredient for the fungal cell membranes development. TBF exhibits a wide range of antifungal action against cutaneous fungal infections. TBF primarily acts as a fungicidal agent against dermatophytes, although it also demonstrates fungistatic activity against Candida albicans [14].

Limitations of traditional formulations for antifungal drug delivery

Medications available in traditional dose formulations for treating external fungus diseases can also be used to treat deeply embedded fungus diseases. Using these formulations can have a number of negative consequences, including burning, redness, and swelling. Furthermore, these formulations' instantaneous drug release has the ability to stimulate the body's immune system and cause a variety of allergic reactions [15].

Treatment options are restricted for deep fungal infections such invasive candidiasis and aspergillosis. Due to its low penetration capability, the traditional topical formulation's ability to release the medicine at the target site is impaired.

Similar issues with limited absorption are displayed by conventional formulations while treating fungus diseases of nails and eyes. Therefore, a number of research concentrating on developing novel topical products and distributing antifungal drugs have been conducted in an effort to get beyond the restrictions of traditional therapy.

Antifungal medication compositions such as niosomes, ethosomes, liposomes, nanoemulsions, nanoparticles, micelles have been recently investigated for topical administration [16].

The microemulsion begins to work faster than traditional dose delivery techniques like cream. Development of colloidal particles has facilitated the prompt and less invasive treatment of fungal diseases [17].

Microemulsions

To effectively transmit medications over the skin, scientists employ microemulsions, a transparent, thermodynamically inert colloid drug transport system. It is an isotropic blend which is hydrophilic plus lipophilic elements that occurs naturally and gets stabilized by the right co-surfactant and surfactant. Its simple construction, extended stability, enhanced solubilization, biological compatibility, skin-safe appearance, attraction for both lipophilic as well as hydrophilic drug molecules make it superior to alternative carrier methods for cutaneous drug administration [18].

Advantages of microemulsion in drug delivery

They superior thermodynamic stability.

- They are simpler to create and don't require an energy input during synthesis.
- They are low viscosity relative to emulsions and reversible microemulsion production make them thermodynamically stable.
- The use of relatively mild conditions during the microemulsion formulation process significantly reduces protein degradation.
- Usage of substances including oils, water, and surfactants that are compatible with proteins. These excipients are widely acknowledged to be safe and are utilized in pharmaceuticalformulations.Theirmetabolicp rofilesandtoxicityarewidelyrecognized [19].

Micro emulsion's function in improving topical medication delivery

Aside from physically influencing the skin, other possible ways to improve medication penetration through the skin include altering the formulation to change the partition, diffusion, or solubility. Combining multiple enhancing approaches, like iontophoresis with fatty acids, results in less skin toxicity and synergistic medication penetration [20].

Microemulsions have a unique mechanism of action when it comes to skin penetration since they have a tendency to interact with the skin's lipids changing the area between cells along with facilitating medication delivery. The droplet size of the dispersed phase is the primary characteristic that separates the emulsion from the microemulsion. Microemulsions are a promising technology for drug delivery systems because they enable both prolonged and regulated drug release for different administration routes. As a drug delivery system, microemulsions are unique in a number of ways, chief among them being their lower toxicity, ability to promote better drug absorption, and ability to control drug release rates [21].

Medications with hydrophilic or lipophilic properties can highly soluble in microemulsions, allowing for the loading of additional drug into the solution and an increase in the change of concentration across the skin without reduction. Prolonging absorption, internal phase's reservoir impact keeps drug's pushing force from the exterior phase on skin constant. The drug is continually delivered to the external part of the microemulsion by its internal part ensuring that medication stays saturated, as the medication diffuses into the skin solely from the external phase [22].

Formulation Components

Essential elements in the creation of microemulsions

Oils

They make the emulsions oil phase. Because of their occlusive and sensory qualities as well as their usage as a medication delivery system, a variety of topically emulsions and mineral oils, either by itself or in conjunction with hard or soft paraffin, are commonly utilized. In addition to oils from fish liver and other vegetable based fixed oils like cottonseed, maize and arachis oils, are utilized as dietary supplements and oral remedies sometimes contain no biodegradable castor and mineral oils, which have a local laxative effect. Oleic acid was used as the oil phase in the development of a microemulsion intended for transdermal distribution of terbinafine [23].

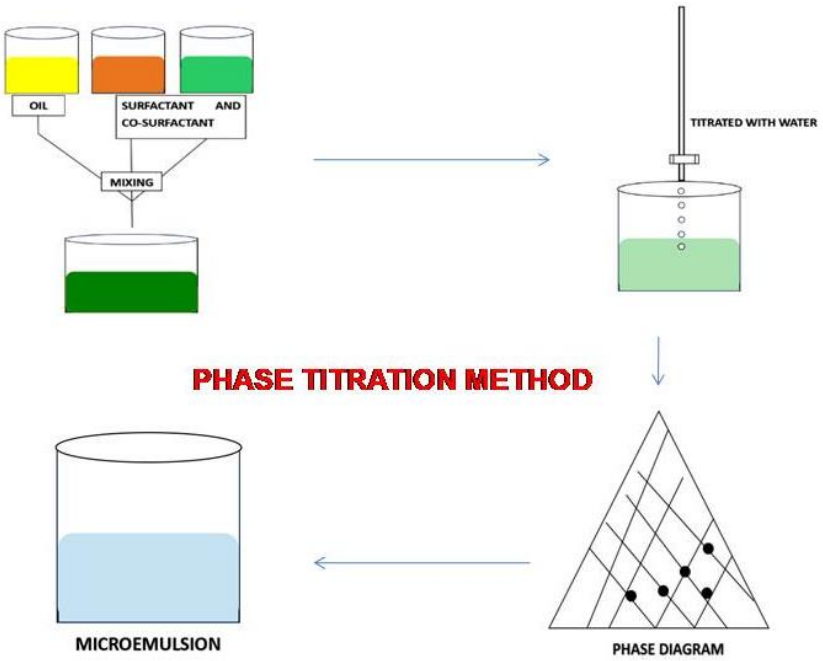
One of the most crucial elements of a microemulsion is oil since it can improve the percentage of lipophilic medications carried by the intestinal lymphatic system and solubilize the necessary dosage of the lipophilic drug. Any liquid with low polarity and low water miscibility is considered oil. Vegetable oil, mineral oil, toluene, and cyclohexane are a few examples of this phase [24].

Surfactants & co-surfactants

Single-chain or double-chain surfactants can be used to produce microemulsions. Cosurfactants are necessary because single chain surfactants are insufficient in lowering the oil-water interfacial tension. By permeating into the surfactant layer, cosurfactant significantly accumulates at the interface layer and increases the fluidity of the interfacial film. Co-surfactants give the interfacial film the flexibility it needs to absorb various curvatures and produce a microemulsion throughout a broad composition range. The lipophilic chains of the surfactant should be suitably short or contain fluidizing groups (such as unsaturated bonds) if a single surfactant film is desired. Alcohols with short to medium chains (C3–C8) are frequently added as co-surfactants to further lower interfacial tension and improve interface fluidity. In order to prevent the formation of a microemulsion, co-surfactants have three functions: they increase the fluidity of the interface, break up liquid crystalline or gel structures, and modify the surfactant partitioning characteristic to modify the HLB value and spontaneous curvature of the interface such as propylene glycol and Tween-80 [25].

Water phase

Preservatives and hydrophilic active substances are typically found in the aqueous phase. Buffer solutions are occasionally employed as the aqueous phase [26].


OIL
SURFACTANT AND CO-SURFACTANT
MIXING
TITRATED WITH WATER
PHASE TITRATION METHOD
MICROEMULSION
PHASE DIAGRAM

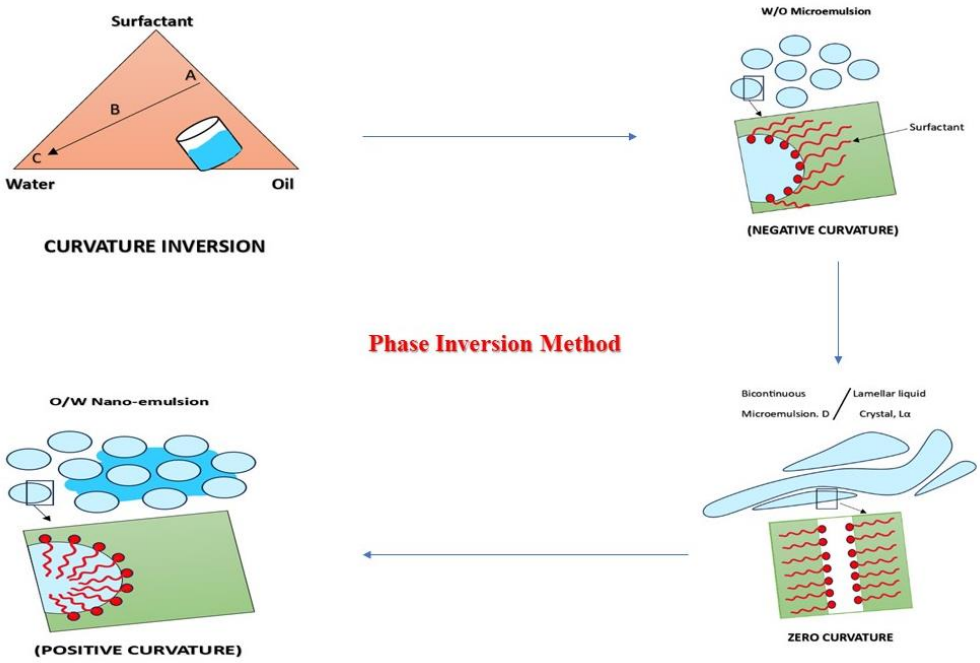

Surfactant
A
B
C
Water
Oil
CURVATURE INVERSION
W/O Microemulsion
Surfactant
(NEGATIVE CURVATURE)
Phase Inversion Method
Bicontinuous Microemulsion, D
Lamellar liquid Crystal, Lα
ZERO CURVATURE
O/W Nano-emulsion
(POSITIVE CURVATURE)

Table no: 1 Properties of Microemulsion and Emulsions [32]

S. No	Property	Microemulsion	Emulsion
1	Appearance	Transparent or translucent	hazy
2	Optical Isotropy	Isotropic	Anisotropic
3	Interfacial tension	extremely low	Elevated
4	Microstructure	dynamic (interface fluctuates continuously and on its own)	unchanging
5	Size of droplets	20-200 nm	> 500 nm
6	Stability	steady thermodynamics and extended shelf life	Kinetically stable yet thermodynamically unstable, they will eventually phase separate
7	Phases	One-phase or monophasic	Biphasic
8	Preparation	Simple preparation and comparatively inexpensive commercial manufacturing	demand a significant energy input and are more expensive
9	Viscosity	Minimal viscosity and Newtonian characteristics	Increased viscosity

Obstacles and Prospective Paths

	Issues with topical medication administration [47]
1	Variability in percutaneous absorption based on illness, age, and other factors
2	Impact of "first-pass" metabolism on the skin
3	The potential of skin as a reservoir
4	Potential for irritability and other side effects from the medication
5	Skin variation and susceptibility to changes in metabolism and turnover
6	The bioequivalence criterion is not specified sufficiently.
7	ignorance of the technologies that can change the rate of percutaneous absorption

Construction of pseudo ternary phase diagram

The pseudo-ternary phase diagram is constructed. In order to construct a phase diagram, we used the difference between the fraction of mixed surfactant and the micro emulsion area to calculate the ideal ratio (Km) of surfactant to cosurfactant. Km was investigated with the use of a basic pseudo-ternary phase diagram. Pseudo-ternary phase diagrams (aqueous phase) were used to examine the production of micro emulsions utilizing a four-component system made up of an oil phase, a non-ionic surfactant, a co-surfactant, and purified water. The pseudo ternary phase diagram was obtained by titrating homogeneous liquid mixes of water, surfactant, and cosurfactant with oil phase at room temperature. The ratio of surfactant to co-surfactant was mixed between 1:9 and 9:1[27].

Preparation of microemulsion

1.Titration method

Phase titration is the procedure used to create microemulsions. This technique is also known as spontaneous emulsification. The phase diagram provides a characterization for microemulsions. A four-compartment system takes a lot of time to set up and is challenging to intercept. Therefore, the pseudo-ternary phase diagram is used in the creation of microemulsions. They have distinct zones as well as microemulsion zones. These displaying all of the specific components at 100%.

We use oils, water, surfactants, and a combination of co-surfactants in predetermined weight ratios in our phase titration approach. The blending of materials is handled by this phase diagram. After agitating each of these mixes at room temperature, a visual inspection will verify whether the system is monophasic or biphasic. The samples should be regarded as biphasic even if turbidity may emerge during phase separation since, with continuous stirring, monophasic mixtures look clear and transparent. The phase diagram needs to be labelled with the obtained points [28].

2. Phase inversion

These emulsions experience a temperature-induced phase inversion into water-in-oil (w/o) emulsions within a specific temperature range. It was demonstrated that, at high enough emulsifier contents, phase inversion produces a one-phase microemulsion or a lamellar phase, which can be used to create a finely distributed, long-term stable oil-in-water emulsion. The associated phase inversion temperature, which is the median value of the phase inversion range, was reached or exceeded when the oil phase was emulsified in the hot state for this purpose. The identical emulsifier composition resulted in an unstable and coarsely dispersed o/w emulsion if the emulsions were made at temperatures lower than the phase inversion range[29].

Antifungal Efficacy

It has been demonstrated that the antifungal medications griseofulvin, amphotericin B, fluconazole, miconazole, and other topical and systemic fungal infections can be treated with micro-emulsions as drug delivery vehicles. As drug delivery vehicles, topical micro-emulsions provided a number of benefits, including improved skin penetration, increased therapeutic efficacy/bioavailability, avoidance of hepatic first pass metabolism, and reduction of systemic side effects[30].

Compared to voriconazole supersaturated solution, drug-loaded microemulsion demonstrated superior antifungal efficacy against candida albicans. In comparison to water-in-oil (w/o) microemulsion, drug penetration from oil-in-water (o/w) microemulsion was comparatively higher [31].

Mechanism of drug release

Two models can be used to explain the drug release from the ME. While the other model views the interfacial barrier between the droplet and its surroundings as the rate-determining phase of drug release, the first model explains drug diffusion throughout the droplet as the rate-limiting stage of drug release. The combination of mass balance and linear dependence of mass fluxes on concentrations was characterized by the most widely accepted model of drug release from ME. Mass transfer constants of the medicines through a biological membrane that divides the ME from the receiver phase are typically used to study drug release from the ME.

In oil-surfactant water mixes, the mass transfer constant and the drug's partition coefficient are

closely correlated. The distribution of the drug across the stages of ME, droplet size, and oil-aqueous phase ratio are the primary factors influencing drug release from ME. The rate at which the drug moves from the disperse phase to the continuous phase and then from the continuous phase through the biological membrane further controls the release pattern. The concentration of the drug in the aqueous phase of the ME is expected to affect the permeability of hydrophilic drugs via the biological membrane that contacts the ME, and vice versa in the case of lipophilic drugs [33].

topical medication administration Transdermal medication distribution may be improved by microemulsions mainly through the following effects: Drugs that are both lipophilic and hydrophilic can be highly soluble in microemulsions, allowing for the loading of additional drug into the solution and an increase in the concentration gradient over the skin without depletion. Prolonging absorption, the internal phase's reservoir effect keeps the drug's pushing force from the exterior phase to the skin constant. The internal phase of the micro emulsion continuously delivers drug to the exterior phase, ensuring that it stays saturated with drug, as the medication diffuses into the skin solely from the external phase [34].

Skin Penetration and Permeation

In comparison to more traditional dosage forms like gel, cream, etc., microemulsions have the advantage of being easier to prepare due to their spontaneous formation, thermodynamic stability, transparent and elegant appearance, increased drug loading, enhanced penetration through biological membranes, and increased bioavailability [35].

The stratum corneum is the main layer of skin that prevents drugs from penetrating. Nonetheless, several mechanisms exist for the transmission of natural compounds through the skin, such as the intracellular, follicular, and intercellular pathways. Drug compounds that are hydrophilic can be transmitted across the intercellular pathway. While the intracellular transport method makes it easier for lipophilic medicinal compounds to penetrate cells, the follicular or trans appendageal channel offers a direct and quick transfer of contents to the infundibulum region. A proper carrier system is extremely desirable to boost the drug's therapeutic efficacy and promote its penetration across the skin. In this order, microemulsion is a possible drug carrier system for topical and transdermal drug delivery to enhance drug transfer via the skin by overcoming skin barriers [36].

Direct effect on the skin

- Increased hydration and swelling are brought on by denaturation or conformational change of intracellular keratin.
- Affection of desmosomes, also called macula adherens, which are specialized cell structures for cell-to-cell adhesion and keep corneocytes (dead cells of the stratum corneum) cohesive.
- Lipid bilayer alterations lessen the barrier to penetration.
- Modifying drug partitioning by changing the stratum corneum's solvent characteristics.
- Using a solvent that can remove the lipids from the stratum corneum and lessen its ability to pierce.

Modification of the formulation

Supersaturation state caused by a volatile solvent that transforms the active ingredient into a state that is more thermodynamically active.

Selecting enhancer molecules for the vehicle that boost penetration into the skin and act as good solvents for the active component will improve the drug's partition into the stratum corneum.

Enhancers that form liquid pools within the bilayers, such as oleic acid, or disrupt the bilayers uniformly, like the Azone® molecules (also known as laurocapram or 1-dodecylazacycloheptan-2-one), can help the active ingredient diffuse through the skin more easily. Azone® is the first molecule created expressly to improve skin permeation. Azone® functions as a surfactant and improves the way that many medications, such as steroids, antibiotics, and antiviral medicines, are transported through the skin[37].

Evaluation

Retention evaluation

Using isopropyl myristate as an oil phase, two surfactants—lecithin and Tween 80—were combined with ethanol as the co-surfactant to create the systems. The study evaluated the in vitro permeation and retention evaluation results on the skin of mice, demonstrating that the ME system had the maximum flow of 33.92 µg/cm2 /h [38].

Globule size and zeta potential measurements

One technique that can be used with a Zetasizer HSA 3000 to ascertain the microemulsion's globule size and zeta potential is dynamic light scattering. Zetasizer was used to calculate the microemulsion's zeta potential [39].

Viscosity measurement

Rheological characteristics are crucial for stability. The digital viscometer made by Brookfield can determine it. It is possible to identify the microemulsion region and distinguish it from other regions by examining changes in the rheological properties [40].

Phase behaviour studies

It is possible to distinguish microemulsions from liquid crystals and coarse emulsions using electron microscopy, phase contrast microscopy, and freeze fracture transmission. Microemulsions are defined as clear, isotropic, one-phase systems, whereas liquid crystalline systems are assumed to be opaque systems exhibitingbirefringent when observed by confined light microscopy [41].

Stability

Microemulsions can be tested for physical stability using techniques including centrifugation, freeze-thaw cycles, and heating-cooling cycles. The surfactant film's elastic characteristics at the O/W interface determine how droplets form, and the surfactants stabilize microemulsions. The film's curvature and rigidity are two crucial characteristics[42].

In-vitro release/permeation studies

To assess the impact of the formulation parameters, the generated microemulsion-based gel's in-vitro penetration rates were measured. Franz diffusion cells, locally constructed with a dialysis membrane pore size of 0.2 mm at 37 ± 0.1 °C, were used for the diffusion studies. 200 ml of phosphate buffer pH 7.4, which serves as receptor fluid, were added to the beaker. Externally powered magnetic beads continuously swirled the fluid within the receptor. Precisely 1 gm of gel based on microemulsion was put into the cylindrical hollow tube, with one end sealed with a 0.2 mm dialysis membrane pore size. It serves as a container for donors.10 ml aliquots were taken at appropriate intervals ranging from thirty minutes to six hours. Following each sample, an equivalent volume of brand-new phosphate buffer was added right away. After the sample was diluted appropriately with a suitable solvent, it was examined using a UV-Visible spectrophotometer at an appropriate wavelength. To determine the total amount of drug release at each time interval, cumulative adjustments were performed [43].

Physical appearances

Micro emulsion’s overall physical quality, one can visually inspect its homogeneity, fluidity, and optical clarity[44].

Thermodynamic stability studies

The efficacy of a lipid-based formulation is contingent upon its physical stability, as drug precipitation inside the excipient matrix might have a detrimental effect on it. Furthermore, inadequate formulation physical stability may result in the excipient's phase separation, which impacts not only formulation performance but also appearance[45].

Percentage Transmittance

For self-microemulsion, visual evaluation is the main method. A UV visible spectrophotometer is used to measure the transmittance of the microemulsion that is produced after self-emulsifying at a dilution to prevent subjectivity [46].

Future prospects for research

It is anticipated that the field of microemulsion technology would see several advancements. Microemulsion systems play a critical role in offering innovative approaches to address the issue of highly lipophilic medicinal compounds poor aqueous solubility and in achieving high, more reliable and repeatable bioavailability.

Furthermore, given the relative expense of commercial production, these formulations ease of scaling up is significant from an industrial perspective. Many topical products using the microemulsion technique are expected to emerge in addition to oral drug delivery. This is noteworthy from the perspective of both the enormous and profitable cosmetic industry prospects as well as the delivery of drugs. Drug targeting can also be accomplished with microemulsions; however, there are still issues, mainly due to the multiple obstacles that these systems must go past in order to reach the target.

The goal of current research is to create safer, more effective, and more suitable microemulsion ingredients, which will increase the usefulness of these innovative vehicles. To characterized the physiochemical behaviour of the microemulsion, a significant amount of work remains. Although this therapeutic system has several limitations, scientists are currently focused on realizing its full potential as a cutting-edge medication delivery technique. [48]

CONCLUSION

With the powerful antifungal drug against fungal diseases, microemulsion provide a fascinating peek into the future of topical antifungal therapy. They appear to be more safe and effective due to their capacity to penetrate the skin's protective layers, solubilize a variety of medications, and reduce systemic exposure. This exciting technology is not without its difficulties, though. Enhanced penetration: Antifungal drugs are delivered directly to the site of action by microemulsions, which storm the stratum corneum and maximize their efficacy.

Drug diversity: They dissolve a broad spectrum of antifungal drug, from hydrophilic to lipophilic, guaranteeing a focused attack on different fungus strains.

SUMMARY

In summary, microemulsions are a two-edged sword. Although they have enormous promise for transforming the battle against topical fungal infections, there are still many obstacles to overcome. We cannot fully utilize this technology until we conduct further research, work together, and plan strategically in order to make sure that whatever successes it achieves help people all across the world. The ultimate objective of this continuous struggle is not simply to win, but to win securely and sustainably, which calls for both inventiveness and pain taking attention to detail. This alternate interpretation emphasizes the advantages and disadvantages of microemulsion technology.

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