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Recent Advances in Emulgel-Based Transdermal Drug Delivery Systems for the Management of Fungal Infections

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Abstract

Emulgels, which feature dual release control (emulsion and gel), have emerged as one of the most intriguing topical drug delivery technologies. The physicochemical parameters of the generated emulgels were assessed, including colour, homogeneity, consistency, spreadability, pH value, rheological behaviour, drug content, drug release, and stability. They are often used as antiseptics, antifungal agents, skin emollients, and protective agents. The action of a topical preparation is determined by a number of parameters, including drug solubility, skin contact time, lipophilicity, and permeability. Gels are a relatively new kind of dosage form in which substantial volumes of aqueous or hydro-alcoholic liquid are entrapped inside a network of colloidal solid particles. When compared to traditional topical medication delivery formulations, gel formulations allow quicker drug release. Despite the numerous benefits of gels, one significant drawback is the difficulty in delivering hydrophobic medicines. Emulgels are created to circumvent these constraints. Emulgels are now being utilised to administer analgesics, anti-inflammatory, anti-fungal, anti-acne medicines, and a variety of cosmetic formulations, with a lot more potential.

Introduction

Emulgels (**Figure 1**) are a hybrid of an emulsion and a gel. Emulsions, either water in oil or oil in water, are gelled by combining with a gelling agent, and this emulsified gel serves as a better carrier for medications that are poorly water soluble or hydrophobic. The delivery of hydrophobic medicines is the main disadvantage of this gel, despite its numerous benefits. As a result, an emulsion-based strategy is being employed to circumvent this limitation, allowing even a hydrophobic medicinal moiety to benefit

from the special features of gels. In recent years, there has been a lot of interest in the use of new polymers as emulsifiers and thickeners. These compounds have a higher gelling capacity, which allows for the production of stable emulsions and creams. This works by raising the aqueous phase's viscosity while simultaneously lowering surface and interfacial tension. A traditional emulsion is transformed into an emulgel when a gelling ingredient is present in the water phase. These topical Emulgels are thixotropic, bio-friendly, water-soluble, greaseless, readily spreadable, emollient, easily removable, non-staining, have a longer shelf life, and have a clear and pleasing look [1].

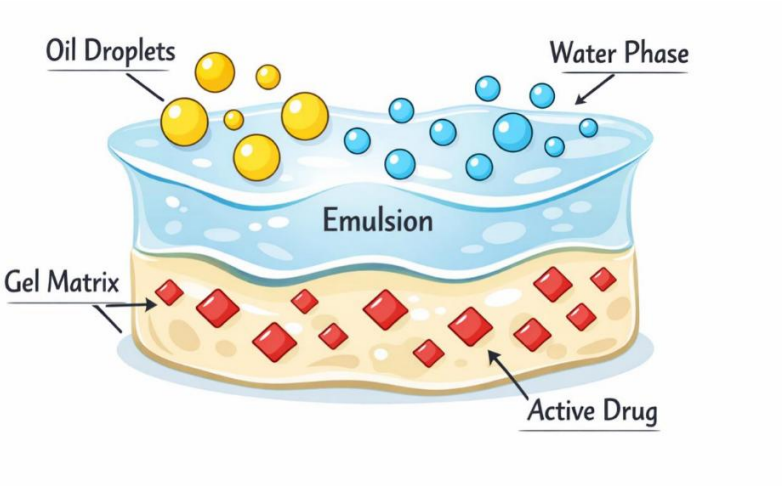

Figure 1. Emulgel.

Emulsion System

Emulsions are thermodynamically unstable two-phase systems made up of two or more immiscible liquids, one of which is distributed in the other liquid as minute droplets, causing the system to become unstable. The biphasic system is stabilized with the addition of an emulsifying agent. There are two types of emulsions: o/w and w/o, which are employed as drug delivery vehicles. Emulsifying compounds are used to stabilis emulsions. They have strong penetration and may be readily removed from the skin [2]. Based on the nature of distribution or size of droplets emulsions are of different types described as follows:

Macroemulsion

The most frequent form of emulsion is macroemulsion. This emulsion's particle size is about 400 nm, and macro emulsions may be seen under a microscope. We can build thermodynamically stable macro emulsions by utilising surface active compounds. The macro emulsion is either O/W or W/O depending on the manner of emulsification and the composition of the emulsifier. They are optically opaque, yet under a microscope, the individual droplets may be seen clearly. Macroemulsions are thermodynamically unstable, although surface active substances may help to stabilize them. Carbopol 940 was used as a gelling agent in the preparation of mefenamic acid emulgel, for example. The oil phase was liquid paraffin. As a penetration enhancer, menthe oil and clove oil were utilized. Then it was subjected to rheological tests, spreading coefficient tests, skin irritation tests, and in-vitro release tests, among other things [3].

Microemulsion

Microemulsions are optically clear and thermodynamically stable. This microemulsion is made up of monodispersed spherical droplets with diameters ranging from 20 to 200 nanometers. Microemulsions are made up of a specified proportion of oil, surfactant, cosurfactant, and water. The chemicals in microemulsion might help the medicine permeate faster by lowering the stratum corneum's diffusion barrier. However, because of their low viscosity, microemulsions have a limited retention capacity in the skin, which limits their use in the pharmaceutical business. To address this limitation, gelling agents such as Carbopol 940, xanthan gum, and carrageenan have been added to the microemulsion in order to generate a microemulsion-based gel with a viscosity acceptable for topical administration. Furthermore, a microemulsion-based gel limits medication absorption into the bloodstream and allows for greater drug accumulation in the skin for more effective action. For example, a vaginal gel based on clotrimazole microemulsion was made using Capryol 90 as the oil phase and Cremophor EL as the surfactant. As a gelling agent, Carbopol ETD 2020 is utilised [4].

Gel

The characteristics of the gel are halfway between those of liquids and solids. These gels appear to be wet and soft, as well as solid material. However, it is often misused to refer to any fluid system with a degree of stiffness. A gel is made up of a polymer that expands when exposed to fluid and perhaps within its structure. The quantity of fluid entrapped in the gel determines its stiffness. These are

capable of undergoing significant physical deformation, such as from solid to liquid [5].

Nanoemulgel

Nanoemulgel is the term used when nanoemulsion is mixed into a gel. Nanoemulsions are transparent (translucent) dispersions of oil and water that are stabilised by an interfacial coating of surfactant and cosurfactant molecules with a droplet size of less than 100 nm. In vitro and in vivo, nanoemulsion formulations have better transdermal and dermal delivery qualities. Many medications have better transdermal absorption in nanoemulsions than in traditional topical formulations like emulsions and gels. e.g. In the oil phase, carvedilol nanoemulgel was made using oleic acid and isopropyl myristate (3:1). Surfactant and cosurfactant were Tween 20 and Carbitol, respectively. As a gelling agent, Carbopol 934 was utilised [6].

Emulgel

Emulgel is a mixture of emulsion and gel, as the name suggests. Emulsions of water-in-oil and oil-in-water are both utilised to deliver medications to the skin. A traditional emulsion becomes an emulgel when the gelling ingredient is present in the water phase. They're also quite good at penetrating the skin. Thixotropic, greaseless, easily spreadable, readily removable, emollient, non-staining, water-soluble, extended shelf life, bio-friendly, translucent, and pleasant look are only a few of the benefits of emulgel for dermatological application.

Molecules enter the skin in one of three ways: via the intact stratum corneum, sweat ducts, or sebaceous follicle. More than 99 percent of the entire skin surface is accessible for percutaneous medication absorption on the stratum corneum's surface. Percutaneous absorption is limited by its ability to pass through this outermost layer. The creation of a concentration gradient, which provides the driving force for drug movement across the skin, the release of drug from the vehicle (partition coefficient), and drug diffusion through the layers of the skin are the primary phases in percutaneous absorption (diffusion coefficient) (**Figure 2**) [7].

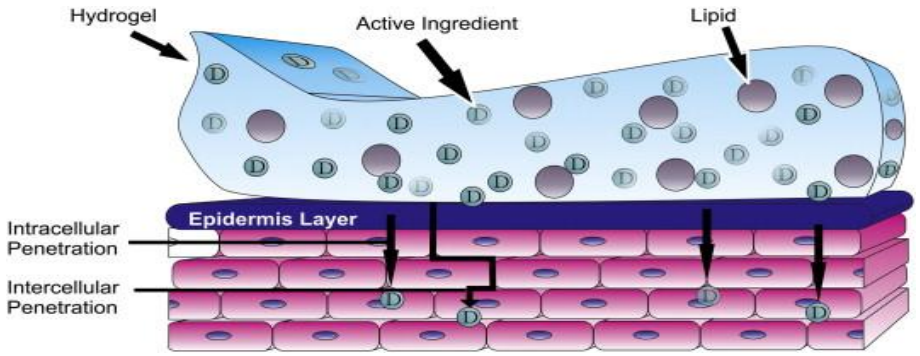

Figure 2. Mechanism of drug absorption.

Emulgel is made by combining an oil-in-water and a water-in-oil emulsion with gel. Lipophilic medications are delivered with oil in water, whereas hydrophobic pharmaceuticals are delivered with water in oil. Thixotropic, greaseless, easily spreadable, readily removable, emollient, non-staining, bio-friendly, attractive appearance, clear and aesthetically acceptable, with excellent skin penetration and a long shelf life, the emulgel has numerous benefits. The characteristics of the emulsion and gel formulations are different. However, the gels have certain drawbacks in terms of hydrophobic drug delivery. Emulgel helps to overcome this constraint. Classical emulsions may be turned to emulgels by using a gelling agent [8].

Human Skin

The skin is our body's biggest sense organ (**Figure 3**), with a surface area of around 2 m^2 and a pH of 4.0 to 5.6. Non-viable epidermis, viable epidermis, viable dermis, and subcutaneous connective tissue are the four layers of the skin.

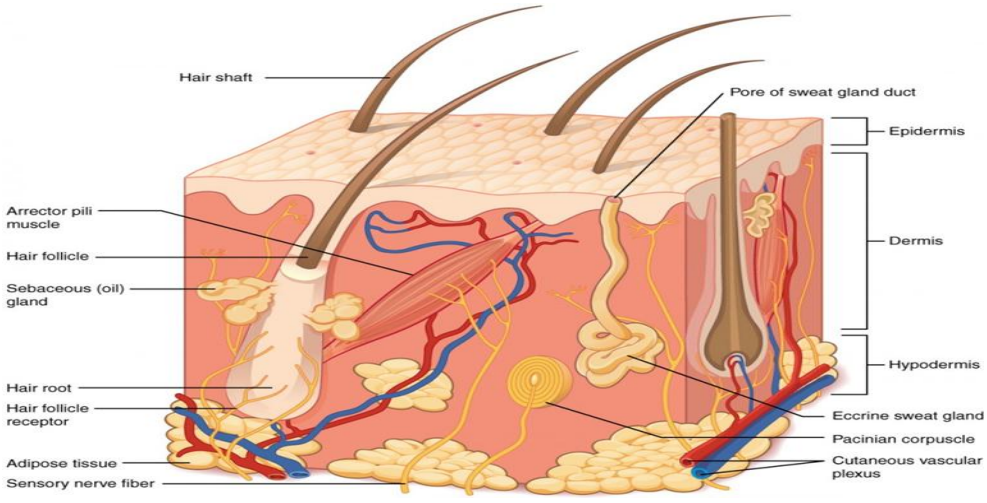

Figure 3. Structure of human skin.

Non- viable epidermis [stratum corneum]

It's the 10-20 cell thick outer layer of skin. The cells are 34-44 µm long, 25-36 µm wide, 0.5- 0.20 µm thick, and have a 750-1200 µm surface area.

Viable epidermis

It has a thickness of 10 µm to 50 µm and is located between the stratum corneum and the dermis. Tonofibrils aid in the merging of cells.

Dermis

It is a structural fibrin that is visible under the viable epidermis. The dermis has a thickness of 2000–3000 µm and comprises loose connective tissue.

Subcutaneous connective tissue

It's a real connective tissue, having a loose texture, fibrous connective tissue, blood vessels, and lymph vessels [9].

Topical Drug Delivery System

Topical medication delivery system (**Figure 4**) is a dosage form that is applied to the skin when other drug delivery methods have failed or for skin problems. The benefit of a topical medication delivery strategy is that it avoids first-pass metabolism. It also helps to avoid the risks and inconveniences associated with intravenous treatment. Topical formulations come in a variety of consistency options, including solid, semisolid, and liquid. In the administration of hydrophobic drugs, the topical delivery technique has failed. Many excipients are utilised in each formulation containing active components. To improve medication distribution, several formulations are sometimes blended; emulgel is an example of this. It's the result of combining emulsion with gel.

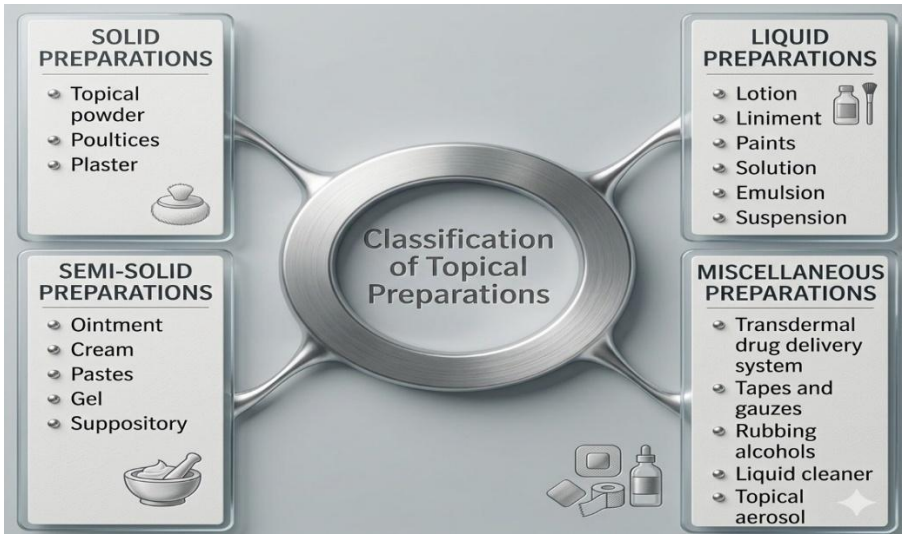

Figure 4. Classification of topical preparation.

There are two kinds of topical delivery products. There are two types of products: exterior and interior. External products are administered by spreading or spraying, whereas internal products are applied orally, vaginally, or rectally, as their names suggest. Solid preparation, liquid preparation, semi-solid preparation, and miscellaneous preparation are the four different types of topical preparation [10].

Factors To Be Considered When Choosing A Topical Preparation

- Vehicle effect; for example, an occlusive vehicle boosts penetration of the active component and effectiveness. The vehicle's own cooling, drying, emollient, or protecting properties are possible.
- Select the appropriate preparation for the lesions. For acute weepy dermatitis, for example, stay away from oily ointments.
- Choose a method of preparation that is appropriate for the location. (For example, for hairy places, a gel or lotion)
- Potential for irritation or hypersensitivity Ointments and w/o creams is often less irritating, while gels are. If you have an allergy to preservatives or emulsifiers, ointments are not for you [11].

Mechanisms Of Topical Drug Absorption

The three ways by which topical drugs are absorbed are transcellular, intercellular, and follicular. Passive diffusion allows the medications to permeate the stratum corneum. Diffusion and dissolution are the rate-limiting processes in this process. Topical medications are used for three different purposes: epidermal, endodermal, and transdermal formulations. The fastest and most direct path is through the transcellular mechanism. The most prevalent method is via intercellular mechanisms. Hair follicles and sweat glands are involved in the follicular process. Chemical (surfactant, water, solvents, etc.), physical (stripping, iontophoresis, ultrasonic, etc.), biochemical (peptides and metabolic inhibitors), and supersaturation augmentation all help to increase drug penetration [12].

TYPES OF EMULGELS

***I.* Based on the Type of API**

a. Herbal/poly-herbal:

i. Cosmetic Emulgel for skin care from field pumpkin.

ii. Anti-psoriatic Emulgel from babchi oil and Gum Guggle.

b. Allopathic:

Diclofenac diethyl Ammonium Emulgel (VOLTAREN®) manufactured by Novartis Ltd.

2. Based on the type of emulsion

Macroemulgel: Dispersed phase droplets with a diameter greater than 400 nm, manufactured using the High Energy and Low Energy Methods.

Microemulgel: Droplet size ranges from 1 to 100 nanometers. The Phase Inversion and Phase Titration Method are used to make it.

Nanoemulgel: The size of a droplet is less than 1 nm [13].

Advantages

- It obviates the need for first-pass metabolism.
- It is possible to prevent gastrointestinal incompatibility.
- The more detail of the site, the better.
- It is possible to increase patient compliance.
- Self-medication is number five.
- Using a medication with a short biological half-life and a small therapeutic window.
- The ability to quickly stop taking medicine if necessary.
- It is simple to use and implement.
- Drugs that are hydrophobic may be used.
- A larger loading capacity is preferable.
- More consistent than other t.d.d.s.
- The expense of preparation is modest.
- It is possible to produce a controlled release.
- There will be no intense sonication [14].

Disadvantages

- Dermatitis produces skin irritation when it comes into touch with it.
- Allergenic responses are the second kind of reaction.
- Some medications have a low permeability through the skin.
- Large-particle drugs are difficult to absorb via the skin.
- Bubbles might appear during the emulgel's creation [15].

Factors Affecting Topical Absorption Of Drug

Physiological factors:

- The thickness of the skin.
- The presence of lipids.
- The number of hair follicles in a given area.
- The number of sweat glands in the body.
- The pH of your skin.
- Blood circulation.

- Skin hydration.
- Skin inflammation.

Physicochemical factors:

- The coefficient of partition.
- The molecular mass (about 400 Daltons)
- The ionisation level (only unionised drugs gets absorbed well).
- Vehicles' impact [16].

Compositions Of Emulgel

Aqueous material

The aqueous phase of the emulsion is formed by this. Agents like as water and alcohol are often utilised.

Oils

The oily phase is formed by these agents. Mineral oils, in combination or alone with hard or soft paraffins, are commonly utilised for externally applied emulsions. Castor oils and non-biodegradable minerals that have a local laxative effect, as well as certain fixed vegetable oils (e.g., arachis, cottonseed, and maize oils) or fish liver oils, are used as nutritional supplements in oral formulations.

Emulsifier

Emulsifying agents are used to enhance emulsification during the manufacturing process and as a shelf life stability controller. Sorbitan monooleate (Span 80), Polyethylene glycol 40 stearate, Stearic acid, Polyoxyethylene sorbitan monooleate (Tween 80), and Sodium stearate are only a few examples.

Preservatives

Microbial assault is prevented by the use of preservatives. For example, methylparaben, propylparaben, benzalkonium chloride, benzyl alcohol, and benzoic acid are all examples of parabens. Butylated Hydroxy Toluene (BHT), Ascorbyl palmitate, Butylated hydroxyanisole (BHA), and other antioxidants are examples.

Humectant

The intended region will be humidified as a result of this. Glycerin, propylene gylcol, and other similar substances are examples.

Gelling agents

These are thickening agents that are also used to make any dose form more consistent. Carbopol 934, carbopol 940, HPMC, HPMC-2910, sodium CMC are some examples.

Permeation enhancers

These are substances that partition into skin components and interact with them to cause a transient and reversible increase in skin permeability. Non-irritating, non-toxic, and non-allergenic permeation enhancers should be used. These permeation enhancers should not bind to receptor sites and have no pharmacological function in the body. They

should look well on the skin and have a good 'feel' about them. Excipients and medications should be compatible with permeation enhancers [17].

Properties of penetration enhancers

- They should be non-toxic, irritant-free, and allergy-free.
- They should operate quickly, with the activity and duration of the impact being predictable and repeatable.
- They must have no pharmacological action in the body, which means they must not bind to receptor sites.
- The penetration enhancers should function in a one-way fashion, allowing therapeutic materials to enter the body while preventing endogenous material from being lost.
- The penetration enhancers should be suitable for incorporation into a variety of topical formulations, and hence compatible with excipients and medicines.
- They should look good on the skin and have a good 'feel' about them [18].

Mechanism of penetration enhancers

Penetration enhancers may work via one of three different mechanisms:

1. Disruption of the stratum corneum lipid's highly organised structure.
2. Interaction with a protein found in the intercellular space.
3. Improved drug, co-enhancer, or solvent partition into the stratum corneum.

The key to changing the polar route is to create a change in protein structure or solvent swelling. The fatty acid enhancers enhanced the fluidity of the stratum corneum's lipid-protein component. By modifying the multi-laminate route for penetration, certain enhancers function on both polar and non-polar pathways. Enhancers may improve drug diffusivity by interacting with skin proteins. The kind of enhancer used has a considerable influence on the product's design and development [19].

Preparation Of Emulgel

Emulgel is made by combining gel with emulsion (**Figure 5**). The emulsion and the gel are made separately and then combined. The aqueous phase and the oil phase are taken separately and combined together to make an emulsion. The gel is then created using a gelling agent. After producing the gel and emulsion, they are gently mixed together. Castor oil, clove oil, liquid paraffin, and other substances are employed as oil phases. The aqueous phase consists of water and alcohol. Tween 80 and water are used to make the

aqueous phase, while paraben and propylene glycol are used to make the oil phase. The medication is dissolved in ethanol, and the two phases are constantly mixed together. The polymers are then dissolved in water with a pH range of 6.0 to 6.5. To make emulgel, the emulsion and gel are prepared separately and then combined together [20].

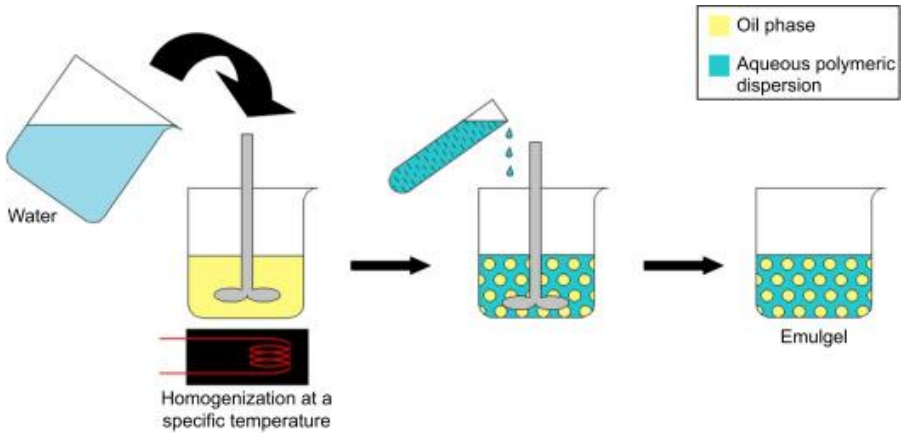

Figure 5. Emulgel development.

Flowchart Of Emulgel Preparation

It consists of three steps (**Figure 6**):

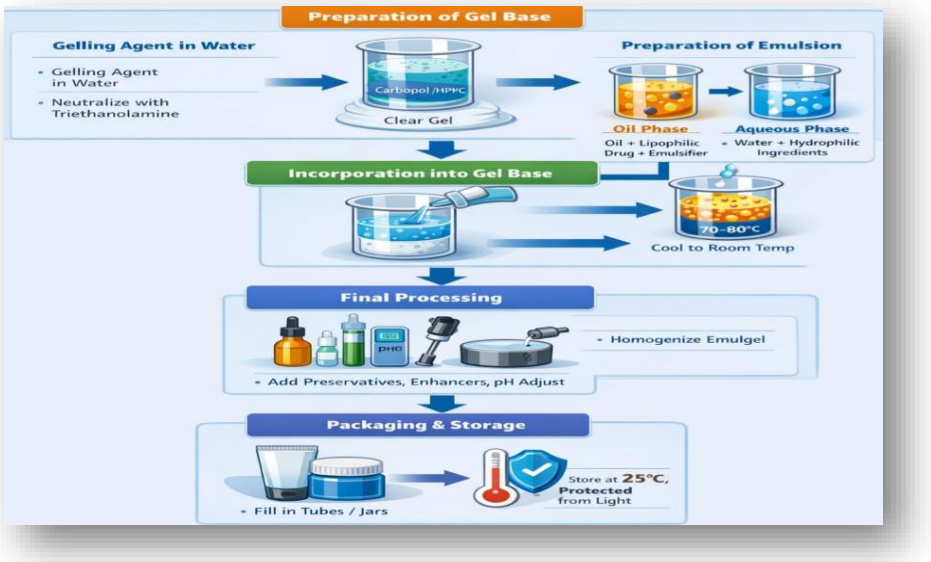

Figure 6. Emulgel preparation flowchart.

Step 1 - Formulation of Emulsion either O/W or W/O

Preparation Of Oil Phase Of Emulsion

The oil phase of the emulsion is made by dissolving an emulsifier, such as span 20, in the oil phase, which is similar to light liquid paraffin.

Preparation of aqueous phase

The aqueous phase is made by dissolving an emulsifier in purified water, such as tween 20.

Preparation of drug solution

In ethanol, the medication is dissolved. Depending on its solubility, the drug is mixed into either oil or an aqueous phase. Both the oily and aqueous phases were heated separately, and then the oily phases were added to the aqueous phase and stirred continuously until the mixture reached room temperature.

Step 2 - Formulation of gel base

The gel phase in the formulations is made by dispersing polymer in purified water using a mechanical shaker while constantly swirling at a moderate speed, then adjusting the pH to 6–6.5 using tri ethanolamine (TEA).

Step 3 - Incorporation of emulsion into gel base

To make the emulgel, add glutaraldehyde to the gel and emulsion in a 1:1 ratio throughout the mixing process [21].

Evaluation Of Emulgel

Physical examination

The homogeneity, colour, consistency, and phase separation of the prepared emulgel were all visually checked.

Determination of pH

The pH of the formulation is measured using a digital pH metre. The pH metre electrode was cleaned with distilled water before being dipped into the mixture to measure pH. This procedure was performed three times and the results were recorded.

Rheological studies

The viscosity of the formulation is measured using a cone and plate viscometer. At 25°C, the viscosity of various emulgel formulations is evaluated using spindle 52, which is coupled to a thermostatically controlled flowing water bath.

Stability studies

The emulgels are manufactured and packaged in aluminium collapsible tubes (5 g) before being submitted to three months of stability testing at 5°C, 25°C/60 percent RH, 30°C/65 percent RH, and 40°C/75 percent RH. Physical appearance, pH, rheological characteristics, drug content, and drug release

patterns were investigated in samples taken at 15-day intervals.

Fourier transforms infrared spectroscopy

The main goal of this study was to find a stable storage environment for the medicine in its solid state, as well as appropriate excipients for formulation.

In Vitro Drug Release

On a Diffusion cell with egg membrane, *in vitro* drug release experiments for produced Emulgel were conducted.

Globule size and distribution

Malvern Zetasizer is the one which determines them. To ascertain the value, the emulgel is dissolved in water, stirred, and placed into the device.

Centrifugation study

This procedure is used to determine the emulgel's stability. After a week of preparation, it is completed. The experiment was carried out in a minicentrifuge at 3000 rpm for 30 minutes.

Swelling index

1 g of produced topical emulgel is put on porous aluminum foil and then placed separately in a 50 mL beaker containing 10 mL 0.1 N NaOH to evaluate the swelling index. After that, samples were taken from beakers at various time intervals and placed in a dry area for a while before being reweighed.

Spreadability

Mutimer et al. (1956) proposed an equipment for determining spreadability, which was modified in the laboratory and employed in the investigation. It is made out of a wooden block with a pulley attached to one end. Spreadability is assessed using this approach based on the emulgel's 'Slip' and 'Drag' qualities. On this block is a ground glass slide. This ground slide has an excess of emulgel (approximately 2 g) under observation. The emulgel is then sandwiched between this slide and a second glass slide with the same dimensions as the fixed ground slide and a hook. For 5 minutes, a 1 kg weight is put on top of the two slides to release air and produce a consistent emulgel coating between the slides. The excess emulgel is scraped away from the edges.

$$S = M \times L / T$$

Where, S = Spreadability, M = Weight tied to upper slide, L = Length of glass slides, T = Time taken to separate the slides completely from each other.

Motic Digital Microscopy

The created Emulgel may be put on a glass slide at room temperature, and the surface morphology of the Emulgel can then be examined using Motic Digital Microscopy. A

Motic Digital Microscopy was used to analyse the morphology of Emulgel. The sample was put on a glass slide and examined at a magnification of 10X.

Zeta potential

Malvern zetasizer was used to assess the zeta potential of an improved emulsion and an optimised Emulgel formulation. The sample was dissolved in purified water and agitated to get a homogeneous dispersion, which was then analysed using a zetasizer.

Skin irritation test

A 0.5 g sample of the test material was then introduced beneath a double gauze layer to an area of skin measuring 1" × 1" (2.54 × 2.54 cm^2) at each location (two sites per rabbit). A rabbit's skin was treated with the Gellified Emulsion. The animals were put back in their cages. The Gellified emulsion is removed after a 24-hour exposure. To eliminate any leftover test article residue, the test locations were cleaned with tap water.

Microbiological assay

The ditch plate technique is employed in this procedure. This approach is used to assess bacteriostastic or fungiststic activity.

Drug content determination

Take 1 g of emulgel and mix it with 1 g of water. It should be mixed with a suitable solvent. To get a clear solution, filter it. Using a UV spectrophotometer, determine its absorbance. In the same solvent, a standard drug plot is created. By placing the value of absorbance on the same standard plot, concentration and drug content may be calculated [22].

Drug Content = (Concentration × Dilution Factor × Volume taken) × Conversion Factor

Packaging Of Emulgels

Emulgels are typically packaged in a membrane-sealed lacquered aluminum tube with an inner coating of phenoxy-epoxy based lacquer and a propylene screw cap, or in aluminum laminated tube with a moulded seal and a propylene screw cap.

Material for laminates tubes

Foil laminates

It creates a barrier against light, air, and moisture.

Plastic laminates

It possesses a chemically impervious barrier [23].

Marketed Preparations

Emulgel products have been created by a number of reputable firms throughout the world and are now on the market (**Table 1)** [24].

Table 1. List of marketed emulgel formulations.

S. No.	Brand Name	Active ingredient	Manufacturer	Uses
1.	Accent Gel	Aceclofenac	Intra Labs India Pvt. Ltd.	Anti-inflammatory
2.	Avindo gel	Azithromycin	Cosme Pharma Lab Ltd.	Anti-bacterial
3.	Cataflam Emulgel	Diclofenac Diethylammonium	Novartis	Anti-inflammatory
4.	Clina Gel	Clindamycin phosphate, Allantoin	Stiefel Pharma Ltd.	Anti-bacterial
5.	Cloben Gel	Clotrimazole, Betamethasone	Indoco Remedies	Anti-fungal
6.	Denacine Emulgel	Clindamycin phosphate	Beit Jala Pharmaceuticals	Anti-acne
7.	Dosanac Emulsion gel	Diclofenac	Siam Pharmaceuticals Ltd.	Anti-inflammatory
8.	Diclon Emulgel	Diclofenac Diethylammonium	Medpharma	Anti-inflammatory
9.	Excex Gel	Clindamycin, Adapalene	Zee Laboratories Ltd.	Anti-bacterial, Anti-acne
10.	Kojivit Gel	Kojic acid, Dipalmitate arbuti	Micro Gratia Pharma Ltd.	Sunscreen
11.	Miconaz-H Emulgel	Miconazole nitrate, Hydrocortisone	Medical Union Pharmaceuticals	Topical Corticosteroid, Anti-fungal
12.	Nadicin cream	Nadifloxacin	Psycho Remedies	Anti-bacterial
13.	Pernox Gel	Benzoyl peroxide	Cosme Remedies Ltd.	Anti-acne
14.	Topinate Gel	Clobetasol propionate	Systopic Pharma	Skin care

15.	Voltaren Emulgel	Diclofinac diethyl ammonium	Novartis Pharma Ltd.	Anti-inflammatory
16.	Voltarol Emulgel	Diclofenac Diethylammonium	Novartis	Anti-inflammatory
17.	Zorotene Gel	Tazarotene	Elder Pharmaceuticals	Total skin care

Anti-Fungal Perspectives of Emulgels

Globally, several researchers have developed Emulgel formulations that have pre-clinical perspectives (**Table 2**).

Table 2. Reported anti-fungal emulgel formulations.

S. No.	DRUG	GELLING BASE	ADVANTAGES	USES	REFERENCE
1.	Itraconazole	Xanthan gum, Guar gum	Enhancing the topical delivery	Treating various fungal infections	26
2.	Ketoconazole	Aqupec HV 505	Better pharmacodynamics	Treating *Microsporum gypseum* and *Candida albicans* infections	27
3.	Tolnaftate	Carbopol-940	Improved penetration and extended drug release	Treating *Candida albicans* infections	28
4.	Atorvastatin	Hydroxyethyl cellulose	Enhancing the topical delivery	Treating oral and vulvovaginal candidiasis	29
5.	Amphotericin B	Carbopol-934	Excellent means of delivery of drug	Treating dermal mycosis	30
6.	Terbinafine	HPMC E15	Controlled release with enhanced	Treating superficial fungal infections	31

			bioavailability and for drug targeting to affected sites		
7.	Chlorphenesin	HPMC K15	Highest drug release observed	Treating various fungal infections	32
8.	Fluconazole	Carbapol 940	Better stability and drug effectiveness	Treating various fungal infections	33
9.	Luliconazole	Carbapol 940	Solution for loading hydrophobic drugs in water soluble gel bases for long-term stability	Treating various fungal infections	34
10.	Clotrimazole	HPMC 2910	Highest drug release and highest antifungal activity	Treating *Candida albicans* infections	35

Discussion

A wide range of formulations are employed in topical drug delivery systems, including ointments, creams, lotions, and gels; however, each of these dosage forms presents specific limitations. Ointments are greasy and cosmetically less acceptable, creams may show phase separation or instability during storage, and gels are often unsuitable for incorporating hydrophobic drugs due to their aqueous nature. Emulgel technology has emerged as an advanced formulation strategy that effectively overcomes many of these drawbacks. By integrating an emulsion system into a gel base, emulgel combines the advantages of both dosage forms, resulting in improved stability, enhanced drug loading capacity, and better patient compliance.

The incorporation of an emulsion within a gel matrix forms a dual controlled-release system. In this structure, the emulsion droplets act as reservoirs for lipophilic drugs, while the gel network regulates drug diffusion and enhances viscosity. This combination minimizes common emulsion-related problems such as creaming, coalescence, cracking, and phase separation. The gel base stabilizes the dispersed droplets, thereby improving the overall physical

stability and shelf life of the formulation. Additionally, the non-greasy and easily spreadable nature of emulgel enhances patient acceptability and ensures uniform drug distribution over the skin surface.

The preparation of emulgel involves three primary steps: first, the preparation of the emulsion by separately heating and mixing the oil and aqueous phases with appropriate emulsifying agents; second, the preparation of the gel base using suitable gelling agents such as carbopol or HPMC; and third, the incorporation of the prepared emulsion into the gel base with continuous stirring to obtain a homogeneous product. Careful selection of ingredients, including oils, surfactants, gelling agents, preservatives, and penetration enhancers, is essential for achieving optimal performance.

Comprehensive evaluation of the formulation is necessary to ensure quality and therapeutic effectiveness. Approximately twenty-five evaluation parameters are commonly employed, including light microscopy for globule size analysis, spreadability testing, viscosity and rheological studies, pH determination, drug content analysis, and in-vitro drug release studies. Today, emulgels such as Miconaz-H emulgel, Isofen emulgel, and Diclon emulgel are widely used, particularly for anti-inflammatory and antifungal therapy, demonstrating the clinical relevance and effectiveness of this advanced topical delivery system.

Future Prospects

Recent advancements in emulgel technology have significantly improved its role as a novel drug delivery system for treating fungal infections. Conventional antifungal formulations such as creams and ointments often suffer from limitations including poor drug penetration, greasiness, instability, and reduced patient compliance. Emulgel overcomes these drawbacks by combining the solubilization capacity of emulsions with the stability and rheological advantages of gels. The development of nanoemulgels, incorporating nano-sized droplets, has enhanced drug solubility and permeation through the stratum corneum, resulting in improved therapeutic efficacy, especially for poorly water-soluble antifungal agents like clotrimazole and ketoconazole. Recent research also focuses on incorporating advanced carriers such as liposomes, solid lipid nanoparticles, and nanostructured lipid carriers within emulgel systems to achieve sustained and controlled drug release. The inclusion of penetration enhancers and bioadhesive polymers further improves

retention time and drug absorption at the infected site. Multifunctional emulgels combining antifungal and anti-inflammatory agents provide synergistic action, reducing both infection and associated inflammation.

Looking ahead, future prospects of emulgel technology are highly promising. Smart and stimuli-responsive emulgels, such as pH-sensitive or thermoresponsive systems, are being explored to enable site-specific and controlled drug release. The integration of natural bioactive compounds and biodegradable polymers aligns with the growing demand for safe and sustainable pharmaceutical formulations. Personalized topical therapy based on individual skin characteristics and infection severity may further optimize treatment outcomes. Additionally, emulgel systems hold potential for expanding into transdermal and mucosal antifungal applications. With continued innovation, clinical validation, and scalable manufacturing approaches, emulgel formulations are expected to play a pivotal role in advancing effective, patient-friendly management of fungal infections.

Conclusion

Following a review of the research, it was determined that emulgels are the most convenient, better, and effective delivery mechanism. It delivers and lacks oily bases due to its non-greasy, gel-like nature, and it provides greater drug release than other topical drug delivery systems. When emulsion is included into a gel, it becomes a dual control release system, and problems such as phase separation and emulsion creaming are overcome, as well as the gel's stability. Emulgels containing particular medications have been discovered to be beneficial in the treatment of several topical illnesses, and they are emerging as a viable drug delivery mechanism in dermatology. In the future, emulgel will be used to deliver hydrophobic medications to the skin. Many of the medications that are useful in the treatment of skin problems are hydrophobic. Such medications may be given as an emulgel, in which they are absorbed into the emulsion's oil phase and mixed with the gel. Emulgels, a relatively new method of topical drug administration, are also useful for integrating hydrophobic medications and are an excellent alternative for combining both hydrophilic and hydrophobic pharmaceuticals. Topical medication delivery will be widely employed in the next years to improve patient compliance, and emulgels, with their non-greasy, gel-like properties and relatively high drug release rates, may be frequently used as innovative

topical drug delivery formulations in the future.

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