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Review Article

Topical Emulgels: A Hybrid System for Improved Dermal and Transdermal Drug Delivery

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Abstract

The goal of this study was to formulate an emulgel formulation for topical administration that would prevent hepatic first-pass metabolism, increase emulsion stability, lower dosage requirements, and increase residence time. An emulgel is a hybrid dosage form that combines the properties of both emulsions and gels, which are particularly significant for the delivery of hydrophobic substances; it enhances drug penetration through the epidermal barrier and promotes effective skin diffusion (especially for medications with low water solubility). This article looks at the advantages, choice of components, preparation methods, development, and characterization of emulgel in drug delivery, all of which are based on the latest research. The pH, viscosity, particle size, zeta potential, drug content, stability study, skin irritation test, and other properties of the prepared formulation are evaluated.

Keywords: Emulgel, hybrid dosage form, hydrophobic substances, future aspect

1. Introduction:

For the treatment of chronic illness, the oral route is the most favored method of drug delivery. However, high lipophilicity makes it difficult to administer nearly 50% of medications orally. Almost 40% of novel medication candidates have poor water solubility, which frequently results in insufficient dosage proportionality and inadequate oral absorption.[1] When it comes to treating skin conditions, the topical method has many advantages over the oral route and a great deal of promise for effective medication administration.[2] Topical drug delivery technique that can be applied topically via the skin, rectal, vaginal, and ocular channels.[3]The topical medications are used to treat localized skin infections or in areas where alternative drug delivery methods are ineffective. In this, the medication is explored on the body's surface in an absorbable format.[4] They have the ability to transport the medication to the site of action smoothly and continuously without causing systemic side effects.[5] And topical treatments have higher bioavailability because they avoid hepatic first-pass metabolism and are administered over longer periods of time. Another benefit of the topical drug delivery method is that it avoids the dangers and hassles of intravenous therapy as well as the various circumstances of absorption, such as pH variations, the presence of enzymes, and gastric emptying time.[6] Topical dosage forms, such as ointments, creams, lotions, gels, and so on, have a number of drawbacks, including stickiness, stability issues, and reduced spreadability. They also result in allergic reactions, poor permeability, absorption, and irritation.[7,8] One of the main drawbacks of gels is the difficulty of delivering hydrophobic medications. To overcome this problem, emulgels are made; so that hydrophobic medications can also enjoy the special qualities of gels.[9] Emulgel-based medications have been found to be the most practical and cost-effective topical treatment options for a variety of skin conditions.[10]

1.2. Emulgel: An emulgel is a hybrid dosage form that combines the properties of both emulsions and gels. Emulsions are colloidal dispersions of immiscible

liquids, and gels are semisolid systems consisting of a network of solid particles dispersed in a liquid.[51] Emulgel mixtures have been made for a number of pharmacological types, such as antiviral, antifungal, anti-inflammatory, medications for plaque, local anesthetics, wound healing medications, and antimicrobials.[11] Emulgels are emulsions of the water-in-oil or oil-in-water type that are gelled by mixing with a gelling agent. The emulsion also functions as a controlled-release drug delivery system in which drug particles trapped in the internal phase go through the external phase to the skin and slowly get absorbed; the drug reaches the external phase of the skin in a controlled manner through the internal phases that act as a reservoir of the drug; and the gel captures small drug particles and provides its release in a controlled manner because of a cross linked network.[12] Encapsulating active compounds, increasing their bioavailability, and inhibiting degradation all depend on nanoemulsion.[13]

Figure 1: Marketed Emulgel Product[51]

1.3 Advantages: Advantages of Emulgel are as follows:-

- Water/oil/water emulsions can be used to quickly integrate hydrophobic drugs into the gel base.
- Emulgel enhanced stability and load capacity.
- It is easy to make and also a low-cost formulation.
- Avoid the first-pass metabolism.
- Also avoid gastrointestinal incompatibility.
- Delivery of a drug at the site of action.
- Enhanced patient adherence.
- Enhanced patient acceptability and appropriateness of self-medication.[16]

1.4 Disadvantages: Disadvantages of Emulgel are as follows:-

- Large-particle drugs are difficult for skin to absorb**.**
- Some medications have poor skin penetration.
- Skin irritation from contact dermatitis.
- During the emulgel formulation, bubbles may form.[29]

1.5 Rational: There are various preparations on the market that can either pharmacologically restore the skin's essential function or change a procedure to the tissue underneath. Lotions, ointments, and cream formulations have a number of disadvantages, such as being sticky, having a low spreading coefficient, and experiencing stability problems. Due to general restrictions in the semisolid preparations, only translucent gels are used in medicinal and cosmetic preparations.[14] In a current situation, more than 40% of therapeutically active compounds are hydrophobic, and handling hydrophobic drugs is a major limitation of gel. Emulsion-based gel is an approach that can successfully incorporate and deliver a hydrophobic therapeutic moiety with improved solubility and penetrability through the skin; additionally, the emulgel can significantly improve the pharmacological action and reduce the dose of drug due to significant penetration.[15]

1.6 Type: Types of emulgel are given in Table 1.

Table 1: Different types of emulgel with their examples

S. N.	Type	Properties	Example	Ref
1.	Macro-emulsion Gel	The most common type of emulgel, where the particle size of droplets of emulsion is more than 400 nm. They are thermodynamically unstable but can be stabilized with surface-active agents. The droplets are imperceptible to the naked eye, but the individual droplets can be easily observed under a microscope.	Mefenamic acid emulgel was prepared using Carbopol 940 as a gelling agent; liquid paraffin as an oil phase and mentha oil and clove oil as penetration enhancers; it was then evaluated for rheological studies, spreading coefficient studies, skin irritation tests, in vitro release, etc.	17,21
2.	Nano-emulgel	The size ranging from 1 nm to 100 nm, nanoemulsions are stable oil-in-water dispersion that appear translucent. They show improved transport capabilities and superior transdermal penetration over conventional emulsions & gels.	Oleic acid and isopropyl myristate (3:1) were used as the oil phase to create carvedilol nanoemulgel. Carbitol and Tween 20 were utilized as co-surfactants and surfactants, respectively. The gelling agent employed was Carbopol 934.	22,18
3.	Microemulsion	Microemulsions are stable, clear mixtures of oil in water that are held together by surfactants. The droplet sizes range from 10 to 100 nm. They improve drug penetration by lowering the stratum corneum diffusion barrier. Their low viscosity restricts the skin retention, which is a present problem of medications. In order to overcome this, gelling agents such as carrageenan, xanthan gum, and carbopol 940 are added to microemulsion-based gels to boost viscosity for topical applications.	Clotrimazole microemulsion based vaginal gel employing Capryol 90 and Cremophor EL was prepared, these gels aid in concentrating the medication in the skin while reducing systemic absorption	22,19

1.7 Mechanism of drug absorption of emulgel: Emulgel enhances topical drug absorption through follicular, intercellular, and transcellular pathways. Its dual-control release technique makes use of both gel and emulsion properties. The subcutaneous layer, which lies beneath the dermis and epidermis, is filled with blood vessels. The most well-liked path is the pilosebaceous pathway, where penetration takes place via the matrix between cells. Drug penetration can be enhanced by organic solvents such as surfactants, DMSO, and propylene glycol. The solubility, partitioning, and fluidization of the crystalline structure are all improved by permeation enhancers. Lipid content, skin thickness, sweat gland density, hair follicle density, skin pH, skin temperature, moisture, inflammation, and blood flow are all factors that affect drug absorption. While thicker skin layers may lead to quicker absorption, less lipid content promotes percutaneous penetration. Faster drug diffusion and systemic uptake are facilitated by increased blood flow.[20]

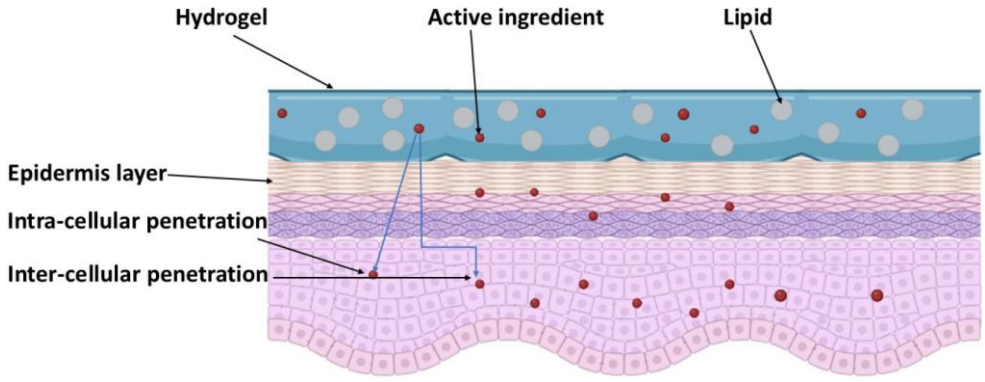

Figure 2: Mechanism of drug absorption from emulgel.[20]

2. Material:

The composition of the emulgel formulation is as follow:

2.1 Active Pharmaceutical Ingredient

The chosen active pharmaceutical ingredient (API) is determined by the particular physicochemical properties of the medication as well as the intended therapeutic results. For lipophilic medications with low water solubility, formulations such as emulgels are particularly beneficial.[23]

2.2 Aqueous Material

The aqueous phase is formed by using aqueous materials. Alcohol and water are commonly used to prepare the aqueous phase.[24]

2.3 Oil Phase

The selection and quantity of oil in a nanoemulgel significantly influence its application and effectiveness. The chosen lipid component, or oil phase, and its amount play crucial roles in determining the permeability, stability, and viscosity of the resulting nano-emulsion. Unless the oil phase acts as an active ingredient, it is generally made up of lipids that can be either naturally sourced or synthetically produced for use in pharmaceutical and cosmetic products. Lipids can vary in texture, ranging from high molecular weight solids to liquids. The stability of an emulsion is heavily reliant on the hydrophobicity of the oil; oils with lower hydrophobicity have been shown to enhance emulsification while also impacting the solubility of lipophilic substances.[25]

Table 2: List of oil used in emulgel[30]

Sr. No.	Oil
1.	Light Liquid Paraffin
2.	Isopropyl myristate
3.	Isopropyl stearate
4.	Isopropyl palmitate
5.	Propylene glycol
6.	Liquid Paraffin
7.	Caprylic/Capric triglyceride
8.	Olive oil
9.	Castor oil

2.4 Emulsifier

Surface-active agents are selected on the basis of their ability to emulsify, route of administration, and consequently how toxic they are. Each surfactant's HLB number indicates the relative amounts of its hydrophilic and lipophilic portions. The majority of a surfactant with a high number is hydrophilic or polar, while the majority of a surfactant with a low number is lipophilic or non-polar. Emulsifying chemicals reduces the interfacial tension between the disperse and continuous phases to ensure emulsion stability throughout the product's shelf life and to encourage true emulsification during manufacturing. It takes trial and error to choose the right emulsifying agent and its appropriate concentration.[26]

Table 3: List of emulsifiers used in emulgel[30]

Sr. No.	Emulsifiers	Type
1.	Tween 80	Non-ionic
2.	Combination of Tween 80 & Span 80	Non-ionic
3.	Combination of Tween 60 & Span 60	Non-ionic
4.	Combination of Tween 20 & Span 20	Non-ionic
5.	Soybean protein isolate	Amphiphilic
6.	Sodium Stearate	Anionic

2.5 Penetration Enhancers

These agents enhance the drug's ability to penetrate the skin. They facilitate the absorption of medications through the skin by temporarily disrupting the well-organized structure of the stratum corneum skin barrier, fluidizing the lipid pathways among corneocytes, modifying how the drug interacts with skin structures, or improving its delivery into the skin.[27] Penetration enhancers help to absorb the drug into the skin.[28]

2.5.1 Mechanism of penetration enhancers:-

Penetration enhancers can operate through one of three mechanisms.

- Alteration of the well-organized arrangement of the lipids in the stratum corneum.
- Engagement with a protein located in the extracellular space.
- Improvement of the partitioning of the drug, co-enhancer, or solvent into the stratum corneum.[31]

Table 4: List of penetration enhancers used in emulgel[15]

Sr. No.	Penetration Enhancers
1.	Oleic acid
2.	Lecithin
3.	Isopropyl Myristate
4.	Linoleic acid
5.	Clove oil
6.	Menthol
7.	Eucalyptus oil

2.6 Gelling Agent

Gelling agents are either dissolved or dispersed in an appropriate medium, forming a loosely cohesive three-dimensional structural network that exhibits a considerable degree of cross-linking, whether physical or chemical, to create semisolid systems. These agents are primarily utilized at concentrations ranging from 0.5% to 10% in semisolid preparations. In emulgel formulations, gelling agents are categorized into natural, synthetic, and semi-synthetic based on their source.[32]

Table 5: List of gelling agents used in emulgel.[30]

Sr. No.	Gelling agents	Type
1.	Carbopol 934	Synthetic
2.	Carbopol 940	Synthetic
3.	Carbopol 980	Synthetic
4.	Poloxamer 407	Synthetic
5.	Sepineo-P600	Synthetic
6.	HPMC	Semi- Synthetic
7.	HEC(hydroxyethyl cellulose)	Semi- Synthetic
8.	Na CMC	Semi- Synthetic
9.	Guar gum	Natural
10.	Xanthan gum	Natural
11.	Whey protein isolate	Natural
12.	Soybean protein isolate	Natural
13.	Alginate	Natural
14.	Combination of carbopol 934 and 940	Synthetic
15.	Combination of carbopol 934 or 940 and HPMC	Synthetic & semi-synthetic
16.	Combination of carbomer interpolymer type A and Xanthan	Synthetic & natural
17.	Combination of xanthan gum and chitosan	Natural

2.7 Preservatives

Preservatives are employed to extend the longevity of products by inhibiting the proliferation of bacteria, filamentous fungi, and yeast, which can lead to illnesses or merely generate oxidative and/or hydrolytic enzymes that can induce physical, chemical, and pharmacological alterations, thus compromising the quality of the end product.[33]

Table 6: List of preservatives used in emulgel.[30]

Sr. No.	Preservatives
1.	Propyl Paraben
2.	Combination of methyl paraben & propyl paraben
3.	Phenoxyethanol
4.	Methyl Paraben
5.	Benzalkonium chloride

3. Method of preparation Emulgel[34]

The particle sizes of nanoemulgel, which range from 10 to 100 nm, enable effective and quick drug delivery or penetration. By reducing surface and interfacial tension in the emulsion and improving transport characteristics, the gelling phase raises the viscosity of the nanoemulgel and stabilizes the formulation. The preparation process is demonstrated as follow:-

The oil and aqueous phase are prepared separately.

↓

The oil phase is added to the aqueous phase by stirring on a magnetic stirrer and allowed to cool.

↓

Next, the emulsification and homogenization process produces a nanoemulsion.

↓

A gelling agent is dispersed in purified water and stirred continuously at a gentle speed with a magnetic stirrer to establish the gel phase in the formulation.

↓

Then the nanoemulsion is combined with the gel bases by gently swirling.

↓

Emulgel is prepared.

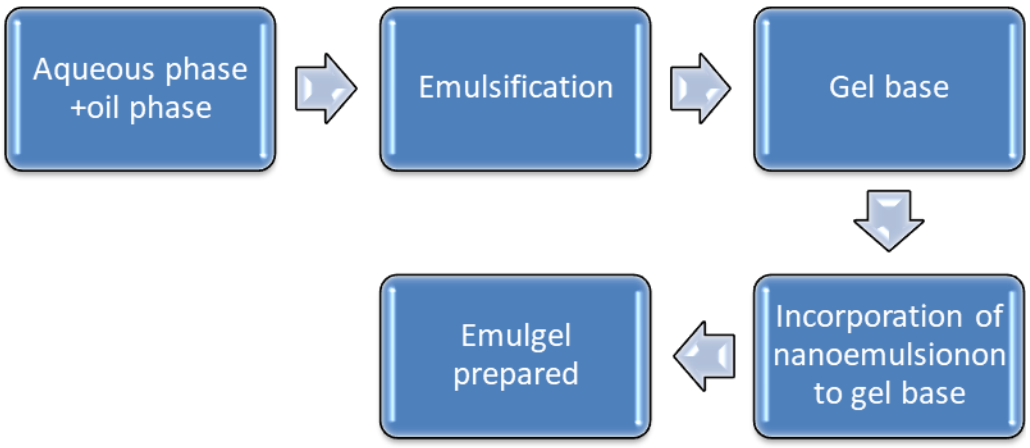

Figure3: Steps in the process of emulgel formulation.

4. Marketed Formulation of Emulgel[20, 35]

Table 7: List of marketed products of emulgel preparation.

S. N.	Brand Name	Manufacturer	Active ingredients	Uses
1.	Diclobar emulgel	Barakat Pharma	Diclofenac diethyl amine	Anti-inflammatory & analgesic
2.	Diclomax emulgel	Torrent Pharma	Diclofenac sodium	Anti-inflammatory
3.	Levorag emulgel	THD Ltd.	Hibiscus, licorice	Emollient
4.	Voltarol 1.16% emulgel	Haleon Consumer Healthcare	Diclofenac sodium	Anti-inflammatory
5.	Cataflam emulgel	Novartis India Ltd.	Diclofenac diethyl ammonium	NSAIDs
6.	Accent gel	Zee Laboratories	Aceclofenac	Anti-inflammatory
7.	Avindo gel	Cosme Pharma Lab	Azithromycin	NSAIDs
8.	Cloben gel	Indoco Remedies	Clotrimazole, betamethasone	Antifungal
9.	Nadicin cream	Psycho Remedies	Nadifloxacin	Fluroquinolone antibiotics
10	Clinagel	Glaxosmithkline Pharmaceuticals Ltd.	Clindamycin phosphate, allantoin	Antibiotic
11.	Voltaren emulgel	GlaxoSmithKline Consumer Healthcare	Diclofenac-diethyl-ammonium	Anti-inflammatory
12.	Miconaz-H-emulgel, Miconazole nitrate, hydrocortisone	Medical Union Pharmaceuticals	Miconazole nitrate, hydrocortisone	Antifungal
13.	Excex gel	Zee Laboratories	Clindamycin, adapalene	Antibiotics
14.	Pernox gel	Eris Oaknet Healthcare Pvt. Ltd.	Benzoyl peroxide	Antimicrobial
15.	Lupigyl gel	Lupin Pharma	Metronidazole, clindamycin	Antibiotics
16.	Topinate gel	Systopic Lab	Clobetasol propionate	Inflammatory & allergic
17.	Kojivit gel	Micro Labs Ltd.	Kojic acid, Dipalmitate arbuti	Skin pigmentation concerns
18.	Zorotene gel	Glenmark Pharmaceuticals Ltd.	Tazarotene	Treat acne, Sun damage
19.	Reumadep emulgel	Erbozeta Energia Verde	Arnica, Ashwagandha, myrrh, ginger, rosemary, cloves, mint	Anti-inflammatory & analgesic
20.	Meloxic emulgel	Provet	Meloxicam	NSIADs
21.	Benzolait Az emulgel	Rordermal	Benzoyl peroxide 10%	Treat acne-prone skin
22.	Coolnac gel emulgel 1%	Chumchon	Diclofenac diethyl ammonium	Anti-inflammatory & analgesic(NSAIDs)

5. Characterization of Emulgel:

The therapeutic activity of pharmaceutical products depends on their quality and consistency. A topical product's quality can be evaluated through several standard tests, such water content uniformity, microbial limits, pH, particle size and sterility. Zeta potential, PDI, spreadability, in vitro release, bio-adhesion, skin irritation, permeability tests, and other tests are also used to characterize nano-emulgel because it contains nano-sized globules.[36]

5.1 Physical Examination

The color, homogeneity, consistency, and phase separation of the prepared emulgel formulations are visually examined.[37]

5.2 Determination of pH

The decision to use a virtual pH meter was based on the pH value of the preparation. After rinsing the pH meter's electrode with distilled water, the preparation is submerged to measure the pH. This procedure is repeated three times.[38]

5.3 Rheological Studies

Rheological behavior is an important factor for emulgels due to their thinning tendency, which generates a thin layer on the skin surface, and improved permeability. The viscosity of the different emulgel formulations is determined at 25 °C using a cone and plate viscometer with spindle 52 and connected to a thermostatically controlled circulating water bath.[39]

5.4 Spreadability

Spreadability is influenced by equipment proposed by Mutimer et al (1956), which is appropriately altered in the lab and utilized for the research. It is made up of a wooden block, which is supported by a pulley at one end. Using this approach, spreadability is evaluated based on the "slip" and "drag" properties of emulgels. A frosted glass slide is secured in this position. An overabundance of emulgel (approximately 2 gm) under study is placed on the ground slide. The emulgel is then positioned between this slide and another glass slide that is equipped with a hook and has the dimensions of a fixed ground slide. To remove air and create a consistent layer of emulgel between the two slides, a 1 kg weight is placed on top of them for five minutes. The excess emulgel is scraped off edges. After that, an 80 gm pull is applied to the top plate. The time (in seconds) needed for the top slide to travel 7.5 cm with the aid of a string fastened to the hook should be recorded. Better spreadability is indicated by a shorter interval. The formula was used to determine spreadability:

$$S = M.L/T$$

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.[40]

5.5 Globule size and its distribution in emulgel

The Malvern zeta sizer determines the size and distribution of globules. To achieve a uniform dispersion, a 1 g sample is dissolved in purified water and shaken. The sample was injected into Zeta Sizer photocell. The distribution and mean globule diameter are found.[41]

5.6 Swelling Index

The swelling index was calculated by weighing 1 gram of prepared topical emulgel on porous aluminum foil and depositing it separately, undisturbed, in a glass beaker with a 50 ml capacity and 10 ml of 0.1N NaOH. After that, the samples are taken out of the beakers at different intervals and left to dry for a while before being weighed again. The following formula was used to determine the swelling index:

$$SW\% = [Wt-Wo/Wo]*100$$

Where,

SW% = Equilibrium percent swelling

Wt = Swollen weight emulgel after time t

Wo = Initial weight of emulgel at time zero.[42]

5.7 Skin Irritation Test

A double layer of gauze covering an area roughly 2.54*2.54cm^2 (1 inch * 1 inch) was used to apply a 0.5 gram sample of the test article to each site (two sites per rabbit). The rabbit's skin was coated with gelled emulsion. The animals went back to their cages. The gelled emulsion is removed after being exposed for a full day. All traces of the test item were eliminated by cleaning the test sites with tap water. If no irritation occurs, then the test is passed. If the skin irritation symptom occurs in more than 2 rabbits, the study should be repeated.[43]

5.8 Stability Studies

The emulgel was packed in aluminum collapsible tubes and tested for three months at 50 °C, 250 °C/60 percent relative humidity, 300 °C/65 percent relative humidity, and 400 °C/75 percent relative humidity. Each month, samples are taken and evaluated according to ICH requirements for physical appearance, pH, rheological properties, drug content, and drug release profile.[42]

5.9 Extrudability Study

Measuring the force needed to extrude the material from the tube is a common empirical test. The technique is used to determine the applied shear in the area of the rheogram where the shear rate exceeds the yield value and results in plug flow. The quantity in percentage of emulgel and emulgel extruded from lacquered aluminum collapsible tube upon application of weight in grams required to extrude at least 0.5 cm ribbon of emulgel in 10 seconds is the method used to evaluate emulgel formulation for extrudability. Extrudability is better when more material is extruded. Each formulation's extrudability is measured in triplicate, and

the average results are shown.[44] The extrudability is then calculated by using the following formula:

Extrudability= Applied weight to extrude emulgel from tube (in gram) / Area (in cm^2)

5.10 In-vitro Release Test

Drug release from the dosage form is linked to the API's efficacy and safety. The FDA states that IVRT studies for semi-solid dosage forms are carried out using either an immersion cell or a vertical diffusion cell, which consists of receptor and donor chambers divided by a receptor membrane; the donor chamber contains the dosage form sample, while the receptor chamber contains the receptor media, which can be a buffer or hydro-alcoholic solution, chosen based on the solubility, sink condition, and stability of the API. The skin-like receptor membrane is selected based on the effective pore size, high permeability, and expected inertness towards the API. If necessary, the receptor membrane should be saturated with release media. The temperature of the media should be maintained around 32°C±1°C for topical administering products; for products intended for mucosal membranes the temperature should be 37°C±1°C. The receptor media is stirred using a magnetic stirrer coated with Teflon. The cell body of the immersion cell model serves as a reservoir. To prevent dosage from leakage, the cell body is sealed with a leakproof seal (retaining ring cap) and covered with a membrane. The top opening of the retaining ring cap should be adjusted so that the membrane is in contact with the dosage form on the bottom and the release media on the top. The immersion cell is placed in a flat-bottomed dissolution vessel with a typical volume of 150-200 ml, and the entire setup is utilized in conjunction with the USP-2 apparatus. The media is stirred or agitated using a tiny spin paddle.[45, 46]

5.11 Microbiological Assay

The ditch plate method was applied. It is a method for assessing a compound's bacteriostatic or fungistatic activity. It is mostly used for semisolid formulations. Sabouraud's agar dried plates that had previously been prepared were utilized. A ditch cut in the plate is filled with three grams of the gelled emulsion. From the ditch to the plate's edge, freshly made culture loops are streaked across the agar at a right angle. Following an 18-24 hour incubation period at 25°C, the fungal growth was monitored, and the percentage inhibition was calculated as follows:

$$\% \text{ inhibition} = L2/L1*100$$

Where, L1= total length of the streaked culture

L2 = length of inhibition.[40]

5.12 Drug Content Determination

Take one gram of emulgel. In the appropriate solvent, mix it. To get a clear solution, filter it. Use a UV spectrophotometer to find its absorbance. The same solvent is used to prepare a standard drug plot. By entering the absorbance value into the standard plot equation, concentration and drug content can be ascertained using the same standard plot.[47]

Drug content = (concentration * dilution factor * volume taken) * conversion factor

5.13 Ex vivo measurement of the bio-adhesive strength of an emulgel (Shaved mouse skin)

Bioadhesive strength was measured using a modified technique. After chopping the fresh skin, wash it with 0.1N NaOH. Two sections of skin were affixed independently to two slides, one to the scales on the right and the other to a piece of wood. By adding weight to the left pan, the left and right pans were brought into balance. One gram of topical emulgel is sandwiched between these two hairless skin preparations. The two skin pieces are then positioned by removing extra weight from the left cup and applying pressure to eliminate any remaining air. For five minutes, the scale is kept in this position. At a rate of 200 mg per minute, the mass is gradually added to the left pan until the patch separates from the surface of the skin. The bioadhesive strength was determined by the mass (force in grams) needed to separate the emulgel from the skin's surface.[43]

Bioadhesive strength = required weight (g) / surface area (cm^2)

5.14 Syneresis Measurement

When the gel is at rest, it shrinks, and a small amount of liquid (known as syneresis) is expelled out. This can be measured using centrifuge tubes in a special device.[49]

Syneresis (%) = liquid separated from emulgel / total mass of emulgel before centrifugation *100

5.15 Drug Release Kinetic Study

In order to describe the appropriate release model, kinetic analysis of the drug release was carried out by fitting the release data to the various release models listed below:

5.15.1 Zero-order equation:

$$Q = k^0 t$$

Where, Q = amount of drug released at time t

k^0 = Zero-order release rate.

5.15.2 First-order equation:

$$\ln (100 - Q) = \ln 100 - K_1 t$$

Where, Q = percentage of drug release at time t

k_1 = first-order release rate constant.

5.15.3 Higuchi's equation:

$$Q = k_2 \sqrt{t}$$

Where, Q = percent of drug release at time t

K_2 = diffusion rate constant.[50]

5.16 Ex-vivo skin permeation and retention studies

Albino rats weighing 200-250 g and aged 10-12 weeks were used. The removed skin was wrapped in aluminum foil, and the skin's dermal side was carefully peeled off to check for any remaining fat and/or tissue beneath the skin. After that, the skin was carefully examined under a magnifying glass to ensure that the specimens had no transdermal penetration research. Fresh skin was used in every experiment after being cleaned with physiological buffer saline. The Keshary-Chien cell was used to investigate the ex vivo skin penetration of drugs from various formulations. The diffusion cell's effective permeation area was 9.8 cm^2, and the receptor compartment had a volume of 37.5 ml. Albino rat skin was firmly sandwiched between the donor and receptor compartments, with the donor compartment containing an epidermis site. The donor compartment was constantly stirred and kept at 37±1 °C. The rat skin's epidermal surface was treated with the emulgel formulation. To guarantee sink condition, 3.0 ml of aliquots were taken out and replaced with an equal volume of new receptor compartment solvent at prearranged intervals of 24 hours (0.5, 1, 2, 4, 6, 8, and 24 hours). At every sampling location, the cumulative percentage of medication that permeated the skin was determined.

The amount of drug that remains on the skin's epidermal surface after subtraction and the amount of free drug content in the receptor compartment. The amount of drug content in the skin was determined by the formulation's initial drug content. The permeation characteristics of the marketed emulgel and ex-vivo permeation study were compared. Every calculation was done in triplicate, and ANOVA was used to compare the data.[12]

6. Packaging of Emulgel

Emulgels are typically packaged in membrane-sealed lacquered aluminum tubes that have an inner layer of phenoxy-enoxy-based lacquer and are capped with a propylene screw cap, or they can be in aluminum laminated tubes sealed with a molded closure and also have a propylene screw cap.

Material used for laminate tube includes:

1. Foil laminates

These offer barriers against light, air, and moisture.

2. All-plastic laminates

These feature a barrier that resists chemicals.

7. Future Prospective

The ongoing research in emulgel formulations is focused on optimizing compositions, exploring new emulsifying agents, and incorporating advanced nanotechnology for targeted drug delivery. Emulsion-based gel is an approach that can successfully incorporate and deliver a hydrophobic therapeutic moiety with improved solubility and penetrability through the skin; additionally, the emulgel can significantly improve the pharmacological action and reduce the dose of drug due to significant penetration. Emulgels are ideal for wound healing, localized anti-inflammatory or antimicrobial therapy, and chronic dermatological conditions because of better local bioavailability, controlled drug release, and improved skin penetration. Emulgel's non-greasy nature, ease of application, and cosmetic acceptability also contribute to their exceptional patient compliance. Their stability, safety, and regulatory potential are further strengthened by the use of QbD-based formulation techniques, biocompatible polymers, and herbal actives. However, going beyond standard formulations in favor of mechanistic comprehension, translational significance, and observable therapeutic advantages is necessary for emulgel systems to succeed in the future. And also, efforts are directed toward expanding the scope of emulgels in personalized medicine and developing formulations for specific therapeutic areas.

Conclusion

A formulation known as "emulgel" combines gels and emulsions in the same dosage. Emulgel mixtures have been ready for a number of pharmacological types, such as antiviral, antifungal, anti-inflammatory, medications for plaque, local aesthetics, wound healing medications, and antimicrobials. According to various studies, emulgel-based medication has been found to be the most practical and cost-effective topical treatment option for a variety of skin conditions. Emulgels are being used more and more in the food, pharmaceutical, and cosmetic industries, and there is a lot of room for growth. Emulgel will become a common drug delivery method because of its advantages in spreadability, adhesion, viscosity, and extrusion. Additionally, they will be used to load hydrophobic medications into gel bases that are soluble in water.

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