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Review Article

Emulgel: New Potential for Enhanced Topical Medication Delivery

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ABSTRACT

Background: Topical medication is a widely utilized and distinctive approach that facilitates the targeted delivery of diverse pharmaceuticals through the skin. It is a popular and unique process that directs the action of various drugs on the skin for the treatment and diagnosis of multiple diseases and disorders such as urticaria, inflammation, rheumatism, etc. Objectives: The major objectives of this review are to explore the rationale behind utilizing emulgel as an effective dosage form for topical drug delivery, assess the key formulation factors influencing emulgel performance, explore the diverse range of therapeutic agents delivered via emulgel, and discuss the challenges and future perspectives of emulgel technology in pharmaceutical applications. This review aims to provide a comprehensive overview of recent advancements in emulgel formulations for topical drug delivery, addressing their formulation strategies, physicochemical characterization, therapeutic applications, patents related to emulgels and innovations in plant based emulgel formulations. Materials & Methods: A comprehensive literature search was carried out using various databases, such as PubMed, Scopus, and Web of Science, to locate pertinent articles published in peer-reviewed journals. The publications were evaluated according to certain criteria for inclusion. Information regarding emulgel formulations, physicochemical properties, drug release profiles, and therapeutic uses was extracted and compiled. Conclusion: Emulgel and other formulations have been considered as potential and promising solutions for lipophilic medications applied over the skin in the future. The objective is to provide an overview of the most recent developments and applications of emulgel in the transdermal delivery of medication, encompassing both superficial and deep drug administration through the skin.

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INTRODUCTION

Human beings have been given drugs in the form of dosage forms by a conventional route over the years, comprising parenteral, rectal, sublingual, oral, and other different types of routes to treat ailments (1). In cases, where conventional forms (oral route) of administering medicine are found to possess less bioavailability, topical medication delivery has proved beneficial (2). Historically, traditional medicines relied on the skin as its primary organ for administering different drugs, consequently getting the necessary therapeutic effect for a long time (3). In a similar spirit, transdermal medication delivery systems have significantly improved health care over the past few decades by offering an alluring substitute for oral drug administration. The advantages of topical drug delivery systems extend beyond their ability to administer medications precisely to a specific location (4). This route of administration provides advantages by overcoming problems such as gastrointestinal incompatibility and metabolic degradation that are frequently linked to oral administration (5). When a medication is applied topically, it diffuses from the delivery system, moves to the intended location, and then becomes absorbed by the skin, avoiding the first-pass metabolic action of the liver. Topical treatment provides a steady distribution for a longer period with an increased bioavailability (6). Topical medication administration facilitates and simplifies localised drug delivery via the skin, ophthalmic, rectal, and vaginal channels. A diverse range of preparations are utilized for both healthy and injured skin, serving both cosmeceuticals and medicinal purposes (7). The formulations are offered in a variety of forms, including solid, semisolid, and liquid. Drugs are administered topically to produce either local or systemic effects, depending on the intended purpose of the medicine. The process of medication absorption via the skin is enhanced when the drug component is dissolved, possesses a favourable lipid/water partition coefficient, and does not exhibit electrolyte properties (8). Various formulations are suitable for topical delivery i.e., lotions, gels, patches, and powders. This principle aim of this review is to provide a comprehensive overview of recent advancements in emulgel formulations for topical drug delivery, addressing their various formulation strategies, their physicochemical characterization, available marketed products, patents related to emulgels and innovations in plant based emulgel formulations.

1.1 Physiology of Human Skin

The skin, covering a surface area of 1.7 square meters, represents the largest and most prominent readily accessible physiological component within the human body. It makes up an estimated 16% of the total body weight of an average individual (9). On average, each square centimetre of human skin surface has approximately 40-70 hair follicles and 200-300 sweat ducts (Figure no. 1.1). The skin's pH ranges from 4 to 5.6. Sebum excretion affects the pH of the skin surface through the release of sweat and fatty acids (10). The protective nature of the skin from harmful substances such as UV rays, allergens, pollutants, and pathogens is due to the outermost layer, known as the epidermis. The epidermis, including the stratum corneum, covers the skin's surface, while the dermis is the middle layer, and the hypodermis is the innermost layer (11).

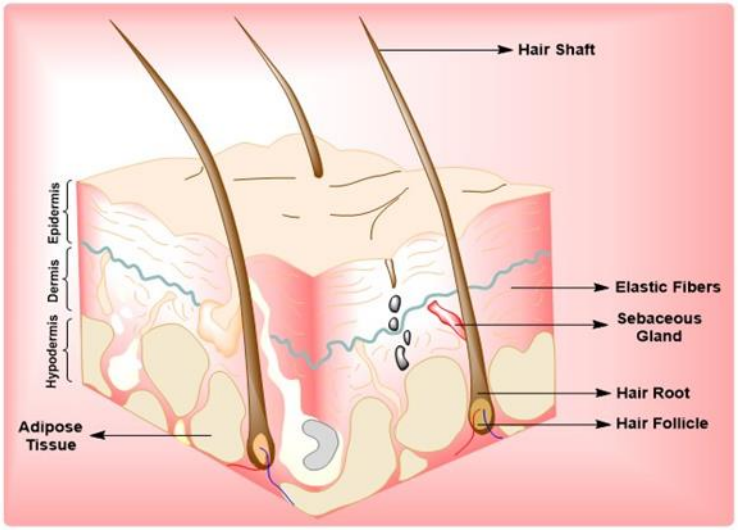

Figure 1.1: Structure of Skin

1.2 Drug Entry Through Skin

The transepidermal and transappendegeal pathways are the two potential passages via which drugs may cross intact skin. In the transepidermal pathway, molecules need to pass through the stratum corneum, which serves as a barrier with diverse architectural characteristics, many layers, and numerous cells (12). The intracellularly located keratinocytes known as corneocytes are responsible for transporting hydrophilic or polar solutes. The movement of polar or lipophilic solutes across the lipid matrix is facilitated by transport through intercellular gaps (Figure no. 1.2). Molecules travel over hair follicles and through sweat glands when travelling via the transappendegeal channel (13).

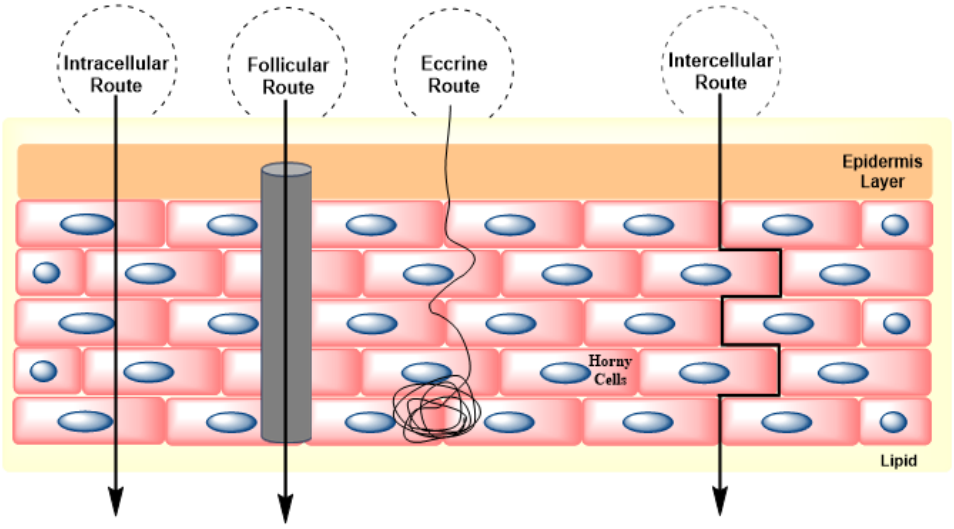

Figure 1.2: Various penetration routes for a drug through the skin

1.3 Methods to Enhance Drug Penetration into The Skin

There are several approaches to improve the permeation of drugs into the skin (Figure no. 1.3) (14).

A. Chemical enhancement
B. Biochemical enhancement
C. Physical enhancement
D. Super saturation enhancement

A. Chemical enhancement

Chemical penetration enhancers (CPEs), alternatively referred to as sorption promoters or accelerants, are useful for transdermal medication delivery for several reasons (15). These include pain avoidance, the lack of invasiveness, and the ability to increase transdermal flux in contrast to passive diffusion (14). Chemical enhancers mainly act by three mechanisms:

1. Interaction with intercellular proteins
2. By the improved partition of drug and
3. Disrupting stratum corneum lipid's orderly structure

Examples: Cyclodextrin, dimethyl sulphoxide, and sodium glycocholate (16).

B. Biochemical enhancement

The use of biochemical enhancers is an innovative method of boosting skin permeability for transdermal medication administration. Biomaterials are used as a biochemical enhancer that could promote the transdermal absorption of insulin *in vitro*. Examples: Ethanol, 2-pyrrolidone, and diethyl sulfoxide (17)

C. Physical enhancement

Chemical and physical techniques can both speed up drug permeation through the epidermis. Iontophoresis, electroporation, ultrasound, microporation, and micro-needles are a few examples of bodily improvements (18). Several physical techniques, including microneedles, heating, electroporation, and ultrasound, have been investigated in the last decade to promote drug penetration and improve its bioavailability (19). Examples: Ultrasound, microneedles, iontophoresis, heating

D. Supersaturation enhancement

The *in vitro* penetration of a lipophilic model molecule (a lavendustin derivative, LAP) through excised pig skin has been improved by supersaturation (20). The medication is dissolved in a variety of liquid and semisolid carriers (which had varying degrees of solubility) that is made by either

1. Employing mixed cosolvents,
2. Solvent evaporation, or
3. Heating the carrier to dissolve the drug.

Independent of the absolute concentration of the medication in the vehicle, saturated formulations demonstrated equivalent penetration rates through the skin (21). Examples: - lemonade with too much sugar, water oversaturated with cocoa powder

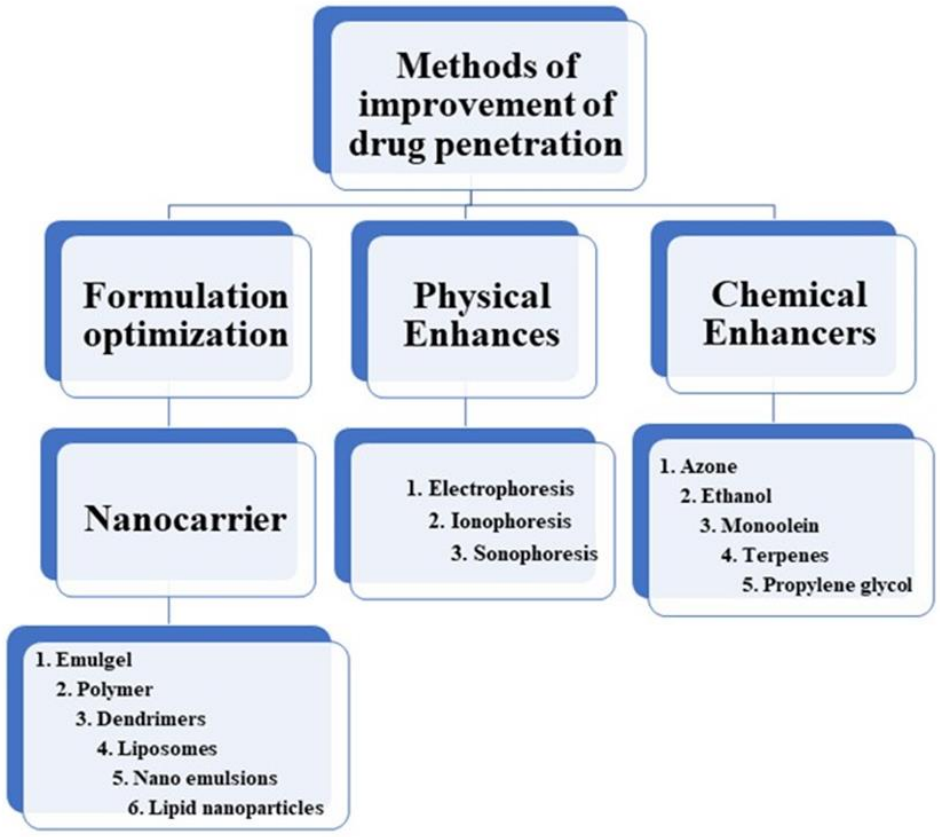

Figure 1.3: Various methods of improvement of drug penetration

1.4 Emulgel

Emulgels are gelled by adding gelatinizer to wate r-in-oil or oil-in-water emulsions. These dependable and efficient medication delivery devices work well for water-repellent drugs. Emulgel provides the advantages of both gels and emulsions (22). The capability of these formulations to carry both lipophilic and hydrophilic medications makes them extensively used by patients (Figure no. 1.4). The emulgel possesses dual characteristics of both emulsion and gel, allowing for dual controlled release (23). In contrast to other topical medications that need vigorous rubbing, these are applied to the skin appropriately because of their non-greasy nature (24).

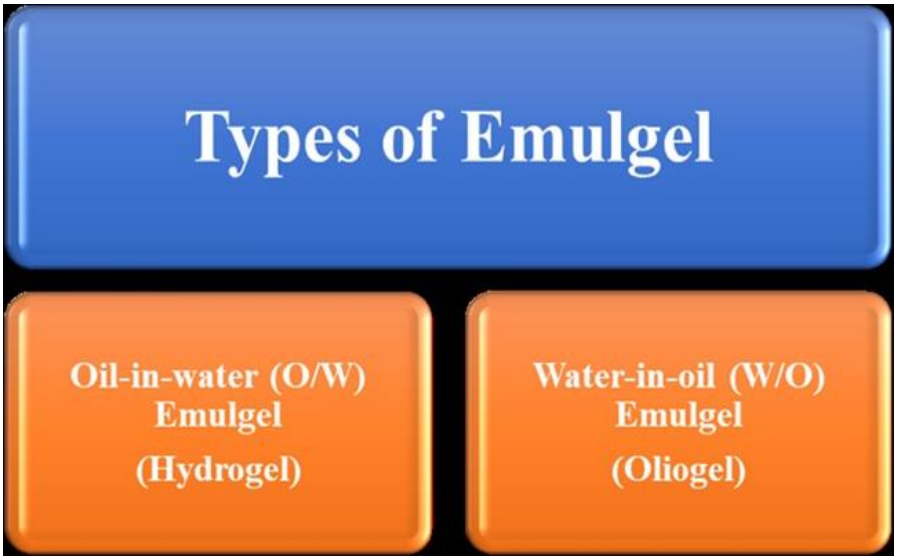

Figure 1.4: Types of Emulgel

Water-in-oil and oil-in-water emulsions are utilized for drug delivery to the epidermis. Furthermore, they demonstrate a notable ability to penetrate the epidermis. The difference between a standard emulsion and an emulgel is determined by the inclusion of a gelling agent within the aqueous phase (25). A dermatologically utilized emulgel possesses several beneficial characteristics, such as thixotropic properties, lack of greasiness, effortless durability, environmentally friendly composition, transparency, and an aesthetically pleasing appearance (26). Drug molecules can penetrate the skin through three pathways: the intact stratum corneum, sweat ducts, or sebaceous follicles. Over 99% of percutaneous medication absorption occurs on the stratum corneum. Percutaneous absorption is limited by this outermost layer. Percutaneous absorption involves producing a concentration gradient, isolating the drug from the carrier based on its partition coefficient, and spreading the medication via the skin layers (27). The merits and demerits of emulgel are tabulated below in table 1 (8).

Table 1: Merits and Demerits of Emulgel

S. No.	Merits	Demerits
1.	Avoid first-pass metabolism	Skin discomfort from contact dermatitis
2.	Avoid gastrointestinal incompatibility	Potential for allergic responses
3.	Suitable for self-medication	Some medications have limited skin absorption
4.	Better stability	Topical absorption of macromolecular medicines is challenging
5.	Appropriate and easy to apply	Appearance of a bubble during emulgel preparation

1.4.1 Classification of emulgel

Emulgel can be categorized into three primary groups based on particle size: macroemulgel, nanoemulgel, and microemulgel (28).

1.4.1.1 Macroemulgel

These emulgels are commonly utilized and have a particle size above 400nm (29). The emulgels

exhibit opacity and homogeneity, yet, the emulsion droplets can be readily detected under a microscope due to their significant particle size. Macroemulgels are unstable in terms of thermodynamics (30, 31).

1.4.1.2 Nanoemulgel

The emulgel is formulated by combining a nanoemulsion with a gel to create a thermodynamically stable dispersion that is both transparent and homogeneous. Nanoemulgel exhibits droplets of a size less than 100nm, resulting in enhanced permeability (32, 33).

1.4.1.3 Microemulgel

Microemulgel is a pharmaceutical formulation blend of microemulsion and gel structures, offering enhanced drug delivery and stability. It combines the advantages of both systems, providing optimal absorption and prolonged localized action (34, 35).

1.4.2 Mechanism of Emulgel Penetration Through Skin

People often use topical medicines like ointments, creams, and lotions, yet have some difficulties. They produce an extremely viscous sensation when applied and cause discomfort for the patient. They also require rubbing action to apply and have a lower spreading coefficient (36). They also show stability issues. All these formulations, categorized as semisolid preparations have increased the utilization of translucent gels in both medicinal and cosmetic products (37). Surface tension immobilizes a colloid, which is often a nearly liquid substance with a tiny quantity of a gelatin substance present to form a macromolecular network of fibres. Gels have several advantages, but not suitable for hydrophobic drugs. To overcome this restriction, a technique based on emulsion is employed, allowing the effective inclusion and administration of hydrophobic medicinal components through gels (Figure no. 1.5) (1).

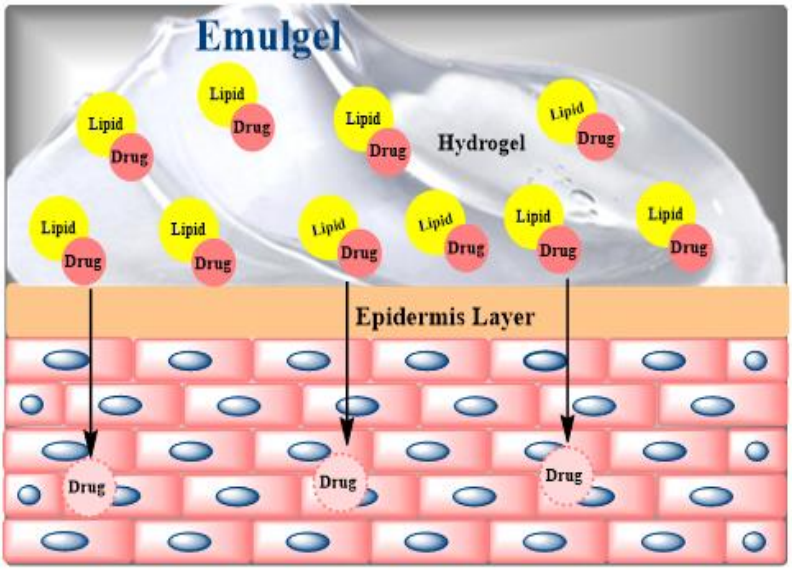

Figure 1.5: Schematic Presentation of Emulgel Penetration Through Skin

1.4.3 Preparation of Emulgel

The emulgel contains various components like a vehicle, aqueous phase, oil, emulsifier, gelling agent, penetration enhancer, humectant, etc.

1.4.3.1 Composition of emulgel

a) **Vehicle:** The vehicle used to prepare emulgel needs to possess certain qualities, including the ability to deposit and distribute medication evenly, release medication for unrestricted movement to the activity site, deliver medicine to correct locations, and maintain the therapeutic level of medication over an extended duration of time (38).

b) **Aqueous material:** Hydrophilic components are used to create the aqueous part of the emulsion. Aqueous phase is typically prepared using alcohol and water. Carbamate and bicarbonate ions make up the lower phase or aqueous phase. Examples: water, alcohol, ethanol, etc (36).

c) **Oil:** Non-biodegradable castor and mineral oils are used to produce the non-aqueous part of the emulsion (39). To prepare emulgel, oils from a variety of plants with varying therapeutic properties can be employed. A nonpolar chemical compound that exhibits hydrophobicity (lack of affinity for water) or lipophilicity (affinity for other oils) and primarily consists of hydrocarbons is known as an oil. Oils are typically surface-active agents and flammable. The majority of oils are liquid and unsaturated lipids at room temperature (40). Examples: Light liquid paraffin, propylene glycol, isopropyl stearate, isopropyl palmitate, etc.

d) Emulsifier: Emulsifying agents are employed to enhance the process of emulsification during production and to maintain stability throughout the product's shelf life. Algin, carrageenan, and agar are just a few of the algae-derived emulsifiers (2). Emulsifying agents include lecithins like those found in egg yolk. An emulsifying agent consists of a hydrophilic portion that can have a positive or negative charge, as well as a hydrophobic portion, typically a fatty acid with an extended carbon chain. The hydrophobic part of the emulsifier dissolves in the oil phase, while the hydrophilic part dissolves in the aqueous phase, dispersing tiny oil droplets. Thus, emulsions of oil and water are created and made stable by emulsifiers (41). Examples: Sorbitan mono-oleate, polyethylene glycol 40 stearate, sodium stearate, stearic

e) **Gelling agents:** Various gelling agents can be used to promote consistency and gelling characteristics. An inverse relationship exists between the medication release and gelling agent concentration (42). In emulgel, carbopol and HPMC are frequently utilised when dissolved in a liquid, the gel-forming agents in colloidal mixtures have a loosely bound internal arrangement. They are either hydrophilic inorganic substances or organic hydrocolloids. Gelling agents are used in semisolid dosage forms at concentrations between 0.5 and 10% (10). They also serve as stabilizers and thickeners, providing thickening without stiffness (43). In semi-solid dosage forms, polymers have been recently used a lot as gelling agents. Carbomers, which are synthetic macromolecular polymers of acrylic acid, are widely recognized as the most prevalent, as they can thicken quickly across a wide pH range (44, 45) Examples: Tragacanth, pectin, starch, carbomer, sodium alginate, gelatin, cellulosederivatives, polyvinyl alcoho l clays, etc.

f) Penetration enhancer: The penetration enhancer will increase the permeability of the drug. It makes it easier for the drug to be absorbed through the skin (46). Agents such as penetration enhancers interfere with the fluidized lipid channels of the corneum which have a highly organized structure, and hence, enhance the transport of drugs through the skin and facilitate their penetration into the skin (47). Examples: Oleic acid, Lecithin, Isopropyl myristate, Linoleic acid, Menthol, etc.

g) Humectant: A compound that retains moisture, as it is hygroscopic (takes in water). They are used in food, cosmetics, medicines, pesticides etc. Humectants are employed in topical formulations to enhance the solubility of a chemical molecule, which in turn increases the active ingredient's ability to penetrate skin or its activity time in cosmetics and pharmaceuticals (48). This hydrating property is also required to counteract the dehydrating nature of some excipients (for example, soaps, corticoids, and some alcohol). Examples: Glycerine, propylene glycol, etc.

1.4.3.2 Methods of preparation of emulgel

Emulgel is a composite substance formed by combining an emulsion and a gel. These are emulsions that have been combined with a gelling agent to create a gel-like consistency. These emulsions can be either water-in-oil (w/o) or oil-in-water (o/w) (49).

Preparation of emulgel requires the following steps

a) Emulsion formation
b) Formation of gel-base
c) Mixing of emulsion into gel-base

Step 1: Emulsion formation, either w/o or o/w

To prepare an emulsion, agitate two liquids together or homogenize the mixture using a colloid mill vigorously. The emulsions prepared in this manner from the pure liquids are typically unstable and get separate when left undisturbed (50). Various techniques can be used to prepare emulsions, depending on the equipment and component types. Emulsions can be produced on a small scale, for instance, in a laboratory or pharmacy, either a desiccated Wedgwood or porcelain mortar and pestle, a mechanical blender, or a mixer can be used (2). A high-speed impeller may be employed in big mixing tanks to create the emulsion on a huge scale. Emulsions are of two types either water in oil (w/o) or oil in water (o/w).

w/o emulsion: A water-in-oil emulsion is a type of mixture where water is dispersed as small droplets within a continuous oil phase. This means that water is the dispersed phase and oil is the continuous phase. The volume proportion of each phase and the type of emulsifier used to determine the outcome of an oil and water mixture that forms an emulsion. These emulsions are commonly used in various industries including cosmetics, pharmaceuticals, and food production (51). Examples: Mayonnaise, milk, etc.

o/w emulsion: An oil-in-water emulsion is a specific form of emulsion in which tiny oil droplets are evenly distributed throughout a continuous water phase. In this emulsion, the oil serves as the dispersed phase, meaning it exists as small droplets suspended within the continuous water phase. These emulsions have specific characteristics and are utilized in various industries for different purposes (51). Examples: Butter, cold cream, cod liver oil

Step 2: Formation of the gel base

Four commercial polymers, including carbopol (CP), hydroxypropyl methylcellulose (HPMC), methylcellulose (MC), and sodium carboxymethylcellulose, are used to make gel bases. The appropriate concentration of the gelling agent in the gel base is 1 to 2 % w/w. A gel base is formed by dissolving the necessary amount of a gelling ingredient in purified water with the application of heat (52).

Step 3: Continuous stirring of the emulsion into the gel base.

Combine the produced emulsion with the gel bases by continuous stirring (Figure no. 1.6) (50)

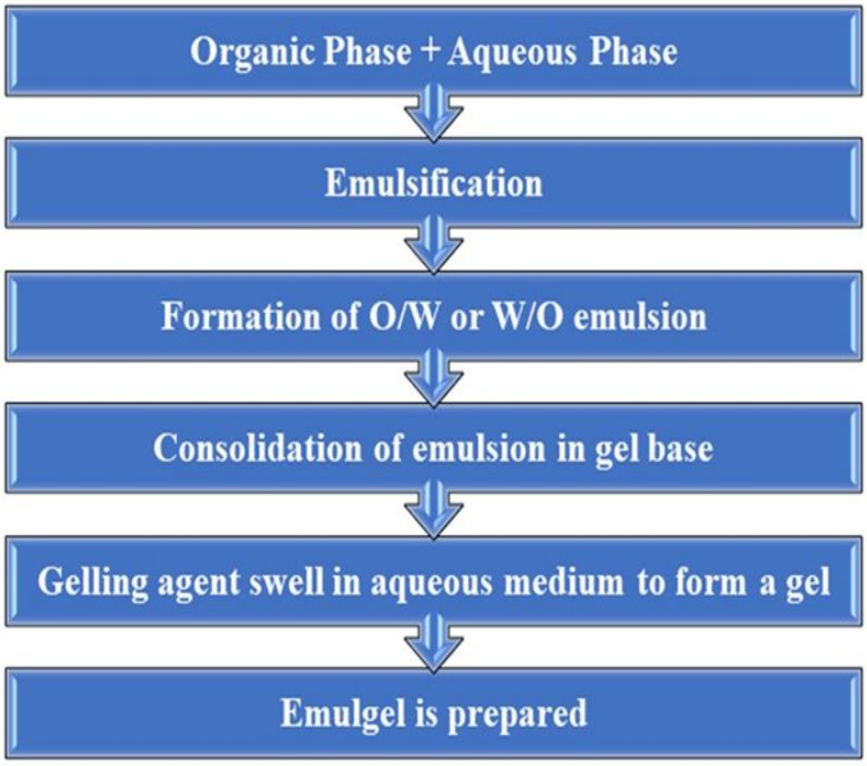

Figure 1.6: Steps For Formulation of Emulgel

1.4.4 Evaluation of Emulgels

Physical inspection: Emulgel formulations are assessed for their visual characteristics, including colour, uniformity, texture, and separation of phases (53).

Rheological studies: The viscosity of several emulgel formulations is measured at a temperature of 25 °C using a cone and plate viscometer. The viscometer is connected to a circulating water bath that is regulated by a thermostat (54).

Spreading coefficient: The spreadability of each gel base is measured individually using a wooden block and glass slide apparatus. To assess the spreadability, a modified device is employed. This apparatus comprised a pair of glass slides, with the specimen positioned in between. The underside of the slides is secured to a wooden block, while the top side is linked to a balance via a hook. All the samples (about 1g) are placed between these two glass slides and pressed together for 5 minutes to expel the air and provide a uniform thickness of

gel by placing a suitable weight. The upper glass slide is identical in dimensions to the stationary base slide. Consequently, a mass of 50 grams is placed onto the pan, and the glass slide is dragged using a stirring stick that is connected to the hook. The duration of the upper glass slide's movement over the lower plate by 10 cm is documented (55). The spreadability is determined by applying the formula shown below:

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

Where,

M = Weight tied to upper slide

L = Length of glass slide

T = Time taken to separate the slides

Topical emulgel extrudability study (Tube test): Measuring the required force to extrude material from a tube is a common empirical test. The approach utilized to determine the shear was implemented in the segment of the rheogram that aligns with a shear rate exceeding the yield value and shows subsequent plug flow. The current study utilizes a method to assess the extrudability of emulgel formulations. This technique quantifies the proportion of emulgel and the volume of emulgel expelled from a lacquered aluminium collapsible tube. The assessment relies on the mass in grams necessary to extrude a 0.5 cm emulgel strip within a 10-second duration. The extrudability of every formulation is assessed in triplicates and the mean values are displayed (56). The extrudability is subsequently determined by employing the following formula:

$$\text{Extrudability} = \text{Applied weight to extrude emulgel from tube (in gm)} / \text{Area (in cm}^2\text{)}$$

Skin irritation test (Patch test): The formulation is applied topically to rat skin that has been appropriately shaved, and any negative consequences, including alterations in skin pigmentation or structure, should be observed for 24 hours (57). The study utilizes the total batch of 8 rats. The test is deemed effective if there is an absence of irritability. If the sensation of skin irritation arises in more than two animals, it is necessary to conduct a repeated trial (42).

***In-vitro* studies on permeation and release:** *In-vitro* release tests are conducted using Franz diffusion cells. The drug release experiments of the emulgel are conducted *in vitro* utilizing a diffusion cell with an egg membrane (58). The item is meticulously affixed to one extremity of the hollow glass tube of the dialysis cell, ensuring a secure attachment. One g dose of emulgel is applied topically onto the egg membrane's surface semipermeable membrane used in dialysis. The receptor chamber is filled with a newly prepared solution of phosphate buffer (pH 7.4) to dissolve the medicine. A magnetic stirrer is employed to induce agitation in the receptor chamber. The samples are collected at regular intervals in 1 ml aliquots and subsequently tested to analyze the drug content using a UV-visible spectrophotometer following suitable dilutions. The total quantity of medication discharged throughout each time interval is determined by aggregating the successive corrections. The total drug release through the egg membrane is measured over time. The total percentage of

medication release is determined by employing a standard calibration curve (59).

Drug Content: Measure 1 gram of emulgel and combine it with an appropriate solvent, then thoroughly mix the two substances. To obtain a definitive resolution, apply a filtering process. Use a UV spectrophotometer to determine its absorbance. A common solvent is utilized for the preparation of drug plots. The concentration and drug content may be determined by employing the absorbance value in the equation of the standard plot (5).

$$\text{Drug Content} = (\text{Concentration} \times \text{Dilution Factor} \times \text{Volume taken}) \div \text{Conversion Factor}$$

Swelling index: To measure the swelling index of the manufactured topical emulsion gel, a quantity of one gram of the gel is spread onto a porous aluminium foil. The foil is then placed inside a separate 50-millilitre beaker, which contains 10 millilitres of a 0.1 normal (N) solution of sodium hydroxide (NaOH). Subsequently, the samples are extracted from the beaker at different time intervals and transferred to a desiccated location for some time, followed by reweighing (60). The swelling index is computed using the following formula:

$$\text{Swelling index (SW)} \% = [(W_t - W_0)/W_0] \times 100$$

Where, (SW)% = equilibrium percentage swelling

W_t= weight of swollen emulsion after time t

W_0 = initial weight of emulsion gel at zero time

1.4.5 Packaging of Emulgel

Emulgel is often packed using either an aluminium laminated tube, closed with a moulded seal and features a propylene screw cap, or a lacquered aluminium tube, sealed with a membrane and has an interior coating of a phenoxy-epoxy-based lacquer (61).

Tubes made of laminated material

a. Laminated foil:

It provides a protective shield against light, air, and wetness.

b. All laminated plastic:

The object possesses a protective barrier that exhibits resistance against chemical substances.

1.4.6 Recent advancements of emulgel

A survey has been done in which authors use the different components to formulate an emulgel that has been shown in Table 2 given below:

Table 2: Recent Advancements in Emulgel with Different Components And API

S. No.	Active ingredient	Excipients	Outcomes	Ref.
1.	5-Fluorouracil	Clove oil, eucalyptus oil	Liposomal emulgel of 5-5-fluorouracil with increased skin permeability and efficacy was obtained	(62)

2.	Dexibuprofen, Capsaicin	Menthol, tween 80, span 80, propylene glycol, liquid paraffin, carbopol 940	A promising synergistic potential of Dexibuprofen capsaicin emulgel was obtained as an alternative to the conventional topical dosage form.	(63)
3.	Piroxicam	Oleic acid, propylene glycol, span 80, tween 80, cetostearyl alcohol	Emulgel of piroxicam with increased skin penetration of drug in comparison with presently marketed preparations of the drugs.	(64)
4.	Aceclofenac	Span 20, tween 20, liquid paraffin, propylene glycol, mentha oil, carbopol 934	Formulation using carbopol 934 revealed a better release profile than HPMC K4M polymer	(65)
5.	Mefenamic acid	Carbopol 940, liquid paraffin, tween 20, span 20, propylene glycol, ethanol, clove oil, mentha oil	Emulgel of mefenamic acid using carbopol 940 as a gelling agent was obtained and possessed effective anti-inflammatory and analgesic activity	(23)
6.	Luliconazole	Oleic acid, tween 80, span 80, propylene glycol, cetostearyl alcohol, carbopol 940	Emulgel of luliconazole with increased skin penetration of drug in comparison to presently marketed preparations of the drug	(41)
7.	Ketoconazole	Carbopol 934, liquid paraffin, tween 80, span80, propylene glycol, ethanol, methylparaben	Nanoemulgel for topical delivery of poor water-soluble drug ketoconazole proved useful in the treatment of fungal infection	(66)
8.	Etodolac	Carbopol 934, liquid paraffin, tween 80, span80, propylene glycol, ethanol, methylparaben	Gastro-intestinal toxicities associated with oral administration of Etodolac were found to reduce, improved drug release as well as permeation, selective absorption of the drug at the site of action and enhanced stability	(67)
9.	Minoxidil	Carbopol 940, liquid paraffin, propylene glycol, ethanol, methylparaben	Minoxidil emulgel was prepared, evaluated and compared with gel for various physicochemical properties, in vitro drug release and ex vivo permeation study. It was proved better than the gel in all aspects.	(53)
10.	Chlorphenesin (CHL)	HPMC, Carbopol 934, liquid paraffin, tween 80, span80,	Chlorphenesin emulgel formulation showed the	(27)

		propylene glycol, ethanol, methylparaben	highest drug release and antifungal activity when compared with conventional formulations	
11.	Amphotericin-B	Polaxmer 407, soybean lecithin, ethanol, and isopropyl palmitate.	Amphotericin-B 3% and oleic acid 5% containing formulation had a more pronounced therapeutic effect in living organisms and reduced toxicity in the body. Use of Amphotericin-B emulgel resulted in improved wound healing with minimized adverse effects	(8)
12.	Chlorphenesin	Hydroxypropyl Methylcellulose (HPMC), Carbopol 934, Span 20, Tween 20, Methylparaben, Propylparaben, and Light Liquid Paraffin.	Emulgel formulated with HPMC and carbopol 934 exhibited stability and favourable physical characteristics. However, emulgel formulated with liquid paraffin had the highest drug release and antifungal efficacy	(42)
13.	Clotrimazole	Hydroxypropyl Methylcellulose (HPMC), Carbopol 934, Span 20, Tween 20, Methylparaben, Propylparaben, and Light Liquid Paraffin.	Emulgel with HPMC K4M exhibited the highest drug release rate, reaching 58.57% after eight hours. Clotrimazole had a consistent and gradual release, indicating excellent stability	(54)
14.	Metronidazole	Xanthan gum, Capmul908, propylene glycol, and methyl and propyl parabens.	When compared to regular gel, the emulgel formulation was found to be more stable and more easily absorbed by the skin	(3)

1.4.7 Various marketed formulations of Emulgels

There are various commercially marketed formulations of emulgel available in the market and those are shown in Table No. 3:

Table 3: Various Marketed Formulations

S. No.	Brand name	Active ingredient	Manufacturer	Ref.
1.	Voltarol emulgel	Diclofenac Diethylammonium	Novatris Pharma	(68)
2.	Diclomax emulgel	Diclofenac sodium	Torrent Pharma	(69)

3.	Miconaz-H-emulgel	Miconazole nitrate, Hydrocortisone	Medical union Pharmaceuticals	(70)
4.	Isofen emulgel	Ibuprofen	BeitJala Pharmaceutical	(71)
5.	Diclona emulgel	Diclofenac diethylamine	Siam bheasach	(72)
6.	Dosanac emulgel	Diclofenac diethylammonium	Med Pharma	(73)
7.	Diclon emulgel	Diclofenac diethylamine	Med Pharma	(74)
8.	Cataflam emulgel	Diclofenac potassium	Novartis Pharma	(75)
9.	Denacine emulgel	Clindamycin phosphate	Beitjala Pharmaceutical	(76)
10.	Voltaren gel	Diclofenac sodium	Endo Pharmaceuticals	(77)
11.	Gaia emulgel	Cucumber gel, camomile essential oil, juniper essential oil, camphor essential oil	Kleraderm Pharma	(10)
12.	Voveran emulgel	Diclofenac sodium	Novartis Pharma	(78)
13.	Nucoxia emulgel	Etoricoxib, Linseed oil, Menthol, Methyl Salicylate	Zydus Cadila	(79)

1.4.8 Innovations in Plant-Based Emulgel Formulations

Innovations in plant-based emulgel compositions have combined nature and technology. Nanoencapsulation improves plant extract stability and bioavailability, while adaptive delivery systems optimize absorption and efficacy over time. Some of the plant-based emulgel formulations are shown in Table 4.

Table 4: Plant-Based Emulgel Formulations

S. No.	Plant Extract	Phytoconstituents	Activity	Ref.
1.	*Ocimum basilicum*	Tannins, sesquiterpenes	Wound healing	(55)

2.	*Avena sativa*	Flavonoids, avenanthramides, flavonolignans	Antipigmentation	(80)
3.	*Coccinia grandis*	Glycosides, alkaloids, phenols	Antibacterial against skin pathogenic bacteria	(81)
4.	*Coriandrum sativum*	Polyphenols, vitamins, phytosterols	Anti-inflammatory	(82)
5.	*Zingiber Officinalis*	Gingerols, shogaols, paradols	Antimicrobial	(83)
6.	*Hibiscus rosa-sinensis*	Alkaloids, flavonoids, mucilage	Anti-inflammatory	(84)
7.	*Saussaria lappa*	Alantolactone, isoalantolactone, guaianolide	Wound healing	(85)
8.	*Polycarpea aurea*	Flavonoids, phenolic compounds	Antibacterial	(6)
9.	*Solanum lycopersicon*	Lycopene	Antibacterial	(86)
10.	*Cardiospermum halicacabum*	Palmitic acid, oleic acid, stearic acid	Anti-arthritic	(87)
11.	*Annona squamoa* Leaf extract	Diterpenes, acetogenins, alkaloids, cyclopeptides	Radical scavenging activity (antioxidant)	(88)
12.	*Cinnamomum tamala extract*	Monoterpenes, sesquiterpenes	Antioxidant	(89)

1.4.9 Patents Related to Emulgel Preparations

Patents related to emulgel preparations cover various aspects of the formulation, manufacturing processes, and applications of emulgel products. Some patents related to emulgel preparations are listed below in Table 5:

Table 5: List of Patents

S. No.	Patent Name	Product	Inventors	Publication Year	Ref.
1.	US 11141242B2	Orthodontic metal brackets with eugenol emulgel	Ahmed Samir Ibrahim Bakry, Mona Aly Abbassy, Amal Linjawi, Ali Habib Hassan, Ahmed Fathy Hanafy, Gihan Salah Labib, Amal Mohammed S Abushal	2021	(90)
2.	US 20170232026 A1	Emulgel for veterinary use	David Quintanar Guerrero, Juan Pablo Martinez Labat, Susana Elisa Mendoza Elvira, Gustavo Vidal Romero, Victor Andres Trenado Hernandez	2017	(91)

3.	CN102525886B	Diclofenac diethylamine emulgel and preparation method thereof	Song JD, Park CM, Choi YK, Lee HH, Shim YH, Yoon HJ	2004	(92)
4.	US20120093882A1	Voveran	Sunilendu Bhushan Roy, Shafiq Sheikh, Jay Kothari, Jitendra Patel	2012	(93)
5.	US 20100286268A1	Topical composition	Fabienne Caillett -Bois, Isabelle Rault, Michel Steiger	2010	(94)
7.	EP2019666A2	Pharmaceutical preparations for transdermal use	Cristina Cavallari, Barbara Luppi, Pietra Anna Maria Di, Lorenzo Rodirguez	2009	(95)
8.	WO2008051186A2	Nanoemulsion-containing composition having anti-inflammatory activity	James R Baker Nanobio Corporation	2008	(96)
9.	EP2055298A1	Diclofenac gel Voltaren Emulgel	Novartis AG	2007	(97)
10.	US 6113921A	Topical and transdermal delivery system utilizing submicron oil spheres	Doron Friedman, Joeph Schwartz, Haim Aviv	2007	(98)
11.	WO2006082596A2	Neem oil contraceptive	Kamalinder Kaur Singh, Pratima Arun Tatke, Shruti Dhuru	2006	(99)
12.	2007129162	Pharmaceutical preparations for transdermal use	Cristina Cavallari, Barbara Luppi, Pietra Anna Maria Di, Lorenzo Rodirguez	2014	(95)
13.	US6004566A	Topical and transdermal delivery system utilizing submicron oil spheres	Doron Friedman, Joeph Schwartz, Haim Aviv	1999	(100)
14.	5639738x	Topical composition containing hyaluronic acid and NSAIDs	Falk, Rudolf Edgar, Asculai, Samuel Simon	1995	(101)

2. CONCLUSION

Various formulations are employed in a topical medication delivery method, each with its own set of drawbacks. The majority of these drawbacks can be reduced by the process of emulgel preparation. The emulgel has been acknowledged as the most suitable, superior, and effective method of distribution of drugs. By incorporating an emulsion into the gel, a dual control release system was established to address several issues related to previous formulations, including emulsion creaming, phase separation, and reduced stability. Currently, emulgel is extensively utilized for the topical administration of several medications. The emulgel that is most frequently utilized is Miconaz-H- emulgel, Diclon emulgel, and other similar products. Typically, emulgels are

employed for their anti-inflammatory, anti-acne, analgesic, and several other therapeutic properties. Having the numerous benefits and innovative uses of emulgel in the delivery of hydrophobic drugs topically, it is highly recommended to further explore emulgel formulations to achieve an efficient method of drug delivery through the skin. This can be achieved by enhancing the stability and penetration rate of the drugs.

3. Future Perspectives

Future of topical medicine administration has great potential for enhancing patient compliance. An innovative approach in drug administration through the topical route is the use of emulgel, which has demonstrated efficacy in delivering hydrophobic medicines. During the process of developing a novel formulation, the most encountered issues are caused by the hydrophobic nature of pharmaceuticals, which in turn leads to challenges related to solubility and bioavailability. In addition, they will formulate a solution for incorporating hydrophobic medications into a gel basis that is soluble in water. Additionally, it can enhance spreadability, viscosity, extrusion, and adhesion. Emulgel, unlike other topical medication delivery methods, exhibits enhanced and expedited drug distribution to the skin by integrating the hydrophobic drug inside the oily base. The benefits of emulgel over other topically applied formulations make it a very successful alternative for drug delivery. These properties can be further applied to formulate many topical medications as an emulgel.

List of Abbreviations

Consent for Publication

NA

Conflict of interest

The authors have declared no conflict of interest financial/others.

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