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REVIEW ARTICLE

Emulgel: An Emerging Candidate in Topical Drug Delivery

Sameer Sarvar Shaikh* and Lalita.S.Nemade
Govindrao Nikam College of Pharmacy Sawarde, Ratnagiri, India.
* **Corresponding Authors:** Sameer Sarvar Shaikh
Email: sameershaikh5488@gmail.com

ABSTRACT
The creation of emulgel formulations, which combine the benefits of gels and emulsions, represents a significant advancement in the topical drug delivery sector. Emulgels are biphasic systems that enhance the stability, spreadability, and drug release characteristics of topical formulations by combining an oil-in-water emulsion with a gel matrix.In this review article, various crucial elements and methodologies are thoroughly examined in relation to the formulation of emulgels. These consist of the choice of gelling agents and emulsifiers as well as the optimisation techniques applied to achieve the required chemical and physical qualities.It also discusses the challenges and most recent developments in the production of emulgels, such as the use of nanotechnology and bioadhesive polymers to improve drug retention and efficacy. The goal of this comprehensive review is to help scientists and formulators develop emulgel systems that work well for a variety of medical applications.
Keywords*: Emulgel, Topical Drug Delivery, Emulsion, Gel Matrix, Formulation.*

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INTRODUCTION

Topical drug administration is the localized administration of medication to any area of the body via the ocular, vaginal, rectal, and epidermal routes. Whether their skin is well or not, they use a wide variety of dermatological and cosmetic preparations on it [1]. Topical formulations are made in three different consistencies: liquid, semisolid, and solid. When hydrophobic medication is used, the topical distribution method is less effective. Excipients are used extensively in any composition that contains active ingredients. Emulgel is one instance of a combination that can be utilized to enhance the administration of medication by combining different formulations. It's the mixture of emulsion and gel[2].

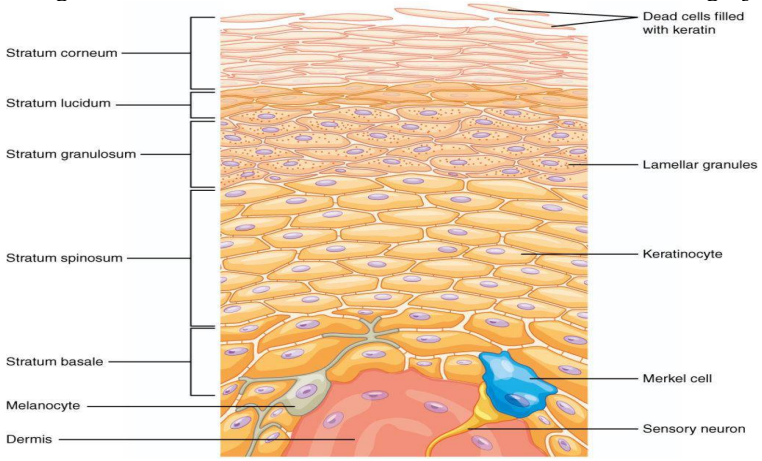

Figure 1: Structure of skin

Compared to oral administration, which avoids hepatic first pass metabolism and maintains delivery for a longer period of time, topical application avoids these issues and enhances bioavailability. Other advantages of topical drug delivery methods include the ability to administer medication more precisely to a particular location and the prevention of stomach intestinal incompatibility and metabolic breakdown linked to oral administration [3]. Topical drug delivery is the dose type used topically when other techniques of medication delivery are not successful or do not work at all in treating skin disorders. One advantage of topical pharmaceutical administration is its ability to negotiate first pass metabolism. It also helps to prevent the risk and inconvenience that come with intravenous therapy [4]. Emulgel is created by combining gel with emulsions of o/w and w/o. Water-in-oil delivery is used for hydrophobic drugs, and oil-in-water delivery is used for lipophilic pharmaceuticals [5]. Among its many advantages are thixotropic, greaseless, easily removable, emollient, and non-staining properties of the emulgel. translucency, aesthetic acceptability, biocompatibility, beautiful appearance, reasonable skin penetration, and extended shelf life[6]. Emulgels are created to overcome this limitation, and when emulsions and gels are applied, even hydrophobic drugs can benefit from the special properties of gels. The term "emulgel" refers to dosage forms.Gels and emulsions are combined. Actually, the inclusion of a gelling component in the water phase is what sets an emulgel apart from a standard emulsion. While hydrophilic medications in the O/W system trap lipophilic substances inside the W/O system [7]. Every gel and emulsion preparation has distinct qualities. However, there are several disadvantages to the hydrophobic drug delivery of the gels. This limitation is being surmounted by Emulgel. A gelling agent can be used to convert a standard emulsion into emulgel[8].

INTRODUCTION TO EMULGEL

Any emulsion that has gelled with the aid of a gelling agent is referred to as "emulgel". They are available in w/o and o/w types. Emulgel is a dependable, improved method that incorporates poor drugs soluble in water. In short, Emulgel is a combo of emulsion and gel. .Gels offer a number of benefits, but one major drawback is the manner hydrophobic drugs are given. In order to get around this restriction, an emulsion-based strategy is being employed, permitting even hydrophobic therapeutic moieties to benefit from the unique properties of the gel. Emulgel has both aqueous and non-aqueous phases, for this reason. It is capable of delivering both lipophilic and hydrophilic drugs. In recent years, they have been used as a control release formulation.[9]. These two-phase systems have better stability and the ability to load drugs. Emulgel has several benefits over the conventional topical formulation, such as better spreadability, grease-lessness, thixotropy, long shelf life, no odour, and a nice appearance. Emulgel is a dual control release system with characteristics of both gel and emulsion [10].

RATIONALE

There are a number of disadvantages to many frequently used topical medications, including ointments, creams, and lotions. They are frequently extremely sticky, which makes the patient uncomfortable when used. They also need to be rubbed to apply and possess a reduced coefficient of spread. They also experience problems with steadiness. These considerations have led to a notable growth in the usage of clear gels in semisolid formulations, including both therapeutic and cosmetic applications. A colloid that is normally 99 percent liquid is called a gel and is kept stable by the surface tension that forms between a fibre network and a liquid that is created from a tiny quantity of a gelling agent. Gels have many benefits, but administering hydrophobic medicines is a major difficulty. This problem is addressed by using an emulsion-based strategy, which makes it possible to incorporate and transport hydrophobic medicinal chemicals through gels in an efficient manner [11].

ROLE OF EMULGEL IN DRUG DELIVERY SYSTEM

1. **Improved Drug Solubility**
   - Many drugs are hydrophobic and difficult to formulate in conventional gels.
   - Emulgels incorporate these drugs in the oil phase of an emulsion, which is then gelled.
   - This enhances drug solubilization and uniform distribution.
2. **Enhanced Skin Penetration**

- Presence of penetration enhancers (oils, surfactants) improves drug permeation through the stratum corneum.
- Emulgels provide better bioavailability than traditional creams or ointments.

3. **Controlled and Sustained Drug Release**

- The gel matrix helps in controlling drug release.
- Provides prolonged therapeutic effect, reducing dosing frequency.

4. **Better Patient Compliance**

- Non-greasy, smooth, and easily spreadable.
- More cosmetically acceptable compared to ointments.
- Easy removal and minimal irritation.

5. Improved Stability

- Emulgel systems reduce problems like phase separation seen in emulsions.
- The gel structure stabilizes the formulation and enhances shelf life.

6. Targeted and Localized Drug Action

- Ideal for localized drug delivery (e.g., anti-inflammatory, antifungal, analgesic drugs).
- Minimizes systemic side effects by delivering drugs directly to the affected site.

7. Versatility in Drug Delivery

- Emulgels are widely used for:
- Dermatological preparations
- Anti-inflammatory drugs (e.g., diclofenac, ibuprofen)
- Antifungal agents
- Antibiotics
- Cosmeceuticals

8. Comparison with Conventional Topical Systems

Feature	Emulgel	Cream/Ointment
Drug solubility	High (for hydrophobic drugs)	Limited
Skin penetration	Enhanced	Moderate
Greasiness	Non-greasy	Often greasy
Stability	High	Lower
Patient compliance	Excellent	Moderate

TYPES OF EMULGEL

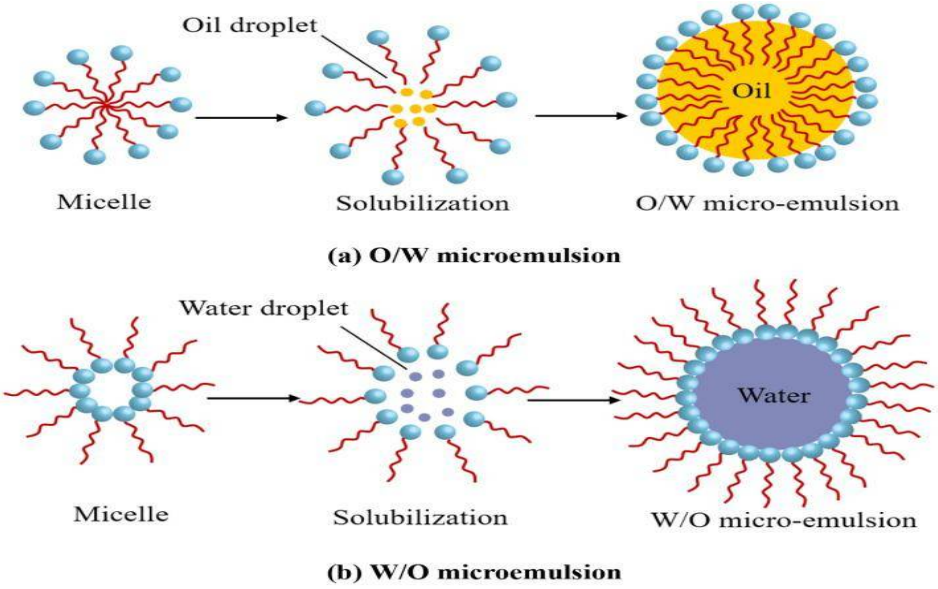

Figure 2: Micro emulsion

MICRO EMULSION

Microemulsions are optically transparent, thermodynamically stable, isotropic mixtures of an oil-in-water system stabilised with a surfactant. The droplets do not coalesce and range in size from 10 to 100 nm. They are made up of precisely the right proportions of water, surfactant, co-surfactant, and oil. The capacity to dissolve both water-soluble and oil-soluble chemicals, as well as having a broad interfacial region and extremely low interfacial tension, are among the special qualities of microemulsions. These components can increase medication penetration via minimising the diffusion barrier in the stratum corneum.But due to their unsatisfactory skin retention and low viscosity, microemulsions are not widely used in the pharmaceutical sector. This is overcome by adding gelling agents to microemulsion-based gels, such as guar gum, Carbopol 940, and HPMC K100M, which have the proper viscosity for topical application.

NANOEMULGEL

The term "nanoemulsion" describes transparent (translucent) oil-water dispersions with globule sizes ranging from 1 nm to 100 nm that are thermodynamically stable because they contain molecules of surfactant and cosurfactant. It is called Nanoemulgel when mixed with a gel. When using Nanoemulsion instead of more conventional formulations like emulsions and gels, many medications gain better transdermal penetration. Both in vivo and in vitro, nanoemulsion demonstrates enhanced transdermal and dermal transport capabilities. Because of its small globule size and high loading capacity, the medication can enter the skin more quickly and have therapeutic effects.

MACROEMULSION GEL

Particle sizes of emulsion droplets bigger than 400 nm are present in emulgels. Under a microscope, individual droplets can be readily detected even though they are invisible to the unassisted eye. Despite their thermodynamic instability, surface-active materials can help to stabilize macroemulsions. [12]

ADVANTAGES AND DIS-ADVANTAGES OF EMULGEL

ADVANTAGES

1. Hydrophobic medicines are easily absorbed into gels by employing d/o/w emulsions. Most hydrophobic medications cannot be directly mixed with other medications. because solubility functions as a barrier and creates problems when the material is discharged, into the gel base. Emulgel spreads oily globules in the aqueous phase, making it easier for hydrophobic medications to be incorporated into the oil phase and produce an oil in water emulsion. Moreover, this emulsion can be used with gel bases. This may be demonstrating better drug stability and release when compared to simply adding drugs to a gel base.
2. Increased stability: Compared to other transdermal preparations, emulgels have a higher level of stability. Creams exhibit phase inversion or breakdown, ointments exhibit rancidity, and powders are hygroscopic. because of the greasy foundation.
3. Increased loading capacity: Liposomes and niosomes have vesicular characteristics and are nanosized, which makes them prone to leaking and other issues. less the trapping's effectiveness. However, the loading capacity of gels with a vast network is much higher.
4. The quicker and easier steps in the emulgel manufacturing process increase the feasibility of production and reduce preparatory costs.production. Specialised equipment is not required for the production of emulgels. The materials are also easily accessible and less priced.lowers the price of making emulgels as a consequence.
5. Lack of powerful sonication: The production of vesicles necessitates intensive sonication, which may lead to drug degradation and leakage. But this There are no problems because sonication is not needed in the emulgel production process.
6. Controlled release: Emulgels can make medications with shorter half-lifes last longer[13,14].
7. avoiding the first-pass metabolic pathway.
8. Keeping the gastrointestinal tract compatible.
9. increased compliance from patients.
10. Easy to use and simple in design[15].

DIS-ADVANTAGES

1. dermatitis resulting in skin irritation upon contact.
2. the possibility of allergic responses.
3. Some drugs don't have enough skin permeability.
4. Large-particle drugs are hard for the skin to absorb.
5. The production of bubbles while making emulgel[16].

COMPONENTS OF EMULGEL

1] AQUEOUS MATERIAL

It creates the emulsion's water phase. A common combination of agents is alcohol and water[17].

2]OILS

The oily phase of the emulsion is produced by these materials. Mineral oils work well for external application emulsions, either on their own or in addition to hard or soft paraffins. Typically employed for both the occlusive and sensory effects of the medicine as well as its delivery system. Oral remedies sometimes contain fish liver oils or other fixed oils of various kinds, as well as nonbiodegradable mineral and castor oils with a laxative effect on the surrounding area.vegetable-based dietary supplements, such as oils derived from arachis, cottonseed, and maize[18,19].

3] EMULSIFIERS

Emulsifying substances are used for purposes other than just encouraging emulsification during manufacturing, but also to regulate stability during a possibly varied shelf life. Days for emulsions created on the spur of the moment, and months or years for commercial formulations. For instance, 40% polyethylene glycol [20].

An emulsifier is used to improve the emulsification of the formulation in order to improve the stability of the shelf life. Stearic acid, Tween 20, Span 80, Tween 80, and other substances are examples of emulsifiers [21].

4]GELLING AGENT

These thickeners also have the ability to improve the consistency of any dosage form. Some of the gelling agents are HPMC-2910, Carbopol 940, and Carbopol 934[22].

5] PENETRATION ENHANCER

These chemicals interact and partition into skin components, causing a temporary and reversible increase in skin permeability [23].

PROPERTIES OF PENETRATION ENHANCERS

1. They must be free of irritants, toxins, and allergies.
2. If they were to act swiftly, their activity and duration would ideally be predictable and repeatable.
3. They shouldn't bind to receptor sites and have no pharmacological action in the body[24].

MECHANISM OF PENETRATION ENHANCERS

One or more of the following main mechanisms may be used by penetration enhancers to carry out their functions:

1. disturbing the lipids in the stratum corneum's well-organised structure.
2. interacting with proteins that are between cells.
3. facilitating better medication, co-enhancer, or solvent partitioning into the stratum corneum[25

PREPARATION OF EMULGEL

To make the gel in the formulations, the polymer was dissolved in purified water and constantly swirled at a reasonable speed. After that, TriEthanolAmine (TEA) was used to adjust the pH to 6.5. Tween 80 was dissolved in filtered water to create the water phase of the emulsion, while Span 80 was dissolved in liquid paraffin to create the oil phaset. Whereas capsaicin was dissolved in ethanol, methyl paraben was dissolved in propylene glycol. The two solutions were subsequently combined with the aqueous phase. Clove oil was added to the oil phase to enhance penetration.

Heats ranging from 40° to 50°C were applied separately to the oily and aqueous phases. Subsequently, the aqueous phase was combined with the oily phase and continuously mixed until the mixture reached room temperature [26].

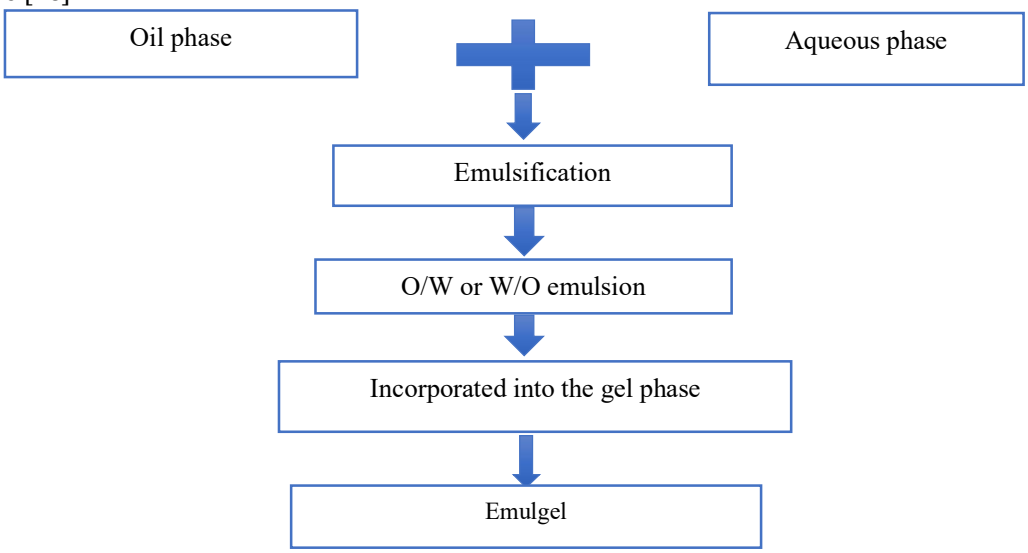

Figure 3: Method for preparation of emulgel

CHARACTERIZATION OF EMULGEL

Physical Appearance

The prepared formulation's physical qualities are observed by visually inspecting it for colour, consistency, and homogeneity [27].

Determination Of PH

A digital pH meter is employed for monitoring each prepared emulgel's pH level. Prior to usage, the pH-meter is calibrated using a standard buffer solution. One gram of the formulation should be dissolved in one millilitre of distilled water to generate a homogenous suspension, and the mixture should be left for two hours. After this period, the glass electrode is dipped into the suspension to measure the pH.[28,29].

Rheological Study

Viscosity is assessed in a rheological analysis at 25 ºC using a cone and plate viscometer [30].

Spreadablity

The spreadability of the emulgel formulations was evaluated 48 hours after manufacture by measuring the diameter of 0.5 g of emulgel, which was deposited inside a pre-marked circle with a diameter of 1 cm on a glass plate over which another glass plate weighing 75 gm was placed. A 425 g weight was left on the upper glass plate for five minutes, during which time it was not expected to spread any further [31].

It was observed that the spreading of the gels had expanded the diameter. The spreadability (g.cm.min-1) should be calculated.

The following equation was applied:

$$S = m \times 1/t$$

where S is the spreadability, m is the weight of the upper plate while it is sitting on it (g), 1 is the diameter (cm) of the spreading emulgel, and t is the required amount of time [32].

Zeta Potential

Zetasizer (Malvern Zetasizer) is used to determine the emulgel preparation's zeta potential. The mixture is put into a clear, single-use zeta cell, and a conclusion is reached. Before the experiment, cuvettes are washed with methanol and then the material is placed inside [33].

Particle Size And Polydispersity Index(PDI)

Making use of a Malvern Zetasizer (the ZS90 device). Emulgel globule size is determined at 250 degrees Celsius. The sample is diluted at the start of the experiment [34].

Stability Study

When conducting stability studies, stress is induced at two different humidity and temperature ranges (room temperature 30C±20C, RH 65%±5%, and room temperature 40C±20C, RH 75%±5%). A stability chamber that has the right number of excipients (API-0.1gm, oil-2.5gm, surfactant-6.665gm, co-surfactant-13.33gm, and double-distilled water 27.15ml) is used. Physical characteristics like turbidity, particle growth, and variations in clarity are tracked during the course of the one-month study[35].

Swelling Index

Separately, In a 50 ml beaker filled with 10 ml of 0.1 N NaOH, 1 mg of gel is spread out over permeable aluminium foil. The sample is removed from the beaker, allowed to air dry, and then weighed once again at different intervals [36].

The formula for calculating the swelling index (SW) is

$$SW=[(Wt - Wo) / Wo] \times 100.$$

Where

The equilibrium percentage swelling is denoted by SW%.

Wo is the emulgel's initial weight at time zero.

Wt is the emulgel's swelling weight.

DRUG CONTENT DETERMINATION

The drug concentration in the gelled emulsion was measured with a spectrophotometer. To determine the drug content, a predefined volume of the gelled emulsion was sonicated and dissolved in methanol. After the appropriate dilution, the absorbance was measured using a UV/VIS spectrophotometer. [37].

9.In Vitro Drug Release Study: -In order to perform the emulgel in-vitro drug release profile, diffusion cells with a dialysis membrane are used. For nine to twelve hours, this membrane is submerged in a pH 5.5 phosphate buffer. Next, it is positioned at one end of the cylindrical tube of the cell, and the emulgel is applied uniformly over it. The same pH 5.5 phosphate buffer is added to the neighboring receptor compartment, and the test is conducted with constant mixing and temperature control at 37°C. The amount of medication released is measured using a UV spectrophotometer by taking 5-millilitre samples at regular intervals. The medication's standard curve and absorbance data are used to compute the percentage of drug release [35].

Skin Irritation Test

Rats that have been shaved are used in this test, which is also known as the patch test. A designated amount of emulgel is applied to a skin area measuring 2.54 cm by 2.54 cm. After that, the application site is observed for any negative side effects, like redness, irritation, morphological changes, or inflammation. Eight rats are used in the test, and if more than two of the rats exhibit negative reactions, the emulgel is deemed to have failed [38].

PACKAGING OF EMULGEL

Emulgel is typically supplied in aluminum-laminated tubes with a moulded seal and a propylene screw cap, or in membrane-sealed, lacquered aluminium tubes with an interior coating based on phenoxy-epoxy (Public Assessment Report of Voltaren Emulgel). The look of plastic and the advantages of aluminium are combined in these laminated tubes. In order to maximise the graphic area, the most recent generation of laminate tubes uses trimming technology. The laminate layer blocks the flow of moisture, light, and air. It is made up of two layers: a plastic layer for visual appeal and an aluminium layer for structural stability [39]. In addition to providing a high-gloss protective lacquer, this barrier can also act as a resistant barrier for products that require maximum compatibility and minimise the absorption of tastes.

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