



# Emulgel: A Boon to Permeability Enhancement

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## Abstract:

Topical drug delivery is a convenient mode of drug delivery to treat local infections. Topical medications are available in many dosage forms, such as creams, ointments, gels, pastes, and lotions. Both emulsions and gels are well known for their benefits as topical preparations with few limitations and called as emulgel. The literature on emulgel formulations was searched in may2023 from various scientific journal articles. From a total of 110 searched articles, 12 duplicated articles and 39 irrelevantly judged on the abstract or full papers were excluded. Finally, 53 articles were selected for review. Emulgel possesses many promising properties for dermatological use such as being greaseless, easily spreadable, emollient, easily removable, non-staining, longer shelf-life, transparent, having a better physical appearance and having less potential to cause serious side-effects due to lower blood exposure. Many formulation scientists have started to develop emulgel by using various active pharmaceutical ingredients, especially those are hydrophobic in nature such as Luliconazole, Ketoconazole, Mefenamic Acid, etc. We conclude that formulated emulgels have shown excellent results in aspects such as appearance, rate of drug penetration to skin, rate of drug release and therapeutic response. This review article is mainly focused on formulation, ingredients, methods, and characterization of emulgel formulations.

**Keywords:** Emulgel; Gelling agent; Gel; Emulsion; Emulsifier

## Introduction:

Topical administration of drug is simplest and easiest route of localized drug delivery system anywhere in the body as compare to other routes such as ophthalmic, rectal, vaginal and skin. These are applied as wide spectrum of preparations in case of both cosmetic and dermatological fields, to the healthy or diseased skin.[1]

A topical drug delivery system is a way to deliver the Active Pharmaceuticals Ingredient that is applied onto a particular part of the body, generally the skin, to obtain the localizing effect of drug.[2] Topical drug delivery system has many advantages over other drug delivery system such as the capability of formulation to deliver drug more selectively to the specific site and it avoid the incompatibilities associated with gastro-intestinal region.[3] along with this, topical delivery of the drug by avoid first pass metabolism which provides an increased bioavailability and consistent delivery for an extended period of time.[4] In topical drug delivery system, drug reaches to the target site via diffusion and their absorption takes place through the skin. Percutaneous absorption can be improved by increasing the rate of the drug release from dosage form.[5] The

rate of drug release from topical drug delivery system depend straight forwardly on various physical, chemical properties of the carrier and the drug which utilized. Since the mid-1980s, emulgel have been picking up significance in pharmaceutical topical semisolid dosage forms.

### What is Emulgel?

Generally emulgel are emulsions having gel like consistency, either it has water-in-oil or oil-in-water phase.[6] The emulsions are the way of drug delivery which provide controlled release dosage form in which the active constituents are entrapped in internal phase with the help of emulsifying agent and passes the external phase to the skin and gets absorbed slowly. The drug reaches to the external phase of the skin in a controlled manner through the internal phase which act as a reservoir of the drug. Gel traps small drug particles which results in its release in a controlled manner due to cross-linked network formed by gel. Because of this emulgel acts as dual control release system It increases the contact time of medication over the skin because of its mucoadhesive property.[7] Emulgel has the properties of both gel and emulsions therefore it is called as emulgel.[8]

Largely, pharmaceutical preparations which are intended to be applied on skin are expected to give some local action and are designed to provide long-term local contact with minimal systemic drug absorption. Some pharmaceutically ingredient applied to the skin for their local action such as antiseptics, antifungal agent, skin emollients and protectants. The topical drug delivery system allows its usage where the others system of drug administration fails or it is mainly used in treatment of fungal infection.

Gels that are used for dermatological property have some positive properties, that is, being emollient[9,10] thixotropic, greaseless, easily removable, non-staining and compatible with various excipients. The rate of drug release, and stability of incorporated drug, can be affected by the type and concentration of polymer which forms the gel. Emulgel may serve as a better alternative when it is concerned with the topical application of less water soluble drug. It is proven better and a stable vehicle for less water-soluble or hydrophobic drugs.[11]

The drug particles can basically penetrate into skin by three routes: through intact stratum corneum, through sweat ducts, or through sebaceous follicle. The outer most layer of skin, that is stratum corneum contains more than 99% of the total skin surface available for percutaneous drug absorption. [12] Penetration of drug through this outer most layer is rate limiting step in percutaneous absorption of drug molecules. The concentration gradient is act as a driving force in percutaneous absorption, So the establishment of a concentration gradient is important for drug movement across the skin, release of drug from the carrier (partition coefficient), and drug diffusion across the layers of the skin (diffusion coefficient). Ideal characteristics for topical drugs dosage form involve molecular mass (600 Da), proper hydrophilic and lipophilic balance, and a high partition coefficient. Except for particles of smaller size, stratum corneum contains lipids therefore water soluble ions and polar molecules do not penetrate intact stratum corneum. Topical formulation can be used to alter the barrier function of the skin, for example, topical anti bacterial and antibiotics help a damaged barrier toward off infection, sunscreens agents and the horny layer protect the skin tissues from Ultraviolet rays and emollient preparations restore pliability to a desiccated horny layer [13]. In this review we represent the overview of emulgels its properties and aspects of the formulation.

### Advantages:[14,15]

**Controlled release:** In case of emulgel, it is possible to give sustain release of those drugs which having shorter half life.

**Better loading capacity:** Gels have higher loading capacity as compare to other dosage forms due to their lower entrapment efficiency shown by them because of their Nano size.[16]

**Better stability:** Most of the transdermal dosage forms are comparatively less stable than emulgels. Like powders are hygroscopic, ointment shows rancidity due to oily base and creams show phase inversion or breaking.[17]

**Incorporation of hydrophobic drugs:** The hydrophobic drug molecules cannot be added directly to the gel bases due to the improper release of drug due to lesser solubility. In case of emulgel, the addition of such hydrophobic drugs in the oil phase which leads to the dispersion of oil globules in aqueous phase which results in a formation of o/w emulsion. Further this emulsion can be simply added to the gel base, and it provides good stability and better drug release to dosage form.[18,19]

**No intensive sonication:** Production Sonication of formulation results in the degradation of drug substance, But this problem is not seen in emulgel production as no sonication is required.

**Low preparation cost:** There are no special instruments required for the production of emulgels. And also materials used are easily available and low cost. This, results in low production cost of emulgels.

**Enhance patient compliance:** Incorporation of drug substance in emulgel dosage form increases patient compliance as they are less greasy and easy to apply on the surface of the skin.[20]

### **Disadvantages:**

There are so many advantages of emulgel formulation over other conventional dosage form, emulgels also have some disadvantages along with advantages which then results in major limitations in the delivery of hydrophobic drugs [21].

The major disadvantages are that the drugs which has a larger particle size is cannot pass through the skin, permeability is poor, skin allergy or contact dermatitis may occur, or a bubble may appear when emulgel is applied. [19,22]

### **Material required for preparation of an emulgel:**

#### **Aqueous material**

Hydrophilic materials that are used mostly for an aqueous phase in emulgels are water and alcohol [23].

#### **Oil**

Various oils are being used in the formation of emulgels. Mineral oil, vegetable oil, or fish liver oil is mostly used for the oil phase. Non-biodegradable mineral oils are most widely used in a preparation of emulgel, Castor oil provides a local laxative effect; other vegetable oils, such as cotton seed, Arachis and maize oil are used as source of nutrition [24,25]. Following are different types of oils; Isopropyl palmitate, Isopropyl myristate, Isopropyl stearate, and liquid paraffin [26].

#### **Emulsifying Agents**

Emulsifier are added in the formulation of emulsion to promote emulsification and to control stability. Tween-20, 40, 60, 80, PEG-40, stearic acid, sodium stearate is most widely used Emulsifying agents [24].

#### **Thickening agent**

Thickening agents are used to enhance consistency and can also be used as gelling agents [27]. Most commonly used agents are Carbomer 934, 940, sodium alginate, sodium CMC and gellan gum [26]. Various gelling agents have been used some of them are as follows; Carbopol-940, HPMC 2910, Carbopol-934, HPMC, Sodium C.M.C., etc. [28].

#### **Permeation enhancer**

These agents are used to increase temporary skin permeability. They cross into and interact with the constituents of skin [29]. Clove oil, olive oil, sodium lauryl sulphate, palmitate, lecithin [5%], and oleic acid [1%] is most widely used [30]. Different penetration enhancers are used some of them are as follows; Lecithin, Oleic acid, Urea, Menthol, Iso-propyl myristate, Eucalyptus oil [29].

### Properties of penetration enhancer

Following are the few characteristics that should be considered before using a penetration enhancer during the preparation of emulgel.

- They does not have any pharmacological action inside the body. It implies that they do not bind to any of the receptor sites [31].
- They are cosmetically available and should not cause any type of skin irritation [32].
- Properties like non-toxicity, less irritability, and non-unfavourably susceptibility should be present [33].
- They show favourable compatibility with the drugs and the excipients added [34].
- When it is removed from the skin, barrier properties should return rapidly [35].

### Preparation method:

There are three basic steps involved in the emulgel preparation, which are demonstrated in Figure 1.

#### Step 1

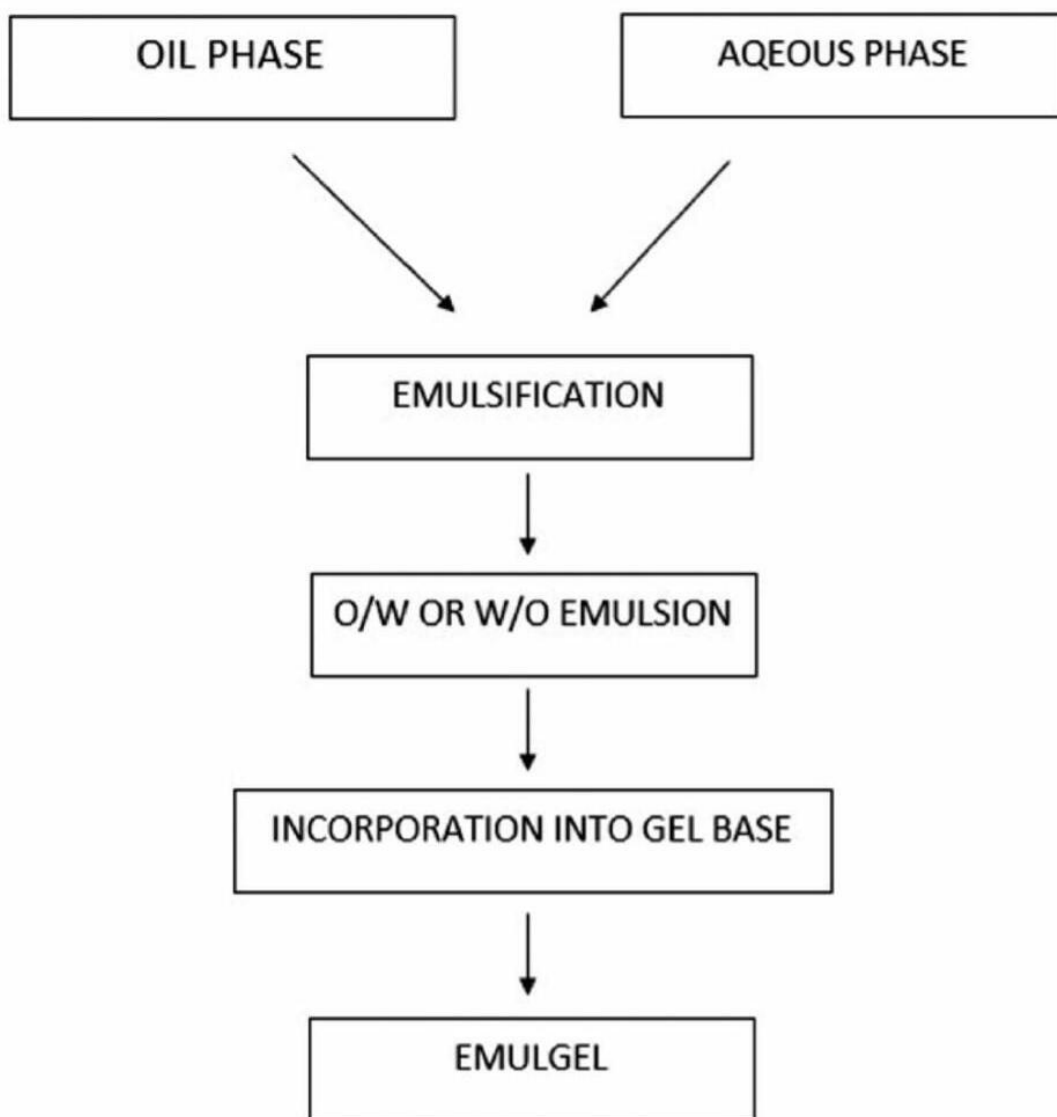
In the initial step the emulsion was formulated which involves the dissolution of oil-soluble substances in the oil vehicle (e.g. dissolving span 20 in liquid paraffin) and the dissolution of the water soluble substances in the aqueous vehicle (e.g. dissolving tween 80 in purified water). Both phases were mixed under turbulent mixing conditions. The formulated emulsion may be O/W or W/O type. [36,37,38]

#### Step 2

After formulation of emulsion a gel base is formulated by adding gelling agents and water with simultaneous stirring and optimization of their pH.

#### Step 3

In last step of emulgel formulation incorporation of the emulsion into gel base with continuous stirring and heating occurs [39].



**Fig.1. Steps of emulgel preparation**

#### **Compatibility studies:**

To check the compatibility of active pharmaceuticals with the excipients used, TheFT-IR spectroscopy (FT IR- 8400-S, Shimadzu, Japan) was employed. The spectra of individual drug substance and the final formulated product containing excipients were compared for confirmation of common peaks.

#### **Evaluation Parameters of emulgel:**

##### **Skin Irritation test**

It is also known as patch test. In all topical preparations the most important evaluation parameter is skin irritation test. In this, a set of rats are chosen for test. Emulgel is applied legitimately on the skin of the rat. Undesirable skin

##### **Globule size**

The globular size obtained was determined using Zetasizer (Malvern Instrument 3000HSA, UK). The sample was diluted and the globule size was measured at 25 °C.

## Determination of pH

The pH of formulated emulgel was find out with the help of pH meter by dipping the glasselectrode into the emulgel.

changes, i.e. alter incolour and skin morphology was observed after 24 hours [40].

## Rheological studies

The viscosity of emulgel formulation is determined at 25°C using a Brookfield viscometer which consists of a spindle, i.e. no 96, at 1.5 rpm [41]. The assembly was connected to a temperature controlled circulating water bath which maintained temperature of 25°C [42]. The sample is added to the beaker, and the spindle was allowed to move freely, and reading was noted [43].

## Physical Appearance

All the prepared formulations were visually checked for the colour, appearance, homogeneity and phase separation.

## Photo-microscopy

One of the best batch of the emulgel was viewed under light micro-scope to study the globular structure in gel base. The emulgel was diluted, pour a drop on glass slide and viewed by light microscope under magnification of 40.

## Swelling index

Weight one gram of sample and take it on a permeable aluminium foil, at that point put in a 50 ml container containing 10 ml of 0.1 NaOH. Further, the samples were taken out from the containers at different periods and were placed at a non-hydrated surface. After a specific time, it is reweighed [44].

## Determination of drug content

Drug content was determined by using U.V Spectrometry. It is done by taking 1 g of sample and mix it with an specific solvent then filter it to obtain a clear solution. Determine its absorbance by using a UV spectrophotometer [45]. On the other hand, a standard calibration curve of a drug was prepared in the same solvent [46]. Its concentration and medicate substance can be decided by utilizing the same standard curve by putting the values of absorbance [47].

## Homogeneity

The formulation is tested for its homogeneity by visual appearance after emulgel was applied on a slide as a thin layer [48].

## Spreadability

Spreadability is one of the criteria for an emulgel to touch an ideal properties. It is a term which expressed to denote the extent the area to which the drug spreads readily on the skin surface when it applied. Mutimer is an apparatus which used to determined the Spreadability of sample [49]. It consists of a wooden block that is attached to a pulley at one end glass slide was placed on a wooden block [50]. An amount of emulgel was placed on the ground slide and then emulgel preparation was sandwiched between both sides [51]. The time required to cover a distance of 5 cm for the top slide was measured [52]. The shorter the time period to travel indicates a better Spreadability [53].

## Conclusion:

This article revised sufficiently about emulgels as author covers all of the major points and issues, also highlighted their importance. Most of the drugs are available in hydrophobic form and there is a challenge to formulate the dosage form by incorporating these drugs. When we consider the delivery of these kind of drug topically (i.e. Creams, lotion, ointments, emulsions, etc.) Due to the water heating nature of the drugs, the issue of stability and bioavailability arises in case of numbers of dosage forms [77]. To overcome this problem, a

modern concept of the formulation is presented, i.e. emulgel. In which the drug is incorporated in the oil phase of the emulsion and the emulsion is merged in gel base which gives the controlled release effect. Furthermore, it also increases the bioavailability of the drug. Emulgel is a very useful topical dosage form and is a great addition to dermatological pharmacotherapy. Since emulgels possess various properties such as Spreadability, viscosity, adhesion, etc. they increase patient compliance; when used for hydrophobic drugs, it will increase its effectiveness and reduce its adverse effects.

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