



EMULGEL: AN EMERGING APPROACH TOWARDS EFFECTIVE TOPICAL DRUG DELIVERY

L V Vigneshwaran^{1*}, Yusra Hameed K A², Azmin Farnaz A H³, Fathimath Anseera P A⁴, Shyma Nasreen⁵, Ajith Babu T K⁶, Sebastian V⁷

Department of Pharmaceutics, Malik Deenar College of Pharmacy Seethangoli, Bela, kasaragod, kerala 671321, India.

*Corresponding Author

L V Vigneshwaran

Department of Pharmaceutics,
Malik Deenar College of Pharmacy
Seethangoli, Bela, kasaragod, kerala
671321, India.

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Abstract: Dosage forms for topical drug delivery systems are applied directly to the skin in order to treat a variety of illnesses. The most recent and widely used drug delivery technology for hydrophobic medications is emulgels. Different polymers are used to prepare emulgel, which serves as both an emulsifying and thickening agent. The gelling capacity reduces surface tension and interfacial tension, increasing the viscosity of the aqueous phase and producing stable emulsions and creams. Emulgels offer significant advantages over both traditional and new vesicular systems when taking into account a number of factors. This formulation, which combines gel and emulsion, is thought to be a novel kind of drug delivery method. Emulgel is a highly promising product for use in dermatology since it is translucent, has an exquisite appearance, is greaseless, readily removed, easily spreadable, emollient, non-staining, and has a longer shelf life. It also has less potential to cause major adverse effects.

Keywords: Topical drug delivery system, Emulgels, hydrophobic drugs.

INTRODUCTION

One of the largest sense organs in the human body, the skin serves as the body's first line of defense and carries out a number of vital tasks. The operation of a drug- containing expression to the skin in order to directly treat a cutaneous condition is known as topical medicine delivery. Topical medicine delivery ways are distributed substantially grounded on density; these density include semi-solids, liquids, solids, and other medications. One of the main downsides of this strategy is that the topical medicine administration styles presently in use can only deliver hydrophilic specifics; they cannot deliver hydrophobic medicinals. Among the lately created phrasings that can give both hydrophilic and hydrophobic specifics is Emulgel. It shares parallels with gels in that they're made of a colloidal network that can hold a lot of water or hydroalcoholic result. Gel phrasings, as opposed to ointments and creams, generally offer briskly drug release. Gels have numerous benefits, but one significant debit is their incapability to distribute hydrophobic specifics. Emulgels are therefore designed to overcome this limitation, and hydrophobic medications can benefit from the unique properties of gels by employing them.^[1] The term "Emulgel" is a blend of emulsion and gel. The medicine's characteristics and the intended point must be taken into consideration while choosing a cure form. In addition, a number of physiochemical variables, similar as skin consistence, pH, hydration, lipid content, blood inflow, hair follicle viscosity, sweat gland viscosity, partition portions, molecular weight, etc., also affect how passable the drug is.

Emulgel

Emulgel is a combinational formulation made up of gel and emulsion; the kind of combination used relies on the medicine's nature in order to maximize bioavailability. Emulgel's advantages over conventional topical treatment including being thixotropic, greaseless, having superior spreadability, being easily removed, being biodegradable, emollient and having lesser convenience. Also, Emulgels high stability and longer shelf life are motivating researchers to produce new products in this class. It shares resemblances with gels in that they are made of a colloidal network that can hold a lot of water or hydroalcoholic solution. It provides advanced solubility of drugs and hence enhanced the penetrability of the drugs and consider as one of the ideal approach of topical delivery of drugs. In addition to the gels' advantages, emulgels were created to get around their inability to deliver lipophilic medications.^[2]

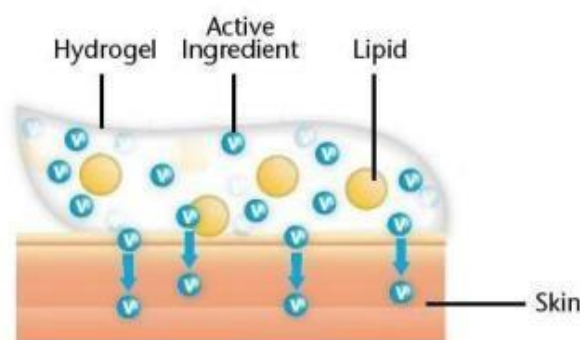


Figure no 1: Structure of Emulgel

Factors Affecting Topical Absorption of Drug

Physiological function

- Skin thickness
- Lipid content
- Density of hair follicle
- Density of sweat gland
- pH of the skin
- Blood flow
- Skin hydration
- Skin inflammation

Physiochemical function

- Partition coefficient
- Molecular weight (<400 Dalton)
- Degree of ionization (only unionized drugs gets absorbed well)
- Effect of vehicles

Factors to be considered when choosing a Topical Preparation

- Effect of vehicle e.g. An occlusive vehicle increases the active ingredient's penetration and boosts its effectiveness. The vehicle itself could function as a drying, emollient, cooling, or protecting agent.
- Match the type of preparation with the type of lesions, for example, avoid greasy ointments for acute weepy dermatitis.
- Match the type of preparation with the site, for example gel or lotion for hairy areas
- Irritation or sensitization potential generally ointments and w/o creams are less irritating, but gels are irritating, do not contain preservatives or emulsifiers if allergy to these agents is a concern. ^[3]

Classification of Emulgel ^[4]

Based on the size of its particles, emulgel can be divided into three main categories: macroemulgel, nanoemulgel, and microemulgel.

Macroemulgel: The most popular emulgels, known as macroemulgels, have particles larger than 400 nm. These emulgels are homogeneous and opaque, but because of their enormous particle sizes, which make them thermodynamically unstable, the emulsion droplets are plainly visible under a microscope.

Nanoemulgel: The goal of creating a clear, uniform, thermodynamically stable dispersion is achieved by combining nanoemulsion with gel to create nanoemulgel. In the case of nanoemulgel, droplet sizes are less than 100 nm, allowing for improved permeability.

Microemulgel: Microemulgels are preparations that function as a thermodynamically stable formulation and have particle sizes between 10 and 100 nm. Microemulgel formulation helps the medication penetrate the skin and go to the intended location. Furthermore, the shortcomings of gels and microemulsions can be solved by microemulgels. The primary benefits of microemulgel

over other conventional topical treatments are its high viscosity, permeability, and homogeneity.

Microemulgel: Emulgels are primarily used to provide the perfect formulation for administering both hydrophilic and lipophilic medications by combining emulsions with the gel. Depending on the type of medication, the emulsion used to produce Emulgel may be water in oil or oil in water. This helps to improve the drug's bioavailability through optimal formulation. Aqueous material, oils, emulsifiers, gelling agent, and permeation enhancer are the main ingredients of Emulgel.

Method of preparation of Emulgel ^[5]

STEP 1: Formulation of Emulsion either O/W or W/O

STEP 2: Formulation of gel base

STEP 3: Emulsion incorporation into gel base while shaking constantly.

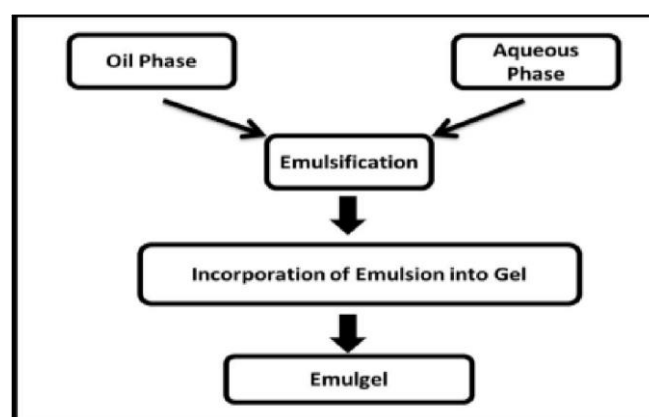


Figure no 2: Flowchart of emulgel formulation

Components of Emulgel

Emulgels mainly incorporate emulsions with the gel to develop ideal formulation for delivering the lipophilic as well as hydrophilic drugs. Depending on the type of medication, the emulsion used to prepare Emulgel may be water in oil or oil in water. This helps to create the optimal formulation, which in turn improves the drug's bioavailability. Aqueous material, oils, emulsifiers, gelling agent and permeation enhancer ^[6]

Aqueous material: The most often employed aqueous materials that make up the aqueous phase of emulsion are water and alcohol.

Oils: Mineral oils are the most widely utilized oils for the formation of emulgels. Oils are used for the development of the oily phase of the emulsion. One can use the mineral oil alone or in combination with other oils, particularly soft and hard paraffin. In addition, considering its laxative qualities, castor oil can also be applied. Jojoba oil, arachis oil, cottonseed oil, maize oil, fish liver oil, and others are more examples of oils that are utilized for their therapeutic qualities.

Emulsifiers: The most essential component for maintaining the stability of emulsion is emulsifier, which are generally surfactants used for the process of emulsification. Mineral oils, such as liquid paraffin, have an HLB of less than 8, which makes them suitable for the development of water in an oil emulsion, whereas nonionic surfactants, such as spans and tweens, with an HLB higher than 8 are employed for the production of oil in water emulsion.

Emulsifiers including sodium stearate, Span 80, Tween 80, stearic acid, and PEG 40 stearate are among the most often used ones.

Gelling agent: These components are utilized to give the formulation gel-like qualities, which enhance consistency. Various studies have shown that the degree of drug release has an inverse relationship with the gelling agent concentration. For the formation of emulgel, the most widely used gelling agents include Carbopol, HPMC 2910, HPMC K4M, etc.

Permeation enhancer: These are the agents responsible for improving the penetration power of drug by implementing various mechanisms to improve the permeability of skin. One of the main mechanisms is the rupture of the stratum corneum or the modification of skin proteins. Some of the most commonly used ingredients for enhancing the permeability are oleic acid, clove oil, lecithin, eucalyptus oil, menthol etc.

EVALUATION OF EMULGEL [7]

Physical appearance: The physical characteristics of the prepared emulgel are examined by considering the pH, phase inversion/separation, grittiness, homogeneity, color, and consistency. An accurate digital pH meter is used to measure the pH after preparing a 1% solution of the emulgel.

Drug content measurement: One gram of emulgel is mixed with a suitable solvent in a sonicator to create a solution, which is then used to measure the drug content. After the solvent has been created, it is filtered, and a UV spectrophotometer is used to detect absorbance.

Drug content = (concentration x Dilution Factor x Volume Taken) x Conversion factor

Rheological Studies: One of the key parameters for emulgel is viscosity, which is determined at a temperature of 25°C using a Brookfield viscometer. The emulgel is added to the beaker, the spindle is free to circulate within the beaker, and the digital indicator's reading is recorded in order to determine the viscosity.

Spreadability: Spreadability, a measurement of the emulgels slip and drug abilities, is calculated by dividing the spreading coefficient with the equipment the Multimer recommends. The ground glass slide was placed over a wooden block that is part of the equipment and is connected by a pulley. The slide is covered with around 2 grams of emulgel, which is then sandwiched between a fixed slide and a moving slide of the same size. After that, a 500g weight is applied to the sandwich and left there for five minutes to create a consistent layer of emulgel on the slides. Next, a specified amount of weight is added, and the time it takes the slides to travel 5 cm is recorded.

$$S = M.L/T$$

Here, S = spreadability M = Weight applied L = Length of glass slide T = time taken to cover distance of 5 cm

Extrudability Test: Extrudability is a measurement that indicates the force needed to extrude the material out of the emulgel-filled tube. It is computed by weighing how much weight is needed to extrude a 0.5-centimeter emulgel ribbon from an aluminum tube in 10 seconds. Typically, this test is run with three readings, and the average of all the measurements is determined using the method that follows:

$$\text{Extrudability} = \text{Weight Applied (gram)} / \text{Area (cm}^2\text{)}$$

Skin Irritation Test: Another name for this test is a patch test. Rats that have had their heads shaved before the test are utilized in this experiment, and a predetermined quantity of emulgel is administered to an area measuring 2.54 cm by 2.54 cm. Next, the application site is checked for any negative side effects, such as redness, irritation, morphological changes, inflammation, etc. Eight rats are used in the test, and if more than two rats experience an adverse event, the emulgel will fail the test.

Globule Size and Zeta potential: Similar to the emulsions, the emulgels are also assessed for zeta potential measurement and globule size, which point to the stability of the formulation. Zetatrac is used for this test, which calculates potential by taking into account charged particle response to an electric field.

Bioadhesive strength Measurement: This test measures the emulgel's force of adhesion and is conducted with the aid of a device that consists of two arm balances. Two glass plates with fresh rat skin are placed in one arm, while a single glass plate is placed in the other. After then, weight is added to both arms to balance them, and the balance is maintained at 10844 for five minutes. In order to conduct the test, approximately 1g of emulgel is taken and sandwiched between the two rat skin-containing slides so that they adhere to one another. Following this, additional weight is applied to the other arm at a rate of 200g per minute until both slides separate. The weight at which the slides separate is taken into consideration as an adhesive strength parameter and is computed using the formula below:

$$\text{Bioadhesive strength} = \text{Weight required (in gram)} / \text{Area(cm}^2\text{)}$$

Stability studies: The ICH guidelines are followed for conducting the stability studies, with an overall preference for quicker studies. After inserting the emulgels into the collapsible tubes, the temperature is adjusted to 37 ± 2°C, 45 ± 2°C, and 60 ± 2°C for three months, with a relative humidity of 60% to 75%. Every 15 days, the samples are analyzed for characteristics like pH, rheology, physical appearance, drug content, and drug release profiles.

In – vitro Drug Release study: Diffusion cells are used to conduct the in-vitro drug release profile of emulgel, a process that requires the usage of dialysis membrane. The dialysis membrane is immersed in phosphate buffer (pH 5.5) for nine to twelve hours in order to perform this test. This membrane is positioned at one end of the cell's hollow tube, and emulgel is evenly deposited on top of it. The phosphate buffer pH5.5 is poured into the receptor compartment, which is next to the donor compartment. Throughout the test, the solution is continuously mixed and the temperature is kept at 37°C. Following that, 5 milliliters of sample are taken out of the solution on a regular basis, and the amount of drug release is estimated using a US spectrophotometer. Next, using the medication's standard curve and absorbance value, the percentage of drug release is computed.

Swelling index: When assessing the emulgel, the swelling index is also taken into account. To measure it, lay one gram of emulgel on aluminum foil and place it in a 50 ml beaker with ten milliliters of 0.1N NaOH. After that, the samples are taken out of the beaker and dried on a regular basis. The following formula is used to determine the change in weight, which is regarded as a parameter of the swelling index:

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

In this case, W_t = Emulgel's weight at time t W_0 = Emulgel's weight at time zero

Ex - Vivo Permeation studies: Male, healthy rats are used in the animal model for the ex-vivo permeation investigations. The rats are first given a thorough cleaning and their hair removed in preparation for the test. The rat's skin is then taken off and linked to the donor compartment. The permeation study is then carried out by covering the skin with emulgel in a way that is similar to in vivo research. The receiver compartment is filled with phosphate buffer, and samples are taken on a regular basis so that the UV spectrophotometer can measure the absorbance.

Microbiological Assay: The purpose of the microbiological assay is to find out if there are any microorganisms in the emulgel. The most popular method for carrying out this test is the ditch plate method, which can identify the semisolid formulations' bacteriostatic and fungistatic activities. To conduct this test, Sabouraud's agar dried plates were used, and the emulgel was placed on these plates at a right angle to the edge. The fungal growth on the plates is monitored after 18 to 24 hours of 25°C incubation. Next, can compute the percentage inhibition using the following formula:

$$\% \text{ inhibition} = L_2/L_1 \times 100$$

Here, L_1 stands for the streak culture's overall length. L_2 is the duration of inhibition

Syneresis Measurement Test: When it comes to emulgel, it is occasionally seen that the formulation shrinks, causing liquid to be released. This process is known as syneresis. The cylindrical tube, which is covered in whatman filter paper and has tiny pores at the bottom, is filled with the emulgel in order to measure this activity. After that, this apparatus is put in a centrifuge and run for fifteen minutes. After the liquid has been separated, it is weighed, and the percentage of syneresis is computed using the formula below:

$$\% \text{ syneresis} = (\text{Weight of separated liquid} / \text{Total weight before centrifugation}) \times 100$$

Advantages of Emulgel

- a. Delivery of lipophilic drugs
- b. High stability
- c. Greater loading capacity
- d. Cost effective
- e. Better penetrability
- f. Improved patient compliance

Disadvantages of Emulgel

- a. Drugs with higher molecular weight and particle size are unable to absorb the drug via skin.
- b. Sometimes, formation of small bubbles may occur in Emulgel, which reduces the penetrability of drug
- c. Skin Irritation is also very common.

CONCLUSION

The advantages of Emulgel and the most current developments in this area relate to the formulations ability to distribute a variety of active ingredients topically. The formulation process is easy, affordable, and takes little time. Given that emulgel exhibits improved spread, adhesion, extrusion, and viscosity, it can be regarded as an innovative drug delivery technology with improved features. The incapacity of traditional therapy to provide lipophilic medications topically has also led to a great demand for innovative formulations, of which emulgels presently meet all the criteria and hence encompass a broad spectrum of indications. As a result, emulgels current benefits and anticipated future developments are encouraging its inclusion in the clinical pipeline and positioning it as a great substitute for topical drug delivery. A number of medications, such as NSAIDs, antimicrobials, and antifungal agents, are anticipated to be administered as emulgels in the future.

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