ejpmr, 2021,8(11), 178-183

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A REVIEW ON EMULGEL: A NOVEL TREND IN TOPICAL DRUG DELIVERY SYSTEM

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Article Received on 28/08/2021 **Article Revised on 18/09/2021** **Article Accepted on 08/10/2021**

ABSTRACT

Gels are one of the commonly used topical drug delivery system. Gels provide faster drug release as compared to ointments and creams. But this dosage form have certain limitations indelivering hydrophobic drug. Hence in order to overcome this limitation emulgels are used. Emulgels are dual drug delivery system which consists of either o/w or w/o emulsion incorporated in base containing gel. Emulgels offer certain advantages like they are thixotropic, non greasy, easily spreadable, non-staining, longer shelf life, transparent and pleasing appearance. Emulgels are the preferred choice in various cosmetic and dermatological preparations and its use will be increasing in coming future.

KEYWORDS: Emulgel, Gels, Topical drug delivery, Swelling index, Spreadability.

INTRODUCTION[2,4]

Approximately 74 percent of medicines administered orally and are not found to be as effective as desired. To address these issues, a transdermal medication delivery method was developed. Transdermal drug delivery varies from standard topical drug administration in that it delivers a medication via the skin to produce a systemic impact.

Drugs that are applied topically have two mechanism of action viz.topical local activity and topical systemic action. If the drug substance is in the form of a solution or has a favourable lipid/water partition coefficient and is a nonelectrolyte, drug penetration through the epidermal membrane is enhanced. Pharmaceutical preparations applied to the skin are primarily intended for local action, and as a result, formulations are designed to offer sustained local contact with the least amount of systemic drug absorption. Antiseptics, antifungal agents, skin emollients, and other drugs administered to the skin for local action.

Topical drug delivery system is used for applying medication to the skin in order to get a localized effect to relieve skin infections. Gels are very ideal form of topical drug delivery system but it possess challenge in delivering hydrophobic drug. A gel is colloid that is typically 99% liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelating substance present. Despite the numerous benefits of gels, a significant limitation exists in the administration of hydrophobic drugs. To overcome this constraint, an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can be successfully incorporated and deliveredthrough gels.

Emulgels are emulsions that are gelled by combining with a gelling agent. They can be oil-in-water or water-in-oil emulsions. The presence of a gelling agent in the water phase transforms a traditional emulsion into an emulgel. Lipophilic drugs are entrapped in direct (oil-in-water) system whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) system. They have a high patient acceptability since they combine the benefits of both emulsions and gels. Emulgels for dermatological use have several favorable properties suchas

1. Thixotropic.
2. Greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, bio-friendly, transparent & pleasing appearance

Molecules can penetrate the skin mainly by three routes which include the intact stratum corneum, through the sweat ducts or through sebaceous follicles. For percutaneous drug absorption, the stratum corneum‟s surface presents more than 99% of the total skin surface for this purpose. Emulgel research has shown to be a trump card in the development of a novel topical drug delivery system.

ADVANTAGES AND DISADVANTAGES OF EMULGEL[4]

1. It avoids first pass metabolism.
2. It avoids gastrointestinal incompatibility
3. It shows site specific activity.
4. It shows site specific activity.
5. It is suitable for self medication.
6. Convenient and easy to apply.
7. It helps in delivering a steady infusion of a drug over an extended period of time.
8. It offers improved patient compliance and reduced inter and intra-patient variability.
9. It increases the therapeutic value of many drugs via avoiding specific problems associated with the drug. E.g. GI irritation, lower absorption, decomposition due to „hepatic first pass" effect.
10. It is non sticky, easily spreadable and has a longer shelf life.

FACTORS AFFECTING TOPICAL ABSORPTION OF DRUG[1,10]

The factors that affect the topical absorption of drug are as follows.

1. **Physiological Factors**
2. **Physiochemical factors**

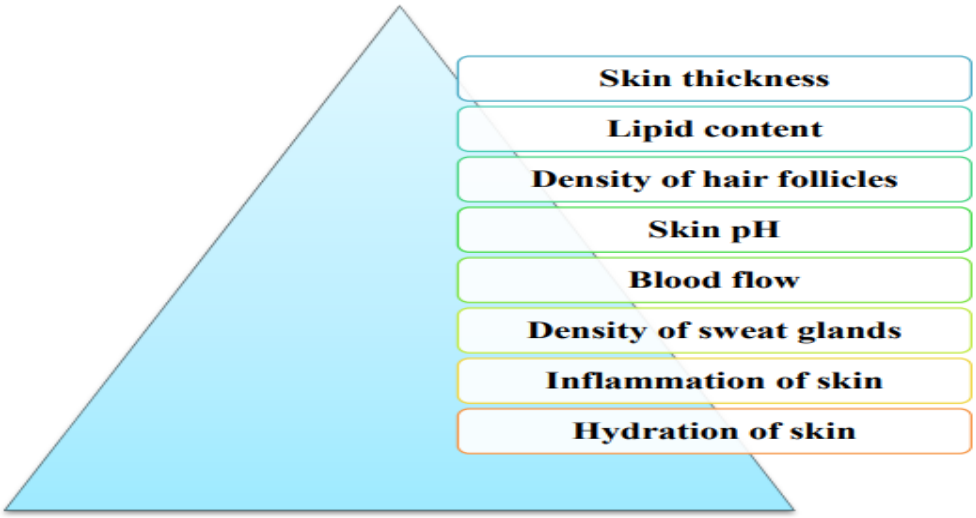

Fig.No. 1: Physiological Factors.

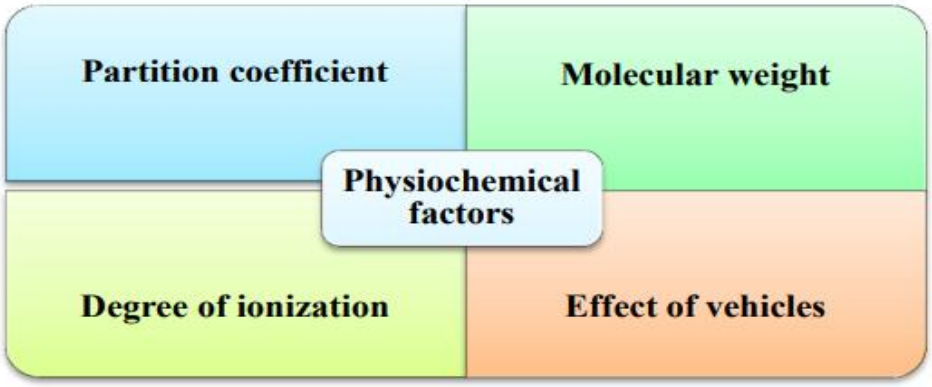

Fig.No.2 Physiochemical factors.

Factors affecting topical absorption of drugs. Many commonly used topical agents, such as ointment, cream, and lotion have numerous drawbacks. When applied, they are extremely sticky, causing discomfort in the patient. Furthermore, they have a lower spreading coefficient and must be applied with rubbing. They also have a problem with stability. Because of all of these factors within the major group of semisolid preparations, the use of transparent gels is recommended.

FORMULATION ASPECTS OF EMULGEL[1,8,13,14]

1. **Aqueous Material:** It mainly consists of the ingredients to formulate the aqueous phase. Commonly used aqueous materials are water, ethanol, propylene glycol etc.

- Properties of vehicles:

✓ Release of drug so that it can freely migrate to site of action.

✓ Delivery of the drug to target site

2. **Oils:** These agents form the oily phase of the

emulsion, for externally applied emulsions, mineral oils, either alone or combined with soft or hard paraffin, are used both as the vehicle for the drug. Widely used oils in oral preparations are non-biodegradable mineral and castor oils that provide a local laxative effect, and fishliver oils or various fixed oils of vegetable origin. The oily phase must have drug release at target site. E.g.: Arachis oil, wheat germ oil, jojoba oil, castor oil.

3. **Emulsifiers:** Emulsifying agents are used both to promote emulsification at the time of manufacture and to control stability during a shelf life that can vary from months oryears. E.g.: polyethylene glycol 40 stearate, Sorbitan mono-oleate (Span 80), polyoxyethylenesorbitanmonooleate (Tween 80), stearic acid, and sodium stearate.
4. **Gelling agent:** These are the agents used to increase the consistency of any dosage form can also be used as thickening agents. Eg: Carbopol-934, Carbopol-940, HPMC.
5. **Permeation Enhancers:** These are substances that partition into skin components andinteract with them to cause a transient and reversible increase in skin permeability. They break the skin barrier temporarily, fluidize the lipid channels between corneocytes, change the drug's partitioning into skin structures, or improve skin delivery. Permeation enhancers such as clove oil and menthol can be utilised. Penetration enhancers should have the following characteristics.

- ✓ They should be non-toxic, non-irritating, and non-allergenic.
- ✓ They should have no pharmacological action within the body, i.e. they should not bind to receptor sites; their activity and duration of impact should be predictable and repeatable.
- ✓ The penetration enhancers should act in a one-way fashion, allowing therapeutic agents to enter the body while preventing endogenous material from being lost.
- ✓ They should be cosmetically acceptable with an appropriate skin „feel".

EMULGEL PREPARATION[1,8,13,14]

Step 1: Gel Base Preparation.

Step 2: Emulsion Preparation Either O/W Or W/OStep 3: Incorporation Of Emulsion Into Gel Base

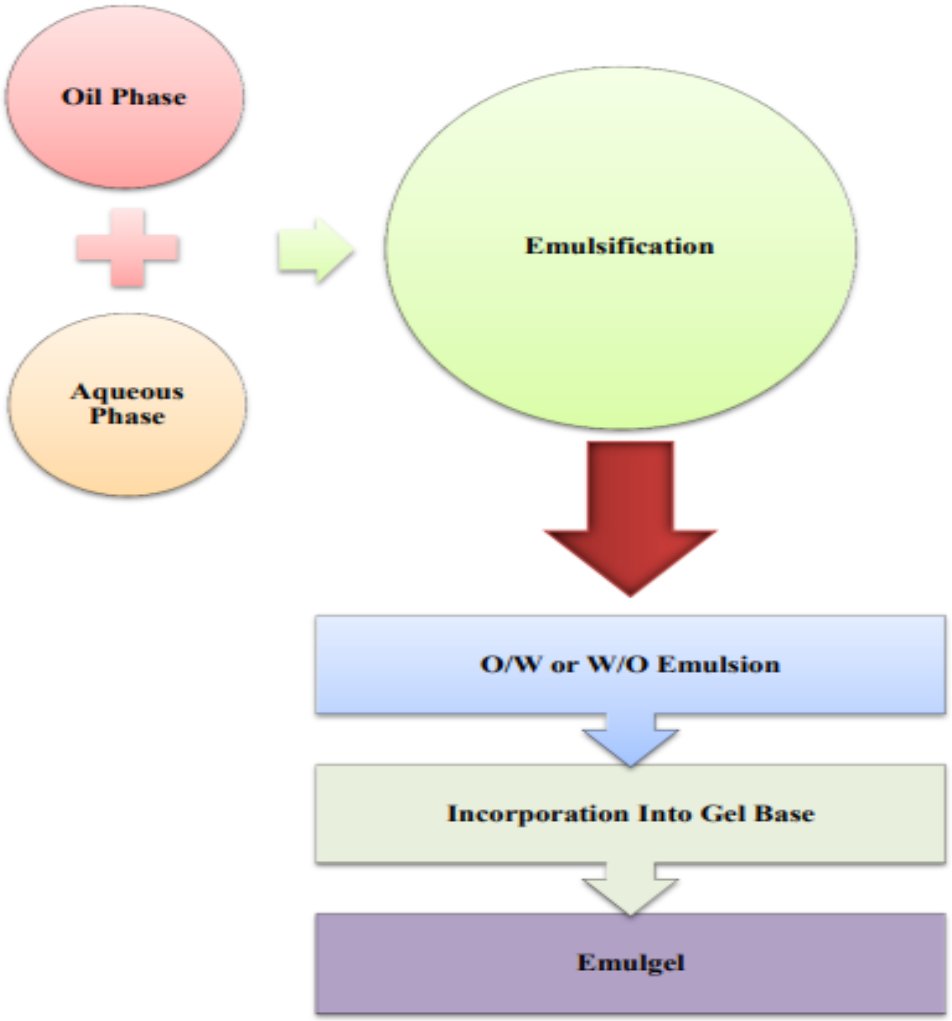

Fig. No 3: Flowchart of Emulgel Formulation.

Packaging of Emulsions[17,14]: Emulgels are typically packaged in a membrane-sealed lacquered aluminium tube with an interior coating of a phenoxy-epoxy based lacquer and a propylene screw cap or an airtight container or aluminum laminated tubes with a propylene screw cap closed by a moulded seal.

Material of construction for laminated tubes

1. Foil laminates - These are employed for sensitive preparations because they provide alight, air, and moisture barrier.

2. All-plastic laminates - These laminates have a chemical-resistant barrier and are utilised in reactive preparations.

CLASSIFICATION OF EMULGEL[15,16]

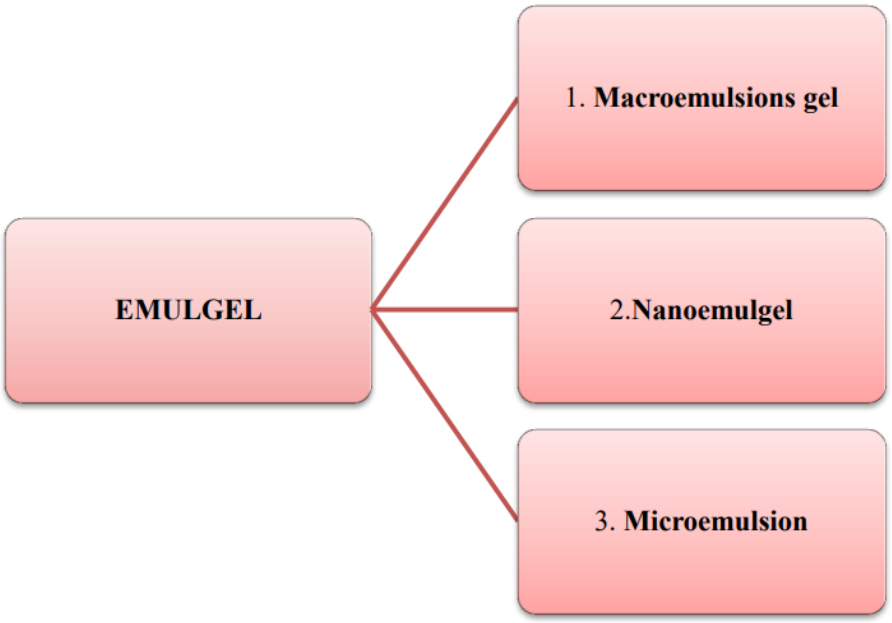

Fig.No 4: Classification of Emulgel.

Macroemulsions gel: The most frequent form of emulgel is one in which the particle size of the emulsion droplets is more than 400nm. Macroemulsions are thermodynamically unstable, however surface active substances can help to stabilize them.

1. **Nanoemulgel:** Nanoemulgel is the term used when nanoemulsion is integrated into agel. Nanoemulsions are transparent (translucent) dispersions of oil and water that are stabilised by an interfacial layer of surfactant and co-surfactant molecules with droplet sizes smaller than 100 nm.
2. **Microemulsion:** Microemulsions are transparent and thermodynamically stable as their droplet size ranges from 10 to 100 nm and they do not coalesce.

CHARACTERIZATION OF EMULGELS[3,5,6,7,9,10,15,18,19]

1. **Physical Examination:** In order to evaluate the created emulgel formulations, it is necessary to observe their color, homogeneity and phase separation. The pH value of aqueous solution of emulgel is measured by a pH meter.
2. **pH:** A digital pH meter was used to determine the pH of the 1% aqueous prepared gels. The pH of the semisolid formulations was measured after the electrodes were completely immersed in them.
3. **Spreadability:** Using a wooden block connected to a pulley at one end, spreadability may be evaluated. Emulgels are evaluated for their 'Slip' and 'Drag' properties in order to determine their spreading coefficient. The wooden block has a ground glass slide attached to it. On this ground slide, around 1 gram of prepared emulgel is placed. Next, the emulgel preparation is squeezed between the fixed ground slide and a second glass slide of the same size. Using the hook, the hook is used to connect a second piece of glass. In order toremove air from the slides, a weight of 100 g is placed on top of them for 5 minutes. Measured quantity of weight is placed in the pan attached to the pulley with the help of hook. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from emulgel and placed in between the slides under the direction of certain load. A shorter interval indicates better spreading coefficient. It is calculated by using the formula.

$$S = M. L / T$$

where M = weight tied to upper slide

L = length of glass slides.

T = Time taken to separate the slides completely from each other.

4. **Extrudability:** It is a common empirical test to determine how much force is necessary to extrude material from a tube. The method is used to determine the amount of applied shear in the rheogram area corresponding to a shear rate exceeding the yield value which results in plug flow. The technique used in this study to assess emulgel

formulation extrudability is based on the percentage of emulgel and emulgel extruded from a lacquered aluminium collapsible tube, as well as the weight in grammes necessary to extrude at least a 0.5 cm ribbon of emulgel in 10 seconds. Extrudability improves as the quantity extruded increases. The measurement of extrudability of each formulation is in triplicate and the average values are presented. The extrudability is than calculated by using the following formula:

Extrudability = Applied weight to extrude emulgel from tube (in gm.) / Area (incm^2)

5. **Globule size and its distribution in emulgel:** Globule size and distribution in emulgel: Malvern zetasizer was used to determine globule size and distribution. To achieve homogenous dispersion, a 1gm sample was dissolved in filtered water and stirred. The sample was injected into the zetasizer's photocell. The average globule diameter and distribution was measured.
6. **Swelling Index:** For the purpose of determining the swelling index of prepared emulgels, 1 gram of the gel is placed on porous aluminium foil and then placed separately in a 50 ml beaker containing 10 ml 0.1 N NaOH. After that, samples were removed from beakers at various time periods and placed in a dry area for a while before being reweighed. The following formula is used to compute the swelling index:

SW % = [Wt – Wo / Wo] × 100

Where, SW % = Equilibrium percent swelling, Wt = Weight of the swollen emulgel after time t, Wo = Initial weight of emulgel at time zero.

7. **Rheological studies:** A Brookfield viscometer with spindle no.18 at 100 rpm is used to determine the rheological properties of the various emulgel compositions at 25^{0}C.
8. **Bioadhesive strength measurement:** The technique is used to determine the bio-adhesive strength of a substance. Fresh skin is sliced into pieces and rinsed in 0.1N NaOH solution. Two strips of skin were connected to two glass slides, one of which was fixed to the wooden piece and the other was tied to the balance on the right hand side. By putting more weight on the left-hand pan, the left and right pans were balanced. Extra weight from the left pan is removed to sandwich the two pieces of skin, and some pressure is applied to remove the presence of air. 1 gm of topical emulgel is placed between these two slides containing hairless skin pieces, and extra weight from the left pan is removed to sandwich the two pieces of skin. For 5 minutes, the balance is held in this posture. Weight is added slowly at 200 mg/min to the left-hand pan until the patch comes away from the skin surface. The bioadhesive strength was determined by the weight (gramme force) required to separate the emulgel from the skin surface. The bioadhesive strength is determined using the formulas below.

Bioadhesive Strength = Weight required (in gm) /Area (cm^2)

9. **Drug content study:** A drug content analysis is conducted to assess the amount of drug contained in a given quantity of formulation. 1 g of emulgel is carefully weighed and transferred to a 10 ml volumetric flask, to which 1 ml methanol is added, and the volume is brought up to 10 ml with phosphate buffer pH 7.4 after vigorous shaking.
   To adequately combine it, the volumetric flask is maintained for 2 hours and shaken in a shaker. After passing the solution through the filter paper, the absorbance is measured with a UV spectrophotometer.

The following formula is used to determine drug content.

Drug Content = (Concentration × Dilution Factor × Volume taken) × ConversionFactor.

10. **In-vitro release study:** A modified Franz diffusion cell is used in the in vitro drug release investigations. The membrane is gently clamped to one end of the hollow glass tube after soaking in phosphate buffer pH 6.8 for 6–8 hours. As a diffusion medium, phosphate buffer with a pH of 6.8 is utilised. The emulgel sample is put to the membrane and then placed in the glass tube between the donor and receptor compartments. Phosphate buffer (100ml) with a pH of 6.8 was stored in the receptor compartment. The solution is agitated constantly by a magnetic stirrer at 500 rpm, and the temperature of the cell is thermostatically controlled at 37^{0}C by circulating surrounding water in the jacket. At appropriate intervals, the sample is removed and replaced with equal volumes of fresh diffusion media. UV spectrophotometric analysis is used to examine the samples.
11. **Skin Irritation Test:** The emulgel formulation is administered topically to the properly shaved skin of rats, and undesirable effects such as changes in skin morphology, such as colour change, should be monitored for up to 24 hours. For the investigation, six numbers of rats (a set) were employed. The test is passed if no irritation develops. The trial should be repeated if the skin irritation symptoms appear in more than two animals.
12. **Stability studies:** The prepared emulgels are packaged in aluminum collapsible tubes (15 gm) and tested for three months at 50°C, 250°C/60% RH, 300°C/65 %RH, and 400°C/75 % RH. Each month, samples are taken and tested according to ICH criteria for physical appearance, pH, rheological characteristics, drug content, and drug release profile, etc.

CONCULSION

Emulgels are a novel drug delivery method that incorporates an emulsion into the gel phase to transport both hydrophobic and hydrophilic drug moiety. When an emulsion is incorporated into a gel, it becomes a dual control release system, and other issues with the emulsion, such as phase partition and creaming, are resolved, and its consistency improves. In comparison to

other conventional topical treatments, emulgel appears as a more effective and beneficial drug delivery system. They are appropriate for nearly all distribution routes and so offer promise in a variety of sectors, including cosmetics, curative medicine, and biotechnology. Because of its non-greasy, gel-like properties, it allows for better drug release.

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