



REVIEW ARTICLE

EMULGEL: A NOVEL APPROACH TO TOPICAL DRUG DELIVERY

Rajesh Asija*, Ravi Sharma, Avinash Gupta

Maharishi Arvind Institute of Pharmacy, Jaipur-302020, Rajasthan, India

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ABSTRACT

Emulgel is an emerging topical drug delivery system to which if more effort is done towards its preparations with more number of topically effective drugs it will prove a boon for derma care products and cosmetic products. Emulgel has emerged as novel drug delivery system to deliver hydrophobic drugs. When gels and emulsions are used in combined form the dosage form are referred as emulgel. The emulgel for topical use has several favorable properties such as being thixotropic, without greasy, easily applicable, removable, emollient, non-staining, water solubility, more shelf life, bio-compatible, transparent & good appearance. Various permeation enhancers can increase the effect, so emulgel referred as better topical drug delivery systems over present drug systems. The use of emulgels can be increased in analgesics and antifungal drugs.

INTRODUCTION:

Topical drug delivery can be defined as the application of a drug containing preparations to the skin to directly treat skin disorders. The topical drug delivery system is generally used where other routes (like oral, sublingual, rectal, parental) of drug administration fails or in local skin infection like fungal infection.¹

Dermatological products which are applied to skin are diverse in formulation and range in consistency from liquid to powder but the most popular products are semisolid preparation. Within the major group of semisolid preparations, the use of transparent gels has been increased both in cosmetics and in pharmaceutical preparations².

Gels are developed as a newer class of dosage form which are formed by entrapment of large amounts of aqueous or hydro alcoholic liquid in a network of colloidal solid particles, which may include inorganic substances, like aluminium salts or organic polymers of natural or synthetic origin³. They have a higher aqueous component that allow greater dissolution of drugs, and also allow easy release of the drug through a vehicle that should be necessarily a liquid, compared with the ointment or cream base. Their use and patient acceptability is superior. Apart from many advantages of gels a major limitation is in the delivery of hydrophobic drugs. Hence, to overcome this limitation, emulgels are formulated and used so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels².

When gels and emulsions are used in combined form the dosage forms are referred as Emulgels. Both o/w and w/o emulsions are extensively used for their therapeutic properties and as vehicles to deliver various drugs to the skin. Emulsions possess a degree of elegance and are easily removed whenever required. They also possess a high ability to penetrate the skin. In addition; the researcher can control the viscosity, appearance and degree of greasiness of emulsions in cosmetic or dermatological preparations. Oil-in-water emulsions are most useful as water washable drug bases and for general cosmetic purposes, while water-in-oil emulsions are used more widely for the treatment of dry skin and emollient applications. Gels for dermatological purpose have several favorable properties such as being thixotropic, without greasy, easily applicable, removable, emollient, non-staining and compatible with several excipients.²⁻⁴

Advantages of emulgel⁵

1. To avoid first pass metabolism
2. Self applied medication
3. Improve patient compliance
4. Medication can be terminated when required
5. Suitable for potent drug and drugs having short half life
6. Site specific drug delivery

Disadvantages of emulgel⁵

1. Large particle sized drugs are not easy to absorb through the skin
2. Some drugs have poor permeability through skin
3. On contact, skin irritation or allergic reaction may occur
4. During formation of emulgel bubbles may occur

Formulation considerations

The challenges in formulating topical emulgel are:

1. Determining those systems which are non toxic, non irritating, non comedogenic and non sensitizing.
2. Preparation of cosmetically elegant emulgel.
3. The emulgel preparations must have low allergic potential, good physiological compatibility and high biocompatibility⁶.

Components of emulgel preparation:

1. Aqueous Materials:

The aqueous phase of the emulsion is formed by aqueous materials. Commonly used agents are alcohols and water.

2. Oils:

The oily phase of the emulsion is formed from oils. For externally applied emulsions, mineral oils are widely used both as the vehicle for the drug and for their occlusive and sensory characteristics either alone or combination with soft or hard paraffins. Widely used oils in oral preparations are non-biodegradable mineral and castor oils that provide a local laxative effect and fish liver oils or various fixed oils of vegetable origin (e.g., arachis, cottonseed, and maize oils) as nutritional supplements.

3. Emulsifiers:

Emulsifying agents are used to promote emulsification at the time of manufacture. These are used to control stability during a shelf life that can vary from days for extemporaneously prepared emulsions to months or years for commercial preparations. eg Polyethylene glycol stearate, Sorbitan monooleate (Span 80), Polyoxyethylene sorbitan monooleate (Tween 80), Stearic acid, Sodium stearate.

4. Gelling Agent:

Gelling agents are used to enhance the consistency of dosage form and can also be used as thickening agent.

5. Permeation Enhancers:

These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability.

Formulation methods^{7,10}

There are various methods of formulation of Emulgel, by using different kinds of ingredient, one method reported by Mohamed (2004) in his research work (optimization of chlorphenesin in

Emulgel) includes preparation of emulsion (o/w or w/o), followed by addition of gelling agent to form Emulgel. First step includes formation of aqueous phase of emulsion. Aqueous phase of emulsion is prepared by first dissolving tween 20 in purified water, then propylene glycol solution is prepared by dissolving methyl paraben and propyl paraben in propylene glycol and then both the solutions are mixed and set aside. Oily phase of emulsion

is prepared by dissolving span 20 in light liquid paraffin. Preparation of emulsion involves separate heating of oily and aqueous phase to 70–80 °C after this both the phases are mixed with constant stirring until cooled to room temperature. Gel phase of emulgel is prepared by dispersing HPMC or Carbopol in water. HPMC is required to soak overnight in water, while Carbopol gel is prepared by simply dispersing it in purified water. When both the components both emulsions & gel get ready then the Emulgel is prepared by mixing emulsion with gel in 1:1 ratio with gentle stirring.

Another method was reported by Perioli et al. (2008). In this research formulation Emulgel formulation involves three step (i) polymer dispersion in water, (ii) neutralization of the polymeric aqueous dispersion and (iii) emulsification of the oil phase. With respect to the first step, three different TR-1 percentages, namely 0.3, 0.4 and 0.5%, w/v, are required. First step involves suspension of polymer in deionized water with continuous stirring at 900 rpm for 20 min at room temperature using a mechanical stirrer equipped with a three blade helical impellers & then slurry is neutralized with NaOH solution (18%w/v) to final pH value of 5.5, 6.0 and 6.5. The neutralization process causes the distension of polymer chains resulting in clear stable gels. Now for the complete hydration of polymer gels are required to be stored at 4 °C for 24 h before the addition of oil phase. After completing the hydration of gel different quantities of oil phase at three o/w ratio (w/w) 0.5, 1.0 and 1.5 respectively are added with stirring at 800 rpm (80 °C) there after it is left for cooling and its pH is measured.

Shahin et al. (2011) followed a different method to develop Emulgel for clotrimazole delivery. In this method the preparation of oily phase of emulsion by dissolving drug and span 60 in oily phase (jojoba oil) with the aid of magnetic stirrer at 75 °C with subsequent cooling followed by addition of Carbopol to the oily phase. In second step aqueous phase is prepared by dissolving Brij-35 in propylene glycol. Third step involves addition of oily phase to the aqueous phase following their emulsification using the over head mixer for 10 min at 1400 rpm, and then introduced emulsion into the homogenizer for 5 min at 10,000 rpm. Gellification of emulsion involves addition of gelling agent triethanolamine (formulae containing Carbopol either alone or in combination) and/or HPMC to the emulsion using over head mixer at 200 rpm for 45 min thereby adjusting the pH of formulation containing Carbopol to 5.5–6.5 using tri ethanol amine.

Dickinson Eric et. al. (2012) prepared a solid-like emulsion gel from a stable liquid-like emulsion by gelling the continuous phase or aggregating the emulsion droplets .

Even simply forcing all the droplets closer together by centrifugation can be sufficient to produce a concentrated protein-stabilized emulsion with gel-like behaviour, *i.e.*, elasticity at small deformations.¹¹⁻¹²

Emulsion gels produced by heat treatment have limited uses, especially for food formulations containing heat-sensitive ingredients. The appearance of emulsion gels prepared by salt-induced gelation is highly dependent on calcium concentrations. Increasing salt concentration produced a particulate gel with poor water holding capacity.

Characterization of Emulgel:

1. **Physical appearance**⁵: The prepared Emulsion preparations were inspected visually for their color, homogeneity, consistency and pH.

2. Spreadability¹¹

For the determination of spreadability, 1gm of emulgel placed between the two glass slides and load of 500 gm was applied. The time needed to slip off the slides is measured and Spreadability was calculated using formula $S = M \cdot L / T$

Where M = wt. tied to upper slide

L = length of glass slides

T = time taken to separate the slides.

3. Extrudability study:

This test is used to measure the force required to extrude the material from tube. The method is used for determination of applied shear in the region of the rheogram corresponding to a shear rate exceeding the yield value and exhibiting consequent plug flow. The study adopted for evaluating emulgel formulation for extrudability is based upon the quantity in percentage of emulgel and emulgel extruded from lacquered aluminum collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of emulgel in 10 seconds. More amount extruded better is extrudability. The measurement of extrudability of every preparations is in triplicate and the average values are presented. The extrudability is then calculated by using the following formula:

Extrudability = Applied weight to extrude emulgel from tube (in gm) / Area (in cm²).

4. Rheological Studies

The viscosity of the different emulgel preparations is determined at 25° C using a cone and plate viscometer with spindle 52 (Brookfield Engineering Laboratories) and connected to a thermostatically controlled circulating water bath¹.

5. Stability of emulasion

Stability of emulsion is determined by visual observation by using creaming index as an indicator.¹³

6. Bio adhesive strength¹⁴⁻¹⁵

The Bioadhesive strength of the emulgel is determined by means of modified analytical two pan balance. The burn human skin is washed with saline solution to 37° C before use. At the time of testing a section of skin was attached to upper glass vial using a rubber band. One vial with a part of tissue was connected to the balance and the other vial was fixed on a height adjustable pan. To the lower vial, emulgel applied. The height of the vial is adjusted so that the gel could adhere to the burn skin of upper vial, which is connected to the pan balance. Weights are added at a certain rate to the pan on the other side of the modified balance of the used device until the gel gets detached from skin. The bioadhesive strength, expressed as the detachment stress in dyne/cm², was determined from the minimal weights required for the detachment using the following equation

Bioadhesive Strength = Weight required (gm) / Area (cm²)

CONCLUSION:

Topical drug administration is a localized drug delivery system anywhere in the body through topical routes (ophthalmic, rectal, vaginal and skin). The major advantage of topical delivery system is to bypass first pass metabolism. In the coming years, topical drug delivery will be used extensively to impart better patient compliance. Emulgel is a popular drug delivery system in terms of viscosity, adhesion, spreadability and extrusion, they will become a popular drug delivery system. Moreover, they will become a solution for loading hydrophobic drugs in a water soluble gel bases.

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