



## EMULGEL: A REVIEW FOR NOVEL TOPICAL DRUG DELIVERY SYSTEM

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### ABSTRACT

Topical drug delivery system can be defined as a direct effect of drug containing medication to the skin to get the effect of drug or to cure disorders. Major disadvantage of gel is the delivery of hydrophobic drug. This can be overcome by Emulgels. Emulgel is the promising drug delivery system for the delivery of hydrophobic drugs. Emulgel is an emulsion which is gelled by mixing it with gelling agents. Many advantages of gels have the major limitation of delivery of hydrophobic drugs. Hence, to overcome this limitation, the emulsion based approach is being used. Emulgel is an interesting topical drug delivery system as it has dual release control system, i.e., gel and emulsion. Due to nongreasy because of the presence of gel phase which favors good patient compliance. In order to understand the potential of emulgel as delivery vehicles, this review gives an overview of the ideal properties, formation, and characterization of emulgels. The use of emulgel based systems as drug delivery vehicles is reviewed, with particular emphasis being placed on recent developments and future directions. The emulgel provide several favourable properties for its dermatological use such as greaseless, thixotropic, easily spreadable, emollient, easily removable, non-staining, water soluble, longer shelf life, transparent, bio-friendly and pleasing appearance.

**KEYWORDS:** Emulgel; Topical drug delivery system; Emulsion.

### INTRODUCTION

Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat the cutaneous disorder. The topical drug delivery system is generally used where other routes (such as oral, sublingual, rectal, and parental) of drug administration fails or in local skin infection like fungal infection.<sup>[1]</sup> Topical drug delivery is an attractive route for local and systemic treatment. A unique aspect of dermatological pharmacology is the direct accessibility of the skin as a target organ for diagnosis and treatment.<sup>[2]</sup> The main advantage of the topical delivery system is to bypass first pass metabolism. Avoidance of the risks and inconveniences of intravenous therapy and the varied conditions of absorption, such as pH changes, the presence of enzymes, and gastric emptying time are another advantage of the topical drug delivery system.<sup>[3]</sup>

As compared with conventional ointments and creams gel formulations generally provide faster drug release. Difficulty in delivery of hydrophobic drugs is major limitation of gels. So to overcome this limitation emulgels are prepared and with their use even a hydrophobic drug can enjoy the unique properties of gels. When gels and emulsions are used in combined form the dosage forms are referred as emulgel. In fact, the presence of a gelling agent in the water phase

converts a classical emulsion into an emulgel. O/W system is used to entrap lipophilic drugs whereas hydrophilic drugs are encapsulated in the W/O system.<sup>[4]</sup> Emulgel as the name suggest they are the combination of gel and emulsion. Both oil- in-water and water-in-oil type of emulsion used as vehicle to deliver various drugs to the skin. The presence of gelling agent in water phase converts a classical emulsion into an emulgel.<sup>[5]</sup> Emulgel for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water soluble, longer shelf life, bio friendly, transparent and pleasing appearance.<sup>[6]</sup>

#### Advantages

- Incorporation of hydrophobic drugs
- Better loading capacity
- Better stability
- Controlled release
- No intensive sonication
- Avoiding first pass metabolism
- Avoiding gastrointestinal incompatibility
- More selective for a specific site
- Improved patient compliance
- Convenient and easy to apply<sup>[7]</sup>

#### Disadvantages

- Skin irritation on contact dermatitis
- The possibility of allergic reactions
- The poor permeability of some drugs through the skin
- Drugs of large particle size are not easy to absorb through the skin
- The occurrence of the bubble during formulation of emulgel<sup>[8]</sup>

### Rationale

Many widely used topical agents like ointment, cream, lotion have many disadvantages. They have very sticky causing uneasiness to the patient when applied. Moreover they also have lesser spreading coefficient and need to apply with rubbing. And they exhibit the problem of stability also. Due to all these factors within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. A gel is colloid that is typically 99% wt liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelling substance present. In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels.<sup>[9]</sup>

### Drug Delivery across the Skin

The superficial layer of the skin is epidermis and it is composed of stratified keratinized squamous epithelium which varies in thickness in different parts of the body. Skin as a target organ for diagnosis and treatment of dermatological problem. The skin acts like a two-way barrier for prevent absorption or loss of water and electrolytes. In topical drug absorption three primary mechanisms are present 1) Transcellular 2) Intercellular 3) Follicular. Mostly drugs pass by the torturous path around corneocytes and through the lipid bilayer to viable layers of the skin. Creams and gels that are rubbed into the skin have been used for many years to deliver as a pain killer medication and antimicrobial drugs to an affected site of the body. These include, among others like a gels and creams for vaginal yeast infections, topical creams for skin infections and creams to soothe arthritis pain. Newer technologies now allow other drugs to be absorbed through the skin (transdermal). These can be used to treat not just the affected areas (for example, the skin) but the whole body (systemic).<sup>[10,11]</sup>

### Important Constituents of Emulgel Preparation Aqueous Material

This forms the aqueous phase of the emulsion. Commonly used agents are water and alcohols.

### Oils

These agents form the oily phase if the emulsion. For

externally applied emulsions, mineral oils, either alone or combined with soft or hard paraffins, are widely used both as the vehicle for the drug and for their occlusive and sensory characteristics. Widely used oils in oral preparations are nonbiodegradable 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.<sup>[12]</sup>

### Emulsifiers

Emulsifiers are used to control emulsification process and stability. By incorporating an appropriate emulsifying agent stability of emulsion can be increased because these are thermodynamically unstable. Surfactants having HLB values greater than 8 such as the nonionic surfactant (spans, tweens) are used in the formulation of o/w emulsions whereas mineral oils such as liquid paraffin have HLB value less than 8 and therefore are used in the formulation of water in oil emulsions. In comparison to the individual system of span or tween, mixtures of span 20 and tween 20 results greater stability of the emulsion.<sup>[13]</sup>

### Penetration enhancers

To promote absorption of drugs, vehicles often include penetration enhancing ingredients that temporarily disrupt the skin barrier, fluidize the lipid channels between corneocytes, alter the partitioning of the drug into skin structures, or otherwise enhance delivery into the skin. Properties of penetration enhancers.

They should be non-toxic, non-irritating, and non-allergenic.

- They would ideally work rapidly, and the activity and duration of effect should be both predictable and reproducible.
- They should have no pharmacological activity within the body, i.e., should not bind to receptor sites.
- The penetration enhancers should work unidirectional, i.e., should allow therapeutic agents into the body while preventing the loss of endogenous material from the body.
- The penetration enhancers should be appropriate for formulation into diverse topical preparations, thus should be compatible with both excipients and drugs.
- They should be cosmetically acceptable with an appropriate skin "feel."<sup>[1]</sup>

### Gelling Agents

Gelling agents are used to forming gel base which by incorporating emulsion to form emulgel. These are also known as thickening agents which expand the consistency of any dosage form by swelling in the aqueous phase and forming gelly like structure.<sup>[14]</sup> Incorporation of gelling agent to a system makes it thixotropic. HPMC based Emulgel was found to be superior to Carbopol based Emulgel since it showed better drug release rate. NaCMC based Emulgels for

vaginal application since it showed higher mucoadhesivity which increased drug residence time and also best *in-vitro* and *in-vivo* performance. HEC based Emulgel showed low mucoadhesion but good drug release profiles and rheological characteristics. Pemulen based Emulgel meant for buccal administration.<sup>[15]</sup>

#### Formulation of emulgel

##### Step1: Preparation of gel using the gelling agent:

Sufficient quantity of Carbopol 940 (1% w/w) was weighed and sprinkled onto warm distilled water with continuous stirring. The dispersion was allowed to hydrate for 1-2 hours. Other ingredients like propylene glycol (10 % w/w) and glycerol (10 % w/w) were added subsequently to the aqueous dispersion with continuous stirring. A required quantity of drug (1 % w/w) was added and properly dispersed. The dispersion was neutralized to pH 6 using triethanolamine and the final weight was adjusted with distilled water. The gel was sonicated for 15 minutes and kept overnight to remove air bubbles.

**Step 2: Preparation of Emulsion:** Depending upon whether oil in water or water in oil emulsion was formulated.

**Step 3: Incorporation of the emulsion into gel base:** Finally emulsion was incorporated in gel base to form emulgel.<sup>[16]</sup>

#### Characterization of Emulgel Physical Appearance

The prepared Emulsion formulations were examined by their colour, homogeneity, consistency and pH value. 1% aqueous solutions of prepared Gellified Emulsion pH value were measured by a pH meter (Digital pH meter).

**PH:** The pH values of 1% aqueous solutions of the prepared gels were measured by a digital pH meter. Electrodes were completely dipped into the semisolid formulations and pH was noted.<sup>[17]</sup>

**Spreadability:** Spreadability is determined by apparatus suggested by Mutimer et al (1956) which is suitably modified in the laboratory and used for the study. It consists of a wooden block, which is provided by a pulley at one end. By this method, spreadability is measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. A ground glass slide is fixed on this block. An excess of emulgel (about 2 gm) under study is placed on this ground slide. The emulgel is then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A 1 Kg weight is placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the emulgel between the slides. Excess of the emulgel is scrapped off from the edges. The top plate is then subjected to pull of 80 gms. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. A shorter interval indicate better spreadability.

Spreadability was calculated by using the formula,

$$S = M.L/T$$

Where, S = spreadability,

M = Weight tied to upper slide,

L = Length of glass slides

T = Time taken to separate the slides completely from each other.<sup>[18]</sup>

#### Swelling index

To determine the swelling index of prepared topical emulgel, 1 g of gel is taken on porous aluminum foil and then placed separately in a 50 ml beaker containing 10 ml 0.1 N NaOH. Then, samples were removed from beakers at different time intervals and put it on a dry place for some time after it reweighed. Swelling index is calculated as follows:

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

Where, (SW) % = Equilibrium percent swelling,

W<sub>t</sub> = Weight of swollen Emulgel after time t,

W<sub>o</sub> = Original weight of Emulgel at zero time.<sup>[19]</sup>

#### Extrudability study

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

$$\text{Extrudability} = \frac{\text{Applied weight to extrude Emulgel from the tube (in g)}}{\text{Area (in cm}^2\text{)}}^{[2]}$$

**Bio-adhesive strength measurement:** A modified balance method was using for bioadhesion measurement. The two pans were removed from physical balance. On the left side, a glass slide was hanged and a 100 ml beaker was used in place of right side pan. A weight of 20 g was hanged on the left side, for balancing the assembly. Another glass slide was placed below the hanged slide. On both slides, portions of hairless fresh rat skin were attached. One gram of gel was placed between two rat skin faces. To form bioadhesion bond, a little pressure was applied, and then slowly water was added to right side beaker, till the gel was separated from one face of rat skin attached. The volume of water added was converted to mass. This gave the bioadhesive strength of

gel in grams.<sup>[20]</sup>

**Drug Content Determination:** Gel formulation (1 gram) was dissolved in suitable solvent. Filtered it to obtain clear solution. The resulting solution absorbance was noted using UV Visible spectrophotometer. Drug content was determined from calibration curve for drug.<sup>[21]</sup>

#### In vitro drug release study

The in vitro drug release studies of the emulgel were carried out on diffusion cell using egg membrane. This was clamped carefully to one end of the hollow glass tube of dialysis cell. Emulgel (1 g) was applied onto the surface of egg membrane dialysis membrane.

The receptor chamber was filled with freshly prepared PBS (pH 7.4) solution to solubilize the drug. The receptor chamber was stirred by a magnetic stirrer. The samples (1 ml aliquots) were collected at suitable time interval sample and were analyzed for drug content by ultraviolet (UV)-visible spectrophotometer after appropriate dilutions.

Cumulative corrections were made to obtain the total amount of drug released at each time interval. The cumulative amount of drug release across the egg membrane was determined as a function of time. The cumulative percentage drug release was calculated using standard calibration curve.<sup>[19]</sup>

*Ex vivo* bioadhesive strength measurement of topical emulgel (mice shaven skin) The modified method is used for the measurement of bioadhesive strength. The fresh skin is cut into pieces and washed with 0.1 N NaOH. Two pieces of skin were tied to the two glass slide separately from that one glass slide is fixed on the wooden piece, and another piece is tied with the balance on the right-hand side. The right and left pans were balanced by adding extra weight on the left-hand pan. 1 g 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, and some pressure is applied to remove the presence of air. The balance is kept in this position for 5 min. Weight is added slowly at 200 mg/min to the left-hand pan until the patch detached from the skin surface. The weight (gram force) required to detach the emulgel from the skin surface gave the measure of bioadhesive strength. The bioadhesive strength is calculated using the following:

**Bioadhesive strength = Weight required (in g)/Area (cm<sup>2</sup>),<sup>[22]</sup>**

**Stability Studies:** The optimized emulgel formulation was selected for stability study. Sufficient quantity of emulgel formulation was sealed in 10 gm collapsible tube in triplicate, and subjected to stability studies at 5°C, 25°C/60%RH, 30°C 65%RH and 40°C/ 75%RH for a period of 3 months. The samples were analyzed at

predetermined time intervals for pH, physical appearance, rheological properties and drug content.<sup>[23]</sup>

**Kinetics modeling:** Data obtained from *ex-vivo* permeation studies were fitted into zero order, first order, Higuchi, and mathematical models for evaluation of drug release kinetics. The model for best fit was predicted from the value of R<sup>2</sup>. For an ideal fit, value of R<sup>2</sup> i.e. higher, the value of R<sup>2</sup> best was the model fitted. Hence, the model which gives the R<sup>2</sup> value nearest to 1 describes the best order of drug release.<sup>[24]</sup>

#### CONCLUSION

Emulgel is the recently developed technique for the topical drug delivery it is best suitable for hydrophobic drugs and obviously it is a better technique for drug delivery of combination of both hydrophilic and lipophilic drugs. It is mainly used for the delivery of both hydrophobic and hydrophilic drug. Emulgel technique contains both oil and aqueous (i.e. gel base) base so it can be used for hydrophobic drugs. Since emulgel shows enhanced spreadability, adhesion, viscosity and extrusion. This novel drug delivery becomes a popular formulation. Many of drugs that have utility in the treatment of skin disorders are hydrophobic in nature. Such drugs can be delivered in the form of emulgel where they can be incorporated in the oil phase of the emulsion and combined with gel.

#### CONFLICT OF INTEREST STATEMENT

We declare that we have no conflict of interest.

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