

A Review on Emulgel: As a Novel Topical Drug Delivery System

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ABSTRACT

Emulgel is Topical preparation Prepared by the combination of emulsion and gel. Emulgel is considered as the one of the most important topical delivery system because it consists of two release control system i.e., gel and emulsion. Emulgels are generally free of serious side effects. The Primary Intention of this New topical Delivery System is to deliver the Hydrophobic drugs into systemic circulation through Skin. Generally emulgel is formed when emulsion is incorporated into gel base. By applying suitable statistical design different grades of emulgel is prepared. There are various favorable properties like be being thixotropic, emollient, greaseless, easily spreadable, easily removable, water-soluble, longer shelf life, non-staining, bio-friendly, transparent and pleasing appearance. Several penetration enhancers can potentiate the effect. So that emulgel is considered as the most conventional systems available in market over other topical drug delivery systems.

INTRODUCTION

Emulgels are generally combination of emulsion and gel. Emulsions, either of the water in oil or oil-in-water type, these emulsions are gelled by mixing with a gelling agent and this Emulsified gel is act as the superior carrier for poorly water soluble or hydrophobic drugs [1].

The major drawback of this gel over many advantages is in the delivery of hydrophobic drugs. So to overcome this drawback an emulsion based approach is being used, so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels.

In recent times, there has been great interest towards the use of novel polymers which can used as emulsifiers and thickeners and the gelling capacity of these compounds is more and allows the formulation

of stable emulsions and creams. This acts by increasing the viscosity of the aqueous phase and at the same time decreasing surface and interfacial tension. Due to the presence of a gelling agent in the water phase converts a classical emulsion into an emulgel. These Emulgels for Topical use have the various useful properties like being thixotropic, bio-friendly, water-soluble, greaseless, easily spreadable, emollient, easily removable, non staining, greater shelf life, clear and pleasant appearance [2,3].

Emulgel is composed of two parts:

1. Emulsion.
2. Gel.

LITERATURE REVIEW

Emulsion

Emulsions are generally thermodynamically unstable two phase system with two or more immiscible liquids one of it dispersed in the form of small droplets in the other liquid due to dispersion the system becomes unstable. An emulsifying agent is used or the stabilization of the biphasic system. There are both o/w or w/o type of emulsions are exists which are used as vehicles to deliver drug. Emulsions are stabilized by use of emulsifying agents. They have good penetration capability and can be easily washed off from skin[4]. Based on the nature of distribution or size of droplets emulsions are of different types described as follows:

Macroemulsion

These macroemulsions are most common type of emulsions the particle size of this emulsion is about 400 nm and these macro emulsions are easily observed by microscope. By using surface active agents we can make thermodynamically stable macro emulsion.

Depending on the method of emulsification and nature of emulsifier the macro emulsion either O/W or W/O.

Microemulsion

Microemulsions are basically thermodynamically stable and optically transparent. This microemulsion is mono dispersed spherical droplets and has the diameter of 20 nm to 200 nm.

Gel

The gel has the properties which is intermediate between those of liquids and solids. These gels look like wet and soft and look like solid material. However, it is often wrongly used to describe any fluid system that exhibits some degree of rigidity. A gel consists of a polymer which swells in the presence of fluid and perhaps it within its structure. The rigidity of the gel is determined by the amount of fluid it entraps. These are capable of undergoing large deformation in their physical state i.e. from solid to liquid [5].

Emulgel

The name emulgel its self tells that it is combination of emulsion and gel. There are both water-in-oil and oil-in-water type of emulsions are used as a vehicle to deliver various drugs to the skin. The presence of the gelling agent in water phase converts a classical emulsion into an emulgel. They also have a high ability to penetrate the skin. Emulgel for dermatological use has several favourable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, bio-friendly, transparent and pleasing appearance.

Molecules are basically penetrate into the skin by three ways: by intact stratum corneum, sweat ducts, or sebaceous follicle. The surface of the stratum corneum presents more than 99% of the total skin surface available for percutaneous drug absorption. Passage through this outermost layer is the rate limiting step for percutaneous absorption. The major steps involved in percutaneous absorption include the establishment of a concentration gradient, which provides the driving force for drug movement across the skin, release of drug from the vehicle (partition coefficient), and drug diffusion across the layers of the skin (diffusion coefficient) [1].

Types of emulgels

1. Based on the Type of API
2. Based on the type of emulsion

Based on the Type of API

- Herbal/poly-herbal:

Example: i. Cosmetic Emulgel for skin care from field pumpkin.

- ii. Anti-psoriatic Emulgel from babchi oil and Gum Guggule.

- Allopathic :

Example: Diclofenac diethyl Ammonium Emulgel (VOLTAREN) by NOVARTIS PHARMA.

Based on the type of emulsion

- Macroemulgel: Size of dispersed phase droplets more than 400 nm and prepared by High Energy and Low Energy Method.
- Microemulgel: Droplet Size between 1 nm to 100 nm. Prepared by Phase Inversion And Phase Titration Method.
- Nanoemulgel: Droplet size is less than 1 nm.

Advantages

1. It avoids the first pass metabolism.
2. Gastrointestinal incompatibility can be avoided.
3. Site specificity is more.
4. Patient compliance can be improved.
5. Self-medication.
6. Providing utilization of drug with short biological half-life and narrow therapeutic window.
7. Ability to easily terminate medication when needed.
8. It is easily applicable and convenient.
9. Hydrophobic drugs can be incorporated.
10. Loading capacity is better
11. Better stability than other t.d.d.s
12. Preparation cost is low
13. Controlled release can be achieved
14. No intensive sonication

Disadvantages

1. On contact to dermatitis causes skin irritation.

2. Allergic reactions.
3. The poor permeability for some drugs through the skin.
4. Drug of large particle size not easy to absorb through the skin.
5. Sometimes bubble during formation of emulgel.

Factors affecting topical absorption of drug

Physiological factors:

1. Skin thickness.
2. Lipid content.
3. The density of hair follicles.
4. The density of sweat glands.
5. Skin pH.
6. Blood flow.
7. Hydration of skin.
8. Inflammation of skin.

Physicochemical factors:

1. Partition coefficient.
2. The molecular weight (<400 Daltons)
3. The degree of ionization (only unionized drugs gets absorbed well).
4. Effect of vehicles.

Materials used in emul gel preparation

Aqueous material: This forms the aqueous phase of the emulsion. Water and alcohols are commonly used agents [3].

Oils: These agents form the oily phase. For externally applied emulsions, mineral oils, either combined or alone with hard or soft paraffin's are widely used. In oral preparations castor oils and non-biodegradable mineral that provide a local laxative effect and various fixed oils of vegetable origin (e.g., arachis, cottonseed, and maize oils) or fish liver oils as nutritional supplements[2].

Emulsifier: Emulsifying agents are used to promote emulsification at the time of Production and it is also used as the stability controller during shelf life. e.g. Sorbitan mono-oleate (Span 80), Polyethylene glycol 40 stearate, Stearic acid, Polyoxyethylene sorbitan monooleate (Tween 80), Sodium stearate [1].

Preservatives: E.g. methyl paraben, Propyl paraben, Benzalkonium chloride, Benzyl alcohol, Benzoic acid etc.

Antioxidants: e.g. Butylated Hydroxy Toluene (BHT), Ascorbyl palmitate, Butylated hydroxyanisole (BHA), etc.

Humectant: E.g. Glycerin, Propylene glycol, etc

Gelling agents: These are used as the thickening agents and also used to increase the consistency of any dosage form. E.g. Carbapol 934, carbapol 940, HPMC, HPMC-2910, sodium CMC

Permeation enhancers: These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability. Permeation enhancers should be non-irritating, non-toxic and non-allergenic. These Permeation enhancers should not bind to receptor site and should

not have any pharmacological activity within the body. They should be cosmetically suitable with an appropriate skin 'feel'. Permeation enhancers should be compatible with both excipients and drugs [5-18].

Mechanism of penetration enhancer

Penetration enhancers may act by one or more of three main mechanisms:

1. Disruption of the highly ordered structure of stratum corneum lipid.
2. Interaction with intercellular protein.
3. Improved partition of the drug, co enhancer or solvent into the stratum corneum.

Method of preparation of emulgel

Step-1: Oil/water or water/oil emulsion.

Step 2: Formation of gel base.

Step 3: Incorporation of emulsion in gel base.

Preparation of gel phase: The gel phase in the formulations is prepared by dispersing polymer in purified water with constant stirring at a moderate speed using mechanical shaker, then the pH was adjusted to 6 – 6.5 using tri ethanol amine (TEA).

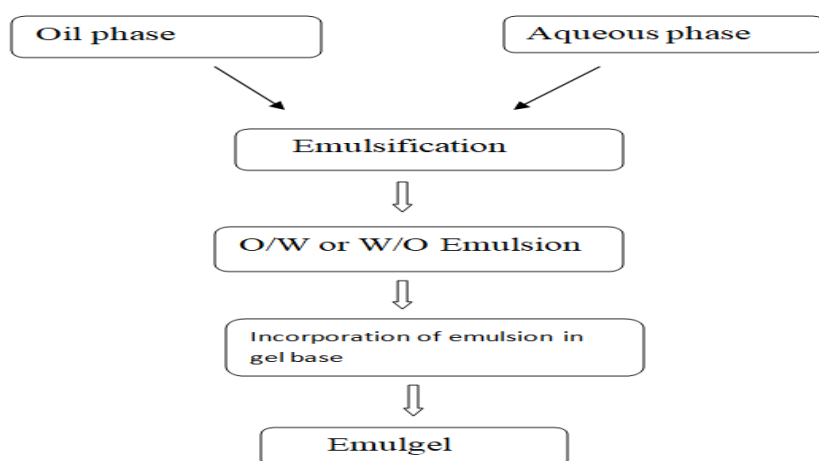
Preparation of oil phase of emulsion:

Oil phase of the emulsion is prepared by dissolving emulsifier e.g. span 20 in oil phase like light liquid paraffin.

Preparation of aqueous phase: The aqueous phase is prepared by dissolving emulsifier e.g. tween 20 in purified water.

Preparation of drug solution: The drug is dissolved in ethanol.

Figure 1. Method of preparation of emulgel.



Evaluation of emulgel

- **Physical examination:** The formulated emulgel was inspected visually for their homogeneity, color, consistency and phase separation (Figure 1).

- **Determination of pH:** Digital pH meter is used for the detection of pH of the formulation. pH meter electrode was washed by distilled water and then dipped into the formulation to measure pH and this process was repeated for 3 times and record the values.
- **Rheological studies:** Cone and plate viscometer are used for the detection of viscosity of the formulation. The viscosity of the different emulgel formulations is determined at 25 °C with spindle 52 and connected to a thermostatically controlled circulating water bath.
- **Stability studies:** The emulgels are prepared and are packed in aluminum collapsible tubes (5 g) and subjected towards stability studies at 5 °C, 25 °C/60% RH, 30 °C/65% RH, and 40 °C/75% RH for a time period of 3 months. Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profiles.
- **Fourier transforms infrared spectroscopy (FTIR):** The major objective of this investigation was to identify the stable storage condition for the drug in solid state and to identify the compatible excipients for formulation.

The *in vitro* drug release studies for prepared Emulgel were carried out on Diffusion cell using egg membrane.

- **Swelling index:** To determine the swelling index of prepared topical emulgel, 1 g of gel is taken on porous aluminium 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_t = Weight of swollen emulgel after time t.

W_o = Original weight of emulgel at zero time.

- **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.

$$S=M \times L/T$$

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.

- **Skin irritation test:** A 0.5 g sample of the test article was then applied to each site (two sites per rabbit) by introduction under a double gauze layer to an area of skin approximately 1" × 1" (2.54 × 2.54 cm² Stability studies). The Gellified Emulsion was applied on the skin of a rabbit. Animals were returned to their cages. After a 24 h exposure, the Gellified emulsion is removed. The test sites were wiped with tap water to remove any remaining test article residue.
- **Drug content determination:** Take 1 gm of emulgel. Mix it in suitable solvent. Filter it to obtain clear solution. Determine its absorbance using UV spectrophotometer. Standard plot of drug is prepared in same solvent. Concentration and drug content can be determined by using the same standard plot by putting the value of absorbance (Table 1).

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

Table 1. Examples of Marketed Preparations.

PRODUCT NAME	DRUG	MANUFACTURER
Voltaren Emulgel	Diclofinac diethyl ammonium	Novartis Pharma
Dosanac Emulsion gel	Diclofenac	Siam Pharmaceuticls
Miconaz-H Emulgel	Miconazole nitrate,Hydrocortisone	Medical-Union Pharmaceutical

CONCLUSION

The advantage of topical drug delivery system is having will better patient compliance. And emulgels are said to be one of the best approach for topical administration and various hydrophobic drugs are formulated as Emulgel for better results. Various penetration enhancers are used for potentiate the effect. Emulgels also possesses an edge in terms of spreadibility, adhesion, viscosity and extrusion, they will become a popular drug delivery system. Emulgels are said to be best conventional systems available in market.

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