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A Review on Emulgel as a Current Trend in 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. Emulgels are used as a recent topical delivery system containing dual release system i.e. gel and emulsion. Since hydrophobic drugs are not soluble in gel bases it causes problem during the release of drug. Emulgel formulation helps the hydrophobic drugs incorporation into the oil phase and then oily globules are dispersed in aqueous phase resulting in o/w emulsion which can be mixed into the gel base. Emulgels are used as better topical drug delivery systems over other systems because of many properties. The use of emulgels can be found in analgesics, anti-inflammatory, anti-fungal, anti-acne drugs and various cosmetic formulations.



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INTRODUCTION

Drugs can be administered by many routes to human body namely oral, sublingual, rectal, parental etc. When drug administration through other routes fails or skin infections occur, transdermal delivery system can be used. Large numbers of dermal products are available for skin as liquids, powders etc. but the most popular products are semisolid preparation. Among the semisolid preparations, the transparent gels are used both in cosmetics and in pharmaceutical preparations. Gels are prepared by entrapment of large amounts of aqueous or hydroalcoholic liquid in a network of colloidal solid particles. Gel formulations generally show better drug release than ointments and creams. A major disadvantage is in the delivery of hydrophobic drugs. Such types of problems are overcome by emulgel preparations and thereby hydrophobic drug shows the characteristics of gels. When gels and emulsion are mixed together emulgel is formed. Water phase containing gelling agent will convert an emulsion into an emulgel. Oil in water system is used for encapsulating lipophilic drugs whereas water in oil system is used for hydrophilic drug. Emulgels can be easily washed away whenever needed and also shows elegant properties. It also shows good penetration through the skin. Emulgels with properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water soluble, longer shelf life, biofriendly, transparent and pleasing appearance are used for dermatological purposes. Drug molecules can enter into the skin by three routes: through intact stratum corneum, through sweat ducts, or through 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, release of drug from the vehicle (partition coefficient), and drug diffusion across the layers of the skin (diffusion coefficient).

Advantages:

- Avoidance of first pass metabolism.
- Avoidance of gastrointestinal incompatibility.
- More selective to a specific site.
- Improve patient compliance.

- Suitability for self medication.
- Drug with short biological half life and narrow therapeutic window can use this method.
- Ability to stop medication when needed
- Convenient and easy to apply.

Disadvantages:

- Skin irritation on contact dermatitis.
- Possibility of allergenic reactions.
- Poor permeability of some drug through skin.
- Larger particle size drugs are not easy to absorb through the skin.

APPLICATION OF EMULGEL IN DRUG DELIVERY SYSTEM

Hydrophobic drugs can be easily incorporated into gels using emulsions.

Since hydrophobic drugs are not soluble in gel bases. Emulgels provide hydrophobic drugs to be mixed into an oil phase and oily globules in aqueous phase result in o/w emulsion. And this emulsion can be mixed into gel base. This shows better stability and release of drug than simply incorporating drugs into gel base.

Production feasibility and low preparation cost

Production feasibility can be increased since emulgel preparation is short and simple. There are no specialized instruments needed for the production of emulgels. Moreover, materials used are easily available and cheaper. Thereby production cost can be reduced for emulgels.

Controlled release

Emulgels can be used to prolong the effect of drugs having shorter $t_{1/2}$.

Patient compliance

They are less greasy and easy to apply.

No intensive sonication

Emulgel is not required to be sonicated but for vesicular molecules, sonication causes drug degradation and leakage.

Better loading capacity

Due to vast network, it shows better loading capacity than other approaches like niosomes, liposomes with nano size.

Better stability

Other preparations like powders which are hygroscopic, creams shows phase inversion or breaking and ointment shows rancidity due to oily base but among all of this emulgels shows better stability.

CONSTITUENTS OF EMULGEL

1. Aqueous Material:

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

2. Oils:

These agents form the oily phase of the emulsion. Mineral oils, either alone or combined with soft or hard paraffin, are used for externally applied emulsion and also used as a vehicle.

3. Emulsifiers:

They are used to maintain stability of a preparation during its shelf life and to cause emulsification during the manufacturing. e.g. Polyethylene glycol 40 stearate, Sorbitan monooleate (Span 80), Polyoxyethylene sorbitan monooleate (Tween 80), Stearic acid, Sodium stearate.

4. Gelling Agent:

It is used to improve the consistency of any dosage form and also used as a thickening agent. e.g. carbopol 934, carbopol 940.

5. Permeation Enhancers:

They are used to improve the absorption of drugs by disrupting the skin barrier, fluidize the lipid channels between corneocytes, altering the partitioning of the drug into skin structures. Commonly used penetration enhancers are oleic acid, lecithin, urea, clove oil, menthol etc..

METHOD OF PREPARATION

The gel is prepared by mixing carbopol 934 in purified water and stirring at a moderate speed and carbopol 940 in purified water with stirring. Then pH is adjusted to 6 to 6.5 using TEA. The oil phase contains span 20 in light liquid paraffin and aqueous phase prepared by tween 20 in purified water. Methyl and Propylparaben are dissolved in propylene glycol whereas drug is dissolved in ethanol and both solutions are mixed with the aqueous phase. Both the oily and aqueous phases are separately heated to 70°- 80°C; then the oily phase is added to the aqueous phase with continuous stirring until cooled to room temperature. And add Glutaraldehyde during of mixing of gel and emulsiolin in 1:1 proportion so as to obtain the emulgel.

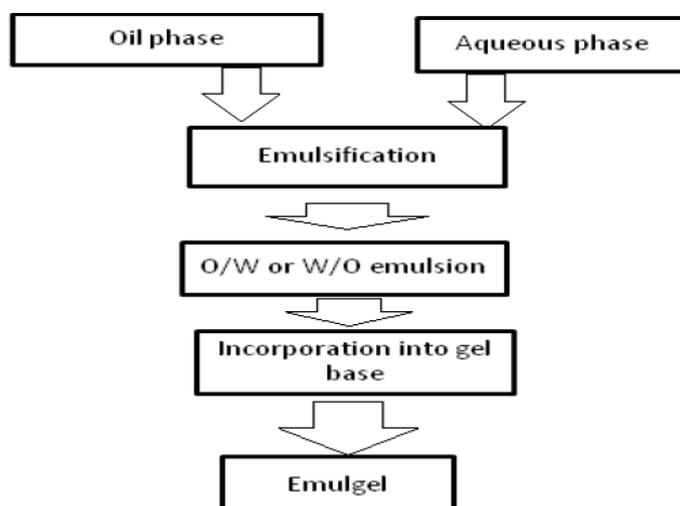
METHOD OF PREPARATION

STEP 1: Formulation of Emulsion either o/w or w/o

STEP 2: Formulation of gel base

STEP 3: Incorporation of emulsion into gel base with continuous stirring

The flow chart of emulgel preparation is shown in figure below



EVALUATION

Physical appearance:

The Emulgel is checked for their color, homogeneity, consistency and pH. The pH values of 1% Emulgel is measured using pH meter.

Spreadability:

Spreadability of emulgel is measured in terms of diameter of emulgel circle produced when emulgel is placed between two glass plates of definite weight. A weighed quantity (350 mg) of emulgel is taken on one glass plate and another glass plate is dropped from a distance of 5 cm. The diameter of the circle of spread emulgel is measured.

Extrudability study:

It is calculated by the force required to extrude the emulgel from the tube. The method applied 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. In this study emulgel extruded from lacquered aluminum collapsible tube on application of weight in grams required to extrude at least 0.5cm ribbon of emulgel in 10 seconds. For better extrudability, more quantity is extruded. For the measurement of extrudability, it is done in triplicate and the average values are calculated. The extrudability is then calculated by using the following formula:

$$\text{Extrudability} = \text{weight applied to extrude emulgel from tube (in gm)} / \text{Area (in cm}^2\text{)}$$

Rheological Studies:

Viscosity of emulgel is determined at 25°C using a cone and plate viscometer with spindle 52 and connected to a thermostatically controlled circulating water bath.

Swelling Index:

It is determined by taking 1g of emulgel in a porous aluminum foil and mixed with 0.1N NaOH kept in a 50ml beaker. Then samples are withdrawn at different time intervals and kept for drying and it is reweighed. Swelling index is calculated as follows:

$$\text{Swelling Index} = \{W_t - W_o / W_o\} 100$$

Where, (SW) % = Equilibrium percent swelling,

Wt = Weight of swollen emulgel after time 't'

Wo = weight of emulgel at zero time.

Drug Content Determination:

Emulgel is mixed in a suitable solvent. Filter it to obtain clear solution. Determine its absorbance using UV spectrophotometer. From the standard equation by putting the absorbance value concentration and drug content can be obtained.

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

Skin Irritation Test (Patch Test):

For this study emulgel is applied on the shaven skin of rat and its adverse effect like change in color, change in skin morphology are evaluated up to 24 hours. About 8 rats can be used for the study. Test passes if no irritation shown. If it fails the test is repeated with another 2 rats.

Ex-vivo evaluation:

Ex vivo release study is conducted using preserved or fresh chicken skin. Then skin is allowed to hydrate for 1 h before being mounted on the Franz diffusion cell with the stratum corneum (SC) facing the donor compartment. The gel sample is applied on the skin and then fixed in between donor and receptor compartment of Franz diffusion cell. The receptor compartment contains phosphate buffer of pH 7.4. The temperature of the medium is thermostatically controlled at $37 \pm 10^\circ\text{C}$ by surrounding water jacket and the medium is stirred with bar magnet using magnetic stirrer. Aliquots, withdrawn at predetermined intervals of time, are spectrophotometrically estimated at maximum wavelength of drug against their respective blank formulation treated in the same manner.

In-vitro Release Study:

Franz diffusion cell is used for the study. Emulgel is applied on the surface of egg membrane is clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber contains freshly prepared PBS (pH 5.5) solution to solubilize the drug. The receptor

chamber is stirred using magnetic stirrer. The samples (1.0 ml aliquots) are collected at different time interval and analyzed for drug content by UV-visible spectrophotometer after appropriate dilutions. Drug release is based on a function of time.

Accelerated stability studies of Emulgel:

Stability studies are carried out as per ICH guidelines. The formulations are stored for 3 months in stability chamber at $37\pm 2^{\circ}\text{C}$, $45 \pm 2^{\circ}\text{C}$ and $60 \pm 2^{\circ}\text{C}$. It is then analyzed for two weeks with UV-Visible spectrophotometer for drug content. Also, the change in pH is checked for determination of stability.

Drug Release Kinetic Study

To determine the drug release, the release data is fitted to following kinetic equations:

Zero – order equation: $Q = k_0 t$

Where, Q is the amount of drug released at time t, and k_0 is zero – order release rate.

First – order equation: $\ln(100 - Q) = \ln 100 - k_1 t$

Where, Q shows drug release at time t, and k_1 is the first – order release rate constant.

Higuchi's equation: $Q = k_2 \sqrt{t}$

Where, Q shows drug release at time t, and K_2 is the diffusion rate constant.

CONCLUSION

Emulgel is used as the recent technique among the topical drug delivery systems. 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.

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