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EMULGEL- A TOPICAL DRUG DELIVERY SYSTEM

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ABSTRACT

Gels are widely used as topical drug delivery system and there are various advantages of gel in topical delivery system. Gel is convinent made of drug delivery to treat localize disnfections. Although there are 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. Emulgel is the dosage combined form of gel and emulsion. Emulgel is the unique dosage form and novel in aspect of dermatological pharmacological accessibility directly to the skin. It acts on the target organ for diagnosis and treatment of diseases and infections, so emulgel can be used as better topical drug delivery system and is for extended period of time in analgesic and antifungal drugs.

KEYWORDS: Emulgel, topical drug delivery, Hydrophobic drugs.

INTRODUCTION

The application of drug containing formulation to the skin to treat cutaneous disorders is known as topical drug delivery system. Topical drug delivery system has several advantages such as ability to deliver drug more selectively to a specific site and prevention of incompatibility associated with gastro-intestinal. Moreover, topical delivery by avoiding first pass metabolism provide an increased bioavailability and consistent delivery for extended period. A technique such as emulgel can aid in the easy penetration of the drug into the skin and provide a rapid onset of action. The topical drug delivery system such as emulgel (gellified emulsion) generally used where the other system of drug administration fail to directly treat cutaneous disorders swuch as fungal, infections, acne, psoriasis etc Nowadays, emulsion ngels have been of growing importance in the field of pharmaceutical semisolid dosage forms. Emulgel for dermatological use has several favoprable propereties such as

being thioxotropic, greaseless, easily spreadable, easily removable, emollient, non staining, water soluble, longer shelf life, bio-friendly, transparent and pleasing appearance.

Fig. 1: An emulgel marketed product

EMULGEL

Emulgel are the combination of gel and emulsion. Both oil-in-water and water-in-oil type of emulsion used as a vehicle to deliver various drugs to the skin. They also have a high ability to penetrate the skin. The presence of the gelling agent in water phase converts a classical emulsion into an emulgel. 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 can basically penetrate into the skin by three routes: through 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).

Advantages

1. Avoidance of first pass metabolism.
2. Avoidance of gastrointestinal incompatibility.
3. More selective to a specific site.
4. Improve patient compliance.
5. Suitability for self-medication.

6. Providing utilisation of drug with short biological half-life and narrow therapeutic window.
7. Ability to easily terminate medication when needed.
8. Convenient and easy to apply.
9. Incorporation of hydrophobic drugs
10. Better loading capacity
11. Better stability
12. Production feasibility and low preparation cost
13. Controlled release
14. No intensive sonication

Disadvantages

1. Skin irritation on contact dermatitis.
2. The possibility of allergenic reactions.
3. The poor permeability of some drug through the skin.
4. Drug of large particle size not easy to absorb through the skin.
5. The occurrence of the bubble during formation of emulgel.

Physiology of skin

Most of the topical preparations are meant to be applied to the skin. So a basic knowledge of the skin and its physiology function are very important for designing topical dosage form. The skin of an average adult body covers a surface area approximately $2m^2$ and receives about one-third of the blood circulating through the body. An average human skin surface is known to contain, on the average 40-70 hair follicles and 200-300 sweat ducts on every square centimetre of the skin. The pH of the skin varies from 4 to 5.6. Sweat and fatty acid secreted from sebum influence the pH of the skin surface. The skin can be considered to have four distinct layers of tissue.

Non-viable epidermis

Stratum corneum is the outermost layer of skin, which is the actual physical barrier to the most substance that comes in contact with the skin. The stratum corneum is 10 to 20 cell layer thick over most of the body. Each cell is a flat, plate-like structure-34-44 µm long, 25-36 µm wide, 0.5 to 0.20 µm thick with a surface area of 750 to 1200 µm stocked up to each other in brick-like fashion. Stratum corneum consists of lipid (5-15%) including

phospholipids, glycosphingolipid, cholesterol sulphate and a neutral lipid, protein (75-85%) which is mainly keratin.

Viable epidermis

This layer of the skin resides between the stratum corneum and the dermis and has a thickness ranging from 50-100 μm. The structures of the cells in the viable epidermis are physicochemically similar to other living tissues. Cells are held together by tonofibrils. The density of this region is not much different than water. The water content is about 90%.

Dermis

Just beneath the viable epidermis is the dermis. It is a structural fibrin and very few cells are like it can be found histological in normal tissue. Dermis thickness ranges from 2000 to 3000 μm and consists of a matrix of loose connective tissue composed of fibrous protein embedded in an amphorphose ground substance.

Subcutaneous connective tissue

The subcutaneous tissue or hypodermis is not actually considered a true part of the structured connective tissue which is composed of loose textured, white, fibrous connective tissue containing blood and lymph vessels, secretary pores of the sweat gland and cutaneous nerves. Most investigators consider drug is permeating through the skin enter the circulatory system before reaching the hypodermis, although the fatty tissue could serve as a depot of the drug.

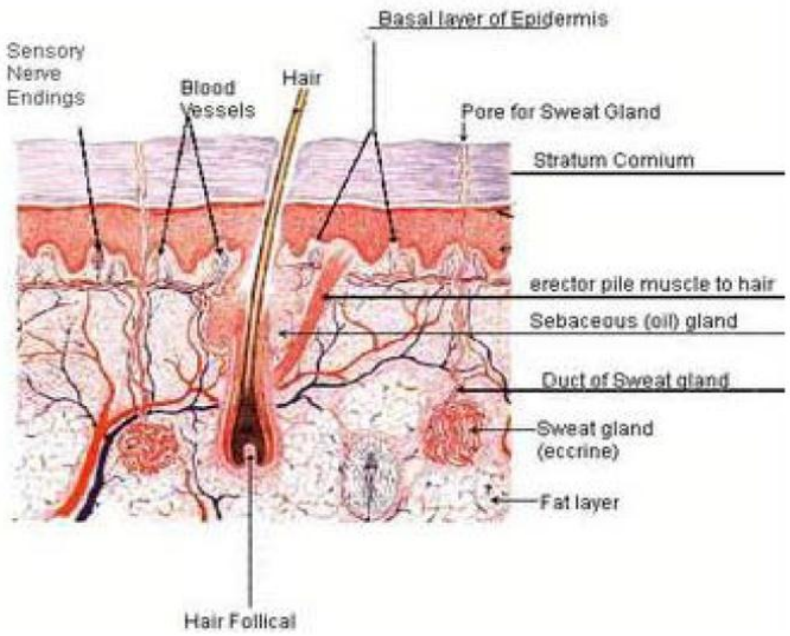

Fig. 2: Physiology of skin.

Drug delivery across the skin

There are two important layers in the skin: the epidermis and dermis. Blood vessels are distributed profusely beneath the skin in the subcutaneous layer. There are three primary mechanisms for drug absorption through the skin: intercellular, trans cellular and follicular. The next most common route of delivery is through the pilosebaceous route permeation tends to occur through the intercellular matrix, but through the transcellular pathway, it has been shown to provide a faster alternative route of highly polar molecules. In normal intact skin, it has been established that the keratinized corneocytes and the largely non-polar lipid intercellular cement of the horny layer are the major factors involved in the maintenance of efficient barrier for drugs.[14] The drug penetration for skin can be enhanced by using organic solvents such as propylene glycol, surfactants and DMSO. The permeation enhancers are altered the barrier properties of the stratum corneum by types of a mechanism including enhancing solubility, partitioning the stratum corneum, fluidising the crystalline structure of the stratum corneum.[15] Creams and gels that are rubbed onto the skin have been used for years for effective treatment against infections and pain by medication. New technologies now allow other drugs to be absorbed through the skin. These can be used to treat not just the affected areas of the skin but the whole body by systemic route.[16]

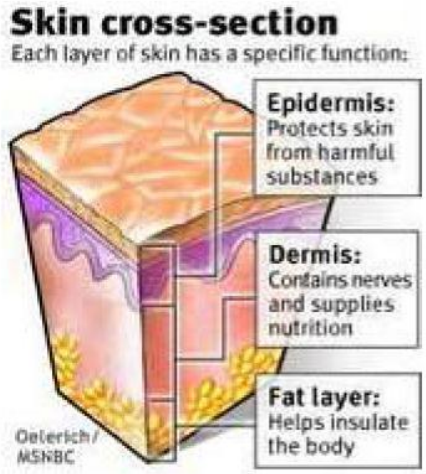

Fig. 3: Drug delivery cross of section

Preparation of emulgel

Emulgel was prepared by the method reported by[28] with minor modification. The Gel in formulations were prepared by dispersing Carbopol 934 in purified water with constant stirring at a moderate speed and carbopol 940 in purified water with constant stirring at a moderate speed then the pH are adjusted to 6 to 6.5 using triethanolamine (TEA). The oil

phase of the emulsion was prepared by dissolving Span 80 in light liquid paraffin having the drug in ethanol solution while the aqueous phase was prepared by dissolving Tween 80 in purified water. Methyl and Propylparaben was dissolved in propylene glycol and was mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70 ° to 80 °C; then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature. And add glutaraldehyde in during of mixing of gel and emulsion in ratio 1:1 to obtain the emulgel.

EVALUATION OF EMULGEL

Fourier transforms infrared spectroscopy (FTIR)

The primary objective of this investigation was to identify a stable storage condition for the drug in solid state and identification of compatible excipients for formulation.

Physical examination

The Prepared emulgel formulations were inspected visually for their colour, homogeneity, consistency and phase separation.

Determination of pH

pH of the formulation was determined by using digital pH meter. pH meter electrode was washed by distilled water and then dipped into the formulation to measure pH and this process was repeated 3 times.

Measurement of viscosity

The viscosity of the formulated batches was determined using a Brookfield Viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, USA) with spindle 63. The formulation whose viscosity was to be determined was added to the beaker and was allowed to settle down for 30 min at the assay temperature (25±1 °C) before the measurement was taken. Spindle was lowered perpendicularly into the centre of emulgel taking care that spindle does not touch the bottom of the jar and rotated at a speed of 50 rpm for 10 min. The viscosity reading was noted.

Spreadability

To determine spreadability of the gel formulations, two glass slides of standard dimensions were selected. Formulation whose spreadability was to be determined was placed over one slide and the other slide was placed over its top such that the gel is sandwiched between the

two slides. The slides were pressed upon each other so as to displace any air present and the adhering gel was wiped off. The two slides were placed onto a stand such that only the lower slide is held firm by the opposite fangs of the clamp allowing the upper slide to slip off freely by the force of weight tied to it. 20 g weight was tied to the upper slide carefully. The time taken by the upper slide to completely detach from the lower slide was noted.

Globule size and its distribution in emulgel

Globule size and distribution is determined by Malvern zeta sizer. A 1.0 g sample is dissolved in purified water and agitated to get homogeneous dispersion. The sample was injected to photocell of zeta sizer. Mean globule diameter and distribution is obtained.

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.

***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 dial y sis cell. Emulgel (1g) 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 were analysed for drug content by 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 % drug release was calculated using standard calibration curve.

Microbiological assay

Ditch plate technique was used. It is a technique used for evaluation of bacteriostatic or fungi static activity of a compound. It is mainly applied for semisolid formulations. Previously prepared Sabouraud's agar dried plates were used. Three grammes of the Gellified emulsion are placed in a ditch cut in the plate. Freshly prepared culture loops are streaked across the agar at a right angle from the ditch to the edge of the plate.

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" x 1" (2.54 x 2.54 cm^2). 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.[32]

Stability studies

The prepared emulgels were packed in aluminium collapsible tubes (5 g) 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 mo. Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profiles.[33]

CONCLUSION

The topical drug delivery system will be used extensively due to better patient compliance. Since emulgel possesses an edge in terms of spreadibilty, adhesion, viscosity 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. Mainly the hydrophobic drugs formulation can be developed using emulgel technique because it contain both oil and aqueous phase while hydrogels are not suitable for hydrophobic drugs. In future topical delivery will be used extensively to impart better patienrt compliance. Since, Emulgel is helpful in enhancing so that tnis novel drug delivery will become a popular formulation in future.

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