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AN OVERVIEW: EMULGEL AS A NOVEL TOPICAL DRUG DELIVERY SYSTEM

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ABSTRACT

Topical drug delivery system is a convenient mode of drug delivery for the treatment of localized skin infection, along with that recently the new approaches are also improving systemic effects. They are generally used as an antiseptic, antifungal, skin emollients and protecting agents. Topical medications are available in many dosage forms such as creams, ointments, paste, gels and lotions. But these dosage forms may have the drawbacks of stickiness, lesser spreading coefficient, irritation, poor penetration properties. To overcome these problems, recently new concept of emugel has been developed with the main aim of delivering the hydrophobic drugs. Emulgel is the combination of emulsion and gel base, they show controlled release of drug due to the combination effect of emulsion and gel. Gels having various advantages like non-greasy and better patient compliance but limited to deliver the hydrophobic drugs. So that emulgels comes to favour to avoid the demerits of gels. Emulgel deliver the hydrophobic drug molecules in controlled manner and possess the various advantages of being thixotropic, greaseless, easily spreadable, bio-friendly, transparent and pleasing appearance. So emulgels can be better semi solid dosage form than other conventional dosage form.

KEYWORDS: Topical drug delivery, Emulgel, antiseptic, antifungal, skin emollients hydrophobic.

INTRODUCTION

Topical drug delivery can be described as the putting on a drug containing formulation to the skin to treat the cutaneous disorders. This type of 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 allergy. Topical drug delivery is an effective route for local and systemic treatment. The dermatological pharmacology has a unique aspect that it gives direct accessibility of the skin as a target organ for diagnosis and treatment. Avoidance of first pass metabolism is the main advantage of topical drug delivery system. 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 other advantages of the drug delivery through skin.[1-3]

Advantages[4-5]

- Incorporation of hydrophobic drugs
- Improved loading capacity
- Better stability
- Controlled release
- No intensive sonication
- Bypasses first pass metabolism
- Avoiding gastrointestinal incompatibility
- More selective for a specific site
- Better patient compliance
- Suitable and easy to apply

Disadvantages

- May causes skin irritation
- The probability of allergenic reactions
- Drugs which have poor permeation through skin cannot be used for topical delivery system.
- Drugs of large particle size do not absorb easily through the skin

Drug delivery across the skin: The epidermis is the superficial layer of the skin and is composed of stratified keratinised squamous epithelium which varies in thickness in different parts of the body. The skin forms a relatively waterproof layer that protects the deeper and more exquisite structures. Blood vessels are distributed profusely underneath the skin. Especially important is a continuous venous plexus that is supplied by inflow of blood from the skin capillaries. In the most exposed areas of the body-the feet, hands, and ears blood is also supplied to the web directly from the small arteries. By preventing the absorption or loss of water and electrolytes skin acts as two-way barrier. The three primary mechanisms of topical drug absorption are: transcellular, intercellular, and follicular. Most drugs pass through the twisted path around corneocytes and through the lipid bilayer to viable layers of the skin. Pilosabaceous route is the next most common route of

delivery and is potentially under recognised in the clinical setting. Stratum corneum is the main barrier for penetration of most of chemicals through whole skin. Creams and gels that are wiped onto the skin have been used for years to deliver analgesic, antibacterial and antifungal drugs to an affected site of the body. It includes, among others, gels and creams for vaginal yeast infections and creams to soothe arthritis pain. Latest technologies now allow other drugs to be absorbed through the skin (transdermal). These technologies allow to treat not just the affected areas (for example, the skin) but the whole body. (systemic).[6]

Factors Affecting Topical Absorption of **Drug**

Physiological Factors

1. Thickness of skin.
2. Lipid content.
3. Density of hair follicles.
4. Density of sweat glands.
5. pH of skin.
6. Blood flow.
7. Skin hydration.
8. Inflammation of skin

Physicochemical Factors

1. Partition coefficient.
2. Molecular weight (less than 400 Dalton).
3. Degree of ionization (only unionized drugs gets absorbed well).
4. Effect of vehicles

Factors to be Considered While choosing a Topical Preparation

1. Effect of the vehicle e.g. An occlusive vehicle improves efficacy and enhances penetration of the active ingredient. The vehicle itself may have a drying, cooling, emollient or protective action.
2. Match of preparation with the type of lesions. Like, avoid greasy ointments for acute weepy dermatitis.
3. Matching the type of preparation with the site. (e.g., gel or lotion for hairy areas)
4. Irritation potential: Generally, ointments and w/o creams are less irritating, while gels are irritating.

Method to improve Drug Penetration and Absorption

1. Chemical enhancement
2. Physical enhancement
3. Biochemical enhancement
4. Supersaturation enhancement

Advantages[7-8]

1. Hydrophobic drugs can be easily incorporated into gels using o/w emulsions. Many of the hydrophobic drugs cannot be added directly into gel base because solubility act as a barrier and problem arises during the release of the drug. Emulgel helps in the incorporation of hydrophobic drugs into the oil phase and then oily globules are dispersed in aqueous phase resulting in o/w emulsion. And this emulsion can be mixed into gel base. This may be proving improved stability and release of drug than simply incorporating drugs into gel base.
2. Improved stability: Other transdermal preparations are comparatively less stable than emulgels. Like powders are hygroscopic, creams show inversion or breaking and ointment shows rancidity due to oily base.
3. Better loading capacity: Other novel approaches like niosomes and liposomes are of nano size and due to vesicular structures may result in leakage and result in lesser entrapment efficiency. But gels due to vast network have comparatively better loading capacity.
4. Production feasibility and low production cost: Preparation of emulgels comprises of easy and short steps which increases the feasibility of the production. There are no specialized instruments needed for the production of emulgels. Moreover, materials used are easily available and cheaper. Hence, decreases the cost of emulgel production.
5. No intensive sonication: Production of vesicular molecules need intensive sonication which may result in drug degradation and leakage. But this problem is not seen during the preparation of emulgels as no sonication is needed.
6. Controlled release: Emulgels can be used to prolong the effect of drugs having shorter half-life.

EMULGEL[9-12]

As the name suggest, emulgels are the combination of gel and emulsion. Both W/O and O/W type of emulsion used as a vehicle to deliver various drugs to the skin. They also have a high ability to permeate through the skin. The presence of the gelling agent in water phase converts a emulsion into an emulgel. Emulgel for dermatological use has several favourable advantages 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 permeate 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 absorption of drug. Passage through the stratum corneum is the rate limiting step for percutaneous absorption. The major steps involved in percutaneous absorption involves 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

- Bypasses first pass metabolism.
- Avoidance of gastrointestinal incompatibility.
- More selective to a specific site.
- Better patient compliance.
- Suitable for self-medication.

- Providing utilisation of drug with short biological t1/2.
- Narrow therapeutic window.
- Termination of medication is easy when needed
- Convenient and easy to apply.
- More suitable for hydrophobic drugs.
- Better loading capacity
- Improved stability
- Production feasibility and low cost
- Controlled release
- No intensive sonication.

Disadvantages

- Skin irritation on contact dermatitis.
- The possibility of allergenic reactions.
- Permeation of some drugs through the skin is poor.
- Drug of large particle size cannot be used for this formulation.
- The occurrence of the bubble during preparation of emulgel.

FORMULATION OF EMULGEL[13]

Steps involved in preparation of emulgel

Step 1: Formulation of O/W or W/O emulsions

The first step of emulsion formulation involves the dissolution of oil-soluble substances in the oil vehicle (e.g., dissolving span 80 in liquid paraffin) and the dissolution of the water-soluble substances in the aqueous phase (e.g., dissolving tween 80 in purified water). Both phases were heated to 70^{o} C and mixed under turbulent mixing conditions to ensure the dispersion of two phases into droplets. In the laboratory, the preparation of emulsions includes the use of a mechanical stirrer, whereas in industrial manufacturing emulsification is generally performed using mechanical stirrers, ultrasonifers, homogenisers, or colloid mills.

Step 2: Formulation of gel base

First, the water-soluble substances or excipients are dissolved in the aqueous vehicle using mechanical stirring in a mixing vessel. To reduce aggregation, the hydrophilic polymer is slowly added to the stirred mixture, and stirring is continued until the polymer has dissolved while the pH remains within the desired range. Superfluous stirring of pharmaceutical gels may result in the entrapment of air, so the mixing rate must be at a moderate pace.

Step 3: Addition of emulsion into gel base with steady blending: the gel stage is mixed into the emulsion stage to the extent of 1: 1 to get emulgel.[13]

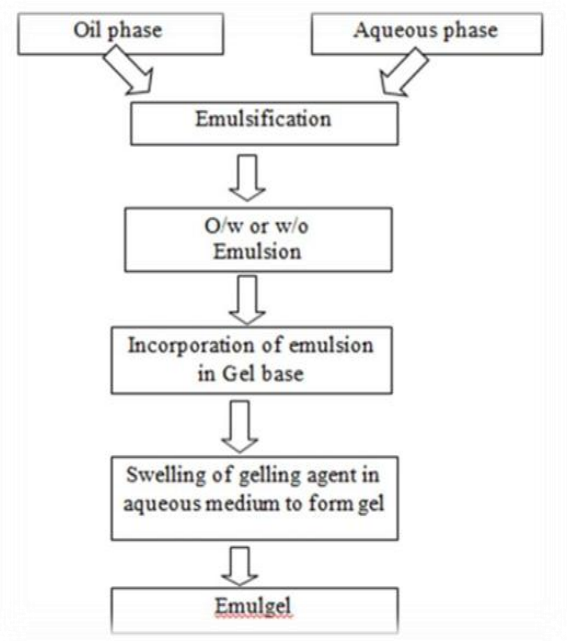

Fig1: Formulation of Emulgel.

Evaluation of emulgel[14-15]

- **Physical appearance**

The prepared emulgel was inspected visually for their color, homogeneity and consistency.

- **pH**

The pH values of 1% aqueous solutions of the formulated gellified emulsion were measured by a pH meter (Digital pH meter DPH 115 pm).[1]

- **Spreadability test**

A sample of 0.5 g of each formula was pressed between two glass slides (divided into squares of 5 mm sides) and left for about 5 minutes where no more spreading was expected (Bachhav et al., 2009). Diameters of spreaded circles were measured in cm and are taken as comparative values for spreadability. The results obtained are average of three determinations.[3]

- **Fourier transforms infrared spectroscopy (FTIR)**

The main objective of this investigation was to identify a stable storage condition for the drug in solid state and identification of compatible excipients for formulation.[3]

- **Measurement of viscosity**

The viscosity of the formulated batches is determined using a Brookfield Viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, USA) with spindle 63. The formulation whose viscosity 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 should not touch the bottom of the jar and rotated at a speed of 50 rpm for 10 minutes. The viscosity reading was noted.[1]

➢ **Swelling index**

To find out 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 taken off from the beakers at different time intervals and put it on a dry place for some time after it is reweighed.

➢ **In vitro drug release study**

Using egg membrane, the in vitro drug release studies of the Emulgel were carried out on Diffusion cell. 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. To solubilize the drug 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 and 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 different 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.

➢ **Globule size and its distribution in emulgel**

Globule size and distribution is detected by Malvern zeta sizer. A 1.0 g sample is solubilised in purified water and stirred to get homogeneous dispersion. The sample is injected to photocell of zeta sizer. Mean globule diameter and distribution is obtained. Or it is determined by motic microscope where the same sample is added on slide and observed under the microscope.

CONCLUSION

The topical route of drug administration is widely used because of better patient compliance. Emugels are best among other topical drug delivery systems and even new technologies due to its better stability and better drug loading capacity. Besides, emugels become a solution for loading hydrophobic drugs in a water-soluble gel basis.

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