A comprehensive Review on Topical Emulgel a Novel Drug Delivery System

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ABSTRACT:
Topical treatments in creams, ointments, gels, and lotions are an important part of the dermatological treatment library. They have relatively no serious side effects. Compared to other semisolid preparations, the use of gels has appeared in cosmetics and pharmaceutical preparations. When gels and emulsions are used in combination, they are called Emulgel. Emulgel is a promising hydrophobic drug delivery system. Emulgel is a gelling emulsion mixed with a gelling agent. The many advantages of gels primarily limit the delivery of hydrophobic drugs. Therefore, to overcome this limitation, emulsion methods are used. Emulgel is an interesting topical drug delivery system because it has a dual release control system, namely gel, and emulsion. Emulgels have several beneficial properties for dermatological use, such as thixotropy, nongreasy, easy to apply, easy to remove, softening, and Nonstaining, long-lasting, clear, and pleasant appearance. Therefore, emulsions can be used as a better local delivery system than existing systems. In a topical drug delivery system, the drug reaches the site of action through a diffuser outside the drug delivery system and its absorption displaces the skin. Percutaneous absorption can be enhanced by accelerating drug release from the dosage form. The rate of drug release from external preparations is directly dependent on the various physical and chemical properties of the carrier and the type of drug used.

KEYWORDS: Emulgel, emulsion, gel, topical preparation.
INTRODUCTION:

People of all ages suffer from all sorts of illnesses that affect their health and well-being. The healing effort has facilitated the discovery of a wide variety of drugs, drugs, and delivery systems. Then, different routes of administration are followed to achieve a therapeutic response to the drugs needed to treat the disease. The route of administration depends on the nature and severity of the disease. For skin conditions, the topical route is usually preferred. A topical drug delivery system is a system in which a formulation containing active pharmaceutical ingredients is applied directly to the skin to achieve the effects of a topical drug. Topical drug delivery systems have several advantages, such as the ability to deliver drugs more selectively to specific sites and prevent incompatibilities involving the gastrointestinal tract. [2] Additionally, topical delivery by avoiding first-pass metabolism may provide higher bioavailability and consistent long-term delivery. [3, 4] In a topical drug delivery system, the drug reaches the site of action via a diffuser outside the drug delivery system and its absorption displaces the skin. Percutaneous absorption can be enhanced by accelerating drug release from the dosage form. 6 The rate of drug release from external preparations is directly dependent on the various physical and chemical properties of the carrier and the type of drug used. [7, 8] Since the mid-1980s, gel emulsions have become increasingly important in topical semi-solid dosage forms. Its widespread use as a pharmaceutical dosage form stems from the widespread use of emulsion systems, especially for dermatological formulations.

Emulgels

Deliver different drugs into the skin. They also have a strong ability to penetrate the skin. The presence of gelling agents in the aqueous phase transforms a regular emulsion into an emulsion. Emulsions are used in dermatology with various beneficial properties, such as thixotropy, they are fat-free, easy to apply, easy to remove, soften, non-staining, water-soluble, and shelf life Use longer, environmentally friendly, transparent, and pleasant. The particles can penetrate deep into the skin in three ways: through the intact stratum corneum of the epidermis, sweat ducts, or sebaceous glands. The surface of the stratum corneum covers more than 99% of the total surface of the skin and can be used for transdermal drug absorption. This passage through the outermost layer is the passage that limits the rate of absorption through the skin.

Merits [9, 10]

• Avoiding gastrointestinal incompatibility.

• More selective to a specific site.

• Improve patient compliance

• Suitability for self-healing.

• Ensuring the use of a drug with a short biological half-life and a narrow therapeutic window. The ability to easily end treatment if needed

• Convenient and easy to apply

• Incorporation of hydrophobic drugs
Demerits-

- Better payload
- Better stability
- Manufacturing feasibility and low cost of preparation
- Controlled release
- No intense sonication
- Disadvantages:
  - Skin irritation with contact dermatitis.
  - Possibility of allergic reactions.
  - Poor skin permeability of some drugs.
  - A drug with a large particle size that is not easily absorbed by the skin.

The rationale for emulgel as a topical drug delivery system:

Many commonly used topical medications, such as ointments, creams, and lotions, have many drawbacks. They are very sticky, causing anxiety to the patient when applied. In addition, they also have a lower spread rate and must be rubbed. And they also have a stability problem. Due to all these factors in the main group of semi-solid preparations, the use of transparent gels has developed both in cosmetics and in pharmaceutical preparations. The gel is a colloidal substance usually 99% by weight that is a liquid fixed by surface tension between it and a network of macromolecular fibers made up of a small amount of viscous material present. Despite the many advantages of gels, the main limitation is hydrophobic drug delivery. To overcome this limitation, an emulsion-based method is employed, in which even a hydrophobic therapeutic radical can be successfully incorporated and delivered by gel [11]. Many drugs are applied to the skin or mucous membranes to improve or restore basic skin function or for pharmacological correction of stated problems. These products are called topical or dermatological products. Many commonly used topical medications, such as ointments, creams, and lotions, have many drawbacks. They are vicious, cause pain when applied to the patient, have a lower rate of spread when applied by rubbing, and also suffer from stability problems. Due to all these factors in the main group of semisolid preparations, the use of transparent gels has developed in cosmetic and pharmaceutical preparations. While there are many benefits of gels, the main drawback is them.

Drug delivery across the skin:

There are two important layers in the skin: the epidermis and the dermis. Blood vessels are widely distributed under the skin in the subcutaneous layer. There are three main mechanisms of drug absorption through the skin: intercellular, transcellular, and follicular.
The next most common route of use is the slime or slime-secreting route, which tends to pass through the extracellular matrix, but has been shown to provide an alternative, faster route for highly polar molecules to cross. transcellular. In normal, intact skin, it has been established that keratinized corneal cells and the largely nonpolar lipid intercellular cementum of the stratum corneum are key factors involved in the maintenance of effective barrier [12]. Skin penetration of drugs can be improved by using organic solvents such as propylene glycol, surfactants and DMSO. Penetration enhancers alter the barrier properties of the stratum corneum through a variety of mechanisms, including enhanced solubility, stratification of the stratum corneum, and fluency of the crystalline structure of the stratum corneum. horns [13]. Creams and gels applied to the skin have been used for many years to effectively treat infections and pain with medication. They can be used to treat not only the affected areas of skin but also the entire body. [14]

**METHOD OF PREPARATION**

**Aqueous material**

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

**Oils**

These agents form the oil phase in the emulsion. In topical emulsions, mineral oils, alone or in combination with soft or hard paraffin, are widely used as a means of drug therapy for their emphysema and sensory properties. The oils commonly used in oral formulations are nonbiodegradable mineral oil and castor oil, which provide a local laxative effect, and cod liver oil or various volatile oils of vegetable origin (eg., Arachis) as a dietary supplement. [15,16] **Table 1: Use of oils**

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Quantity</th>
<th>Dosage form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light Liquid Paraffin</td>
<td>7.5%</td>
<td>Emulsion and Emulgel</td>
</tr>
<tr>
<td>Isopropyl myristate</td>
<td>7-7.5%</td>
<td>Emulsion</td>
</tr>
<tr>
<td>Isopropyl stearate</td>
<td>7-7.5%</td>
<td>Emulsion</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>3-5%</td>
<td>Gel</td>
</tr>
<tr>
<td>Isopropyl palmitate</td>
<td>7-7.5%</td>
<td>Emulsion</td>
</tr>
</tbody>
</table>

**Emulsifiers**

Emulsifying agents are used both to aid in emulsification during manufacture and to control stability during a storage period, which can range from days in the case of on-demand emulsions to months or years in the case of commercial formulations to salt. Polyethylene glycol 40 stearate, sorbitan monooleate, polyoxyethylene sorbitan monooleate (tween 80), stearic acid, sodium stearate. [17, 18]

**Gelling agent**

These are the agents used to increase the consistency of any dosage form and can also be used as a thickening agent [19, 20].

**Permeation enhancers**

These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability [21].
Use of gelling agents:

<table>
<thead>
<tr>
<th>Gelling agent</th>
<th>Quantity</th>
<th>Dosage form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbopol-934</td>
<td>0.5%-2%</td>
<td>Emulgel</td>
</tr>
<tr>
<td>Carbopol-940</td>
<td>0.5%-2%</td>
<td>Emulgel</td>
</tr>
<tr>
<td>HPMC-2910</td>
<td>2.5%</td>
<td>Emulgel</td>
</tr>
<tr>
<td>HPMC</td>
<td>3.5%</td>
<td>Gel</td>
</tr>
<tr>
<td>Sodium CMC</td>
<td>1%</td>
<td>Gel</td>
</tr>
</tbody>
</table>

Use of penetration enhancers:

<table>
<thead>
<tr>
<th>Penetration enhancer</th>
<th>Quantity</th>
<th>Dosage form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oleic acid</td>
<td>1%</td>
<td>Gel</td>
</tr>
<tr>
<td>Lecithin</td>
<td>5%</td>
<td>Gel</td>
</tr>
<tr>
<td>Urea</td>
<td>10%</td>
<td>Gel</td>
</tr>
<tr>
<td>Isopropyl myristate</td>
<td>5%</td>
<td>Gel</td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>5%</td>
<td>Gel</td>
</tr>
<tr>
<td>Clove oil</td>
<td>8%</td>
<td>Emulgel</td>
</tr>
<tr>
<td>Menthol</td>
<td>5%</td>
<td>Emulgel</td>
</tr>
<tr>
<td>Cinnamon</td>
<td>8%</td>
<td>Emulgel</td>
</tr>
</tbody>
</table>

Properties of penetration enhancers

They should be non-toxic, non-irritating, and non-sensitizing.
Ideally they would act quickly and the activity and duration of the effect should be predictable and repeatable.
Penetration enhancers should act unidirectional, i.e. they should let the therapeutic agents flow into the body while preventing the loss of endogenous material from the body.
Penetration enhancers should be suitable for formulation into various topical formulations and, therefore, should be compatible with both excipients and medicaments.

Should be cosmetically acceptable with an appropriate “feel” on the skin.

**Mechanism of penetration enhancers**

Penetration enhancers can act according to one or more of three main mechanisms: Disruption of the highly ordered lipid structure of the stratum corneum.

Interaction with intercellular protein.

Improved distribution of the drug, co-enhancer, or solvent into the stratum corneum.

The amplifiers work by changing one of the three paths. The key to altering the polar pathway is to cause the protein conformational change or the solvent swelling. Fatty acid enhancers increased the fluidity of the lipid-protein part of the stratum corneum. Some enhancers work on both the polar and non-polar pathways, altering the multilayer pathway for penetration. Enhancers can increase the diffusion of a drug through skin proteins. The type of amplifier used has a significant impact on the design and development of the product.

**Preparation of Emulgel**

The emulgel was prepared using the method described by [22] with a slight modification. The gel formulations were prepared by dispersing Carbopol 934 in purified water under constant stirring at moderate speed and carbopol 940 in purified water under constant stirring at moderate speed, then adjusted to pH 6 to 6.5 using triethanolamine (TEA). The oil phase of the emulsion was prepared by dissolving the Span 80 in the light liquid paraffin containing the drug in an ethanol solution, while the aqueous phase was prepared by dissolving the Tween 80 in purified water. propylparaben and Methyl were dissolved in propylene glycol and mixed with the aqueous phase. Both the oil and water phases were separately heated to 70 to 80 °C; then the oil phase was added to the water phase with continuous stirring until it was cooled to room temperature. And add glutaraldehyde while mixing gel with emulsion in 1:1 ratio to get an.
EVALUATION OF EMULGEL [23-25]

Physical examination:
The prepared emulsion formulations were visually checked for their color, homogeneity, consistency, and phase separation.

Fourier transforms infrared spectroscopy (FTIR)
The main purpose of this study was to identify stable solid-state drug storage conditions and to identify compatible formulation excipients.

Determination of pH
The pH of the formulation was determined with a digital pH meter. The pH meter electrode was rinsed with distilled water and then immersed in the slide to measure the pH, and this process was repeated 3 times.

Spreadability
The emulgel was prepared using the method described by [22] with a slight modification. The gel formulations were prepared by dispersing Carbopol 934 in purified water under constant stirring at moderate speed and carbopol 940 in purified water under constant stirring at moderate speed, then adjusted to pH 6 to 6.5 using triethanolamine (TEA). The oil phase of the emulsion was prepared by dissolving the Span 80 in the light liquid paraffin containing the drug in an ethanol solution, while the aqueous phase was prepared by dissolving the Tween 80 in purified water. propylparaben and Methyl were dissolved in propylene glycol and mixed with the aqueous phase. Both the oil and water phases were separately heated to 70 to 80 °C; then the oil phase was added to the water phase with continuous stirring until it was cooled to room temperature. And add glutaraldehyde while mixing gel with emulsion in 1:1 ratio to get an emulsion.
Measurement of viscosity

The viscosity of the formulated batches was determined using a Brookfield viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, 9 USA) with a spindle 63. The formulation, whose viscosity was to be determined, was added to the beaker and allowed to settle for 30 min. at the assay temperature (25 ± 1 ° C) before measurement. The spindle was lowered perpendicularly to the center of the emulgel, taking care not to touch the bottom of the jar and to rotate at 50 rpm for 10 min. The viscosity reading was recorded.

Swelling index

To determine the swelling ratio of the prepared topical emulgel, 1 g of the gel is applied to a porous aluminum foil and then placed separately in a 50 ml beaker containing 10 ml of 0.1 N NaOH. The samples were then removed from the beakers at various intervals and, after reweighed, placed in a dry place for some time.

Globule size and its distribution in emulgel

The size and arrangement of the spheres are determined by the Malvern zeta meter. A 1.0 g sample is dissolved in purified water and mixed to obtain a homogeneous dispersion. The sample was injected into the zeta sizer photocell. The mean diameter and distribution of the spheres were obtained.

**In vitro drug release study**

In vitro, drug release studies with Emulgel were performed in a diffusion cell using an egg membrane. It was attached carefully to one end of the hollow glass tube of a dialysis cell. Emulgel (1g) was applied to the surface of the dialysis membrane of the egg membrane. The receptor chamber was filled with freshly prepared PBS solution (pH 7.4) to dissolve the drug. Samples (aliquots of 1 ml) were collected at appropriate intervals. The samples were analyzed for drug content using a UV-visible spectrophotometer after appropriate dilution. Cumulative corrections were made to obtain the total amount of drugs released in each time interval. The cumulative amount of drug released by the egg membrane was determined as a function of time.

Cumulative% drug release was calculated using a standard calibration curve.

**Microbiological assay**

The ditch slab technique was used. It is a technique used to evaluate the bacteriostatic or fungistatic effect of a compound. It is mainly used for semi-solid preparations. Pre-prepared plates dried on Sabouraud agar were used. Three grams of gelled emulsion are placed in a ditch cut into a plate.

Freshly prepared culture loops are spread over the agar at right angles 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 applying under the double layer of gauze to the skin surface of approximately 1 "x 1" (2.54 x 2.54 cm2). The gelled emulsion was applied to the skin of a rabbit. The animals returned to their cages. After 24 hours of exposure, the gelled emulsion is removed. The test sites were wiped with tap water to remove any residue of the test item [26].

**Stability studies**

The prepared emulates were packed in aluminum collapsible tubes (5 g) and subjected to stability tests at 5 ° C, 25 ° C / 60% RH, 30 ° C / 65% RH, and 40 ° C / 75% RH for 3 months. Samples were taken at 15-day intervals and evaluated for physical appearance, pH, rheology, drug content, and drug release profiles. [26]
CONCLUSION

A local drug delivery system will be widely used due to improved patient compliance. As emulsifiers have advantages in terms of lubricity, adhesion, viscosity, and extrusion, they will become a popular drug delivery system. In addition, they will become a solution for the incorporation of hydrophobic drugs into water-soluble gel bases.

REFERENCES:


