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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 semi-solid 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 by mixing with a gelling agent. The many advantages of gels primarily limit the delivery of hydrophobic drugs. Therefore, in order 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, non-greasy, easy to apply, easy to remove, softening, and Non-staining, long-lasting, clear and pleasant appearance. Therefore, emulsions can be used as a better local delivery system than existing systems.

Key Words: *Emulgel, emulsion, gel, topical preparation.*

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INTRODUCTION:

People of all ages experience all sorts of diseases that affect their health and well-being. Efforts to cure disease have facilitated the discovery of a variety of drugs, drugs, and delivery systems. Various routes of administration are then followed to achieve a therapeutic response with drugs necessary 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 local drug delivery system is a system in which a formulation containing active pharmaceutical ingredients is applied directly to the skin to achieve local drug action.

Topical drug delivery systems have several advantages, such as the ability to more selectively deliver drugs to specific sites and prevent incompatibility related to the gastrointestinal system. [2] In addition, local administration by avoiding first-pass metabolism can provide higher bioavailability and long-term consistent administration. [3, 4] In a local drug delivery system, the drug reaches the site of action through a diffuser outside the drug delivery system, and its absorption replaces the skin. The transdermal absorption can be enhanced by increasing the release rate of the drug from the dosage form. 6[ ]The drug release rate of external preparations directly depends on the various physical and chemical properties of the carrier and the drug used. [7, 8] Since the mid-1980s, emulsion gels have become increasingly important in topical semi-solid pharmaceutical forms. Its widespread use as a pharmaceutical dosage form stems from the widespread use of emulsion systems, especially for dermatological formulations.

Emulgels

Deliver various medications onto the skin. They also have a strong ability to penetrate the skin. The presence of gelling agents in the water phase turns classic emulsions into emulsions. Emulsions Emulgels used in dermatology have various beneficial properties, such as thixotropy, they are fat-free, easy to apply, easy to remove, softening, non-staining, water-soluble, longer shelf life, bio-friendly, transparent and pleasant in appearance.

The particles can penetrate deep into the skin in three ways: through the intact horny layer of the epidermis, sweat ducts or sebaceous glands. The surface of the stratum corneum covers more than 99% of the total skin surface and can be used for transdermal drug absorption. The passage through this outermost layer is the passage which limits the rate of percutaneous absorption.

Advantages [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
- 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 skin.

Rationale of emulgel as a topical drug delivery system:

Many commonly used topical agents, such as ointments, creams, lotions, have many disadvantages. They are very sticky, causing patient anxiety during application. In addition, they also have a lower spreading ratio and must be applied by rubbing. 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 expanded both in cosmetics and in pharmaceutical preparation. The gel is a colloid that is typically 99 wt.% a liquid that is immobilized by the surface tension between it and the macromolecular fiber network made up of the small amount of gelatinous material present. Despite the many advantages of gels, the main limitation is the delivery of hydrophobic drugs. To overcome this limitation, an emulsion-based approach is used, whereby even a hydrophobic therapeutic moiety can be successfully incorporated and delivered by gels [11]. Many medicinal products are applied to the skin or mucosa to enhance or restore the basic function of the skin or pharmacologically change the action in the highlighted tissues. Such products are referred to as topical or dermatological products. Many commonly used topical agents, such as ointments, creams, and lotions, have many disadvantages. They are viscous in nature, causing distress to the patient during application, have a lower spread rate so applied by rubbing, and also suffer from stability

problems. Due to all these factors in the main group of semi-solid preparations, the use of transparent gels has expanded in both cosmetics and pharmaceutical preparations. Despite the many advantages of gels, a main limitation is them.

Drug delivery across the skin:

There are two important layers in the skin: the epidermis and the dermis. Blood vessels are profusely distributed under the skin in the subcutaneous layer. There are three primary mechanisms for drug absorption through the skin: intercellular, transcellular, and follicular. The next most common route of delivery is the sebaceous-sebaceous route, which tends to cross the extracellular matrix but has been shown to provide a faster alternative route for highly polar molecules via the transcellular route. In normal, intact skin, it has been established that keratinized corneocytes and the largely nonpolar lipid intercellular cementum of the stratum corneum are the main factors involved in maintaining an effective drug barrier [12]. The skin penetration of the drug can be enhanced by the use of organic solvents such as propylene glycol, surfactants, and DMSO. Penetration enhancers alter the barrier properties of the stratum corneum by various mechanisms, including solubility enhancement, stratification of the stratum corneum, and fluidization of the stratum corneum crystal structure [13]. Creams and gels rubbed into the skin have been used for years to effectively treat infections and pain with medications. They can be used to treat not only the affected areas of the skin, but the entire body through the systemic route. [14]

Emulgel preparation

Aqueous material

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

Oils

These agents form an oil phase in the emulsion. In topical emulsions, mineral oils, alone or in combination with soft or hard paraffin, are widely used both as a drug carrier and for their occlusive and sensory properties. Commonly used oils in oral formulations are non-biodegradable mineral and castor oils, which provide a local laxative effect, and fish liver oils or various non-persistent oils of vegetable origin (eg, Arachis) as a dietary supplement.15,16]

Table 1: Use of oils

Chemical	Quantity	Dosage form
Light Liquid Paraffin	7.5%	Emulsion and Emulgel
Isopropylmyristate	7-7.5%	Emulsion
Isopropyl stearate	7-7.5%	Emulsion
Propylene glycol	3-5%	Gel
Isopropyl palmitate	7-7.5%	Emulsion

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 can also be used as 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:

Gelling agent	Quantity	Dosage form
Carbopol-934	0.5%-2%	Emulgel
Carbopol-940	0.5%-2%	Emulgel
HPMC-2910	2.5%	Emulgel
HPMC	3.5%	Gel
Sodium CMC	1%	Gel

Use of penetration enhancers:

Penetration enhancer	Quantity	Dosage form
Oleic acid	1%	Gel
Lecithine	5%	Gel
Urea	10%	Gel
Isopropyl myristate	5%	Gel
Linoleic acid	5%	Gel
Clove oil	8%	Emulgel
Menthol	5%	Emulgel
Cinnamon	8%	Emulgel

Properties of penetration enhancers

1. They should be non-toxic, non-irritating and non-sensitizing.
2. Ideally, they would act quickly and the activity and duration of the effect should be predictable and repeatable.
3. 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.
4. Penetration enhancers should be suitable for formulation into various topical formulations and therefore should be compatible with both excipients and medicaments.
5. Should be cosmetically acceptable with an appropriate & quot; feel & quot; 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 the gel with the emulsion in a 1: 1 ratio to get an emulgel.

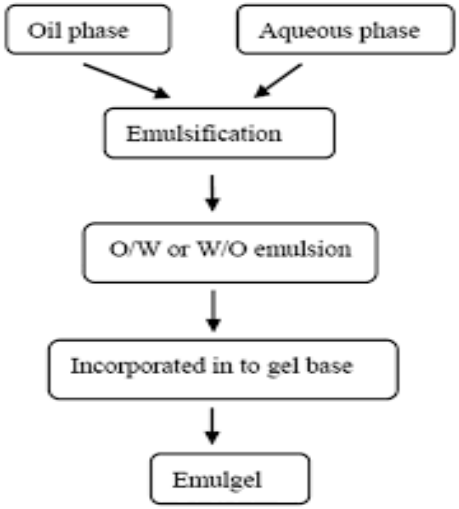

Fig: Preparation of Emulgel

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

Two standard size slides were selected to determine the spreadability of the gel preparations. The slide of which was to be determined was placed on one slide and the other slide was placed on top of it so that the gel was placed between two glass slides. Slides were pressed together to displace any air present, and the adhering gel was wiped away. Two guides are placed on the tripod in such a way that only the lower slide is firmly held by the opposing jaws of the clamp, allowing the upper slide to slide freely under the influence of the weight attached to it. A 20 g weight was carefully attached to the top slide. The time taken for the upper spool to completely disengage from the lower spool is recorded.

Measurement of viscosity

The viscosity of the formulated batches was determined using a Brookfield viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, 9USA) 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) prior to 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

In order 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 is 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 drug 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 is 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 emulgels 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 a period of 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.

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