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Emulgel as Topical Drug Delivery System

Prachi N. Raipure, Akshada U. Raghatwan, Priti B. Pote

Shankarrao Ursal College of Pharmaceutical Science and Research centre Kharadi, Pune.

Savitribai Phule Pune University, Pune-14

ABSTRACT

To treat localized and systemic infections, topical drug delivery is an effective drug delivery method. There are multiple dosage forms for topical drugs, including creams, ointments, gels, pastes, and lotions. Major disadvantages of gel are the delivery of hydrophobic drug. This can be overcome by Emulgels. Emulgel is the term referring to the dosage form made by combining gels and emulsions. Emulgel is an interesting topical drug delivery system as it has dual release control system, i.e., gel and emulsion. Emulgels are thixotropic, greaseless, easily spreadable, easily washable, emollient, non-staining, having long shelf life, transparent, and have a pleasing appearance, which are all beneficial for dermatological use. Emulgel is used to treat aches and pains caused by injuries, arthritis, headaches, muscle aches, backaches, and other conditions. Hence, emulgels can be used as better topical drug delivery system over present systems. This review gives knowledge about emulgel including its properties, advantages, and formulation considerations.

KEY WORDS: Emulgel, Emulsifier, Gel, Topical Drug Delivery.

INTRODUCTION

Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat the cutaneous disorder. The topical drug 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 fungal infection.[1] Delivery of medications topically is a desirable method of local and systemic therapy. The direct access to the skin as a target organ for diagnosis and treatment is a special feature of dermatological pharmacology.[2]

Pharmaceutical semisolid dosage forms, especially emulgels, have gained increase in interest from both academic and industrial researchers during the past ten years. For both systemic and local medication administration, the skin is a vital organ. Despite being a convenient route for drug delivery, some medications

may not penetrate the skin.[3] An emulsion and gel-based preparation is called emulgel. Oil-in-water (O/W) or water-in-oil (W/O) emulsions can be utilized, and both can be combined with a gelling agent to create an emulgel. The development of this new formulation for topical medication administration in recent years has revealed its effectiveness for carrying medicines that has hydrophobic nature. Additionally, it is anticipated that emulgel will become a vital method for loading hydrophobic pharmaceuticals.[4]

The formulations are available in a wide range of forms, including solid, semisolid, and liquid. Topically applied medications are used for their actions at the application site or systemic effects. Drug absorption is enhanced by the skin if the medication is in solution, if its lipid/water partition coefficient is favorable, and if it is non electrolyte.5 Gel formulations typically offer faster medication release than standard ointments and lotions. Gels' main drawback is their difficulty in delivering hydrophobic medications. Emulgels are prepared in order to overcome this limitation, and even with a hydrophobic medication that can benefit from the special properties of characteristics of gels when emulsions and gels are utilised. The dosage forms are referred to as emulgel when gels and emulsions are combined. In actual, the water phase's existence of a gelling agent makes an emulgel from a conventional emulsion. The O/W system whereas hydrophilic medications are utilised to entrap lipophilic substances contained within the W/O system.[6] Gels have many favorable properties like spreadability, non-staining, greaseless, and thixotropic but a major drawback in delivering hydrophobic drugs to the skin. Active ingredients with a hydrophobic nature exhibit improper drug release in gels due to lack of solubility in the aqueous phase, hence they are not suitable to be added into the gel base.[7, 8]

Advantages [9]

- Incorporation of hydrophobic drugs
- Better loading capacity
- Better stability
- Controlled release
- No intensive sonication
- Avoiding first pass metabolism
- Avoiding gastrointestinal incompatibility
- More selective for a specific site
- Improved patient compliance
- Convenient and easy to apply [9]

Disadvantages: [5]

- Skin irritation on contact dermatitis
- Possibility of allergenic reactions
- Poor permeability of some drugs through the skin
- Drugs of large particle size are not easy to absorb through the skin
- The occurrence of the bubble during formulation of emulgels.

FORMULATION OF EMULGEL

Vehicle[2]

The vehicle has following properties:

• Efficiently deposit the drug on the skin with even distribution.
• Release the drug so it can migrate freely to the site of action.
• Deliver the drug to the target site.
• Sustain a therapeutic drug level in the target tissue for a sufficient duration to provide a pharmacologic effect.
• Appropriately formulated for the anatomic site to be treated.
• Cosmetically acceptable to the patient.
• Due to the efficiency of the epidermal barrier, the amount of topical drug that gets through the stratum corneum is generally low. Rate and extent of absorption vary depending on characteristics of the vehicle but is also influenced by the active agent itself.

Aqueous material[12]

This forms the aqueous phase of the emulsion. The commonly used agents are water and alcohols. Eg sodium chloride

Oils[1]

Mineral oils are appropriate for emulsions that are applied externally, commonly used either alone or in combination with soft or hard paraffin employed as the drug's delivery system as well as their occlusive and properties of the senses. Oils commonly used in oral preparations are mineral and castor oils that are not biodegradable and provide a fish liver oils or other stable oils, local laxative effects vegetable origin (for instance, oils from Arachis, cottonseed, and maize) as dietary supplements.

Emulsifiers[11]

Emulsifying agents are used to enhance emulsion during manufacturing and to control stability during a temporary shelf life that can range from days' months or years to prepare emulsions for commercial substances like polyethylene glycol 40 stearate, Polyoxyethylene sorbitan (Span 80) and sorbitan mono-oleate sodium stearate, stearic acid, and monooleate (Tween 80).

Gelling agents[14,15]

These are the agents used to increase the consistency of any dosage form can also be used as thickening agent.

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

Penetration Enhancer[1]

Vehicles frequently contain penetration-enhancing components that temporarily interfere with fluidizing the lipid channels between corneocytes, protect the skin barrier affect the drug's distribution into skin structures, or otherwise, improve skin penetration.

Properties of penetration enhancers[1]

1. They should be non-toxic, non-irritating and non-allergenic.

2. They would ideally work rapidly, and the activity and duration of effect should be both predictable and reproducible.

3. They should have no pharmacological activity within the body i.e. should not bind to receptor sites.

Mechanism of penetration enhancers[14, 16]

Penetration enhancers may act by one or more of three main mechanisms:

1. Disruption of the highly ordered structure of stratum corneum lipid.
2. Interaction with intercellular protein.
3. Improved partition of the drug, coenhancer, or solvent into the stratum corneum.

The enhancers act by altering one of three pathways.

Methods involved in preparation of emulgels

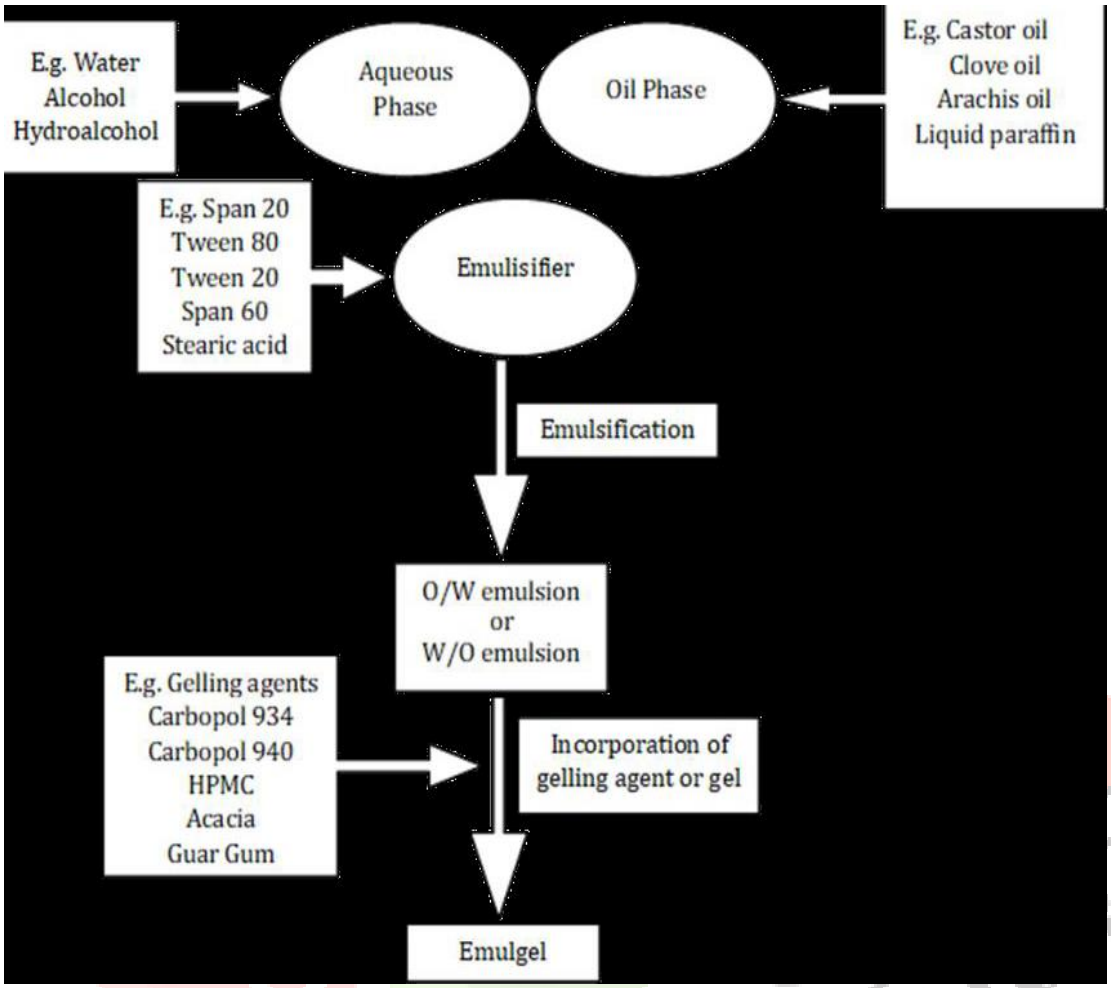
Step 1: Formulation of O/W or W/O emulsions

The initial step of emulsion formulation involves the dissolution of oil-soluble substances in the oil vehicle (e.g. dissolving span 20 in liquid paraffin) and the dissolution of the water soluble substances in the aqueous vehicle (e.g. dissolving tween 80 in purified water). Both phases were mixed under turbulent mixing conditions to ensure the dispersion of two phases into droplets[5,17]. In the laboratory, the preparation of emulsions involves the use of a mechanical stirrer, whereas the emulsification of industrial manufacturing is generally performed using mechanical stirrers, ultrasonicator, homogenisers, or colloid mills[18].

Step 2: Formulation of gel base

To begin, the water-soluble substances or excipients are dissolved in the aqueous vehicle using mechanical stirring in a mixing vessel. To avoid 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[19,20]. 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



General steps involved in the preparation of Emulgels

Evaluation of emulgels[21, 22, 23]

Fourier transforms infrared spectroscopy (FTIR)

The primary objectives of this investigation were to find a stable storage environment for the medication in its solid state and to find formulation-compatible excipients.

Physical examination

The prepared emulgel formulations, colour, homogeneity, consistency, and phase separation were all inspected visually.

Determination of pH

With the use of a digital pH metre, the formulation's pH was determined. The pH metre electrode was rinsed with distilled water before being dipped into the mixture to measure pH.

Measurement of viscosity

Using a Brookfield Viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, USA) with spindle 63, the viscosity of the formulated batches was evaluated. The formulation whose viscosity was to be evaluated was added to the beaker, and before the measurement was taken, it was allowed to settle for 30 minutes at the assay temperature (25±1 °C). Spindle was lowered perpendicularly into the centre of the emulgel, being careful not to let it touch the jar's bottom, and rotated for 10 minutes at a speed of 50 rpm. The viscosity reading was noted.

Spreadability

Two glass slides of standard diameters were used to test the gel compositions' spreadability. One slide was covered with the formulation whose spreadability was to be evaluated, and the other slide was placed on top, such that the gel is sandwiched between two slides. The sticking gel was removed after the slides were pressed together to remove any air that might have been present. The upper slide may slide off freely due to the force of the weight attached to it because only the lower slide is held firmly by the opposing fangs of the clamp. 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 emulgels

Malvern zeta sizing determines globule size and distribution. For homogenous dispersion, a 1.0 g sample is dissolved in filtered water and stirred. The sample was injected into the zeta sizer's photocell. The distribution and mean globule diameter are determined.

Swelling index

A 50 ml beaker containing 10 ml of 0.1 N NaoH and 1 g of produced topical emulgel are used separately to calculate the swelling index of the gel. After then, samples were taken out of the beakers at various intervals and placed on a dry surface for a while before being weighed again.

***In vitro* drug release study**

Egg membrane was used in the in vitro drug release tests for the Emulgel on diffusion cells. This was securely attached to one end of the dial-y-sis cell's hollow glass tube. Egg membrane dialysis membrane's surface was treated with emulgel (1g). To solubilize the medicament, freshly prepared PBS solution (pH 7.4) was injected into the receptor chamber. A magnetic stirrer was used to stir the receptor chamber. After the proper dilutions,

the samples (1 ml aliquots) were collected at suitable intervals and tested for drug content using a UV-visible spectrophotometer. To determine the overall amount of medication released at each time interval, cumulative corrections were done. 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

The ditch plate method was employed. It is a method for evaluating a compound's bacteriostatic or fungal static activity. It is mostly used for compositions that are semisolid. The Sabouraud's agar dried plates were previously produced. In a ditch cut plate three grammes of the gellified emulsion are added. Freshly made culture loops are streaked at an angle across the agar from the ditch to the plate's edge.

Skin irritation test[24]

The test article was then introduced into each site (two sites per rabbit) under a double layer of gauze to a skin region that measured about 1" × 1" (2.54 x 2.54 cm2 for stability tests). A rabbit's skin was treated with the Gellified Emulsion. The animals were placed back in their cages. The Gellified emulsion is removed after a 24-hour exposure. To get rid of any last traces of test article residue, the test areas were cleaned with tap water.

Stability studies[25]

The prepared emulgels were packed in aluminium collapsible tubes (5 g), and stability tests were conducted on them for three months at 5 °C, 25 °C/60% RH, 30 °C/65% RH, and 40 °C/75% RH. At intervals of 15 days, samples were taken out and examined for their physical appearance, pH, rheological characteristics, drug content, and drug release profiles.

PACKAGING OF EMULGELS[26]

Packaging of emulgels are usually done in membrane sealed lacquered aluminum tube with inner coating of a phenoxy-epoxy based lacquer closed with propylene screw cap or an aluminum laminated tubes closed by a moulded seal, with a propylene screw cap.

MARKETED FORMULATIONS

SR No	Brand Name	Active Ingredient	Manufacturer	Uses
1	Voltarol 1.16% Emulgels	Diclofenac Diethyl ammonium Salt	Novartis	Anti Inflammatory
2	Miconaz H-emulgel	Miconazole Nitrate Hydrocortisone	Medical union Pharma ceuticals	Topical corticosteroid
3	Denacine Emulgel	Clindamycin Phosphate	Beit jala Pharmaceutical Company	Anti-acne
4	Diclon Emulgels	Diclofenac Diethylamine	Medpharma	Anti-Inflammatory
5	Cataflam emulgel	Diclofenac potassium	Novartis	Anti-inflammatory

Conclusion:

Due to improved patient compliance, the topical drug delivery system will be utilised extensively. The spreadability, adhesion, viscosity, and extrusion advantages of emulgel will make them an increasingly popular drug delivery method. In the future, these physical and physico-chemical properties will be utilized to deliver a greater number of topical medications, such as emulgel.

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