Emulgel: A dual release system for hydrophobic drug delivery

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Abstract

Emulgel is NDDS that is in recent light for its capacity to deliver hydrophobic drugs. In a topical drug delivery system, the most important task is to pass the drug through the barrier and the proper diffusion of the drug in the skin. Emulgel is made up of emulsion and gel where emulsion helps in the delivery of hydrophobic drugs while gel gives proper diffusion, spread ability and improves the stability of an emulsion. It’s a dual release system in which the emulsion is jellified by gelling agents giving us characteristics of both emulsion and gel along with improved patient compliance. In the following review, we will discuss about the emulgel and its types along with its method of preparation, evaluation and applications in a comprehensive way.

Keywords: Emulgel; Dual release system; Hydrophobic drugs; Topical drug delivery

1. Introduction

Topical drug administration is a localized drug delivery system anywhere in the body such as ophthalmic, vaginal, rectal and skin as topical routes. These are applicable for wide range such as for both cosmetics and dermatological preparations to healthy or diseased skin [7].

When a person has cutaneous disorders like acne, eczema, psoriasis, etc., then topical drug delivery is preferred, in which the required drug is applied to the skin. This route of administration has many years of history and new methods and technologies are continuously being investigated and developed for better patient compliance. This route of administration is the best option for cutaneous purposes as the skin is the most accessible organ [37,39] and facilitates the delivery of drugs with better efficacy when compared to the other routes of administration [15].

Drugs are topically administered for their action at the site of application for local or systemic effects. Drug absorption is enhanced through the skin if the drug substance is in solution, if it has a favorable lipid/water partition coefficient and if it is a non-electrolyte [3].

Topical drug delivery is an attractive route for local and systemic treatment [40]. Some topical administrations are applied on the skin but they actually work towards being absorbed systemically [38]. The advantages of topical drug delivery system includes; bypass first pass metabolism, avoidance of the risks and inconveniences of intravenous therapy and the varied conditions of absorption, such as the presence of enzymes, pH changes, and gastric emptying time are another advantage of the topical drug delivery system [1].

Topical products are divided into two types; external topical and internal topical. The external topical product spreads to the tissues to cover the diseased areas of the body. In contrast, internal topical products are applied topically to the mucous membrane in the oral cavity, rectal tissues, or vagina to achieve local effect [15].
Following are the different types of topical drug delivery systems that are being widely used around the world.

- **Solid**: Solid topical dosage forms being used are powders, plasters, etc.
- **Semi-solid**: Semi-solid dosage forms being used are ointments, creams, poultries, gels, pastes, etc.
- **Liquid**: this dosage form includes tinctures, emulsions, paints, lotions, etc.
- **Miscellaneous**: Miscellaneous dosage forms being used are topical aerosols, gauzes, rubbing alcohols, liquid cleansers, tapes, etc. [15].

### 1.1. Emulsion

Emulsions are made by combining two or more immiscible liquids. In this system, the aqueous phase is miscible with the oil phase using an emulsifying agent. The emulsifying agents help to stabilize emulsions. They have good penetration capability and can be easily washed off from the skin [4, 18].

### 1.2. Gels

The entrapment of large amounts of aqueous or hydroalcoholic liquid in a network of colloidal solid particles, which may be inorganic or organic polymers of natural or synthetic origin, constitute a gel. The high amount of aqueous component permits greater dissolution of drugs, and permits easy migration of the drug as compared to the ointment or cream base. However, this makes gels a poor vehicle for hydrophobic drugs [25].

### 1.3. Emulgel

Emulgel are emulsion, either of oil-in-water or water in oil type, which are gelled by mixing with a gelling agent [24]. Emulsified gel is stable one and superior vehicle for hydrophobic or poorly water-soluble drugs [18].

While gel captures small drug particles and provides its release in a controlled manner by forming a cross-linked network. It prolongs the contact period of medication over the skin due to its mucoadhesive property. Within biphasic liquid doses forms, emulsion is a controlled release system where entrapped drug particles in internal phase pass through the external phase to the skin and slowly get absorbed. Internal phases (act as reservoir of drug) slowly release drug in a controlled way through the external phase to the skin. In spite of many advantages of gels and emulsions, a major limitation is their inability to deliver the hydrophobic drugs and instability during storage respectively. Therefore, to overcome these limitations an emulsion-based approach i.e., Emulgel is being used in which a hydrophobic therapeutic moiety is successfully incorporated into gel and enjoy the unique property of gels. Since Emulgel possesses the property of both emulsion and gel it acts as dual control release system.

Emulgel offers the capability of delivering both hydrophilic and lipophilic drug moieties due to the presence of both aqueous and non-aqueous phases.

It is believed that the usefulness of any topical preparation lies on its penetration ability. If emulsion is thixotropic, the processes of penetration into skin are simplified. Thus, to improve stability of emulsion and its penetration ability it is incorporated into gel. Further, Emulgel for dermatological use has several favourable properties, such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, greater shelf life, bio-friendly, clear & pleasant appearance [26].

### 1.4. Types of emulgel

#### 1.4.1. Macroemulsion gel

Emulgel with emulsion having particle sizes greater than 400 nm are known as macroemulsion gel. They are physically invisible, but the individual droplets can be seen clearly under a microscope. Macroemulsions are thermodynamically unstable, but surface-active agents can help to stabilize them [4].
1.4.2. Microemulgel

Micro-emulsion are transparent and thermodynamically stable as their droplet size range from 100 to 400 nm and they do not coalesce. Microemulsion are composed of oil, surfactant, co-surfactant, and water in particular ratios [25,22].

1.4.3. Nanoemulgel

When Nano-emulsion are incorporated into gel, it is called Nano-emulgel. Nanoemulsion are thermodynamically stable, transparent dispersion of oil and water stabilized by an interfacial film of surfactant and cosurfactant molecule having a globule size of less than 100 nm [21].

1.4.4. Submicron emulgel

When submicron-emulsion are incorporated into gel, it is called submicron-emulgel. Submicron emulsion (SE) possess a dispersed phase mean droplet diameter under 1 µm and also referred to as miniemulsion, ultrafine emulsions, nanoemulsions. SE can be given by a variety of route such as parenteral, topical, ophthalmic, and nasal delivery and as a vehicle in cosmetics [2].

1.5. Advantages of Emulgel [41]

- Incorporation of hydrophobic drugs
- Better loading capacity
- Better stability
- Production feasibility and low preparation cost
- Controlled release
- No intensive sonication
- Improve Patient Compliance

1.6. Disadvantages of Emulgel [26]

- Skin irritation on contact dermatitis.
- The possibility of allergenic reactions.
- Some drugs show poor permeability through the skin.
- Difficult to absorb the large drug particle through the skin.
- During formation of emulgel the occurrence of bubble is seen.

2. Rationale of emulgel as a topical drug delivery system [16,32]

To enhance or restore a fundamental function of skin or pharmacologically alter an action in the underlined tissues, a number of medicated products are applied to the skin or mucous membrane. These products are known as topical or dermatological products. Many widely used topical agents like, creams, ointments, lotions have many disadvantages. They cause uneasiness to the patient due to their sticky nature. Moreover, they exhibit the problem of stability, they also have lesser spreading coefficient and need to apply with rubbing also. Therefore, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations due to all these factors within the major group of semisolid preparations. A gel is a colloid that typically contain 99% liquid, which is immobilized by surface tension between it and a macromolecular network of fibres built from a small amount of a gelatin substance present. In spite of many advantages of gels, the delivery of hydrophobic drugs in gels is a major limitation. So, to overcome this limitation, emulgel; an emulsion-based approach is being used so that even a hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels.

3. Formulation of emulgel

3.1. Active pharmaceutical ingredients

Active pharmaceutical ingredients are the main action producing agents in the emulgel formulations. The generally used active pharmaceutical ingredients are NSAIDs, antibiotics, antifungal agents, antimicrobial agents, antiseptics, etc. [22].

3.2. Vehicle

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.
- Delivery of the drug to the target site.
- They sustain a therapeutic drug level in the target tissue to provide a pharmacologic effect for a sufficient duration.
- Formulated Appropriately for the anatomic site to be treated.
- Cosmetically acceptable to the patient [16].
- The amount of topical drug that gets through the stratum corneum is generally low due to the efficiency of the epidermal barrier. Rate and extent of absorption vary depending on characteristics of the vehicle but is also influenced by the active agent itself [1].

These are of two types –

- Aqueous material

These are used to form the aqueous phase of the emulsion. Commonly used agents are water and alcohols.

- Oils

These form the oily phase of the emulsion. Mineral oils, either alone or combined with soft or hard paraffin, are widely used for externally applied emulsions. In oral preparations, widely used oils are non-biodegradable mineral and castor oils that provide a local laxative effect, and fish liver oils or various fixed oils of vegetable origin like Arachis, cottonseed, and maize oils are used as nutritional supplements [3,27].

**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>Isopropyl palmitate</td>
<td>7-7.5%</td>
<td>Emulsion</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>3-5%</td>
<td>Gel Emulsifier</td>
</tr>
</tbody>
</table>

### 3.3. Emulsifiers

Emulsifying agents are used both to promote emulsification at the time of manufacture and to control stability during a shelf life that can vary from days for extemporaneously prepared emulsions to months or years for commercial preparations. e.g. polyethylene glycol 40 stearate, sorbitan monooleate (span 80), polyoxyethylene sorbitan monooleate (tween 80), stearic acid, sodium stearate [3].

### 3.4. Gelling agent

**Table 2** Use of gelling agent

<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>
<tr>
<td>Poloxamer 407</td>
<td>1</td>
<td>gel</td>
</tr>
</tbody>
</table>
These are the agents used to increase the consistency of any dosage form and can also be used as thickening agent. [3] Various gelling agents have been used some of them are as follows; Carbopol 940, HPMC 2910, Carbopol-934, HPMC, Sodium CMC, etc. [46].

3.5. pH adjusting agent
These agents are used to maintain the pH of the formulation. Example: triethylamine, NaOH, etc. [4].

3.6. Preservatives
Preservatives are used to inhibit the growth of micro-organisms and are added to emulgel to avoid spoilage of the formulation from micro-organism. E.g., Propyl paraben, methyl paraben, Benzalkonium chloride, Benzoic acid, Benzyl alcohol etc.

3.7. Antioxidants
The antioxidants are used for the emulgels to enhance the stability of therapeutic agents. E.g., BHA, BHT, etc.

3.8. Humectants
The humectant is used for the maintenance of the moisture in the emulgel formulations. Glycerine, Propylene glycol are the commonly used humectants [22].

3.9. Permeation enhancers
These are agents that induce a temporary and reversible increase in skin permeability [3].

Table 3 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>

3.9.1. Properties of penetration enhancers: [3]
- They should be non-irritating, non-toxic, and non-allergenic.
- They ideally work rapidly, and should have predictable and reproducible activity and duration of effect.
- They should have no pharmacological activity within the body i.e., should not bind to receptor sites.
- They should work unidirectional i.e., should allow therapeutic agents into the body whilst preventing the loss of endogenous material from the body.
- They should be appropriate for formulation into diverse topical preparations, thus should be compatible with both excipients and drugs.
- They should be acceptable cosmetically with an appropriate skin ‘feel’.
3.9.2. Mechanism of penetration enhancers: [3,27,29]

The penetration enhancers act by altering any one of the three pathways. The key to change the polar pathway is to cause solvent swelling or conformational change of protein. The fatty acid enhancers elevate the fluidity of the lipid-protein portion of the stratum corneum. Some enhancers act on both non-polar and polar pathway by changing the multi-laminate pathway for penetration. Permeation Enhancers can also elevate the drug diffusivity through proteins present in skin. The type of enhancer used has a significant impact on the development and design of the product.

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

- The disruption of the highly ordered structure of stratum corneum.
- Interaction with intercellular protein.
- Improved partition of the co-enhancer, drug or solvent into the stratum corneum.

Re-organisation of lipid domain and barrier disruption is shown by the use of terpenes, which enhance the drug diffusion by extracting lipids from stratum corneum.

3.9.3. Pathways of Transdermal Permeation: [17]

Permeation can occur by diffusion via:

- Transdermal permeation, through the stratum corneum.
- Intercellular permeation, through the stratum corneum.
- Trans-appendaged permeation through the hair follicle, sebaceous and sweat glands.

Most molecules penetrate into the skin via intercellular route and therefore, most of the enhancing techniques aim to bypass or disrupt the molecular architecture.

3.9.4. Methods to Enhance Drug Penetration: [31]

- Chemical enhancement
- Biochemical enhancement
- Physical enhancement
- Super saturation enhancement

4. Preparation of emulgel

- Step 1: Formulation of either O/W or W/O emulsion.
- Step 2: Formulation of gel base.
- Step 3: Incorporation of emulsion into gel base with continuous stirring [1].

4.1. Formulation of either o/w or w/o emulsion

The emulsion is prepared by slowly mixing oil phase and aqueous phase of the emulsion containing an emulsifying agent like spans and tweens. Before mixing the two phases, both the oily and aqueous phase are separately heated to 70-80°C; then the oily phase can be added to the aqueous phase with continuous stirring for 15 to 20 minutes and cooled to room temperature. Preservative may also be added to the emulsion in any phase depending on its solubility.

4.2. Formulation of gel base

The gel in formulation is prepared by dispersing a suitable polymer in purified water with constant stirring at a moderate speed to allow complete hydration and swelling of polymers. Then the pH of this formulation is adjusted to 6 to 6.5 using Triethanolamine (TEA).

4.3. Incorporation of emulsion into gel base

The obtained emulsion is mixed with the gel in 1:1 ratio with gentle stirring to obtain the emulgel [28].
5. Evaluation of emulgel

5.1. Fourier transforms infrared spectroscopy (FTIR)
The main objective of the FTIR investigation was to identify a stable storage condition for the drug in solid state and identification separation [1].

5.2. Determination of pH
It was determined by using digital pH meter. For this the electrode of pH meter was washed by distilled water and then dipped into the formulation to determine pH. This process was repeated 3 times [3,30].

5.3. Measurement of viscosity
To carry out the rheological studies, we use a cone and plate viscometer. The various emulgel formulations are taken and their viscosity is determined at 25°C by using the above-mentioned apparatus connected to a circulating water bath which is controlled thermostatically [11].

5.4. Spreadability
The two glass slides of standard dimensions were selected to determine spreadability. Formulation whose spreadability was to be determined was placed over one slide and the other slide was placed over it such that the gel was sandwiched between the two slides. The slides were pressed upon each other to displace any air present and the adhering gel was wiped off. The two slides were placed over a stand in such a way that only the lower slide was held firm [34,35].

5.5. Physical examination
The prepared emulgel formulations were inspected visually for their colour, homogeneity, consistency and phase separation [23].

5.6. Globule size and its distribution in emulgel
Globule size and distribution is determined by Malvern zeta sizer. A 1.0 g sample is dissolved and agitated to get a homogeneous dispersion. The sample was injected into the photocell of zeta sizer. Mean globule size and distribution is determined [5].

5.7. Swelling index
1 gm of gel sample is taken on a porous aluminium foil and then placed in a 50 ml beaker containing 10 ml 0.1 N NaOH separately. Then the samples were removed from beakers at different time intervals and kept it at a dry place for some time, then it was reweighed.

5.8. In vitro drug release study
The in vitro drug release studies of the Emulgel were carried out on Diffusion cell using egg membrane. Emulgel (1g) was applied onto the face of egg membrane dialysis membrane. The receptor chamber was filled with newly prepared PBS (pH7.4) solution to solubilize the medicament. The receptor chamber was stirred using a magnetic stirrer. The samples (1 ml aliquots) were collected at suitable time interval. The sample were analysed for medicament content by UV-visible spectrophotometer after proper dilutions. Cumulative corrections were made to attain the total quantity of drug released at each time interval. The cumulative quantity of drug release across the egg membrane was determined as a function of time. The cumulative percentage of medicament release was calculated using standard calibration curve.

5.9. Microbiological assay
Ditch plate approach was used for microbiological assay and mostly applied for semisolid formulations. It’s an approach used for evaluation of fungistatic or bacteriostatic activity of an emulsion. Already prepared Sabouraud’s agar dried plates were used. Three gm of the jellified emulsion are placed in a ditch cut in the plate. Newly prepared culture loops are streaked across the agar at a right angle from the ditch to the edge of the plate.

5.10. Skin irritation test
The skin irritation study of emulgels can be determined by using shaven skin of a rat or rabbit. The weighed sample of medicament is applied to either side of the area of the skin and keep them in cage for the following 24 hrs. After 24 hrs,
examine the rat or rabbit skin area and check for any color change or any adverse effect noted. If no adverse effects were shown, the formulation passes the test [19].

5.11. 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 months. Samples were withdrawn and evaluated for pH, physical appearance, rheological properties, drug content, and drug release profiles at a 15-day time interval [1].

5.12. Extrudability study
It is a usual empirical test to measure the force required to extrude the material from the tube. The method adopted for the determination of applied shear in the region of the rheogram corresponding to a shear rate exceeding the yield value and exhibiting consequent plug flow. In the present study, the method adopted for evaluating emulgel formulation for extrudability is based on the quantity in the percentage of emulgel and emulgel extruded from the lacquered aluminium collapsible tube on the application of weight (in grams) required to extrude at least 0.5 cm ribbon of emulgel in 10 s. More quantity extruded better is extrude ability. The measurement of extrudability of each formulation is done in triplicate, and the average values are recorded. The extrudability is calculated using the following formula:

$$\text{Extrudability} = \frac{\text{Applied weight to extrude Emulgel from the tube (in g)}}{\text{Area (cm}^2\text{)}}$$

5.13. Drug content determination
Gel formulation (1 gram) was dissolved in suitable solvent and sonicated [36]. Filtered it to obtain clear solution. The resulting solution absorbance was noted using UV Visible spectrophotometer. Drug content was determined from calibration curve for drug [12].

5.14. Ex vivo bioadhesive strength measurement of topical emulgel (mice shaven skin)
The modified approach is used for the measure of bioadhesive strength. The fresh skin was cut into pieces and washed with 0.1 N NaOH. Two pieces of skin were tied to the two- glass slide independently from that one glass slide is fixed on the wooden piece, and another piece is tied with the balance on the right- hand side.

The right and left pans were balanced by adding spare weight on the left- hand pan. 1 g of topical emulgel is placed between these two slides containing furless skin pieces, and spare weight from the left pan is removed to squeeze the two pieces of skin, and some pressure is applied to remove the presence of air. The balance is kept in this position for 5 min. Weight is added slowly at 200 mg/ min to the lefthand pan until the patch detached from the skin surface. The weight (gram force) needed to detach the emulgel from the skin surface gave the measure of bio-adhesive strength. The bio-adhesive strength is calculated using the following: [20]

$$\text{Bio-adhesive strength} = \frac{\text{Weight required (in g)}}{\text{Area (cm}^2\text{)}}$$

5.15. Ex–vivo evaluation
Ex – vivo release study is conducted using saved or fresh chicken skin. Also skin is allowed to hydrate for 1 hr before being mounted on the Franz diffusion cell with the stratum corneum (SC) facing the donor compartment. The gel sample is applied on the skin and also fixed in between donor and receptor chamber of Franz diffusion cell. The receptor chamber contains phosphate buffer of pH7.4. The temperature of the medium is thermostatically controlled at 37 ± 10ºC by circling water jacket and the medium is stirred with bar magnet using magnetic stirrer. Aliquots, withdrawn at predetermined intervals of time, are spectrophotometrically estimated at maximum wavelength of drug against their respective blank formulation treated in the same manner [10].

5.16. Drug release kinetic study
To analyse the mechanism of drug release from the topical gel, the release data were fitted to the following eq.

$$\text{Zero – order equation: } Q = k0 \times t$$

Where, Q is the percent amount of drug released at time t, and k0 is zero-order release rate constant.

First-order equation: $$\ln (100 - Q) = \ln 100 - k1 \times t$$

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Where, $Q$ is the percent of drug release at time $t$, and $k_1$ is the first-order release rate constant.

Higuchi's equation: $Q = k_2 \sqrt{t}$

Where, $Q$ is the percent of drug release at time $t$, and $K_2$ is the diffusion rate constant. [9]

5.17. Accelerated stability studies

Stability studies were performed according to ICH guidelines. The formulations were stored in a hot air oven at 37 ± 2°C, 45 ± 2 °C, and 60 ± 2 °C for 3 months. The samples were analysed for drug content every 2 weeks by UV-visible spectrophotometer. Stability study was carried out by measuring the change in pH of the gel at regular interval of time [10, 33].

5.18. Syneresis measurement test

On rest, gel shrinks and a little liquid is pressed out called syneresis. This could be measured by means of centrifuge tubes in specific apparatus [8].

$$\text{Syneresis (\%)} = \frac{\text{Liquid separated from Emulgel}}{\text{Total weight of Emulgel before centrifugation}} \times 100$$

5.19. Zeta potential

The Zeta potential of the emulgel compound is determined by zetasizer (Malvern Zetasizer) The preparation is placed in a clear, disposable zeta cell, and the result is determined. The cuvettes are washed with methanol before experimenting and also the sample is placed [14].

5.20. Particle size and polydispersity index (PDI)

The globule size of emulgel is measured at 25°C, by using a zetasizer (Malvern zetasizer instrument, ZS90). The sample is watered down before the experimentation [4].

5.21. Ex-vivo skin permeation and retention studies

Albino rat 10-12 weeks old weighing 200-250 g was used. The excised skin was placed in aluminium foil. The dermal side of the skin was delicately teased off for any following fat and/or subcutaneous tissue. The skin was then precisely checked through a magnifying glass to guarantee that specimens were free from any surface inconsistencies, for example, small openings or cervices in the part that was utilized for transdermal permeation studies. The skin was washed with physiological buffer saline and freshly obtained skin was used in all experiments. The ex-vivo skin permeation of drug from different formulations was studied using Keshary-chien cell. The effective permeation area of the diffusion cell was 9.8 cm$^2$. The receptor compartment has a volume of 37.5 ml. Albino rat skin was stuffed securely between donor and receptor cell with the donor cell having epidermis site. The donor compartment was maintained at 37±1°C with constant stirring. The emulgel formulation was applied to the epidermal surface of the rat skin. At a predetermined time interval for 24 hr (0.5hr, 1hr, 2hr, 4hr, 6hr, 8hr, and 24hr), 3.0 ml of aliquots were withdrawn and were replaced with an equal volume of fresh receptor compartment solvent to ensure sink condition. The cumulative percentage drug diffused across the skin was calculated at each sampling point. The amount of free drug content in the receptor compartment and the amount of drug remained on the epidermal surface of the skin on subtraction from the initial drug content of the formulation applied resulted the amount of drug content in the skin. The marketed emulgel is compared with the ex-vivo permeation study of emulgel for permeation characteristics. All the determinations were carried out in triplicate and the data were compared by ANOVA [6].

5.22. Kinetics Modeling

Data obtained from ex-vivo permeation studies were fitted into zero order, first order, Higuchi, and mathematical models for evaluation of drug release kinetics. The model for best fit was predicted from the value of R$^2$. For an ideal fit, value of R2 is higher, the value of R2 best was the model fitted. Hence, the model which gives the R2 value nearest to 1 describes the best order of drug release [6].

5.23. Photomicroscopy

Emulgel was viewed under light microscope to study the globular structure in gel base. The emulgel was suitably watered down, mounted on glass slide and viewed by light microscope under magnification of 40x [13].
5.24. Dilution test
50 to 100 times aqueous dilution of emulgels was done by adding Continuous phase and visually checked for phase separation and clarity [13].

5.25. Homogeneity
The formulation is tested for its homogeneity by visual appearance after emulgels were applied on a slide as a thin layer [15].

5.26. Effect of temperature
It was studied by maintaining the optimized batch at room temperature for 3 months. After storage, the emulgels were tested for their pH, physical appearance, viscosity and drug content after every month. Freeze thaw study was also carried out at 40°C and -20°C for 7 days. The emulgels are tested for pH, physical appearance and drug content after 7 days [22].

6. Marketed preparations
The various preparations of Emulgels available in market are shown in Table [1,4,6,7,13,19].

Table 4 Marketed preparations

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Drug</th>
<th>Manufacturer</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voltaren emulgel</td>
<td>Diclofenac-diethyl-ammonium</td>
<td>Novartis pharma</td>
<td>Anti-inflammatory</td>
</tr>
<tr>
<td>Miconaz-H-Emulgel</td>
<td>Miconazole nitrate hydrocortisone</td>
<td>Medical union Pharmaceuticals</td>
<td>Topical corticosteroid antifungal</td>
</tr>
<tr>
<td>Exceex gel</td>
<td>Clindamycin, Adapalene</td>
<td>Zee laboratories</td>
<td>Anti-acne Anti-inflammatory</td>
</tr>
<tr>
<td>Pernox gel</td>
<td>Benzoyl peroxide</td>
<td>Cosme remedies Ltd.</td>
<td>Anti-acne</td>
</tr>
<tr>
<td>Lupigel gels</td>
<td>Metronidazole, clindamycin</td>
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<td>Barakat Pharma</td>
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<td>Hibiscus, licorice, natural extract</td>
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<td>Novartis</td>
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<tr>
<td>Product</td>
<td>Active Ingredient</td>
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<td>Activity</td>
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<td>------------------------</td>
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<tr>
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<td>Herbitas</td>
<td>Intense moisturizing and exfoliation activity</td>
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7. Conclusion

The emulgel is a good alternative for other semisolid preparations and can be used in local and systemic treatment. Along with properties like viscosity, spreadability, extrudability, drug release and stability, it also shows good penetration characteristics and ease of application. Most of the drug not being able to convert into topical system is their hindrance due to hydrophobicity (hydrophobic nature leads to poor water solubility and bioavailability of drugs). But emulgel makes it easy for them without affecting the release unlike ointment or creams.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflicts of interest, financial or otherwise.

References


