World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

Emulgel: A dual release system for hydrophobic drug delivery

Muskan Kankane *, Vijay Nigam, Shailendra Modi, Sanjay Jain and Pooja Adhikari

Department of Pharmaceutics, Daksh Institute of Pharmaceutical Science (DIPS), Chhatarpur, M.P., India.

World Journal of Biology Pharmacy and Health Sciences, 2022, 12(03), 335–347

Publication history: Received on 07 November 2022; revised on 20 December 2022; accepted on 23 December 2022

Article DOI: https://doi.org/10.30574/wjbphs.2022.12.3.0258

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].

* Corresponding author: Muskan Kankane

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, poultices, 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].

Creams, ointments and gels are the semisolid formulations which are commonly used for local and regional skin disorders. Semisolids can change their shape because of plastic behaviours, except gels having viscoelastic effect because of showing liquid and solid properties [42–44]. Ointments, creams, lotions, gels, etc., are a few examples of topical dosage forms. These have many disadvantages like stickiness, stability problems, and less spreadability plus, it also causes allergic reactions, poor permeability, absorption, and causes irritation [45].

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 as 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 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

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

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

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
Poloxamer 407	1	gel

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-organism 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

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

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 colour 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 applied 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:

$$Extrudability = \frac{Applied\ weight\ to\ extrude\ Emulgel\ from\ the\ tube\ (in\ g)}{Area\ (cm2)}$$

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]

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

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.

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

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

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

Where, Q is the percent of drug release at time t, and k1 is the first-order release rate constant.

Higuchi's equation: $Q = k2\sqrt{t}$

Where, Q is the percent of drug release at time t, and K2 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].

Syneresis (%) = Liquid separated from Emulgel/Total weight of Emulgel before centrifugation × 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 R2. 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 emulgel 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 emulgel was 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

Product Name	Drug	Manufacturer	Use
Voltaren emulgel	Diclofenac-diethyl-ammonium	Novartis pharma	Anti-inflammatory
Miconaz-H-Emulgel	Miconazole nitrate hydrocortisone	Medical union pharmaceuticals	Topical corticosteroid antifungal
Excex gel	Clindamycin, Adapalene	Zee laboratories	Anti-acne Anti-inflammatory
Pernox gel	Benzoyl peroxide	Cosme remedies Ltd.	Anti-acne
Lupigyl gel	Metronidazole, clindamycin	Lupin pharma	Topical antibiotic
Clinagel	Clindamycin phosphate, allantoin	Stiefel pharma	Anti-acne
Topinate gel	Clobetasol propionate	Systopic pharma	Anti-inflammatory
Kojivit gel	Kojic acid dipalmitate arbuti	Micro gratia pharma	Hyperpigmentation
Acent gel	Aceclofenac	Intra Labs India Pvt. Ltd.	Anti-inflammatory
Avindo gel	Azithromycin	Cosme pharma lab	Antibiotic
Cloben gel	Clotrimazole beclomethasone	Indoco remedies	Anti-fungal Anti-bacterial Anti-inflammatory
Zorotene gel	Tazarotene	Elder pharmaceutical	Anti-acne
Diclobar emulgel	Diclofenac diethyl amine	Barakat Pharma	Anti-inflammatory, analgesic
Diclomax emulgel	Diclofenac sodium	Torrent Pharma	Anti-inflammatory
Levorag emulgel	Hibiscus, licorice, natural extract	THD Ltd. Emollient	Emollient
Voltarol 1.16% emulgel	Diclofenac sodium	Novartis	Anti-inflammatory

Dermafeet Emulgel	Urea 40%	Herbitas	Intense moisturizing and exfoliation activity
Denacine emulgel	Clindamycin phosphate	Beit jala pharmaceutical company	Anti-acne
Isofen emulgel	Ibuprofen	Beit jala pharmaceutical company	Anti-inflammatory
Diclona emulgel	Diclofenac diethylamine	Kuwait Saudi pharmaceutical industries co.	Anti-inflammatory
Dosanac emulsion gel	Diclofenac diethylammonium	Siam bheasach	Anti-inflammatory
Diclon emulgel	Diclofenac diethylamine	Medpharma	Anti-inflammatory
Cataflam emulgel	Diclofenac potassium	Novartis	Anti-inflammatory

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

Acknowledgments

Authors have the honor to express deep gratitude to Mr. Ajay Lal Nigam (Director, Daksh Institute of Pharmaceutical Science) for providing us all the facilities and opportunities.

Disclosure of conflict of interest

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

References

[1] Phad AR, Dilip NT, Ganapathy RS, Emulgel: A Comprehensive Review for Topical Delivery of Hydrophobic Drugs, Asian Journal of Pharmaceutics, Apr-Jun 2018 (Suppl), 12 (2) S382.

[2] Pandey D, Jain D, Formulation and Evaluation of Submicron Emulsion Containing Entrapped Fluoroquinolone For Ocular Delivery, Asian J Pharm Clin Res, Vol 11, Issue 7, 2018, 431-435.

[3] Yadav SK, Mishra MK, Tiwari A, Shukla A, Emulgel: A New Approach for Enhanced Topical Drug Delivery, Int J Curr Pharm Res 2017;9(1):15-19.

[4] Patel BM, Kuchekar AB and Pawar SR, Emulgel Approach to Formulation Development: A Review, Biosciences Biotechnology Research Asia, September 2021. Vol. 18(3), p. 459-465.

[5] Varma V N.S, Maheshwari PV, Navya M, Reddy SC, Shivakumar HG, Gowda DV, Calcipotriol delivery into the skin as emulgel for effective permeation, Saudi Pharm J 2014;22(6):591-599.

[6] Kumar D, Singh J, Antil M and Kumar V, Emulgel-novel topical drug delivery system–a comprehensive review, Int J Pharm Sci Res 2016; 7(12): 4733-42.

[7] Akki R, BS and Kiranmai J, A novel approach for topical delivery using emulgel, The Pharma Innovation Journal 2019; 8(4): 35-42.

[8] Kumar G N. S, Dr. Nallaguntla L, Dr. Kulkarni GS, A Review On: Microemulgel as A Topical Drug Delivery System, Volume 6, Issue 4 July-Aug 2021, pp: 1542 -1549.

[9] Hardenia A, Jayronia S and Jain S: Emulgel: An emergent tool in topical drug delivery, Int J Phar Sci Res 2014; 5(5):1653-60.

[10] Thomas J, Kuppuswamy S, Sahib AA, Benedict A, George E, A Review on Emulgel as a Current Trend in Topical Drug Delivery System, IJPPR June 2017 Vol.:9, Issue:3.

[11] Parihar N, Saini M, Soni SL, Sharma V, Emulgel: A Topical Preparation, Asian Journal of Pharmaceutical Research and Development. 2020; 8(3):196-201.

[12] Dhawas V, Dhabarde D and Patil S .2020, Emulgel: A Comprehensive Review for Novel Topical Drug Delivery System, Int J Recent Sci Res. 11(04), pp. 38134-38138.

[13] Sah SK, Badola A, Nayak BK., Emulgel: Magnifing the application of topical drug delivery, Indian J. Pharm. Biol. Res.2017; 5(1):25-33.

[14] Ojha A, Ojha M and Madhav N.V. S, Recent Advancement in Emulgel: A Novel Approach for Topical Drug Delivery, International Journal of Advances in Pharmaceutics 2017; 06(01): 17-23.

[15] Talat M, Zaman M, Khan R, Jamshaid M, Akhtar M & Mirza AZ (2021): Emulgel: an effective drug delivery system, Drug Development and Industrial Pharmacy.

[16] Shaik. Sultana S, Parveen P, M. Sri Rekha, K. Deepthi, Ch. Sowjanya, Dr. A. Seetha Devi, Emulgel – A Novel Surrogate Appraoch for Transdermal Drug Delivery System, Indo American Journal of Pharmaceutical Research, 2014 :4(11).

[17] Singla V, Saini S, Joshi B, Rana AC., Emulgel: a new platform for topical drug delivery, Int J Pharm Biol Sci 2012;3:485-98.

[18] Kute SB, Saudagar RB; Emulsified gel A Novel approach for delivery of hydrophobic drugs: An overview; J. Adv. Pharm. Edu. & Res. 2013: 3(4): 368-376.

[19] Charyulu NR, Joshi P, Dubey A, Shetty A., Emulgel: A Boon for Enhanced Topical Drug Delivery, J Young Pharm. 2021;13(1):76-9.

[20] Vanpariya F, Shiroya M, Malaviya M, Emulgel: A Review, International Journal of Science and Research (IJSR) ISSN: 2319-7064 SJIF (2019): 7.583.

[21] Shaker DS, Ishak R AH., Ghoneim A, and Elhuoni MA, Nanoemulsion: A Review on Mechanisms for the Transdermal Delivery of Hydrophobic and Hydrophilic Drugs, Sci. Pharm. 2019, 87, 17.

[22] Gopalasatheeskumar K, Komala S, Soundarya R, Parthiban S, Bharathi BD, Elango S, Review on Emulgel Formulations With Non-Steroidal Anti-inflammatory Drugs For Topical, Pharma Science Monitor 8(1), Jan-Mar 2017.

[23] Kullar R, Saini S, Steth N, Rana AC., Emulgel a surrogate approach for topical used hydrophobic drugs; Int J Pharm Biol Sci 2011;1:117-28.

[24] Mohamed MI, Optimization of chlorphenesin emugel formulation, AAPS J 2004;6:81-7.

[25] Rode RJ, Dixit GR, Upadhye KP, Bakhle SS and Durge RT, A Comprehensive Review on Emulgel: A New Approach For Enhanced Topical Drug Delivery, IJMPR 2021, 5(3), 222-233.

[26] Patel N, Chaudhary S, Chaudhary A, Emulgel – Emerging as a Smarter Value-Added Product Line Extension for Topical Preparation, Indo Global J. Pharm. Sci., 2022; 12: 92-103.

[27] Vats S, Saxena C, Easwari TS, Shukla VK, Emulsion Based Gel Technique: Novel Approach for Enhancing Topical Drug Delivery of Hydrophobic Drugs, International Journal for Pharmaceutical Research Scholars (IJPRS) V-3, I-2, 2014.

[28] Sharma P, Saini S And Gill N, Formulation and Evaluation of Ketoconazole Emulgel for Topical Drug Delivery, IJBPAS, December, Special Issue, 2021, 10(12): 159-170.

[29] Gaur PK, Mishra S, Purohit S, Dave K., Transdermal drug delivery system: a review. Asian J Pharm Clin Res 2009;2:14-20.

[30] Singla V, Saini S, Rana AC, Singh G., Development and evaluation of topical emulgel of lornoxicam using different polymer bases. Int Pharm Sci 2012;2:36-44.

[31] Baibhav J, Singh G, Rana A C, Saini S, Singla V, Emulgel: A comprehensive review on recent advancement on topical drug delivery. IRJP, 2011; 2(11): 66-70.

[32] Panwar AS, Upadhyay N, Bairagi M, Gujar S, Darwhekar GN, Jain DK., Emulgel: A review. Asian J Pharm Life Sci. 2011; 1(3): 333-343.

[33] Deveda P, Jain A, Vyas N, Khambete H, Jain S, Gellified emulsion for sustained delivery of itraconazole for topical fungal diseases. Int. J. Pharm. Pharm. Sci. 2010; 2: 104– 112.

[34] Khullar R, Kumar D, Seth N, Saini S: Formulation and Evaluation of Mefenemic acid emulgel for topical delivery, Saudi Pharm. J. 2011: 63–67.

[35] Gupta A, Mishra AK, Singh AK, Gupta V, Bansal P., Formulation and evaluation of topical gel of diclofenac sodium using different polymers, Drug Invention Today. 2010; 2:250-253.

[36] Aher S.D., Banerjee S.K., Gadhave M.V., Gaikwad D.D., Emulgels –A New Dosage Form for Topical Drug Delivery. International Journal of Institutional Pharmacy and Life Sciences. (2013); 3(3): 1-10.

[37] Rashmi M., 'Topical gel: A review', Pharmainfo.com, August vol. 2008.

[38] Dhawas V, Dhabarde D and Patil S, Emulgel: A Comprehensive Review for Novel Topical Drug Delivery System, Int J Recent Sci Res. 2020 11(04), pp. 38134-38138.

[39] Purushottam SS, Bhaskarrao GS, Bhanudas SR. Gelified emulsion: a new born formulation for topical delivery of hydrophobic drugs. World jurnal of pharmacy and pharmaceutical sciences. 2013;3:233- 251.

[40] Sonaje PS, Bhaskarrao GS, Bhanudas S., Gellified Emulsion: A New Born Formulation for Topical Prepration of Hydrophobic drugs, Pharm Tech Med 2013; 2:370-76.

[41] Singh RP, Parpani S, Narke R, Chavan R. Emulgel: A Recent Approach for Topical Drug Delivery System. AJPRD 2014;2:112-23.

[42] Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. Saudi Pharm J 2012;20:63-67.

[43] Lachman L, Lieberman HA, Kang JL. Theory and Practice of Industrial Pharmacy, Bombay, India: Verghese Publishing House; 1991.p. 534-63.

[44] Swarbrick J, Boylan JC. Encyclopedia of Pharmaceutical Technology, Vol. 14, New York: Marcel Dekker; 1996. p. 31-59.

[45] Baibhav J, Vikas S, Gurpreet S. Emulgel: a comprehensive review on the recent advances in topical drug delivery. Int Res J Pharmacy. 2011;2(11):66–70.

[46] Jain A, Deveda P, Chuhan J., Development of Antifungal Emulsions based gel for topical fungal infections, Int J Pharma Res Dev. 2011;2:12.