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EMUGEL: AN INSIGHT

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ABSTRACT

Emulgel is emulsions, either of the oil-in-water or water-in-oil type, which are gelled by mixing with a gelling agent. Emulsion in gel have emerged as one of the most interesting topical drug delivery system as it has dual release control system i.e. emulsion and gel. Also the stability of emulsion is increased when it is incorporated in gel. Emulgel have major advantages on novel vesicular systems as well as on conventional systems in various aspects. The emulgel for dermatological purpose has several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water soluble, longer shelf life, bio-friendly, transparent & pleasing appearance. Various permeation enhancers can potentiate the effect, so emulgel can be used as better topical drug delivery systems over present systems.

KEYWORDS: Emulgel, Skin, Emulsion, Hydrophobic Drug, Topical drug delivery, Gelling Agent.

INTRODUCTION

The delivery of drugs across the skin is gaining wide acceptance among patients and termed as Topical drug delivery. It is a viable administration route for potent, low molecular weight therapeutic agents susceptible to first pass metabolism. Topical drug delivery is referred to as a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Skin is one of the most readily accessible organs on human body for topical administration and is main route of topical drug delivery system. In developing a

transdermal delivery system, two criteria are considered: one is achieving adequate flux across the skin and the other is minimizing the lag time in skin permeation.[1] The main advantage of topical delivery system is to bypass first pass metabolism, avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption, like pH changes, presence of enzymes, gastric emptying time, include prolonged drug levels in the blood stream, reduced side effects, improved bioavailability, better patient compliance and easy termination of drug administration are other advantage of the topical drug delivery system is generally used where the others system of drug administration fails. Moreover this type of drug delivery is easy and painless. Human skin is a uniquely engineered organ that permits terrestrial life by regulating heat and water loss from the body whilst preventing the ingress of noxious chemicals or microorganisms. It is also the largest organ of the human body, providing around 10% of the body mass of an average person, and it covers an average area of 1.7 m^2. Emulgel are a relatively newer class of dosage form created by entrapment of large amounts of aqueous or hydro alcoholic liquid in a network of colloidal solid particles, which may consist of inorganic substances, such as aluminum salts or organic polymers of natural or synthetic origin. Emulgel have a higher aqueous component which permits greater dissolution of drugs, and also permit easy migration of the drug through a vehicle that is essentially a liquid. So, the gelling agent in the water phase which converts a classical emulsion into an emulgel. [2] Emulgel is emulsions, either of the oil-in-water or water in oil type, which are gelled by mixing with a gelling agent. Emulsified gel is stable one and better vehicle for hydrophobic or poorly water soluble drugs. They have a high patient acceptability since they possess the advantages of both emulsions and gels. Direct (oil-in-water) systems are used to entrap lipophilic drugs, whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) systems. Emulgel allow dual control of the drug release from the formulation, i.e. emulsion and gel. Emulsions possess a certain degree of elegance and are easily washed off whenever desired [3, 4].

In recent years, there has been great interest in the use of novel polymers with complex functions as emulsifiers and thickeners because the gelling capacity of these compounds allows the formulation of stable emulsions and creams by decreasing surface and interfacial tension and at the same time increasing the viscosity of the aqueous phase [5,6].

PHYSIOLOGY OF SKIN

Most of the topical preparations are meant to be applied to the skin. So, basic knowledge of the skin and its physiology function are very important for designing topical drug delivery. The skin of an average adult body covers a surface area approximately $2m^2$ and receives about one third of the blood circulating through the body. An average human skin surface is known to contain, the average 40-70 hair follicles and 200-300 sweat ducts on every square centimeter of the skin. The pH of the skin varies from 4 to 5.6. Sweat and fatty acid secreted from sebum influence the pH of the skin surface. The skin can be considered to have four distinct layers of tissue as shown in figure 1.

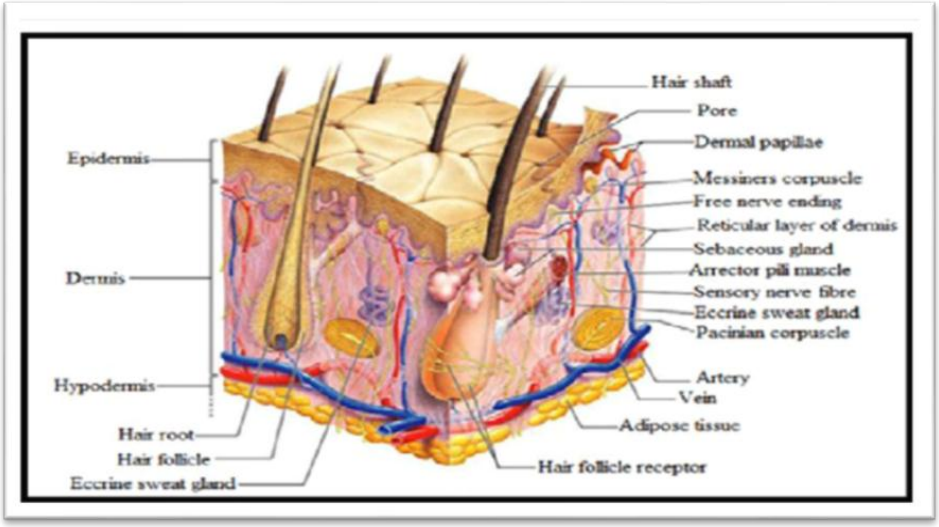

Figure 1: Distinct layers of skin

1. **Non-viable epidermis:** Stratum corneum is the outer most layer of skin, which is the actual physical barrier to most substance that comes in contact with the skin. The stratum corneum is 10 to 20 cell layer thick over most of the body. Each cell is a flat, plate like structure about 34-44 µm long, 25-36 µm wide, 0.5 to 0.20 µm thick with surface area of 750 to 1200 µm stocked up to each other in brick like fashion. Stratum corneum consists of lipid (5-15%) including phospholipids, glycophospholipid, cholesterol sulfate and neutral lipid, protein (75-85%) which is mainly keratin [7, 8].
2. **Viable epidermis:** This layer of the skin resides between stratum corneum and dermis and has a thickness ranging from 50-100 µm. The structures of the cells in the viable epidermis are physiochemically similar to other living tissues. Cells are held together by tonofibrils. The water content is about 90%.

3. **Dermis:** Just beneath the viable epidermis is the dermis. Dermis thickness ranges from 2000 to 3000µm and consists of a matrix of loose connective tissue composed of fibrous protein embedded in an amorphous ground substance.
4. **Subcutaneous connective tissue:** The subcutaneous tissue or hypodermis is not actually considered a true part of the structured connective tissue which is composed of loose textured, white, fibrous connective tissue containing blood and lymph vessels, secretory pores of the sweat gland and cutaneous nerves. Most investigators consider drug permeating through the skin enter the circulatory system before reaching the hypodermis, although the fatty tissue could serve as a depot of the drug [9].

DRUG DELIVERY ACROSS THE SKIN

A unique aspect of dermatological pharmacology is the direct accessibility of the skin as a target organ for diagnosis and treatment. The skin acts as a two-way barrier to prevent absorption or loss of water and electrolytes. There are three primary mechanisms of topical drug absorption: transcellular, intercellular, and follicular. Most drugs pass through the torturous path around corneocytes and through the lipid bilayer to viable layers of the skin. The next most common (and potentially under recognized in the clinical setting) route of delivery is via the pilosebaceous route. The barrier resides in the outermost layer of the epidermis, the stratum corneum, as evidenced by approximately equal rates of penetration of chemicals through isolated stratum corneum or whole skin. Creams and gels that are rubbed into the skin have been used for years to deliver analgesic and anti-infective drugs to an affected site of the body. These include, among others, gels and creams for vaginal yeast infections, topical creams for skin infections and creams to soothe arthritis pain. New formulations like Emulgel now allow other drugs to be absorbed through the skin (transdermal). These can be used to treat not just the affected areas (for example, the skin) but the whole body (Systemic) [10].

ADVANTAGES OF EMULGEL

1. **Delivery of hydrophobic drugs:** Most of the hydrophobic drugs cannot be incorporated directly into gel base because solubility act as a barrier and problem arises during the release of the drug. Emulgel helps in the incorporation of hydrophobic drugs into the oil phase and then oily globules are dispersed in aqueous phase resulting in o/w emulsion, this emulsion can be mixed into gel base providing better stability and release of drug than simply incorporating drugs into gel base [11].

2. **Better stability:** Other transdermal preparations are comparatively less stable than emulgel e.g. powders are hygroscopic, creams shows phase inversion or breaking and ointment shows rancidity due to oily base.
3. **Better loading capacity:** Other novel approaches like niosomes and liposomes are of nano size and due to vesicular structures may result in leakage and result in lesser entrapment efficiency. But gels due to vast network have comparatively better loading capacity.
4. **Production feasibility and low preparation cost:** Preparation of emulgel comprises of simpler and short steps which increases the feasibility of the production. There are no specialized instruments needed for the production of emulgel. Moreover materials used are easily available and cheaper resulting in lower production cost [12].
5. **No intensive sonication:** Production of vesicular molecules needs intensive sonication which may result in drug degradation and leakage. But this problem can be avoiding during the production of emulgel as no sonication is needed.
6. **Controlled release:** Emulgel can be used to prolong the effect of drugs having shorter $t_{1/2}$.
7. **Improve patient compliance**: They are less greasy and easy to apply [13].
8. More selective to a specific site.
9. Increases contact time and mean residence time of the drug [14].
10. It is a non-invasive mode of drug delivery with no trauma or risk of infection [15].

Formulation Considerations

The challenges in formulating topical emulgel are [16]:

1. Determining systems that are non-toxic, non-irritating, non-comedogenic and non-sensitizing.
2. Formulating cosmetically elegant emulgel.
3. The emulgel formulation must have low allergenic potential, good physiological compatibility and high biocompatibility.

CONSTITUENTS OF EMULGEL

A) Drug substances-. Mainly NSAID's agent, antifungal agent, antibacterial agent etc. can be used for delivery. Judicious choice of the drug plays an important role in the successful development of a topical product. The important drug properties that effect its diffusion through the device as well as through skin are as follow [17, 18],

a. Physicochemical properties

- Molecular wt. should be less than 500 Daltons.
- Adequate lipophilicity of drug must be required.
- pH of saturated aqueous solution of drug should be between 5 and 9.
- Drugs which are highly acidic or alkaline in solution are not suitable candidates for topical delivery.

b. Biological properties

- The drug should not irritate the skin.
- The drug should not stimulate an immune reaction in the skin.
- Drugs, which degrade in gastrointestinal tract or are inactivated by hepatic first pass effect, are suitable for topical delivery.
- Tolerance to the drug must not develop under the near zero order release profile of topical delivery.
- Drugs which have to be administered for a long time or which cause adverse effects to non-targeted tissue can also be formulated for topical delivery.

(1) Vehicle

The vehicle must have 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 pharmacological effect
- Cosmetically acceptable to the patent.

(a) Aqueous material: The aqueous materials like Water or Alcohols can be used.

(b) Oils: They form the oily phase of the emulsion. Most commonly used oils are mineral oils either alone or in combination with soft and Hard Paraffin. Non biodegradable mineral oil and Castor oils can be used which provide local laxative effects. Oils extracted from different types of plant with various medicinal values can be employed in emulgel formulation. One such oil of medical importance is of Geranium. Geranium is used to staunch bleeding, healing of wounds, ulcers and skin disorder and in treatment of Diarrhea, Dysentery

and colic. Similarly, garlic has been found to possess burning wound healing properties. Some other medicinal plants were also investigated for their antimicrobial potency; these include *Arnelia nobilis, Garciana indica, Boehavia diffusa, Solanum albicaule, Vitex nigundu, Bunium persicum, Acacia concinna* and *Albizia lebbeck*. The oil has insecticidal and anti-bacterial properties. Shahin et al. (2011) carried one such of the research work using jojoba oil as oil phase for Emulgel. They prepared antifungal Emulgel of Clotrimazole using Jojoba oil as oil phase. Jojoba oil is a wax ester consisting of a complex mixture of naturally-occurring long-chained linear esters. It also contains tocopherols, sterols, and other unsaponifiable matter. It is an excellent moisturizer that does not block skin pores and helps restore normal oil balance of the skin. The oil is stable to oxidation and imparts photo-protection. It also possesses anti-inflammatory and antibacterial properties, thereby; making it useful in acne treatment. Reason of selecting Jojoba oil as oil phase was that it might help to reduce inflammation commonly associated with fungal infections. Moreover, it was found effective in combating inflammation in several experimental animal models [19]. The other example include almond oil, the main constituents of almond oil are Glycerides of Oleic and Linoleic Acid, Phytosterols, α-Tocopherol, and Vitamin K. Fatty acids are metabolized in the skin when applied topically, thereby normalizing the cell lipid layer and improving the water retention capability. α-Tocopherol improves water-binding ability, improving the appearance of rough and damaged skin. In addition to these, it does not clog pores or leave the skin oily. Wheat germ oil is one of the richest sources of Vitamin A, E, and D. It has a high content of lecithin and proteins. It is extensively used for external application as it helps in combating skin irritation, including skin dryness and cracking. It is also a good source of fatty acids and minimizes symptoms of dermatitis. Sesame oil is mostly composed of triglycerides of singly unsaturated Oleic acid and the doubly unsaturated Linoleic acid, besides a small percentage of saturated fats. It contains powerful antioxidants. The most important ingredient that makes it very beneficial for skin is Vitamin E, which imparts exceptional moisturizing and emollient properties. Moreover, it is valuable in the prevention and cure of acne due to its oil-pulling property. Table: 1 includes some examples of oils which are used in the Emulgel Formulation.[20]

Table: 1 Examples of oils used in the Formulation are

Sr. No.	Chemical Name	Quantity	Dosage Form
1.	Isopropyl Myristate	According to phase diagrams	Emulsion
2.	Isopropyl Stearate	According to phase diagrams	Emulsion
3.	Isopropyl Palmitate	7-7.5%	Emulsion
4.	Isopropy Acetate	7-7.5%	Emulsion
5.	Light Liquid Parrafin	7.5%	Emulsion
6.	Propylene Glycol	3.5%	Gel

2. Emulsifiers

Emulsifying agents are used both to promote emulsification at the time of manufacture and to control stability during a shelf life [21]. Emulsions are thermodynamically unstable system however stability can be increased by using appropriate emulsifying agent. Nonionic surfactants such as spans, tweens have HLB values greater than 8 and are used in the formulation of o/w emulsions whereas mineral oils such as liquid paraffin have HLB values less than 8 & therefore are employed in the formulation of water in oil emulsions [16]. Emulgel was developed using Tween 20 as emulsifiers in its aqueous phase & Span 20 in its oily phase .Both surfactants are Sorbitan Lauric acid esters with the same cyclic structure. However, Tween 20 contains additional Polyoxyethylene units. Tween surfactants are Polysorbate molecules each attached to a hydrophilic head group of Oligo Ethylene Glycol) (OEG) chains and a hydrophobic tail of fatty acid ester moiety. Span 20/Tween 20 Mixtures contribute towards greater stability of the emulsions as compared with pure Tween or Span systems [18]. Joshi baibhav et al (2012) has prepared Clarithromycin emulgel using Tween 80 and Span 80 as emulsifying agents. However, these surfactants possess problem of toxicity which can be replaced by using biosurfactant. Biosurfactant are produced by microbes and have short fatty acid tail and polar head groups. They are sticky to both hydrophilic and hydrophobic molecules. They have lower toxicity, high biodegradability and are environment friendly. Better foaming properties and stability at extreme pH and temperature is reported. Biosurfactant is produced by microbes and has short fatty acid tail and polar head groups. They are sticky to both hydrophilic and hydrophobic molecules. They have lower toxicity, high biodegradability and are environment friendly. Better foaming properties and stability at extreme pH and temperature is reported. Various biosurfactant used in medical field are rhamnolipid obtained from *Pseudomonas aeruginosa*, surfactin (very powerful surfactant

commonly used as an antibiotic) obtained from microbial strains of *Bacillus subtilis*[16]. Some of the example of emulsifier is Polyethylene Glycol Stearate, Sorbitan Monooleate (Span 80), Polyoxyethylene Sorbitan Monooleate (Tween 80), Stearic Acid, and Sodium Stearate [22].

3. Gelling agent

These are used to increase consistency of dosage forms and provide gelled behavior. Gelling agent are of two types, natural and synthetic. Incorporation of gelling agent to a system makes it thixotropic. According to the Swedish National Encyclopedia (1989-1996) thixotropy is "property of viscous (viscid) or gel-like product turning more liquid as the longer time and the more vigorous, which is deformed (e.g. by stirring). It is generally accepted that thixotropy is the phenomenon of the fluid which shows a reversible structural transition (i.e., gel-sol-gel conversion) due to the time-dependent changes in the viscosity induced by temperature, pH or other components without any changes in the volume of the system. Gel-sols-gel behavior imparts stability as well as improves bioavailability of system. It has been found that there exist an inverse relationship between concentration of gelling agent and extent of drug released. The gelling agents like Carbomers readily absorb water, get hydrated and swell. Besides its hydrophilic nature, its cross-linked structure and it's insolubility in water makes Carbopol a potential candidate for use in controlled release drug delivery system. HPMC based emulgel shows better drug release than Carbopol based emulgel. Various gelling agent used are Carbopol-934, HPMC 2910, HPMC K4M etc [23]. Table: 2 comprise various gelling agent which are used in various formulations.

Table: 2 Examples of Gelling Agent

Sr. No.	Chemical Name	Quantity	Dosage Form
1.	Carbopol-934	1%	Emulgel
2.	Carbopol-940	1%	Emulgel
3.	Hpmc2910	2.5%	Emulgel
4.	Sodium CMC	1%	Gel
5.	Xanthan Gum	1%	Gel
6.	HPMC	3.5%	Gel

4. Penetration Enhancers

These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability. In order to promote absorption of drugs thorough skin barrier, vehicles often include penetration enhancing ingredients which temporarily disrupts the highly ordered structure of stratum corneum skin barrier, fluidize the lipid channels between corneocytes, alter the partitioning of the drug into skin structures, and

enhance delivery into skin [23, 24]. E.g. Oleic Acid, lecithin, Isopropyl Myristate, Urea, Eucalyptus oil, Chenopodium oil, Pyrrolidone, Laurocapran, Dimethyl Sulphoxide, Linoelic acid, Menthol etc. Table: 3 comprises various penetration enhancers

Table: 3 Examples of Penetration Enhancers

Sr. No.	Chemical Name	Quantity	Dosage Form
1.	Isopropyl Myristate	5%	Gel
2.	Lecithin	5%	Gel
3.	Oleic Acid	1%	Gel
4.	Urea	10%	Gel
5.	Eucalyptus oil	Na	None
6.	Chenopodium oil	NA	None
7.	Menthol	4-6%	NA
8.	Linoleic Acid	5%	Gel

Formulation Methods of Emulgel

i. **Mohamed (2004**) in his research work (optimization of Chlorphenesin in Emulgel) includes preparation of emulsion (o/w or w/o), followed by addition of gelling agent to form Emulgel. First step includes formation of aqueous phase of emulsion. Aqueous phase of emulsion was prepared by first dissolving Tween 20 in purified water, then Propylene glycol solution was prepared by dissolving Methyl Paraben and Propyl Paraben in Propylene Glycol and then both the solutions are mixed and set aside. Oily phase of emulsion was prepared by dissolving span 20 in light Liquid Paraffin. Preparation of emulsion involves separate heating of oily and aqueous phase to 70–80° C after that both the phases were mixed with constant stirring until cooled to room temperature. Gel phase of emulgel was prepared by dispersing HPMC or Carbopol in water. HPMC was required to soak overnight in water, while Carbopol gel was prepared by simply dispersing it in purified water. When both the components both emulsions & gel get ready then the Emulgel was prepared by mixing emulsion with gel in 1:1 ratio with gentle stirring [25].

ii. **Method reported by Perioli et al. (2008)** uses three steps for formulation of Emulgel (I) polymer dispersion in water (ii) neutralization of the polymeric aqueous dispersion and (iii) emulsification of the oil phase. With respect to the first step, three different TR-1 percentages, namely 0.3, 0.4 and 0.5%, w/v, are required. First step involves suspension of polymer in deionized water with continuous stirring at 900 rpm for 20 min at room temperature using a mechanical stirrer equipped with a three blade helical impellers &

then slurry was neutralized with NaoH solution (18%w/v) to final pH value of 5.5, 6.0 and 6.5. The neutralization process causes the distension of polymer chains resulting in clear stable gels. Now for the complete hydration of polymer gels were stored at 4° C for 24 h before the addition of oil phase. After completing the hydration of gel different quantities of oil phase at three o/w ratio (w/w) 0.5, 1.0 and 1.5 respectively were adding it stirring at 800 rpm (80 °C) there after it was left for cooling and its pH was measured[26].

iii. **Shahin et al. (2011)** followed a different method to develop Emulgel for Clotrimazole delivery. In this method the preparation of oily phase of emulsion by dissolving drug and span 60 in oily phase (Jojoba oil) with the aid of magnetic stirrer at 75° C, with subsequent cooling, followed by addition of Carbopol to the oily phase. In second step aqueous phase was prepared by dissolving Brij- 35 in Propylene glycol. Third step involves, addition of oily phase to the aqueous phase following their emulsification using the over head mixer for 10 min at 1400 rpm, and then introduced emulsion into the homogenizer for 5 min at 10,000 rpm. Gellification of emulsion involves, addition of gelling agent Tri ethanolamine (formulae containing Carbopol either alone or in combination and/or HPMC to the emulsion using over head mixer at 200 rpm for 45 min thereby adjusting the pH of formulation containing Carbopol to 5.5–6.5 using Tri ethanol amine [27].

iv. **Dickinson Eric et al. (2012)** prepared a solid-like emulsion gel from a stable liquid-like emulsion by gelling the continuous phase or aggregating the emulsion droplets. Even simply forcing all the droplets closer together by centrifugation can be sufficient to produce a concentrated protein-stabilized emulsion with gel-like behavior, i.e., elasticity at small deformations. Emulsion gels produced by heat treatment have limited uses, especially for food formulations containing heat sensitive ingredients. The appearance of emulsion gels prepared by salt-induced gelation was highly dependent on calcium concentrations. Increasing salt concentration produced a particulate gel with poor water holding capacity [28].

Characterization of Emulgel

Physical appearance

Emulgel can be tested for their visual appearance, consistency, grittiness and phase separation. The formulations can be tested for their homogeneity by visual appearance after the emulgel was applied as a thin layer on the slide [29].

Stability of Emulsion

Stability of emulsion can be determined by visual observation by using creaming index as an indicator [30].

Microscopic Evaluation

Globule size of the prepared emulgel can be determined by optical microscopy. A compound microscope can be used for this purpose and the globules can be observed under 40x magnification. Prior to observation, the eye-piece micrometer was calibrated with a stage micrometer and calibration factor was obtained. Subsequently, mean globule size can be calculated [31, 32].

pH determination

The pH value of emulgel formulation can be measured by using pH meter (Digital pH meter). The pH meter was calibrated with standard buffer solution having pH 4 and 7 before use. And then the 1% aqueous solution of the prepared emulgel can be made. 1 gm of formulation was dissolved in distilled water and stirred until it forms uniform suspension, kept it aside for 2 hr. The volume made up to 100ml and pH of the suspension can be measure with the digital pH meter [33, 34].

Spreading Coefficient

It is the term expressed to denote the extent of area to which gel readily spreads on application to skin or affected part Spreading coefficient (Spreadability), can be determined by apparatus suggested by Lalit Kumar et.al. 2010. It consists of a wooden block, which is attached to a pulley at one end. Spreading coefficient can be measured on the basis of 'Slip' and 'Drag' characteristics of emulgel. A ground glass slide can be fixed on the wooden block. An excess of emulgel (about 2 gm) under study can be placed on this ground slide. The emulgel preparation was then sandwiched between this slide and second glass slide having same dimension as that of the fixed ground slide. The second glass slide is provided with the hook. Weight of 500 mg was placed on the top of the two slides for 5 min to expel air and to provide a uniform film of the emulgel between the two slides. Measured quantity of weight was placed in the pan attached to the pulley with the help of hook. Time in seconds taken by two slides to slip off from emulgel and placed in between the slides under the direction of certain load. Lesser the time taken for separation of two slides, better the spreadability. It is calculated by using the following formula [35]:

S = M. L / T

Where, M = wt. tied to upper slide; L = length of glass slides; T = time taken to separate the slides.

And the other method is one of the criteria for an emulgel to meet the ideal quantities is that it should possess good spreadability. The therapeutic efficacy of a formulation also depends upon its spreadability. Spreadability of emulgel and marketed gel can be measured in terms of diameter of emulgel circle produced when emulgel is placed between two glass plates of definite weight. A weighed quantity of emulgel or gels can be taken on one glass plate and another glass plate was dropped from a distance of 5 cm. The diameter of the circle of spread emulgel can be measured [36].

Extrudability

It can be a usual empirical test to measure the force required to extrude the material from tube. The method applied for determination of applied shear in the region of the rheogram corresponding to a shear rate exceeding the yield value and exhibiting consequent plug flow, the method adopted for evaluating emulgel formulation for extrudability can be based upon the quantity in percentage of emulgel and emulgel extruded from lacquered Aluminum collapsible tube on application of weight in grams required to extrude at least 0.5cm ribbon of emulgel in 10 seconds. More quantity extruded better is extrudability. The measurement of extrudability of each formulation can be triplicate and the average values are presented. The extrudability can be calculated by using the following formula [37]:

Extrudability = Applied weight to extrude emulgel from tube (in gm) / Area (in cm2).

Another method to check the Extrudability of emulgel formulation can be carried out using hardness tester. A 15 gm of gel can be filled in Aluminum tube. The plunger was adjusted to hold the tube properly. The presence of 1 kg/cm was applied for 30 sec. the quantity of gel extruded can be weighed. The procedure can be repeated at 3 equidistance places of the tubes.[38]

Drug content/Drug entrapment efficiency

Drug concentration in Gellified Emulsion can be measured spectrophotometrically. Emulgel was dissolved in Methanol and subjected to sonication and the absorbance can be measured after suitable dilution in UV Visible spectrophotometer [39, 40].

Drug content = (concentration × dilution factor × volume taken) × conversion factor

Swelling index

To determine the swelling index of prepared topical emulgel, 1 gm of gel can be taken on porous aluminum foil and then placed separately in a 50 ml beaker containing 10 ml 0.1 N NaoH. Then samples can be removed from beakers at different time intervals and put it on dry place for some time after it reweighed. Swelling index can be calculated as follows [41, 42]:

% Swelling index (SW) = [(Wt – Wo) / Wo] × 100 …… (2)

Where, % SW = Equilibrium percent swelling

Wt= Weight of swollen emulgel after time t

Wo = Original weight of emulgel at zero time.

Viscosity

Viscosity of the prepared gels can be determined using Brookfield viscometer at the temperature of 37^0 C. The gel sample was filled in the sample holder and the particular spindle immersed into the sample. Then it can be allowed to rotate at a particular speed and viscosity of the formulation can be measured after 2 minutes [43, 44].

Phase Separation

All prepared formulations can be subjected to centrifugations at 10,000 rpm for 10 min and examined for any change in phase separation [45].

Determination of thixotropic characteristics

The formulations can be subjected to different rates of shear using Rheometer, at constant temperature (25^0C). The measuring system employed can be the cone and plate system having 40 mm diameter and 4^0 angles. The rheogram can be constructed by plotting rate of shear against shear stress [46].

Syneresis measurement

Upon standing sometimes gel system shrinks a bit and little liquid is pressed out. This phenomenon is known as syneresis. In this test, emulgel can be put in cylindrical plastic tube with a perforated bottom which can be covered with filter paper (Whatmann No. 4). These tubes are then placed in centrifuge tubes and centrifuged for 15 min. the cylindrical plastic tube and liquid which had separated from emulgel can be weighed. The percentage of syneresis can be calculated as the ratio of weight of liquid separated from the emulgel to the total weight of emulgel before centrifugation and multiplied by 100. The data can be calculated [47].

In vitro Release/permeation Study

In vitro release studies can be carried out using Franz diffusion cell. In this effective diffusion area 3.14 cm2 and 15ml cell volume can be used for the drug release studies. Emulgel can be applied onto the surface of egg membrane evenly the egg membrane was clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber was filled with freshly prepared PBS solution to solubilize the drug. The receptor chamber was stirred by magnetic stirrer a sample (1.0 ml aliquots) was collected at suitable time interval. Samples can be analyzed for drug content by UV visible after appropriate dilutions. Cumulative corrections can be made to obtain the total amount of drug release at each time interval. The cumulative amount of drug released across the egg membrane can be determined as a function of time [48, 49].

Ex vivo Drug permeation Study

The *Ex vivo* drug release study of selected formulations can be carried out in a modified Diffusion cell, using wistar male rat skin. A section of skin was cut and clamped carefully to one end of the hollow glass tube of dialysis cell (2.3 cm diameter; 4-16 cm^2 area) keeping the dorsal side upward. Then emulgel can be spread uniformly on the membrane. PBS pH 7.4 can be used as dissolution media. The donor compartment was kept in contact with receptor compartment. This whole assembly can be kept on a magnetic stirrer and the solution on the receptor side can be stirred continuously using a magnetic bead and temperature of the cell can be maintained at 37±0.5°C. Sample (5 ml) can be withdrawn at suitable time intervals and replaced with equal amounts of fresh dissolution media. Samples can be analyzed spectrophotometrically and the cumulative % drug release can be calculated [50, 51].

Stability studies

The stability study can be performed as per ICH guidelines. The formulated gels can be stored at different temperatures, viz. 4^0c ± 2^0C, 25^0C ± 2^0C, and 40^0C ± 2^0C for a period of three months and studied for appearance, pH spreadability, extrudability, drug content and in vitro diffusion studies at one month intervals [52].

CONCLUSION

Emulgel is one of the best approaches for topical drug delivery of hydrophobic drugs, as emulgel has several favorable properties Such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, bio-friendly, transparent & pleasing appearance. Emulgel have properties of both emulsion and

gels and thus can be used for controlling release rate of drugs with short half-life. Currently, very few marketed emulgel formulation are available in market however, it offers a vast field for development and research. However, regarding various advantages and future prospective emulgels offer a wide utility in derma care. Due to lack of excessive oily bases and excipients, it shows better drug release and thus could be formulation of choice in various dermatological diseases.

FUTURE SCOPE

In the coming years, topical drug delivery will be used extensively to impart better patient compliance. Since emulgel possesses an edge in terms of spreadability, adhesion, viscosity and extrusion, they will become a popular drug delivery system. Moreover, they will become a solution for loading hydrophobic drugs in a water soluble gel bases.

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