GELLIFIED EMULSION: A NEW BORN FORMULATION FOR TOPICAL DELIVERY OF HYDROPHOBIC DRUGS

Sonaje Sumeet Purushottam¹, Gondkar Sheetal Bhaskarrao², Saudagar Ravindra Bhanudas³

¹Department of Pharmaceutics, KCT’S R.G.Sapkal College of Pharmacy, Anjaneri, Nashik, 422213. Maharashtra, India.

²Department of Pharmaceutics, KCT’S R.G.Sapkal College of Pharmacy, Anjaneri, Nashik, 422213. Maharashtra, India.

³Department of Pharmaceutical Chemistry, KCT’S R.G.Sapkal College of Pharmacy, Anjaneri, Nashik, Maharashtra, India.

ABSTRACT

Emulgel has emerged as promising drug delivery system for the delivery of hydrophobic drugs. When gel and emulsion are used in combined form the dosage form are referred as Emulgel. Emulgel are either emulsion of oil in water or water in oil type, which is gelled by mixing it with gelling agent. Incorporation of emulsion into gel increases its stability and makes it dual release control system. The presence of gelling agent in the water phase converts a classical emulsion into an emulgel. The major objective behind this formulation is delivery of hydrophobic drugs to systemic circulation via skin. These emulgel are having major advantages on novel vesicular systems as well as on conventional systems in various aspects. The emulgel for dermatological use has several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, bio-friendly, transparent and pleasing appearance. Various permeation enhancers can potentiate the effect, so emulgels can be used as better topical drug delivery systems over present systems. The use of emulgels can be extended in analgesics, antiviral and antifungal drugs.
Keywords: Emulgel, Hydrophobic drugs, Dermal delivery, Thixotropic, Penetration enhancers.

INTRODUCTION
Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorder. Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. These apply a wide spectrum of preparations for both cosmetic and dermatological to their healthy or diseased skin. Topical drug delivery is an attractive route for local and systemic treatment.[1] The topical drug delivery system is generally used where the others system of drug administration fails or it is mainly used in fungal infection.[2] A unique aspect of dermatological pharmacology is the direct accessibility of the skin as a target organ for diagnosis and treatment. The combination of hydrophilic cornified cells in hydrophobic intercellular material provides a barrier to both hydrophilic and hydrophobic substances.[3] Dermatological products applied to skin are diversified in formulation and range in consistency from liquid to powder but the most popular products are semisolid preparation. Within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. Gels are a relatively newer class of dosage form created by entrapment of large amounts of aqueous or hydroalcoholic liquid in a network of colloidal solid particles, which may consist of inorganic substances, such as aluminium salts or organic polymers of natural or synthetic origin. They have a higher aqueous component that permits greater dissolution of drugs, and also permit easy migration of the drug through a vehicle that is essentially a liquid, compared with the ointment or cream base. These are superior in terms of use and patient acceptability.[4]

In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels. When gels and emulsions are used in combined form the dosage forms are referred as “Emulgel”. As the name suggest they are the combination of emulsion and gel. 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. In fact, the presence of a gelling agent in the
water phase converts a classical emulsion into an emulgel. The emulsion gels are hydrogels containing randomly distributed oil microdroplets. Both oil-in-water and water-in-oil emulsions are extensively used for their therapeutic properties and as vehicles to deliver various drugs to the skin. Emulsions possess a certain degree of elegance and are easily washed off whenever desired. They also have a high ability to penetrate the skin. Emulsion itself 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 and slowly release drug in a controlled way through the external phase to the skin. Gel forms cross linked network where it captures small drug particles and provides its release in a controlled manner. In addition, the formulator can control the viscosity, appearance, and degree of greasiness of cosmetic or dermatological emulsions. Oil-in-water emulsions are most useful as water washable drug bases and for general cosmetic purposes, while water-in-oil emulsions are employed more widely for the treatment of dry skin and emollient applications. Emulgels are emulsions, either of the oil-in-water or water-in-oil type, which are gelled by mixing with a gelling agent. They have a high patient acceptability. Therefore, they have been recently used as vehicles to deliver various drugs to the skin. Emulgels for dermatological use have several favourable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, nonstaining, long shelf life, bio-friendly, transparent and pleasing appearance.

Formulation Considerations

The challenges in formulating topical emulgels are:

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 allergic potential, good physiological compatibility and high biocompatibility.

**ADVANTAGES OF TOPICAL DRUG DELIVERY SYSTEMS**[^8,9]

- Avoidance of first pass metabolism.
- Convenient and easy to apply.
- Avoidance of the risks and inconveniences of intravenous therapy and of varied conditions of absorption like pH changes, presence of enzymes, gastric emptying time.
- Ability to easily terminate the medications, when needed.
- Ability to deliver drug more selectively to a specific site.
- Avoidance of gastro-intestinal incompatibility.
- Providing utilization of drugs with short biological half-life, narrow therapeutic window.
- Improve patient compliance.
- Provide suitability for self-medication.

**DISADVANTAGES OF TOPICAL DRUG DELIVERY SYSTEMS**[^8,9]

- Skin irritation on contact dermatitis may occur due to the drug and/or excipients.
- Poor permeability of some drugs through the skin.
- Possibility of allergenic reactions.
- Drugs of larger particle size not easy to absorb through the skin

**RATIONAL**

Various types of topical formulations are available or used to apply on to the skin or mucous membrane restores a fundamental function of skin or pharmacologically alters an action in the underlined tissues. On the same time the topical agents such as ointment, cream, lotion have many disadvantages also. They are sticky causing uneasiness to the patient and also have lesser spreading coefficient and need to apply with rubbing. They exhibit the problem of stability also. Due to all these factors within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. Despite of offering several benefits, Gels a colloid system shows a major limitation in delivery of hydrophobic drugs. So to overcome this approach an emulsion based approach is being used so that even hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels.
**PHYSIOLOGY OF SKIN**[10,11]

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 dosage form. The skin of an average adult body covers a surface area approximately $2 \text{m}^2$ and receives about one third of the blood circulating through the body. An average human skin surface is known to contain, on 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 2.

![Fig. 2: skin structure][11]

1. Non-viable epidermis
2. Viable epidermis
3. Viable dermis
4. Subcutaneous connective tissue

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 - 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, glycosphingolipid, cholesterol sulfate and neutral lipid, protein (75-85%) which is mainly keratin.
2. Viable epidermis
This layer of the skin resides between the stratum corneum and the 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 density of this region is not much different than water. The water content is about 90%.

3. Dermis
Just beneath the viable epidermis is the dermis. It is a structural fibrin and very few cells are like it can be found histological in normal tissue. Dermis thickness ranges from 2000 to 3000 µm and consists of a matrix of loose connective tissue composed of fibrous protein embedded in an amphorphose 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, secretary 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.

DRUG DELIVERY ACROSS THE SKIN [10,11]
The epidermis is the most superficial layer of the skin and is composed of stratified keratinized squamous epithelium which varies in thickness in different parts of the body. It is thickest on with elastic fibers. The skin forms a relatively waterproof layer that protects the deeper and more delicate structures. Blood vessels are distributed profusely beneath the skin. Especially important is a continuous venous plexus that is supplied by inflow of blood from the skin capillaries. In the most exposed areas of the body-the hands, feet, and ears blood is also supplied to the plexus directly from the small arteries through highly muscular arteriovenous anastomoses. 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 pain medication and infection fighting 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 technologies now allow other drugs to be absorbed through the skin (transdermal). These can be used to treat not just the affected areas (the skin) but the whole body (systemic).

FACTORS AFFECTING TOPICAL ABSORPTION OF DRUG\textsuperscript{[12]}

**Physiological Factors**
1. Skin thickness
2. Lipid content
3. Density of hair follicles
4. Density of sweat glands
5. Skin pH
6. Blood flow
7. Hydration of skin
8. Inflammation of skin

**Physiochemical Factors**
1. Partition coefficient
2. Molecular weight (<400 Dalton)
3. Degree of ionization (only unionized drugs gets absorbed well)
4. Effect of vehicles

FACTORS TO BE CONSIDERED WHEN CHOOSING A TOPICAL PREPARATION\textsuperscript{[13]}
1. Irritation or sensitization potential. Generally ointments and w/o creams are less irritating while gels are irritating, Ointments do not contain preservatives or emulsifiers if allergy to these agents is concern.
2. Match the type of preparation with the type of lesions. For example, avoid greasy ointments for acute weepy dermatitis.
3. Match the type of preparation with the site (e.g., gel or lotion for hairy areas).
4. Effect of the vehicle e.g. an occlusive vehicle enhanced penetration of the active ingredient and improves efficacy. The vehicle itself may have a cooling, drying, emollient or protective action.
5. The medication should not affect skin type.

METHOD TO ENHANCED DRUGS PENETRATION AND ABSORPTION\[14\]

1. Chemical enhancement
2. Physical enhancement
3. Biochemical enhancement
4. Supersaturation enhancement

ADVANTAGES OF USING EMULGELS AS A DRUG DELIVERY SYSTEM\[15\]

1. Hydrophobic drugs can be easily incorporated into gels using d/o/w emulsions: 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. And this emulsion can be mixed into gel base. This may be proving better stability and release of drug than simply incorporating drugs into gel base.

2. Better stability: Other transdermal preparations are comparatively less stable than emulgels. Like 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 emulgels comprises of simpler and short steps which increases the feasibility of the production. There are no specialized instruments needed for the production of emulgels. Moreover materials used are easily available and cheaper. Hence, decreases the production cost of emulgels.

5. No intensive sonication: Production of vesicular molecules need intensive sonication which may result in drug degradation and leakage. But this problem is not seen during the production of emulgels as no sonication is needed.

6. Controlled release: Emulgels can be used to prolong the effect of drugs having shorter T1/2.
CLASSIFICATION OF TOPICAL DRUG DELIVERY SYSTEM[^16]

Table 1: Classification of topicals

<table>
<thead>
<tr>
<th>Liquid preparations</th>
<th>Semi-solid preparations</th>
<th>Solid preparations</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liniments</td>
<td>Ointments</td>
<td>Topical powders</td>
<td>Transdermal drug delivery system</td>
</tr>
<tr>
<td>Lotions</td>
<td>Creams</td>
<td>Poultices</td>
<td>Tapes and gauzes</td>
</tr>
<tr>
<td>Paints</td>
<td>Pastes</td>
<td>Plaster</td>
<td>Rubbing alcohols</td>
</tr>
<tr>
<td>Topical solution</td>
<td>Gels</td>
<td></td>
<td>Liquid cleaner</td>
</tr>
<tr>
<td>Topical tinctures</td>
<td>Poultices</td>
<td></td>
<td>Topical aerosols</td>
</tr>
</tbody>
</table>

FORMULATION OF EMULGEL[^16]

1. **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.
   - Deliver the drug to the target site.
   - Sustain a therapeutic drug level in the target tissue for a sufficient duration to provide a pharmacologic effect.
   - Appropriately formulated for the anatomic site to be treated.
   - Cosmetically acceptable to the patient.

Due to the efficiency of the epidermal barrier, the amount of topical drug that gets through the stratum corneum is generally low. Rate and extent of absorption vary depending on characteristics of the vehicle but is also influenced by the active agent itself.

(A) **Aqueous Material**

This forms the aqueous phase of emulsion. The commonly used agents are water, alcohols etc.

(B) **Oils**

These agents form the oily phase of the emulsion. For externally applied emulsions, mineral oils, either alone or combined with soft or hard paraffin, are widely used both as the vehicle for the drug and for their occlusive and sensory characteristics. Widely used oils in oral preparations are non-biodegradable mineral and castor oils that provide a local laxative
effect, and fish liver oils or various fixed oils of vegetable origin (e.g., arachis, cottonseed, and maize oils) as nutritional supplements. Some are discussed in table 2.

Table 2: Uses of oil

<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 &amp; 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</td>
</tr>
</tbody>
</table>

2. 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 mono-oleate (Span 80), Polyoxyethylene sorbitanmonooleate (Tween 80), Stearic acid and Sodium stearate.

3. Gelling Agents

These are the agents used to increase the consistency of any dosage form can also be used as thickening agent. The examples are given in table 3.

Table 3: 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>1 %</td>
<td>Emulgel</td>
</tr>
<tr>
<td>Carbopol – 940</td>
<td>1 %</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>
Table 4: Different grades of carbopol

<table>
<thead>
<tr>
<th>POLYMER</th>
<th>VISCOSITY</th>
<th>PROPERTIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbopol</td>
<td>9103000-7000</td>
<td>Effective in low concentration and will provide a low viscosity formulation.</td>
</tr>
<tr>
<td>Carbopol</td>
<td>93430,500-39,400</td>
<td>Effective in thick formulations such as emulsions, suspensions, sustain release formulation, transdermals and topical forms clear gels with water.</td>
</tr>
<tr>
<td>Carbopol</td>
<td>934 P29,400-39,400</td>
<td>Same properties as 934, but intended for pharmaceutical formulation purified water.</td>
</tr>
<tr>
<td>Carbopol</td>
<td>94040,000-60,000</td>
<td>Effective in thick formulation, very good clarity in water or hydroalcoholic topical gels. Forms clear gels with hydro alcoholic system.</td>
</tr>
</tbody>
</table>

4. Penetration Enhancers[18]

In order to promote absorption of drugs, vehicles often include penetration enhancing ingredients that temporarily disrupts the skin barrier, fluidize the lipid channels between corneocytes, alter the partitioning of the drug into skin structures, or otherwise enhance delivery into skin. So called penetration enhancers some of these materials given in table 5.

Table 5: Use of penetration enhancer

<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>Lecithine</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>Eucalyptus oil</td>
<td>NA</td>
<td>None</td>
</tr>
<tr>
<td>Chenopodium oil</td>
<td>NA</td>
<td>None</td>
</tr>
</tbody>
</table>

PROPERTIES OF PENETRATION ENHANCERS[18]

•They should be non-toxic, non-irritating and non-allergenic.
They would ideally work rapidly, and the activity and duration of effect should be both predictable and reproducible.

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

The penetration enhancers should work unidirectional i.e. should allow therapeutic agents into the body whilst preventing the loss of endogenous material from the body.

The penetration enhancers should be appropriate for formulation into diverse topical preparations, thus should be compatible with both excipients and drugs.

They should be cosmetically acceptable with an appropriate skin ‘feel’.

**MECHANISM OF PENETRATION ENHANCERS**<sup>[19]</sup>

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

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

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

**PATHWAY OF TRANSDERMAL PERMEATION**<sup>[19]</sup>

Permeation can occur by diffusion via:

1. Transdermal permeation, through the stratum corneum.
2. Intercellular permeation, through the stratum corneum.
3. Transappendaged permeation, via the hair follicle, sebaceous and sweat glands.

Most molecules penetrate through skin via intercellular micro route and therefore many enhancing techniques aim to disrupt or bypass its elegant molecular architecture.
EMULGEL PREPARATION\textsuperscript{[20]}

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

Emulgel was prepared by the method reported by Mohammad et al (2004) with minor modification. The Gel in formulations were prepared by dispersing Carbopol 934 in purified water with constant stirring at a moderate speed and Carbopol 940 in purified water with constant stirring at a moderate speed then the pH are adjusted to 6 to 6.5 using Triethanolamine (TEA). The oil phase of the emulsion were prepared by dissolving Span 20 in light liquid paraffin while the aqueous phase was prepared by dissolving Tween 20 in purified water. Methyl and propyl paraben was dissolved in propylene glycol whereas drug was dissolved in ethanol and both solutions was mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70° to 80°C; then the oily phase were added to the aqueous phase with continuous stirring until cooled to room temperature. And add glutaraldehyde in during of mixing of gel and emulsion in ratio 1:1 to obtain the emulgel.
CHARACTERIZATION OF EMULGEL\textsuperscript{[21,22,23]}

1. Physical Examination: The prepared emulgel formulations are inspected visually for their color, homogeneity, consistency and phase separation.

2. Rheological Studies: The viscosity of the different emulgel formulations is determined at 25°C using a cone and plate viscometer with spindle 52 (Brookfield Engineering Laboratories,) and connected to a thermostatically controlled circulating water bath.

3. Spreading Coefficient: Spreadability is determined by apparatus suggested by Mutimer et al (1956) which is suitably modified in the laboratory and used for the study. It consists of a wooden block, which is provided by a pulley at one end. By this method, spreadability is measured on the basis of ‘Slip’ and ‘Drag’ characteristics of emulgels. A ground glass slide is fixed on this block. An excess of emulgel (about 2 gm) under study is placed on this ground slide. The emulgel is then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A 1 Kg weight is placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the emulgel between the slides. Excess of the emulgel is scrapped off from the edges. The top plate is then subjected to pull of 80 gms. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. A shorter interval indicates better spreadability.

4. Extrudability Study of Topical Emulgel (Tube Test): It is 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. In the present study, the method adopted for evaluating emulgel formulation for extrudability is 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 0.5 cm ribbon of emulgel in 10 seconds. More quantity extruded better is extrudability. The measurement of extrudability of each formulation is in triplicate and the average values are presented. The extrudability is then calculated by using the following formula:

\[
\text{Extrudability} = \frac{\text{Applied weight to extrude emulgel from tube (in gm)}}{\text{Area (in cm}^2\text{)}}
\]

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

\[
\text{Swelling index (SW)} \% = \frac{(\text{Wt} - \text{Wo})}{\text{Wo}} \times 100.
\]

Where,

(SW) % = Equilibrium percent swelling,

Wt = Weight of swollen emulgel after time t,

Wo = Original weight of emulgel at zero time.

6. **Drug Content Determination**: Take 1gm of emulgel. Mix it in suitable solvent. Filter it to obtain clear solution. Determine its absorbance using UV spectrophotometer. Standard plot of drug is prepared in same solvent. Concentration and drug content can be determined by using the same standard plot by putting the value of absorbance.

\[
\text{Drug Content} = (\text{Concentration} \times \text{Dilution Factor} \times \text{Volume taken}) \times \text{Conversion Factor}
\]

7. **Skin Irritation Test (Patch Test)**: The preparation is applied on the properly shaven skin of rat and its adverse like change in color, change in skin morphology should be checked upto 24 hours. The total set of 8 rats can be used of the study. If no irritation occurs the test is passed. If the skin irritation symptom occurs in more than 2 rats the study should be repeated.

8. **Ex–Vivo Bioadhesive Strength Measurement of Topical Emulgel**: (MICE SHAVEN SKIN): The modified method is used for the measurement of bioadhesive strength. The fresh skin is cut into pieces and washed with 0.1 N NaoH. Two pieces of skin were tied to the two
glass slide separately from that one glass slide is fixed on the wooden piece and other piece is tied with the balance on right hand side. The right and left pans were balanced by adding extra weight on the left hand pan. 1 gm of topical emulgel is placed between these two slides containing hairless skin pieces, and extra weight from the left pan is removed to sandwich 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 minutes. Weight is added slowly at 200 mg/ min to the left hand pan until the patch detached from the skin surface. The weight (gram force) required to detach the emulgel from the skin surface gave the measure of bioadhesive strength. The bioadhesive strength is calculated by using following:

\[
\text{Bioadhesive Strength} = \frac{\text{Weight required (in gms)}}{\text{Area (cm}^2\text{)}}
\]

![Fig.5: setup for bioadhesive test](image)

9. In Vitro Release/Permeation Studies: In vitro release studies were carried out using Franz diffusion cell.

10. Stability Studies: The prepared emulgels were packed in aluminum 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 at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profiles.

MARKETED PREPARATIONS

<table>
<thead>
<tr>
<th>Product name</th>
<th>Drug</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>VOLTAREN EMULGEL</td>
<td>Diclofenac diethyl</td>
<td>Novartis Pharma ammonium</td>
</tr>
<tr>
<td>MICONAZ-H-EMULGEL</td>
<td>Miconazole nitrate,</td>
<td>Medical union Pharma</td>
</tr>
<tr>
<td></td>
<td>Hydrocortison</td>
<td></td>
</tr>
</tbody>
</table>
FUTURE PROSPECTIVE
Hydrophobic behavior of drugs is one of the most common problems faced during formulation & development of any new formulation. This behavior is responsible for poorwater solubility and bioavailability of drugs. Many numbers of drugs are hydrophobic in nature. Their delivery to the biological system has been challenging. For topical delivery of drugs different delivery systems such as ointments, lotion, creams and pastes are applied. These topical formulations generally include large number of oleaginous bases such as petrolatum, bees wax or vegetable oils that themselves are hydrophobic in nature that do not allow the inclusion of water or aqueous phase. It makes them an excellent emollient but retards the release of drugs and makes the product thick & greasy. Whereas gel provides aqueous environment to drug, favors its dissolution and provides quicker release of drug as compared to other topical delivery systems. Emulsion based gel provides a suitable medium for delivery of such hydrophobic drugs where such drugs can be incorporated into its oily phase and delivered to skin. All such advantages of Emulgel over other topical delivery systems make them more efficient & productive. In future these properties will be used to deliver more number of topical drugs in the form of Emulgel.

CONCLUSION
After thorough literature survey we reached into a conclusion that Emulgels have proven as most convenient, better and effective delivery system. Due to its non-greasy, gel like property it provides & lacks of oily bases and it provides better release of drugs as compared to other topical drug delivery system. Incorporation of emulsion into gel makes it a dual control release system further problem such as phase separation, creaming associated with emulsion gets resolved and its stability improves. Emulgel loaded with specific drugs has been found effective in some topical disorders & it is emerging as potential drug delivery system in area of dermatology. In future Emulgel will provide a solution for topical delivery of hydrophobic drugs. Many of drugs that have utility in treatment of skin disorders are hydrophobic in nature. Such drugs can be delivered in the form of Emulgel where they can be incorporated in oil phase of emulsion and combined with gel. Drugs which are still unexplored in this area are Retinoic Acid, Adapalene, Tolnaftate, Betamethasone, Dexamethasone etc.

REFERENCES


