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Review Article

# A Review on Emulgels-A Novel Approach for Topical Drug Delivery

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## ABSTRACT

Emulgels have emerged as one of the most interesting topical delivery system as it has dual release control system i.e. gel and emulsion. The major objective behind this formulation is delivery of hydrophobic drugs to systemic circulation via skin. A unique feature of topical drug delivery is the direct accessibility of the skin as a target organ for the diagnosis and treatment. When gel and emulsion are used in combined form the dosage form are referred as Emulgel. This may be proving better stability and release of drug than simply incorporating drugs into gel base. 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.

**Key words:** Emulgels, gel, emulsion, loading capacity and topical drug delivery

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## INTRODUCTION

Over the last decades, the treatment of illness has been accomplished by administering drug to human body via various routes namely oral, sublingual, rectal, parental etc. The topical drug delivery system is generally used where these systems of drug administration fails or in local skin infection like fungal infection. Topical drug delivery system can be defined as direct effects of formulation or drug containing medication to the skin to get localizing effect of drug or directly cure cutaneous disorders. Dermatological products applied to skin are diverse in formulation and range in consistency from liquid to powder but the most popular products are semisolid preparation. Topical drug delivery system has several advantages such as ability to deliver drug more selectively to a specific site, avoidance of gastro-intestinal incompatibility & metabolic degradation associated with oral administration. The release rates of drugs from topical preparations depend directly on the physiochemical properties of the carrier and the drug employed. In topical drug delivery system drug diffuses out of the delivery system, reaches to the site of action and gets absorbed by the skin. Increasing the release rate of the drug from the dosage form might therefore improve percutaneous absorption. Moreover topical deliveries provide an increased bioavailability by avoiding first pass metabolism effect by liver and a consistent delivery for extended period. When gels and emulsions are used in combined form the dosage forms

are referred as emulgel[1].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. Both oil-in-water and water-in-oil emulsions are used 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. Emulgels for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, and emollient, no staining, water- soluble, longer shelf life, and bio-friendly, transparent & pleasing appearance.

Now emulgels have been used for treatment of various kinds of skin disorder such as those infected by viral, bacterial, and fungal species (eczema, Herpes simplex ,acne).Research works on antifungal drugs incorporated to Emulgel have been carried by different scientist to judge its efficacy against fungal infection such as candidacies. Species causing candidacies are Candida albicans, Candida glabrata, Candida parapsilosis, Candida tropicalis and Candida krusei. Preparing Emulgels was found useful in combating fungalinfection.Scientist has been trying to develop Emulgel of various drugs to treat various kinds of skin disorder[2]. Acne is one of the major skin disorder common among adolescents. Factors that are responsible for acne are hormones, excess sebum, dead cells, Propionibacterium acne's and inflammatory response. Approaches should be taken to develop emulsion based, gel for treatment of such kinds of disorder. Anti-aging areas are yet to be explored researches on its cream based formulations have been done using varieties of herbal moieties such as Glycyrrhizaglabra, Curcuma longa, seeds of P. coliforlia, Cassia tora, Acacia catechu & Punicagranatum. Emulgel containing anti-inflammatory drug (Diclofenac) is used for relief of pain in muscle and joints[3].

Effort to cure diseases has been leading in the discovery of various drugs, medicine and delivery systems. To get therapeutic response of drug required for treatment of disease different routes of administration are followed. Route of administration depends on type and severity of disease. For skin disorders topical route is most preferred. Use of topical agents requires an appreciation of the factors that influence percutaneous absorption[4]. Molecules can penetrate the skin by three routes:

- Through intact stratumcorneum,
- Through sweat ducts,or
- Through the sebaceousfollicle.

The surface of the stratum carenum presents more than 99% of the total skin surface available for percutaneous drug absorption. Passage through this outermost layer is the rate-limiting step for percutaneous absorption. The major steps involved in percutaneous absorption include the establishment of a concentration gradient, which provides the driving force for drug movement across the skin; release of drug from the vehicle (partition coefficient); and drug diffusion across the layers of the skin (diffusion coefficient)[5].

Preferable characteristics of topical drugs include low molecular mass (600 Da), adequate solubility in oil and water, and a high partition coefficient. Except for very small particles, water soluble ions and polar molecules do not penetrate intact stratum carenum. Topical formulation can be used to manipulate the barrier function of the skin, for example, topical antibiotics and antibacterial help a damaged barrier to ward off infection, sun screening agents and the horny layer[6].

## RATIONALE OF EMULGEL AS A TOPICAL DRUG DELIVERY SYSTEM

There are many medicated products are applied to the skin or mucous membrane that either enhance or restore a fundamental function of skin or pharmacologically alter an action in the underlined tissues. Such products are referred as topical or dermatological products[7]. Many widely used topical agents like ointments, creams lotions have many disadvantages. They have very sticky causing uneasiness to the patient when applied. Moreover they also have lesser spreading coefficient and need to apply with rubbing, and 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. A gel is colloid that is typically 99% wt. liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelating substance present. 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 be successfully incorporated and delivered through gels[8].

## ADVANTAGES OF USING EMULGELS AS A DRUG DELIVERY SYSTEM

### Hydrophobic drugs can be easily incorporated into gels using 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[9].

**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.

**Controlled release**

Emulgels can be used to prolong the effect of drugs having shorter T1/2.

**Patient compliance**

They are less greasy and easy to apply.

**No intensivesonication**

Production of vesicular molecules needs 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[10].

**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.

**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.

## FACTORS AFFECTING TOPICAL ABSORPTION OF FORMULATIONS

**Physiological Factors**

- Skin thickness.
- Skin pH.
- Hydration of skin
- Inflammation of skin
- Lipid content.
- Blood flow
- Density of hair follicles.
- Density of sweat glands.

**Physiochemical Factors**

- Partition coefficient.
- Molecular weight (<400Dalton).
- Degree of ionization (only unionized drugs gets absorbed well).
- Effect of vehicles

## FACTORS TO BE CONSIDERED WHEN CHOOSING A TOPICAL FORMULATION[11]

- Effect of the vehicle e.g. an occlusive vehicle enhances penetration of the active ingredient and improves efficacy. The vehicle itself may have a cooling, drying, emollient, or protective action.
- Match the type of preparation with the type of lesions. For example, avoid greasy ointments for acute weepy dermatitis.
- Match the type of preparation with the site (e.g., gel or lotion for hairy areas).
- 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 a concern.
- The medication should not affect the skin type.

## PHYSIOLOGY OF SKIN[12]:

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. 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, 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.

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

**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, glycosphingo lipid, cholesterol sulfate and neutral lipid, protein (75-85%) which is mainly keratin.

**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%[13].

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[14].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.

## METHOD TO ENHANCE DRUG PENETRATION[15]:

**1.** Chemical enhancement

**2.** Biochemical enhancement

**3.** Physical enhancement

**4.** Super saturation enhancement

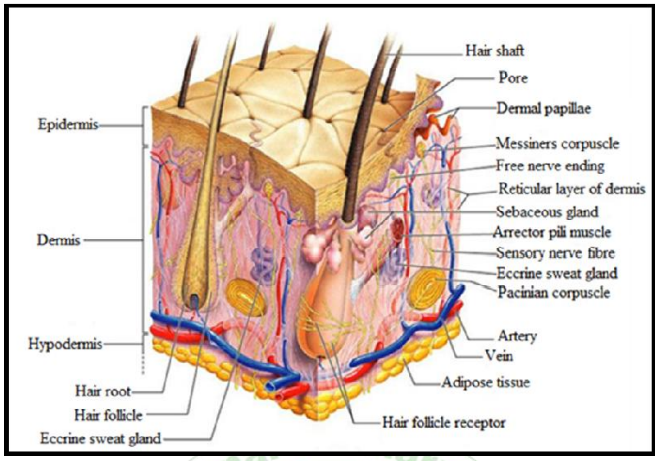
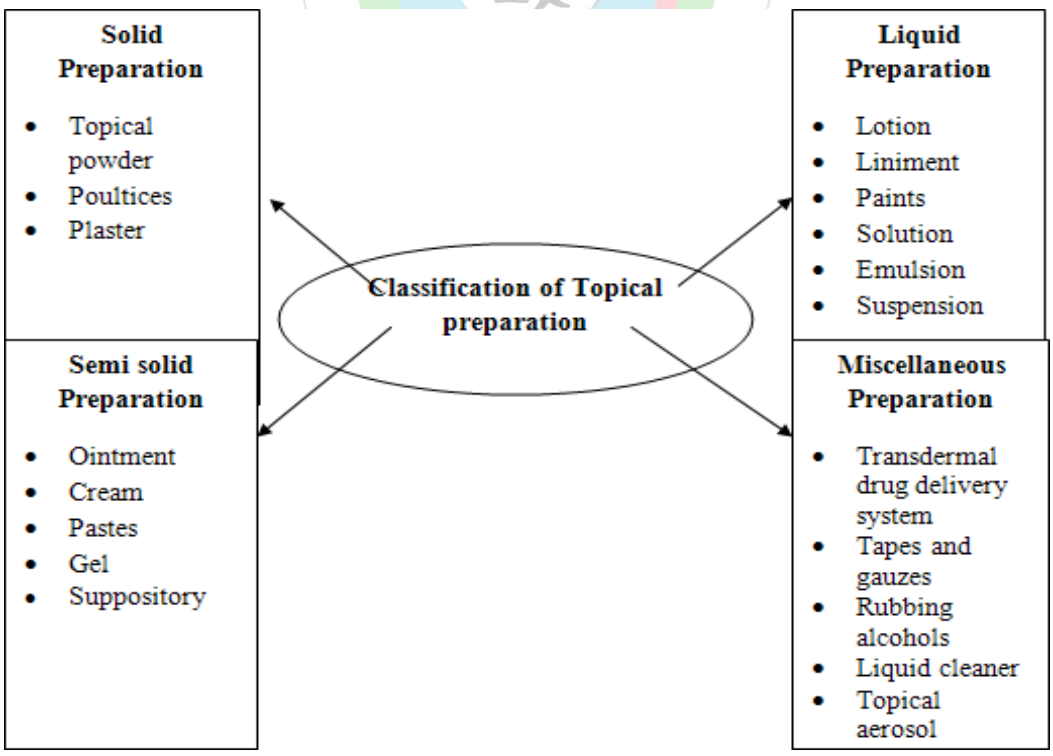



**Figure.1**Cross section of section

**Various Approaches Used For Topical Drug[16]**

**Delivery Formulation of Emulgel:**



**Vehicle[17]:**

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 patent.

**Aqueous Material:**

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

**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[17]. Some are discussed in table2.

**Table 2** : Use of oils

| Oil | Quantity | Dosage Form |
|---|---|---|
| **LightLiquidParaffin** | 7.5% | Emulsion & Emulgel |
| **Isopropylmyristate** | 7-7.5% | Emulsion |
| **Isopropylstearate** | 7-7.5% | Emulsion |
| **Isopropylpalmitate** | 7-7.5% | Emulsion |
| **Propyleneglycol** | 3-5% | Gel |

**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 (Span80), Stearic acid and Sodium stearate**.**

**Gelling Agents:**

These are the agents used to increase the consistency of any dosage form can also be used as thickening agent[18]. The examples are given in table3.

**Table 3** : Use of gelling agents

| Gelling agent | Quantity | Dosage Form |
|---|---|---|
| **Carbopol-934** | 1% | Emulgel |
| **Carbopol-940** | 1% | Emulgel |
| **HPMC-2910** | 2.5% | Emulgel |
| **HPMC** | 3.5% | Gel |
| **SodiumCMC** | 1% | Gel |

**Penetration Enhancers:**

In order to promote absorption of drugs, vehicles often include penetration enhancing ingredients that temporarily disrupts the skin barrier, fluidize the lipid channels between coenocytes, alter the partitioning of the drug into skin structures, or otherwise enhance delivery into skin[19]. So called penetration enhancers some of these materials given in table 4.

**Table 4:** Use of Penetration enhancer

| Penetration Enhancer | Quantity | Dosage Form |
|---|---|---|
| **Oleic acid** | 1% | Gel |
| **Lecithine** | 5% | Gel |
| **Urea** | 10% | Gel |
| **Isopropyl myristate** | 5% | Gel |
| **Linoleic acid** | 5% | Gel |
| **Clove oil** | 8% | Emulgel |
| **Menthol** | 5% | Emulgel |

**PROPERTIES OF PENETRATION ENHANCERS[20]:**

- 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[21]:

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 theproduct[22].

## PATHWAY OF TRANSDERMAL PERMEATION:

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[23].

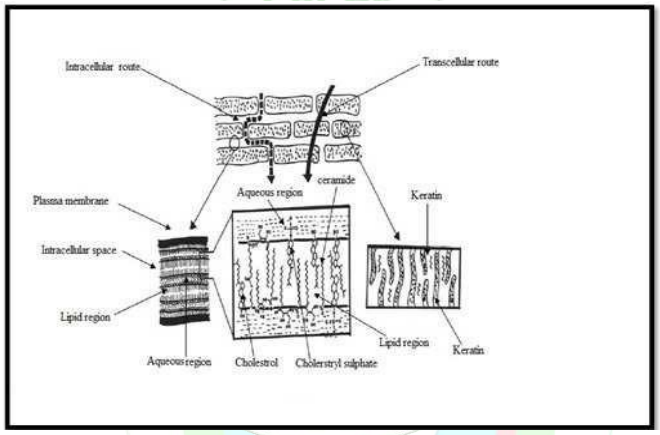



**Figure.2:** Mechanism of Penetration in to skin

## METHOD OF PREPARATION:

STEP1: Formulation of Emulsion either O/W or W/O
STEP2: Formulation of gel base
STEP3:Incorporation of emulsion into gel base with continuous stirring the flow chart of emulgel preparation is shown in figure 3.

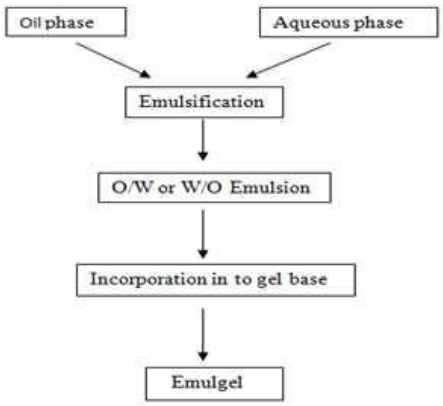



Figure.3: Flow chart of Emulgel formulation

**Table 5:** Marketed preparations

| Product name | Drug | Manufacturer |
|---|---|---|
| Voltarenemulgel | Diclofenac diethyl ammonium | Novartis Pharma |
| Miconaz-H-emulgel | Miconazole nitrate, Hydrocortisone | Medical union Pharmaceuticals |
| Excex gel | Clindamycin, Adapalene | Zee laboratories |
| Pernox gel | Benzoyl peroxide | Cosme Remedies Ltd |
| Lupigyl gel | Metronidazole | Lupin Pharma |
| Clinagel | Clindamycin phosphate Allantoin | Stiefel Pharma |
| Topinate gel | Clobetasol propionate | Systopic Pharma |
| Kojivit gel | Kojic acid, Dipalmitate Arbutin, Octinoxate | Micro Gratia Pharma |
| Acent gel | Aceclofenac, Methyl salicylate, Capsaicin | Intra labs India Pvt Ltd |
| Avindo gel | Azithromycin | Cosme Pharma laboratories |
| Cloben gel | Clotrimazole,Beclomethasone Dipropionate, Neomycin | Indoco Remedies |
| Nadicin cream | Nadifloxacin | Psychoremedies |
| Zorotene gel | Tezarotene | Elder Pharmaceuticals |

## CHARACTERIZATION OF EMULGELS[24]

**Physical Examination:**

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

**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.

**Spreading Coefficient:**

Spreadibility 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 isprovidedbyapulleyatoneend.Bythis a distance of 7.5 cm be noted. A shorter interval indicates betterspreadibility[41].

method, spreadibility 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.

**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 therheogramcorresponding 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 than calculated by using the following formula:

Extrudability=Applied weight to extrude emulgel from tube (in gm) / Area (in$cm^2$)

**SwellingIndex**:

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:

Swelling Index (SW) % = [(Wt – Wo) / Wo] ×

100. Where (SW) % = Equilibrium percent swelling, Wt = Weight of swollen emulgel after time t, Wo = Original weight of emulgel at zero time[42].

**Drug ContentDetermination:**

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 the same solvent. Concentration and drug content can be determined by using the same standard plot by putting the value of absorbance in the standard plot equation

Drug Content = (Concentration × Dilution Factor× Volume taken) × Conversion Factor.

**Skin Irritation Test (PatchTest):**

The preparation is applied on the properly shaven skin of rat and its adverse effect like change in color, change in skin morphology should be checked up to 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.

**In Vitro Release/PermeationStudies**:

In vitro release studies were carried out using Franz diffusion cell.

## REFERENCES


1. Kanikkannan N, Kandimalla K, Lamba SS, Singh M. Structure-activity relationship of chemical penetration enhan-cers in transdermal drug delivery. Current medicinal chemistry. 2000; 7(6):593-608.
2. Singh PB, Choudhury PK. Penetration enhancers for transdermal drug delivery of systemic agents. J Pharm Res. 2007; 6(2):44-50.
3. Kalia YN, Guy RH. Modeling transdermal drug release. Advanced drug delivery reviews. 2001; 48(2-3):159-72.
4. Ayub AC, Gomes AD, Lima MV, Vianna-Soares CD, Ferreira LA. Topical delivery of fluconazole: in vitro skin penetration and permeation using emulsions as dosage forms. Drug development and industrial pharmacy. 2007; 33(3):273-80.
5. Singla V, Saini S, Joshi B, Rana AC. Emulgel: A new platform for topical drug delivery. International Journal of Pharma and Bio Sciences. 2012 ; 3(1):485-98.
6. Subramanian N, Ghosal SK, Moulik SP. Enhanced in vitro percutaneous absorption and in vivo anti-inflammatory effect of a selective cyclooxygenase inhibitor using microemulsion. Drug development and industrial pharmacy. 2005; 31(4-5):405-16
7. Pathan IB, Setty CM. Chemical penetration enhancers for transdermal drug delivery systems. Tropical Journal of Pharmaceutical Research. 2009; 8(2).
8. Kshirsagar NA. Drug delivery systems. Indian Journal of Pharmacology. 2000; 32(4):S54-61.
9. Panwar A, Upadhyay N, Bairagi M, Gujar S, Darwhekar G, Jain D. Emulgel: a review. Asian J Pharm Life Sci. 2011; 2231:4423.
10. Sharma S. Topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membranes. Pharmaceutical reviews. 2008; 6(1).
11. Laithy HM. El shaboury KMF. The development of Cutina Lipogels and gel microemulsion for topical administration of fluconazole. Ame Pharm Sci. PharmSciTech. 2003; 3:10-25.
12. Kumar L, Verma R. In vitro evaluation of topical gel prepared using natural polymer. International journal of drug delivery. 2010 ;2(1).
13. Remington AR. The science and practice of pharmacy, Easton. PA, Mack publishing. 1995; 1:250-1.
14. Panchal B, Rathi S. Topical Emulgel: A Review on State of Art. Pharma Science Monitor. 2018; 9(1).
15. Panwar A, Upadhyay N, Bairagi M, Gujar S, Darwhekar G, Jain D. Emulgel: a review. Asian J Pharm Life Sci. 2011; 2231:4423.
16. Remington AR. The science and practice of pharmacy, Easton. PA, Mack publishing. 1995;1:250-1
17. Mohamed MI. Topical emulsion gel composition comprising diclofenac sodium. AAPS J. 2004; 6(3):1-7.
18. Mohamed MI. Optimization of chlorphenesin emulgel formulation. The AAPS journal. 2004; 6(3):81-7.
19. 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(5):250-3.
20. Korhonen M, Hellen L, Hirvonen J, Yliruusi J. Rheological properties of creams with four different surfactant combinations-effect of storage time and conditions. International journal of pharmaceutics. 2001; 221(1-2):187-96.
21. Stanos SP. Topical agents for the management of musculoskeletal pain. Journal of pain and symptom management. 2007; 33(3):342-55.
22. Jain A, Deveda P, Vyas N, Chauhan J, Khambete H, Jain S. Development of antifungal emulsion based gel for topical fungal infection (s). IJPRD. 2011;2(12):18-22.
23. Blumenthal D, Brunton Ll, Buxton Il, Parker Kl. Goodman & Gilman's manual of pharmacology and therapeutics.
24. Singla V, Saini S, Joshi B, Rana AC. Emulgel: A new platform for topical drug delivery. International Journal of Pharma and Bio Sciences. 2012; 3(1):485-98.