

EMULGEL: A COMBINATION OF EMULSION AND GEL***Patel Chirag J¹, Satyanand Tyagi², Anil Kumar Gupta³, Prabhakar Sharma⁴, Parimal M. Prajapati⁵, Mrugendra B. Potdar⁶**¹Editor-in-Chief, Tyagi Pharmacy Association (TPA) & Scientific Writer (Pharmacy), Patan, Gujarat, India.²President & Founder, Tyagi Pharmacy Association (TPA) & Scientific Writer (Pharmacy), Chattarpur, New Delhi, India.³Jyoti Vidyapeeth women's University, Jaipur, discipline of Pharmaceutical Science, Jaipur, Rajasthan, India.⁴GRKIST Pharmacy College, Barela, Kukrikheda, Jabalpur, Madhya Pradesh, India.⁵I. K. Patel College of Pharmaceutical Education and Research, Samarth Campus, Himmatnagar, District-Sabarkantha, Gujarat, India.⁶Smt. S. S. Patil College of Pharmacy, Chopda, Maharashtra, India.**ABSTRACT:**

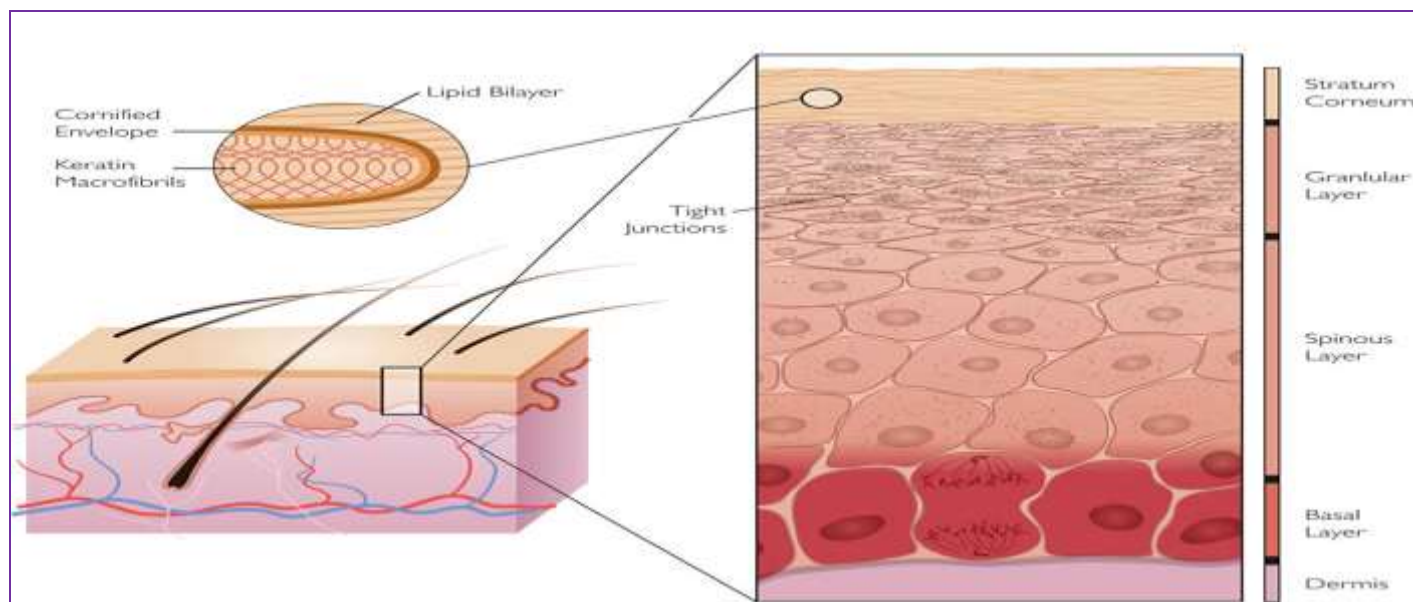
Dermatological products applied to skin are diverse in formulation and range in consistency from liquid to powder but the most popular products are semisolid preparation. Emulgels have emerged as one of the most interesting topical delivery system as it has dual release control system i.e. gel and emulsion. When gel and emulsion are used in combined form the dosage form are referred as emulgel. Emulgels 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 & 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 and antifungal drugs.

KEY WORDS: Emulgel, Skin, Gel, Emulsion, Hydrophobic Drugs**INTRODUCTION:**

Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorder. The topical drug delivery system is generally used where other routes (like oral, sublingual, rectal, parental) of drug administration fails or in local skin infection like fungal infection¹.

Human skin² (Fig. 1 & 2) 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 m². Whilst such a large and easily accessible organ apparently offers ideal and multiple sites to administer therapeutic agents for both local and systemic actions, human skin is a highly efficient self-repairing barrier designed to keep the insides in and the outside out³.

**Figure 1: Layer of human skin²**

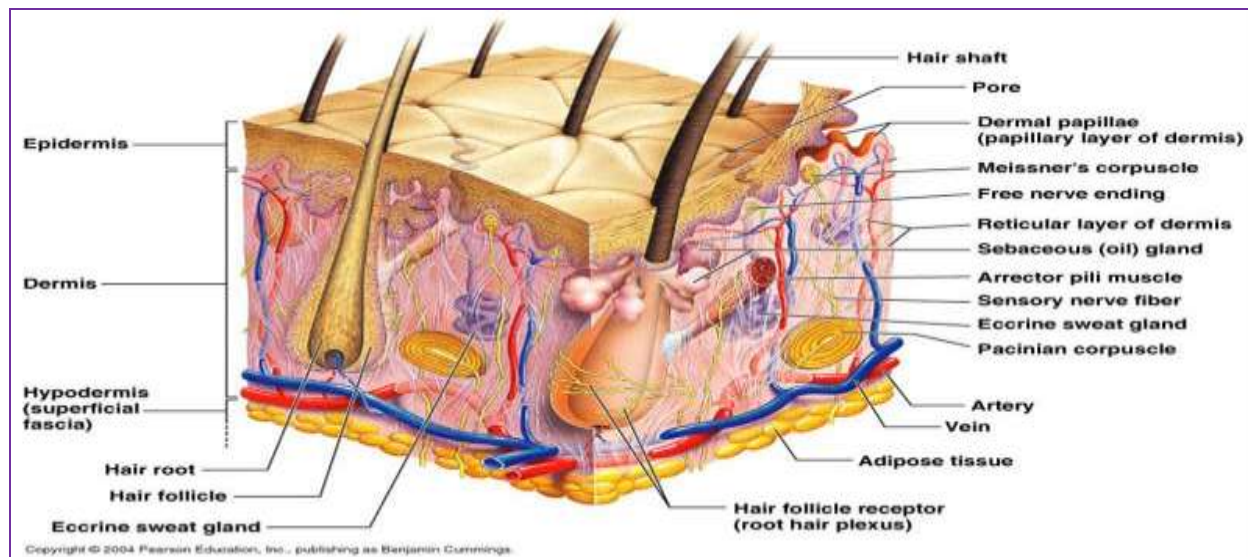


Figure 2: Anatomy of human skin²

Many widely used topical agents like ointments, creams, lotions have numerous disadvantages. They are usually very sticky causing uneasiness to the patient when applied. Moreover they also have less spreading coefficient and need to apply with rubbing. They also exhibit the problem of stability^{1,4}.

Due to all these factors, within the major group of semisolid preparations, the use of transparent gels has increased both in cosmetics and in pharmaceutical preparations. A gel is colloid that is typically 99% by weight liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelatin substance present. Gels 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. Gel formulations generally provide faster drug release compared with ointments and creams^{1,5}.

In spite of many advantages of gels a major limitation is their inability to delivery hydrophobic drugs. To overcome this limitation an emulsion based approach is being used so that a hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels. When gels and emulsions are used in combined form the dosage forms are referred as emulgels⁶.

In fact, the presence of a gelling agent in the water phase converts a classical emulsion into an emulgel. Direct (oil-in-water) system is used to entrap lipophilic drugs where as hydrophilic drugs are encapsulated in the reverse (water-in-oil) system. Emulsions possess a certain degree of elegance and are easily washed off whenever desired. They also have a high ability to penetrate the skin¹.

ADVANTAGES:

- 1. Incorporation 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. 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 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.
- 3. 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.
- 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. Controlled release:** Emulgels can be used to prolong the effect of drugs having shorter $t_{1/2}$.
- 6. No intensive sonication:** 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^{3,7}.

CONSTITUENTS USED IN EMULGEL PREPARATION

1. Aqueous Materials:

Aqueous Materials form the aqueous phase of the emulsion. Commonly used agents are water, alcohols.

2. Oils:

Oils form the oily phase of the emulsion.

For externally applied emulsions, mineral oils, either alone or combined with soft or hard paraffins, 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.

3. Emulsifiers:

Emulsifying agents are used both to promote emulsification at the time of manufacture and to control stability during a shelf life that can vary from days for extemporaneously prepared emulsions to months or years for commercial preparations. eg Polyethylene glycol stearate, Sorbitan monooleate (Span 80), Polyoxyethylene sorbitan monooleate (Tween 80), Stearic acid, Sodium stearate.

4. Gelling Agent:

These are the agents used to increase the consistency of any dosage form can also be used as thickening agent.

5. Permeation Enhancers:

These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability^{3,8-10}.

EMULGEL PREPARATION:

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 Tri ethanol amine (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 were 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^{3,6}.

MARKETED PREPARATIONS:

Some marketed preparation shown in table 1.

Table 1: Marketed Emulgel Preparations¹

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

CHARACTERIZATION OF EMULGELS:^{1, 6, 11-13}

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 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 gm. 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. 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:

$$\text{Swelling Index (SW) \%} = [(W_t - W_o) / W_o] \times 100$$

Where, (SW) % = Equilibrium percent swelling, W_t = Weight of swollen emulgel after time t , W_o = Original weight of emulgel at zero time.

5. 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:

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

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 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:

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

7. Ex-Vivo Bioadhesive Strength Measurement of Topical Emulgel

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 200mg/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 formula.

$$\text{Bioadhesive Strength} = \text{Weight required (in gm)} / \text{Area (cm}^2\text{)}$$

8. In Vitro Release/Permeation Studies

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

9. Skin Irritation Test (Patch Test)

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.

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.

CONCLUSION:

Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. 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 are other advantages of topical preparations. Since emulgel possesses an edge in terms of

spreadibility, 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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