



A Emulgel Review: Topical Drug Delivery System

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ABSTRACT:

The Topical drug delivery system make local administration of the drug in the body through vaginal , ophthalmic, skin and rectal routes. The topical formulations mainly used in the skin disease intended for cosmetic or dermatological application . Emulgel is used to treat in osteoarthritis ,acute and chronic pain, migration, misery, colic other conditions and injuries .The drug may be administered for systemic inflammatory response syndrome. The topical drug prepration can be formulated in following physico-chemical properties as solid, semisolid or liquid .These drug also known as hydrophobic drugs .Gel and emulsion are used in the combination is called as emulgel. Emulgel is an emulsion is gelled are by mixing it with gelling agent.The prepared emulgel for various parameter like pH, appearance, spreadability, viscosity, globule size, greaseless, shelf life. Emulgel are used in the various delivery of the analgesic ,anti-inflammatory anti-fungal, anti-acne drugs.[1][12]

KEYWORDS:

Topical Drug Delivery, Emulgel, Gel, Emulsion, Hydrophobic drug, gelling agent, Binary control release.

INTRODUCTION:

A topical drug delivery system is a medication that is applied to a particular place on or in the body. Most often topical administration means application to body surfaces such system is generally used in the local skin infection like fungal infection. A topical drug delivery system is medication is an attractive route for local and systemic treatment. Topical medication can be defined as the application of a drug containing formulation to the skin to treat cutaneous disorder. The main advantages of topical drug delivery system is diversion first pass metabolism.[25]

The topical drug can be administered in various route to human body namely oral, sublingual, rectal, parental etc. The mostly drug product available in large number skin as liquids, powders. In most popularly used in semisolid preparation in topically. Gels are prepared using aqueous and hydro- alcoholic liquids. Combined with colloidal solid particles. The many formulations available in different forms like solid through semisolid to liquid. These gels and emulsions are used in the combination is called as emulgel. Both phases are used in preparation water-in-oil and oil-in-water. Emulsion are easily washable and gracefulness properties. The emulgels preparation of dermatological use have several beneficial properties such as being thixotropic, smoothness, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, transparent and pleasing appearance.[3][8]

The molecules penetrate the skin by three route system: stratum corneum, sweat ducts or sebaceous follicle. The surface of stratum corneum presence in the skin in drug absorption by more than 99%. In the emulgel presence of gelling agents in water phase. The pH of skin various from 4.7 to 5.75.[11]

Topical Drug Delivery System:

Topical drug delivery system there are two types of topical drug delivery products, externally and internally used topicals for local activity. Main benefit of topical drug delivery system are avoided first pass metabolism, avoided gastrointestinal incompatibilities, specific site selective, improving patients compliance, possible and self-medication, and drugs with short shelf-life and narrow therapeutic index are also subjected to be used, facility is utilized to easily terminate medicines whenever required. Move across the skin membrane is obviously a complex process and challenge in analysis. Factors affecting the topical drug delivery system can be physiological factors e.g. thickness, hydration, inflammation and pH of skin, lipid content, densities of hair follicles and sweat glands, blood flow etc., and physico-chemical factors like partition coefficient, molecular weight, degree of ionization, effect of vehicle etc.[15] [2]

Classification of topical drug delivery systems:

1. **Solid preparation:** Topical Powders, Plasters Ointments, poultics.
2. **Semi solid preparation:** Creams, Poultrices, Gels, Pastes, ointment.
3. **Liquid preparation:** Liniment, Lotions, solution, tinctures, Emulsions, Suspensions, Paints.
4. **Miscellaneous preparation:** Transdermal drug delivery systems, Tapes and Gauzes, Rubbing alcohols, Liquid cleanser, and Topical aerosol.

Factors affecting topical absorption of drug :

Physiological factors

1. Thickness of skin.
2. Lipid content.
3. Density of hair follicles.
4. Density of sweat glands.
5. pH of skin.
6. Blood flow.
7. Skin hydration.
8. Inflammation of skin.

Physicochemical factors

1. Partition coefficient.
2. Molecular weight (<400 Dalton).
3. Degree of ionisation.
4. Effect of vehicles.[9]

Physiology of skin:

Most of the topical preparation are meant to applied to the skin. So basic knowledge of the skin and its physiology function are very important for designing topical drugs.[6]

The skin can be considered to have four distinct layers of tissue:

- Non-viable epidermis:
- Viable epidermis:
- Dermis:
- Subcutaneous connective tissue :

1)Non- viable epidermis:

It is the outer layer of skin. Thickness of cell is 10-20 and 34-44 μ m long and 25-36 μ m wide.

2)viable epidermis:

It between stratum corneum and dermis with 10-50 μ m thick.

3)Dermis;

It is called as viable dermis. Thickness range 2000-3000 μ m.

4)subcutaneous connective tissue:

It is consider true connective tissue with loose texture, fibrous connective tissue, blood and lymph vessels

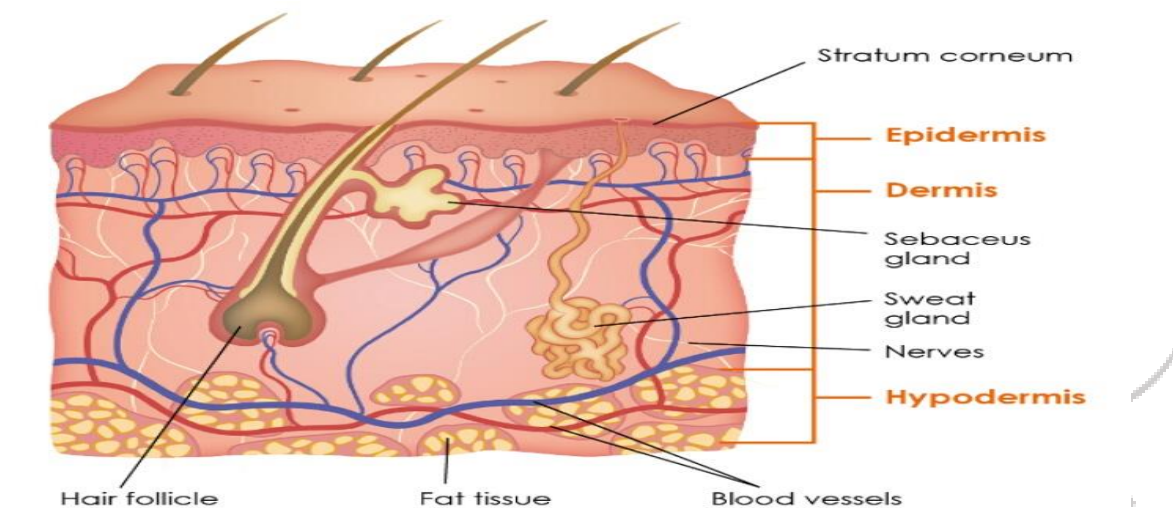


Fig: Physiology of skin

Factors to be considered when choosing a topical preparation:

1. Infuriation or sensitization potential. Generally, ointments and water with oils creams are less irritating, while gels are infuriating. Ointments do not contain preservatives or emulsifiers if allergy to these agents is a concern. [7]
2. Match the type of preparation with the type of lesions.
3. Match the type of preparation with the site. (e. g., gel or lotion for hairy areas)[20]

Different Method to Enhance Drug Penetration and Absorption :

1. Chemical enhancement
2. Biochemical enhancement
3. physical enhancement
4. Supersaturation enhancement [5]

Advantages :

- Hydrophobic drugs can be easily incorporated into gels using d/o/w emulsions.
- Better stability.
- No intensive sonication.
- Avoid first pass metabolism.
- More selective to a specific site.
- Avoid gastrointestinal incompatibility.
- Improving patient compliance.
- Suitable for self medication.
- Providing utilization of drug with short biological half life and narrow therapeutic window.
- Ability to easily terminate medication.
- Offer targeted drug delivery.
- Easy to formulate and cost effective preparation.
- Better loading capacity.
- Controlled release.
- No intensive sonication.
- Convenient and easy to apply.[19]

Disadvantages:

- Skin infuriation .
- The possibility of allergenic reaction.
- The poor permeability of some drug through the skin.
- Drug of large particle size not easy to absorb through the skin.
- The occurrence of the bubble during formulation of emulgel.[17][19]

Important Constituents of Emulgel Preparation :**1. Aqueous Material:**

This forms the aqueous phase of the emulsion. For example: commonly used agent- water, alcohols.

2. Oils:

These agents form the oily phase if the emulsion. Commonly used oils in oral preparations are non-biodegradable mineral and castor oils that provide a laxative effect, and fish liver oils or various fixed oils of vegetable origin (e.g., arachis, cottonseed, and maize oils) as nutritional supplements. [22]

3. Emulsifiers:

Emulsifiers used for preparation of emulsion. Some example: Polyethylene glycol 4031 stearate, Sorbitan monooleate (Span 80), Polyoxyethylene sorbitan monooleate (Tween 80), Stearic acid, Sodium stearate.[16]

4. Gelling Agent:

Gelling 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.

6.pH adjusting agent:

EMULGEL PREPARATION:

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). [23]

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 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.[14]

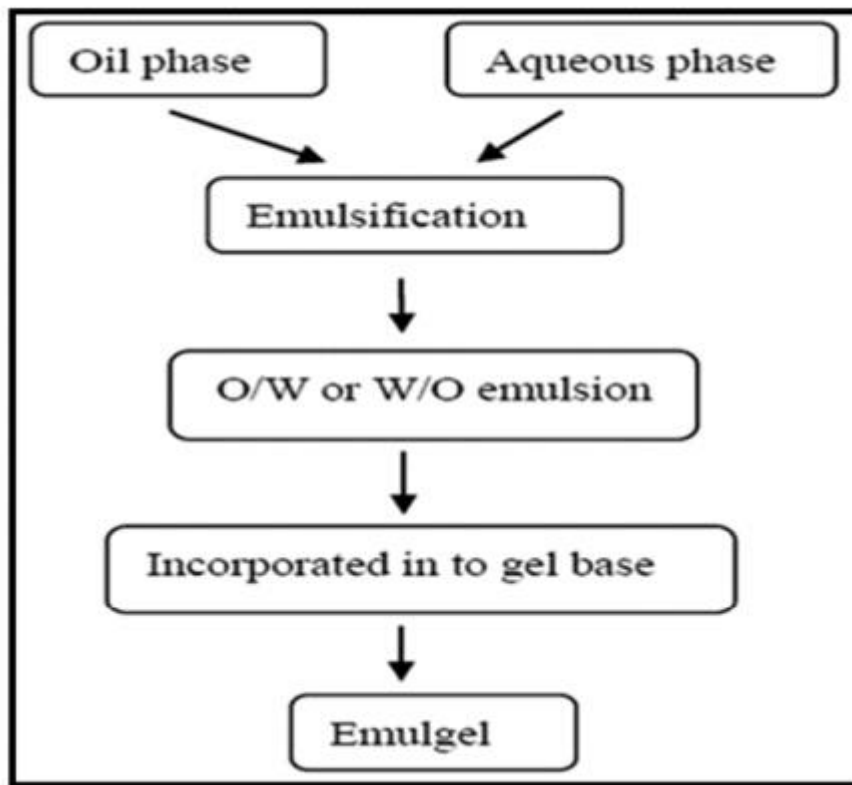


Fig: Flow chart of emulgel preparation.

CHARACTERIZATION OF GELLIFIED EMULSION :

Physical appearance:

The colour, homogeneity, consistency and pH. The pH values of 1% aqueous solutions of the prepared Gellified Emulsion were measured by a pH meter (Digital pH meter).[19]

Spreadability:

Spreadability is checked by “slip” and “drag” character of emulgel. The 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. A ground glass slide is fixed on this block. An excess of emulgel 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 indicate better spreadability. Spreadability was calculated by using the formula, [24]

$$S = M.L/T$$

Where, S = spreadability,

M = Weight tied to upper slide,

L = Length of glass slides

T = Time taken to separate the slides completely from each other.

Extrudability study:

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 than calculated by using the following formula:[4]

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

Globule size and its distribution in emulgel:

Globule size and distribution was determined by Malvern zetasizer. A 1.0 gm sample was dissolved in purified water and agitated to get homogeneous dispersion. Sample was injected to photocell of zetasizer. Mean globule diameter and distribution was obtained. [18]

Rheological Study:

The viscosity of the different emulgel formulations is determined at 25°C using a cone and plate viscometer with spindle 52 and connected to a thermostatically controlled circulating water bath.

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: [20]

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

Where, (SW) % = Equilibrium percent swelling,

W_o = Original weight of emulgel at zero,

W_t = Weight of swollen emulgel after time t

Ex-vivo Bioadhesive strength measurement of topical emulgel:

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

Drug Content Determination:

Take 1 gm 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 standard plot equation.[1][23]

$$\text{Drug content} = (\text{Concentration} \times \text{Dilution factor} \times \text{Volume taken}) \times \text{Conversion factor}$$

In Vitro Release/Permeation Studies:

Franz diffusion cell (with effective diffusion area 3.14 cm² and 15.5 ml cell volume) was used for the drug release studies. Gellified Emulsion (200 mg) was 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 (pH 5.5) solution to solubilize the drug. The receptor chamber was stirred by magnetic stirrer. The samples (1.0 ml aliquots) were collected at suitable time interval. Samples were analyzed for drug content by UV visible spectrophotometer after appropriate dilutions. Cumulative corrections were made to obtain the total amount of drug release at each time interval. The cumulative amount of drug released across the egg membrane was determined as a function of time. [13]

Microbiological assay:

Ditch plate technique was used. It is a technique used for evaluation of bacteriostatic or fungistatic activity of a compound. It is mainly applied for semisolid formulations. Previously prepared Sabouraud's agar dried plates were used. Three grams of the Gellified Emulsion are placed in a ditch cut in the plate. Freshly prepared culture loops are streaked across the agar at a right angle from the ditch to the edge of the plate. After incubation for 18 to 24 hours at 25°C, the fungal growth was observed and the percentage inhibition was measured as follows. [24]

$$\% \text{ inhibition} = L2 / L1 \times 100$$

Where, L1 = total length of the streaked culture, and

L2 = length of inhibition.

Skin irritation test:

The preparation is applied on the properly shaven skin of rat and its adverse effect like change in colour, change in skin morphology should be checked up to 24 hrs. 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. [21]

Accelerated stability studies of Gellified Emulsion:

Stability studies were performed according to ICH guidelines. The formulations were stored in hot air oven at 37 ± 2°, 45 ± 2° and 60 ± 2° for a period of 3 months. The samples were analyzed for drug content every two weeks by UV-Visible spectrophotometer. Stability study was carried out by measuring the change in pH of gel at regular interval of time. [16]

CONCLUSION:

In the recent years, topical drug delivery will be used extensively due to 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 a loading hydrophobic drug in a water soluble gel bases.

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