

EMULGEL: AN EMERGING TOOL AND MAGNIFYING APPLICATION OF TOPICAL DRUG DELIVERY

Gaurav Ramesh Chale ^{1*}, A. S. Jeughale¹, K. B. Erande¹, Dr. S. R. Tambe³ and Dr. M. A. Tayde²

^{1*}Department of Pharmaceutical Quality Assurance, M.G.V.'S Pharmacy College, Panchavati, Nashik, India.

²Department of Pharmaceutical Chemistry, M.G.V.'S Pharmacy College, Panchavati, Nashik, India.

³Department of Pharmaceutical Chemistry, S.P.H. College of Pharmacy, Malegaon, Nashik, India.

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*Corresponding Author

Gaurav Ramesh Chale

*Department of
Pharmaceutical Quality
Assurance, M.G.V.'S
Pharmacy College,
Panchavati, Nashik, India.
gauravchale74401@gmail.com

ABSTRACT

Emulgel is topical drug delivery system used to treat pains caused by headache, cold, muscle aches, backaches and others conditions and injuries. The patients adherence to topical formulation is significant in relation to chronic skin diseases, like fungal infections, acne, and psoriasis. Emulgel is one of the recent and advanced technology in NDDS used topically having characteristics of dual control release i.e emulsion as well as gel.

KEYWORDS: Topical drug delivery, Skin diseases. Emulgel, Gelling agents.

INTRODUCTION

Emulgel topical dosage form means the combination of emulsion and gel. Several topical formulations are available in cream and other dermatological dosage forms. Emulgel are emulsion, either water in oil / oil in water type that are formulated in gel by mixing with gelling agent. Gel in emulsion proves better over creams and ointment as good application property 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 across the skin. Emulsions possess a some degree of

elegance and are easily washed off whenever desired and also have a high ability to penetrate the skin.

The dermatologicals^[2] in emulgels have several favourable characteristics like easy spreadability, emollient, easily removable, non-staining, water soluble, longer shelf life, bio-friendly, thixotropic, greaseless, transparent & pleasing appearance. There are three major steps involved during percutaneous absorption. First is Establishment of concentration gradient, it will cause the movement of drug across skin, second is partition coefficient across skin release drug from a vehicle, third is Diffusion coefficient drug diffusion across layer of skin. The major steps involved in percutaneous absorption include the establishment of a concentration gradient, which is a driving force for drug movement across the skin; release of drug from the vehicle is partition coefficient and drug diffusion across the layers of the skin that is diffusion coefficient. Preferable characteristics of topical drugs include low molecular mass is about 600 Daltons, adequate solubility in oil and water, and a high partition coefficient. Drug for topical formulation should have molecular mass (600 Dalton) water and oil solubility and high partition coefficient.

TYPES OF EMULGEL

Table no. 1: Classification of Topical drug delivery system.^[3]

SOLID PREPARATION	LIQUID PREPARATION	SEMISOLID PREPARATION	MISCELLANEOUS PREPARATION
Topical Powder Poultices Plaster	Lotion Liniment Paints Solution Emulsion Suspension	Ointment Cream Pastes Gel Suppository	Transdermal drug delivery system Tapes and Gauzes Rubbing Alcohols Liquid cleaner Topical aerosol

ADVANTAGES AND DISADVANTAGES

Advantages of Topical Drug Delivery Systems^[4]

1. Emulgel is used for avoidance of first pass metabolism.
2. Patients Convenient and easy to apply.
3. Easily terminate the medications, when needed.
4. Deliver drug more selectively to a specific site.
5. Avoidance of gastro-intestinal incompatibility.
6. Providing utilization of drugs with short biological half-life, narrow therapeutic window.
7. Improve patient compliance.

8. Provide suitability for self-medication
9. The Avoidance of the risks and inconveniences of intravenous therapy and of varied conditions of absorption like, presence of enzymes, pH changes, gastric emptying time.

Disadvantages of Topical Drug Delivery Systems^[4]

1. Poor permeability of some drugs through the skin.
2. Drugs of larger particle size are not easy to absorb through the skin.
3. Skin irritation on contact dermatitis may occur due to the drug or excipients.

RATIONALE OF EMULGEL TOPICAL DELIVERY SYSTEM

In the pharmaceutical industry number of medicated product is applied to the skin or mucous membrane. There are various topical/ dermatological product available in market which applied an skin. Such products referred as topical or as dermatological products. Many widely used topical agents like creams, ointments, lotions have many disadvantages. They are sticky in nature and causing uneasiness to the patient when applied, It have lesser spreading coefficient so applied by rubbing and thair are also exhibit the problem of stability. Because to all these factors within the major group of semisolid preparations, use of transparent gels has expanded both pharmaceutical preparations and in cosmetics. Topical delivery system as a cream, ointment, lotion have many disadvantages like sticky in nature, less spreadability property, less stability. So to overcome this limitation on an emulsion based approach is used so that even a hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels as a emulgel.^[5]

Physiology of Skin

Many topical preparation are applied on skin and consideration of such so a basic Physiology of the skin and its function are very important for designing and formulations topical dosage form. The skin of an average adult body covers the surface area approximately 2m^2 and receives about a one-third of the blood circulating through the body. An the average human skin surface is known to contain, the 200-300 sweat ducts on every square centimetre of the skin and average 40-70 hair follicles.

Non-viable epidermis

The Stratum corneum is the outermost layer of skin is stratum corneum and is actual physical barrier to the most substance that comes in contact with the skin. Stratum corneum is of 10 to 20 cell layer thick over the most of the body. Each cell is flat, 25-36 μm wide, plate-like

structure-34-44 μm long, 0.5 to 0.20 μm thick with a surface area of 750 to 1200 μm stocked up to each other in brick-like fashion. Stratum corneum consists of lipid (5-15%) including, cholesterol sulphate, phospholipids and a 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 of thickness ranging from 50-100 μm . The structures of cells in the viable epidermis are physicochemically similar to the other living tissues. The density of this region is not much to different than water. The water content is of about 90%.

Dermis

Just beneath of viable epidermis is the dermis. It is a structural fibrin and very few cells are of like it can be found histological in normal tissue. Dermis thickness ranges from 2000 to 3000 micrometer.

Subcutaneous connective tissue

The skin has subcutaneous tissue or hypodermis is not actually considered true part of the structured connective tissue which is composed of loose textured, fibrous connective tissue containing blood and lymph vessels, white secretory pores of the sweat gland and cutaneous nerves.

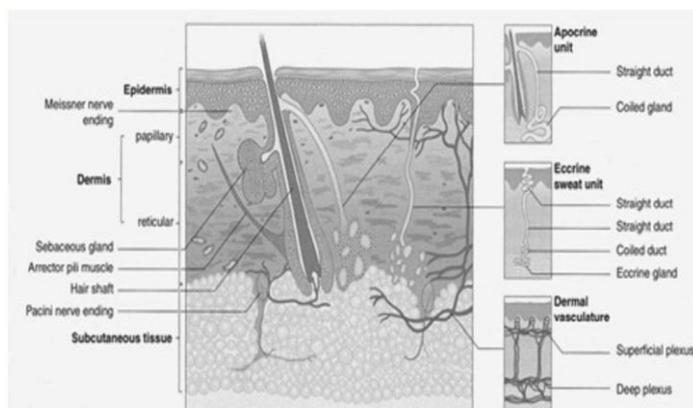


Fig. 2: Skin Physiology.^[6]

FORMULATION OF EMULGEL^[2]**Vehicle****Properties of Vehicle**

1. Efficiently deposit the drug on the skin with even distribution.
2. Release the drug so it can migrate freely to the site of action.
3. Deliver the drug to the target site.
4. Sustain a therapeutic drug level in the target tissue for a sufficient duration to provide a pharmacologic effect.
5. Appropriately formulated for the anatomical site to be treated.
6. Cosmetically acceptable to the patient.
7. Due to the efficiency of the epidermal barrier, the amount of topical drug that gets through the stratum corneum is generally low. The Rate and extent of absorption vary depending on characteristics of the vehicle but is also influenced by the active agent itself.

Aqueous Material

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

Oils: 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 sensory and occlusive characteristics. Widely used oils in the oral preparations are non-biodegradable mineral and castor oils that provide a local laxative effect.

Emulsifiers

The agent used both to promote emulsification at the time of manufacture and to control stability during the shelf life that can vary from days for extemporaneously prepared emulsions to months or years for commercial preparations e.g., Sorbitan mono-oleate (Span 80), Polyethylene glycol 40 stearate Polyoxyethylene sorbitan monooleate (Tween80), Stearic acid and Sodium stearate.

Gelling Agent: The agents used to increase the consistency of any dosage form can also be used as thickening agent. 1% HPMC-2910, Carbopol-940.

Penetration Enhancers

In order to promote absorption of drugs, vehicles often include penetration enhancing ingredients for that temporarily disrupts the skin barrier, fluidize the lipid channels between coenocytes, alter the partitioning of the drug into skin structures, or otherwise to enhance delivery into skin. E.g, Menthol 5%, Clove oil 8%.



Fig. 1: An Emulgel Marketed Product.

METHOD OF PREPARATION FOR EMULGEL^[7]

It is simple and cost effective method of preparation that including three steps; first the preparation of oil in water or water in oil emulsion where the drug is incorporated as per formulation requirement then second step is to formulate the gel base and finally the addition of emulsion to gel in continuous stirring to form emulgel . in detail for the formulation of emulsion and aqueous phase is prepared by taking the purified water to which the soluble ingredient are added and heated up to 70°C including emulsifying agent as tweens and then the oil phase was prepared by dissolving the surfactant such as spans is also heated to same temperature with the addition of hydrophobic drug. The gel phase is prepared by dispersing the polymer in to purified water with constant stirring at a moderate speed and then the pH are adjusted to 6 to 6.5 as per the requirement of the polymer. For example pH of gel with carbopol is adjusted by Triethanolamine (TEA). Preservatives 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. Now the emulsion is added to the gel base in ratio 1:1 to obtain the emulgel.

Evaluation of Emulgel

Appearance^[8]

The prepared Emulgel formulations were visually inspected for colour, appearance and homogeneity.

pH

pH is one of the most important parameters involved in the evaluation of Emulgels. The pH values has an effect on the balance of the ionized and unionized form of the drug, and ionized and unionized forms of the drug would show different penetration behavior. The pH of all the formulations was evaluated using a pH meter and the pH was measured at room temperature.

Spreadability

Spreadability of the Emulgel was determined 48 hours after preparation of the Emulgel by using the wooden block and the glass slide apparatus. 1 g of the prepared Emulgel was placed between two 10 × 10 cm glass plates(125g each). A weight of 25g was placed it in a pan and the time required for the upper glass plate to completely separate from the fixed glass plate was recorded. The spreadability was then calculated from the equation as unde $S = \frac{m \times L}{T}$

T

Where S = Spreadability

L = length of the glass plate used

M = weight tied to the upper slide

T = time taken to separate slide completely from each other. Spreadability was measured in terms of g.cm/sec.

Extrudability

The Extrudability method was adopted for evaluating gel formulation for a extrudability was based upon quantity in percentage of gel extruded from lacquered aluminum collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of gel in a 10 seconds. More quantity extruded better was extrudability. The measurement of extrudability of each formulation was in triplicate and a average values were presented. The Extrudability calculated by using the following formula:

Extrudability = Applied weight of to extrude gel from tube (in gm) / Area (in cm²)

Swelling Index

Emulgel of known weight 1 gram was wrapped with Aluminium Foil (pricked with a pin to make holes) and placed in phosphate buffer pH 6.8 for 6 hours. After 6 hours, the gels were scrapped and the wet weight of the swollen gel was determined by first blotting the gels with filter paper to remove absorbed water on surface and then it was immediately weighed on a

electronic balance. Then weight of the swollen gels was determined using an electronic balance. Swelling index was calculated using the following formula,

$$Sw = (Wt - Wo) / Wo \times 100$$

Where, Sw = Percentage of swelling of Emulgel

Wt = Weight (g) of the gels at time t, Wo = Initial weight (g) of the Emulgel.

Drug Content Uniformity

The content uniformity of Drug from the various Emulgel formulations was determined by weighing 1 g of the Emulgel formulation and extracting the drug from it using suitable medium and finally determining the amount of Drug present. 1 g of the Emulgel was transferred to a 100 ml volumetric flask and to this about 70 ml of phosphate buffer pH 6.8 was added. This mixture was then shaken for about 15 mins so as to completely extract the drug from the Emulgel. The volume was finally made up to 100 ml using Phosphate Buffer pH 7.4. The solution was filtered and then the dilution was made taking 1 ml of the filtrate and diluting to 25 ml (dilution Factor 25). The absorbance of this solution was measured at 363 nm. Phosphate Buffer pH 7.4 was used as blank. The drug content was calculated from the following formula:

$$\text{Content uniformity} = \frac{\text{conc in mcg/ml} \times 100 \times \text{Dilution Factor}}{1000}$$

The percentage content uniformity is calculated by :

$$\% \text{ Content Uniformity} = \frac{\text{Practical Yield}}{\text{Theoretical yield}} \times 100$$

Theoretical yield.

In-Vitro Release Studies of Prepared

Emulgel Formulations

The Franz diffusion cell with effective^[9] diffusion area 3 cm² and 30ml cell volume. Cellophane membrane previously soaked in the respective dissolution medium overnight was used as the permeation membrane. 200 ml of Phosphate buffer pH 7.4 was placed in a beaker (receptor compartment). An accurately weighed quantity (1) of the formulated Emulgel was then uniformly spread on the cellophane membrane (donor compartment) and this membrane was tied to the diffusion tube (a hollow tube open on both sides). One side of the cellophane membrane was kept in contact with the medium Phosphate Buffer pH 7.4. The medium was constantly agitated using a magnetic stirrer and the temperature was maintained at a constant

of $37 \pm 1^\circ\text{C}$ throughout the operation. Samples of 10 ml volume were then withdrawn from the receptor compartment at intervals of 1 hour over a period of 8 hours and the amount withdrawn was replaced with fresh volume of the medium. The samples withdrawn were then analysed for the amount of Drug released by UV spectrophotometric method by measuring the absorbance of the samples at 363 nm against Phosphate Buffer pH 7.4 taken as blank.

Stability Studies^[8,9]

The Stability of the drug has been defined the ability of a particular formulation in a specific container to remain within its physical, chemical, toxicological and therapeutic specification. Stability studies were performed (8) on the optimal Formulation F9 b which was subjected to 3 different storage conditions: $5^\circ\text{C} \pm 2$, 45°C and room temperature at 75% RH for a period of 2 months.

CONCLUSION

Emulgels have proven as most convenient, better and effective delivery system. It provides gel like property due to its non-greasy nature and lacks oily bases therefore 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 and solves the bases such as petrolatum, bees wax or vegetable oils that themselves are hydrophobic in nature that do not allow the inclusion of a water or an aqueous phase.

Further problem such as creaming, phase separation associated with emulsion gets resolved and its stability improves. Emulgel loaded with specific drugs has been found effective in some topical disorders and it is emerging as potentially drug delivery system in area of dermatology.

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