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Review Article

A Brief Review On Emulgel

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ABSTRACT

Emulgel systems are currently attention to the pharmaceutical sectors because of their substantial potential to act as drug delivery vehicle by incorporating a broad range of drug molecules and higher stability compared to the other dosage form like cream, lotion, gel, etc. Emulsions are either available in an oil in water or water in oil type. These are prepared by the incorporation of the emulsion into the gel with constant stirring at a moderate speed. Incorporation of emulsion into a gel makes it a dual control release system, thereby, increasing its stability. It has better drug release if we compare to other topical drug delivery system. It is non-greasy because of the presence of gel phase which enhances patient compliance. Gels has a major limitation for the delivery of hydrophobic drugs, so to overcome this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic drug can enjoy the unique properties of gels. In recent years, these have also been a great interest in the use of novel polymers. These emulgels are having major advantages on vesicular drug delivery systems as well as on conventional systems in various aspects. Various permeation enhancers can enhance the effect; due to this emulgels can be used as better topical drug delivery systems over current drug delivery systems. The emulsion can be used for analgesics and antifungal drugs.

INTRODUCTION

Skin is the most readily accessible part of human body for topical administration; small molecules penetrate into the skin by three major routes: that is 1) stratum corneum 2) sweat ducts and 3) sebaceous follicle1. The topical drug delivery system is generally used where these systems of drug administration fails or in local skin infection mostly in the case of fungal infection. Topical drug delivery system can be defined as direct effects of drug containing medication to the skin to get localizing effect of drug or directly cure cutaneous disorders2. It has major advantage that it negotiating the first pass metabolism and also helps to avoid the risk and inconvenience of I.V. route therapy. These type of drug delivery system used for localized action on the body through vaginal, rectal, ophthalmic, and skin as topical

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routes. The topical drug delivery system such as emulgel is generally used where the other systems of drug administration fails to directly treat skin or cutaneous disorders such as fungal infections, acne, psoriasis, bullous pemphigoid etc. if the drug substance present in solution, Absorption of drug through the skin is enhanced. If lipid/water partition coefficient of drug substances has favorable and if it is a non electrolyte.3 Pharmaceutical formulation applied to the skin to produce local action and as such preparations are prepare to provide prolonged local contact with minimal systemic drug absorption. Mostly drugs like antifungal agent, antiseptics, and skin emollients are applied to the skin for their local action and also avoidance of first pass metabolism. The main advantage of topical drug delivery system, it also Avoid the risks and inconveniences of intravenous therapy. and of the diverse conditions ofabsorption like pH changes, presence of dissimilar enzymes, gastric emptying time are other advantages of topical preparations4. If we compared to the conventional pharmaceutical dosage form like creams, gel, ointments, they have faster drug release only the difficulty is it can not use for the hydrophobic drugs. So to overcome this problem emulgels are formulated and with this, even hydrophobic drugs can use without any problem. Emulgel is referred as a combined of gel and emulsion in one dosage form. It is mainly available in two type O/W and W/O. O/W system is used to entrap lipophilic drugs whereas hydrophilic drugs are encapsulated in the W/O system5. It has many advantages like thixotropic, non-staining, greaseless, easily spreadable, emollient, bio-friendly, pleasing appearance, easily removable, transparent and cosmetically acceptable, which also have a good skin penetration and long shelf- life6. The emulsion and gel preparations have their individual properties but the gels show some limitations as hydrophobic drug delivery. This limitation is overcomes by the emulgel. By the use of gelling agent good emulsion can be converted in to emulgel7.

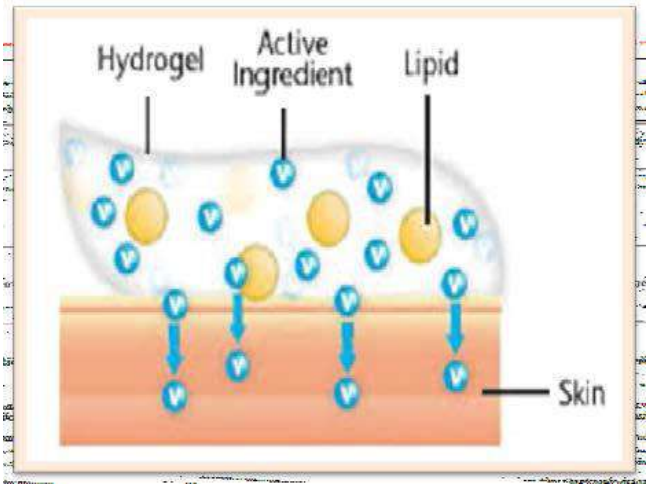

Figure 1: Emulgel Structure8

Topical gels are semisolid systems in which a liquid phase is constrained within a 3D polymeric matrix of natural or synthetic gum. A gel is colloid that is typically 99% by weight.9 Topical preparations can be categorized into two forms that are external and internal preparations. The external products are applied by spreading and the internal products are applied orally, vaginally or rectally10. Topical preparation can be classified by their uniformity, which is solid preparation, liquid preparation, semi-solid preparation and miscellaneous preparation etc11. Factors can affect the absorption of the drugs through every route. Some factors like skin pH, partition coefficient, molecular weight, molecular size as well as skin thickness. Topical drug delivery system has several advantages like it avoids first pass metabolism and gastrointestinal incompatibility. Topical preparations are applied on the skin surface. It penetrates into the skin and gives result at right site. The skin is the largest sense organ in human body which consists of approximately 2 m2 of total surface area and pH is 4.0-5.6. It consist of 4 layers; non-viable epidermis, viable epidermis, viable dermis and subcutaneous connective tissue.

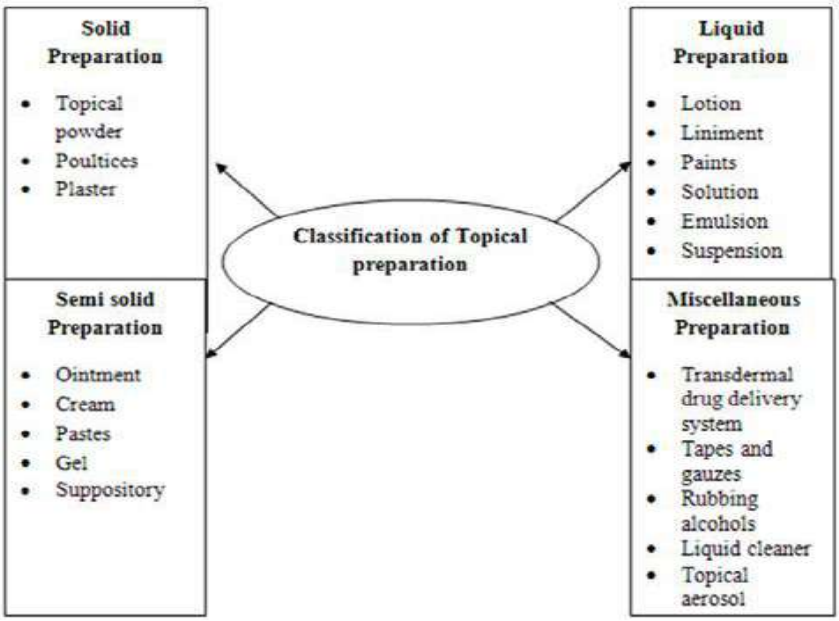

Figure 2: Classification of Topical Preparation12

a. Non- viable epidermis [stratum corneum]:

It is the outer layer of skin, 10-20 cells thick. The cells are 34- 44 µm long, 25- 36 µm wide, 0.5-0.20 µm thick with surface area of 750- 1200 µm.

b. Viable epidermis:

It lies between stratum corneum and dermis with 10 - 50 µm thickness. The tonofibrils helps it for joining the cells.

c. Dermis:

It is seen under the viable epidermis, and it is a structural fibrin. Thickness of the dermis ranges from 2000 – 3000 µm and contains loose connective tissue.

d. Subcutaneous connective tissue:

It is considered as a true connective tissue with loose texture, fibrous connective tissue, blood and lymph vessels.

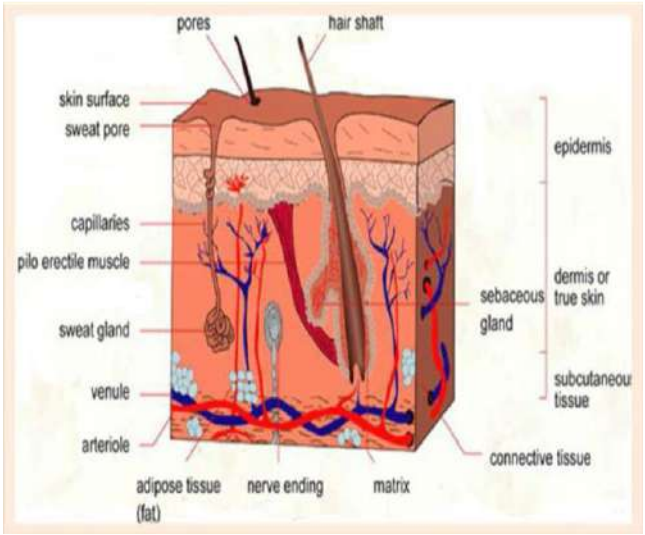

Figure 3: Structure of Skin13

Three mechanisms involved in drug absorption are- transcellular, intercellular, and follicular. The drugs penetrate the stratum corneum by passive diffusion14 in which dissolution and diffusion are rate limiting steps. It has three major functions i.e. epidermal formulation, endodermal formulation and transdermal formulation. In which Transcellular mechanism is the shortest and direct

route and intercellular mechanism is the common route. The follicular mechanism is through hair follicles and sweat glands15. Penetration of the drugs can be enhanced by some chemical like; (surfactant, water, solvents, etc.), physical (stripping, iontophoresis, ultrasound, etc.), biochemical (peptides and metabolic inhibitors) and super saturation enhancement16.

Advantages of Emulgel17:

- Better stability
- Incorporation of hydrophobic drugs
- Better loading capacity
- Controlled release
- No intensive sonication
- Avoiding first pass metabolism
- Avoiding gastrointestinal incompatibility
- More selective for a specific site
- Improved patient compliance
- Convenient and easy to apply

Disadvantages of Emulgel18:

- The poor permeability of some drugs through the skin
- Skin irritation on contact dermatitis
- The possibility of allergenic reactions
- Drugs of large particle size are not easy to absorb through the skin
- The occurrence of the bubble during formulation of emulgel

Ideal Properties of Drug to Formulate As Emulgel19

- Drug dose should be low i.e. less than 10mg.
- Molecular weight of drug should be 400 Dalton or less.
- Half life of drug 10 hr or less.
- Partition coefficient i.e. Log p (Octanol-water) between 0.4-0.8
- Having a skin permeability coefficient more than 0.5 x 10 -3cm/hr
- Oral bioavailability and therapeutic index should be low.
- Drug should be non irritating and non-sensitizer having a less polarity.

Important Constituents of Emulgel Preparation:

1. Aqueous Material:20

It mainly consists of the ingredients to formulate the aqueous phase. Commonly aqueous materials are used in preparation is water, alcohol, propylene glycol etc.

2. Oils:21,22

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

3. Emulsifiers:

These agents are required to promote the emulsification at the time of formulation preparation and to provide long term stability to the formulation. E.g. Polyethylene glycol 40 stearate23, Sorbitan monooleate (Span 80)24 Polyoxyethylene sorbitan monooleate (Tween 80)25, Stearic acid26, Sodium stearate27.

4. Gelling agent:28, 29

These agents are used to formulate the gel phase of the emulgel and also use as a thickening agent. It also increases the consistency of the preparation.

5. Permeation enhancer:

These are the agents used for the enhancement of the permeation of the drug by modifying the skin membrane characteristics by interacting with the skin membrane.30

Table 1: Quantity of Different Gelling Agents Used In Preparation of Gel and Emulgel31 Gelling agent

Table 1: Quantity of Different Gelling Agents Used In Preparation of Gel and Emulgel31 Gelling agent	Quantity	Dosage form
Carbopol-934	0.5%-2%	Emulgel
Carbopol-940	0.5%-2%	Emulgel
HPMC-2910	2.5%	Emulgel
HPMC	3.5%	Gel

EMULGEL PREPARATION:

The gel preparation in formulations were prepared by dispersing Carbopol 934 in water with constant stirring at a moderate speed and by the addition of Carbopol 940 in purified water with constant stirring at a moderate speed and the pH is adjusted to 6 to 6.5 using Triethanolamine (TEA). The oil phase of the emulsion was prepared by dissolving Span 20 in oil and the aqueous phase was prepared by dissolving Tween 20 in purified water. Methyl paraben and Propyl paraben was dissolved in a propylene glycol, whereas drug was dissolved in ethanol. Both the solutions were mixed with the aqueous phase. Both the oily and aqueous phases were individually heated to 70° to 80°C then the oily phase were added to aqueous phase with continuous stirring until it cooled to room temperature. And add Glutaraldehyde in during of mixing of gel and emulsion in ratio 1:1 to obtain a final emulgel.32 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.33

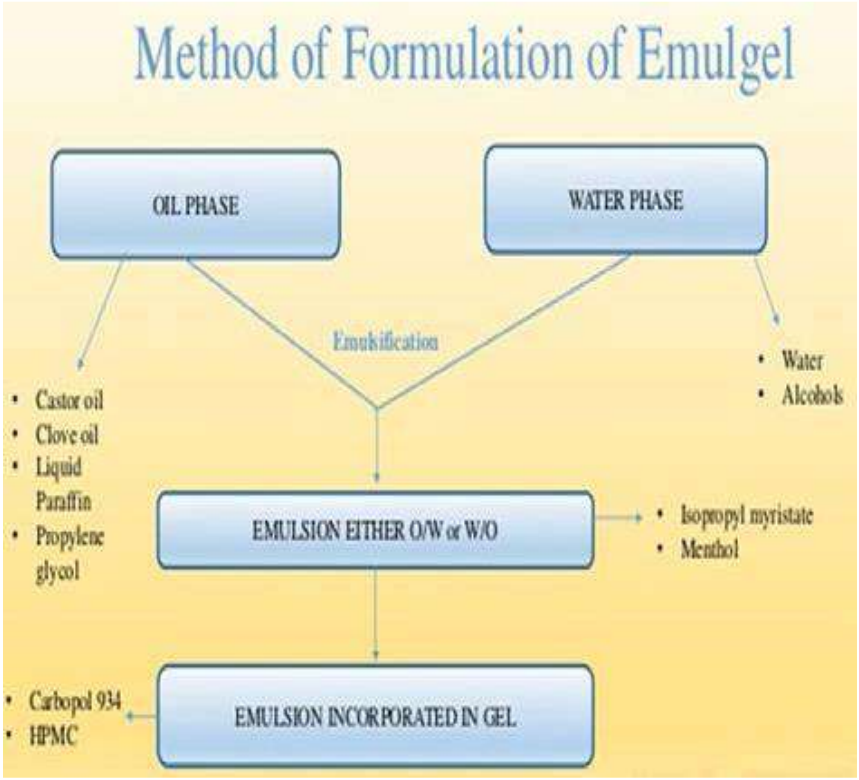

Figure 4: Method of Formulation of Emulgel34

EVALUATION TECHNIQUES:

Evaluation of emulgel:

Physical examinations:

Physical examinations like Color, homogeneity, consistency, texture, etc.

Dilution test35:

This can be done by 50 to 100 times aqueous dilution of emulgel by adding continuous phase and visually checked for phase separation and clarity.

pH:

This can be done by use of 1% solution in water of emulgel subjected to measure pH by the digital pH meter. pH meter electrode was washed by distilled water and then dipped into the formulation to measure pH and this process was repeated 3 times.

Photo microscopy36:

Emulgel was viewed under light microscope to study the globular structure in gel base. The emulgel was suitably diluted, mounted on glass slide and viewed by light microscope under magnification of 40x.

Spreadability measurement:

0.5 gm of emulgel is placed on a clean and dry glass slide and a made circle around it. Then a second clean slide is placed over it and a predetermined weight is put on it for a specific time period. The increase in diameter is noted as gm-cm/sec.37

Measurement of viscosity:

The viscosity of the formulated batches was determined using a Brookfield Viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, USA) with spindle 63. The formulation (Emulsion) was added to the beaker and was allowed to settle down for 30 minutes at the temperature (25±1°C) before the measurement was taken. Spindle was lowered perpendicularly into the centre of emulgel take careful that spindle does not touch to the bottom of the jar and rotated at speed 50 rpm for 10 min. The viscosity reading was noted.

Fourier transforms infrared spectroscopy (FTIR):

The aim of this investigation was to identify a stable storage condition for the drug in solid state and identification of the excipients for formulation.

Globule size and its distribution in emulgel:

It is determined by Malvern zeta sizer. 1g of sample was dissolved in purified water and agitated to get homogeneous dispersion. The sample was injected to photocell of zeta sizer. By this system particle and molecular size, particle charge, mean globule diameter, and particle concentration is obtained.

Swelling index:

1gm of prepared formulation (Emulgel) was taken on porous aluminum foil and was dispersed in 10ml of 0.1 N NaOH solutions. A sample was removed on various time intervals and notes the weight till no further change in weight:

Swelling Index (SW) % = [Wt-Wo]/Wo]*100

Where, (SW) % = Percentage swelling,

Wo = Original weight of emulgel

Wt = Weight of bloat emulgel at time t.

Measurement of bio adhesive strength:

Accurately 1 gm of formulation was applied between a slide containing rat's hairless skin pieces. Putting weight on single glass slide and created some pressure to remove it from two slides. Adding extra weight is considered as 200mg/min to until it detachment of the skin surface. Required weight to detach the emulgel from skin will give bio adhesive strength. It can be calculated by using this following formula:

Bio adhesive Strength = W / A

Where, W= Weight required (in gms) and A=Area (cm2)

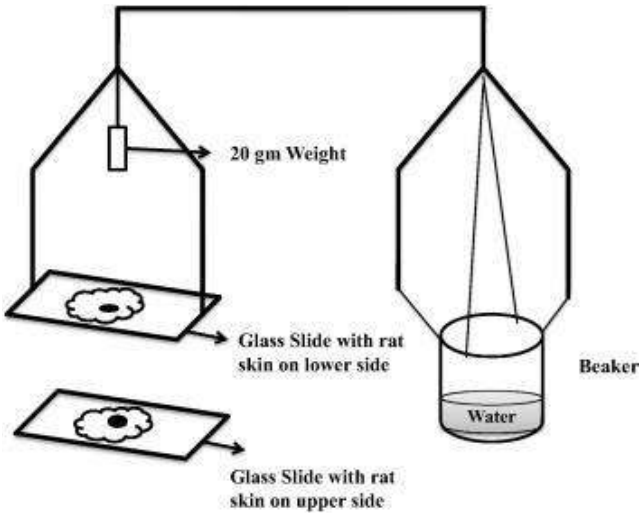

Figure 5: Schematic Diagram Illustrating Bio adhesion Measurement by the Modified Balance Method38

Accelerated stability studies:

Described in ICH guidelines, the emulsion is kept in oven at 37±2°C, 45±2°C and 60±2°C differently for 3 months. Drug content is examined in every 2 week by an analytical method. Stability measurement is based on change in pH of gel.36

Microbiological assay:

In this experiment ditch plate technique was used. It is a technique used for evaluation of bacteriostatic activity of a compound. It is mainly applied for semisolid formulations. Previously prepared Sabouraud's agar dried plate was used. 3gm of the jellified emulsion are placed in a ditch cut in plate. Freshly prepared culture loops are streaked across the agar at a right angle from the ditch to the edge of the plate.

Skin irritation test:

Small amount of sample was taken on skin article then applied to each site (two sites per rabbit) by introduction under a double gauze layer to a skin area approximately 1" x 1" (2.54 x 2.54 cm2). The jellified Emulsion was applied on the skin of a rabbit. Animals were returned to their cages. After 24 hours exposure, the jellified emulsion will remove. The test sites were wiped with tap water to remove any remaining test article residue.39

Table 2: Some Marketed Emulgel Preparation40 Product Name	**Drug**	**Manufacturer**
VoltarenTM	Diclofenac Diethyl Ammonium	Novartis Pharma
Miconaz-H-emulgelTM	Miconazole Nitrate, Hydrocortisone	Medical Uniun Pharmaceutical
Diclomax EmulgelTM	Diclofenac Diethyl Amine	Torrent Pharma

CONCLUSION:

In the coming years, topical drug delivery system is extensively due to better patient compliance. It has a several advantages in which the main advantage is to avoidance first pass metabolism. Emulgel is one of the best solutions for the delivery of the hydrophobic drugs as it provides controlled release. Since Emulgel is helpful in nhancing spreadability, viscosity, adhesion, and extrusion, this novel drug delivery will become a popular formulation in future. Moreover, they will become a solution for loading hydrophobic drugs in a water soluble gel bases.

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