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A COMPREHENSIVE REVIEW ON EMULGEL: A NEW APPROACH FOR ENHANCED TOPICAL DRUG DELIVERY

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ABSTRACT

Emulgel is a new approach and recent technology of NDDS for topical drug transport having characteristics of dual controlled release i.e emulsion and gel Emulsion used for treating for muscle pain, headache, acne, psoriasis, rheumatoid arthritis. When emulsion and gel used in combination its known as Emulgel. Emulgel is transparent gel which is used in pharmaceutical and cosmetic product. Emulgel overcome the problem which is come in gel and emulsion. Gel is a new class of formulation, gel release drug faster in comparison of ointment, cream, lotion etc. Limitation of gel in the delivery of hydrophobic drug through the skin. Overcome the limitation on emulsion based approach is being used so that even a hydrophobic therapeutic moiety can exhibit the unique properties of gels. Emulgel is prepared by different polymers which act as an emulsifying agent and thickening agent because the gelling capacity of these polymers give rise to stable emulsions by decreasing interfacial and surface tension while at the same time increasing the viscosity of the aqueous phase. Emulgel are having major advantages on novel vesicular systems as well as on conventional systems considering various aspects. The emulgel provide several favourable properties for its dermatological use such as greaseless, thixotropic, easily spreadable, emollient, easily removable, non-staining, water soluble, longer shelf life, transparent, bio-friendly and pleasing appearance.

KEYWORDS: Emulgel, Emulsion based gel, Hydrophobic drugs, Topical drug delivery system, novel drug delivery.

INTRODUCTION

Topical drug administration is simplest and easiest route of localized drug delivery anywhere in the body by routes as ophthalmic, rectal, vaginal and skin. These are applied as wide spectrum of preparations in case of both cosmetic and dermatological, to the healthy or diseased skin. Topical drug delivery can be defined as the application of a drug containing formulation to the skin to treat cutaneous disorder directly. 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 a fungal infection. The main advantage of the 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, the presence of enzymes, gastric emptying time are another advantage of The topical drug delivery system is generally used where the others system of drug administration fails.

Topical drug delivery can be defined as the application of drug containing formulation to the skin to directly treat cutaneous disorders (e.g acne) or the cutaneous mainfestations of a general disease (e.g psoriasis) with the intent of confining the pharmacological or other effect of the drug to the surface of the skin or within the skin.

Topical drug delivery system include a large variety of pharmaceutical dosage form like semisolids, liquid preparation, sprays, and solid powders. Most widely used semisolid preparation for topical drug delivery includes gels, creams, and ointments.[1]

Emulsion

Emulsions are phases of two or more immiscible liquids. The one phase is dispersed into dispersed medium. Several types as oil in water (O/W), water in oil (W/O), oil in oil (O/O), micro-emulsions, double and multiple emulsions, mixed emulsions etc. for preparation and stability of emulsion the emulsifier is necessary. 3 Various factors could affect the process of emulsification, such as the nature of oil, emulsifier, the emulsifier concentration used, rpm, as well as, the temperature.[2]

Gels

Gels are constituted by entrapment of large amounts of aqueous or hydroalcoholic liquid in a network of colloidal solid particles, which may be inorganic or

organic polymers of natural or synthetic origin. The higher aqueous component permits greater dissolution of drugs, and permits easy migration of the drug as compared to the ointment or cream base. However, this makes gels poor vehicle for hydrophobic drugs. This limitation of gels can be overcome by making emulgel.[3]

Emulgel

Emulgel is prepared both in oil-in-water and water-in-oil type emulsion mixed with gel. oilin-water type is used for lipophilic drugs and water-in-oil type is used for hydrophobic drugs delivery. 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 emulgel have many advantages like thixotropic, greaseless, easily spreadable, easily removable, emollient, nonstaining, bio-friendly, pleasing appearance, transparent and cosmetically acceptable, which also have a good skin penetration and long shelf-life. The emulsion and gel preparations have their own properties. The use of transparent gels has expanded both in cosmetics and pharmaceutical preparations. But the gels show some limitations as hydrophobic drug delivery. This limitation is overcome by emulgel dosage form. i.e by the use of gelling agent classical emulsion can be converted in to emulgel.[4]

The emulsion also acts as controlled release drug delivery system in which drug particles entrapped in internal phase go through the external phase to the skin and slowly get absorbed. The drug reaches the external phase of the skin in a controlled manner through the internal phases which act as a reservoir of the drug. Gel captures small drug particles and provides its release in a controlled manner because of a cross-linked network.[5]

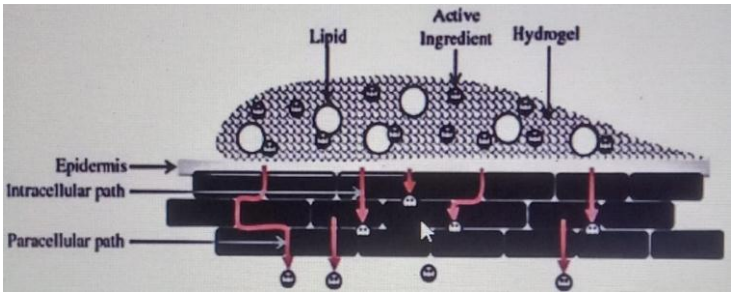

Fig. 1: Structure of Emulgel.

Types of Emulgels

Macroemulgel: These are most common type of emulgels in which the particle size of droplets of emulsion is more than 400 nm. They are visually opaque but the individual droplets can be easily observed in microscope.

Microemulgel: Micro-emulsion are transparent and thermodynamically stable as their droplet size range from 100 to 400 nm and they do not coalesce. Micro-emulsion are the composed of oil, surfactant, co-s surfactant, and water in particular ratios.

Nanoemulgel: When Nano-emulsion are the incorporated into gel it is called as Nano-emulgel Nanoemulsion are thermodynamically stable transparent dispersion of oil and water stabilized by an interfacial flim of surfactant and cosurfactant molecule having a globule size of less than 100 nm. Nano-emulsion formulation possess development transdermal and dermal delivery properties in vitro as well as invivo. Nano-emulsion have improved transdermal permeation of drug over the conventional topical formulation such as emulsion and gels.[6]

Ideal Properties of Emulgel

- Being greaseless.
- Easily spreadable.
- Easily removable.
- Emollient.
- Non-staining.
- Longer self-life, bio friendly.
- Pleasing appearance.[7]

Objectives

Fig. 2: Objectives of Emulgel.[8]

Advantages of Emulgel

1. Avoidance of first pass metabolism, and gastrointestinal incompatibility
2. More selective to a specific site.
3. Improve patient compliance.
4. Suitability for self-medication.
5. Hydrophobic drugs can be easily incorporated into gels using o/w 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.

6. 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 oily base.

7. 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.

8. 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.

9. Controlled release

Emulgels can be used to prolong the effect of drugs having shorter $t^{1}/_{2}$.

10. No intensive sonication

Production of vesicular molecules need 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.[9,10]

Disadvantage of Emulgel

1. Skin irritation on contact dermatitis.
2. The possibility of allergenic reactions.
3. The poor permeability of some drug through the skin.
4. Drug of large particle size not easy to absorb through the skin.
5. The occurrence of the bubble during formation of emulgel.[11]

Rationale of Emulgel as a Topical Drug Delivery System

Many widely used topical agents such as ointment, cream, and lotion 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. Moreover, they exhibit the problem of stability also. Due to all these factors within the major group of semisolid preparation, the use of transparent gels has expanded both in cosmetics and a pharmaceutical preparation.

A gel is a 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 gelatin substance present. In spite of many advantages of gels, a major limitation is in the delivery of hydrophobic drugs. Hence, to overcome this limitation, an emulsion based approach is being used.

Numbers of medicated products are applied to the skin or mucous membrane that either enhances or restores a fundamental function of skin or pharmacologically alters an action in the underlined tissues. Such products are referred as topical or dermatological products. Many widely used topical agents such as ointments, creams, and lotions have many disadvantages. They are sticky in nature causing uneasiness to the patient when applied, have lesser spreading coefficient so applied by rubbing, and they also exhibit the problem of stability. Due to all these factors within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and pharmaceutical preparations. In spite of many advantages of gels, a major limitation is in the delivery of hydrophobic drugs. so that even a hydrophobic therapeutic moiety can be successfully incorporated and deliver through gels.[12,13]

Physiology of Skin

The skin is the largest single organ of the body, accounting for about 15% of the total adult body weight. It combines with the mucosal lining of the respiratory, digestive, and urogenital tracks to form a capsule which separates the internal body structure from external environment. For an average 70 kg human with skin surface area of 1.8 m^2, a typical square covers 10 hair follicle, 12 nerves, 15 sebaceous glands. 100 sweat glands, and 3 blood vessel with 92 cm total length. The pH of the skin varies from 4 to 5.6 sweat and fatty acid secreted form sebum which influence the pH of the skin surface.

Temperature of skin varies in a range of 30 to 40 degree depending of the environmental conditions. It performs many vital functions, including protection against external physical, chemical, and biologic assailants, as well as prevention of excess water loss from the body and a role in thermoregulation. The skin is continuous, with the mucous membrane lining the body's surface.[14]

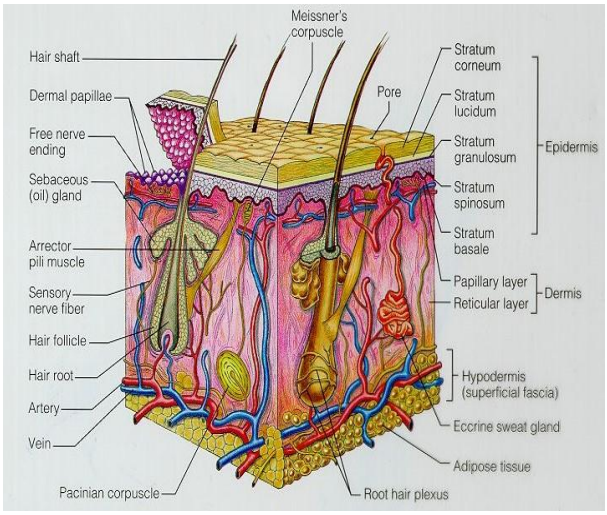

Fig. 3: Structure of Skin.

Epidermis

It is the outermost layer of the skin, which is approximately 150 micrometers thick. it consist of epithelial cells. Among these cells, both living cells and dead cells can be found. These new cells at the bottom of epidermis divide fast and push the older cells upward. The source of energy for lower portions of epidermis is glucose and the end of product of metabolism, lactic acid, accumulates in the skin.

The layer of epidermis are

- Stratum Germinativum (Growing layer)
- Malpighion Layer (pigment Layer)
- Stratum Spinosum (prickly cell layer)
- Stratum Granulosum (Granular Layer)
- Stratum Lucidum
- Stratum Corneum (Horny layer)

Dermis

Dermis is non – descriptive region lying between the epidermis and the subcutaneous fatty region It consist mainly of the of the dense network of structural protein fiber i.e collagen, reticulum and elastin embedded in the semi gel matrix of mucopolysaccharaidic 'ground substance' The elasticity of the skin is due to network or gel structure of the cells. Beneath the dermis the fibrous tissue open outs and merges with the fat containing subcutaneous tissue. Protein synthesis is a key factor in dermal metabolism.

Subcutaneous Tissue (hypodermis)

This layer consist of sheet of fat rich areolar tissue known as superficial fascia, attaching the dermis to the underlying structure. Large arteries and vein are present only in the superficial region.

Function of Skin

- Containment of body fluid and tissuses.
- Protection from external stimuli like chemicals, light, heat, cold, and radiation.
- Reception of stimuli like pressure, heat, pain etc.
- Biochemical synthesis.
- Metabolism and disposal of biochemical wastes.
- Regulation of body temperature.
- To control blood pressure.
- Prevent penetration of noxious foreign material and radiation.[15,16]

Permeation through the Skin

Trans -epidermal absorption

The trans-epidermal route across the continuous stratum corneum and the epidermis involves two route of entry: via the intercellular spaces which includes passive transport of small molecules, active transport of ionic and polar compound and endocytosis and transcytosis of macromolecule and via intracellular spaces which transport molecule around or between the cells. Tight junctions or similar situations exist between the cells. The partition coefficient (log k) decides the principal patway for the permeate (0/w log k greater than 2) pass through stratum corenum by both routes. However the indirect intercellular pathway is widely considered to provide the principal route and the major barrier to the permeation of most drugs.

Trans- follicular absorption

Appendageal route comprises of transport via sweat glands and along hair follicle with their associated sebaceous glands. These route circumvent penetration through the stratum corneum and are therefore known as "shunt" routes This route is considered to be of small importance as it has a small area , approximately 0.1% of the total skin area. In addition, the skin appendages exercise some influence on percutaneous absorption due to their secretions which affect the lipid and the water content of the stratum corneum and so can modify the absorption of molecules.

The skin is the largest and the most visible organ of the human body but, for people with skin diseases, this visibility is often the worst aspect of their conditions. It has been shown that relatively minor skin complaints often cause more anguish to people than more serious medical problem. Common skin disorders with impaired quality of life are topic eczema, vitiligo, acne urticarial, dermatitis, leg ulcers, skin disease involving the scalp, psoriasis etc.[17]

Classification of Topical Drug Delivery System

Classification of Topical Drug Delivery System based on the physical state

1. **Solid:** Powder, Aerosol, Plaster.
2. **Liquid:** Lotion, Solution, Emulsion, Suspension, Aerosol.
3. **Semi-solid:** Ointment, Cream, Paste, Gel, Jelly.[18,19]

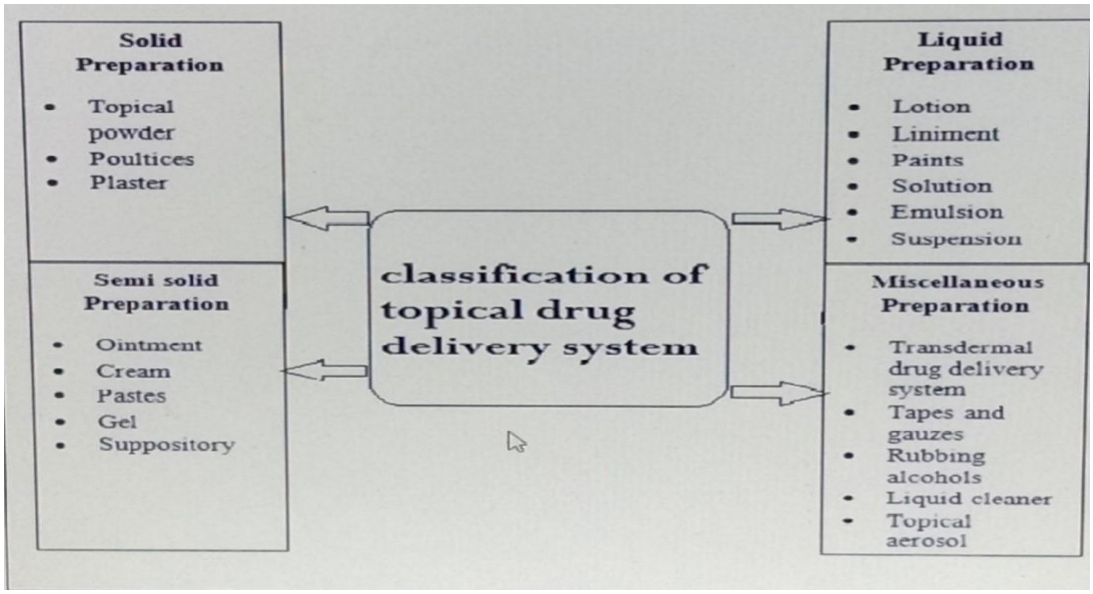

Fig. 4: Classification of topical drug delivery system.

Factor Affecting Topical Drug Delivery System

Physiological Factor

1. **Skin thickness**: Varies from epidermis to subcutaneous layer. Epidermis has high thickness about 100–150 µm. Skin on the sole and palm has a high rate of diffusion.
2. **Lipid content**: It is an effective water barrier, percutaneous penetration increases when lipid weight in stratum corneum is low.
3. **The density of hair follicles**: Hair follicle infundibulum has a large storage capacity about 10 times more than the stratum corneum.
4. **The density of sweat glands**.
5. **Skin pH**: Sweat and fatty acid secreted from sebum influence the pH of the skin surface.
6. **Blood flow.**
7. **Hydration of skin**: Can enhance permeation of drug.
8. **Inflammation of skin**: That disrupts the continuity of stratum corneum increases permeability.
9. **Skin temperature**: Increase in temperature gives rise to increase in the rate of skin permeation.[20]

Physiochemical Factor

- Partition coefficient
- Molecular coefficient
- Degree of ionization
- Effect of vehicle.[21]

Method to Enhance Drug Penetration and Absorption

- Chemical enhancemen.
- Physical enhancement.
- Biochemical enhancement.
- Supersaturation enhancement.[22]

Factor to Be Cosidered When Choosing Topical Preparation

1. Effect of the vehicle is to be checked 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.
2. The type of preparation should be matched with the type of lesions. For example, avoid greasy ointments for acute weepy dermatitis.
3. Match the type of preparation with the site (e.g., gel or lotion for hairy areas).
4. Irritation or sensitization potential. Should be notified. Generally, ointment and w/o creams are less irritating, while gels are irritating Ointment do not contain preservative or emulsifiers if allergy to these agent is a concern.[23]

Important Consistuent Used In Formulation of Emulgel

Vehicle

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 patient.
- Due to the efficiency of the epidermal barrier, the amount of topical drug that gets through the stratum corneum is generally low. Rate and extent of absorption vary depending on characteristics the vehicle but is also influenced by the active agent itself.[24]

Aqueous material

It's a aqueous phase of emulsion. Commonly water and alcohol are used as a aqous phase for Emulgel.[25]

Oils

These are use developing oil phase for Emulsion. There are differing kinds of oil phase that is employed within the Emugel formulation eg. mineral oil alone or paraffine combination, and non-biodegradable oil. Mineral oil are use commonly alone or with hard and light paraffin combination(according to drug and formulation). For eg, emulsions, mineral oils, either alone or combined with soft or hard paraffin, are widely used each because the vehicle for the drug and for their occlusive and sensory characteristics. Wide used oils in oral preparations are non-biodegradable mineral and castor oils that give a local laxative impact, and fish liver oils or numerous fixed oils of vegetable origin (e. g., Arachis, cottonseed, and maize oils) as nutritionary supplements.[26]

Table 1: Examples Oil.

Chemical	Quantity	Formulation
Light Liquid Paraffin	7.5%	Emulgel
Propylene glycol	3-5%	Emulsion and gel
Isopropyl sterate	7-7.5%	Emulsion
Isopropyl Palmiate	7-7.5%	Emulsion

Emulsifiers

Emulsifying agents are used both to promote emulsification at the time of manufacture and to regulate stability during a shelf life that can vary from days for extemporaneously prepared emulsions to months or years for commercial preparations. There are different kind of emulsifying agent are employed in the preparation of emulsion. Emulsion are thermodynamically unstable or biphasic system, with use of emulsifying agent stability will increase. Emulsifying agents are selected by according to formulation and HLB value. Non ionic surfactant that have greater HLB value than 8 (eg; spans, tween) are use within the formulation of o/w emulsion whereas mineral oil having HLB value less than eight are use in the formulation of w/o emulsion. mostly Emulgel formulation are prepare by the use of tween as a emulsifying agent in aqueous phase and span twenty in its oily phase. But span, tweens as a emulsifying agent might cause the toxicity and stability problem thus overcome this problem we use biosurfactant. Some of the emulsifying agents are below.[27,28]

Table 2: Examples of Emulsifiers.

Chemical	Formulation
Polyethylene glycol 40 stearate	Emulsion and Emulgel
Sorbitan monooleate (span40)	Emulgel and Emulsion
Polyoxyethylene sorbitan monooleate (tween 80)	Emulgel and Emulsion
Stearic acid	Emulsion
Sodium Stearate	Emulsion

Gelling agent

These are the agents used to increase the consistency of any dosage form also can be used as thickening agent. mainly these are two type natural and synthetic. the main purpose of using gelling agent, they make the formulation thixotropic. Carbapol and HPMC these are the 2 gelling agents that is often use for Emulgel. Carbapol is instantly absorb the water compared of HPMC. Carbapol and HPMC show a much better control release property. HPMC containing Emulgel show better control release.[29,30]

Table 3: Examples gelling agent.

Synthetic gelling agent	Natural gelling agent	Formulation
Carbopol 934	Xanthan gum	Emulgel and gel
Carbopol 940	Guar gum	Emulgel and gel
HPMC 2910	Tragacanth	Emulgel and gel
Sodium CMC		Gel

Preservatives

Preservatives are the used for inhibit the growth of micro-organism and which is added to emulgel to avoid spoilage of the formulation from micro-organism. E.g. Propyl paraben, methyl paraben, Benzalkonium chloride, Benzoic acid, Benzyl alcohol etc.[31]

Antioxidants

The antioxidants are the used for the emulgels to enhance the stability of therapeutic agents. E.g. BHA, BHT, etc.[32]

Humectants

The humectant is used for the maintenance of the moist in the emulgel formulations. Glycerin, Propylene glycol are the commonly used humectants.[33]

Permeation enhancer

These are agents that partition into and interact with skin constituents to induce a temporary and reversible increase in skin permeability. In order to promote absorption of drugs thorough skin barrier, vehicles often include penetration improving ingredients which temporarily disrupts the highly ordered structure of stratum corneum skin barrier, fluidize the lipid channels between corneocytes, modify the partitioning of the drug into skin structures, and increase delivery into skin. E.g. Oleic Acid, lecithin, Isopropyl Myristate, Urea, Eucalyptus oil, Chenopodium oil, Pyrrolidone, Laurocapran, Dimethyl Sulphoxide, Linoelic acid, Menthol etc.[34]

Properties of Permeation enhancers

- The Permeation enhancers must 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 inside the body i.e. should not bind to receptor sites.
- The Permeation enhancers should work unidirectional i.e. should allow therapeutic agents into the body at the same time as avoids loss of endogenous material from the body.
- They should be suitable for formulation into different topical preparations, thus should be companionable with both excipients and drugs.

Mechanism of penetration enhancers

Penetration enhancers may act by one or more of three main mechanisms:

- Disruption of the highly ordered structure of stratum corneum lipid.
- Interaction with intercellular protein.
- 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 the product. The Permeation enhancer should be cosmetically acceptable with an appropriate skin.[35,36]

Table 4: Examples of Penetration enhancers.

Chemical	Formulation
Oleic acid	Emulgel and gel
Lecithine	Emulgel and gel
Urea	Emulgel and gel
Isopropyl myristate	Emulgel and gel
Linoleic acid	Emulgel and gel
Menthol	Emulgel and gel

METHOD OF PREPARATION

Step 1: Formulation of emulsion either O/W or W/O
Step 2: Formulation of gel base
Step 3: Incorporation of emulsion into gel base with continuous stirring.

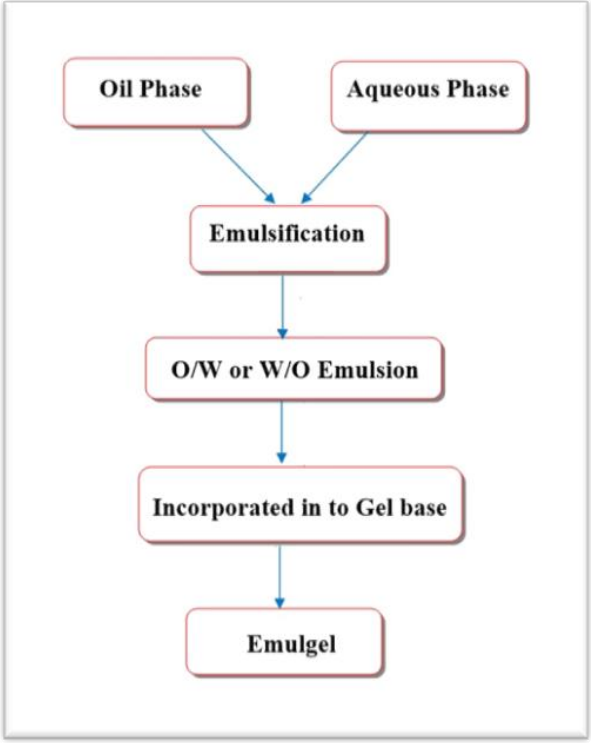

Fig. 5: Flowchart of Emulgel.

Preparation of Emulsion

The oil phase was prepared by dissolving certain amount of span 20 in liquid paraffin, while the aqueous phase was prepared by dissolving the required amount of tween 20 in purified water. Drug in weighed quantity was dissolved in suitable solvent, while required quantity of methyl paraben and propyl paraben were dissolved in propylene glycol and both were mixed with aqueous phase.

Both the oily and aqueous phases were separately heated to 70-80° C. Then, the oil phase was added to the aqueous phase with continuous stirring at 50 rpm until cooled to room temperature.[37]

Preparation of Gel

Gel was prepared by dispersing Carbopol powder in purified water with aid of moderate speed stirrer (50 rpm), and then the pH was adjusted to 6 – 6.5 using Tri-ethanolamine. Also methyl cellulose gel was prepared by dispersing methyl cellulose powder in heated purified water (80 °C), and the dispersion was cooled to room temperature and left overnight to ensure hydration of the gel.[38,39]

Preparation of Emulgel

Incorporation of prepared emulsion into gel base in ratio 1:1 with continuous stirring until the homogenous emulgel was obtained.[40]

Evaluation Parameter of Emulgel

1. Fourier transforms infrared spectroscopy (FTIR)

The primary aim of analysis of FTIR was to find a stable storage condition for the drug in solid state and excipient compatibility for Emulgel formulation.[41]

2. Physical appearance

Each prepared Emulgel formulation is displayed for there physical representation like colour, grittiness homogeneity, consistency, Uniformity. Wether colour is white, pale yellow, offwhite. Homogeneity and uniformity are examined by applying the Emulgel formulation on thin glass slide.[42]

3. pH determination

pH meter is used for measuring the pH value of Emulgel formulation. Before use, ph meter should be caliberated with standard solution having ph 4-7. In distilled water 1gm of prepared Emulgel formulation was dissolved and stirred it to form a uniform suspension, kept it for 2hr. The volume made up to 100 ml and pH of the suspension can be measure with the digital pH meter.[43]

4. Viscosity measurement

Brookfield Viscometer was used to determine viscosity of prepared Emulgel formulation. For the determination of viscosity, prepared Emulgel formulation was added to the beaker and setteled it for 30 mint at 25-30 °C. Adjust the spindal in that way that spindal does not touch the bottom of the jar and rotate at a moderate speed 40-70 RPM for 10 min. The viscosity reading was noted.[44]

5. Spreadability measurement

Two glass slide was used, which is same dimension used for determination of the prepared Emulgel formulation. Prepared Emulgel was placed over one slide and the other slide was placed over its top. The slide pressed upon each other like sandwich and remove the air bubble. Apply 2 gm of Emulgel is place between the slide and put 1 kg of weight on upper slide. Top plate was then subjected to pull of 80 grams. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5cm be noted. A shorter time to reach standard distance show a better Spreadability.[45]

6. Globule size and its distribution

Malvern zeta sizer is used for the determination of the globule size in prepared Emulgel formulation. Emulgel Formulation, whom globule size was determined, dissolved in distilled water and shakes it to get a uniform solution. Take well-defined amount of sample in photocell of zeta sizer. Mean globule size and its distribution in prepared Emulgel is collected.[46]

7. Swelling index

Swelling index of prepared Emulgel was determined by the porous aluminum foil. Take 1- 2gm of prepared Emulgel place it in 1N NaOH solution. Sample was taken from beaker at different time period and place it on dry place for some time re weight.[47]

Swelling index was calculated by following formula

Swelling Index (SW) % = [(Wt – Wo) / Wo] × 100

Where, (SW) %=equilibrium swelling percent

Wo= emulgel weight at zero time Wt= weight of swollen Emulgel

8. Drug content determination

UV spectrometer was used for the determination of drug content of Emulgel formulation. Dissolve well-defined amount of Emulgel in suitable solvent with sonication. Absorption was determined by using proper dilution in UV spectrometer and Result were noted.[48]

9. In vitro release study

Emulgel in vitro study was done on the Franz diffusion cell using egg membrane. Egg membrane clamped carefully at one end of glass tube of dylasis. A well-defined a amount of Emulgel was applied on the egg membrane surface. The assembly has two chamber. Receptor chamber and donor chamber. Receptor chamber is filled by the freshly prepared phosphate buffer having pH 7-8 for solubilizing the drug. Donar chamber use for sample withdrawing. Sample were collected different time interval and analyzed after suitable dilution in UV spectrometer. Cumulative % of drug release was calculated by the help of standard calibration curve.[49]

10. Drug content = (Conc.×D.F.×V.T.)×C.F.

D.F = dilution factor

V.T.= Volume taken

C.F.= Conversion factor

11. Phase separation

Phase separation was done by using the centrifugation. All prepared Emulgel formulation were keep in centrifugation for 10 mint at 10,000 RPM and check if any phase separation obtained.[50]

12. Skin irritation test

Skin irritation test of Emulgel was determined by using properly shaven skin of rat and rabbit. A group of 8 rat and rabbit can be used for the study. Weight accurately 1gm of Emulgel on the rat and rabbit skin and keep them in cage for next 24 hr. After 24 hr examine the rat and rabbit skin area, where the Emulgel formulation were applied check for any change occur in skin, colour change, any adverse effect noted. When no adverse effect were found formulation passed the test. If any adverse effect obtained in 2 or more then 2 rat then study should repeated.[51]

13. Extrudability

It is a typical observational test to quantify the power required to expel the material from tube. The technique connected for assurance of connected shear in the locale of the rheogram relating to a shear rate surpassing the yield esteem and showing resulting plug stream. In the present examination, the technique received for assessing Emulgel definition for extrudability depends on the amount in level of Emulgel and Emulgel expelled from lacquered aluminum collapsible tube on utilization of weight in grams required to expel no less than 0.5 cm lace of Emulgel in 10 seconds. More amount expelled better is extrudability. The estimation of extrudability of every detailing is in triplicate and the normal esteems are displayed. The extrudability is than ascertained by utilizing the accompanying recipe.[52]

14. Extrudability = weight applied to extrude Emulgel from tube (in gm) / Area(in cm^2).

Another technique to visualize the Extrudability of Emulgel formulation is applied using hardness tester. A fifteen weight unit of gel is stuffed in Al tube. The plunger was adjusted to carry the tube properly. The presence of one kg/cm was applied for thirty sec. the amount of gel extruded is weighed. The procedure is recurrent at three equidistance places of the tubes.

15. Ex-Vivo Bio-adhesive Strength Measurement of Emulgel (Mice shaven skin)

The modified method is used for the measurement of bio-adhesive 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 another piece is tied with the balance on the right-hand side. The right and left pans were balanced by adding extra weight on the left-hand pan. 1 g 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 min. Weight is added slowly at 200 mg/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 bio-adhesive strength. The bio-adhesive strength is calculated using the following. Bio-adhesive strength = Weight required (in g)/Area (cm2).[53]

16. Microbiological Assay

Ditch plate technique is 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 are used. Three grams of the gel based 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 18–24 h at 25°C, the fungal growth is observed, and the percentage of inhibition is measured as follows.[54]

% inhibition = L2/L1 × 100,

Where, L1 = Total length of the streaked culture, and L2 = Length of inhibition

17. Stability study

All Emulgel formulation were examined for the stability study. A well-defined amount (5gm) of Emulgel formulation was fill in alimunium tube place them for different temperature and RH enviourment. Temperature and RH is 5°C, 25°C/65%, 40°C/75% for next 3 months. Sample were taken at fifteen-day time interval and evaluate physical appearance, pH, rheological property, drug content, drug release profile.[55]

18. Drug release kinetic study

Drug release of topical formulation were calculated by the following equation.

(1) Zero order equation; Q=ko t

Q=amount of drug release

T=time Ko=zero-order release constant

(2) 1 ST order equation; In (100-Q)=In 100-k1t

Q= % of drug release

T= time

K1= 1st order release constant

(3) Higuchi equation; Q= k2√t

Q= % of drug release

T= time

K2= rate constant of diffusion.[56]

Emulgel Formulation Are Used For Following Diseases

Acne

Acne is disorder of skin sebaceous gland and result in clogged pores and lesions commonly called pimples or jits. Prescription topical medications are erythromycin, clindamycin.

Psoriasis

It is fundamentally an inflammatory skin condition with reactive abnormal epidermal differentiation and hyper proliferation affecting 2-3% of world population. Topical treatments are usually the first to be tried when fighting psoriasis that includes emollients, dithranol, tar, deltanoids, corticoids, tacrolimus etc.

Atopic Dermatitis

It is a familial, chronic inflammatory skin disease that commonly presents during early infancy and childhood but can persist or start in adulthood. First line treatment includes Skin hydration and topical corticosteroids.

Atopic Eczema

Atopic eczema is the commonest inflammatory skin disease of childhood. Itching, skin damage, redness, sores, sleep loss are various characteristics of eczema.

Topical corticosteroids, topical calcinurin inhibitors, various emollients are used in its treatment.[57]

Various Marketed Emulgel Formulations

Emulgel are commercially available in markets; some preparations of which are listed as following in Table. Isofen Emulgel, Voltaren Emulgel is a topical analgesic gel that provides relief in shoulder pain, back pain and reduces swelling.Denacine act as topiacal antibiotic. Voltaren Emulgel is non-greasy, white pleasant-smelling gel which is available in a 100g tube having a active ingredient diclofenac sodium 1% w/w (as diclofenac diethylamine Indogel Emulgel acts as anti-rheumatic were Diclomax Emulgel as Anti-inflammatory. Another emulgel is Diclomax Emulgel which is used in treatment inflammation of the tendons, ligaments, muscles and joint and manufactured by Torrent Pharma.

Miconaz H emulgel which is manufactured by medical union pharmaceuticals having active ingredient miconazole nitrate and hydrocortisone posses bactericidal, fungicidal, antiinflammatory and anti-pruriginous properties.[58,59]

Table 5: Various Marketed Emulgel Formulation.

Sr. No	Brand Name	Active ingredients	Manufacture	Use for
1	Voltarol Emulgel	Diclofenac Diethylammonium	Novartis	Anti- inflammatory
2	Miconaz-H-Emulgel	Miconazole nitrate, Hydrocortisone	Medical Union Pharmaceuticals	Topical corticosteroid and antifungal
3	Diclomax Emulgel	Diclofenac sodium	Torrent pharma	Intense moisturizing and exfoliation activity
4	Dermafeet Emulgel	Urea 40%	Herbitas	Anti-inflammatory
5	Isofen Emulgel	Ibuprofen		Anti-inflammatory

Fig. 6: Various Marketed Emulgel Formulation.

Future Prospective

Many drugs are hydrophobic in nature. Their delivery to the biological system has been challenging. For topical delivery of drugs different delivery systems such as ointments. lotion, creams, and pastes are applied. These topical formulations generally include large number of oleaginous bases such as petrolatum, beeswax, or vegetable oils those themselves are hydrophobic in nature that does not allow the inclusion of water or aqueous phase. It makes them an excellent emollient but retards the release pattern of drugs and makes the product thick and greasy. Whereas gel provides an aqueous environment to the drug, favors its dissolution and provides quicker release of drug as compared to other topical delivery systems. Emulsion-based gel provides a suitable medium for delivery of such hydrophobic drugs where such drugs can be incorporated into its oily phase and delivered to the skin.

CONCLUSION

The Emulgel drug delivery system can be effective novel approach for topical drug delivery for the treatment of various conditions. It is better suitable for hydrophobic drugs and it is a very good technique for drug delivery of combination of both hydrophilic and hydrophobic drugs. Mainly the hydrophobic drug formulation can be developed using emulgel technique because it contain both oil and aqueous phase while hydrogels are not suitable for hydrophobic drugs. Moreover, emulgel will become a solution for loading hydrophobic drugs in a water soluble gel bases. So that less dosage and dose

frequency are required compared to conventional dosage form. In the recent years, topical drug delivery system will be used extensively due to better patient compliance.

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