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A Review on Emulgel Drug Delivery System

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ABSTRACT

Topical drug delivery is the delivery of drugs anywhere in the body via skin, vaginal, ophthalmic and rectal routes. Pills may be given for localized or systemic results. Topical formulations with varying physicochemical homes, which includes solid, semisolid, or liquid, may be developed. The topical system is created by means of preparing a drug emulsion and incorporating it into an emulgel. Emulgel is a thermodynamically strong method with low interfacial anxiety that is made through combining a surfactant and a co-surfactant and has numerous properties which include multiplied permeability and accurate thermodynamic stability. Emulgel has a twin control and a sustained release pattern. Emulgel improves bioavailability in addition to affected person compliance. The pH, viscosity, particle size, zeta capacity, drug content material, stability study, pores and skin inflammation test, and other properties of the organized formula are evaluated.

INTRODUCTION:

Topical drug shipping refers back to the utility of a drug-containing system to the skin to treat a cutaneous condition. This machine is used when different routes of drug management (including oral, sublingual, rectal, and parental) fail, or while a neighborhood pores and skin infection, along with a fungal infection, occurs[1]. Topical drug management is a commonplace treatment technique for each neighborhood and systemic conditions. Inside the topical shipping machine, the drug is absorbed by way of the pores and skin and reaches the website of motion to offer a healing impact. The fee of drug launch from a topical education relies immediately at the physiological functions of the service [2]. The number one advantage of a topical transport system is that it avoids the first-skip metabolism. The term micro emulsion is based on particle length. Due to their smaller size, the drug debris can easily diffuse thru the pores and skin and reach their web page of action. The gel will hold the micro emulsion for a long time and will useful resource inside the sustained release of the drug. Various fungal infections are developing in recent times that are a primary problem for society. Fungal infections inclusive of Tinea capitis, Tinea pedis and Tinea corporis infect the pores and skin critically. A technique which includes emulgel can aid in the easy penetration of the drug into the pores and skin and provide a rapid onset of action.

Many blessings of gels a primary hindrance is inside the shipping of hydrophobic capsules. So, to overcome this drawback an emulsion based totally approach is being used so that even a hydrophobic healing moiety can revel in the particular residences of gels. While gels and emulsions are used in mixed form the dosage shape are referred as emulgel. In recent years, there was remarkable hobby in the use of novel polymers. A completely unique thing of dermatological pharmacology is the direct accessibility of the pores and skin as a goal organ for diagnosis and remedy. The combination of hydrophilic cornified cells in hydrophobic intercellular cloth presents a barrier to each hydrophilic and hydrophobic materials. Inside the essential organization of semisolid arrangements, the use of transparent gels has extended both in cosmetics and in pharmaceutical preparations. Polymer can feature as emulsifiers and thickeners because the gelling potential of these compounds lets in the method of stable emulsions and lotions by lowering surface and interfacial anxiety and on the equal time increasing the viscosity of the aqueous segment. In truth, the presence of a gelling agent in the water segment converts a classical emulsion into an emulgel. Those emulgel are having primary advantages on novel vesicular systems in addition to on traditional structures in

various elements. Numerous permeation enhancers can potentiate the impact; So emulgels may be used as higher topical drug transport systems over gift systems. Using emulgels can be extended in analgesics and antifungal drugs.[2, 3]

Topical drug management is a localized drug shipping gadget everywhere inside the frame through ophthalmic, rectal, vaginal and skin as topical routes. Those are observe a wide spectrum of arrangements for each cosmetic and dermatological, to their healthful or diseased skin.1 those formulations range in physicochemical nature from stable via semisolid to liquid. Drug substances are seldom administered on my own, however as a substitute as part of a method, in combination with one or greater non medicated marketers that serve various and specialized pharmaceutical characteristic. Drugs are administered topically for his or her motion at the site of utility or for systemic consequences.[2] Drug absorption through the pores and skin is enhanced if the drug substance is in answer, if it has a beneficial lipid/water partition coefficient and if it is a nonelectrolyte. For the most element, pharmaceutical arrangements carried out to the pores and skin are supposed to serve a few neighborhood action and as such are formulated to provide prolonged nearby touch with minimum systemic drug absorption. Drug implemented to the skin for their neighborhood action include antiseptics, antifungal agent, skin emollients and protectant. The main advantages of topical delivery system are to pass first pass metabolism. Avoidance of the dangers and inconveniences of intravenous therapy and of the varied conditions of absorption like pH changes, presence of enzymes, gastric emptying time are other advantages of topical arrangements.[3-5]

The topical drug delivery gadget is usually used where the others gadget of drug management fails or it's miles in particular used in fungal contamination. Hu guy skin is a uniquely engineered organ that perm its terrestrial lifestyles by way of regulating heat and water loss from the frame even as preventing the ingress of noxious chemical substances or microorganisms. it is al so the largest organ of the human body, providing around 10% of the body mass of a median man or woman, and it covers a mean location of 1.7 m^2. Whilst any such huge and easily on hand organ reputedly gives best and a couple of websites to manage healing retailers for each neighborhood and systemic movements, human skin is a especially efficient self-repairing barrier designed to hold the internal in and the out of doors out.[5]

Gels are an enormously more recent elegance of dosage shape created by way of entrapment of big amounts of aqueous or hydroalcoholic liquid in a network of colloidal solid debris,

which may additionally consist of inorganic substances, including aluminum salts or natural polymers of herbal or artificial beginning.[6] they have a better aqueous element that lets in more dissolution of medicine, and additionally allow clean migration of the drug via an automobile that is essentially a liquid, in comparison with the ointment or cream base.[7] these are advanced in phrases of use and patient acceptability. No matter many blessings of gels a chief obstacle is inside the shipping of hydrophobic drugs. So to conquer this trouble, emulgels are prepared and used so that even a hydrophobic healing moiety can enjoy the specific homes of gels.[8]

In reality, the presence of a gelling agent inside the water segment converts a classical emulsion into an emulgel.[12] both oil- inwater and water-in-oil emulsions are used as vehicles to deliver various pills to the pores and skin. Emulgels for dermatological use have several favorable homes which include being thixotropic, greaseless, without difficulty spreadable, effortlessly detachable, emollient, no-staining, long shelf life, bio- pleasant, obvious & alluring appearance.[10]

Use of topical seller's calls for an appreciation of the factors that influence percutaneous absorption.[14] Molecules can penetrate the pores and skin by way of three routes: thru intact stratum corneum, through sweat ducts, or via sebaceous follicle. The surface of the stratum corneum gives extra than 99% of the entire skin surface to be had for percutaneous drug absorption.[15]

Passage thru this outer most layer is the rate limiting step for percutaneous absorption. The major steps concerned in percutaneous absorption consist of the establishment of a attention gradient, which offers the using force for drug motion throughout the pores and skin, release of drug from the car (partition coefficient), and drug diffusion throughout the layers of the pores and skin (diffusion coefficient). Ultimate traits of topical capsules consist of low molecular mass (600 Da), ok solubility in oil and water, and an excessive partition coefficient. Besides for very small debris, water soluble ions and polar molecules do no longer penetrate intact stratum corneum. Topical components can be used to manipulate the barrier function of the skin, for instance, topical antibiotics and antibacterial assist a damaged barrier closer to off infection, solar screening marketers and the horny layer defend the possible tissues from Ultraviolet radiation and emollient preparations repair pliability to a desiccated attractive layer.[16]

For the duration of improvement of semi-solid preparations for cutaneous utility whose formula contains an antimicrobial preservative, the need for and the efficacy of the chosen preservative will be validated to the satisfaction of the equipped authority. An appropriate check method collectively with criteria for judging the preservative houses of the components are furnished in efficacy of antimicrobial maintenance. Sterile semi-strong preparations for cutaneous software are prepared the use of materials and techniques designed to make certain sterility and to avoid the advent of contaminants and the growth of microorganisms.[17]

The efficacy of an antimicrobial preservative can be more advantageous or faded by means of the energetic constituent of the education or by using the system wherein it is included or by the field and closure used. Preparation for topical use should have microbiological fine and its miles checked with test for sterility. Overall possible aerobic depend ought to now not be more than 102 micro-organisms (cardio bacteria plus fungi) according to gram. It must now not have more than 101 enter bacteria, sure different gram-bad bacteria per gram and absolutely without Pseudomonas aeruginosa and Staphylococcus aureus.[18-19]

Need of Emulgel:

Many widely used topical sellers like ointment, cream, lotion have many negative aspects. They have very sticky inflicting uneasiness to the affected person when carried out. Moreover additionally they have lesser spreading coefficient and need to use with rubbing. And they showcase the problem of balance also. Due to these kinds of elements inside the most important organization of semisolid arrangements, the usage of obvious gels has accelerated each in cosmetics and in pharmaceutical arrangements.

A gel is colloid that is generally 99% wt. liquid, that's immobilized via surface anxiety among it and a macromolecular community of fibers constructed from a small quantity of a gelatin substance gift. Despite many advantages of gels a chief limitation is in the transport of hydrophobic drugs. So to triumph over this difficulty an emulsion primarily based approach is getting used in order that even a hydrophobic therapeutic moiety may be efficiently integrated and added via gels.[20]

Emulsion

Emulsions are made by combining two or more liquids that are normally incompatible. In this system, the oil phase is miscible with the aqueous phase using an emulsifying agent. The use

of emulsifying agents helps to stabilize emulsions. They are easy to wash off and they also penetrate well [8].

Gel

The word "gel" refers to enhancing the viscosity of liquid preparations without changing other properties. Gels can be used as a thickening agent and also help to improve the homogeneity and consistency of a formulation. This agent is used to create a gel base, which is then mixed with emulsion to create emulgel.

A gel is made up of a polymer that enlarges when exposed to fluid and possibly within its structure. The amount of fluid entrapped in the gel determines its rigidity. These gels are wet and smooth, with the appearance of being solid. These are capable of significant physical deformation, from solid-state to liquid state [9].

Introduction to Emulgel

Emulgel is known as an emulsion that has been gelled by using a gelling agent. They can be made either o/w or w/o type. Emulgel is a stable and superior system that incorporates poor water-soluble drugs. In brief, emulgel is a combination of emulsion and gel. Despite the numerous advantages of gels, one significant disadvantage is the delivery of hydrophobic medications. As a result, an emulsion-based solution is being used to overcome this limitation, allowing even hydrophobic therapeutic moieties to benefit from the unique properties of the gel.

Emulgel can deliver both hydrophilic and lipophilic drugs due to the presence of both aqueous and non-aqueous phases. In recent years, they have been used as a control release formulation. These are biphasic systems that have better drug loading capacity and better stability [10,11]. Emulgel has several good properties, such as good spreadability, greaseless, thixotropic, good shelf life, odorless, and a pleasant appearance over the conventional topical formulation. Emulgel has both gel and emulsion properties and functions as a dual control release system [12].

$$\text{Emulgel system} \Longrightarrow \text{Emulsion} + \text{gel}$$

Types of Emulgel

Microemulsion

Microemulsions are isotropic mixtures of a biphasic o/w systemic stabilized with a surfactant that is thermodynamically stable and optically clear. Droplets vary in size from 10 to 100nm and do not coalesce. It is made up of specific amounts of oil, co-surfactant, surfactant, and water. Microemulsions may have unique properties, including extremely low interfacial tension, a broad interfacial region, and the ability to dissolve both aqueous and oil-soluble compounds. The ingredients in microemulsion could help the drug permeate faster by lowering the stratum corneum's diffusion barrier.

However, because of their low viscosity, the use of microemulsions in the pharmaceutical industry is limited due to their low skin retention ability. To address this limitation, gelling agents like HPMC K100M, Carbopol 940, and guar gum are added to the microemulsion to form microemulsion-based gels with a viscosity appropriate for topical application [13,14,15].

Nanoemulgel

Nanoemulsion is transparent (translucent) oil-water dispersions that are thermodynamically stable due to surfactant and cosurfactant molecules with a globule size range from 1nm to100 nm. When the emulsion is mixed with gel, the term Nanoemulgel is used. Many drugs have higher transdermal permeation with Nanoemulsion than with traditional formulations such as emulsions and gels. The Nanoemulsion possesses enhanced transdermal and dermal delivery properties in vivo as well as in vitro. Because of its high loading capacity and small globule size, the drug easily penetrates the skin and provides less therapeutic effect in a short period.

Macroemulsion gel

Emulgel with emulsion droplet particle sizes greater than 400nm. They are physically invisible, but under a microscope, the individual droplets can be seen clearly. Macroemulsions are thermodynamically unstable, but surface-active agents can help to stabilize them.

Advantages of Emulgel

Using water/oil/water emulsions, hydrophobic drugs can be quickly implemented into the gel base.

Improved stability and load capacity.

Easy for production and a low-cost mechanism.

Avoid sonication.

The first metabolism is avoided.

Avoid gastrointestinal incompatibility.

Target drug delivery on the body.

Improved patient compliance.

Improved patient acceptability and suitability for self-medication.

Ability to easily terminate medication [16].

Disadvantages of Emulgel

The drug and/or excipients can lead to skin irritation in people with contact dermatitis.

Some medications have low permeability through the skin.

Possibility of allergenic reactions.

Larger-particle-size drugs are not easily incorporated into the skin [17].

The Rationale of Emulgel As Topical Drug Delivery

Various semisolids and other preparations are available on the market for restoring the skin's fundamental role or pharmacologically altering an operation to the underline tissue [18]. The formulations, such as lotions, ointments and creams have several drawbacks, including being sticky, having a low spreading coefficient, and having stability issues. Only transparent gels have exposure in pharmaceutical and cosmetic preparations due to overall limitations within the semisolid preparations [19]. As a result, an emulsion-based solution is used to address this

limitation. Hence, the hydrophobic moiety of the drug should be incorporated and provided through gels. Drug/oil/water emulsions may be used to integrate hydrophobic drugs into emulgel. Since solubility acts as a barrier, most drugs cannot be inserted directly into gel bases, causing problems during drug release. The emulgel system helps to incorporate a hydrophobic drug into the oil phase, after which oily globules are easily dispersed into the aqueous phase, resulting in an oil/water emulsion. The emulsion can be mixed into the gel base. This may result in enhanced drug stability and release over simply incorporating the drug into the gel base [20].

Drug delivery across the skin

The epidermis is the most superficial layer of the pores and pores and pores and skin and includes stratified keratinised squamous epithelium which varies in thickness in a single-of-a-type additives of the frame. Its miles thickest on with elastic fibres. The pores and skin forms a quite water resistant layer that protects the deeper and more sensitive structures. Blood vessels are dispensed profusely underneath the skin. Mainly critical is a non-prevent venous plexus this is provided thru inflow of blood from the pores and skin capillaries. Within the maximum exposed regions of the body-the palms, feet, and ears blood is likewise furnished to the plexus straight away from the small arteries through especially muscular arteriovenous anastomoses. A completely unique factor of dermatological pharmacology is the direct accessibility of the skin as a goal organ for assessment and treatment. The pores and pores and skin acts as a -way barrier to prevent absorption or loss of water and electrolytes. There are three number one mechanisms of topical drug absorption: transcellular, intercellular, and follicular. Most drugs bypass through the torturous path round corneocytes and through the lipid bilayer to viable layers of the pores and skin. The subsequent most common (and probably below diagnosed inside the scientific placing) path of transport is through the pilosebaceous path. The barrier is living within the outermost layer of the dermis, the stratum corneum, as evidenced by using way of using approximately identical charges of penetration of chemical substances via remoted stratum corneum or entire pores and pores and skin. creams and gels which can be rubbed into the pores and skin were used for years to deliver ache remedy and infection stopping capsules to an affected net on-line of the body. Those consist of, among others, gels and creams for vaginal yeast infections, topical creams for pores and pores and skin infections and lotions to assuage arthritis pain. New generation now allow one-of-a-kind tablets to be absorbed via the pores and pores and skin (transdermal).

Those can be used to deal with no longer absolutely the affected regions (for example, the pores and skin) however the whole body.

Factors Affecting Topical Absorption of Drug[21-22]

Physiological Factors

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

Physiochemical Factors

1) Partition coefficient.
2) Molecular weight (<400dalton).
3) Degree of ionization (only unionized drugs gets absorbed well).
4) Effect of vehicles

Factors to be considered when choosing a Topical Preparation [23-24]

1) Effect of the automobile e.g. an occlusive automobile complements penetration of the energetic aspect and improves efficacy. The automobile itself may additionally have a cooling, drying, emollient or shielding action in shape the sort of practice with the kind of lesions. For example, avoid greasy ointments for acute weepy dermatitis.

2) Match the kind of guidance with the website online.(e.g., gel or lotion for bushy regions)

3) Inflammation or sensitization capacity. Typically, ointments and w/o lotions are less tense, while gels are nerve-racking. Ointments do not include preservatives or emulsifiers if allergic reaction to those retailers is a subject.

Method to Enhance Drug Penetration and Absorption[25]

1) Chemical enhancement

2) Physical enhancement

3) Biochemical enhancement

4) Super saturation enhancement

Advantages[26-27]

1) Hydrophobic pills may be without problems integrated into gels the usage of d/o/w emulsions. Maximum of the hydrophobic pills cannot be included without delay into gel base due to the fact solubility act as a barrier and trouble arises at some stage in the release of the drug. Emulgel enables inside the incorporation of hydrophobic drugs into the oil segment and then oily globules are dispersed in aqueous segment ensuing in o/w emulsion. And this emulsion may be combined into gel base. This may be proving better balance and launch of drug than honestly incorporating drugs into gel base.

2) **Higher stability:** other transdermal preparations are relatively less stable than emulgels. Like powders are hygroscopic, lotions indicate segment inversion or breaking and ointment suggests rancidity because of oily base.

3) **Better loading ability:** different novel strategies like noisome and liposomes are of Nano size and because of vesicular systems may result in leakage and result in lesser entrapment efficiency. However gels because of significant network have relatively better loading potential.

4) **Manufacturing feasibility and occasional preparation fee:** preparation of emulgels accommodates of less complicated and brief steps which will increase the feasibility of the manufacturing. There are no specialized gadgets wanted for the manufacturing of emulgels. Furthermore substances used are effortlessly to be had and less expensive. For this reason, decreases the production cost of emulgels.

5) **No intensive sonication:** manufacturing of vesicular molecules need in depth sonication which may also bring about drug degradation and leakage. But this trouble is not seen for the duration of the manufacturing of emulgels as no sonication is wanted.

6) **Managed launch:** Emulgels may be used to lengthen the impact of medication having shorter $t_{1/2}$.

Important components of Emulgel:

1) **Aqueous material:** This forms the aqueous phase of the emulsion. Normally used marketers are water, alcohols.[28]

2) **Oils:** Those dealers shape the oily phase if the emulsion. For externally carried out emulsions, mineral oils, both by myself or blended with soft or hard paraffins, are extensively used each as the automobile for the drug and for his or her occlusive and sensory traits. broadly used oils in oral preparations are non-biodegradable mineral and castor oils that offer a nearby laxative effect, and fish liver oils or various constant oils of vegetable origin (e.g., arachis, cottonseed, and maize oils) as dietary supplements.[29-30]

3) **Emulsifiers:** Emulsifying agents are used both to promote emulsification on the time of manufacture and to manipulate balance at some point of a shelf existence which could vary from days for extemporaneously prepared emulsions to months or years for commercial arrangements.eg Polyethylene glycol 40[31] stearate, Sorbitan monooleate[32] (Span 80), Polyoxyethylenesorbitan monooleate (Tween 80)[33], Stearic acid[34], Sodium stearate.[35]

4) **Gelling Agent:** these are the agents used to increase the consistency of any dosage form can also be used as thickening agent.[36-37]

5) **Permeation Enhancers:** These are dealers that partition into and have interaction with skin materials to induce a brief and reversible boom in skin permeability.[38]

Emulgel Formulation:

Emulgel turned into organized by way of the approach mentioned via Mohammad et al (2004) with minor modification. The Gel in formulations have been prepared by means of dispersing Carbopol 934 in purified water with constant stirring at a slight speed and Carbopol 940 in purified water with regular stirring at a moderate pace then the pH are

adjusted to 6 to 6.5 the usage of Tri ethanol amine (TEA).

The oil section of the emulsion were organized by dissolving Span 20 in mild liquid paraffin while the aqueous phase changed into prepared by using dissolving Tween 20 in purified water. Methyl and Propyl paraben became dissolved in propylene glycol while drug changed into dissolved in ethanol and both solutions became blended with the aqueous phase. Each the oily and aqueous stages were one at a time heated to 70° to 80°C; then the oily segment had been delivered to the aqueous phase with continuous stirring until cooled to room temperature. And upload Glutaraldehyde in all through of blending of gel and emulsion in ratio 1:1 to gain the emulgel.[39]

Characterization of Emulgel

Physical appearance

The color, consistency and homogeneity of the prepared formulation are visually inspected for observations of physical properties [29].

pH measurement

A digital pH meter is used to determine the pH of all prepared emulgel. Calibration of the pH meter is performed before using a standard buffer solution. 1 gm of the formulation is dissolved in distilled water until a uniform suspension is formed and is kept aside for 2 hours. After 2 hours the glass electrode is dipped in the suspension and the pH is measured [30,31].

Rheological study

The viscosity of the prepared formulation is determined at 37^0C using a cone and plate Brookfield viscometer [32].

Stability study

Stability studies are carried out by inducing stress at different temperatures and humidity (room temperature of 30^0C±2^0C, RH of 65%±5% and room temperature of 40^0C±2^0C, RH of 75%±5%) using a stability chamber with proper excipient quantity (API-0.1gm, oil-2.5gm, surfactant-6.665gm co-surfactant-13.33gm, double-distilled water 27.15ml).

The study is done for 1 month and observation is done for physical changes such as a change in clarity, observance of turbidity and detection of particle growth [33,34].

Skin irritation test

Skin irritation test is usually done in skin of human volunteers with proper written consent. The prepared formulation is applied to the skin of the hand and observation is done to check for any undesirable effects[35].

Zeta potential

The Zeta potential of the emulgel preparation is determined by zetasizer (Malvern Zetasizer) The formulation is placed in a clear, disposable zeta cell, and the result is determined. Before experimenting, cuvettes are washed with methanol and then the sample is placed [36].

Particle size and polydispersity index (PDI)

The globule size of emulgel is measured at 25^0C by using a zetasizer (Malvern zetasizer instrument, ZS90). The sample is diluted before the experiment[37].

Swelling Index

1 mg of gel is placed on porous aluminium foil separately in a 50 ml beaker that contained 10 ml of 0.1 N NaOH. The sample is removed from the beaker at various time intervals and kept in a dry place for some time after it is reweighed [38,39].

Swelling index (SW) = [(Wt.-Wo)/Wo] x a hundred.

Where (SW) %= Equilibrium percentage swelling.

Wo= Original weight of emulgel at zero time where time t,

Wt= Weight of swollen emulgel

Drug Content determination

A spectrophotometer is used to determine the drug concentration in the emulsion. The drug content of an emulsion is determined by sonicating a known amount of emulsion in a solvent

(methanol). In a UV/VIS spectrophotometer, absorbance is measured after appropriate dilution [40].

CONCLUSION

Emulgel is a novel technique that has been verified to be the most convenient, superior, and efficient transport system. Because of its non-greasy nature and shortage of oily bases, it gives gel-like homes and offers superb drug release whilst in comparison to traditional topical transport structures. Emulgel has a high drug loading capability and is effective in drug delivery on the goal website online. Penetration of a drug thru the skin is effective due to its small particle size. Emulgel is fashioned by incorporating emulsion into the gel base and presents a twin manipulate release effect. The emulgel method enables to solve special problems, which include creaming, segment separation and its balance improves. Hydrophobic pills can be delivered with the help of emulgel and they can be integrated into the oil phase of the emulsion and blended with gel. This approach improves affected person compliance and will increase the bioavailability of the drug in specific regions.

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