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A Review on Microemulgel for Topical Drug Delivery System

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ABSTRACT

Microemulgel is made by screening oils, emulsifiers, and co-emulsifiers based on the solubility of an API in them, as opposed to gel and other topical preparations. Due to its great solubility and potential for pharmacological properties, oil may complement the therapeutic activity of API. Because there is an oil component, the API penetrates the skin more deeply. The oil micelle size was smaller than 500 nm, which gives the skin greater surface area for API absorption, increasing penetration and effectiveness compared to macro-emulsion. In addition to having the advantages of both micro-emulsion and gel, microemulgel also offers a number of other advantageous qualities, such as a good consistency, thyrotrophic, greaseless, readily spreadable, and detachable.[1]Micro-emulsions are micronized, thermodynamically stable systems with low interfacial tension that are made by adding co-surfactant and offer a number of advantages, including improved permeability, strong thermodynamic stability, and extended release. Emulgel enhances patient compliance, extends the duration of medication release, and stabilizes the emulsion. While the produced emulgel is assessed for a number of characteristics, including spreadability, globule size, pH, and viscosity, the micro-emulsion is assessed for a number of characteristics, including viscosity, pH, and zeta-potential.[2]

Keywords: Microemulgel, Micro-emulsion, Emulgel, Topical drug delivery system, gelling agent.

INTRODUCTION

The last few years have seen the administration of drugs to the human body through a variety of channels, including oral, sublingual, rectal, parental, etc., in order to cure sickness. In cases when other drug delivery methods are ineffective, or primarily for localized skin infections such as fungal infections, the topical drug delivery system is employed. A medication-containing formulation applied topically to the skin to treat cutaneous disorders directly is known as topical drug delivery.[3,4]Topical drug delivery, which has the benefits of bypassing first-pass metabolism and boosting the therapeutic efficacy of the medicine, is described as the administration of a formulation directly via skin to treat disorders . [5]

Emulgel:
Emulgels are emulsions of water in oil or oil in water that have been gelled through the addition of a gelling agent. Emulsified gel is a stable and better carrier for drugs that are hydrophobic or have low water solubility. Emulsions mixed with gels are known as emulgels.

Microemulgel:
When both micro-emulsion and gel are used in combinationdosage forms the prepared formulations are called as microemulgel, having the advantages of both emulgel as well as micro-emulsion.Drugs that are hydrophilic or hydrophobic are combined in dosage formulations. Their vast surface area facilitates medication absorption, and the oil part improves the permeability of the drug, increasing its bioavailability.Incorporating micro-emulsion into gel also increases its stability. In

contrast to micro-emulsions, microemulgels are more elegant and are simple to clean when needed. [6] By penetrating the underlying layers of skin or mucous membranes, topical medicines have localized effects at the application site. It offers the freedom to administer medication to a targeted location more successfully. It allows the use of medications with a brief biological half-life and a constrained therapeutic window to extend the time of effect. The topical medication can be applied topically to any part of the body via the ophthalmic, rectal, vaginal, and cutaneous routes. The kind and severity of the ailment determine the administration route. A drug delivery device can apply a formulation directly to the skin, giving the medication a localized effect. Due to its ability to distribute medications more precisely to a targeted area, topical drug delivery systems provide several benefits. The goal of topical distribution is to circumvent the metabolic breakdown and gastrointestinal incompatibilities that come with oral delivery. [7]

Anatomy and physiology of skin:

The skin on an average adult body has a surface area of roughly 2 m² and receives one-third of the blood that circulates throughout the body. Per square meter of skin, the average human skin surface has between forty and seventy hair follicles and two to three hundreds of sweat ducts.

Skin has a pH range of 4 to 5.6. The pH of skin is influenced by fatty acids released from sebum and sweat. The skin is made up of four different tissue layers: the dermis, the subcutaneous connective tissues, the viable epidermis, and the nonviable epidermis.[8-10]

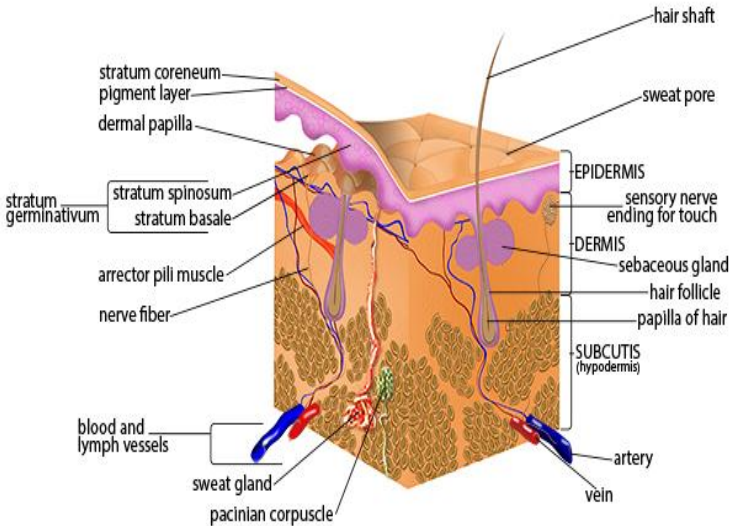

Fig: Anatomy of skin

Advantages:[11]

1] The capacity to prevent metabolism by first pass.
2] Micro- emulgel provide a large surface area foe drug absorption.
3] Gentle on the skin.
4] Suitable for self-administration of medicines.
5] The sufferer quickly moves past it.
6] Oil portion increases the bioavailability by improving permeability of drugs.

Disadvantages:[12]

1] In pharmaceutical applications, the surfactant used shouldn't be harmful.
2] Contact dermatitis is linked to itchy skin.
3] There were bubbles in the emulgel formulation.
4] The possibility of experiencing allergic responses

Components of Microemulgel:[13]

1] Aqueous phase:

Typically, the microemulgel composition is made using ultra-purified or distilled water.

2] Oil phase:
The choice of oil or other lipid constituents needs to guarantee the presence of an oily phase that is protected against contaminants such as peroxides, free radicals, and other fatty acids like sterols and polymers. Usually, the oils utilized in the microemulsion are the same oils that are used to carry the drug. Aperient and abundant fixing oils include olive, peanut, soy bean, and essential oils like clove, rose, and other oils.

3] Surfactants and Co-surfactants:
Two commonly used non-ionic surfactants are polyoxyethylene fatty acid esters and sorbitan esters. Co-surfactants are usually used to increase the thermodynamic stability of the product and lower the surfactant concentration. Ethyl alcohol, PGs, glycerine, Transcutol HP, and PEGs are a few examples of co-surfactants.

4] Penetration Enhancers:
Using penetration enhancers has shown to be one of the best ways to increase the efficiency of transportation through the skin and associated layers. Penetration enhancers are a mainstay of the conventional drug delivery strategy and are commonly used in topical microemulgel.

5] Gelling agent:
The gelling agent is one of the essential ingredients of microemulgel that gives the formulation its perfect structure. Logically, they are agents that cross-link. Tragacanth, HPMC, and Carbopol are a few of the gelling agents used.

6] Antioxidants:
Antioxidants are chemical substances that are added to compositions to stop certain components from oxidizing. As an illustration, consider butylated hydroxyl toluene and ascorbylpalmitate.

7] Preservatives:
Preservatives are substances that are added to products to prolong their shelf life and shield them against microbial deterioration. Preservatives such as phenoxyethanol, benzalkonium chloride, propyl paraben, and methyl paraben are often used.

Preparation method for Microemulgel: [14-16]
Microemulgel is a specific type of gel formulation that mixes hydrophilic matrix with microscale oil or other hydrophobic substance droplets. The following are the general methods used to create Microemulgel:

1] High- pressure Homogenization method:
By utilizing a high-pressure homogenizer, this approach breaks down the oil phase into microsized droplets that are readily disseminated in a hydrophilic gel matrix. The homogenization process generates high shear pressures, which help to reduce droplet size and create a stable microemul gel.

2] Ultra sonication Method:
This method creates microemul gel using ultrasonic vibrations. High-frequency ultrasonic waves are delivered to the mixture following the combination of the hydrophilic matrix and oil phase. The ultrasonic energy fragments the oil phase into microsized droplets, which are then uniformly disseminated throughout the gel matrix.

3] Solvent Evaporation Method:
This method uses a water soluble solvent to dissolve both the oil phase and the hydrophilic matrix. The solvent is then extracted under low pressure, producing a microemulgel with oil droplets the size of microparticles dispersed throughout the gel matrix.

4] Micro fluidization Method:
Through the use of a microfluidizer, the hydrophilic matrix and the oil phase are combined to create microemul gel. The oil phase was dispersed into microscale droplets inside the gel matrix by the high shear forces generated by the microfluidizer.

5] Self Emulsifying Gel Method:
This method includes the use of a self-emulsifying drug delivery system (SEDDS) that can create microemul gel in situ. The oil, surfactants, and co-solvents in the SEDDS mixture have the ability to emulsify on their own when exposed to water. When SEDDS is mixed with a hydrophilic gel matrix, microemulgel is produced.

6] Phase inversion temperature (PIT):
Using a thermosensitive surfactant, which transitions from its water-soluble to insoluble state at a certain temperature, is the foundation of this method. By raising or lowering the system's temperature, the surfactant can create a gel-like structure that traps the dispersed phase.

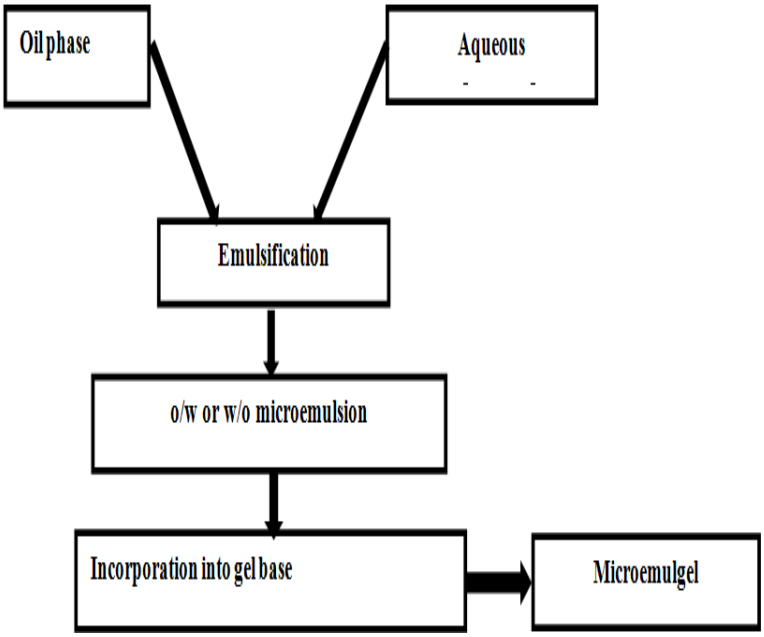

Fig: Preparation Method of Microemulgel

Future Prospective:
One of the main challenges in the formulation and development of pharmaceuticals is their hydrophobic character. Hydrophobic medications have low water solubility and absorption, which is their biggest drawback. It could be challenging to distribute a medication of this kind within the biological system. There are a number of drawbacks to their topical formulations, such as lotion, cream, and ointment. They are inherently sticky, making application uncomfortable. They also have a lower spreadability and are less effective when rubbed. Additionally, they demonstrate stability issues. Gels are now used more often in both medicinal preparation and cosmetics. A gel may consist of a solid preparation rendered immobile by a physical phenomenon and a network of molecules composed of fibers created from a little amount of gelatin.

Evaluation of Microemulgel:
1) Spreadability:[17]
The spreading diameter between two glass slides can be used to determine the microemulgel'sspreadability. Weigh around 0.5g of the sample and place it in the center of the glass plate to determine the spreadability of the gel in centimeters (creating a circle). After that, push between the two slides, set a second glass plate on top of the first one, and wait five minutes.

2) Skin irritation test: [18]
The preparation is applied to neatly shaved rats' skin; any adverse reactions, including color or morphological changes, should be watched for up to 24 hours. In most studies, the whole group of eight rats is used. If there's no irritation, the test passes. If the sign of skin irritation affects more than two animals, a second trial need to be carried out.

3) Study of Drug Release Kinetics:
To examine the drug release kinetics and process, the combined release data were fitted to models that represented Zero order, First Order, and Higuchi Models.

4) Stability Study:[19]
Samples of the drug microemulsion formulation were placed in stability chambers for two months, with temperatures ranging from 250 C to an accelerated 40±20 C34. The samples were sealed in ampoules. For the purpose of assessing their chemical and physical stability, duplicate samples were eliminated at 0, 1, and a few months. A globule size analyzer was

used to quantify the mean globule size and zeta potential following dilution with water, and the physical stability was assessed visually for physical alterations (drug precipitation, phase separation, etc.). The molecule's UV visible spectroscopic process at 257 nm was measured in order to assess its chemical stability.

5) Physical Examination: [20]
The physical characteristics of the generated microemulgel formulations, including color, texture, homogeneity, phase separation, and pH, are visualized.

6) Droplet size micro emulsion: [21]
Using a particle size analyzer, the microemulsion's globule size distribution is ascertained.

7) Viscosity: [22]
The viscosity is tested in order to ascertain the formulations' rheological characteristics. Brookfield Viscometer The viscosity is measured using the rotational r type. The average of the three duplicate results is taken into account.

8) Conductivity: [23]
Using a digital conductometer, the electric conductivity of the micro-emulsion is measured at room temperature. After obtaining three copies of the results, an average is calculated.

9) Rheological study:
Viscosity at 37 °C is measured using a Brookfield viscometer.

10) Franz Diffusion Cell:
The drug release investigations employ a Franz diffusion cell, which has an effective diffusion area of 3.14 cm2 and a cell volume of 15.5 ml. When 1 g of microemulgel is put to the surface of egg emulsion-based emulgel, it has an effect that is 2, 3, or 4 times more than that of a typical marketed product, requiring less dosage and dosing frequency in comparison to traditional medications.In the end, there are far fewer adverse effects and a higher level of patient acceptability.

CONCLUSION

Microemulgel is said to be the greatest method for topical distribution because of its numerous advantageous qualities, including its prolonged shelf life, biocompatibility, and ease of dispersal and removal. By mixing microemulsion into the gel basis, microemulgel may deliver hydrophobic drugs while still offering the advantages of both. Though there aren't many commercially available microemulgel formulations at the moment, there is a lot of room for advancement and study. In the future, microemulgel will be very useful for cutaneous care.

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