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REVIEW ON EMULSION AND MICROEMULSION IN TOPICAL DELIVERY SYSTEM

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ABSTRACT

Microemulsions have emerged as novel vehicles for drug delivery which allow sustained or controlled release for percutaneous, peroral, topical, transdermal, ocular and parenteral administration of medicaments. Microemulsions are thermodynamically stable o/w emulsions of mean droplet size approximately 100–400 nm, whereas nanoemulsions are thermodynamically unstable o/w emulsions of mean droplet size approximately 1 to 100 nm. Their inner oil phase allows the solubilization of lipophilic drugs, achieving high encapsulation rates, which are instrumental for drug delivery. While most of the micro/nanoemulsions on the market are held by the cosmetic industry to enhance the activity of drugs used in skincare products, the development of novel pharmaceutical formulations designed for the topical, dermal and transdermal administration of therapeutic drugs is being considered. The delivery of poorly water-soluble molecules through the skin has shown some advantages over the oral route, since drugs escape from first-pass metabolism; particularly for the treatment of cutaneous diseases, topical delivery should be the preferential route in order to reduce the number of drugs used and potential side-effects, while directing the drugs to the site of action. Thus, nanoemulsions and microemulsions represent versatile options for the delivery of drugs through lipophilic barriers, and many synthetic and natural compounds have been formulated using these delivery systems, aiming to improve stability, delivery and bioactivity. Many widely used topical agents like ointments, creams, lotions have many disadvantages like sticky in nature, causing uneasiness to the patient when applied, have lesser spreading co-efficient so applied by rubbing and they also exhibit the problem of stability. Microemulsion is having stability problem due to having low viscosity but can be overcome by incorporation into topical DDS causes improved viscosity and hydrating stratum corneum which will increase drug dermal permeation and the skin flux. Microemulsion based gel helps in the, incorporation of hydrophobic drugs into the oil phase and then oily globules are dispersed in an aqueous phase resulting in oil/water emulsion.

Keywords: Microemulsion, Nanoemulsion, Skin Drug Delivery, Skin Bioavailability, Formulations.

I. INTRODUCTION

In 1959, Schulman et al. visualized the existence of small emulsion-like structures by electron microscopy and subsequently coined the term “microemulsions” . The term has been defined and redefined by many authors. In this review, however, we will use the most general definition provided by Danielsson and Lindman in 1981 . a microemulsion is a single, optically isotropic structured solution of surfactant, oil, and water.

Current skin drug delivery methods play a pivotal role in achieving effective therapeutic outcomes and addressing various dermatological conditions. One such promising technology is microemulsions (MEs), which have gained significant attention in the pharmaceutical research field due to their unique properties and potential applications in delivering both hydrophilic and hydrophobic drugs. To reach the target site, the administered drug undergoes a pharmaceutical phase (i.e., characterized by its release from the dosage form), a pharmacokinetic phase (i.e., undergoing absorption, distribution, metabolization and, eventually, a portion of it is excreted from the body before reaching the target site) and a pharmacodynamic phase (when reaching the systemic circulation and the site of action)

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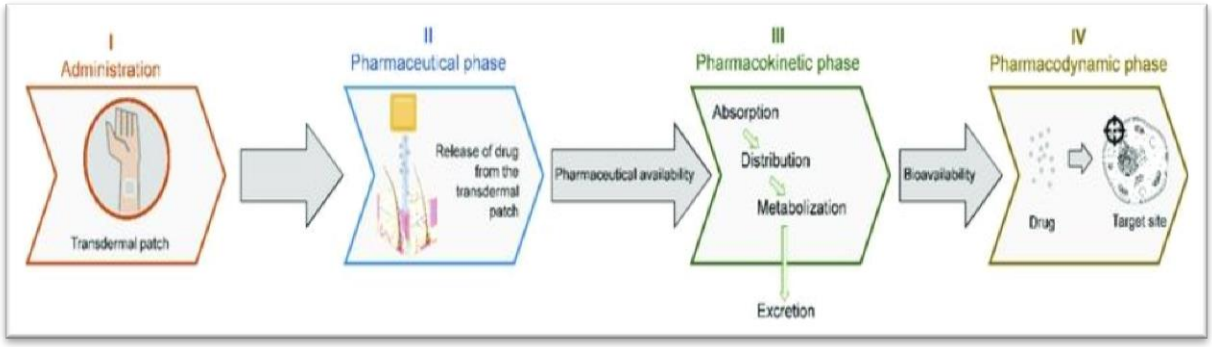

FIGURE - Drug administration to it's pharmacological effect.

Among the various formulations in the field of nanotechnology, nanoemulsion represents a versatile option for the delivery of drugs through lipophilic barriers. Currentlyhis technology is already under use in several industries, as is the case in food, biomedical and cosmetic industries .Nevertheless, the development of nanoemulsions for skin delivery of either cosmetics or therapeutic drugs has arisen as a strategy to overcome some limitations, such as the penetration and absorption of these active molecules.

In this comprehensive review, we aim to provide a detailed overview of microemulsions as an advanced drug delivery system, with a particular emphasis on their potential for cutaneous drug delivery. We will discuss the formulation and characterization of microemulsions, including the different types of microemulsions, their composition, stability, and characterization techniques. Moreover, we will highlight the advantages and limitations of microemulsions as a drug delivery system, as well as their potential use in topical formulations. Overall, this review aims to provide valuable insights into the role of microemulsions in overcoming drug delivery

☆ PHARMACEUTICAL EMULSION

DEFINATION:

Emulsion are heterogeneous system composed of at least two immiscible liquid,water and oil ,one of which is usually uniformly dispered as fine droplets throughout the other liquid phase by mechanical agitation process.

• CLASSIFICATION OF EMULSION

Emulsions are commonly used for topical pharmaceutical and cosmetic products, such as lotions and creams. The largest group of emulsions commercially available as medicines are dermatological products for topical application. Emulsions can be designed to facilitate drug penetration into and/or through the skin. Both oil-in-water and water-in-oil emulsions have been extensively used to deliver drugs and cosmetic agents to the skin, depending on the property of active agents and the indications of the medicines. Droplet size of the emulsion may influence the drug penetration through the skin, but the effect often is not clinically significant. The evaporation of volatile excipients can occur and so affect the drug permeation across the skin. Judicious selection of an appropriate emulsifying agent and additional stabilizer is a critical factor in the design and development of emulsions.

Additionally, o/w emulsions are the most appropriate for topical application, as they allow the penetration of hydrophilic substances through the Stratum corneum of the skin. emulsions exhibit metastable colloid behavior, exhibiting flocculation, creaming and separation phenomena as a result of droplet interactions . To counter this type of phenomenon, it is necessary to maintain the stability of the emulsion. In this sens number of mechanisms are available, such as electrostatic, steric stabilization or stabilization by solid particles .However, the stability of most pharmaceutical formulations is guaranteed by the addition of surfactants. The amphiphilic nature of surfactants induces a reduction in the interphase voltage of the systems. As can be seen below figure . the structure of the surfactants causes them to be adsorbed at the interface of the mixture, as they have a lipophilic "tail" and a hydrophilic "head".

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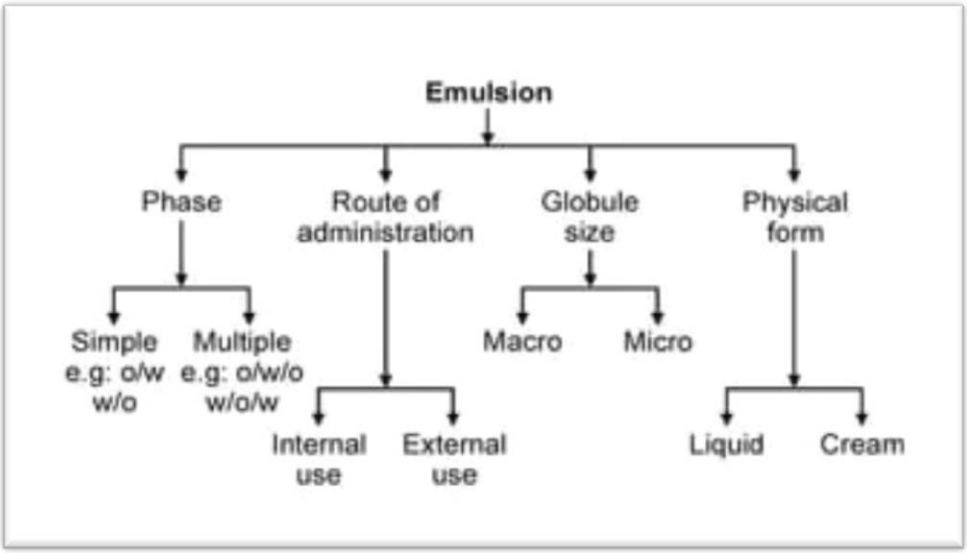

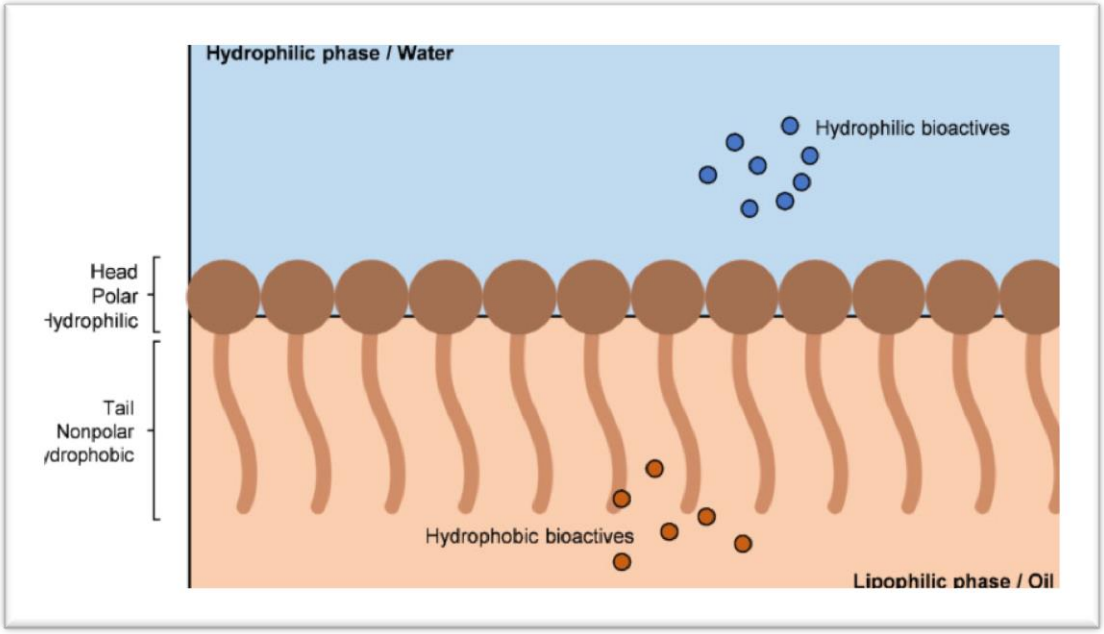

FIGURE – Schemetic representation of surfactant placement in the oil &water interface.

The primary surfactants are those whose properties allow the stabilization of the emulsions without the need to add any other component for this purpose . Secondary surfactants, or cosurfactants, have polar and nonpolar structures in the same molecule (amphiphilic characteristics) and serve to increase the thermodynamic stability of these systemsIn order to ensure the long-term stability of the emulsion, avoiding or postponing phenomena such as coalescence, an appropriate choice of surfactants is important.

The addition of one or more surfactants to this immiscible mixture guarantees the formation of a macroscopically homogeneous and microscopically heterogeneous phase. When considering the aforementioned steps, it is possible to summarize the production of an emulsion by shown in below figure 3.

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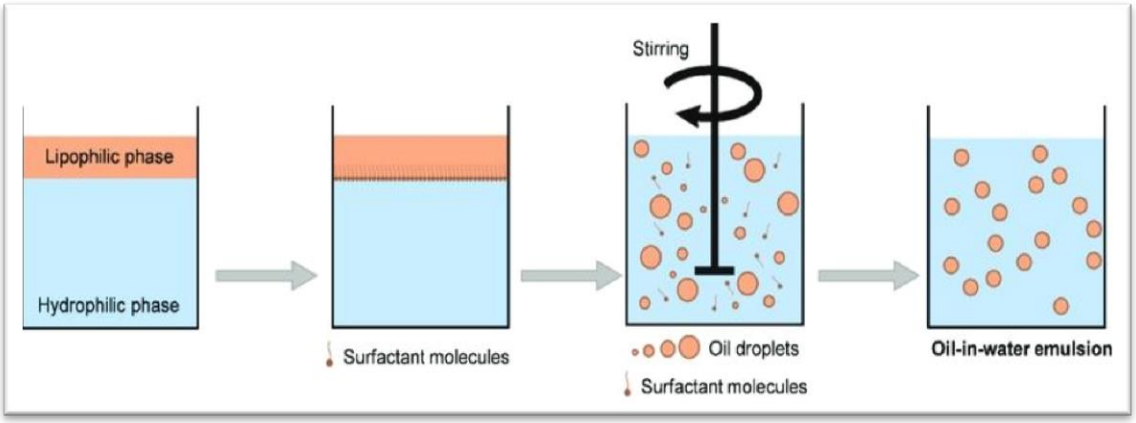

FIGURE - Production of an O/W Emulsion

II. METHOD OF FORMULATION

Commercially, emulsions are prepared in large volume mixing tanks and refined and stabilized by passage through a colloid mill or homogenizer. Extemporaneous production is more concerned with small scale methods. Several methods are generally available to the pharmacist. Each method requires that energy be put into the system in some form. The energy is supplied in a variety of ways: trituration, homogenization, agitation, and heat.

The methods commanly used to prepare the emulsion are broadly classified into two types.

A) Trituration Method

B) Bottle Method

A) Trituration Method

The method consist of two methods.

a) Dry gum mehod

b) Wet gum method

a) Dry gum method:

It is also known as continental method. The continental method is used to prepare the initial or primary emulsion from oil, water, and a hydrocolloid or "gum" type emulsifier (usually acacia). The primary emulsion, or emulsion nucleus, is formed from 4 parts oil, 2 parts water, and 1 part emulsifier. The 4 parts oil and 1 part emulsifier represent their total amounts for the final emulsion.

In a mortar, the 1 part gum is levigated with the 4 parts oil until the powder is thoroughly wetted; then the 2 parts water are added all at once, and the mixture is vigorously and continually triturated until the primary emulsion formed is creamy white and produces a "crackling" sound as it is triturated (usually 3-4 minutes).

Additional water or aqueous solutions may be incorporated after the primary emulsion is formed. Solid substances (e.g., active ingredients, preservatives, color, flavors) are generally dissolved and added as a solution to the primary emulsion. Oil soluble substance, in small amounts, may be incorporated directly into the primary emulsion. Any substance which might reduce the physical stability of the emulsion, such as alcohol (which may precipitate the gum) should be added as near to the end of the process as possible to avoid breaking the emulsion. When all agents have been incorporated, the emulsion should be transferred to a calibrated vessel, brought to final volume with water, then homogenized or blended to ensure uniform distribution of ingredients.

b) Wet Gum Method:

In this method, the proportions of oil, water, and emulsifier are the same (4:2:1), but the order and techniques of mixing are different. The 1 part gum is triturated with 2 parts water to form a mucilage; then the 4 parts oil is added slowly, in portions, while triturating. After all the oil is added, the mixture is triturated for several minutes to form the primary emulsion. Then other ingredients may be added as in the continental method.

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Generally speaking, the English method is more difficult to perform successfully, especially with more viscous oils, but may result in a more stable emulsion.

B) Bottle Method:

It is also known as forbes method. This method may be used to prepare emulsions of volatile oils, or oleaginous substances of very low viscosities. It is not suitable for very viscous oils since they cannot be sufficiently agitated in a bottle. This method is a variation of the dry gum method. One part powdered acacia (or other gum) is placed in a dry bottle and four parts oil are added. The bottle is capped and thoroughly shaken. To this, the required volume of water is added all at once, and the mixture is shaken thoroughly until the primary emulsion forms. It is important to minimize the initial amount of time the gum and oil are mixed. The gum will tend to imbibe the oil, and will become more waterproof.

It is also effective in preparing an olive oil and lime water emulsion, which is self-emulsifying. In the case of lime water and olive oil, equal parts of lime water and olive oil are added to the bottle and shaken. No emulsifying agent is used, but one is formed “in situ” following a chemical interaction between the components. What emulsifying agent is formed?

□ INSTABILLITY OF EMULSION:

An emulsion is said to be stable.If it remain such as after its preparation i.e dispersed globules are uniformly distributed throughout the dispersed medium during it storage.

Deviations from the ideal behavior of an emulsion is knownas instabillity of emulsion.

Instabillity of emulsion may be classified into four phenomenon those are-

1) cracking and Brecking(Coalescence)

2) Creaming

3) Phase inversion

4) Flocculation

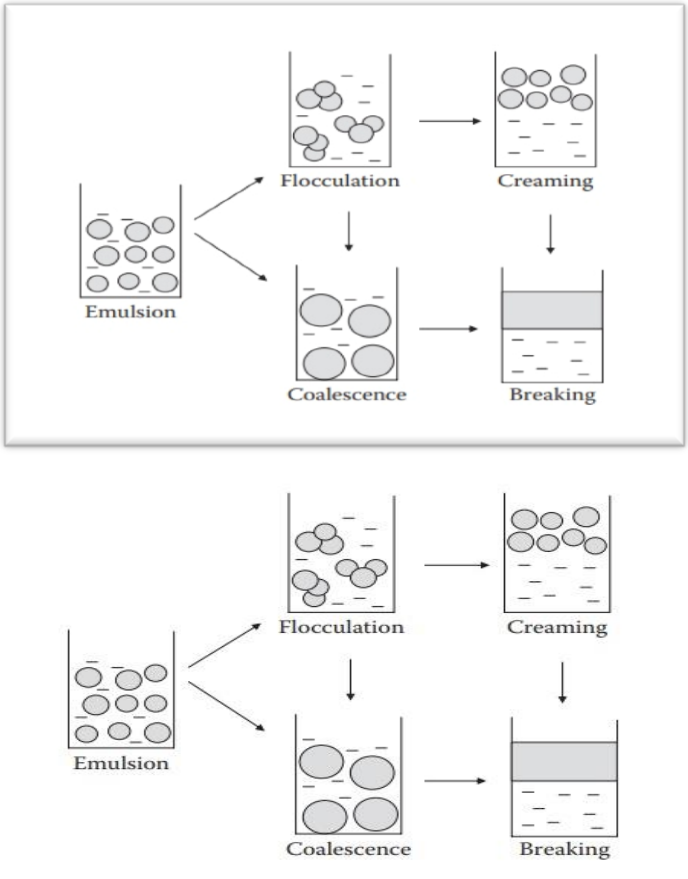

FIGURE - Different types of instabillity of emulsion

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1) Cracking and Brecking :

Cracking mean the separation of two layers of disperse and continuous phase, Due to the coalescence of disperse phase globules which are difficult to redispers.

Cracking of emulsion can be due to:

1. addition of an incompatible emulsifying agent,
2. chemical or microbial decomposition of emulsifying agent,
3. addition of electrolytes,
4. exposure to increased or reduced temperature or change in pH
5. By addition of common solvent

2) Creaming:

Creaming is the upward movement of dispersed oil droplets in an o/w emulsion, whereas sedimentation, the reverse process, is the downward movement of dispersed-phase droplets. Creaming involves visually evident separation of two layers that differ primarily in the number density of the dispersed phase, and, thus, show optical differences. These processes take place due to the density differences in the two phases and can be reversed by shaking. Creaming is undesirable because a creamed emulsion increases the likelihood of coalescence due to the closer proximity of the globules in the cream and because of the nonuniformity of the creamed emulsion.

3) Phase inversion:

An emulsion is said to invert when it changes from an o/w to a w/o emul-sion, or vice versa. Phase inversion can occur by the addition of an elec-trolyte or by changing the phase volume ratio. Addition of monovalent cations promotes the formation of o/w emulsions, whereas the addition of divalent cations increases the propensity toward the formation of w/o emulsions. For example, an o/w emulsion stabilized with sodium stearate can be inverted to a w/o emulsion by adding calcium chloride to form cal-cium stearate.

4) Flocculation:

Is the process that occurs when the emulsion droplets aggregate into small or large clusters or “flocks” without breacking the stabillizing layer at the interface.

Flocculation is defined as a weak reversible association of globules in emulsions.

However these aggregates can easily be redispersed upon shaking.Flocculation can be reversed by agitation. increasing the concentration of the emulsifier or adding a higher HLB emulsifier.

☆ MICROEMULSION:

Defination:

Microemulsions are thermodynamically stable, optically transparent, isotropic dispersions of aqueous and hydrocarbon liquids stabilized by an interfacial film of surfactant molecules.

Microemulsions show diverse structural organizations due to wide range of surfactant concentrations, water-oil ratios, temperature etc...

CLASSIFICATION:

On the basis of composition of water and oil portion microemulsion are classified into three types:

1. Oil in water microemulsion (O/W):

Oil droplet are scatter in water phase or aqueous phase.

2. Water in oil microemulsion(W/O):

Water droplet are scatter in oil phase or lipophilic

3. By contineous microemulsion:

Micro area oil & water are interspersed within system.

ADVANTAGES OF MICROEMULSION:

1. Increase the rate of absorption
2. Eliminates variability in absorption
3. Helps solubilize lipophilic drug

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4. Provides a aqueous dosage form for water insoluble drugs
5. Increases bioavailability
6. Various routes like tropical, oral and intravenous can be used to deliver the product.
7. Rapid and efficient penetration of the drug moiety
8. Helpful in taste masking

DISADVANTAGES OF MICROEMULSION:

1. Use of a large concentration of surfactant and co-surfactants.
2. Limited solubilizing capacity for high-melting substances.
3. The surfactant must be nontoxic for using pharmaceutical applications.
4. Microemulsion stability is influenced by environmental parameters such as temperature and pH.
5. It is exagerrated by temperature associate hydrogen ion cocentration.

☆ MICROEMULSION AS TRANSDERMAL DRUG DELIVERY VEHICLE:

Transdermal drug delivery offers several advantages over the oral route of administration: it avoids hepatic metabolism, the administration is simpler and more convenient for th e patient, and the treatment can be discontinued immediately if necessary.
Despite the enormous potential of transdermal delivery of pharmaceuticals, only a few medication formulations are commercially accessible.
The primary cause is the barrier function of human skin, which is thought to be the most impenetrable epitheliu m to external chemicals .

☆ MECHANISM OF SKIN PERMEATION:

The epidermis is the outermost layer of the skin, covering the dermis, the active layer of the skin that contains the blood supply, sebaceous glands, nerve receptors, and hair muscles.Beneath the dermis is a layer of fat. Although the stratum corneum, a layer that regulates drug penetration, is only 15-20 μm thick, it offers a highly efficient barrier to penetration. The skin is a very diverse membrane with a diversity of cell types. Transcellular, intercellular, and appendageal (via eccrine (sweat) glands or hair follicles) are the three ways that the medicine can penetrate the skin. Since appendages occupy very low surface area this means permeation is less significant under normal condition.

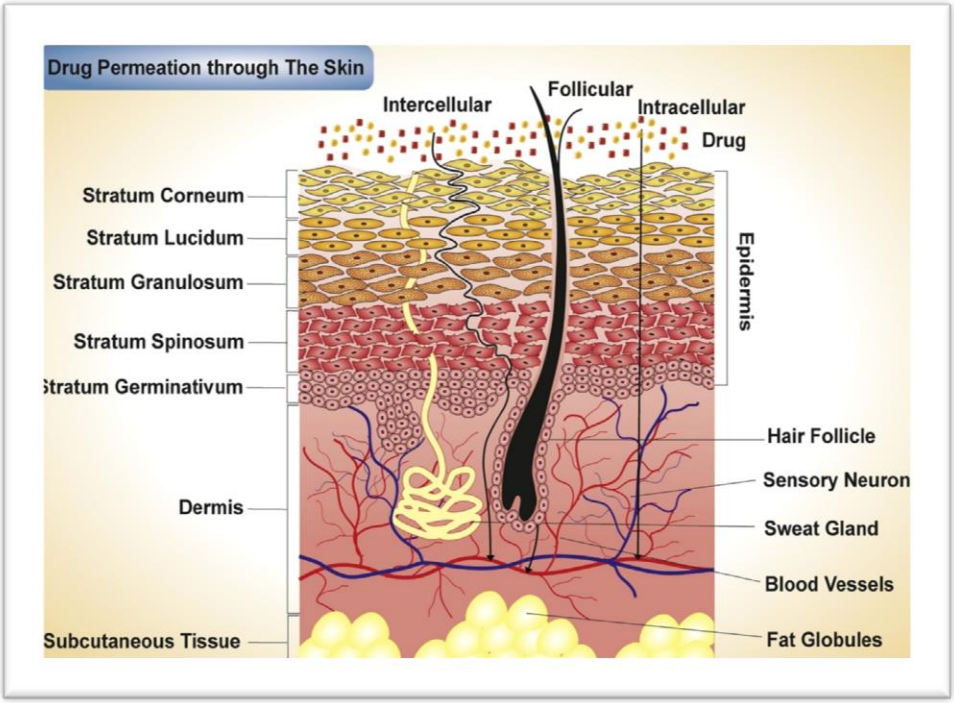

FIGURE - Schemetic representation of drug permeation through the skin.

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Nevertheless, this route is more important in iontophoretic delivery . The intercellular spaces are made up of a mixture of lipids, including cholesterol and its sulphates, free fatty acids and their esters, and cem-
mides. Recent advancements in spectroscopic techniques provide intriguing molecular insights that could expla in the skin's impermeability through repeated partition and diffusion across structured bilayers . Three factors primarily influence transdermal drug permeability: the drug's mobility in the vehicle, the drug's release from th e vehicle, and drug penetration through the skin As a result, researchers are challenged to develop formulation s that increase the drug's permeability without permanently altering the function of the skin barrier.

1. Direct affect on skin

a) Intracellular keratin denaturation or medification Swelling and increased hydration are caused by conformation.

b) The affection of desmosomes, which are cell structures called macula adherens that are specialised for cell-to-cell adhesion and that keep corneocytes (dead cells of the stratum corneum) cohesive c)Lipid bilayer modification lowers penetration resistance. d. Modifying the stratum corneum's solvent characteristics to alter drug partitioning e. Applying a solvent capable of removing the stratum corneum's lipids and reducing its resistance to penetration.

2) Modification of formulation

a) A volatile solvent creates a supersaturation state, which reduces the active ingredient to a state that is only thermodynamically active.

b) Selecting enhancer molecules for the vehicle that improve skin penetration and act as good solvents for the active ingredient will improve the drug's partition into the stratum corneum.

c) Enhancers that produce liquid pools within the bilayers, such as oleic acid, or that uniformly disrupt the bilayers, such as Azone melecules (Azone (1-dodecylazacycleheptan-2-one or lauro capram), are the first molecules specifically made as a skin permeation enhancer. These enhancers can help the active ingredient diffuse through the skin.

As a surfactant, azone improves the skin transport of many medications, such as steroids, antibiotics, and antiviral medicines .The desired substance's permeability can occasionally be increased more when many enhancing effects work in concert. Recent comprehensive reviews by Handgraft and Williams and Barry provide more thorough explanations and a variety of instances of the enhancing methods.

☆FORMULATION OF MICROEMULSION

When creating microemulsions for drug delivery applications, formulation is an essential component.The microemulsion system can have the appropriate physicochemical characteristics, including stability, size, and drug loading capacity, thanks to a carefully planned formulation The oil phase, surfactant, co-surfactant, and aqueous phase are the four fundamental parts of microemulsions The drug's physicochemical characteristics and the preferred mode of administration determine which of these ingredients are used One important factor in determining the stability of the microemulsion is the oil phase, which can be either hydrophilic or hydrophobic The drug's solubility and compatibility with the surfactant are two examples of the factors that go into choosing the right oil phase . Another essential element that stabilises the microemulsion system and reduces the interfacial tension between the water and oil phases is the surfactant The choice of surfactant is based on its compatibility with the co-surfactant and its capacity to form a monolayer at the oil-water interface . Usually a short-chain alcohol or a glycol, the co-surfactant improves the surfactant's solubility and aids in microemulsion stabilisation .p Depending on the system's intended pH, either water or an aqueous buffer can make up the aqueous phase .Furthermore, the drug's solubility in microemulsion can be enhanced by the presence of co-solvents, such as ethanol .

Microemulsions can be prepared using a variety of techniques, such as ultrasound-assisted emulsification , spontaneous emulsification .and phase inversion temperature (PIT). By heating the mixture of oil, surfactant, co-surfactant, and water above the phase inversion temperature and then cooling it to room temperature, the PIT method creates a microemulsion . With continuous stirring, the aqueous phase is gradually added to the mixture of oil, surfactant, and co-surfactant in the spontaneous emulsification method . In order to create

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microemulsions, high-frequency ultrasound waves are applied to a mixture of oil, surfactant, co-surfactant, and aqueous phase in a process known as ultrasound- assisted emulsification .

The intended mode of administration, the drug's physicochemical characteristics, and the stability of the microemulsion system should all be taken into account when formulating microemulsions .Enhancing the stability and drug loading capacity of the microemulsion can be achieved by utilizing appropriate oils, surfactants, and co-surfactants .The quality of the microemulsion system is also highly dependent on the formulation technique chosen.

COMPONENT OF FORMULATION:

1) Surfactant:

When formulating microemulsions for drug delivery, the choice of surfactant is crucial for achieving successful outcomes Several factors should be considered when selecting a surfactant, including microemulsifying properties, compatibility with the route of administration, and the solubility of active ingredients. There are different classes of surfactants . Ionic and nonionic surfactants are the two main types with ionic surfactants being further divided into anionic, cationic, and amphoteric surfactants based on the dissociation of their hydrophilic group in water . Cationic surfactants such as hexadecyltrimethylammonium bromide and dodecyl trimethyl ammonium bromide , anionic surfactants such as dioctyl sodium sulfosuccinate and sodium dodecyl sulfate , and amphoteric surfactants such as lecithins and phospholipids have been commonly used in studies. Nonionic surfactants, which include a wide range of options such as polysorbate 80, PEG-8 , Pluronic F-68 and vitamin E TPGS , do not dissociate into ions in aqueous solutions, and are classified based on their specific hydrophilic group . Alkyl polyglycosides such as Oramix CG-110 have gained attention for their excellent biodegradability and renewable sources, making them an attractive option for microemulsion formulation for various applications, including skin delivery . The selection of surfactant should be based on the specific requirements of the intended application.

The selection of a surfactant is essential for the successful formulation of microemulsions for drug delivery . When choosing a surfactant, a number of factors should be taken into account, such as the solubility of the active ingredients, compatibility with the route of administration, and microemulsifying properties. Surfactants are classified into various classes .The two primary types of surfactants are ionic and nonionic , Ionic surfactants can be further classified as anionic, cationic, or amphoteric surfactants according to how their hydrophilic group separates in water . Research has often used cationic surfactants like sodium dodecyl sulfate and hexadecyl trimethylammonium bromide and dodecyl trimethyl ammonium bromide amphoteric surfactants like lecithins and phospholipids .and anionic surfactants like dioctyl sodium sulfosuccinat. and sodium dodecyl sulfate , and cationic surfactants like lecithins and phospholipids .

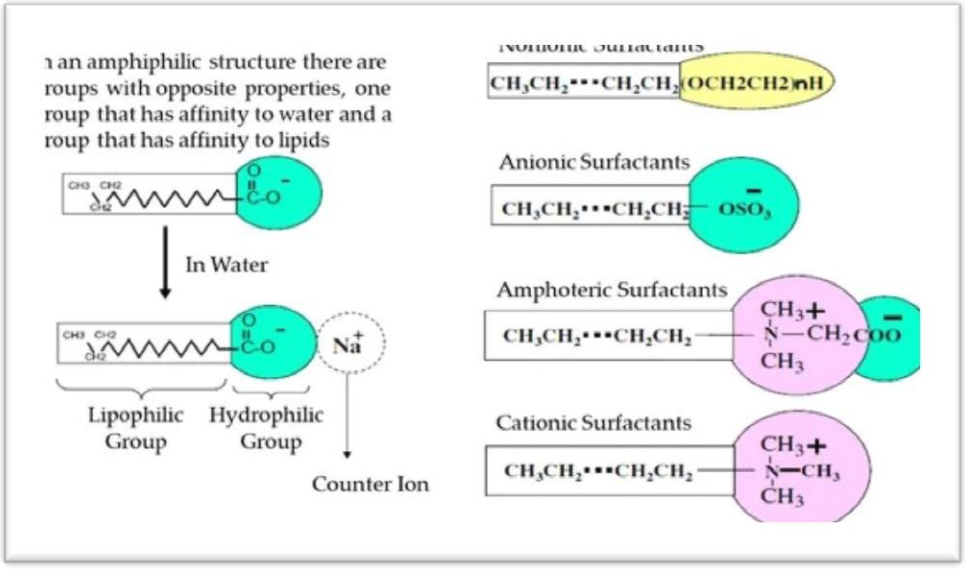

FIGURE - Structure &Classification of surfactant.

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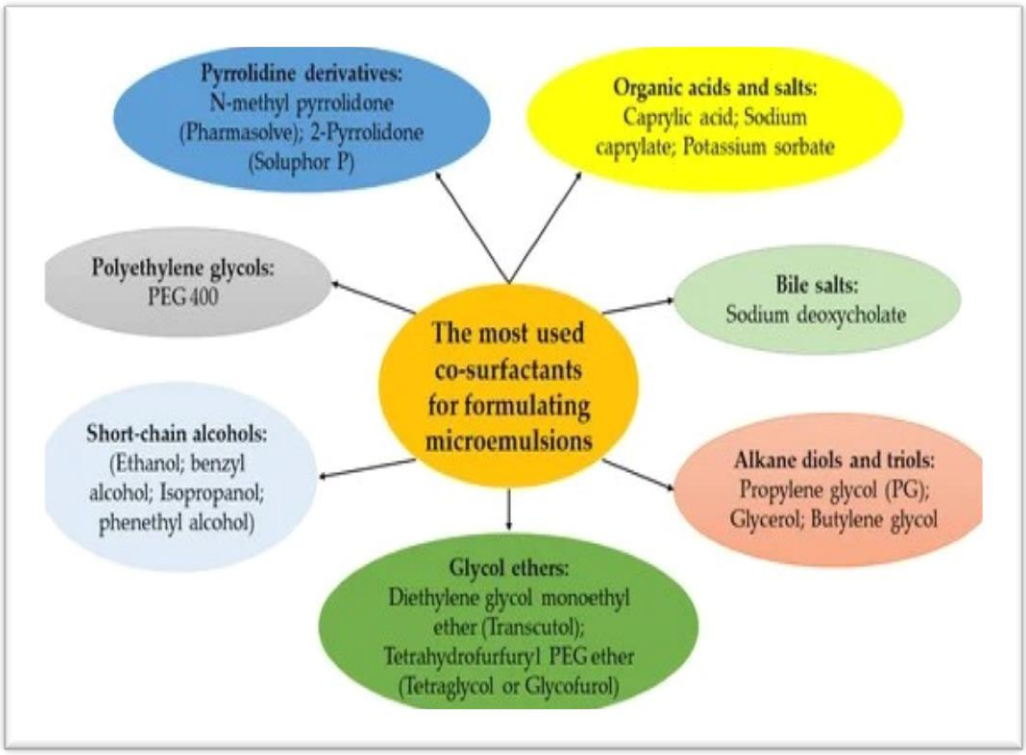
When surfactants—which come in a variety of forms and are categorized according to their particular hydrophilic group—do not dissociate into ions in aqueous solutions. Examples of nonionic surfactants are polysorbate 80, PEG-8 Pluronic F-68 and vitamin E TPGS . Oramix CG-110 and other alkyl polyglycosides have drawn interest due to their exceptional biodegradability and renewable source, which makes them a desirable choice for microemulsion formulation for a range of applications, including skin delivery . The particular needs of the intended application should guide the surfactant selection process.

2) CO-Surfactant:

In microemulsion formulations, the addition of a co-surfactant is frequently required to induce a much lower interfacial tension decrease .Co-surfactants that are frequently used include short-chain alcohols like ethanol and isopropanol, alkanediols like propylene glycol, sucrose ethanol blends, medium chain monoglycerides and diglycerides, alkyl monoglycosides, and geranio Furthermore, studies have demonstrated the amphiphilic and absorption-enhancing qualities of glycol ethers, like Transcutol®, which makes them popular co-surfactants for oral and dermal applications because of their strong solubilizing potency



Examples of the most often used co-surfactants in microemulsion formulations

The interfacial film may thin as a result of the addition of contaminants. Coch inhibits the development of liquid crystals.

Additionally dispersed between the aqueous and oil phases, these co-surfactants aid in reducing the hydrophilicity and lipophilicity of the two phases [5,6,13,14, 15]. Recent research has also looked into the formulation of microemulsions using natural co-surfactants such phospholipids and lecithin, which have been demonstrated to have good biocompatibility and the potential to be used in drug delivery applications.

3) Oil Phase:

Many types of compounds, such as fatty acids like oleic acid, alcohols like octanol and decanol, and esters of fatty acids or alcohols like isopropyl myristate, isopropyl palmitate, ethyl oleate, isostearyl isostearate, and cetearyl octanoate, can make up the oil phase in microemulsions . In oil phase formulations, medium-chain triglycerides of caprylic or capric acid as well as triesters of glycerol and acetic acid, including triacetin, are frequently used Furthermore, various terpenes have also been utilized in recent investigations , including limonene, cineole, camphor, and menthol. The drug's solubility, the intended use, and the stability of the microemulsion are some of the variables that influence the oil phase choice.

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4) Aqueous Phase

In order to achieve the necessary characteristics and functioning, the choice of aqueous phase in the microemulsion formulation is essential . The viscosity and stability of the microemulsion can be adjusted in addition to water by using viscosifiers like xanthan gel and Carbopol® . To assure the osmolarity with plasma and tear fluid in microemulsions meant for parenteral or ocular routes, NaCl is added. When lecithin is employed as a surfactant, buffer solutions are also added to maintain pH values between 7 and 8, which is crucial to preventing the degradation of phospholipids and triglycerides. Drug distribution can be enhanced by adding absorption enhancers , but their compatibility with the other ingredients in the microemulsion needs to be carefully considered to prevent any chemical incompatibilities that could damage

5) Active Pharmaceutical Ingredient

When creating microemulsions for drug delivery applications, choosing the right active pharmaceutical ingredient (API) is essential . The phase behaviour and microemulsion structure can be greatly influenced by the API's physicochemical characteristics, including logP, pKa, structure, molecular weight, and the presence of ionisable groups . For instance, the presence of diclofenac sodium hydrochloride may alter the characteristics of the resulting microemulsions by influencing ionic surfactants like dioctyl sodium sulphosuccinate. However, some surface-active active ingredients can increase the area where microemulsions form ,while others, like tricyclic amines, can function as co-surfactants and lower the amount of surfactant needed.

It is noteworthy that certain lipophilic substances have the potential to function as oils and either compete with or supplement the oil phase during the generation of microemulsions. Consequently, the quantity of surfactant or co-surfactant employed may need to be adjusted . In order to create a stable and efficient drug delivery system using microemulsions, it is imperative that the API be chosen and thoroughly studied .

The use of high surfactant concentrations in microemulsion formulation is another significant problem to take into account, since this may raise toxicity issues . Recent research has looked into ways to lower the surfactant concentration while enhancing the stability and performance of materials by using natural surfactants and co-surfactants, as well as the addition of stimuli-responsive polymers and particles.

☆ CHARACTERIZATION OF MICROEMULSION:

The characterization of microemulsions has been extensively researched in the literature due to their significance in the pharmaceutical industry . Microemulsions can be characterized using a variety of techniques, which can reveal details about their viscosity, droplet size, zeta potential, and thermodynamic stability.

Dynamic light scattering (DLS), which quantifies the size distribution of the droplets in the microemulsion, is a frequently used technique for microemulsion characterization. The polydispersity index, zeta potential, and particle size distribution of the droplets can all be determined using DLS, a quick, accurate, and non-invasive technique . The structure of the microemulsion droplets can also be seen using additional techniques like cryogenic transmission electron microscopy (Cryo-TEM) and transmission electron microscopy (TEM).

The thermodynamic stability of microemulsions can be assessed using different techniques, such as conductivity measurements, phase behavior studies, and centrifugation tests Measurements of conductivity can reveal details regarding the kind and quantity of surfactants contained in the microemulsion. Ternary phase diagrams are created as part of phase behavior studies in order to pinpoint the areas where microemulsion formation occurs and to ascertain the ideal microemulsion composition . Through the measurement of the droplet coentation rate, centrifugation tests can yield information regarding the stability of the microemulsion.

Microemulsion composition, preparation technique, and storage conditions are some of the variables that can impact microemulsion characterization . The droplet size and stability of the microemulsion can also be affected by the preparation technique, including the order of addition and speed of mixing . Temperature and duration of storage can have an impact on the microemulsion's physical and chemical characteristics, changing its stability.

When developing a drug delivery system, toxicity or biocompatibility must be taken into account. Numerous characterization techniques are used to appraise the possible toxicity and biocompatibility of microemulsions in order to determine their suitability as drug carriers . Assessing the impact of microemulsions on cell viability and proliferation is largely done through cytotoxicity assays. Cell viability and the cytotoxic effects of

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microemulsions are frequently assessed using methods like the MTT assay , Alamar Blue assay . and LDH release assay . Hemocompatibility assays, which include measurements of hemolysis, coagulation, platelet activation, and complement activation, are used to determine whether microemulsions are compatible with blood components.

In addition, tests for skin sensitivity and irritation, like the Draize test and patch testing, are carried out to ascertain whether microemulsions have the capacity to induce allergic reactions or skin irritation.

Furthermore, histological analysis, the evaluation of inflammatory responses, immunotoxicity assessments, and systemic toxicity studies in animal models are examples of in vitro and in vivo biocompatibility studies that shed light on how living tissues or organisms react to microemulsions . To find out if microemulsions cause DNA damage or mutations, genotoxicity and mutagenicity tests are conducted . For this, methods like the comet assay , micronucleus assay , and Ames test are used. Additionally, enzymatic degradation tests and research on the fate and clearance of microemulsions in biological systems are used to assess their biodegradation and biocompatibility .Researchers may assess the toxicity and biocompatibility profiles of microemulsions using these characterisation techniques, which offers important information about their safety and potential as efficient drug delivery systems.

In summary, the effectiveness and safety of microemulsions as a drug delivery mechanism depends heavily on their characterisation. Different methodologies can be used to evaluate the stability of the microemulsion and to characterise the microemulsion droplets. The best formulation and characterisation of microemulsions depend on a comprehensive understanding of the various aspects that can impact microemulsion characterisation. It is important to note that a variety of methods are available for assessing the toxicity and compatibility of microemulsions.

☆ LIFE SCIENCE APPLICATIONS OF MICROEMULSION

Due to their special qualities and possible uses in drug delivery, microemulsions have been thoroughly researched in the pharmaceutical research field . As previously stated, they are a desirable alternative for drug delivery due to their optical transparency, thermodynamic stability, and capacity to deliver both hydrophilic and hydrophobic drugs.

Microemulsions have demonstrated significant potential in resolving bioavailability issues and facilitating steady medication delivery. When it comes to medication delivery, Microemulsions have been applied in a number of applications, such as parenteral, topical, and oral management.

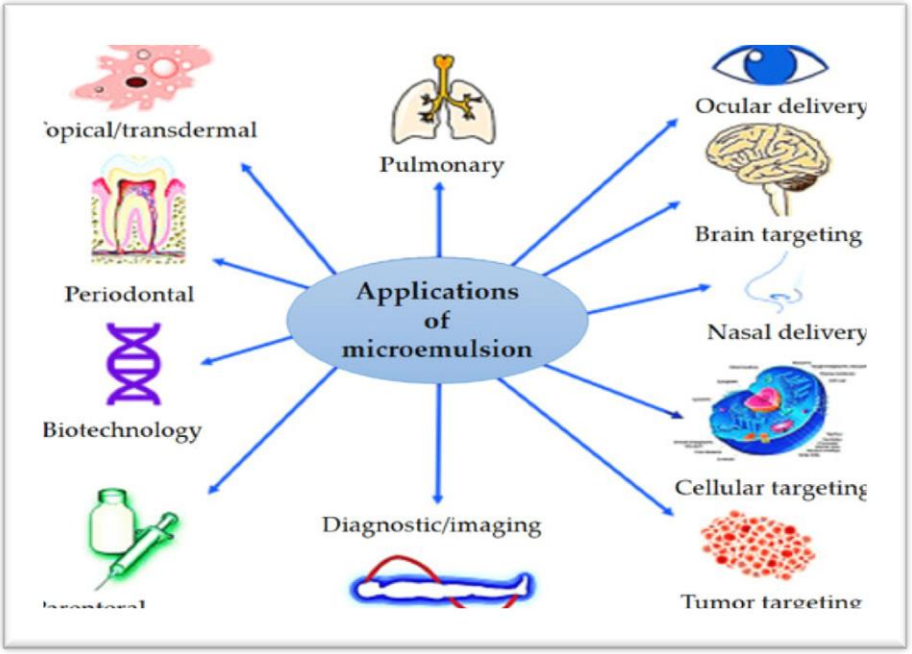

FIGURE - Application of microemulsion in drug & gene delivery

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In the past, oral microemulsions utilized to increase poorly soluble compounds' bioavailability medications [57]. As demonstrated by topical microemulsions potential to improve medication delivery throughout the epidermis [21]. Utilizing parenteral microemulsions in order to administer lipophilic medications and target the system of lymph.

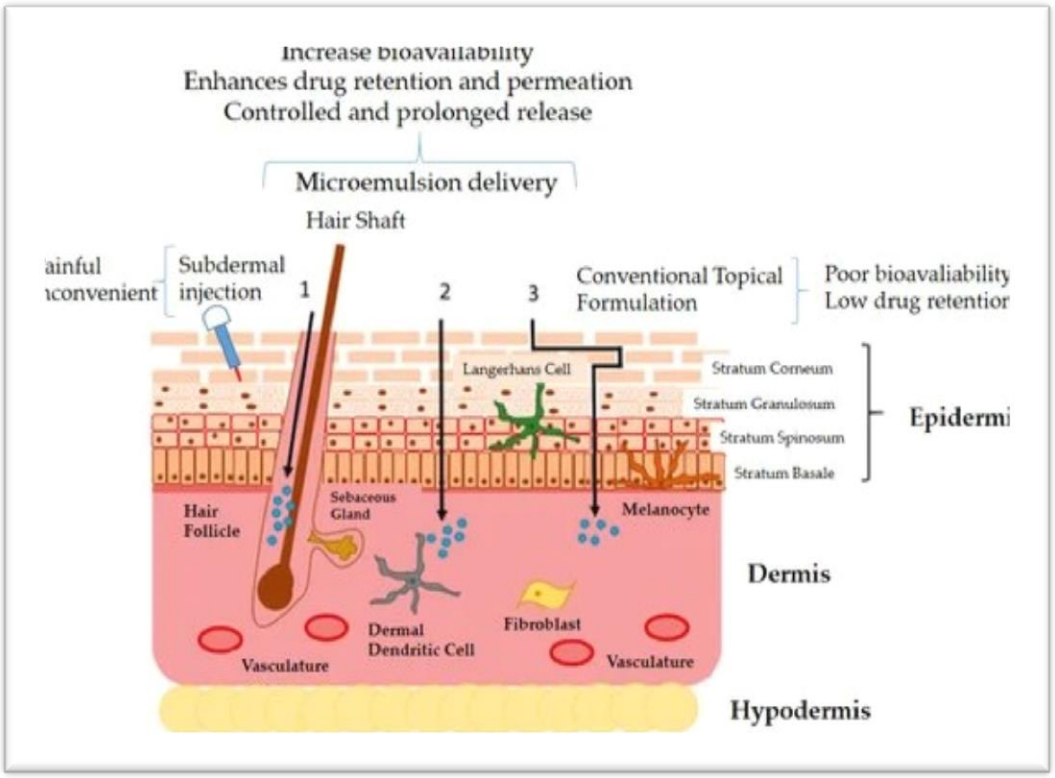

FIGURE - Different route of penetration of microemulsion through the skin

III. CONCLUSION

The skin is definitely a very promising route for drug administration and delivery. The ability to release drugs into the bloodstream at constant concentration levels, coupled with its high application area, the exemption of the first-pass effect and application comfort, make it the route of choice. Both microemulsions and nanoemulsions are carriers able to act as permeation/penetration enhancers through the skin due to the characteristics they bring together, allowing to overcome the barrier of the Stratum corneum. They may also increase the liposolubility of hydrophilic drugs, because a more nonpolar chain can be added to its more polar side, which gives ambivalence to molecules with bioavailability problems. The same happens with lipophilic substances, so that their more nonpolar side is added to a more polar chainMicroemulsions and nanoemulsions have similar macroscopic characteristics. Although they are microemulsions, they have a droplet size smaller than that of nanoemulsions, which can cause some confusion. However, what distinguishes nanoemulsions is their kinetic behavior, conferred by the Brownian motion of the particle. Microemulsions have a high thermodynamic stability, making their shelf life longer com- pared to classic emulsions. On the other hand, despite having unstable thermodynamics, nanoemulsions have kinetic stability, which makes them resistant to degradation problems. These characteristics make these systems advantageous in the preservation of drugs, so that they remain in good condition until the moment of application. The high thermodynamic stability, as well as the kinetics, make these systems able to increase the permeation capacity in the skin and the drug's sharing quotient, which promotes a good ability to overcome transdermal barriers. Both the behavior of these systems and the components of which they are made make these systems great promoters of skin permeation, which makes them good vehicles for transdermal drug delivery. The extensive study of these systems gave rise to a set of production methods, with different characteristics chosen according to the availability of the laboratory and the properties of the molecules to be transmitted. It should be noted that in the case of nanoemulsions, it is possible to produce systems capable of successfully increasing the bioavailability of drugs that are poorly

soluble in hydrophilic and lipophilic media, which can be a good solution to the problems faced by many drugs on the market. The existence of spontaneous production methods is of great value, especially in periods of resource containment, so there is a significant reduction in energy costs as well as high-cost machinery. These methods can be very advantageous in the case of large-scale produc- tion. However, it would be important to conduct further comparative studies between microemulsion and nanoemulsions system, in order to distinguish them unequivocally, which is the best method for application to the skin. This gap is due to the fact that they are still very novel in the scientific world.

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