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A BRIEF REVIEW ON METHOD PREPARATION AND IMPORTANCE OF MICROEMULSION IN DRUG DELIVERY SYSTEM

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ABSTRACT

The term "micro emulsion" refers to an unstable, isotopically transparent dispersion of two immiscible liquids, such as oil and water, stabilised by an interfacial coating of surfactant molecule. At the moment, micro emulsion is a growing industry with significant global impact in many technical applications. Among these uses are increased oil recovery, combustion, enzymatic catalysis, organic and bio-organic processes, the chemical synthesis of nanoparticles, cosmetics, medicines, agriculture, metal cutting, lubrication, food, and others. The purpose of this review article is to discuss the use of micro emulsions. An overview of the micro emulsion's structure, type, features of formation, stability, phase behavior, and the impact of additives, pressure, and temperature on that behavior is provided. It is crucial to be aware of the different techniques that can be used to fully define a micro emulsion system. Although micro emulsion is employed in many different industries, the pharmaceutical applications are highlighted in this review. [1,2,3,4]

KEYWORDS: Micro emulsion, surfactant, and delivery system

INTRODUCTION:

A surfactant and co-surfactant interfacial coating stabilizesmicro emulsions, which are thermodynamically stable isotopically transparent dispersions of two immiscible liquids, such as oil and water. In comparison to traditional emulsions, suspensions, and micellar solutions as well as the colloidal systems under investigation, micro emulsions have several advantages. Micro emulsions offer many types of medication carriers. The benefits of micro emulsions include spontaneous creation, simplicity in manufacturing and scaling up, thermodynamic stability, enhanced drug solubilization of hydrophobic medicines, and bioavailability . Based on the components, there are three different forms of microemulsions:

• Continuous aqueous phase micro emulsions of oil in water, in which oil droplets are scattered

• Bi-continuous micro emulsions, in which microdomains of both oil and water are interspersed within the systems. Water in oil micro emulsions, in which water droplets are scattered in the continuous oil phase.

An adequate mixture of surfactants and/or co-surfactants stabilizes the interface in all three forms of micro emulsions. [1-4]

HISTORY :

Hoar and Schulman introduce micro emulsions. A standard coarse emulsion can be made into a transparent solution by titrating it with medium-chain alcohols. By using the proper surfactants and co-surfactants, two immiscible liquids (oil and water) are combined to form a single phase in micro emulsions, which are thermodynamically stable isotropic systems. In the micro emulsion system, short to medium chain alcohols are typically regarded as co-surfactants. Surfactant and co-surfactant use lowers interfacial tension. Consequently, micro emulsions spontaneously occur, and their average droplet diameter ranges from 10 to 140 nm [1-4]

FORMULATION :

The micro emulsions are colloidal dispersions made up of an adequate amount of an oil phase, an aqueous phase, a surfactant, and a co-surfactant

Surfactants :

Stabilizing the system involves the application of surfactants. Surfactants are utilized to create micro emulsions by lowering the interfacial tension, which ultimately speeds up the dispersion process and creates a micro emulsion surrounding the droplet. They might be anionic, cationic, swatter ion, or non-ionic surfactants.

Co-surfactants :

Co-surfactants are chemicals that are added to a process to increase a surfactant's efficacy. These are employed to improve the micro emulsion surfactant system's ability to solubilize oil . Co-surfactants are short to medium chain length alcohols that have the ability to increase the fluidity of a surface by lowering interfacial tension. They are amines, alcohols, and Cholesterol

Oils :

Through its capacity to enter the tail group region of the surfactants, the oil component affects curvature. Short chain oil increases the negative culture and decreases HLB when compared to long chain alkenes .

Different types of oils are employed in the creation of micro emulsions, including:

- saturated fatty acids: auric acid, meristic acid, caprice acid. Unsaturated fatty acids include, for example, oleic, linoleic, and linolenic acids..
- Oleic acid, meristic acid, and auric acid methyl or ethyl esters are examples of fatty acid esters. Oil selectin is primarily used to ensure that a medication has a high soluble content. Utilize the oil to reduce the 750.the formulation's volume.

- Low allergic potential, good physiological compatibility, and high biocompatibility,

Component	Example
Oil	1)-saturated fatty acid- lauric acid, carpic acid 2)unsaturated fatty acid-oleic acid, linolic acid, linolenic acid 3)fatty acid ester-ethyl or methyl ester of lauric, oleic acid and myristic acid
Surfactant	1-polyoxyethylene/polysorbate/tween 20,40,60,80 2-sorbitan monolaurate, eggs lecithin 3-sodium dodecyl sulphate
Co-surfactant	1-ethanol, proranol, butanol, isopropanol, pentanol, hexanol 2-polyoxyethylene-10-oelyl ether 3-sodium monohexyl phosphate 4-cinnamic alcohol, cinamic alcohol

table no 1: component of microemulsion system [6-12]

The general composition of micro emulsions consists of the following elements:

(a) an oil phase;

(b) an aqueous phase containing hydrophilic active ingredients (preservatives and buffers may be present);

(c) a primary surfactant (anionic, non-ionic, or amphoteric); and

(d) secondary surfactant or surfactants. [1-4]

The Micro Emulsion's Structure Micro emulsions, also known as Micellar emulsions, are dynamic systems in which the interface fluctuates continually and arbitrarily.

They are structurally divided into three groups: water in oil, bi-continuous micro emulsions, and oil in water (o/w). Water droplets are distributed across the continuous oil phase to create w/o micro emulsions, whereas oil droplets are dispersed throughout the continuous aqueous phase to form o/w micro emulsions. When the proportions of water and oil are comparable in a system, bi-continuous micro emulsions may form. The mixing of oil, water, and surfactants can produce a variety of structures and phases, depending on the component ratios. Micro Emulsion's composition: Microemulsions, also known as Micellar emulsions, are dynamic systems in which the interface fluctuates continually and arbitrarily. They are separated structurally into three groups: bi-continuous micro emulsions, water in oil, and oil in water (o/w).

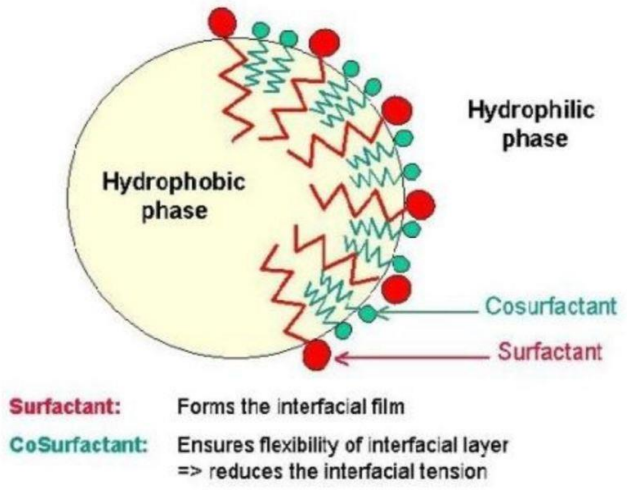

figure no :1structure of micro emulsion [6-12]

Classification of Micro Emulsion :

Winsor identified four different types of micro emulsion phases that are present in equilibrium and are referred to as Winsor phases.

- Winsor I (two phase system): upper oil layer and lower (o/w) micro emulsion phase are in equilibrium.
- The Winsor II (two phase system) upper (w/o) micro emulsion and lower surplus water are in equilibrium.
- Winsor III (three phase system): middle bi-continuous phase of o/w and w/o called) exists in equilibrium with upper phase oil and lower phase water.
- The Winsor IV (single phase system) creates a homogeneous mixture of oil, water, and surfactant. [6,-12]

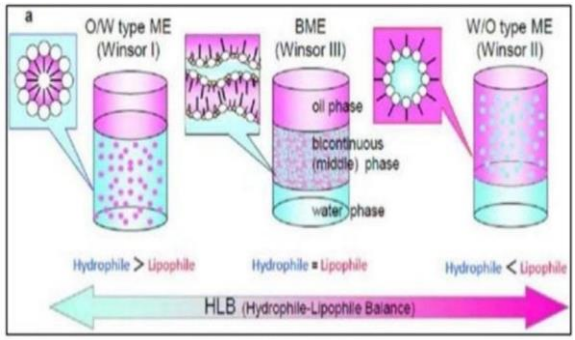

figure no 2: types of microemulsion [6-12]

MICROEMULSION PREPARATION METHODS :

Only when the oil/water interface's interfacial tension is kept at a very low level and the interfacial layer is kept highly flexible and fluid do micro emulsions occur. To stabilize the micro droplets created by extremely low interfacial tension, the surfactant concentration must be high enough to supply the necessary number of surfactant molecules.

PROCEDURE TO MAKE MICROEMULSION:

Titration Technique :

Fatty acid and oil are combined with a caustic solution to create a micro emulsion, which is then titrated with an alcohol surfactant until the combination becomes clear. It has been discovered that oils with larger chain lengths can create micro emulsions with considerable transmittances by the visible spectrum as the chain length of the surfactant increases. Additionally, it has been discovered that certain alcohols have varied effects on how micro emulsions develop. Short or branched alcohols produce the best results in terms of the highest percent transmittance and the widest range of oil (dispersed in water) concentration

Agitation Technique :

Oil and water phases can be mixed with a surfactant, and a surfactant is then added at a slow rate with gradual stirring until the system is transparent. The medicine is then dissolved in the lipophilic portion of the micro emulsion. The pseudo-ternary phase diagram will be used to calculate the quantity of surfactant and surfactant that needs to be added as well as the percentage of oil phase that can be included. Finally, the ultrasonicator can be used to produce distributed globules in the required size range. [14-20]

1. Factors influencing the development of the microemulsion system :

The packing ratio, oil phase, temperature, chain length, type, and nature of co-surfactant are all factors that affect how an oil or water swelling micro emulsion forms.

Ratio of packing: The type of micro emulsion is determined by the surfactant's HLB(Hydrophilic Lipophilic Balance), which has an impact on molecular packing and film curvature. In terms of packing ratio, also known as the crucial packing parameter, Israclachvili et al. (1976) and Mitchell and Ninham

(1977) outlined how the study of film curvature for surfactant connections leading to micro emulsion production works.

v/a/l is the critical packing parameter (CPP).

Where is the ideal head group area, l is the length of the surfactant tail, and v is the partial molar volume of the hydrophobic portion of the surfactant.

If the CPP (0-1) interface has a positive curvature toward the water and favors o/w systems.

When CPP is more than 1, the interface spontaneously curves in the direction of the oil (negative curvature), favoring micro-free emulsions.

Depending on the stiffness of the film, either continuous or lamellar structures may emerge at zero curvature when the HLB is balanced (p = 1). (zero curvature).

Oil phase, temperature, and surfactant property: The kind of micro emulsion that forms is dependent on the surfactant. A surfactant has a lipophilic tail group and a hydrophilic head group. When calculating the surfactant HLB in a specific system, the areas of these groups which are a measure of the differential tendency of water to swell the head group and oil to swell the tail area are crucial for specific formulation. The degree of polar group dissociation increases lessened in the presence of salt or when the surfactant is applied in high concentrations, and the resulting system may be typeless.

The chain length, co-surfactant kind, and nature Alcohols are frequently employed as a co-surfactant in the creation of micro emulsions.

Longer chain co-surfactants favour w/o type w/o type due to alcohol swelling more in the chain region than the head region, whereas adding shorter chain co-surfactants has a positive curvature effect because alcohol swells the head region more than the tail region, making it more hydrophilic and favoring o/w type. [14-20]

2. Elements That Influence Phase Behavior :

Salinity: O/W micro emulsion droplet size rises at low salinity. This is consistent with an increase in oil solubilization. The system becomes bi-continuous over an intermediate salinity range as salinity rises more. A continuous micro emulsion forms as salinity rises while globule size decreases. A complete phase change eventually ensues from additional salinity increase.

Alcohol concentration: Increasing the amount of low molecular weight alcohol used as a co-surfactant causes the w/o/bi continuous phase transition to happen, which then results in an o/w type micro emulsion. The phase transition for high molecular weight alcohol is exactly the reverse.

Surfactant Hydrophobic Chain Length: The expansion of the surfactant's hydrophobic chain length demonstrates the transition from an o/w micro emulsion to a w/o micro emulsion via a continuous phase.

pH: The micro emulsions that contain pH sensitive surfactants are affected by changes in ph. When using acidic or alkaline surfactants, this effect is more evident. By raising pH, carboxylic acids and amines change the phase behavior from w/o to o/w.

Oil's nature: Increasing an oil's aromaticity causes a phase change from o/w to w/o, which is the reverse of what happens when an oil's alkane carbon number rises.

Ionic Strength: The system transitions from an o/w micro emulsion in equilibrium with excess oil to the middle phase, and then to a w/o micro emulsion in equilibrium with excess water as the ionic strength increases.

TEST FOR MICRO EMULSION IDENTIFICATION:

1)Dilution test:

The continuous phase won't split or fracture if it is added in micro emulsions. It will continue to be stable if water is introduced to the o/w kind of micro emulsions.

2) Test for stains:

Water-soluble dyes like methylene blue or amaranth are added, and an oil-and-surfactant micro emulsion is created. Under a microscope, a drop of Micro emulsions is seen. The background is discovered to be either blue or red, and the globule will seem colourless.

3) A diluted aptitude test:

In order to determine whether the system exhibits any signs of separation, the micro emulsions created are diluted in ratios of 1:10 and 1:100 with double distilled water. It must be negative or neutral, indicating that the system is stable and that the micro-emulsion droplets have no charge. Zetasizer is used to calculate zeta potential. Since electrical charges on particles affect the rate of flocculation, zeta potential is essentially useful for evaluating flocculation.

4) A polydispersity :

The Abbes refractometer describes this feature. [1,9,10,11]

APPLICATION OF MICRO EMULSION :

Applications for Pharmaceuticals:

1. intravenous delivery.

2. Oral medication administration

3. Topical medication administration.

4. Delivery via the lungs and eyes.

5. Biotechnology uses micro emulsions.

Parenteral Administration: Due to the extremely low concentration of drug actually delivered to a targeted site, parenteral administration (particularly via the intravenous route) of medicines with restricted solubility is a significant concern in industry. When administered parenterally, micro emulsion formulations have specific advantages to macroemulsion systems due to the fine particle

Micro emulsions have a longer residence duration in the body because they are removed more slowly than coarse particle emulsions.

For parenteral distribution, o/w and w/o micro emulsion are both utilized. Few of the many micro emulsion systems described in the literature can be employed for parenteral delivery due to surfactant toxicity and parenteral use. By using a different strategy, Von Corsewant and Thorne 50 produced an almost balanced middle phase micro emulsion by substituting C3-C4 alcohols with parenterally acceptable co-surfactants, polyethylene glycol (400)/polyethylene glycol (660)/12-hydroxystearate/ethanol, while maintaining a flexible surfactant film and spontaneous curvature close to zero. In this application, the middle phase structure was chosen since it could integrate significantquantities of water and oil with little surfactant present.

Oral Administration: Micro emulsion formulations have various advantages over traditional oral formulations for oral administration, including improved clinical efficacy, increased absorption, and reduced drug toxicity 51. Therefore, it has

been suggested that micro emulsion is the best method for delivering medications such steroids, hormones, diuretics, and antibiotics.

Pharmaceutical peptide and protein medications have very strong physiological effects and are very targeted. The majority, though, are challenging to provide orally. less than 10% oral bioavailability in traditional formulations (those not based on micro emulsions)By oral administration, they are typically not therapeutically effective. The majority of protein medicines are only offered as parenteral formulations due to their poor oral bioavailability. Peptide medications, however, need to be dosed more than once since their biological half-lives are so short when given parentral. [1-3]

a cyclosporine micro emulsion formulation, has been introduced to replace Sand immune®, a cyclosporine crude oil-in-water emulsion formulation. Since Neural® is made with a finer dispersion, it absorbs more quickly, predictably, and with less variation between and among patients.

Delivery Through the Skin: Topical administration of medications can be superior to oral delivery for a number of reasons, one of which being the avoidance of the drug's hepatic first pass metabolism and associated adverse consequences. The drug's direct delivery to the damaged area of the skin or eyes, as well as its target ability, come in second. The delivery of prostaglandin E1 has been examined in hairless mouse models using both O/W and W/O micro emulsions. The Labra sol (C8 and C10 polyglycolysed glycerides) and Plural Oblique CC 497 as the surfactant mixture stabilized the micro emulsions, which were based on oleic acid or Glacier 44/14 as the oil phase.

Despite the fact that the o/w micro emulsion showed improved delivery rates, the authors came to the conclusion that neither system's penetration rates were sufficient for practical application. It has also been reported that indomethacin and diclofenac are trans dermally transported using a lecithin/IPP/water micro emulsion. After a one-day incubation, the IPP organ gel had altered the lipid organization in the human stratum cornea, according to FTIR spectroscopy and differential scanning calorimetry (DSC) .

The transdermal delivery of the hydrophilic drug diphenhydramine hydrochloride from a w/o micro emulsion through the excised human skin has also been investigated. Tween 80 and Span 20, two surfactants, were used in conjunction with IPM to create the formulation. However, two other formulations that contained oleic acid and cholesterol, respectively, were evaluated. Although oleic acid had no detectable effect and cholesterol improved medication penetration, the authors clearly showed that penetration characteristics can be modified by compositional choice 55.

Drugs are primarily used topically to treat eye problems. Ocular and pulmonary delivery O/W micro emulsions have been researched for use in ocular administration, to break down poorly soluble medicines, to boost absorption, and to achieve a prolong release profile.

Lecithin, propylene glycol, and PEG 200 were used to create the pilocarpine-containing micro emulsions, with IPM serving as the oil phase. The formulations had a refractive index that made them suitable for ophthalmologic applications 56 and had a low viscosity. A water-in-HFA propellant micro emulsion that is intended for pulmonary distribution and is stabilized by a fluorocarbon non-ionic surfactant has been disclosed. [1,9,10,11]

PROPERTIES :

According to the size of the particles, there are two different types of emulsions: macroemulsions are those with particle sizes between 0.5 and 50 micrometres. These can be seen clearly under a microscope. The second kind of emulsions are known as microemulsions, and they have particles that range in size from 10 to 200 nm (0.01-0.20 m) (Schuster, 1996). Emulsions can be categorised based on the system's structure or the emulsifier's characteristics (Table 1). (Schuster, 1996). Surprisingly, an emulsion's appearance to the unaided eye depends on the size of the scattered particles. The emulsion is milky white if the dispersed particle diameter is 1 m, blue white if it is 1-0.1 m, grey and semitransparent if it is 0.1-0.05 m, and transparent if it is 0.05 m. Macroemulsion is opaque as a result.

CONCLUSION :

In a technique called a microemulsion, a lot of surface-active chemicals are used to solubilize the medicines. Consequently, it can also boost the drug's solubility in the case of lipophillic medicines. A helpful answer to the stability

and bioavailability issues is a dose form like microemulsions. Oil, a surfactant, and a co-surfactant were used to create microemulsions, which were stable and clear for an acceptable amount of time. It is also a highly helpful method of drug delivery when quick access to the medication is required.

It has been demonstrated that microemulsion can be used to create preparations that are suited for the majority of delivery routes, as well as to protect labile drugs, control drug release, increase drug solubility, boost bioavailability, and lower patient variability. Before they may fully realise their potential as versatile drug delivery systems, however, a significant amount of fundamental research defining the Physico-chemical behaviour of microemulsions needs to be done.

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