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A REVIEW ON MICROEMULSION – A RECENT APPROACH FOR TOPICAL DRUG DELIVERY SYSTEM

Vaibhav D. Mane*, Vipul M. Patil, Manisha V. Mane, Sachinkumar V. Patil.

Department of Pharmaceutics,

Ashokrao Mane College of Pharmacy, Peth-vadgaon, Maharashtra, India-416112

Abstract: A drug delivery method has been explored as microelectric emulsions that are optically isotropical, and thermodynamically stable water, oil, surfactant and/or surfactants due to their potential to solubilize poorly water soluble medicines and to their increased topical and systemic availability. The lipophilic drugs mobility may be solubilized and the skin can be entered quickly and effectively. Thus the topical administration of drugs is helpful. Many commonly utilized topical treatments such as salts, creams and lotions have numerous drawbacks such as sticky texture, causing discomfort when applied, They have a lower coefficient of propagation so applied by rubbing and they also show a stability concern. The difficulty of stability of the microemulsion is low viscosity, but it may be solved by adding viscosity and the moisturizing stratum corneum into topical DDS, which increases dermal penetration and skin flow of medical devices. Because of all these considerations, the use of transparent gels in pharmaceutical preparations has grown in the main semi-solid preparation category.

Key words- Microemulsion, Topical drug delivery, Polymers.

INTRODUCTION

Application of a medication containing formulation in the skin to directly treat cutaneous diseases can be characterized as the topical drug delivery. The topical mode of medication delivery is normally utilized in cases when other routes, such as oral, sublingual, rectal, parental or local infections, such as fungal infections, fail. Human skin is a remarkable organ that allows earth life by controlling bodily heat and water loss and prevents harmful substances or germs from entering. Also the largest organ in the human body, with an average body weight of about 10 percent, is 2 square meters in average. While such a big, easy-to-use organ seems to offer an excellent and multiple location for the administration of therapeutic medicines, the human skin remains a highly efficient barrier that allows the inside and the outside to be remedied. Many commonly used topical medications have a lot of drawbacks such as oints, creams and lotions. Usually they become quite stubborn, creating discomfort for the sufferer. In addition, the spreading coefficient is also smaller and must be used with rubbing.

Micro-emulsion is dispersion of the anisotropic, dispersed domain diameter of about 1 to 100 nm, generally 10 to 50 nm, water, oil and surfactant(s)[1].

microemulsion, usually combined with a co-extractive agent, are transparent, thermodynamically stable, isotropic mixes of oil, water and surfactants. In this aqueous phase, salt(s) and other components may be found and in fact, "oil" can be a complicated mix of many olefins and hydrocarbons[2]. The word "microemulsion" covers a combination including at least three components. The term is oily, aqueous and a surface active species, known as surfactants. The fourth component, i.e., may or should be

present with the cosurfactant. In both extremes, the microstructure for the micro-emulsions varies according to the ratios between the components, from the extremely small water droplets scattered in oil phase (w/o micro emulsion) to oil droplets scattered in water phases (o/w micro emulsions). The microstructure of the mixture continually varies from one extreme to another: spherical to cylindrical, tubular and linked continuous petroleum and water stages with a very thin layer of surfactant molecules in the centre, designated as intermittent micro emulsion. Thermodynamically stable and transparent solutions are the microemulsions of each kind. There are major structural and stability variations between emulsions and microemulsions. Unlike the microemulsions, emulsions are unstable systems and phase separation occurs without agitation. The further distinction is that the droplets in emulsions are within the range of micrometers whereas in micro-emulsions the droplets are between 5 and 100 nm, depending on the degree of their distribution, depending on certain factors such as surfactants type and concentration. Therefore the micro-emulsion phrase often turns out to be deceptive, because this does not reflect the size of the phase droplets in the nanoscale range of the system. The presence of the electrolytes in the aqueous phase is another crucial feature, depending on the kind of surfactant used in the production of the microemulsion[2].

History and Terminology

The work of Hoar and Schulman in 1943, reporting spontaneous emulsion of water and oil on the addition of a strong surface-active ingredient, was not really acknowledged for microemulsions. In 1959, Schulman et al[3] utilized the word 'micro-emulsion' even later to characterize, in a clear manner, a multi-phase system made of water, oil, surfactant and alcohol.[4] The phrase 'micro emulsion' was widely discussed to characterize those systems. While it has not been utilized systematically today, some prefer "swollen micelles' or "micellar emulsions." [5] Micro-emulsions were presumably found far earlier than Schulmann's studies: since early previous century, Australian homewives utilized the liquid waxes discovered by Rodawald in 1928 with water and eucalyptus oils/soap flakes/whites spirits mixed to wash wool. Micro emulsion interest really increased in the late 1970s and early 1980's, when recognition became that these systems were able to improve the petroleum recovery and when the petroleum price reached the levels at which tertiary recovery methods have become profit-making methods[6]. This is no longer the case now but 60 additional micro-emulsions, e.g. catalysis, submicron particle preparation, solar energy conversions, liquid-liquid extraction, were identified (mineral, proteins, etc.). The topic is sufficiently significant to continue to attract several scientists in combination with the conventional applications in detergence and lubrication. In the last 20 years there was considerable development in the knowledge of micro-emulsion characteristics from a fundamental scientific point of view. In particular, thanks to novel and strong methods such as small-angle neutron diffusion interfacial film stability and the microemulsion structure can now be studied in detail. The next sections discuss basic microemulsion characteristics, such as formation and stability, surfactant films, gradation and behavior of phases.

Structure of Micro Emulsion

In a structure split into oil into water (o/w), oil water (w/o) and bilateral microemulsions. microemulsions or micellar emulsions are dynamic systems in which the interface is fluctuated constantly and spontaneously[7]. Water droplets are distributed in the continuous oil phase in w / w of micro-emulsions during the continuous aqueous phase of the oil droplets. The two-continuous microemulsions may occur in systems with comparable quantities of water and oil[8]. The combination of oil water and surfactants can create a broad range of phases and structures depending on the component quantities.

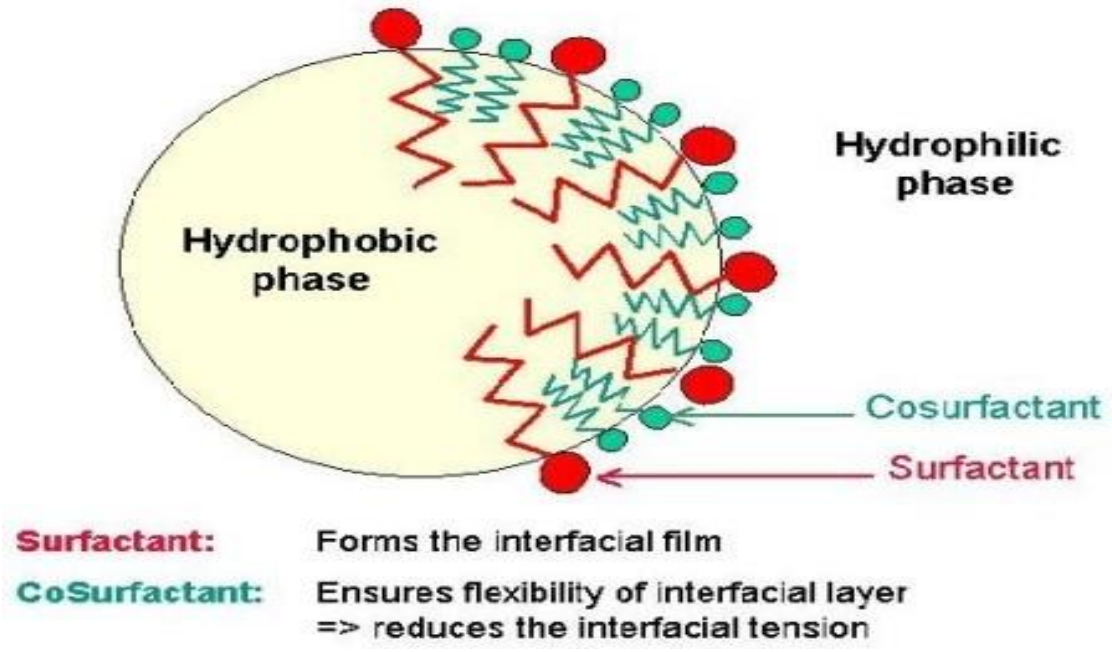

Figure 1: Structure of Microemulsion

Characteristics

A distinct oil and water system shall be created, provided the surfactant with balanced hydrophilic and lipophilic characteristics is employed at a correct concentration. The system remains an emulsion, but has features which differ from the previously mentioned milk emulsions. These are "micro-emulsions." There are low viscosity and newtonian flow characteristics of the interfacial tension between phases and energy required for creation, droplet size. When exposed to a number of shear rates, heir flow remains constant. Some non-Newtonian flow and plasticity may display discontinuous formulations. Even at high droplet levels, micro-emulsion viscosity is near to water. This continually alters the microstructure, creating highly dynamic systems with reversible gout coalescence. A number of approaches are used to characterize distinct micro-emulsion characteristics. We employed extensively light dispersion, X-ray diffraction, UC, electrical conductivity and viscosity tests[9].

Classification of Micro Emulsion [10-15]

According to Winsor, there are four types of micro emulsion phases exists in equilibrium, these phases are referred as Winsor phases. they are:

- Winsor I (two phase system): upper oil layer exists in equilibrium with lower (o/w) micro emulsion phase
- Winsor II (two phase system): the upper (w/o) micro emulsion exists in equilibrium with lower excess water.
- 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.
- Winsor IV (single phase system): it forms homogenous mixture of oil, water and surfactant

The ratio is among the characteristics that Winsor initially presented to describe the impact on interface curvature of amphiphiles and solvents. R-ratio relates an amphiphile's affinity in the oil to its affinity in the water.

Advantages of Microemulsion system [16-21]

1. Microemulsions are ready and require no energy during preparation due to the improvement of thermodynamic stability.
2. Microemulsion creation can be reversed. At low or high temperatures, they can be unstable, but the microemulsion reforms when the temperature returns to stability.

3. The thermodynamically stable system of microemulsions allow the system to selfemulsify.
4. Compared to emulsions, microemulsions have low viscosity.
5. Microemulsions are supersoluble to medicines and may solve both hydrophilic and lipophilic medications, including insoluble pharmaceuticals in both hydrophobial and aqueous solvents.
6. The capacity to take lipophilic and hydrophilic medicinal products.

Disadvantages of Microemulsion Systems [16-18]

1. Having limited solubilizing capacity for high- melting substances.
2. Require large amount of Surfactants for stabilizing droplets.
3. Microemulsion stability is influenced by environmental parameters such as temperature and pH.

INGREDIENTS OF MICROEMULSION [18-20]

In the formulation and development of microemulsions, several substances are employed. In microemulsion, most oils and surfactants should be biocompatible, not poisonous and therapeutically acceptable. Main microemulsion components

1. Oil Phase
2. Aqueous
3. Surfactant
4. Co-solvent

Table 1: Basic difference between Macroemulsion and Microemulsion [22-24].

MACROEMULSION	MICROEMULSION
They are lyophobic in nature.	They are the border between lyophilic and lyophobic.
Droplet diameter 1 to 20 mm.	Droplet diameter 10 to 100 mm.
Macroemulsion droplets exist as individual entities.	Microemulsion droplets disappear within fraction of seconds.
Emulsion droplets are roughly spherical droplets of one phase dispersed into the other phase.	Microemulsions are the structures of various droplets like bi-continous to swollen micelles.
Macroemulsions requires quick agitation for their formation.	Microemulsions are obtained by gentle mixing of ingredients.
Most of the emulsions are opaque (white) in appearance.	Microemulsions are transparent or translucent in nature.

Oil phase [28]

The oil is an important part of microemulsion because the dose required of a lipophilic medicinal product can be solubilized and the fraction of lipophilic medicinal product carried by a lymphatic intestinal system rises. Oil is a liquid with low polarity and low water miscibility. Cyclohexane, mineral oil, toulene and vegetable oil etc. are examples of such a phase.

Aqueous phase

The hydrophilic active components and preservatives usually form in the aqueous phase. Buffer solutions are sometimes employed as an aqueous phase.

Surfactant [29]

Surfactant (surface-active-agent) is a word used to describe a chemical that has some superficial or interfacial activity and is used to reduce surface or interface tension. It is attracted to both polar and nonpolar liquids. The molecules that have a polar head and a polar tail are surfactants. Surfactant molecules are independent because of different inter- and intramolecular forces and entropy concerns.

The many surfactants that contribute to the gradual microemulsion development system are

1. Cationic
2. Anionic
3. Non-ionic
4. Zwitterionic surfactants.

Co-solvent [30]

The single chain surfactants have been shown to be unable to decrease the o/w interfacial voltage enough to produce a microemulsion. The inclusion of co-surfactants makes it flexible to use various curvatures necessary to produce the microemulsion across a variety of excipients. If a single surfactant film is needed, the surfactant lipophilic chains should be short enough or include fluidisation groups (e.g. unsaturated bonds).

STEPS IN MICROEMULSION PREPARATION [31]

- **Preparing Water Phase-**

(Dissolving water soluble components)

↓

(Solids dissolve possible by heating)

↓

(Undissolved material separated by centrifugation)

- **Preparing Oil Phase-**

(Dissolving oil soluble component)

- **Emulsifying Water & Oil Phases-**

(Mixed in suitable vessel & given time to equilibrate)

↓

(Using emulsification techniques – stirring, Use of membranes, applying shear, ultrasound etc)

Ternary Phase Diagram

Ternary Phase Diagram a basic three-component microemulsion diagram is split into two or 4 areas with a constant temperature and pressure. Each compositional point above the demising line corresponds to the microemulsion in each case inside the single-phase area. The following components reflect multiphase areas that in general include the micro-emulsions in the balance of the aqueous or organic phase or both, i.e. systems of type Winsor.

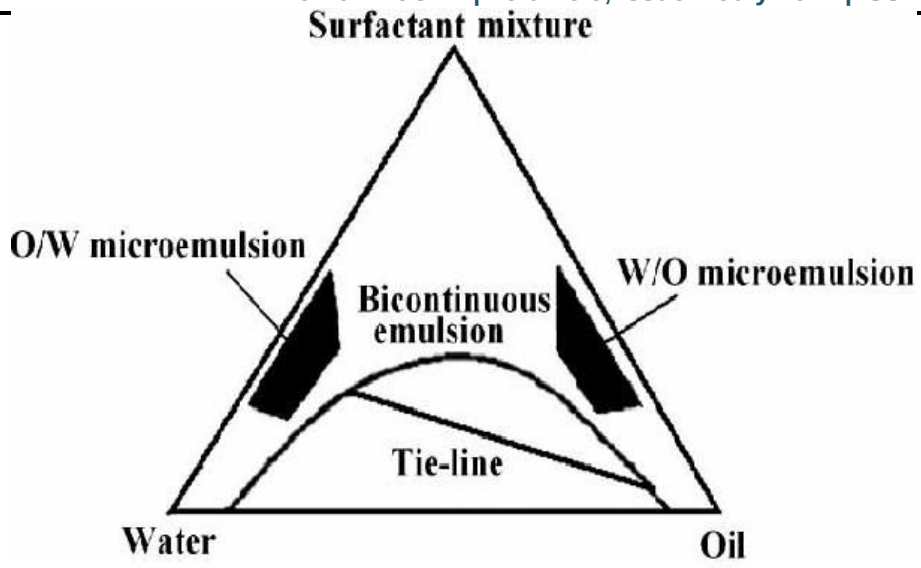

Figure 2 : Ternary Phase Diagram

Phases Involved

Water phase

Water may become a water pool or function as dispersion media in the micro emulsion system, depending on the amount of water present in the system.

Oil phase

The selection of additional ingredients for the micro-emulsion should be chosen correctly because two principal aspects need to be addressed before picking the suitable oil stage. The oil phase must be considered.

Composition [32-41]

The Major component in microemulsion system are-

1) Oil phase
2) Surfactant (primary surfactant)
3) Co-surfactant (secondary surfactant)
4) Co-solvent

Table 2: Component of Microemulsion system

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

Factor affecting Microemulsion [42-44]

Factor affecting the microemulsion are as follows

- Packing ratio[45]

  HLB of surfactant influences the kind of microemulsion by affecting the packaging and the curvature of the film.

- Property of surfactant

  Two lipophilic group and hydrophilic group include surfactants. Hydropyl single-chain surfactants, such cetyl ammonium bromide, are totally dissociated into a diluted solution and tend to produce o/w microemulsion.

- Property of oil phase

  By its capacity to enter and swell the tail group area of a surfactant monolayer, the oil phase influences a curvature, swelling the tail resulting in an enhanced negative curvature to w/o microemulsion.

- Temperature[46]

  The efficient head group size of nonionic surfactants is very essential to determine the temperature. The hydrophilic and the typical O/W system are formed at low temperatures. They are lipophilic and w/o systems at higher temperatures.

APPLICATION OF MICROEMULSION SYSTEM

Microemulsion in Pharmaceutical

From last two decades there has been a revolution in the utilization of microemulsion systems in a variety of pharmaceuticals.

- **Parenteral Delivery** [47]

The administration of medicinal medicines with restricted solubility (particularly through the intravenous method) is an important challenge for the business since the very tiny amount of medicine really delivers to a specific location.

- **Oral Delivery** [48]

A number of benefits compared to traditional oral formulation including greater absorption, improved clinical strength and lower drug toxicity are provided with micro-emulsion formulations.

- **Topical delivery** [49]

  For a number of reasons, the topical administration of medicines may have benefits over other approaches, including the prevention of first-pass Hepatic metabolism, salivary and stomach degradation and associated consequences of toxicity.

- **Ocular and Pulmonary Delivery** [50]

Drugs are mostly administered topically for the treatment of eye disorders. For ocular delivery, O/W micro-emulsions were explored to dissolve poorly soluble medicines, improve absorption and achieve a long-term release profile.

Other pharmaceutical applications [51-54]

- Nasal delivery
- Drug targeting
- Cellular targeting
- Brain targeting
- Periodontal delivery
- Tumor targeting

CONCLUSION

Both for the medication delivery system and for the industrial process, microemulsions are of critical relevance. They can be utilized to maximize medication targeting without increasing systemic absorption at the same time. Micro-involvement emulsion's in giving new methods for addressing the challenges of poor water solubility and high bioavailability in highly lipophilic substances. However, problems persist, largely due to the layers of barriers these systems must overcome to reach the target, microemulsions may also be employed to reach the drug target. The ability to safeguard labile drugs, regulate the discharge of pharmaceutical drugs and reduce patient variability.

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