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Review Article

A Review on Formulation and Evaluation OF Micro-Emulsion

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ABSTRACT

Microemulsions are among the greatest options for innovative drug delivery systems since they are stable, transparent, and isotropic combinations of water, oil, and surfactants, frequently combined with co-surfactants. They have the following advantages: long shelf-life, improved drug solubilization and bioavailability, optical isotropy, thermodynamic stability, ease of manufacturing and scale-up, and spontaneous formation. They are also promising drug carrier systems for oral, topical, and parenteral administration.

INTRODUCTION

Danielsson. and Lindman defines a microemulsion as "a system of water, oil, and an amphiphile which is a single optically isotropic and thermodynamically stable liquid solution."[1] This is one of the better definitions of microemulsions. In some ways, microemulsions may be considered miniature versions of emulsions, which are droplet-type dispersions of either water-in-oil (w/o) or oil-in-water (o/w), with drop radiuses ranging from 5 to 50 nm. Unfortunately, because microemulsions and regular emulsions differ greatly, such a definition is imprecise. The discovery of a spontaneous emulsion of water and oil upon the addition of a potent surface-active agent by Hoar and Schulman in 1943 marked the beginning of the true recognition of microemulsions [2]. Even later, in 1959, Schulman et al. [3] used the term "microemulsion" to refer to a multiphase system that consists of alcohol, water, oil, and surfactant that produces a clear solution. The term "microemulsion" to refer to such systems has been hotly debated [4]. Some people prefer the terms "micellar emulsion" [5] or "swollen micelles," even though they are not used consistently nowadays [6]

Objectives of micro-emulsion:-

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- The goal is to combine organic, aqueous, and surfactant phases to optimize w/o microemulsions. Ternary phase diagrams show the resultant microemulsions along two dilution lines inside the monophasic zone.
  - By adding sodium chloride, a model hydrophilic guest molecule, to the water domains of continuous oil microemulsions, the conductivity-based salt-release capabilities of certain salt-containing microemulsion compositions can be evaluated, and the mechanism of release may be determined.

Types of micro-emulsion –

Microemulsion types: Three types of microemulsions are most likely to develop, depending on the composition:
1. Oil in water (O/W) microemulsions, in which dispersed oil droplets make up the continuous aqueous phase.

2. Bi-continuous microemulsions, where the system is interspersed with oil and water microdomains;

3. Microemulsions of water in oil (W/O), where water droplets are dispersed throughout the continuous oil phase. In all three types of microemulsions, the interface is stabilized by a suitable combination of surfactants and co-surfactants.[7]

The advantages of microemulsion over alternative dosage methods -

1. Easy manufacturing and scalability.
2. Colloidal drug delivery systems have several applications for medicine targeting and controlled release.
3. Promotes lipophilic drug solubilization, which improves the absorption and bioavailability of medications.
4. Eliminates fluctuations in absorption.
5. Provides an aqueous dosage form for drugs that are insoluble in water.
6. There are other ways to give drugs, including as intravenous, oral, and tropical.[8]

7. The drug moiety penetrates quickly and effectively.
8. Beneficial for disguising flavor.
9. Both hydrophilic and lipophilic medications can be transported by the same microemulsions.
10. Offers defense against oxidation and hydrolysis as the medicine in the oil phase of the O/W microemulsion is shielded from air and water attack.
11. Patient compliance is increased by liquid dose forms.
12. A lower energy consumption.
13. Alcohol-free microemulsions have been shown to have a significantly decreased propensity for skin irritation.
14. Extended shelf life in contrast to alternative colloidal drug delivery methods.
15. A high loading of drugs.
16. Increase the therapeutic effectiveness of medications and enable the drug delivery vehicle's volume to be reduced, hence reducing harmful side effects.[9]

17. Simple to provide to adults and children who have trouble swallowing solid dose forms.

Requirements of formulations: microemulsions are colloidal dispersions made up of the proper ratios of oil phase, aqueous phase, surfactant, and co-surfactant.[10]

1. Surfactants: The system is stabilized with the addition of surfactants. Surfactants are utilized to formulate microemulsions to reduce the interfacial tension, which in turn helps the dispersion process and creates a microemulsion surrounding the

droplet. They might be cationic, anionic, zwitter ion, or non-ionic surfactants.

2.Co-surfactants: Co-surfactants are chemicals that are added to a process to increase a surfactant's efficacy. These are employed to improve the microemulsion surfactant system's ability to solubilize oil. Co-surfactants are alcohols with short to medium chain lengths (C3–C8) that have the capacity to improve the fluidity of the interface while lowering interfacial tension. They are cholesterol, amines, and alcohols.[11-14]

3.Oils: Through its capacity to permeate the surfactants' tail group area, the oil component affects curvature. Short-chain oil is more likely to boost the negative culture and lower the HLB than long-chain alkenes.[15]

The following types of oils are employed in the formation of the microemulsions:

• Saturated fatty acids: capric acid, myristic acid, and lauric acid.

Oleic acid, linoleic acid, and linolenic acid are examples of unsaturated fatty acids. •Fatty acid ester: Lauric acid, myristic acid, and oleic acid methyl or ethyl esters. The primary purpose of oil selection is to ensure that the medicine has a high solubility. The oil should be used to reduce the formulation's volume. The therapeutic dosage of the medication should be administered by the oil in an encapsulated form. Microemulsion formulations need to be low in allergic reactions, have good physiological compatibility, and be highly biocompatible. A primary surfactant (anionic, non-ionic, or amphoteric), an aqueous phase with hydrophilic active ingredients (preservatives and buffers may be included), a secondary surfactant or cosurfactants, and an oil phase are the components involved in the general formulation of microemulsions.

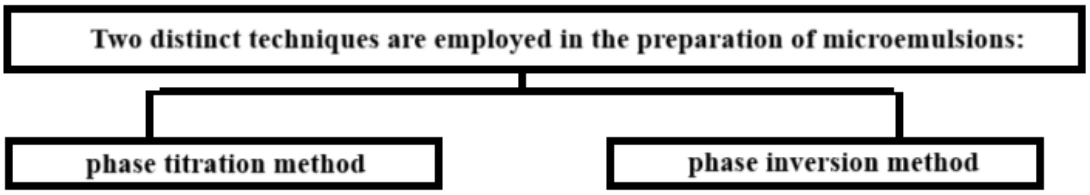

Figure 1.Two Distinct Techniques Are Employed in The Preparation of Micro-Emulsions.

1] phase titration method; Microemulsions are prepared by the phase titration method. These is also called as spontaneous emulsification method. Microemulsions can be characterized by the phase diagram. As four four-compartment system is difficult to intercept and time-consuming process. So, in the preparation of microemulsions, we are using the pseudo-ternary phase diagram. These have the different zones and microemulsion zones. These show the 100% of the particular components. In this phase titration method, we are using the oils, water, surfactants & mixture of co-surfactants in fixed weight ratios. This phase diagram is responsible for the mixing of ingredients. All these mixtures will be stirred at room temperature, then the monophasic/biphasic system will be confirmed by the visual inspection. In phase separation turbidity may appear, the samples should be considered biphasic because the monophasic is visualized as clear and transparent mixtures after continuous stirring. The obtained points should be marked in the phase diagram. When turbidity occurs during phase separation, the

samples should be regarded as biphasic since, with constant stirring, the monophasic mixes appear as clear and transparent. In the phase diagram, the points that were acquired should be indicated.

2] phase inversion method; The microemulsion undergoes phase inversion when an excess of the dispersed phase is added or when the temperature changes. Drug release in vitro and in vivo may be impacted by physical and particle size changes that may arise during the phase inversion procedure. It is possible to create non-ionic surfactants by altering the system's temperature; in these procedures, an o/w microemulsion at low temperatures transforms into a w/o microemulsion. The transitional phase inversion method is another name for this technique.As the system cools, it maintains surface tension, breaks the zero-point spontaneous structure, and increases the dispersion of oil droplets. In addition to temperature, pH level and salt content may be taken into account.
By altering the water volume percentage, this phase inversion technique can cause a radius change. When water is added to oil, water droplets are first created in a continuous oil phase. Temperature can be used to stabilize a w/o microemulsion with surfactants and raise the water volume fraction to an o/w microemulsion.

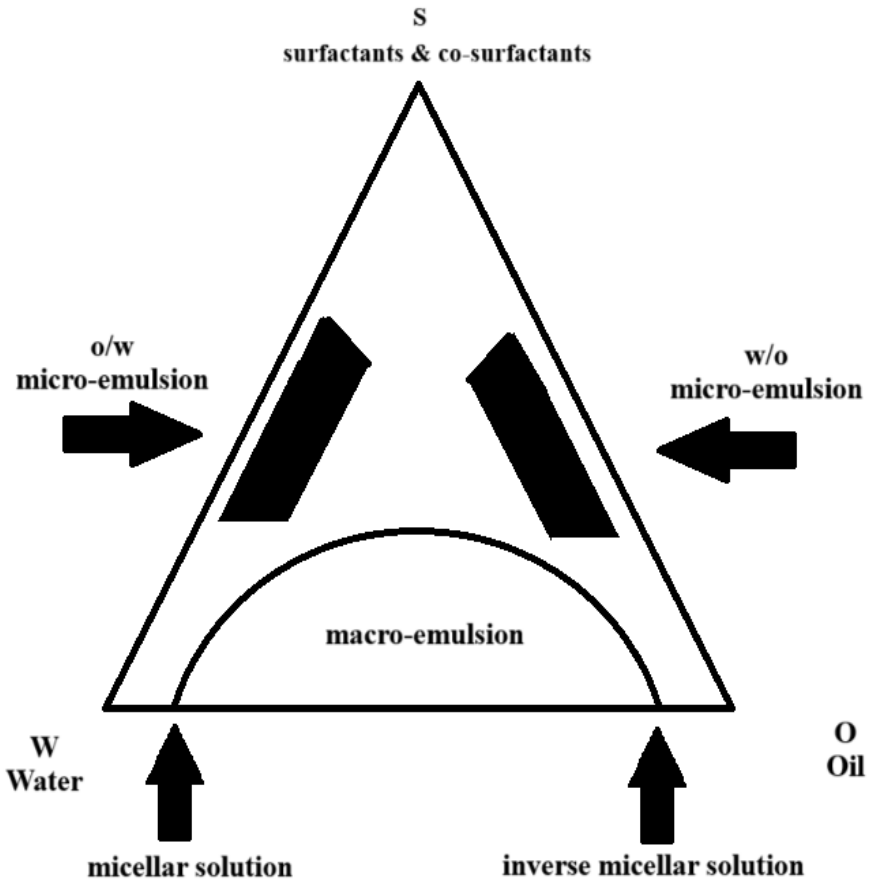

Figure 2.Hypothetical phase regions of microemulsion system of oil (O), water (W), and surfactant + cosurfactant (S) [16]

Comparison between emulsion[macro-emulsions] and micro-emulsions [17-22];-

Sr.no	Emulsions[macro-emulsions]	Micro-emulsions
1.		
2.	Emulsions consist of roughly spherical droplets of one phase dispersed into the other.	They alternate between different configurations all the time, from bi-continuous to droplet-like inflated micelles.
3.	Size of droplets: 1–20 mm	size of droplets: 10–100 nm
4.	Since most oils have higher refractive indices than water and the bulk of their droplets is larger than the wavelength of light, most emulsions are opaque (white).	Microemulsions scatter little light since their droplet width is less than ¼ of the wavelength of light, making them transparent or translucent
5.	Ordinary emulsion droplets, no matter how tiny, remain distinct entities until they merge or undergo Ostwald ripening.	While another droplet develops spontaneously elsewhere in the system, a microemulsion droplet may vanish in a matter of seconds.
6.	In order to reach a minimum in free energy, they will eventually go through phase separation after remaining stable for extended periods of time. They are thermodynamically unstable yet kinetically stable.	More thermodynamically stable than macroemulsions, they don't tend to split, and they can last virtually forever if no changes are made to the composition, temperature, or pressure.
7.	They're lyophobic.	Between lyophobic and lipophilic colloids, they are situated.
8.	need a great deal of agitation to develop.	This is often accomplished by slowly mixing components

Evaluation parameters of micro-emulsion: -

To evalutate the microemulsions, measurements of the droplet size, density, turbidity, viscosity, refractive index, phase separation, and pH must be made.

1] Droplet size -The droplet size distribution of microemulsions is ascertained using electron microscopy or the light scattering method. This method is the most effective way to forecast the stability of microemulsions.

- **Dynamic Light-Scattering: -**

  Using a neon laser with a wavelength of 632 nm, the DLS measurements are completed at 90° in a dynamic light-scattering spectrophotometer. With the instrument, the integrated computer processes the data.[23]

- **Polydispersity:-** Using an Abbe refractometer, the polydispersity is studied.

- **Phase analysis: -**A conductometer is used to measure the electrical conductivity to identify the kind of microemulsion (o/w or w/o) constituting the phase system.

- **Viscosity measurments:-**The viscosity of microemulsions is measured using a Brookfield rotational viscometer. This involves measuring the viscosity of microemulsions with varying compositions at various temperatures and shear rates. Before testing, the measurement samples must be submerged in a Thermo-bath that maintains the instrument at 37 ± 0.2°C.[24]

- **Nuclear magnetic resonance study:-**The structure and behavior of microemulsions are investigated using the Nuclear Magnetic Resonance method. Self-diffusion measurements, often radio labelling, are used in various tracing methods to provide information on component mobility. Fourier transform pulsed-gradient spin-echo (FT-PGSE) may be used to quickly and simultaneously determine the self-diffusion coefficients when there is a magnetic gradient on the samples.[25-26]

- **Interfacial tension :-**The interfacial tension may be measured to study the development and characteristics of microemulsions. In low ultra-values, this interfacial tension is associated with phase behavior, indicating the presence of middle-phase or surfactant-phase microemulsions in equilibrium with the aqueous and oil phases. Using the spinning-drop technique, ultra-low interfacial tension is determined... The form of a drop of the low-density phase is measured and rotated in a cylindrical capillary filled with high-density phase to produce these. [27]

- **Electron Microscope Characterization** Microstructure analysis of microemulsions The most crucial method is transmission electron microscopy (TEM), which may immediately create high-resolution pictures and record any coexisting structure as well as microstructural transformations. • The freeze fracture TEM technique is used to create pictures of the specimen under room temperature. • The cryo-TEM is used to analyze the samples that are directly observed after quick freezing and freezing fructose in the cold microscope.

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