

**MICROEMULSION: A NOVEL DRUG CARRIER APPROACH****\*Shish Kumar, Shardul Chauhan, Ankit Kumar Pandey, Shashank Patel, Anurag Goel**

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**ABSTRACT**

Microemulsions are liquid mixtures of water, oil, and surfactant that are isotropic transparent, and thermodynamically steady often in combination with a co-surfactant. The "oil" might be a complex blend of different olefins and hydrocarbons, while salts and other materials could be present in the aqueous phase. Microemulsions create by merely mixing the components, in contrast to conventional oils, that required severe shear conditions to produce. Furthermore, the droplet size in these microemulsions is consistent, falling between 100 and 1000 Å (10 and 100 nm), and the oil/water interfacial tension is remarkably low. Nowadays, the use of microemulsion in a variety of technological applications is a rapidly expanding business with global relevance. Since the droplet size of

microemulsions is less than 25% of the wavelength of visible light, they are transparent. This article attempts to illustrate the importance of microemulsions as DD Vehicles by giving a general review of their creation, characterization, and use in different drug delivery routes.

**KEYWORDS:** Microemulsion, Surfactants, Co-surfactants, Bioavailability.

**INTRODUCTION**

A microemulsion that is a single, optically isotropic, thermodynamically stable liquid solution based on water, oil, and amphiphiles. "The term microemulsion was coined in 1959 by Jack H. Shulman. It is also known by the names easily visible emulsion, swelling micelle, micellar solution solubilized oil. An interfacial coating of surfactant molecules stabilises microemulsions, which are thermodynamically stable, clear solutions of oils and water. One can utilize a co-surfactant alone or in combination with the surfactant used, like a medium-chain alcoholic (butanol, pentanol). These uniform systems are all fluids with a low viscosity

that may be produced in an oil: water ratio range of 20–80% and with surfactant concentrations ranging widely.

Transparency, low viscosity, and more importantly, thermodynamic stable and spontaneous formation are characteristics that easily set microemulsions apart from regular emulsions.<sup>[1]</sup>

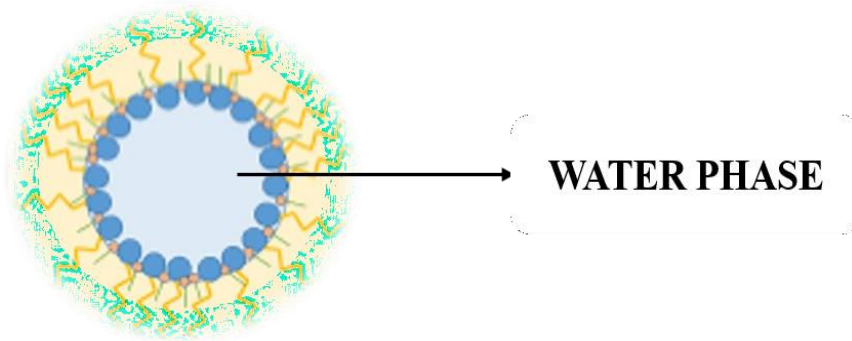
A mixture consisting of three components at minimum is referred to as a micro emulsion: an aqueous form, an oily form, and a surface-active species, also known as surfactants. Co-surfactant is the fourth component that occasionally needs to or can be present. In the two extremes, the microstructure of the micro emulsions varies according to the component ratios. The microstructures of the micro emulsions range from an oil phase dispersed in water phase (o/w micro emulsion) to extremely small water droplets scattered in oil phase (w/o micro emulsion).<sup>[2]</sup>

Thermally stable microemulsion systems with a minimum oil percentage of 30% that spontaneously form, 1. –30% non-ionized surfactant system with hydrophilic–lipophilic balance (HLB) consisting of 20% water, 9–18% co-solvent, and at least 30% oil.

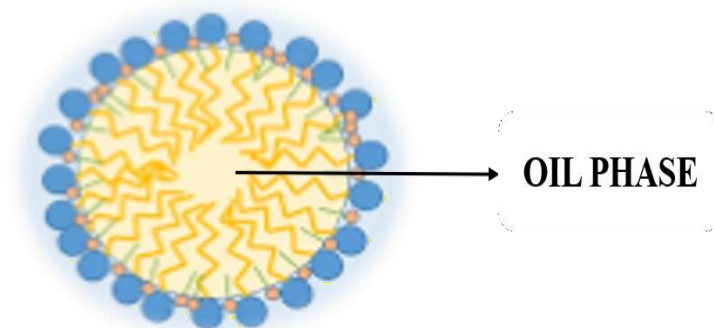
As a result, under typical circumstances, microemulsion systems have an infinite shelf life, in contrast to the limited life of macroemulsions. In addition, the droplets in these microemulsions maintain a consistent size within the range of 100-1000 Å (10-100 nm) and exhibit a very low oil/water interfacial tension. Microemulsions are transparent because their droplet size is less than 25% of the visible light wavelength.<sup>[3,4]</sup>

### **Types Of Microemulsions**

Thermodynamically stable microemulsions are found only in specific, well-defined conditions. Winsor states that there are 4 different kinds of microemulsion phases that can be found at equilibrium these stages are sometimes referred to as Winsor stages. The following are four different methods of microemulsion solubilization that can be applied to pharmaceuticals. i.e., **Water in oil type-** In the continuous oil phase, water droplets are scattered. Fatty acid tails face the oil phase, while the surfactant's polar headgroups face the water droplets. These are also called as "reverse micelles." The aqueous biological system can cause a w/o microemulsion that is administered orally or parenterally to become unstable.



**Oil in water type** - In the ongoing aqueous phase, oil droplets are distributed. This type of the microemulsion has a higher interaction ratio than w/o microemulsions.



**Microemulsions that are bicontinuous type-** Within the systems, there are pockets of water and oil and this instance, the phases of water and oil are both continuous. An uneven water and oil channel that resembles a "sponge-phase" is created. Transition from o/w to w/o in microemulsions can cross this bi-continuous state. Bi-continuous microemulsions can be plastic and flow non-Newtonian. They are particularly helpful for intravenous injection or topical drug delivery because of these characteristics.

**Homogenous Single-Phase Mixture type-**The oil, water, and surfactants are combined uniformly in a single-phase homogeneous mixture.<sup>[5,6,7,8,9,10]</sup>

#### ADVANTAGES OF MICROEMULSION SYSTEM

1. The enhanced thermodynamic stability of microemulsions makes their production energy-free and simple.
2. The process of microemulsion production is reversible.
3. Temperature fluctuations can cause the microemulsion to become unstable, but it always returns to its stable range as the temperature drops.
4. In comparison to emulsions, microemulsions are less viscous.

5. Microemulsions are super solvents that may dissolve hydrophilic and lipophilic medications as well as drugs which are intractable in aqueous and polar solvents.
6. Able to transport hydrophilic and lipophilic medications.
7. Microemulsions are a thermodynamically stable system that enable the system to self-emulsify.<sup>[11,12,13,14]</sup>

### DISADVANTAGES OF MICROEMULSION SYSTEM

1. Have a high surfactant requirement in order to stabilise droplets.
2. Having a restricted ability to dissolve highly combustible materials.
3. Environmental factors like pH and temperature influence the microemulsion's stability.<sup>[15,16,17,18]</sup>

It is necessary to have large concentrations of surfactant and co-surfactant.<sup>[19]</sup>

### Theories Of Microemulsion

There are three hypotheses about the creation of microemulsions these are-

**Interfacial or Mixed Film Theory**-This theory is also known as a negative interfacial tension theory, postulates that when surfactant and co-surfactant interact, a microemulsion can form instantly and spontaneously, creating a negative interfacial tension. The film, which may contain molecules of surfactant and co-surfactant, is viewed as an oily "two dimension" third phase that is in balance with oil as well as water.

A monolayer that has different characteristics on its water and oil sides is called a duplex film. According to the duplex film theory, the tension between two surfaces  $\gamma T$  may be found using the formula that follows.

$$\gamma \cdot T = \gamma \cdot (o/w) \text{ --- } \pi$$

**Where,**  $\gamma$  (o/w)

$\gamma$ (o/w) a is significantly lower than  $\gamma$ (O/W) in the absence of the alcohol.

[Patel V, Kukadiya H, Mashru R, Surti N, Mandal S. Development of microemulsion for solubility] enhancement of clopidogrel.

**Solublization Theory**- Micelles in micellar gradually grow and swell to a certain size range, forming a microemulsion. These micelles might be oil soluble phase or reverse micelles.

**Thermodynamic Theory-** A simple thermodynamic process can explain the formulation and stability of microemulsions. Therefore, the extent to which a surfactant reduces surface pressure at the interface between the oil and the water and the entropy shift of the system can affect the unrestricted energy of microemulsion production. that is,

$$D.G.f = \gamma.D.A - T DS$$

**Where,** DG f = Free Energy of formation,

$\gamma$  =Surface Tension of the oil–water interface,

DA = Change in interfacial area on micro emulsification,

DS = Change in entropy of the system which is effectively the dispersion entropy, and T = Temperature.

It is shown that the production of a microemulsion results in an enormous number of really small droplets, which drastically modifies the DA. Though  $\gamma$  is usually positive, it is vital to realize that it is very tiny and is compensated for by the entropic factor.

The main beneficial entropic contribution comes from the extremely large dispersion entropy that is produced when one phase mixes with the other in the form of many little droplets.<sup>[20]</sup>

### **Composition Of Microemulsion**

A range of materials are used in the development and formulation of the microemulsions. Surfactants that are & oils are the primary elements needed to create microemulsions.

They ought to be non-toxic, biocompatible, and approved by doctors. These are the main parts of a microemulsion. Mainly, microemulsions contains-

**A. Oil Phase**

**B. 2. Aqueous Phase**

**C. Surfactant**

**D. Co-Solvent**

Therefore, these all are briefly explained as-

#### **Oil phase**

Oil phase is the second most significant vehicle after water because it can dissolve a lipophilic molecules of drugs and improve absorption across the body's lipid barrier. Oil has a special ability to penetrate cell membranes, which makes it highly helpful for administering lipophilic active drugs.

The oil phase has an impact on the surfactant's tail group area swelling. For examples- lauric acid, oleic acid, capric acid.<sup>[21]</sup>

### Aqueous Phase

Hydrophilic active agents & preservatives are typically included in the aqueous phase. As an aqueous phase, buffer solutions are occasionally employed.


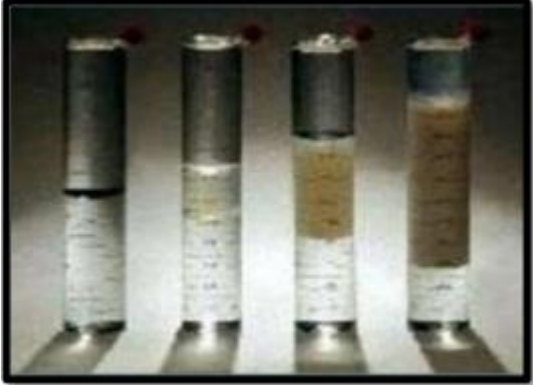
### Surfactants

To stabilise the system, surfactants are employed. when creating the microemulsions. Reducing the interfacial tension is the function of surfactants. Surfactants surround the droplet in a microemulsion formulation, which is the last step in the dispersion process. These surfactants might be non-ionic, anionic, zwitter ionic, or anionic.

### Co-solvent

Organic solvents like ethanol, propylene glycol (PG), and polythene glycol (PEG) are examples of co-solvents. which aid in the dissolution of lipid-soluble medications and surfactants at relatively high concentrations. As a result, co-solvents and co-surfactants are synonymous terms.

**Table 1: Comparisons B/W Emulsion and Microemulsion.**

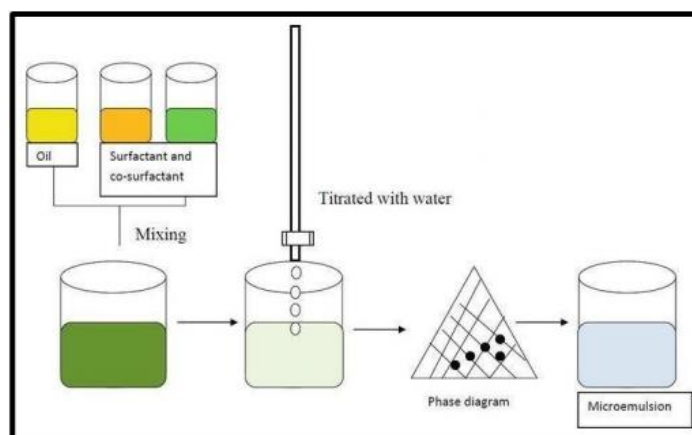
Emulsion	Micro-emulsion
	
<p>These are the familiar oil-in-water (o/w) or water-in-oil(w/o) emulsions</p>	<p>A microemulsion is a type of emulsion that is thermodynamically stable. Microemulsion used for better drug absorption and bioavailability</p>
<p>Formed by mixing oil and water with the help of high shear conditions for their creation.</p>	<p>They do <b>not require high shear conditions</b> for their creation.</p>
<p>The oil and water phases remain separate unless an emulsifying agent.</p>	<p>Microemulsions consist of tiny droplets of one phase dispersed within another phase. Three basic types of microemulsions exist: ❖ <b>Direct Microemulsion (o/w):</b> Oil droplets</p>

	<p>dispersed in water.</p> <ul style="list-style-type: none"> <li>❖ <b>Reversed Microemulsion (w/o):</b> Water droplets dispersed in oil.</li> <li>❖ <b>Bicontinuous Microemulsion:</b> A continuous network of both oil and water phases.</li> </ul>
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**Preparation Method of Micro-Emulsion:** Following are the method used for the preparation of the microemulsion:

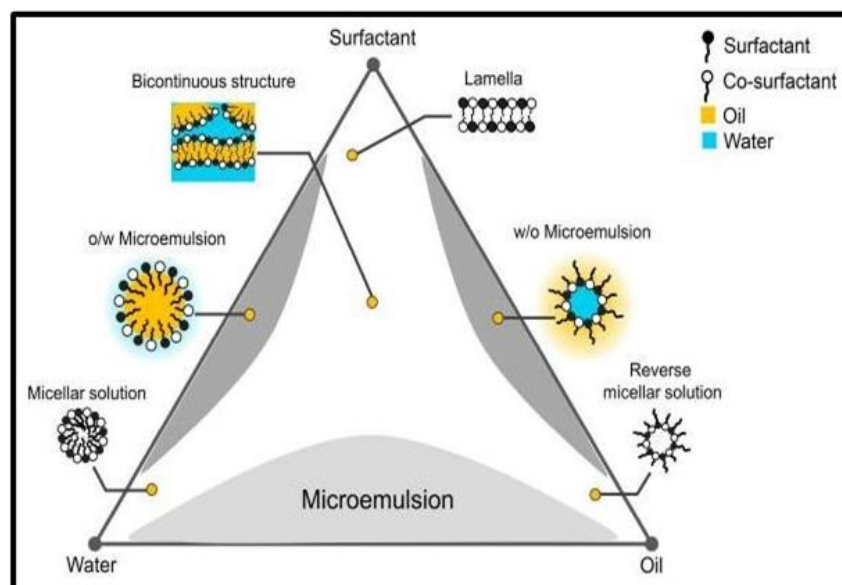
- 1) **Phase titration method**
- 2) **Phase inversion method**

**Titration Method:** Micro emulsions are prepared by the spontaneous emulsification method (phase titration method) and can be depicted with the help of phase diagrams. Construction of phase diagram is a useful approach to study the complex series of interactions that can occur when different components are mixed. Micro emulsions are formed along with various association structures (including emulsion, micelles, lamellar, hexagonal, cubic, and various gels and oily dispersion) depending on the chemical composition and concentration of each component. The understanding of their phase equilibrium and demarcation of the phase boundaries are essential aspects of the study. As quaternary phase diagram (four component system) is time consuming and difficult to interpret, pseudo ternary phase diagram is often constructed to find the different zones including microemulsion zone, in which each corner of the diagram represents 100% of the particular component. The region can be separated into w/o or o/w micro emulsion by simply considering the composition that is whether it is oil rich or water rich. Observations should be made carefully so that the metastable systems are not included.



**Figure: Phase titration method.**

**Phase Inversion Method:** Phase inversion of micro emulsions occurs as a result of addition of excess of the dispersed phase or in response to temperature. During phase inversion drastic physical changes occur including changes in particle size that can affect drug release both in vivo and in vitro. These methods make use of changing the spontaneous curvatures of the surfactant. For non-ionic surfactants, this can be achieved by changing the temperature of the system, forcing a transition from an o/w micro emulsion at low temperatures to a w/o micro emulsion at higher temperatures (transitional phase inversion). During cooling, the system crosses a point of zero spontaneous curvature and minimal surface tension, promoting the formation of finely dispersed oil droplets. This method is referred to as phase inversion temperature (PIT) method. Instead of the temperature, other parameters such as salt concentration or pH value may be considered as well instead of the temperature alone. Additionally, at transition in the spontaneous radius of curvature can be obtained by changing the water volume fraction. By successively adding water into oil, initially water droplets are formed in a continuous oil phase. Increasing the water volume fraction changes the spontaneous curvature of the surfactant from initially stabilizing a w/o micro emulsion to an o/w micro emulsion at the inversion locus. Short chain surfactants form flexible monolayer at the o/w interface resulting in a discontinuous microemulsion at the inversion.



The ternary phase diagram depicts various structures.

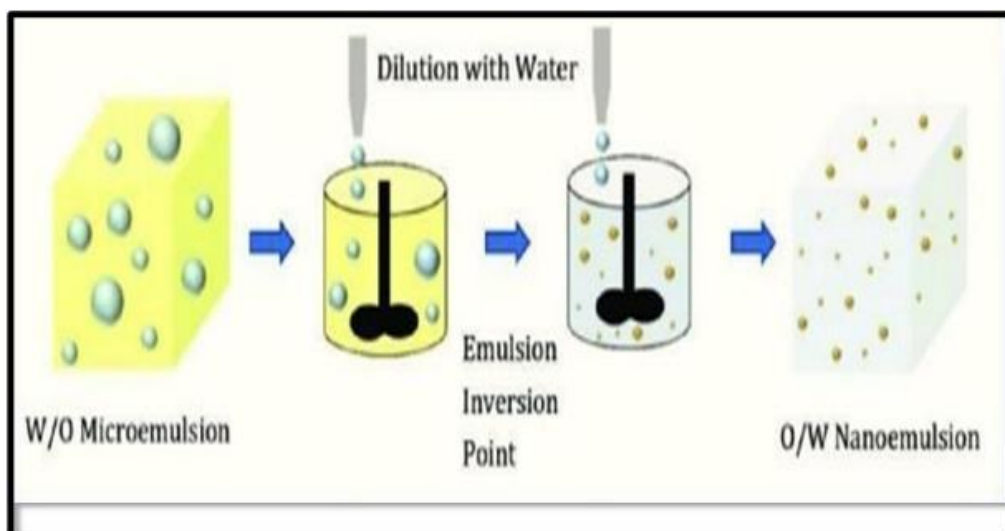


Figure- Phase inversion method.

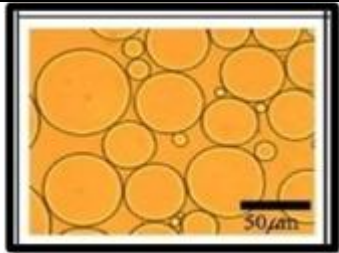
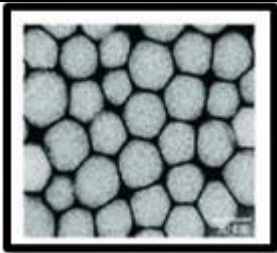
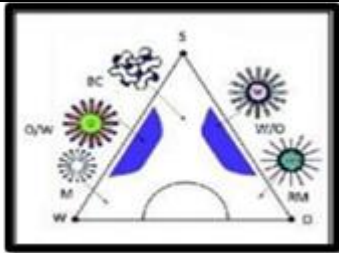
### EVALUATION PARAMETERS OF MICROEMULSION SYSTEM

- Phase behaviour
- Size and shape
- Physical appearance
- Scattering Techniques
- Limpidity Test (Percent Transmittance)
- Drug stability
- Globule size and zeta potential measurements
- Assessment of the Rheological Properties (viscosity measurement)
- Electrical conductivity
- Drug solubility
- In-vitro drug release
  
- **Electron Microscope Characterization Phase behaviour**

Lavender essential oil (LO) is widely used as a bioactive component in cosmetics. In this study, the pseudo ternary phase diagrams of microemulsions composed of oil phase (LO: short-chain alcohol = 1:1, w/w), non-ionic surfactant (Tween 80) and water were constructed to evaluate the impact of co-surfactant type on the dilute ability of micro-emulsion systems. The solubilization of LO was improved in the presence of 1, 3-butylene glycol. For this reason, microstructural inversion of a water titration line D82 was investigated by dye diffusion, conductivity, viscosity and DSC. Microemulsions transition from W/O to bi-continuous occurred at 20% water content, and then to O/W structure at 50% water content. In the

bicontinuous phase, the viscosity reduced rapidly by the rise of temperature. The structure transition affected the free radical scavenging activity. The DPPH radical scavenging activity continuously with water content from 10% to 90%, indicating that increasing free water may accelerate the interaction between LO and DPPH radicals. The ABTS radical scavenging activity of W/O and bi-continuous formulations was concentration dependent while increased again and peaked at 70% water content in O/W regions. The microemulsion techniques could be applied as potential delivery systems to improve the application of poorly water-soluble essential

### Size And Shape

Content	Macroemulsion	Nano-emulsion	Microemulsion
			
Size	1-100 $\mu\text{m}$	20-500 nm	10-100 nm
Shape	Spherical	Spherical	Spherical lamellar
Stability	Thermodynamically	Thermodynamically stable, kinetically stable	Thermodynamically stable
Method of preparation	High and low energy method	High and low energy method	low energy method
Polydispersity	After high ( $\geq 40\%$ )	After high ( $\geq 10-20\%$ )	After high ( $\geq 10\%$ )

### Physical appearance

For Physical appearance microemulsion can be inspect visually for homogeneity, fluidity and optical clarity.

### Scattering Techniques

Scattering techniques such as small angle neutron scattering, small angle X-ray scattering and light scattering have found applications in studies of microemulsion structure, particularly in case of dilute monodisperse spheres, when polydisperse or concentrated systems such as those frequently seen in microemulsions.

### Limpidity Test (Percent Transmittance)

The limpidity of the microemulsion can be measured spectrophotometrically using spectrophotometer.

**Drug stability**

The optimized microemulsion was kept under cold condition (4-8°C), room temperature and at elevated temperature ( $50 \pm 2$  °C). After every 2 months the microemulsion can be analysed for phase separation, % transmittance, globule size and % assay.

**Globule size and zeta potential measurements<sup>[39]</sup>**

The globule size and zeta potential of the microemulsion can be determined by dynamic light scattering, using a Zetasizer HSA 3000.

**Assessment of the Rheological Properties (viscosity measurement)**

The rheological properties play an important role in stability. It can be determined by Brookfield digital viscometer. Change in the rheological characteristics help in determining the microemulsion region and its separation from other region. Bicontinuous microemulsion are dynamic structures with continuous fluctuations occurring between the bicontinuous structure, swollen reverse micelle, and swollen micelles.

**Electrical conductivity**

The water phase was added drop wise to a mixture of oil, surfactant and co-surfactant and the electrical conductivity of formulated samples can be measured using a conductometer at ambient temperature and at a constant frequency of 1 Hz.

**Drug solubility**

Drug was added in excess to the optimized microemulsion formulation as well as each individual ingredient of the formulation. After continuous stirring for 24 h at room temperature, samples were withdrawn and centrifuged at 6000 rpm for 10 min. The amount of soluble drug in the optimized formulation as well as each individual ingredient of the formulation was calculated by subtracting the drug present in the sediment from the total amount of drug added. The solubility of drug in microemulsion was compared with respect to its individual ingredients.

**In-vitro drug release**

The diffusion study can be carried out on a modified Franz diffusion cell, within volume of 20mL. The receptor compartment was filled with of buffer The donor compartment was fixed with

### **Electron Microscope Characterization**

the investigation of microemulsions' microstructure. The most crucial method is transmission electron microscopy (TEM), which can record any coexisting structure as well as micro structural transformations and directly generates images at high resolution.

- An image of the material is taken under room temperature (RT) via the freezing fracture TEM method and the cryo-TEM is utilised to study the samples after rapid freezing and fructose freezing in the cold microscope.<sup>[50]</sup>

### **LIMITATIONS OF MICROEMULSION**

A few things that restrict the application of the microemulsion in therapeutic settings. Among these are

1. The amount of surfactants and co-surfactants used must be maintained low for toxicological reasons.
2. Phase separation is another problem for microemulsions.
3. The need for pharmaceutically approved chemicals limits the choice of microemulsion components (oil, surfactant, and co-surfactant), which poses difficulties in the formulation process.
4. Excipient toxic effects, or the harmful effects of surfactants and co-surfactants, is the primary drawback. The development of studies in this field may be aided through looking at safe excipients as well as assessing the toxicity characteristics of excipients currently in use.

### **IDENTIFICATION TESTS FOR MICROEMULSION**

#### **1. Dilution test**

The following stage will not separate or break if it is applied in microemulsions. It will remain stable if water is introduced to the o/w kind of microemulsions.

#### **2. Staining test**

Water-soluble dyes like methylene blue or amaranth are added, and an oil-and-surfactant microemulsion is produced. Microscopically, a drop of microemulsion can be observed. The background is discovered to be either blue or red, and the globule can appear colourless.

#### **3. Dilute ability test**

To determine if there are any indications of separation in the system, the produced microemulsions are diluted in ratios of 1:10 and 1:100 when using double-distilled water.

#### 4. Zeta potential measurement

It is destructive and illogical, signalling the fact that the micro-emulsion droplets are not charged and that the system is stable. The zeta potential is computed using zetasizer. This potential is most useful for assessing flocculation because the electrical charges on particles alter the flocculation rate.

#### 5. Poly dispersity

Abbes refractometer is used to describe this characteristic.<sup>[24]</sup>

### MICROEMULSION APPLICATIONS IN FORMULATION

#### 1. Controlled release solid state microemulsion

The controlled-release products are produced from microemulsions, which are dispersed in a carrier and thoroughly mixed. The drug is then released in a controlled manner from the solidified microemulsions when the solvent is eliminated using techniques like spray drying, reduced pressure evaporation, etc.<sup>[30]</sup>

#### 2. Nano capsules from w/o microemulsions

The advantages of interfacial polymerization of water-in-oil microemulsions over other approaches in the preparation of PECA nano capsules may have consequences for preserving stability and obtaining effective trapping of specific bioactives, particularly proteins and peptides. By adjusting some of the formulation variables, which include the volume of polymer used, the water weight percentage of the aqueous component of the microemulsion, and the pH<sub>22</sub>, it is possible to control the size, wall thickness, polymer molecular weight, and release rate of the nanocapsules. Anju Graf et al. also described the interfacial polymerization process used to create insulin nanoparticles from w/o microemulsions.<sup>[31]</sup>

**Nanosuspension:** Michele Trotta et al. describe the synthesis of griseofulvin particles from water-dilutable microemulsions. This nanosuspension may be made by using optimal formulations and medicinally appropriate solvents that are such as butyl lactate; low polydispersity griseofulvin nanoparticles smaller than 100 nm were attained. Griseofulvin particles made using the solvent diffusion approach dissolved more quickly than those made using the commercial product.<sup>[32]</sup>

## **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**

Parenteral administration (especially via the intravenous route) of drugs with limited solubility is a major problem in industry because of the extremely low amount of drug actually delivered to a targeted site. Microemulsion formulations have distinct advantages over macroemulsion systems when delivered parenterally because of the fine particle microemulsion is cleared more slowly than the coarse particle emulsion and, therefore, have a longer residence time in the body.

#### **Oral Delivery**

Microemulsion formulations offer the several benefits over conventional oral formulation including increased absorption, improved clinical potency, and decreased drug toxicity. Therefore, microemulsions have been reported to be ideal delivery of drugs such as steroids, hormones, diuretic and antibiotics.

#### **Topical delivery**

Topical administration of drugs can have advantages over other methods for several reasons, one of which is the avoidance of hepatic first-pass metabolism, salivary and degradation of the drug in stomach and related toxicity effects. Another is the direct delivery and targetability of the drug to affected areas of the skin or eyes. Now a day, there have been a number of studies in the area of drug penetration into the skin. They are able to incorporate both hydrophilic (5-fluorouracil, apomorphine hydrochloride etc) and lipophilic drugs (estradiol, finasteride, keto profenetc) and enhance their permeation. Since formation of microemulsion formation requires high surfactant concentration, the skin irritation aspect must be considered especially when they are intended to be applied for a longer period.

#### **Ocular and Pulmonary Delivery**

For the treatment of eye diseases, drugs are essentially delivered topically/W microemulsions have been investigated for ocular administration, to dissolve poorly soluble drugs, to increase absorption and to attain prolong release profile.

**Pharmaceutical applications for current review**

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

**Other application****Microemulsions in analytical applications**

Microemulsions are widely used in the field of analytical techniques such as chromatography etc. In microemulsion electrokinetic chromatography (MEEKC), characterization of solute hydrophobicity was carried out, which provides a quick and reproducible method to obtain hydrophobic parameters for solvents. Microemulsions are able to enhance analytical spectroscopic techniques by functioning as solubilized media, spectral shift reagents, intensity amplification agents, etc. The utilization of microemulsion media in analytical spectroscopy and the analytical sensitivities of the three systems o/w, w/o and bi continuous microemulsion have been assessed. A series of studies have been reported on the determination of aluminium, zinc, copper, manganese ions using both microemulsion and mixed microemulsion systems.

**Microemulsions in biotechnology**

Many biocatalytic and enzymatic reactions are conducted in aquo-organic or pure organic as well as in biphasic media. Their use is seriously limited because they can inactivate or denature the biocatalysts. Recently, interest on microemulsions is being focused for various applications in biotechnology, viz, enzymatic reactions, immobilization of proteins and bioseparation.

**Microemulsions in enhanced oil recovery**

The understanding of the mechanisms of enhanced oil recovery (EOR) using surfactant and microemulsion can help in obtaining unrecoverable underground oil. If the interfacial tension between the crude oil and reservoir brine can be reduced to around  $10^{-3}$  N/m, a substantial fraction of the residual oil in the porous media in which it is trapped can be mobilized. Low interfacial viscosity of the system is also advantageous.

- **Microemulsions for bio separations**
- **Microemulsion as a chemical sensor material**
- **Microemulsions as lubricants, cutting oils and corrosion inhibitors**
- **Microemulsions as coatings and textile finishing.**
- **Microemulsions in detergency.**
- **Microemulsions in cosmetics.**
- **Microemulsions in agrochemicals.**
- **Microemulsions in food.**
- **Microemulsions in environmental remediation and detoxification.**
- **Microporous media synthesis (microemulsion gel technique).**
- **Microemulsions in analytical applications.**
- **Microemulsions as liquid membranes.**
- **Novel crystalline colloidal arrays as chemical sensor materials.**

#### **CURRENT AND FUTURE DEVELOPMENTS**

Over the past 20 years, a lot of research has been conducted on the microemulsion system in an effort to find novel solutions for the problems of repeated bioavailability and low solubility in water of highly lipophilic pharmaceutical compounds. Scaling up is easy from an industrial perspective when evaluating the relative costs of commercial manufacturing.

A microemulsion can be used cosmetically and to target medications. The focus of current research is on developing safer, more appropriate, and effective microemulsion ingredients to extend the use of this cutting-edge delivery method.

<b>S.NO</b>	<b>Drug</b>	<b>Category</b>	<b>Route</b>
<b>1</b>	Fluconazole	Antifungal	Topical
<b>2</b>	Piroxicam	NSAID	Topical
<b>3</b>	Acyclovir	Antiviral	Topical
<b>4</b>	Acetogenic	NSAID	Percutaneous
<b>5</b>	Fluconazole	Antifungal	Topical
<b>6</b>	Diclofenac Sodium	NSAID	Transdermal
<b>7</b>	Timolol	Antihypertensive	Ophthalmic

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