

Microemulsion as a Novel Drug Delivery System: A Review

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Abstract:

A novel, rapid, The microemulsion approach was introduced in the 1940s by Hoar and Schulman. A microemulsion is one of the clear transparent, thermodynamically stable, and longer shelf life novel drug delivery systems because of their long shelf life and improved drug solubility with ease to formulate and administer. The Microemulsion may be dispersed in oil in the water phase with stabilization in the interfacial film of surfactant and co-surfactant. The drug circulates in water-soluble and a lipid-soluble as a drug pathway because of its improved drug solubility capacity, long shelf life, ease of preparation, and increase bioavailability. Its optically isotropic liquid solutions of oil, water and amphiphile. They have emerged new soluble agents or vehicles for drug delay, allowing controlled or sustained release for topical, transdermal, parenterally administering medication. Microemulsions are low viscosity, transparency. This nano-structured vehicle exhibited better solubilization of a drug, higher skin permeation of drugs than conventional formulations when applied on the skin. Improved drug solubility, improved flux across the skin, reduction in diffusion coefficients are significant virtues of the microemulsion system owing to the internal phase being in the nanosize droplet, ultralow interfacial tension with increased surface free energy. The present review focuses on different characterization methods available to establish phase behavior, type of Microemulsion, microstructure details, rheological properties, etc. Microemulsion-based systems find a significant increase in topical delivery of antifungal, antiviral, anti-inflammatory, antioxidant, and local anesthetics. The primary purpose of this review article is to discuss the complete data of Microemulsion.

Keywords: Micro emulsion, Amphiphile formulations, Surfactant-based Formulations, Characterization, Pharmaceutical application.

Introduction

The formulate and development of a new drug delivery system that added the nature of increasing an existing drug's efficacy is an ongoing pharmaceutical research pathway. Nowadays, many types of drug delivery systems have been developed. The microemulsion approach has been introduced in the 1940s by hoar and Schulman ^[1]. Microemulsions are clear, thermodynamically stable, isotropic liquid mixtures of oil, water, and surfactant, frequently combined with a co-surfactant. The aqueous phase may contain salt(s) and other ingredients, and the "oil" may be a complex mixture of different hydrocarbons and olefins ^[2]. Microemulsions are used as the carrier

for protein and peptide delivery to the GI tract. The droplet size of the dispersed phase in a microemulsion is less than 100 nm. Microemulsions are known to increase drug absorption on topical application. Microemulsion-based formulations as prepared in liquid forms, which are preferable for patients with difficulties in swallowing solids ^[3]. Microemulsion has been shown to possess very-low interfacial tension (sometimes negative) as it can adapt a large fraction of co-surfactant/surfactant mixture at the interface, thus thermodynamic stable. The interface between the regular and internal phases has stabilized by a suitable combination of surfactants

and co-surfactant. There is a detailed theoretical basis that explains the stability of Microemulsion in terms of surface free energy, interfacial tension, and solubilization of its components ^[3, 4]. The

into several distinctive types. (4) Water in- Oil (w/o) type vconsists of the oil phase dispersed in the continuous water phase. Most of the topical vehicles investigated belong to this type and found to be more effective in drug delivery than w/o types. Oil-in-water (o/w) microemulsion comprises water droplets internally dispersed into a continuous aqueous phase. However, both types of systems gained equal importance in topical delivery. Bi-regularly structures are also known as lamellar structures, where phases in oil and water microdomains are inter dispersed ^[1, 4]. These systems' complementary names are often such as bloated micelle, visible emulsion, soluble in oil, and micellar solution. Microemulsions are presently the subject of many researchers because of their wide range of potential and actual utilization. The high capacity of microemulsions for drugs makes them interesting formulations for the pharma industry. These systems also offer several benefits for oral administration, including improves absorption, increase clinical efficacy, and reduce toxicity ^[4].

Advantages of microemulsion drug delivery system ^[5,7]

The following advantages of microemulsion drug delivery are maintained below;

1. A microemulsion is allowed self emulsification of the system and thermodynamically stable system.
2. Microemulsions have low viscosity compared to emulsions.
3. This delivery system improves the efficacy of drugs and reduces side effects.
4. The dispersed phase lipid-soluble or hydrosoluble (o/w or w/o microemulsions) can act as an ability reservoir of lipophilic or hydrophilic drugs.

academic details of Microemulsion and its stabilization are given elsewhere in the literature. Micro-structural variations appear when the internal phases have been rearranged

5. Microemulsion having the capacity to carry both lipophilic and hydrophilic drugs.
6. Easy to manufacture and formulate.
7. A microemulsion also improves or enhances amphiphile bioavailability.
8. A microemulsion is helpful for taste masking.
9. Less amount of energy requirement.
10. A microemulsion also improves the absorption of lipophilic and hydrophilic drugs.
11. It is helpful for complete applications for the colloidal drug delivery system.
12. Better long time storage stability.

Disadvantages of Micro emulsion Drug Delivery System ^[5,8]

The following disadvantages of microemulsion drug delivery are maintained below;

1. Microemulsion stability is affected by environmental factors such as pH and temperature.
2. Microemulsion requires a large number of surfactants for stabilizing droplets.
3. It has limited solubilizing potency for high melting materials.
4. Microemulsion having limited storage conditions.
5. A sustained-release short period (biodegradable).
6. Low amount of drug conjugates.
7. Safety is unclear in vivo.
8. Low entrapment and time-consuming drug delivery system.
9. Viscosity issues.
10. Microemulsion having Limited tumor penetrate.

A microemulsion is a thermodynamically, stable, Amphiphile nature. The Microemulsion

may be defined as the precise, thermodynamically stable, isotropic liquid mixtures of oil, water, and surfactant, very ingredients, and the "oil" may be a complex mixture of different hydrocarbons and olefins.

often in combination with a co- surfactant. The water phase may contain salt(s) and other

Following types of Micro emulsion are maintained below;

Table 1: Basic Differences b/w Macroemulsion and Micro emulsion ^[5,9]

S.NO	PARAMETER	MACROEMULSION	MICROEMULSION
1.	Nature	Lyotropic	Amphiphile
2.	Diameter	1to20 mm	10to100 mm
3.	Droplet entities	Individual	Disappear within a fraction of seconds.
4.	Droplet shape	Roughly spherical	Lamellar, spherical
5.	Appearance	White	Transparent
6.	Stability	Thermodynamically unstable	Thermodynamically
7.	Method of preparation	Low and high energy Method	Low energy method
8.	Surface area	Low	High
9.	Types	O/W, W/O.	W/O, O/W, and Bicontinuous.
10.	Surfactant concentration	2-3%	5-8%
11.	Co surfactant	NO	YES

Types of Microemulsions [9-12]

Following types of Micro emulsion are maintained below;

1. Oil/water microemulsion or Winsor I
4. Single phase homogenous mixture or Winsor IV.

2. Water/ oil microemulsion or Winsor II
3. Biscontinuous microemulsion or Winsor III.

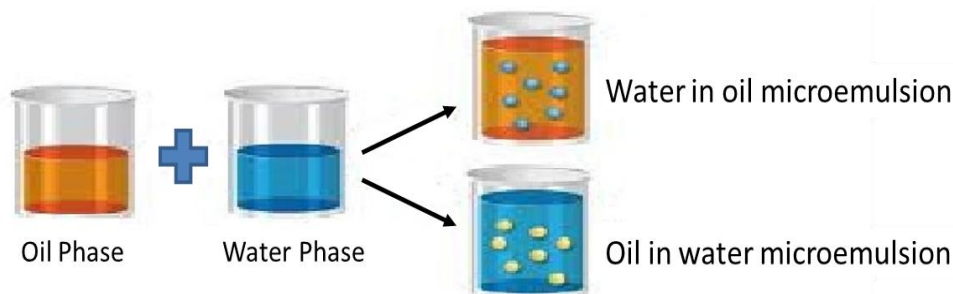


Figure 1 Development of Micro emulsion

Oil-in-water microemulsion: Oil/Water microemulsions are obtained spontaneously by mixing two immiscible liquids (water and oil) in the presence of a surfactant. This type of Micro emulsion mostly has a more significant infraction volume than the water-in-oil microemulsions. In this type, microemulsions maybe oil in a droplet circle by a surfactant (and co-surfactant) film that forms an oil phase distributed in water, which is a repeated phase. This type of Micro emulsion typically has a more intermittent volume than w/o microemulsion.

Water-in-oil Micro emulsion: Water-in-oil type microemulsion may be defined as the process of droplets of water surrounded by a regular oil phase. These are verified as "revertmicelles," where polar head groups of surfactants are encountered in the oil phase with fatty acid tails in water droplets. An

aqueous biological system can undermine a w / o microculture used orally or paternally.

Bicontinuous Micro emulsion: The Bicontinuous Micro emulsion system may be defined as the process amount of water and oil present are the same; in this case, both water and oil are present as a continuous phase. A variable channel of oil and water is combined and resembles a "sponge-phase". Transitions from O/W to W/O microemulsions can pass through this dipole state. The untreated Micro emulsion may show non-Newtonian flow and plasticity. These belongings make the particularly useful for topical delivery or intravenous administration of drugs.

Single-Phase Homogeneous Mixture: Single-phase, the homogeneous mixture may be defined as the process that is homogeneously mixed with oil, water, and surfactants.

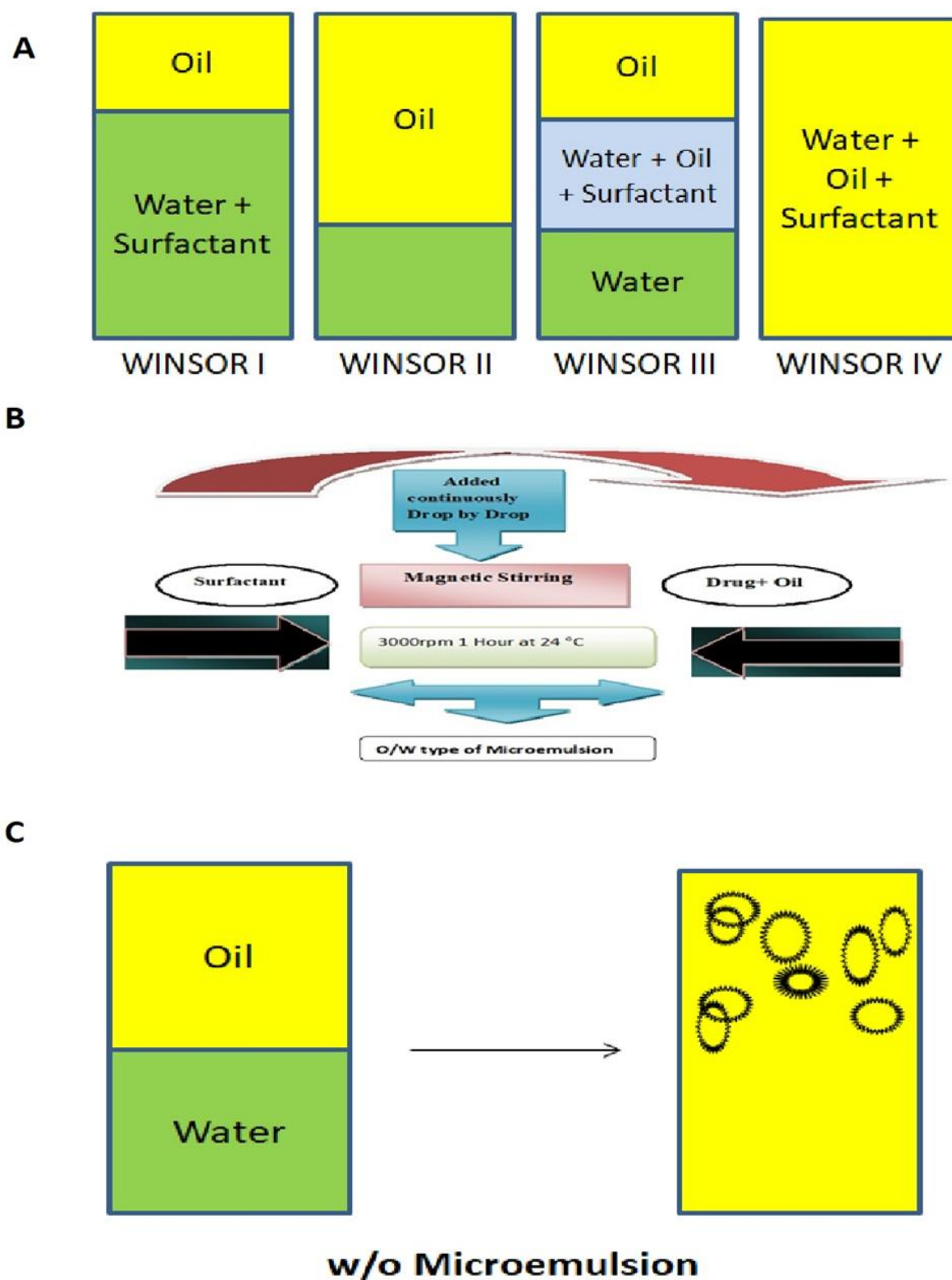


Figure 2 Various type of emulsions

Oil-in-Water Microemulsion: Oil/Water microemulsions are obtained spontaneously by mixing two immiscible liquids (water and oil) in the presence of a surfactant. This type of Micro emulsion mostly has a more significant infraction volume than the water-in-oil microemulsions. In this type, microemulsions maybe oil in a droplet circle by a surfactant (and cosurfactant) film that forms an oil phase distributed in water, which is a repeated phase. This type of Micro emulsion typically has a more intermittent volume than w/o microemulsion.

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Ingredients of Micro emulsion ^[12-16]

The following types of components are used for formulating and developing microemulsions. Generally, lipids and surfactants are used in Micro emulsion that should be nontoxic, clinically acceptable, biodegradable, and biocompatible.

Five main components of Microemulsion are:

aqueous biological system can undermine a w / o microculture used orally or paternally.

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Single-Phase Homogeneous Mixture: Single-phase, the homogeneous mixture may be defined as the process that is homogeneously mixed with oil, water, and surfactants,

1. Oil phase
2. Water phase
3. Surfactant
4. Cosurfactant
5. Cosolvent

Oil phase: The oil phase is the most variable constituents of Microemulsion because it can solubilize the lipophilic drugs and improve the fraction of lipophilic medications delivered through the intestinal

lymphatic system. Generally, the oil phase selects based on the solubility of active pharmaceutical ingredients. Many triglycerides and hydrocarbons are used as oil phases like isopropyl myristate, olive oil, castor oil, oleic acid, triacetin, and other semi-synthetic oils available in markets. Oil refers to the process as any liquid having low miscible and low polarity with water. The same examples of oil phases are cyclohexane, vegetable oil, mineral oil, and toluene. The oil phase is also called the lipid phase.

Water phase: The water phase may contain hydro lover active ingredients and protecting agents. Many times buffer solutions are used as water phase, "water phase also called aqueous phase". An aqueous phase is a liquid medium with water as its principal component and some water-soluble materials.

Surfactant: These substances lower the surface tension (or interfacial tension) between two liquids, between a gas and a liquid, or between a liquid and a solid. The surface-active agent may act as detergents, wetting agents, emulsifiers, foaming agents, and dispersants. The term surfactant (surface active agent) gives a substance that exposes the same superficial and interfacial

action. surfactant are the molecules used to lower the surface or interface tension.

Natural (also known as bio-based or oleo), the surfactant may be found from plant oils, mainly coconut and palm kernel. The plant oils are chemically performed (including through esterification, hydrogenation, and distillation) to give fatty alcohol. Surface active agents play a vital role as cleaning, wetting, dispersing, emulsifying, foaming, and anti-foaming agents in many applications and products, including paints, emulsions adhesives, inks, sanitizers, shampoos, toothpaste, foams, detergents, insecticides, deinking of recycled papers, ski waxes, spermicides. Surface active agent self affiliate due to various inter and intramolecular forces as well as entropy concern.

The types of surfactants, its help in the modern development of the microemulsion system are maintained below;

1. Nonionic Surfactant
2. Anionic Surfactant
3. Cationic Surfactant
4. Zwitter ion Surfactant

Cationic surfactant: Cationic surfactant is contacted an aqueous phase; it gives amphiphilic cation and negative forms, its

halogen types. These are surfactants made up of a positively charged head. Most of the cationic surfactants find use as

The cationic nature of the surface-active agent is not typically consistent with the world of nonionic and anionic charges, and they disrupt cell membranes of bacteria and viruses. Permanently charged quaternary ammonium cations include Alkyltrimethylammonium salts, cetyltrimethylammonium bromide (CTAB), and cetyltrimethylammonium chloride (CTAC).

Anionic surfactant: The anionic surfactant has come with water; it gives amphiphilic anion and a cation, which is, in general, a complimentary metal (Na, K) or quaternary ammonium. The anionic surface-active agent contains anionic functional groups at their head, such as sulfonate, phosphate, sulfate, and carboxylates. Alkyl sulfates involve ammonium lauryl sulfate, sodium lauryl, and the related alkyl-ether sulfate sodium Laureth sulfate, also known as sodium lauryl ether sulfate (SLES), and sodium myreth sulfate. These are the most regularly used surfactants and commonly the alkyl carboxylates (soaps), such as sodium stearate.

antimicrobials, antifungals, etc. Cetylpyridinium chloride (CPC), Benzethonium chloride (BZT).

Nonionic surfactant: Nonionic surface-active agents may stabilize dipole and hydrogen bond interactions with the hydration layer of water and its hydrophilic surface. Its non ionize water solution is that its hydro lover group is non-separable, becoming phenol, alcohol, ester, amides, etc. A nonionic surfactant has no charged groups in its head. A large proportion of these nonionic surface-active agents is derived from hydrophilic by a polyethylene glycol chain.

Zwitterionic surfactant: The zwitterionic surface-active agent is also called amphoteric surfactants. The zwitterionic surface-active agent may have both cationic and anionic centers attached to the same molecule, or both charges positively and negatively charged groups and form microemulsions by the addition of co-surfactants. The anionic part can be variable and include sulfonates, as in the sultaines CHAPS(3-[(3-Cholamidopropyl) dimethylammonio]-1-propanesulfonate). Betaines such as Cocamidopropyl betaine have a carboxylate with the ammonium. The cationic part is based on primary, secondary,

or tertiary amines or quaternary ammonium cations. Zwitterionic surfactants are often sensitive to pH and will behave as anionic or cationic based on pH. Fast dry ("coacervation") latex traffic paints are based on this concept, with a drop in pH triggering the paint's latex to coagulate. Most commonly zwitterionic surface-active agent soybean and egg. Its biocompatibility surface active agent.

Cosolvent

These are the substances that deal with a mixture of two or more separate substances that are ordinarily immiscible to make them mixable, and these are added to increase the solvent power of the primary substance in the mixture, also known as cosolvent. Cosolvent Observing that a single-chain surface-active agent cannot decrease the oil/water interfacial tension sufficiently to form a microemulsion. Cosolvents that are commonly used are methanol, ethanol, and water. Its solubility power determines the effectiveness of a cosolvent. This is the maximum rate of dissolution of a solute in mixtures of various formulations. Cosolvents work best in the presence of another solvent that, in conjunction, improved the dissolution of a solute. The use of co-surfactant is to damage liquid

crystalline or gel structures that come in place of a microemulsion phase.

Co-surfactant

Are mainly alcohols or amines ranging from C4 to C10 and promote the formation and stabilization of micelles/microemulsions. These chemical substances used in addition to surfactant to improve its performance are mostly a second surfactant used in conjunction with a primary surfactant.

Method of formulation ^[16-20]

The microemulsion is an anisotropic, thermodynamically stable, transparent system with oil, water, and surfactant. The following method for the preparation of microemulsions is described and maintained below;

Microemulsions are preparing in a four-step process:

- Firstly selected surfactant, which is rarely soluble in the oil phase.
- Thus, the surfactant chosen is dissolved in the oil, therefore, emulsified in an amount useful to yield a fine emulsion of the emulsified oil in an aqueous phase.

- The oil, closely with its dissolved surfactant, is added to the water phase and jolted or stirred.
- At last, there is a second surfactant in the water phase, which is somewhat more soluble in water than the first surfactant improved a substantially clear microemulsion.

Two types of method prepare and the development of Micro emulsion;

1. Phase inversion method
2. Phase titration method

Phase inversion method

Phase inversion of the Microemulsion is taken out upon adding an excess amount of the dispersed response and temperature phase. During phase inversion, drastic physical changes occur, including changing a particle size that can finally affect drug release in vivo and in vitro. The phase inversion method may be phase inversion of microemulsions and occurs in a large amount of dispersed phase. Its phase inversion unexpected physical changes. For nonionic surfactants in this fully converted by changing the temperature, power of transition from oil in water microemulsion, and low-temperature water in oil microemulsion at a higher temperature

(transitional phase inversion). After cooling, these processes cross a point of zero curvature and minimal surface tension, improving the formation of finely dispersed oil droplets. "Phase inversion also called phase inversion temperature (PIT)." Other than temperature and another parameter such as salt concentration, pH value may be considered more than the effects of the temperature alone. It can also obtain a change in the spontaneous radius of curvature by converting the volume fraction of water. By consecutively adding water to the oil, water droplets form in a regular oil phase. By improving the fraction of water molecules, stabilized w / o microemulsion at the converse point into an o / w microemulsion changes the surface-active agent's impulsive curvature.

Phase titration method

The Microemulsion may be prepared and formulated by the spontaneous emulsification method, shown in the phase diagram. "Phase titration method is also called an emulsification method." The emulsification method may be defined as a mixture of fatty acid and oil added to an acoustic solution to prepare and formulate Microemulsion. As the quaternary phase diagram (four-component system) is time

overwhelming and challenging to interpret, the pseudo ternary phase diagram is made up to find out the different zones and the microemulsion zone, each corner of the graph, represents the particular components. Pseudo-ternary phase diagram of oil, water, and co-surfactant, a mixture of surfactants is constructing at fixed cosurfactant/ surfactant weight ratios. Phase diagrams are obtained by mixing the components, which shall be pre-weighed into glass vials, titrated with water, and stirred well. The formation of a monophasic/ biphasic system is confirmed by visual inspection. It is found as the long-chain length of surfactant. This extended length of surfactant also improved microemulsions with significant transmittances by visible spectrum formed with oils of longer chain lengths. It has been found that different alcohols affect the formation of microemulsions in different ways. The best results are obtained from small or branched alcohols, combined with a wide range of oil (dispersed in water) concentrations in terms of the most excellent percentage transmittance.

Theories of microemulsion ^[20-22]

Various theories related to microemulsion formation, stability, and phase behavior have been proposing over the years. For

example, one explanation for their thermodynamic equilibrium is that the surfactant present stabilizes the oil/water dispersion and their formation includes the elastic properties of the surfactant film at the oil /water interface, including the parameters, curvature. And hardness. Of the film. These parameters may have an eclipse or measured pressure and temperature dependence (salinity of the aqueous phase), which can be used to divide the area of stability of the Microemulsion or to divide this area.

The following theories give based upon effect and control their stability and phase behavior, these theories are maintained below;

- 1.Thermodynamic theory
- 2.Solubilisation theory
- 3.Interfacial theory.

Thermodynamic theory

The formation and stability of microemulsions can be explicitly based on a normally thermodynamic mechanism. The free energy of microemulsion formation can hang on the extent to which the surface-active agent decreases the surface tension of

the oil-water interface and in the entropy of the system, therefor-

$$\Delta G_f = \gamma \Delta A - T \Delta S$$

Where;

ΔG_f = Energy released from formation,

γ = Surface tension of the oil-water interface,

ΔA = Interfacial area change in micro emulsification,

ΔS = Change in the entropy of the system, which is effectively the dispersion entropy,

T = Temperature.

When a microemulsion is formed, the ΔA is changed significantly due to many tiny droplets' formation. It is essential to know that, although the γ value always is positive, this is very small and is met by the entropic component.

The significant, timely entropic extension is the extensive dispersion entropy resulting in many small droplets mixing from one phase to another. However, favorable entropic contributions also come from other kinetic processes, such as monomer – micelle surfactant exchange and these Surfactant diffusions in the interfacial layer. When a massive reduction in surface tension is found by significantly favorable entropy change, the negative free energy of formation is obtained. In that case, the

Microemulsion is spontaneous, and the resulting dispersion is thermodynamically stable.

Solubilisation theory

Microemulsions may be thermodynamically stable monophasic solutions of water-swelling (w/o) or oil-swelling (o/w) spherical micelles. The relationship between microemulsions and W/O microemulsions can be studied with phase diagrams. The ternary system's inversion is the formation of reverse micelles dissolving in SDS water in the mycelium region, i.e., water, pentanol, and sodium dodecyl sulfate (SDS) pentanol.

The addition of O-xylene up to 50% gives rise to a transparent W / O region with a maximum of 28% water containing 5% pentanol and 6% surfactant (i.e., microevolution). The quaternary phase diagram, constructed on the addition of p-xylene, represents the relationship of these regions to the isotropic inverted micellar phase. These four component systems could be prepared by adding hydrocarbons. The microemulsion is a soluble oil phase, and the water phase by reverse micelles becomes bigger and swelling to a specific range of size results.

Interfacial theory

"In this theory also called a mixed-film theory." The relatively large entropy of the droplet mixture and the continuous medium suggest the spontaneous formation. Shulman emphasized the importance of the interfacial film. They assumed that microemulsion droplets' spontaneous formation was due to a complex film's shape at the oil-water interface by surfactants and co-surfactants. This caused a decrease in the oil-water differential stress to a deficient value (near zero to negative), which is indicated by the following equation;

The film which consists of surfactant and cosurfactant molecules, is taken as a "two-dimensional" third phase is equal with both oil and water.

Factor affecting formulation of microemulsion ^[22-25]

These factors are affecting the formulation and development of the microemulsion system. The formation of oil or water-swollen microemulsion depends on the packing ratio, property of the surfactant, oil phase, temperature, chain length, type, and nature of the co-surfactant.

The following factor affecting the formulation and development of Microemulsion is maintained below;

1. Packing Ratio,
2. Properties of Surfactant, Oil phase, and temperature
3. Factor affecting phase behavior
 - Salinity
 - Surfactant
 - Hydrophobic
 - Chain length
 - Alcohol concentration pH
 - Ionic strength.
4. Property of Surfactant

Packing ratio

HLB of the surface-active agent elects the type of Microemulsion through molecular packing and its effect on film curvature. The determination of film curvature for leading surfactant alliance for microemulsions formation is called a critical packing parameter (CPP).

$$CPP = v / a * l \quad (3)$$

Where v is the partial molar volume of the surfactant's hydro-soluble portion, an optical head group area, and L is the length of the surfactant tail. If the CPP value is between 0 and 1 interface, water (positive curvature) and oil/water favor the system, but when CPP is > 1 , the interface alliance currently

reduces dilute solution and can form oil/water microemulsion. When the surfactant is in the presence of salt or when a high concentration of surfactant is used, the degree of dissociation of polar groups becomes lesser, and the resulting system may be water/oil type.

Properties of Surfactant, Oil phase, and temperature

This type of Microemulsion depends on the nature of the surfactant. Surfactants include water-soluble head groups and lipid-soluble tail groups. These clusters, which are determined by the water gap's capacity to expand the head region and the oil to tail region, are important for specific formulation when evaluating surfactant HLB in each system. When high concentrations of the surface-active agent are use or when a surfactant is in the presence of salt, the degree of dissociation of polar groups decreases and may result in system water/oil types. Dissolving with water can improve dissociation and convey towards the Oil / Water system. Ionic surfactants are mostly influenced by temperature. Mainly causes surfactant counterion dissociation. The oil component also affects curvature by penetrating and swaying the surfactant monolayer's tail group region. Small-chain

oils enter the lipid-soluble group zone to a large extent and improve the negative curvature. Temperature is critical in determining the size of the influential head group of non-surfactants. At low temperatures, these are water-soluble and form a typical Oil/Water system. At high temperatures, they are lipid-soluble and Water/Oil systems. At an average temperature, Microemulsion coexists with additional water and oil phases and forms a tectonic structure.

pH

pH changes may have improved the microemulsions containing pH-sensitive surfactants. This is more affected pronounced in the case of acidic or basic surfactants. Carboxylic acids and amines change the phase behavior from water/oil to oil/water by increasing the pH. An increase in the aromaticity of oil leads to a phase transition from oil/water to water/oil and is the opposite of an increase in the oil alkane carbon number. As the ionic strength improves, the system passes from oil/water microemulsion in balance with excess oil to the intermediate phase and finally to water/oil microemulsion in equilibrium with excess water.

Property of surfactant

The surfactant contains two group lipophilic and hydrophilic groups. Hydrophilic single-chain surfactants such as cetyl-ethyl ammonium bromide dissociate completely in dilute solution and tend to form oil/water microemulsion. When the surface-active agent is in the presence of salt or when a high concentration of surfactant is used, the degree of dissociation of polar groups becomes lesser, and the resulting system may be Factors Affecting phase behavior.

Salinity

low salinity, the droplet size of oil/water microemulsion increases, corresponds to an improvement in oil solubilization. As salinity further increases, the system becomes bi-continuous over a between salinity range. Increase in salinity towards the formation of continuous Microemulsion with a reduction in globule size. Further, the rise in salinity currently results in a complete phase transition.

Alcohol concentration

Increasing the concentration of low molecular weight alcohol as a co-surfactant leads to the phase transition from water/oil to bicontinuous and currently to oil/water type microemulsion. Exactly opposite phase

transition is noticed in the case of high molecular weight alcohol.

Surfactant hydrophobic chain length:

The surfactant's hydrophobic chain length also increases and shows the change of oil/water microemulsion to water/oil via the bicontinuous phase.

Evaluation Parameters of Micro emulsion System ^[26-30]

Following the evaluation parameter of the microemulsion system also maintained below ;

1. Physical appearance
2. Scattering techniques
3. Limpidity test
4. Drug stability
5. Globule size.
6. Zeta potential
7. Rheological properties
8. Electrical conductivity
9. Drug solubility
10. In-vitro drug release

Physical appearance

Microemulsion can be inspected for physical appearance for uniformity, fluidity, and optical clarity.

Scattering techniques

These techniques, such as small-angle neutron scattering, small-angle X-ray scattering, and light scattering, have found application in microemulsion structure studies, particularly in thinning monodisperse regions when in polydispersed or concentric systems such as microemulsions.

Limpidity test

Under the measurement of percent transmittance, this test can measure the limpidity of the Micro emulsion spectrophotometrically.

Drug stability

The optimized Microemulsion was kept in cold conditions (4-8 ° C), room temperature, and moderate temperatures (50.2 ° C). After every two months, microemulsions can be analyzed for phase separation, % transmittance, spherical shape, and % test.

Globule size and zeta potential

The microemulsion globule size and zeta potential can be measured by dynamic light scattering using a zeta sizer HST3000.

Rheological properties

Stability plays a vital role in rheological properties. It can be the measurement by the Brookfield Digital Viscometer. converting in

rheological features that help determine the microemulsion area and its separation from another area. Bicontinuous micro solutions are dynamic structures between continuous structure fluctuations, inverted micelles, and swollen micelles.

Electrical conductivity

The aqueous phase has added a drop to drop in a mixture of oil, surfactant, and co-surfactant, and the electrical conductivity of the prepared samples can be measured using one kilometer at room temperature and a constant frequency of 1 Hz.

Drug solubility

The drug was added to a custom microemulsion formulation and an excess of every formulation component. After regularly stirring for 24 hours at room temperature, the samples were removed and centrifuged at 6000 rpm for 10 minutes. The amount of soluble drug is the optimized formulation, and each formulation component was calculated by subtracting the drug present in the sediment from the total drug volume. The solubility of the drug in Microemulsion was compared concerning its ingredients.

In vitro drug release

Proliferation studies can be performed on a modified Franz diffusion cell within a volume of 20ml. The receptor compartment was filled with a buffer and fixed with the donor compartment, and cellophane membrane, containing the Microemulsion formulated and simple medication solutions. Predetermined time intervals samples were drawn from the receptor analyzed for drug molecules using Ultra Violet spectrophotometer.

Application of microemulsion system^[30-35]

These microemulsion systems find utility in various applications, including consumer and industrial cleaning formulations, chemical reaction media, polymerization, and active ingredient delivery. Following application are also divided many industries are maintained below

1. Pharmaceutical industries
2. Agrochemicals
3. Cutting oils
4. Biotechnology
5. Food industry
6. Cosmetic industry
7. Analytical method
8. Environmental detoxification

Micro emulsion in pharmaceuticals^[31, 35]

Nowadays, many revolutions in the utilization of the microemulsion system in a variety of Pharmaceuticals.

- Parenteral delivery
- Oral delivery
- Topical delivery
- Ocular delivery
- Pulmonary delivery
- Nasal delivery
- Drug targeting delivery
- Cellular targeting delivery
- Brain targeting delivery
- Tumor targeting delivery
- Periodontal delivery

Parenteral delivery

Intravenous drug administration delivery route a rare solubility is a significant problem in pharmaceuticals because of the low amount of drug delivered in the target site. These formulations have many advantages over the microemulsions system because of fine particles, clear solutions, and longer residence time in the biological system.

Oral delivery

The oral drug delivery system has several advantages of oral formulations because it increases absorption, improves clinical

potency, and decreases toxicity. Therefore, many oral formulations for the ideal delivery of drugs such as hormones, antibiotics, steroids, etc.

Topical delivery

Topical drug delivery systems also are used in the microemulsion, such as nowadays, there have been several studies in the area of drug penetration into the skin. Because it is the avoidance of hepatic first-pass metabolism, salivary, and degradation of the drug in the stomach and toxic effect, this system requires a high surfactant concentration.

Ocular and pulmonary delivery

These drug delivery systems are used in the treatment of eye disease. The drug is delivered topically; oil and water microemulsion has been magnifying for ocular drug delivery administered. In this drug delivery system, to dissolve poorly soluble drugs, improve absorption, and prolonged time.

Nasal delivery

In recent times, Microemulsion has been studied as an administration of the nose to brain increase drug uptake through the nasal mucosa. In addition to mucus adhesives, the

polymer helps extend the time spent in the mucosa. The nose to brain route for administered Microemulsion with diazepam may be a useful approach for quick action during emergency treatment of status epilepticus due to improved penetration and improved bioavailability.

Drug targeting

Drug targeting to various tissues has developed as the most desirable target of drug delivery. Improved targeted action by changing the pharmacokinetics and biodistribution of drugs and improved their tissue to attain drug potency with concomitant reduction of their toxic effect. Nowadays, Microemulsion for tumor targeting of the lipid-soluble antitumor antibiotic salinomycin. A was an effective method of targeting emulsions to tumor cells.

Periodontal delivery

Periodontal disease is a collective term for progressive oral pathological pain like inflammation and deterioration of the gums, periodontal ligaments, cementum, and promoting bone.

Cellular targeting

Nucleic acid, Conway to cells are encouraging therapeutics. The initiation of the insertion of nucleic acid into a reverse micelle for cell delivery proved very encouraging. They referred to water/oil microemulsions as reverse micelles. The reverse micelle has been the property to close the nucleic acid for relaxed delivery.

Tumor targeting

The microemulsions as vehicles used to deliver chemotherapeutic or diagnostic agents to tumor cells while avoiding normal cells were advised.

Brain targeting

Nose to brain drug delivery is administration confers a simple, practical, cost-effective, convenient, and non-invasive route of administration for rapid drug delivery to the brain. It allows direct transport of drugs to the brain, Conway the brain barriers.

Microemulsions in biotechnology

Many biocatalysts and biocatalytic reactions are strategies in pure organic or aqua-organic media. Biphasic media are also utilized for these types of responses. The use of pure apolar media causes the denaturation of biocatalysts. The use of water-proof media is mainly advantageous. Enzymes are

a low water content, Thus improved solubility in apolar reactants, Prospect of shifting thermodynamic equilibria in favor of deliquescence. Improvement of thermal stability of the biocatalyst, Allow reactions to be carried out at higher temperatures.

Mostly enzymes consist of lipases, esterases, dehydrogenases, and oxidases, often work in the cells in microenvironments that are hydrosoluble. In biological systems, enzymes manage the interactions between hydrophobic and hydrophilic domains, and these usual interfaces are stable by polar lipids and other natural amphiphiles. Enzymatic catalysis in microemulsions has been utilized for various reactions, such as the synthesis of esters, peptides, sugar acetals transesterification; different hydrolysis reactions, and steroid transformation.

Conclusion

The microemulsions as drug delivery vehicles have been used as a stimulating and agreeable research field because of its many prospective and excellent advantages. In microemulsions, one can design the interaction of such nanometer-sized droplets so that droplet stability and shelf life in humans can be made to last from a few milliseconds to minutes, or even to hours.

The microemulsion droplets' abbatial severity plays the primary role in the drugs' flux from such droplets to the cells and tissues. Tailoring microemulsion systems to control the drugs' fluctuation can customize drug delivery according to individual patient requirements or specific pharmaceutical needs. Microemulsions offer an absorbing and potentially completely powerful

different carrier system for drug delivery because of their high soluble capacity, transparency, thermodynamic stability, ease of preparation, and increased diffusion and absorption rates when compared to solvent without the surfactant system. Anyway, toxicological estimation and evaluation of the prepared Microemulsion can be used in the future.

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