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Microemulsions: A possible food bioactive delivery method

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Abstract
Microemulsions are thermodynamically stable, transparent, low viscosity, and isotropic dispersions consisting of oil and water stabilized by an interfacial film of surfactant molecules, typically in conjunction with a cosurfactant. Microemulsions (so-called due to their small particle size; 5–100 nm) have found application in a wide variety of systems, such as pharmaceutical and oil recovery, but their application in food systems has been hindered by the types of surfactant permissible for use in food. Microemulsions contain definite boundary between oil and water phases at which surfactant is located. Conventional surfactant molecules comprised polar head group region and a polar tail region. Microemulsions may be asymmetric in shape, frequently adopting the shape of prolate ellipsoid. Microemulsions can be applied as liquid membrane carriers to transport lipophilic substance through an aqueous medium or to carry hydrophilic substances across lipoidal medium. As the size of the particle is much smaller than the wavelength of visible light, microemulsions are transparent and structure cannot be observed through an optical microscope. Microemulsions are liquid behave as a Newtonian liquid. They offer the advantage of spontaneous formation, ease of manufacturing and scale-up, thermodynamic stability, and improved drug solubilization and bioavailability. Preparing a pharmaceutically acceptable dosage form demands a clear understanding of the micro-emulsion structure, phase behavior, factors leading to its thermodynamic stability and the potential uses and limitations of the microemulsion system.

Keywords: Microemulsion, thermodynamically stable, surfactant.

Introduction
Microemulsions are clear, stable, isotropic mixtures of oil, water and surfactant, frequently in combination with a cosurfactant. These systems are currently of interest to the pharmaceutical scientist because of their considerable potential to act as drug delivery vehicles by incorporating a wide range of drug molecules [3]. The aqueous phase may contain salt(s) and/or other ingredients, and the "oil" may actually be a complex mixture of different hydrocarbons and olefins. In contrast to ordinary emulsions, microemulsions form upon simple mixing of the components and do not require the high shear conditions generally used in the formation of ordinary emulsions. The two basic types of microemulsions are direct (oil dispersed in water, o/w) and reversed (water dispersed in oil, w/o) [4]. Microemulsions forms spontaneously with an average droplet diameter of 10 to 140 nm. Microemulsions contain definite boundary between oil and water phases at which surfactant is located. Conventional surfactant molecules comprised polar head group region and an apolar tail region. Microemulsions may be asymmetric in shape, frequently adopting the shape of prolate ellipsoid. Microemulsions can be applied as liquid membrane carriers to transport lipophilic substance through an aqueous medium or to carry hydrophilic substances across lipoidal medium. As the size of the particle is much smaller than the wavelength of visible light, microemulsions are transparent and structure cannot be observed through an optical microscope. Microemulsions are liquid behave as a Newtonian liquid.They are not very viscous [5]. A microemulsion is a transparent or nearly transparent, quasi-homogeneous, thermodynamically stable mixture of two immiscible liquid stabilized by surfactant (or mixture of surfactant). As pharmaceuticals drug delivery systems, microemulsion have unique properties, including clarity, high stability and ease of preparation. Due to their physicochemical properties, microemulsion often advantages over traditional topical and transdermal drug delivery systems. Moreover, microemulsion dispersion are promising candidates as means for controlled drug delivery, and as drug carriers for oral, topical, and parenteral administration furthermore, microemulsion have been shown to process promising

potential in the fields of cosmetic and various consumer products [6]. The structure, dynamics and transport behaviors of microemulsions are physicochemically unique and need exploration for basic understanding of their formation, state of aggregation, internal interaction, and stability with reference to their probable uses. Microemulsions w1x are compartmentalized liquids of potential current and future application prospects. They are dispersions of either 'water in oil' or 'oil in water' stabilized by pure or mixed amphiphiles, the latter is required for significant lowering of the oil water interfacial tension by way of their interfacial adsorption, thus to help minimize the related positive free energy change of dispersion associated with surface formation [8].

The structures within these phases may be spheroid (e.g., micelles or reverse micelles), cylinder-like such as rod-micelles or reverse micelles), plane-like (e.g., lamellar structures), or sponge-like (e.g., bicontinuous). Appropriate analytical methods are required to accurately identify the structures formed within a SOW system under a particular set of conditions, such as microscopy (e.g., light, electron, or atomic force), scattering methods (e.g., light, X-ray, or neutrons), electrical conductivity, nuclear magnetic resonance, and rheology. When using the term ''microemulsion'' one must therefore clearly state which kind of microemulsion system is being considered [9]. The tremendous potential of microemulsions as modern colloidal carriers for topical and transdermal drug delivery are well recognized [1]. Microemulsions, a system of water, oil and amphiphiles, provide a variety of advantages for pharmaceutical use, such as nanometer-sized aggregations, long-term stability, biocompatibility, straightforward preparation and high solubilization capacity for drug molecules and enhanced drug delivery [2–4]. Oil soluble drugs can be formulated in oil-in-water microemulsions whereas, water soluble ones are better suited for water-in-oil microemulsions [12].

Microemulsion polymerization of monomers may be achieved by incorporating a monomer in any of the water and oil phases of the system. Replacing dispersed phase by a monomer in an o/w microemulsion produces spherical latex particles of optimum diameter. However, solid materials may be produced if the continuous phase is polymerized, entrapping the dispersed phase in its matrix. This latter approach that has been successfully used for producing solid materials by microemulsion polymerization [13]. Microemulsions have ultralow interfacial tension, large interfacial area and capacity to solubilize both aqueous and oil-soluble compounds.

Depending on the proportion of various components and hydrophilic–lypophilic balance (HLB) value of the used surfactant microemulsions can be classified as water-in-oil (W/O), oil-in-water (O/W) and intermediate bicontinuous structural types that can turn reversibly from one type to the other.

The dispersed phase consists of monodispersed droplets in the size range of 5-100 nm. The nanodroplet size can be modified by varying concerned parameters, e.g. the type of stabilizer, continuous phase, the precursor content dissolved within the nanodroplets, and the water content, referred to as molar ratio of water to surfactant (*W*). In addition, the stability of the microemulsion can be influenced by addition of salt, concentration of reagents, temperature or pressure [13].

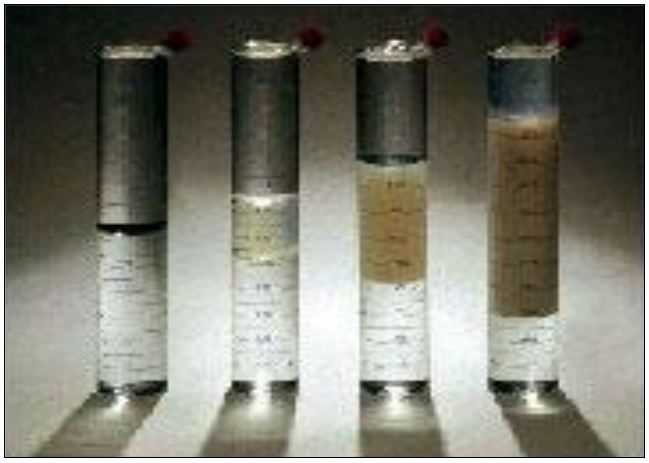


Fig 1: Show surfactant-poor oil phase

Historical background

The combination of water and oil, made into a single-phase system with the aid of a third component (surfactant), was patented in mid1930's. However, it was not until 1943 when the first academic studies were performed. Hoar and Schulman showed, with the help of a strong surface active agent, it is possible to induce spontaneous emulsification. This is now attributed to microemulsion formation, owing to very low interfacial tensions promoted by the surfactants. Five years later, Winsor studied the phase behavior of water-oil-surfactant mixtures in the presence of different additives and classified four types of phase equilibria:

Type I: Surfactant-rich water phase (lower phase) coexists with surfactant-poor oil phase (Winsor I).

Type II: Surfactant-rich oil phase (the upper phase) coexists with surfactant-poor water phase (Winsor II).

Type III: Surfactant rich middle-phase coexists with both water (lower) and oil (upper) surfactant-poor phases (Winsor III)

Type IV: Single phase homogeneous mixture.

In 1959, Schulman *et al*., titrated a multiphase system (consisting of water, oil and surfactant) with alcohol and obtained a transparent solution which they termed 'a microemulsion'. At that early stage some researchers preferred to identify these systems with 'swollen micelles' others used the term 'micellar emulsion'. Nevertheless, the term 'microemulsion' is a commonly used name nowadays. A detailed historical background of microemulsions can be found elsewhere [4]. Since the discovery of microemulsions by Jack H. Shulman, there have been huge progresses made in applying microemulsion syst ems in a plethora of research and industrial processes. Microemulsions are clear, stable, isotropic mixtures of oil, water and surfactant, frequently in combination with a cosurfactant. Microemulsions are optically isotropic and thermodynamically stable liquid solutions of oil, water and amphiphile. To date microemulsions have been shown to be able to protect labile drug, control drug release, increase drug solubility, increase bioavailability and reduce patient variability. Furthermore, it has proven possible to formulate preparations suitable for most routes of administration. Since the discovery of microemulsions, they have attained

increasing significance both in basic research and in industry. Due to their unique proper ties, namely, ultralow interfacial tension, large interfacial area, thermodynamic stability and the ability to solubilise otherwise immiscible liquids, uses and applications of microemulsions have been numerous. Microemulsions are readily distinguished from normal emulsions by their transparency, low viscosity and more fundamentally their thermodynamic stability. Microemulsions are shown to be effective dermal delivery mechanism for several active ingredients for pharmaceutical and cosmetic applications [4].

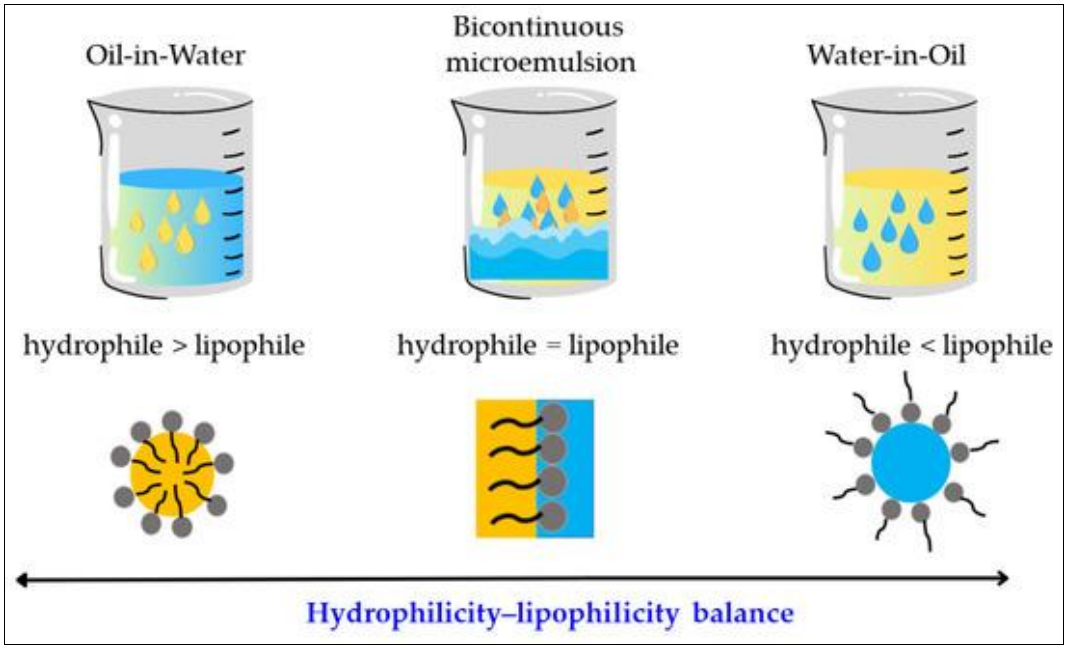


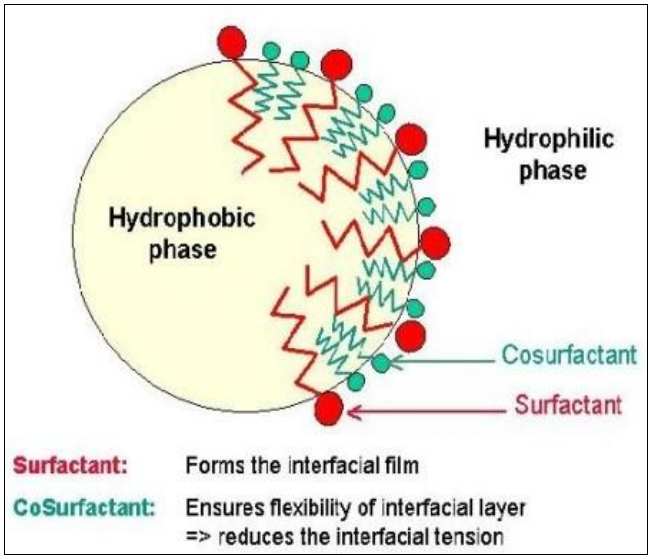
Fig 2: Show Hydrophilicity-lipophilicity balance

Structure of Microemulsion

Microemulsions are dynamic systems in which the interface is continuously and spontaneously fluctuating. Structurally, they are divided into oil-in-water (o/w), water in oil (w/o) and bicontinuous microemulsions. In w/o microemulsion, water droplets are dispersed in the continuous oil phase while o/w microemulsion is formed when oil droplets are dispersed in the continuous aqueous phase. In systems where the amounts of water and oil are similar, a bicontinuous microemulsion may result. In all three types of microemulsions, the interface is stabilized by an appropriate combination of surfactants and/or co-surfactants. The mixture of oil, water and surfactants is able to form a wide variety of structures and phases depending upon the proportions of the components.

The flexibility of the surfactant film is an important factor in this regard. A flexible surfactant film will enable the existence of several different structures like droplet like shapes, aggregates and bicontinuous structures, and therefore broaden the range of microemulsion existence. A very rigid surfactant film will not enable existence of bicontinuous structures which will impede the range of existence.

Besides microemulsions, structural examinations can reveal the existence of regular emulsions, anisotropic crystalline hexagonal or cubic phases, and lamellar structures depending on the ratio of the components. The internal structure of a microemulsion vehicle is very important for the diffusivity of the phases, and thereby also for the diffusion of a drug in the respective phases. Researchers have been trying zealously to understand the complicated phase behavior and the various microstructures encountered in the microemulsion systems [16, 5].



Structure of microemulsion

Fig 3: Show hydrophobic phase

Advantages of Micro Emulsion based systems

Microemulsions exhibits several advantages as a drug delivery system:

1. Microemulsions are thermodynamically stable system and the stability allows self-emulsification of the system.
2. Microemulsions act as super solvents for drug. They can solubilize both hydrophilic and lipophilic drugs including drugs that are relatively insoluble in both aqueous and hydrophobic solvents.
3. The dispersed phase, lipophilic or hydrophilic (oil in water, O/W, or water-in-oil, W/O microemulsions) can

act as a potential reservoir of lipophilic or hydrophilic drugs, respectively. Drug release with pseudo-zero-order kinetics can be obtained, depending on the volume of the dispersed phase, the partition of the drug and the transport rate of the drug.
4. The mean diameter of droplets in microemulsion is below 0.22 mm. The small size of droplet in microemulsions e.g. below 100 nm, yields very large interfacial area, from which the drug is released rapidly into external phase when absorption (*in vitro* or *in vivo*) takes place, maintaining the concentration in the external phase close to initial levels.
5. Same microemulsions have the ability to carry both lipophilic and hydrophilic drugs.
6. Because of thermodynamic stability of microemulsions, they are easy to prepare and require no significant energy contribution during preparation. Microemulsions have low viscosity compared to primary and multiple emulsions.
7. The use of microemulsion as delivery systems can improve the efficacy of a drug, allowing the total dose to be reduced and thus minimizing side effects.
8. The formation of microemulsion is reversible. They may become unstable at low or high temperature but when the temperature returns to the stability range, the microemulsion reforms [3].

Disadvantages of Micro Emulsion based systems
1. Require large amount of S/Cs for stabilizing droplets.
2. Limited solubilizing capacity for high-melting substances used in the system.
3. The surfactant should be nontoxic for use in pharmaceutical applications.
4. Microemulsion stability is influenced by environmental parameters such as temperature and pH. These parameters change as microemulsion delivered to patients [5].

Limitations

Factors which limit the use of micro Emulsion in pharmaceutical applications
1. The concentration of surfactants and co-surfactants used must be kept low for toxicological reasons.
2. Microemulsion also suffers from limitations of phase separation.
3. For intravenous use, the demand of toxicity on the formulation is rigorous and very few studies have been reported so far.
4. Use of those surfactants which are included in "generally regarded as safe" (GRAS) category can reduce toxicity.
5. The need of pharmaceutically acceptable ingredients limits the choice of microemulsion
6. components (e.g., oil, surfactant and cosurfactants) leading to difficulties in formulation.
7. The major limitation is the toxicity of excipients i.e. surfactant/ co-surfactants. Exploration of safe excipients and evaluation of the toxicity parameters of available excipients may help in further expansion of research in this field [3, 4].

Components of Micro Emulsion System

The availability of oils and surfactant is abundance but their use is restricted due to their toxicity, irritation potential and unclear mechanism of action. Oils and surfactant which will be used for the formulation of micro emulsion should be biocompatible, non-toxic, and

Clinically acceptable. The emphasis is on selecting the component which comes under "generally regarded as safe" (GRAS)
1. Oil phase
2. Aqueous phase
3. Primary surfactant
4. Secondary surfactant (co-surfactant)
5. Co-Solvent

1. Oil phase

The oil being one of the most important excipients in the formulation not only because it can solubilize the required dose of the lipophilic drug, it can increase the fraction of lipophilic drug transported via the intestinal lymphatic system, thereby increasing absorption from the GI tract depending on the molecular nature of the triglyceride. The oil component influences curvature by its ability to penetrate and hence swell the tail group region of the surfactant monolayer. Short chain oils penetrate the tail group region to a greater extent than long chain alkanes, and hence swell this region to a greater extent, resulting in increased negative curvature (and reduced effective HLB).

Following are the different oils are mainly used for the formulation of microemulsion
- Saturated fatty acid-lauric acid, myristic acid, capric acid
- Unsaturated fatty acid-oleic acid, linoleic acid, linolenic acid
- Fatty acid ester-ethyl or methyl esters of lauric, myristic and oleic acid.

2. Aqueous phase: The aqueous phase may contain hydrophilic active ingredients and preservatives. Buffer solutions are used as aqueous phase by some researchers [5].

3. Primary Surfactants: The surfactant chosen must be able to lower the interfacial tension to a very small value which facilitates dispersion process during the preparation of the microemulsion and provide a flexible film that can readily deform around the droplets and be of the appropriate lipophilic character to provide the correct curvature at the interfacial region. It is generally accepted that low HLB surfactants are favored for the formulation of w/o microemulsion, whereas surfactants with high HLB (>12) are preferred for the formation of o/w microemulsion. Surfactants having HLB greater than 20 often require the presence of cosurfactants to reduce their effective HLB to a value within the range required for micro Emulsion formation (18).

4. Co-surfactants: Microemulsion formation may also require the presence of a cosurfactant. Medium chain length alcohols, and to a lesser extent amines and acids, have been used as cosurfactants and perform a variety of functions to aid in microemulsion formation. The cosurfactant has the effect of further reducing the interfacial tension, whilst increasing the fluidity of the interface, thereby increasing the entropy of the system. Cosurfactants may also adjust the curvature of the interfacial film by partitioning between the tails of the surfactant chains, allowing greater penetration of the oil between the surfactant tails. Furthermore, the

presence of alcohol may influence the solubility properties of the oil and water phases, due to its partitioning between these phases.21 Cosurfactants can also destabilize the lamellar liquid crystalline phase [21].

5. Co-solvents: The production of stable microemulsion requires relatively high concentrations (generally more than 30% w/w) of surfactants. Organic solvents such as, ethanol, propylene glycol (PG), and polyethylene glycol (PEG) are suitable for oral delivery, and they enable the dissolution of large quantities of either the hydrophilic surfactant or the drug in the lipid base. These solvents can even act as co-surfactants in microemulsion systems [5].

Method of Preparation

1. Phase Titration Method
2. Phase Inversion Method

1. Phase Titration Method

Microemulsions 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. Microemulsions 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 equilibria 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 microemulsion 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 [6, 21].

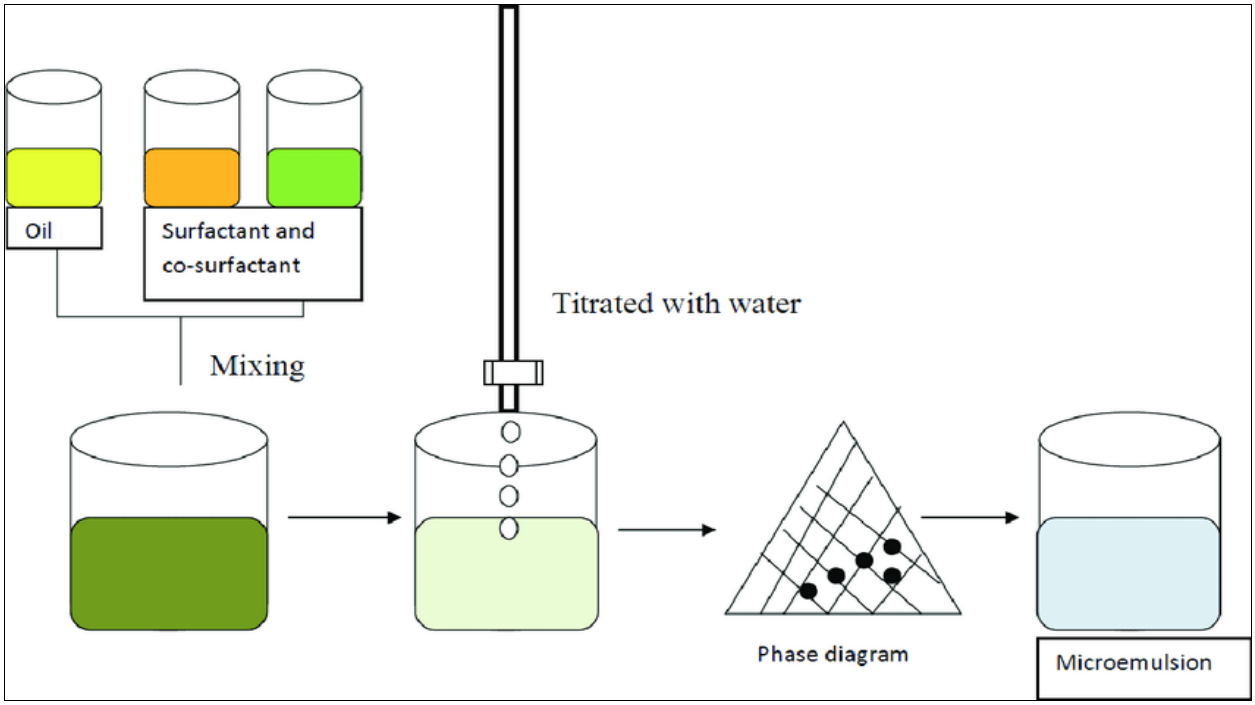


Fig 4: Show Diagrammatic representation of the titration method of Micro Emulsion.

2. Phase inversion method

Phase inversion of microemulsions 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 curvature 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 microemulsion at low temperatures to a w/o microemulsion 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, a 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 microemulsion to an o/w microemulsion at the inversion locus. Short-chain surfactants form flexible monolayers at the o/w interface resulting in a bicontinuous microemulsion at the inversion point [5, 18].

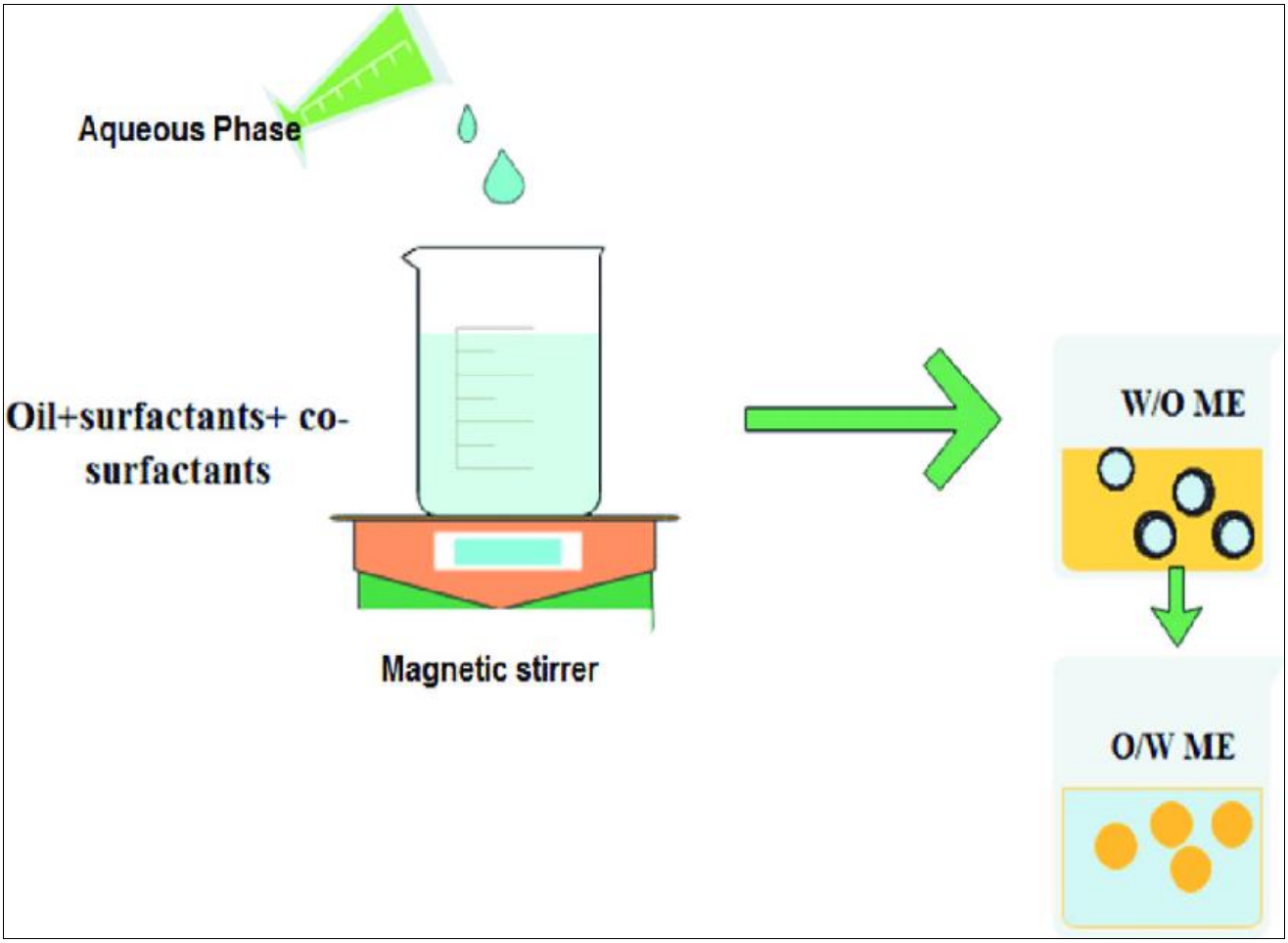


Fig 5: Show Diagrammatic representation of the phase inversion method of Micro Emulsion.

Characterization of Microemulsion

Microemulsions can be characterized by different techniques. The characterization of microemulsions is a difficult task due to their complexity, variety of structures and components involved in these systems, as well as the limitations associated with each technique but such knowledge is essential for their successful commercial exploitation. Therefore, complementary studies using a combination of techniques are usually required to obtain a comprehensive view of the physicochemical properties and structure of microemulsions.

The basic component in a physicochemical characterization of microemulsions systems are

- Phase stability and phase behavior.
- Microstructure, dimension.
- Shape and surface futures such as specific area, charge and distribution.
- Local molecular rearrangement.
- Interaction and dynamics.

Among these properties particle size, interactions, and dynamics are fundamental importance because they control many of general properties of microemulsions. The release of drug from Microemulsions depends on various process parameters like oil aqueous phase ratio, droplet size, the distribution of drug in the phases of Microemulsions system and rate of diffusion or absorption in both phases [6].

Microemulsion characterization can be divided into 2 main areas, characterization at the macroscopic level and characterization at the microscopic level. Viscosity, conductivity, and dielectric measurements provide useful information at the macroscopic level. The presence of worm-like reverse micelles and the transition between microemulsion structures can be implied by changes in viscosity. The rheological properties of microemulsions has been recently reviewed by Gradzielski. Conductivity measurements can be used to determine whether a microemulsion is oil-continuous or water-continuous, and may also be used to monitor percolation or phase inversion phenomena. Dielectric measurements have been used to probe both the structural and dynamic features of microemulsions. The optical clarity of microemulsions along with their isotropic nature makes their study by light-scattering methods quite straightforward; however, it is the minute particle sizes encountered in microemulsions which require special techniques. A variety of methods, such as freeze fracture electron microscopy, and a range of light scattering methods, such as small-angle X-ray scattering, small-angle neutron scattering, total intensity light scattering, photon correlation spectroscopy, may be used to determine the particle size of a microemulsion [20].

Applications of Microemulsions:

Pharmaceutical Applications

1. Parenteral delivery.
2. Oral drug delivery.
3. Topical drug delivery.
4. Ocular and pulmonary delivery.
5. Microemulsions in biotechnology.

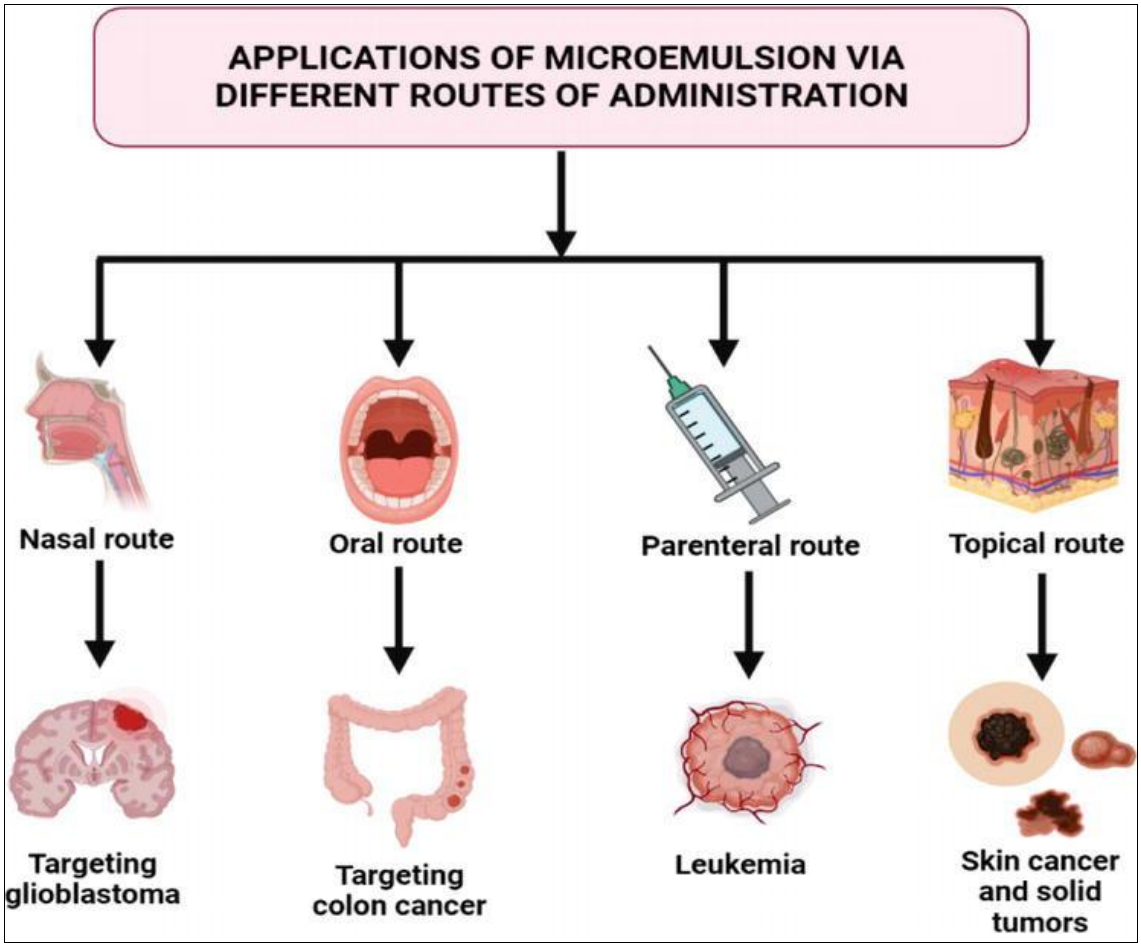


Fig 5: Show applications of Micro Emulsion via different routes of administration

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 [4].

Oral Delivery

Microemulsion formulations offer the several benefits over conventional oral formulation for oral administration including increased absorption, improved clinical potency and decreased drug toxicity 51. Therefore, microemulsion has been reported to be ideal delivery of drugs such as steroids, hormones, diuretic and antibiotics. Pharmaceutical drugs of peptides and proteins are highly potent and specific in their physiological functions. However, most are difficult to administer orally. With on oral bioavailability in conventional (i.e. non-microemulsion based) formulation of less than 10%, they are usually not therapeutically active by oral administration. Because of their low oral bioavailability, most protein drugs are only available as parenteral formulations. However, peptide drugs have an extremely short biological half-life when administered parenterally, so require multiple dosing.

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 of the drug and related toxicity effects. Second is the direct delivery and targetability of the drug to affected area of the skin or eyes. Both O/W and W/O microemulsions have been evaluated in a hairless mouse model for the delivery of prostaglandin E1. The micro emulsions were based on oleic acid or Gelucire 44/14 as the oil phase and were stabilized by a mixture of Labrasol (C8 and C10 polyglycolysed glycerides) and Plurol Oleique CC 497 as surfactant.

Ocular and Pulmonary Delivery

For the treatment of eye diseases, drugs are essentially delivered topically. O/W microemulsions have been investigated for ocular administration, to dissolve poorly soluble drugs, to increase absorption and to attain prolong release profile. The microemulsions containing pilocarpine were formulated using lecithin, propylene glycol and PEG 200 as co-surfactant and IPM as the oil phase. The formulations were of low viscosity with a refractive index lending to ophthalmologic applications 56. The formation of a water-in-HFA propellant microemulsion stabilized by fluorocarbon non-ionic surfactant and intended for pulmonary delivery has been described.

Microemulsions in Biotechnology

Many enzymatic and bio-catalytic reactions are conducted in pure organic or aqua-organic media. Biphasic media are also used for these types of reactions. The use of pure a polar media causes the denaturation of biocatalysts. The use of water-proof media is relatively advantageous. Enzymes

in low water content display and have; 1. Increased solubility in non-polar reactants 2. Possibility of shifting thermodynamic equilibrium in favor of condensations 3. Improvement of thermal stability of the enzymes, enabling reactions to be carried out at higher temperatures [4].

Nasal delivery

Recently, microemulsions are being studied as a delivery system to enhance uptake of drug through nasal mucosa. In addition, with mucoadhesive polymer helps in prolonging residence time on the mucosa. Lianly *et al*. investigated the effect of diazepam on the emergency treatment of status epilepticus. They found that the nasal absorption of diazepam fairly rapid at 2 mg kg-1 dose with maximum drug plasma concentration reached within 2-3 min.

Periodontal Delivery

Periodontal disease is a collective term for a number of progressive oral pathological afflictions like inflammation and degeneration of the gums, periodontal ligaments, cementum and its supporting bone. It is a major cause of tooth loss. The invention of Brodin *et al*. included a novel pharmaceutical composition comprising local anaesthetic in oil form, surfactant, water and optionally a taste masking agent. The composition was in the form of an emulsion or microemulsion and had thermoreversible gelling properties i.e. it was less viscous at room temperature than after introduction onto a mucous membrane of a patient. The surfactant in the formulation imparted the thermoreversible gelling properties. Preferred surfactants were Poloxamer 188®, Poloxamer 407® and Arlatone 289®. The composition could be used as a local anaesthetic for pain relief within the oral cavity in conjunction with periodontal scaling and root planning and overcame the problem with the existing topical products (jelly, ointment or spray) such as lack of efficacy due to inadequate depth of penetration, too short duration and difficulties in administration due to spread, taste etc. [5].

Other Applications

1. Microemulsions can improve skin penetration of lycopene.
2. Microemulsion as a vehicle for transdermal permeation of nimesulide.
3. Microemulsion in enhanced oil recovery, detergency, cosmetics, agrochemicals, food. Microemulsions in environmental remediation and detoxification.
4. Microemulsions as fuels, as lubricants, cutting oils and corrosion inhibitors, coatings and textile finishing.
5. Microemulsions in microporous media synthesis (microemulsion gel technique) Microemulsions in analytical applications.
6. Microemulsions as liquid/membranes Novel crystalline colloidal arrays as chemical sensor materials.
7. Microemulsion in enhanced oil recovery.
8. Microemulsions as fuels.
9. Microemulsions as coatings and textile finishing.
10. Microemulsions in detergency.
11. Microemulsions in cosmetics.
12. Microemulsions in agrochemicals.
13. Microemulsions in food.
14. Microemulsions in environmental remediation and detoxification.
15. Microemulsions in analytical applications.
16. Micro emulsions as liquid membranes (4).

Conclusion

Microemulsion have been shown to be able to protect labile drug, control drug release, increase drug solubility, increase bioavailability and reduce patient variability Furthermore it has proven possible to formulate preparations suitable for most routes of administration. Recently, several research papers have been published for the improvement of drug delivery, but still there is a need to emphasis on its characterization part including *in vitro* evaluation. Many research papers shows higher percentage of surfactant (much higher than CMC level) used for the formation of microemulsion, irrespective of different routes of administration, but there is a lack of toxicological evaluation of the prepared microemulsion, which can be a broad research area in future.

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