Indian Journal of Pharmaceutical Education and Research | Association of Pharmaceutical Teachers of India

# Microemulsions as Promising Delivery Systems: A Review

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## ABSTRACT

Microemulsions are clear, stable, isotropic liquid mixtures of oil, water and surfactant, frequently in combination with a cosurfactant. 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.

Microemulsion are having unique properties, namely, ultralow interfacial tension, large interfacial area, thermodynamic stability and the ability to solubilize otherwise immiscible liquids. Microemulsion are having wide applications and uses such as in pharmaceuticals, cosmetics, cutting oils, biotechnology, food , agrochemicals, environmental detoxification, analytical applications, microporus media synthesis etc.

*Submitted: 8-11-2010* *Revised: 14-1-2011* *Accepted: 25-4-2011*

## INTRODUCTION

It is well established that large amounts of two immiscible liquids (e.g. water and oil) can be brought into a single phase (macroscopically homogeneous but microscopically heterogeneous) by addition of an appropriate surfactant or a surfactant mixture. This unique class of optically clear, thermodynamically stable and usually low viscous solutions, called 'microemulsions', have been the subject of extensive research over the last two decades primarily because of their scientific and technological importance.

Microemulsions are clear, stable, isotropic liquid mixtures of oil, water and surfactant, frequently in combination with a cosurfactant. Microemulsions are bicontinuous systems that are essentially composed of bulk phases of water and oil separated by a surfactant/cosurfactant rich interfacial region. These systems have advantages over conventional emulsions in that they are thermodynamically stable liquid systems and are spontaneously formed.[1]. Microemulsions are currently the subject of many investigations because of their wide range of potential and actual utilizations. The high capacity of microemulsions for drugs makes them attractive formulations for pharmaceuticals. These systems also offer several benefits for oral administration, including increased absorption, improved clinical potency and decreased toxicity.[2]

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Microemulsions containing the oil and aqueous phase, surfactant and cosurfactant (cos), are optically transparent mixtures with a very small droplet size (G140 nm).[3,4] Microemulsions have been increasing in popularity and garnering more attention in recent years, because they may enhance the transdermal absorption of drug molecules by increasing drug solubilities and modifying their partition coefficients.[5] A hydrogel base is used very often in topical formulations.[6,7] . The hydrogel formulation was prepared and studied as a vehicle for its permeation potential.

**Advantages :**

a. Thermodynamically stability and require minimum energy for formation.

b. compatibility in manufacturing

c. Enhanced drug solubilization and improved bioavailability.

d. Micro emulsion are having wide applications in colloidal drug delivery systems for the purpose of drug targeting and controlled release.

**Method of Preparation**

**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.

**2. Phase Inversion Method**

Phase inversion of microemulsions occurs upon 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.

Microemulsions can be prepared by controlled addition of lower alkanols (butanol, pentanol and hexanol) to milky emulsions to produce transparent solutions comprising dispersions of either water-in-oil (w/o) or oil-in-water (o/w) in nanometer or colloidal dispersions (~ 100 nm). The lower alkanols are called cosurfactants, they lower the interfacial tension between oil and water

sufficiently low for almost spontaneous formation. The miscibility of oil, water and amphiphile (surfactant plus cosurfactant) depends on the overall composition which is system specific.

When English chemist J.H. Schulman introduced the term "microemulsion" in 1943 he described the transition from a stable oil-rich mixture to a stable water-rich mixture. Microemulsions contain a polar component, water, and a non polar component, oil, which makes them capable of solubilizing a wide spectrum of substances. They measure in size from 3 to 300 nanometers in droplet diameter, are transparent and thermodynamically stable. Due to these special properties microemulsions offer a high potential for numerous practical applications. Consequently, microemulsions may be used for enhanced oil recovery, cosmetic formulations, edible coatings for food, and for drug delivery systems as both transdermal or oral administrative vehicles for the controlled release of dosages. Microemulsions also have industrial applications, one of them being the synthesis of polymers. Microemulsion polymerization is a complex heterogeneous process where transport of monomers, free radicals and other species (such as chain transfer agent, co-surfactant and inhibitors) between the aqueous and organic phases, takes place.[8] Compared with other heterogeneous polymerization processes (suspension or emulsion) microemulsion polymerization is a more complicated system. Polymerization rate is controlled by monomer partitioning between the phases, particle nucleation, and adsorption and desorption of radicals. Particle stability is affected by the amount and type of surfactant and pH of dispersing medium.

Several authors have reported preparation of microemulsions using alcohols of short or medium length chains (e.g., butanol, heptanol or pentanol) as co-surfactants.[9] These substances limit the potential application of microemulsion due to their toxic and irritant properties. A selection of components for microemulsions suitable for pharmaceutical use involves a consideration of their toxicity and, if the systems are to be used topically, their irritation and sensitivity properties.[10] The ionic surfactants are generally too toxic to be used for preparation of lipid emulsions; therefore, non ionic surfactants, such as the poloxamers, polysorbates, polyethylene glycol are preferred. Polysorbate 80 is widely applied to pharmaceutical preparations, including ophthalmic

preparations, due to its history of usefulness and safety, and it is listed in the United States Pharmacopoeia- National

Formulary, the European Pharmacopoeia and the Japanese Pharmacopoeia.[11]. With the recent improvements in aseptic processing and the availability of new well-tolerated emulsifieres (polysorbate 80), emulsion technology is currently under evaluation for topical cyclosporine A delivery. Ding [12] developed a castor oil in water microemulsion. This microemulsion is stabilized by polysorbate 80 where the active substance cyclosporine A remains stable over 9 months and causes only mild discomfort and slight hyperemia on the rabbit eyes applied 8 times per day during 7 days. This encouraging result allowed the formulations to undergo clinical trials of phase II and III in dry eye disease. The II phase trial performed on 162 patients demonstrated good tolerance of the emulsion.[13]

**Ternary and quaternary phase diagrams:**

The knowledge on the phase manifestations of the pseudo-ternary (water/amphiphile/oil) or explicitly quaternary (water/surfactant/cosurfactant/oil) mixtures has been systematized. At low surfactant concentration, there is a sequence of equilibria between phases, commonly referred to as Winsor phases[14], they are

**Winsor I:** with two phases, the lower (oil/water, o/w) microemulsion phase in equilibrium with the upper excess oil;

**Winsor II:** with two phases, the upper microemulsion phase (water/oil, w/o) in equilibrium with excess water;

**Winsor III:** with three phases, middle microemulsion phase (o/w plus w/o, called bicontinuous) in equilibriumwith upper excess oil and lower excess water;

**Winsor IV:** in single phase, with oil, water and surfactant homogeneously mixed.

Inter-conversion among the above-mentioned phases can be achieved by adjusting proportions of the constituents. Simultaneous presenceof two microemulsion phases, one in contact with water and the other in contact with oil is also possible. [15]. This may be considered as an extension of Winsor's classification forming the fifth category. A microemulsion forming systems is shown in figure 1.

Another important consideration in the formation of microemulsions is related to the packing parameter, which is important for structures with high curvatures (Fig. 2). Surfactants must have the proper molecular volume dimensions and proportions to effectively pack into a micellar structure. Oil phases with high molecular volume fractions (such as triglycerides) will pack less efficiently and will have difficulties in entering between the surfactant tails. This is also reflected in the isotropic regions of a phase diagram. It

**Fig.1: Microemulsion Forming System**

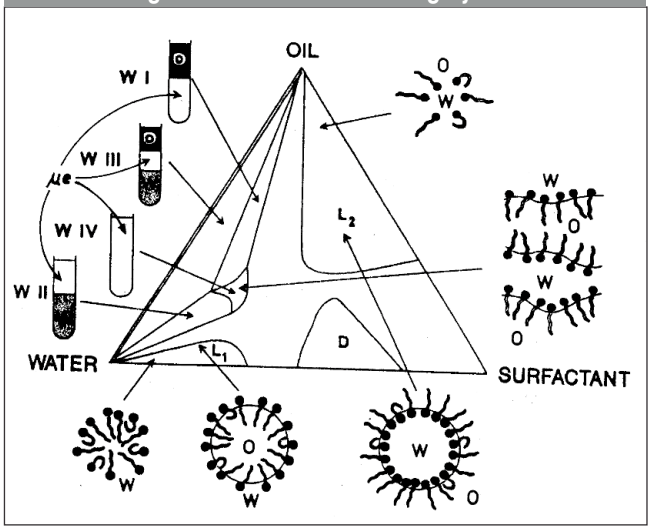
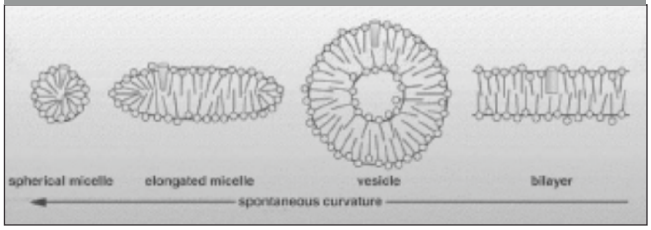



**Fig. 2: Schematic representation of microemulsion microstructures**




should be stressed that the o/w microemulsion droplets generally have a larger effective interaction volume than w/o droplets. Also, whereas emulsions consist of roughly spherical droplets of one phase dispersed into the other, microemulsions constantly evolve into various structures ranging from "droplet-like" swollen micelles to bicontinuous structures, frequently making the usual o/w and w/o distinctions irrelevant. Because the size of the particles is much smaller than the wavelength of visible light, microemulsions are transparent and their structure cannot be observed through an optical microscope.

The extents of formation of w/o, o/w and bicontinuous microemulsions can be understood from the phase equilibrium studies. Such studies may often become complex with the appearance of tiny or extended additional zones of viscous gel and liquid crystalline phases [16], the establishment of their boundary demarcations is time consuming and laborious.

Most commonly used methods and techniques to acquire information on the particle dimension and shape, their diffusion coefficient and polydispersity, aggregation and dynamics of coalescence, state of the water pool, thermodynamics of formation, etc. of the compartmentalized systems of microemulsion are related to conductance,

viscosity, ultrasound, static and dynamic light scattering, neutron and low angle X-ray scattering, nuclear magnetic resonance,

dielectric relaxation, time resolved fluorescence quenching, transmission electron microscopy, calorimetry, etc.

**Differences between Emulsion & Microemulsion**

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).

The main difference between emulsions and microemulsions is in the size and shape of the droplets that are dispersed in the continuous phase, reflecting the differences in the thermodynamic stability of the two systems (Table 1). Emulsions are kinetically stable but thermodynamically unstable, and after storage or aging, droplets will coalesce and the two phases separate. In contrast, microemulsions are thermodynamically stable and will not separate into the corresponding phases. It should be stressed that the term "mini-emulsions" was coined by some authors to describe emulsion droplets of submicron size with improved stabilities, other scientists may call those emulsions "nanoemulsions." While nanoemulsions do not have a long shelf life, they frequently are freshly prepared and used. It should also be stressed that in some studies, the authors neglect to test stability and consider mini- or nanoemulsions to be true microemulsions. The kinetics of microemulsion polymerization has much in common with emulsion polymerization kinetics, the most characteristic feature of which is the compartmentalization, where the radicals growing inside the particles are separated from each other, thus suppressing termination to a high extent and, as a consequence, providing high rates of polymerization.

Microemulsions can be sterilized by filtration and their production is relatively simple and inexpensive. Because of these properties, they have attracted a great interest as drug delivery vehicles[17,18]. Microemulsions can be applied as liquid membrane carriers to transport lipophilic substances through an aqueous medium or to carry hydrophilic substances across lipoidal medium. They are proposed for oral, topical, dermal, transdermal, parentenal and pulmonary administration of drugs[19]. Although microemulsions have been known for a long period, their potential as vehicles for topical ocular drug delivery has been investigated only within the last decade[20]. The main problem in a microemulsion application is a high concentration and a narrow range of physiologically acceptable surfactants and co-surfactants. [21,22]. On the other hand, the large surfactant concentration determines their stability.

**Factors Affecting the Microemulsion:**

The formation of microemulsion will depend on the following factors

**a. Packing ratio**: The HLB of surfactant determines the type of microemulsion through its influence on molecular packing and film curvature. The analysis of film curvature for surfactant association's leadings to the formation of microemulsion.

**Table 1: Difference between miniemulsion, macroemulsion and microemulsion.**

| | Emulsions | | Microemulsions |
|---|---|---|---|
| Properties | Miniemulsion | Macroemulsion | NSSL |
| Visual aspect |  |  |  |
| Typical characteristic size | 20–200 nm | >1 μm | 10–100 nm |
| Stability | Kinetic | | Thermodynamic |
| Formation | Energy input | | Spontaneous |
| Surfactant concentration | Low | | High |

**b. Property of surfactant, oil phase and temperature**: The type of microemulsion depends on the nature of surfactant. Surfactant contains hydrophilic head group and lipophilic tail group. The areas of these group, which are a measure of the differential tendency of water to swell head group and oil to swell the tail area are important for specific formulation when estimating the surfactant HLB in a particular system. When a high concentration of the surfactant is used or when the surfactant is in presence of salt, degree of dissociation of polar groups becomes lesser and resulting system may be w/o type. Diluting with water may increase dissociation and leads to an o/w system. Ionic surfactants are strongly influenced by temperature. It mainly causes increased surfactant counter-ion dissociation. The oil component also influences curvature by its ability to penetrate and hence swell the tail group region of the surfactant monolayer. Short chains oils penetrate the lipophilic group region to a great extent and results in increased negative curvature. Temperature is extremely important in determining the effective head group size of nonionic surfactants. At low temperature, they are hydrophilic and form normal o/w system. At higher temperature, they are lipophilic and form w/o systems. At an intermediate temperature, microemulsion coexists with excess water and oil phases and forms bicontinuous structure.

c. The chain length, type and nature of cosurfactant: Alcohols are widely used as a cosurfactant in microemulsions. Addition of shorter chain cosurfactant gives positive curvature effect as alcohol swells the head region more than tail region so, it becomes more hydrophilic and o/w type is favoured, while longer chain cosurfactant favours w/o type w/o type by alcohol swelling more in chain region than head region.

**Evaluation / Characterization of microemulsion**

The microemulsions are evaluated by the following techniques. They are

***(I) Phase behavior studies:*** visual observations, phase contrast microscopy and freeze fracture transmission electron microscopy can be used to differentiate microemulsions and coarse emulsions. Clear isotropic one-phase systems are identified as microemulsions whereas opaque systems showing bifringence when viewed by cross polarized light microscopy may be taken as liquid crystalline system.

***(II) Scattering Techniques:*** Scattering techniques such as

**Some Research Work on Microemulsions**

| Drug Name | Route | Purpose/Result |
|---|---|---|
| Acyclovir [23] | oral | Improved bioavailability |
| Flurbiprofen [24] | Parenteral | Increased the solubility |
| Apormorphine HCL [25] | Transdermal | Increased the permeability |
| Ketoprofen [26] | Transdermal | Enhancement of permeability |
| Prilocainne-HCL [27] | Transdermal | Increased the solubility |
| Estradiol [28] | Transdermal | Improvement in solubilization |
| Aceclofenac [29] | Dermatological | Increased the solubility |
| Piroxicam [30] | Oral | Increased the solubility |
| Diclofenac [31] | Transdermal | Permeability enhancement |
| Dexamethasone [32] | Topical Ocular | Enhanced the Bioavailability |
| Carbamazepine [33] | Intranasal | Enhanced bioavailability |
| Chloramphenicol [34] | Ocular | Increased the solubility |
| Ibuprofen [35] | Parenteral | Increased the solubility |
| Sumatriptan [36] | Intranasal | Enhanced the Bioavailability |
| Ibuprofen [37] | Topical | Increasing the solubility |
| Clonixic acid [38] | transdermal | For better absorption |
| Itraconazole [39] | Parenteral | For better absorption |
| Timolol [40] | Ophthalmic | For better absorption |
| Terbinafine [41] | Transdermal | Permeability enhancement |
| Fenofibrate [42] | Self-Micro emulsifying | Increasing the solubility |
| Progesterone 43 | Dermal | Increased the chemical Stability |
| Clopidogrel 44 | oral | Solubility enhancement |

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 monodisperese spheres, when polydisperse and/or concentrated systems such as those frequently seen in microemulsions.

***(III) Transmittance test***

Stability of the optimized microemulsion formulation with respect to dilution was checked by measuring transmittance at a specific wavelength with a UV spectrophotometer .

***(IV) Globule size and zeta potential measurements***

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

***(V) Viscosity measurements***

Rheological behavior of the formulation can be observed by using a Brookfield LVDV III+ cone and plate (CP) viscometer (Mfg: Brookfield, USA) using rheocal software at a temperature. 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

***(VI) 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 (CM 180 conductivity meter, Elico, India) at ambient temperature and at a constant frequency of 1 Hz.

***(VII) Drug stability***

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

***(VIII) 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.

***(IX)Drug release studies***

***(A) 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 cellophane membrane , containing the microemulsion formulation and the plain drug solution, separately. At predetermined time intervals samples were withdrawn from the receptor compartment and analyzed for drug content, using a UV spectrophotometer at specific wavelength.

***(B) Ex-vivo drug release***

Ex -vivo drug release into buffer was studied using intestinal membrane within a Franz diffusion cell. Microemulsion formulation and plain drug solution were placed in the donor compartment of two separate diffusion cells and the temperature of each cell was maintained at 37 ±2°C. The amount of drug released from the microemulsion formulation can be estimated spectrophotometrically at specific wavelength, by withdrawing samples from the receptor compartment at predetermined time intervals.

**Applications of microemulsions**

There has been a revolution in the last two decades in the utilization of microemulsion systems in a variety of pharmaceutical, chemical, industrial processes etc.

***Microemulsion in pharmaceutical***

Liquid crystalline, miceller and emulsion forming systems are widely used in pharmaceutical preparations. The easy formation, remarkable environment independent stability, excellent solubilization capacity, etc. favour microemulsions to be a better proposition over other compartmentalized systems. The dispersed phase, lipophilic or hydrophilic(o/w or w/o type) can act as a potential reservoir of lipophilic or hydrophilic drugs that can be partitioned between the dispersed and the continuous phases. Coming in contact with a semipermeable membrane, such as skin or mucous membrane, the drug can be transported through the barrier. [45]. Both lipophilic and hydrophilic drugs can be administered together in the same preparation.

Low viscous formulations using microemulsions with suitable protein compatible surfactants can be used as injection solutions, for they are miscible with blood in any ratio. In contrast to emulsions, microemulsions cause minimum immuno reactions or fat embolism. Proteins are not denatured in microemulsions although they are unstable at high or low temperatures. The total dose of the drug can be

reduced when applied through the microemulsion route and thus side effects can be minimized.

Toxicity, bio-incompatibility of surfactants and cosurfactants, requirement of high concentrations for formulations and other relevant factors such as maintenance of thermodynamic stability in the temperature range between 0 $^0$C and 40 $^0$C, salinity, constant pressure during storage, low solubilizing capacity for high molecular weight drug (and oil), etc. limit the uses of microemulsions in the pharmaceutical and medicinal fields.

An application of o/w microemulsion in the pharmaceutical industry is the use of strongly hydrophobic fluorocarbons (as oils) to produce short-time blood plasma substitutes to maintain the supply of oxygen in the living systems. The components to be used must have low allergic potential, good physiological compatibility and high biocompatibility. The biocompatibility requirements of the amphiphiles are fulfilled by lecithins, non-ionic surfactants (Brijs, Arlacel 186, Spans and Tweens).

Garcia-Celma [45] has reviewed microemulsions as drug delivery systems for different types of drugs, viz. antineoplastics/ antitumour agents (doxorubicin, idarubicin, tetrabenzamidine derivative), peptide drugs (cyclosporine, insulin, vassopressin), sympatholytics (bupranolol, timolol, levobunolol, propanolol), local anesthetics (lidocaine, benzocaine, tetracaine, heptacaine), steroids (testosterone, testosterone propionate, testosterone enanthate, progesterone, medroxyprogestorane acetate), anxiolytics(benzodiazepines), antiinfective drugs (cloitrimazole, ciclopirox olamine, econazole nitrate, tetracycline hydrochloride), vitamins (menadione, ascorbic acid), anti-inflammatory drugs(butibufen, indomethacin), and dermological products( tyrocine, azelaic acid, octyl dimethyl PABA, 2- ethyl hexyl *p*-methoxy cinnamate).

Enzyme doped silica nanoparticles (ceramic drug carrier) in the aqueous core of reverse micelles and microencapsulation of diospyrin, a plant-derived bisnapthoquinol of potential chemotherupic activity have been very recently reported. [46]

***Microemulsions in cosmetics***

It is believed that microemulsion formulation will result in a faster uptake into the skin. Cost, safety, appropriate selection of ingredients are key factors in the formulation of microemulsions. Skin care microemulsions contain [47], sodium alkyl sulfate, tetraethylene glycol monododecyl ether, lecithin, dodecyl oligoglucoside, alkyl dimethyl amine oxide, propanol,hexadecane, isopropyl myristate have been used as surfactants, cosurfactants and oils respectively.

Hair care microemulsions contain an amino-functional polyorganosiloxane (a nonionic surfactant) and an acid and/or a metal salt.

Cosmetic microemulsions (transparent and translucent) of silicone oils was produced by emulsion polymerization tehnique. Ultrafine emulsions prepared by condensation method have some advantages in cosmetic and medical products, as they have excellent stability and safety and their droplet size can be readily controlled. Ultrafine emulsions can be regarded as thermodynamically unstable microemulsions, as they are o/w emulsions with droplet size similar to microemulsion. Tokuoka *et al.*[48] studied the solubilization of several systems consisting of water, surfactant and synthetic perfumes (viz. d-limonene, *a*-ionone, benzyl accetate, linalol, eugenol and *a*-hexylcinnamaldehyde), clarifying (a) the influence of fragrance structure on the phase regions in a water/nonionic surfactant systems, (b) the distribution co-efficient between micelles and the bulk phase, and (c) the partition between dissolved and solubilized perfume components on their volatility. In this, the phase equilibria in water, lecithin, soybean oil and vanillin have been studied.

***Microemulsions in analytical applications***

Microemulsions are widely used in the field of analytical techniques such as chromatography, laser-excited photoionization spectroscopy, etc. In microemulsion electrokinetic chromatography (MEEKC), characterization of solute hydrophobicity was carried out [49], 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 bicontinuous microemulsion have been assessed. A series of studies have been reported on the determination of aluminium, zinc, copper, cadmium, manganese ions using both microemulsion and mixed microemulsion systems. These studies are mostly published in the journals published by the Chinese Chemical Society.[50]

***Microemulsions in biotechnology***

Recently, interest on microemulsions is being focused for various applications in biotechnology, viz, enzymatic reactions, immobilization of proteins and bioseparation. Microemulsions are advantageous over other multiphase equilibrium systems because of simultaneous solubilization of polar and nonpolar reactants in the same solution, shifting of the equilibrium position of the reaction and the separation of products by physical means. However, bio-incompatibility

of the amphiphiles used poses a serious limitation in the advancement of this field. The prospects of biotechnological applications have also been reviewed [51,52]. Enzyme reactions (catalysis) in microemulsion media have widely been studied. The use of microemulsion for enzyme catalysis is not arbitrary for enzymes under *in vivo* condition function in the cell as well as at the interface of hydrophobic and hydrophilic domains of cell and tissue containing lipids and other natural amphiphiles.

***Enzymatic reactions in microemulsions:***

The potential advantages of employing enzymes in media of low water content, i.e. w/o microemulsions are: (i) increased solubility of nonpolar reactants; (ii)possibility of shifting thermodynamic equilibria in favour of condensation; (iii) improvement of thermal stability of the enzymes, enabling reactions to be carried out at higher temperature. Catalysis by a large number of enzymes in microemulsion media has been studied for a variety of reactions, such as synthesis of esters, peptides and sugar acetals; transesterifications; various hydrolysis reactions; glycerolysis; oxidation and reduction and steroid transformation. The conformation and activity of an enzyme depend on ([water]/[surfactant]); the enzyme is thus sensitive to amount of surrounding water.

Gomez-Puyon has carried the work on behaviour of enzymes in microemulsions[53]

***Immobilization of protein in microemulsion****:* In the field of protein immobilization, microemulsion medium has been found to be a good proposition. Immobilization of a variety of proteins on suitable solid surfaces using microemulsion media has been successfully carried out[54].

***Microemulsions for bioseparations****:* The possibility of microemulsions to extract biopolymers (proteins and enzymes) from an aqueous phase has been explored. Microemulsions are gentle solvents for extraction of proteins without altering their enzymatic or functional properties although the process can readily be scaled by conventional liquid–liquid extraction techniques. The pH, ionic strength, type of salt, concentration of solvent and temperature influence the partition of a protein.[55,56]

***Microemulsion as a chemical sensor materials.***

Microemulsions as novel crystalline colloidal arrays (CCA) are new findings which acts as novel chemical sensors. A intelligent photoionic crystalline colloidal array self assemblies have been developed, [57] which can have use in medicine, environmental chemistry, process control and remote sensing. These are mesoscopically periodic fluid materials, that diffract light satisfying the Bragg condition. The crystalline colloidal array self assemble into either face centered or body centered cubic form. Just as atomic crystals diffract X-rays that fulfill the Bragg condition, CCAs diffract ultraviolet, visible and near-infrared light, depending on the lattice spacing. Colloidal particles of inorganic materials, such as silica or organic polymers, such as poly (*N*-isopropylacrylamide) have been synthesized having periodicity of the order of ~200 nm. Asher *et al.* [58] and Holtz *et al.*[59] have developed a novel sensing material from a polymerized crystalline colloidal array (PCCA) which is a mesoscopically periodic crystalline colloidal array of spherical polystyrene colloids within a thin, intelligent polymer hydrogel film. They have fabricated a sensor, utilizing a crown ether as the recognization agent that can detect Pb2+ in the 0.1 □M– 20 mM (~20 ppb – ~ 400 ppm) concentration range. The sensors for glucose and galactose utilising glucose oxidase or *b*-D-galactosidase as the recognization entities have been developed. Besides sensing glucose, this sensor can estimate dissolved oxygen concentration in the presence of constant glucose concentration. Development of thermally tunable photonic crystal of poly (*N*-isopropylacrylamide) (PNIPAM), a novel CCA photoionic crystals with variable sphere sizes and variable array periodicity and sensors that change volume in response to nonionic molecular recognition processes such as antibody/antigen interactions have been attempted.

## CONCLUSION

Microemulsions are having a vast and significant potential in drug delivery as well as in the industrial process. Researchers are working in this field for drug release, coatings, dyes, agrochemicals and in enzyme reaction. In the future prospects, microemulsions will be used in synthesis of nanoparticles and as a industrial chemical sensors. The role of microemulsion in providing novel solutions to overcome the problems of poor aqueous solubility of highly lipophilic drug compounds and provide high, more consistent and reproducible bioavailability. Furthermore, these formulations can be easily manufactured in term of the relative cost of commercial production. Topical products are now employing the microemulsion technology are likely to emerge. Microemulsions can also be used to achieve drug targeting however challenges remain, primarily because of the layers of barriers that these systems need to overcome to reach to the target. Recent research work is focused on the production of safe, efficient and more compatible microemulsion constituents which will further enhance the utility of these novel vehicles. Microemulsion in today's world can be accepted as full of potential in a novel drug delivery systems.

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