

Chapter I

Introduction

1.1. Physicochemical studies: An overview

Physicochemical studies are concerned with, or relating to physical chemistry or both physics and chemistry of the systems. It is the method of investigation that makes possible a determination of the interactions between the components of a system through the study of the relations between the system's physical properties and composition. The principles of physicochemical analysis were established in the late 19th century by J. Gibbs, D. I. Mendeleev, and J. van't Hoff. Further, the method received its development in the research of H. Le Châtelier, G. Tammann and H. Roozeboom [1-2]. Physicochemical analysis involves the measurement of various physical properties of the systems, most often the phase rule and on the principles of continuity and correspondence, phase transition temperatures and other thermal properties (thermal conductivity, heat capacity, thermal expansion), electrical properties (conductivity, dielectric permittivity), and optical properties (refractive index, rotation of the plane of polarization of light). Also, the density, viscosity, and microstructural aspects, as well as the dependence of the rate of the transformations occurring in a system on the system's composition, are measured. Most recently, scattering techniques (X-ray and neutron scattering), diffraction analysis, diffusion coefficient measurement, spectroscopic probing techniques and techniques of microscopic imaging are extensively used in physicochemical analysis [1-4]. Physicochemical analyses are made by constructing and geometrically analyzing composition-properties diagrams and phase diagrams. Since the analytical expressions describing phase equilibria are unwieldy and determine the regions of phase existence approximately, a geometric analysis of the diagrams is the most common procedure for judging the composition and boundaries of phase existence of a system without separating the phases from the mixture and subjecting them to ordinary chemical analysis. For this reason, physicochemical analysis is an important method of studying systems made up of two, three, or more components, for example, alloys,

minerals, semiconductors, superconductors, and solutions. In the recent past, single and mixed surfactant solutions which are the most fascinating self-organized assemblies in particular, are exploited for physicochemical studies of the same [3-4].

1.2. An outline of surfactant (amphiphilic) molecules

Surfactants, a common contraction of the term surface-active agents, are versatile chemical substances that modify the surfaces or interfaces of the systems in which they are confined. Surfactants have the ability to adsorb (or locate) at interfaces, thereby alter significantly the physical properties of the interfaces [5]. Surfactants possess these special characteristics since their molecular structures are amphiphilic (from the Greek *amphi* meaning ‘on both sides’ and *philein* meaning ‘to love’) having polar as well as apolar components within the same molecular unit. The polar component is called “head” and the apolar component usually a long chain hydrocarbon, is called “tail” (Figure 1.). These compounds are most comfortable in a situation when each component is located in an appropriate environment, which is only possible at the interface between two media [6].

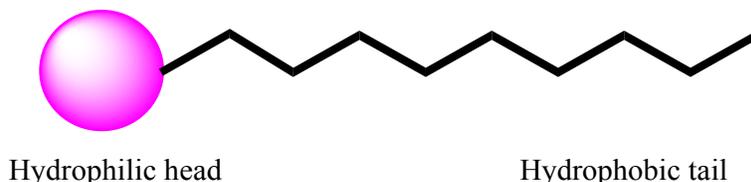


Figure 1. Common schematic representation of a surfactant molecule.

Apolar or hydrophobic components can be aliphatic or aromatic. The sources of hydrophobic components are normally natural fats and oils, petroleum fractions, relatively short synthetic polymers, or high molecular weight synthetic alcohols. The hydrophilic groups contribute the primary classification to surfactants, and are anionic, cationic and nonionic in nature. The anionic hydrophiles are the carboxylates (soaps), sulfates, sulfonates and phosphates. The cationic hydrophiles are some form of an amine or both quaternary ammonium alkyl and alkyl pyridinium salts. The nonionic hydrophiles associate with water at the ether oxygen of a polyethylene glycol chain. Some surface-

active amphiphilic molecules that contain both anionic and cationic centers at the head group, and are called zwitterionic surfactants. Surfactants can also have two hydrocarbon chains attached to a polar head and are called double chain surfactants. On the other hand, surfactants containing two hydrophobic and two hydrophilic groups are called “gemini” surfactants. Amphiphilic molecules can also have two head groups (both anionic or cationic or one anionic and the other cationic) joined by hydrophobic spacer [7]. These types of molecules are termed “bola-amphiphiles” and commonly known as “bolaforms”. Surface activity of these molecules depends on both the hydrocarbon chain length and the nature of head group(s).

1.3. Self-organized assemblies of surfactant (amphiphilic) systems

Surfactant (amphiphilic) molecules have been the realm of interest in chemistry for over a century with attention not only from theoretical perspectives but also from the view point of wide applications in industry. Self-assembly is a spontaneous organization of molecules driven by noncovalent interactions into stable aggregates. Self-assembly phenomenon is also well recognized in biological systems, e.g., lipid bilayers, the DNA duplex, and also, tertiary and quaternary structure of proteins. The process of spontaneous aggregation of simple molecules in solution into larger structures with a certain order, is also an important phenomenon in every-day-life as well as an interesting topic for scientific investigation. The best-known example of aggregation in every-day-life is the formation of micelles by surfactant or detergent molecules. However, the most important type of aggregation, which is essential to life, is the formation of the lipid bilayer membrane by phospholipids. Interestingly, both chemists and physicists were motivated to study these types of aggregates including other similar types, because they mimic biological systems [5]. Aggregation of molecules often occurs at the borderline of solubility. An important molecular property in this respect is polarity, for which solubility follows the rule 'like dissolves like'. Polar (hydrophilic) compounds are well soluble in polar solvents, e.g. salt in water, and the same is true for apolar (hydrophobic) compounds and solvents, e.g. vitamin E and oil. Furthermore, polar compounds are insoluble in apolar solvents and vice versa.

Amphiphiles with longer hydrocarbon chains are found to be more surface-active compared to those having shorter hydrocarbon tail [8]. However, amphiphiles with fluorocarbon chain are more surface-active than those with hydrocarbon chain [9] When surfactants are added to water, they are adsorbed at the water-air interface, which actually originates from their dualistic character (both polar and apolar characters composed in the same molecule). In aqueous solution, the hydrophobic chain interacts weakly with the water molecules, whereas the hydrophilic head interacts strongly via dipole or ion-dipole interactions. This strong interaction renders the surfactant soluble in water. However, the cooperative action of dispersion and hydrogen bonding between the water molecules tends to squeeze the surfactant chain out of the water (hence, these chains are referred to as hydrophobic). Therefore, surfactants tend to accumulate at the surface, which allows lowering the free energy of the phase boundary, i.e. the surface tension [8].

1.4. Classifications of diverse self-organized assemblies made by surfactant molecules

1.4.1. Micelles

The most intensely studied and deliberated molecular self-assembly, and perhaps the simplest in terms of the structure of the aggregate, is the micelle. Micelles formed by ionic and nonionic amphiphilic molecules in aqueous solution are dynamic associations of surfactant molecules that achieve segregation of their hydrophobic portions from the solvent via self-assembly. They are loose, and commonly spherical aggregates above their critical micellization concentration (cmc) in water or organic solvents [5]. Also, micellar aggregates are short-lived dynamic species, which rapidly disassemble and reassemble [10]. Hence, only average shape and aggregation numbers of micelles can be determined.

1.4.2. Vesicles

Vesicles are closed bilayered or hollow spherical structures similar to those of the lamellar phase characterized by two distinct water compartments, one forming the core and other the external medium (Figure 2). Like micelles, the formation of vesicles is a result of energetically favorable hydrophobic association of the hydrocarbon tail(s) of an

amphiphilic molecule. However, unlike micelles, vesicles have two distinct domains: the lipophilic membrane and the interior aqueous cavity. Specifically, the surface of micelles is a lipid monolayer, while that of liposomes is a lipid bilayer. Whereas, the inner core of micelles is composed of hydrocarbon chains, and that of vesicles is an aqueous phase [11,12].

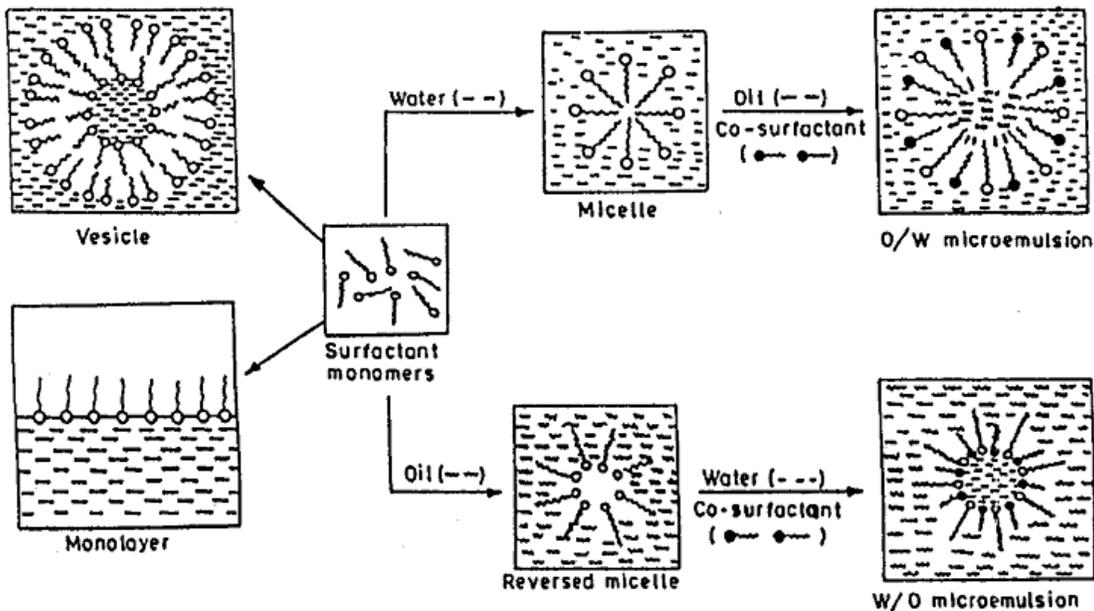


Figure 2. Schematic representation of different self-organized assemblies

1.4.3. Microemulsions

Microemulsions are another class of self-organized assemblies in which oil and water are homogeneously mixed due to the presence of surfactant molecules (amphiphiles). Sometimes, a co-surfactant is used in combination with the surfactant as a stabilizer (Figure 2). They differ from conventional emulsions not only by their much smaller droplet size, but in respect of their thermodynamic stability, which renders them very interesting micro heterogeneous systems. Moreover, they allow for a long-lived stabilization of mixed oil/water systems, which otherwise can not be achieved. Microemulsions can be thought to be the type of oil swollen micelles [oil-in-water (o/w) microemulsion] or water swollen reverse micelles [water-in-oil (w/o) microemulsion]. The physical characteristics of water/oil microdroplet in microemulsions are at variance from those of the bulk water or oil [3].

1.4.4. Reverse micelles

Surfactants associate to form inverted or reverse micelles in non-polar solvents containing a little water. The polar head groups of the surfactant monomers are directed to the centre containing water with the hydrophobic tails extending outward into the bulk organic solvent phase. Reverse micelles can solubilize an appreciable amount of water to form a spherical pool in the centre (Figure 2) [13].

1.5. Microemulsions and their special characteristics

Microemulsions are a trending class of compartmentalized liquids that has incredible application in current and future perception [14, 15]. Microemulsions have been the topic of comprehensive research for more than 40 years with a particularly intense period in the late 70s and early 80s in the context of tertiary oil recovery [16]. Currently, microemulsions are becoming increasingly complex systems due to exploration of more sophisticated surfactants, mixed surfactants, polymers, biomolecules and inorganic nanoparticles etc. within their constricted environments. [17]. It contains distinct microstructural features, i.e. topologically ordered oil and water coated with surfactant film. They are isotropic with typical structural units in the size range of 3–100 nm from which their transparent appearance results. As defined by Danielsson and Lindman, “a microemulsion is a system of water, oil and an amphiphile which is a single optically isotropic and thermodynamically stable liquid solution” [18]. Herein, surfactants are the most important amphiphiles. Their amphiphilic character is strong enough to be driven to the interface where the polar part is located in the polar region and vice versa. The term “oil” refers to an organic phase which is immiscible or at least partially miscible with the polar phase. Therefore, nonpolar substances such as hydrocarbons, partially or totally chlorinated or fluorinated hydrocarbons, single-chain alkanes, cyclic or aromatic hydrocarbons. However, triglyceride natural oils or polar lipophilic oils can be used [19, 20]. Straight chain hydrocarbons or *n*-alkanes are the most frequently used non-polar components in microemulsions.

However, microemulsions were not really recognized until the term “oleopathichydromicelle” was proposed by Schulman and Hoar dates back in 1943 for describing the spontaneous formation of transparent emulsion of water and oil upon

addition of a strong surface-active agent [21]. But the concept had appeared in the U.S. patent literature before that [22]. The term “microemulsion” was first coined even later by Schulman, Stockenium and Prince in 1959 [23] to describe a multiphase system consisting of water, oil, surfactant and alcohol, which forms a transparent solution (Figure 2). There has been much debate about the word “microemulsion” to describe such systems [24]. Although not systematically used today, some authors prefer the names “micellar emulsion” [25] or “swollen micelles” [26]. Being a ternary (water/surfactant/oil) or quaternary (water/surfactant/alcohol/oil) system, it has the advantage of offering a better compartmentalization than the other organized assemblies. In addition, microemulsions have experienced continuous scientific and industrial development since their inception [14]. The knowledge gained on the fundamental aspects of these systems has made it possible to improve some established applications and to develop new ones. In view of these growing research activities in this area, this review (presented in this section) is devoted to the detailed discussion on the various aspects, more precisely, the basic aspects viz. formation characteristics, properties and structural characterization of microemulsions and reverse micelles stabilized by single and mixed surfactants in nonpolar, polar and biocompatible oils. However, numerous books and review articles appeared concerning various aspects of microemulsions/reverse micelles, which will be discussed in subsequent sections. Hence, it is obvious that everything known about microemulsions cannot be summarized within a few pages. An attempt has been made to present the most important facts and concepts that are closely related with the topic of the thesis, in the following sections with special reference to the self-organized molecular assemblies of single and mixed surfactant microemulsions. The basic intention of this thesis is an attempt on the studies emphasizing on the formation and characterization of microemulsions formed from both single and mixed surfactants of different charge types and mixing ratios, in linear hydrocarbons and alkyl ester oils, as a blend of surfactants can provide better performance than pure surfactants for a wide variety of applications. Further, major aspect of my dissertation aims at physicochemical studies of mixed surfactant microemulsions.

1.6. Classification of microemulsions

Three types of microemulsions are most likely to be formed depending on the composition: oil-in-water (o/w), water-in-oil (w/o) and bicontinuous. A schematic representation is also depicted in Figure. 3. Oil-in-water (o/w) microemulsions are droplets of oil surrounded by a surfactant film that forms the internal phase distributed in water, which is the continuous phase. The monolayer of surfactant forms the interfacial film, which is oriented in a “positive” curve, where the polar head groups face the continuous water phase and the hydrophobic tails face into the oil droplets. The o/w systems are interesting because they enable hydrophobic drugs to be more soluble in an aqueous based system, by solubilizing it in the internal oil droplets [27].

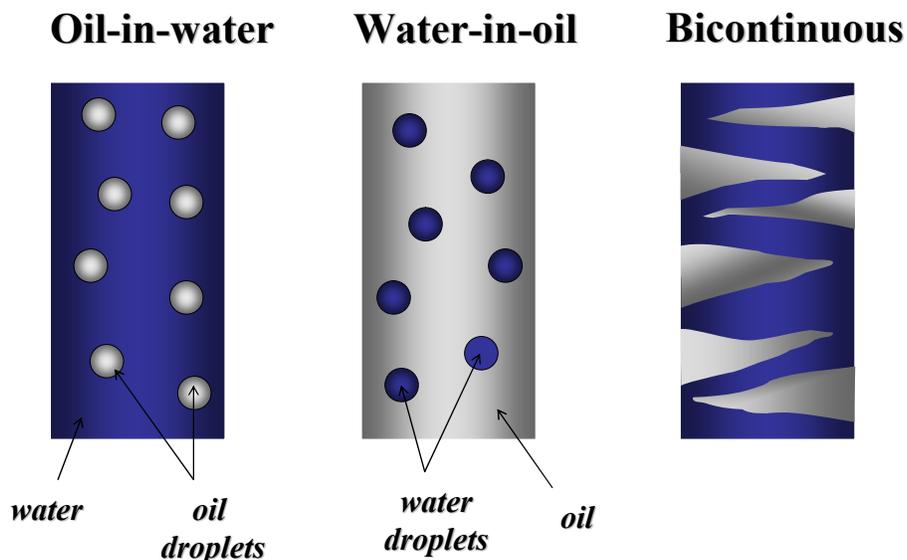


Figure 3. Schematic representation of different types of microemulsion systems

Water-in-oil (w/o) microemulsions are made up of droplets of water surrounded by an oil continuous phase stabilized by an interfacial film of surfactant (sometimes in presence of cosurfactant). These are generally known as “reverse micelles” (RMs), where the polar head groups of surfactant are facing into the droplets of water, with the hydrophobic tails facing into the oil phase. In the RMs, the amount of water present is low and is limited to

the maximum capacity of hydration of the hydrophilic head group of the surfactants; hence, the water pool

is rigid. A term ω , defined as $[\text{water}]/[\text{surfactant}]$ has been taken as a criterion as to whether a RMs or a w/o microemulsion has been formed [28]. It was suggested that when $\omega < 10$, it is a RMs and when $\omega > 10$, it is a w/o microemulsion [29]. However, some evidence exists that the cut-off point may be $\omega = 15$ [13]. When the amount of water and oil present are at equivalence, a bicontinuous microemulsion system may result. In this case, both water and oil exist as a continuous phase. Transition from o/w to w/o microemulsion may pass through this bicontinuous state. Bicontinuous microemulsions are useful for topical delivery of drugs or for intravenous administration, where upon dilution with aqueous biological fluids, form an o/w microemulsion [27]. Irregular channels of oil and water are intertwined, resulting in what looks like a “sponge phase”.

1.7. Winsor representation

Winsor representation [30] is a cut of the phase prism/tetrahedron where only one variable is varied and measures the relative volume of the phases obtained on varying the single variable. Each data point represents one sample and is a direct picture of the observed phases in the test tube. There are four commonly observed phase behaviors as described by Winsor (Figure 4):

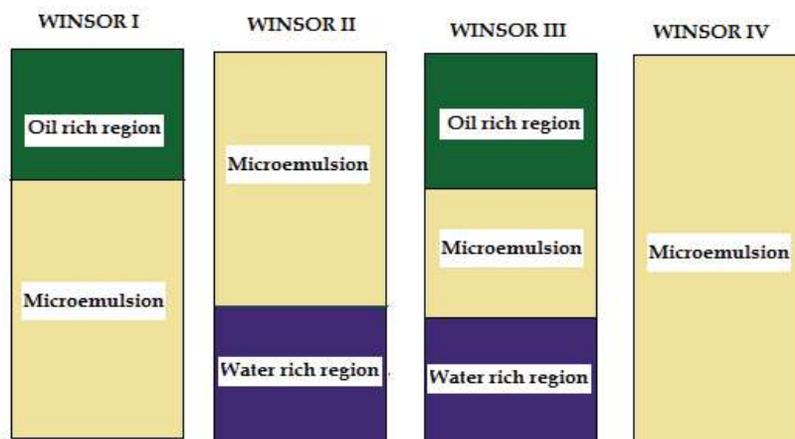


Figure 4. Winsor classifications of microemulsion systems

1. Winsor I ($\underline{2}$), a water rich microemulsion in equilibrium with an excess oil phase.
2. Winsor II ($\bar{2}$), an oil-rich microemulsion in equilibrium with an excess water phase.

3. Winsor III (3), a microemulsion phase in equilibrium with an excess oil phase and an excess water phase.
4. Winsor IV (1), a single-phase microemulsion.

1.8. Basic aspects of microemulsions

1.8.1. Role of surfactants in microemulsions

An understanding of the basic phenomena involved in the application of surfactants, such as in the preparation of emulsions and microemulsions and their subsequent stabilization, is of vital importance in arriving at the right composition and control of the system involved [31]. 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 also, attains appropriate lipophilic character to provide the correct curvature at the interfacial region. It is generally accepted that lower hydrophile–lipophile balance (HLB) of surfactants favour the formulation of w/o microemulsion, whereas surfactants with high HLB (>12) can form o/w microemulsion [32].

A simple classification of surfactants based on the nature of the hydrophilic group is commonly used. Two main classes may be distinguished, namely ionic and nonionic [33]. Ionic surfactants can be anionic, cationic or zwitterionic.

Anionic surfactants are the most widely used class of surfactants in industrial applications due to their relatively low cost of manufacture and are used in practically every type of detergent [34]. For optimum detergency, the hydrophobic chain should be a linear alkyl group with a chain length in the region of 12–16 carbon atoms. Linear chains are preferred since they are more effective and also degradable than branched ones [34].

Alkali alkanoates, also known as soaps, are the most common anionic surfactant. The anionic charge in this surfactant comes from the ionized carboxyl group. Sodium bis(2-ethylhexyl) sulfosuccinate or commonly known as AOT, is the most widely studied anionic surfactant. It has twin tails and is particularly a good stabilizer of w/o microemulsions. Other important classes of anionic surfactants include, alkyl sulphates, alkyl ether sulphates, methylester sulphonates, aryl sulphonates.

Cationic surfactants generally fall into the class of quaternary ammonium alkyl salts. Alkylammonium halides are excellent hydrogen bond donors and interact strongly with water. The most well known examples from the cationic surfactant class are hexadecyltrimethylammonium bromide (CTAB) and didodecyldimethylammonium bromide (DDAB). Although less numerous, phosphorous can be quaternized with alkyl groups to create alkyl phosphonium cationic surfactants as well. Cationic surfactants are generally water soluble when there is only one long alkyl chain. They are generally compatible with most inorganic ions and hard water, but they are incompatible with metasilicates and highly condensed phosphates. They are also incompatible with protein-like materials. They are generally stable towards pH changes, both acidic and alkaline. Cationic surfactants are incompatible with most anionic surfactants, but they are compatible with nonionic surfactants. These cationic surfactants are insoluble in hydrocarbon oils. In contrast, cationic surfactants with two or more long alkyl chains are soluble in hydrocarbon solvents viz. didodecyldimethylammonium bromide (DDAB), but they become only dispersible in water (sometimes forming bilayer vesicle type structures). In most cases, they are chemically stable and can tolerate electrolytes [35, 36].

Amphoteric (Zwitterionic) Surfactants are surfactants containing both cationic and anionic groups [37, 38]. The most common amphoteric surfactants are the N-alkyl betaines, which are the derivatives of trimethyl glycine $(\text{CH}_3)_3\text{NCH}_2\text{COOH}$ (described as betaine). An example of betaine surfactant is lauryl amido propyl dimethyl betaine, $\text{C}_{12}\text{H}_{25}\text{CON}(\text{CH}_3)_2\text{CH}_2\text{COOH}$. These alkyl betaines are sometimes described as alkyl dimethyl glycinates. Phospholipids, such as lecithin are common zwitterionic surfactants. Unlike other ionic surfactants, which are somewhat toxic, they show excellent biocompatibility. This is most likely due to the fact that lecithin is obtained naturally from soyabean or egg, which contains diacylphosphatidylcholine as the major constituent. The main characteristic of amphoteric surfactants is their dependence on the pH of the solution in which they are dissolved. In acidic pH solutions, the molecule acquires a positive charge and behaves like a cationic surfactant, whereas in alkaline pH solutions they become negatively charged and behave like an anionic one.

Classification of Surfactants

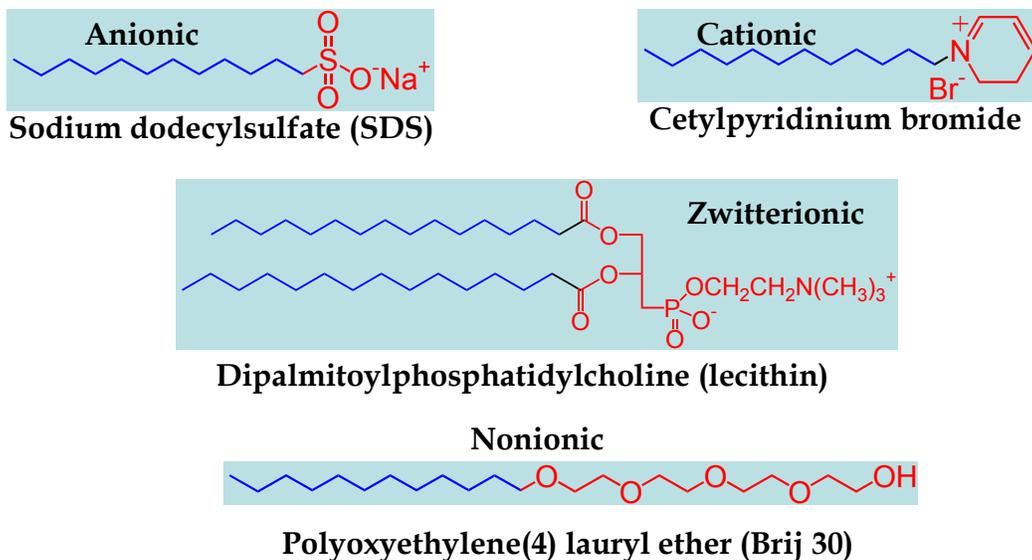


Figure 5. Pictorial representation of various types of surfactants.

A specific pH can be defined at which both ionic groups show equal ionization (the isoelectric point of the molecule). The change in charge with pH of amphoteric surfactants affects their properties, such as wetting, detergency, foaming, etc. [37].

Most of the nonionic surfactants are structurally similar to the ionic surfactants, except the head groups are uncharged or neutral. The interaction between these nonionic head groups are governed by steric forces, as no electrostatic charges emerges from their head groups. Ethoxylated alcohols are the most common nonionic surfactants.

These alcohols contain a wide-ranging degree of ethoxylation, where ethylene oxide is added to fatty acids to make them more water soluble. They are considered to be amphiphiles, with oil loving hydrocarbon tail and a water loving ethoxylated alcohol group. Examples of nonionic surfactants include polyoxyethylene surfactants, such as Brij's (viz. Brij-35, Brij-58 *etc.*), or sugar esters, such as sorbitan esters (viz. Span-20, Span-80 *etc.*). Ethoxylated derivatives of Spans are known as Tweens. Polysorbates are

partially fatty acid esters of sorbitol. Sorbitans are partial esters of sorbitol and mono and di-anhydrides with fatty acids. These are considered as lipophilic nonionic surfactants. Alkanol amides and polyamines are the primary nitrogen-based nonionic surfactant types [39, 40]]. Figure 5 depicts different type of surfactants.

Safe non-ionic surfactants, for example, sucrose laurate and ethoxylated mono-diglyceride have been extensively used by Fanun and co-worker for the formulation of biocompatible single and mixed nonionic surfactant microemulsions [41-45]. Further, the use of short-chain glycerol-based surfactants viz. diglycerol monocaprate, diglycerol monolaurate, and diglycerol monomyristate has been reported by Aramaki and coworkers the formulation of nonionic reverse micelles [46-57] published a series of papers on the formulation of food grade microemulsions by using polyol nonionic surfactants like sucrose stearate (S-1570), sucrose laurate (L-1695), sucrose palmitate (P-1570), sucrose monooleate (O-1570) etc. or Tweens as stabilizers.

Sugar-based surfactants such as alkyl glucosides can be made from renewable material and are biodegradable. They can be used in various applications as substitutes for other surfactants that are not environmentally benign. In addition, sugar-based surfactants exhibit some unusual properties. Their solubility comes from the hydroxyl groups and not from the ether oxygens (as in alkyl polyethyleneglycol ethers) (C_iE_j). They do not show the inverse solubility versus temperature, unlike nonionic alkyl polyethyleneglycol ethers which are temperature sensitive [58].

Amino acids have become increasingly popular in recent years as starting material for surfactants [59-63]. Approximately, one-third of the 20 natural amino acids as well as several non-natural amino acids are utilized for this purpose [64, 65]. An important example of the latter category is sarcosine, also referred to as N-methyl glycine, which constitutes the polar head group in an important type of anionic surfactants [66, 67]. Amino acids based surfactants belong to the class of surfactants with high biodegradability, low toxicity and excellent surface active properties. They possess excellent emulsifying and detergency properties and also, form fine lather. These surfactants are environment friendly, mild to skin and eyes, and possess hard water tolerance. Very recently, Chandra et al. [68] reviewed synthesis, surface active properties [such as, cmc (critical micelle concentration), surface tension, phase behavior, Kraft

temperature, aggregation properties and interfacial adsorption of these surfactants. The biological properties such as antimicrobial activity, aquatic toxicity, biodegradability and hemolytic activity, have also been focused. Further, various applications of these surfactants in the area of life sciences, viz. gene transfection, formation of liposomes and drug delivery systems have been reviewed.

1.8.2. Role of cosurfactant on the formation of microemulsions

Surfactants, due to their diphilic nature, get adsorbed at the oil/water interface of microemulsion systems to render stability to the dispersion by preventing coalescence. However, to fulfill the interfacial thermodynamic requirements often the presence of cosurfactant is required [69]. Generally, short to medium chain (C₄-C₈) lipophilic alcohols have been used as cosurfactant for the formulation. Sometimes, propanol is used as a cosurfactant, depending on the other constituents used for preparation of microemulsion. The addition of alcohol (cosurfactant) effectively changes the originally unfavorable packing geometry of the surfactant molecules, which in turn, adjust the spontaneous curvature of the film to a negative value (curvature towards aqueous domain) and produces a stable surfactant/alcohol mixed interfacial film. By changing alcohol content, imparts an additional advantage to modulate size of the water pools and surface dynamics. Therefore, without a quantitative description of the dependence of the partition equilibria on the system composition under varied physicochemical environments, a full understanding of quaternary microemulsions can not be attained [70-73].

It is apparent that the presence of surfactant vis-à-vis the interaction of surfactant with cosurfactant and the accommodation of these amphiphiles at the interface plays an important role for the formation of stable w/o microemulsions. Hence, this phenomenon can be understood by the packing parameter (P) of the molecular geometry [74]. Israelachvili [74] defined the dimensionless packing parameter (P) of the molecular geometry as $v_c/(a_0l_c)$ where, v_c is the volume and l_c is the length of the hydrophobic tail and a_0 is the area of cross section of the surfactant head group. Most of the cationic surfactants cannot satisfy this condition when they are alone in the organic phase. The addition of an alcohol which accommodates in the interfacial region of these systems has

an effect of increasing the volume of surfactant tail, v_c and reducing the effective surface area a_0 , thus facilitating the formation of stable w/o microemulsions [75]. Recently, Mathew and Juang [75] reported that alcohols play important roles in the formation of w/o microemulsions, such as (i) alcohols act as a weak amphiphile when added into a binary water-in-oil mixture. They act as “co-solvents” in some cases where they partition between the aqueous domain and the amphiphilic film. However alcohol acts as a “co-surfactant,” and it preferentially dissolves in the amphiphilic film, making the (surfactant+alcohol) mixture more hydrophobic. Further, (ii) the amount of alcohol added to the microemulsion system is also considered to be critical. At lower concentration of alcohol the water uptake in the organic phase may be almost zero giving rise to Winsor I type system and at very high concentration of alcohols also the water uptake decreases, (iii) for alcohols with hydrocarbon chain longer than C_{10} , the concentration of alcohol required to form w/o microemulsion eventually start increasing with an increase in the chain length. For a fixed alcohol concentration, the longer the hydrocarbon chains of alcohol, the smaller the water uptake of w/o microemulsion systems [76, 77].

1.8.3. Role of oil on the formation of microemulsions

The oil component influences curvature by its ability to penetrate and hence, swell the tail group region of the surfactant monolayer. More precisely, short chain oils penetrate the tail group region of the surfactant monolayer to a greater extent than long chain alkanes, and subsequently, swell this region to a greater extent, resulting in increased negative curvature (and reduced effective HLB) [73, 78]. Further, starting from a short chain alkane, increasing the oil chain length would gradually reduce the cohesive interaction between the hydrocarbon chains of the interface and decrease the interfacial rigidity due to decreasing oil penetration. Consequently one would expect a decrease in water solubilization in microemulsion with the increase in oil chain length [79]. However, fatty acid esters, such as ethyl, methyl or isopropyl esters of lauric, palmitic, oleic and myristic acid, have also been employed as the oil phase [27, 79, 80-83]. An interesting point is to be noted that saturated (for example, lauric, myristic and capric acid) and unsaturated fatty acids (for example, oleic acid, linoleic acid and linolenic acid) possess penetration enhancing property of their own and they have been studied for a long time [84].

1.8.4. Thermodynamics and stability of microemulsions

For understanding of the thermodynamics of the microemulsion, different types of interactions existing between the components [viz. oil, water, surfactant and/or cosurfactant] present in the system and the microstructure of the system, need to be taken into consideration. Nevertheless, the interaction between oil and water establishes the repulsive forces, and the presence of surfactant molecules changes the balance between cooperative forces towards the attractive forces. The formation of different types of microemulsions made possible due to the stabilizing effect of the surfactants under the auspices of stabilizing interactions. Hence, the understanding of the microstructures of the microemulsions is of prime importance. [85].

The stability of microemulsions is a well-known issue and was dealt by Overbeek and Ruckenstein et al. from theoretical aspects [86]. The understanding of the stability of microemulsions was further developed considerably with the proposition of several thermodynamic theories by Nagarajan et al.[87]. It was considered that the free energy of formation of microemulsion involves three thermodynamic contributions; (1) interfacial free energy, (2) free energy of interaction between the droplets, and (3) entropy of dispersion of droplets in the continuous medium. These studies led to the conclusion that microemulsions are thermodynamically stable, as the interfacial tension between oil and water is too low to compensate the dispersion entropy. Therefore, an essential requirement for the formation of o/w or w/o droplets and their stability is the attainment of a very low interfacial tension (γ). Since microemulsions possess a very large interface between oil and water due to the small droplet size, they can be thermodynamically stable if the interfacial tension is so low that the positive interfacial energy (given by γdA) can be compensated for by the negative free energy of mixing (ΔG_{mix}). If the enthalpy of mixing (ΔH_{mix}) is assumed to be zero for an ideal solution, the free energy of mixing can be given as,

$$\Delta G_{\text{mix}} = -T\Delta S_{\text{mix}} = k_{\text{B}}T \quad (1)$$

(Where, k_{B} is the Boltzman constant and ΔS_{mix} is the entropy of mixing).

$$\text{This follows, } k_{\text{B}}T = \gamma dA = 4\pi r^2\gamma \quad (2)$$

(Where, r is the droplet radius.

So, if $r = 10 \text{ nm}$, γ should be $\sim 0.03 \text{ mN m}^{-1}$. Hence, to prepare microemulsion, the interfacial tension must reach such an ultralow value. Generally, the interfacial tension between oil and water lies in the order of $\sim 50 \text{ mN m}^{-1}$. The role of surfactant is to reduce this value to such an ultralow value [88, 89]. Except for some double chain ionic surfactants and also, for a few nonionic surfactants, it is not possible to achieve the required interfacial area with the use of a single surfactant. However, addition of a second amphiphile (either surfactant or cosurfactant) to a single surfactant system, the effect of both can be additive, provided that the adsorption of one does not adversely affect that of the other. Consequently, they are cooperatively accommodated at the interface and result in decrease of the interfacial tension of the blended system. The accumulation of both surfactant and cosurfactant at the interface results in a decrease in chemical potential, which generates an additional negative free energy change, which is known as dilution effect. Further, the thermodynamic theories explain the role of both cosurfactant and salt in the formation of a microemulsion with ionic surfactant. The cosurfactant produces an additional dilution effect and decreases interfacial tension further. Also, the addition of a salt to systems containing ionic surfactants causes similar effects by shielding the electric field produced by the adsorbed ionic surfactants in the adsorption of large amount of surfactants at the interface. [90]. Recently, an approach to the thermodynamics of microemulsions based on the use of the two-phase model was reported by Kartsev et al. [91]. In this model, one phase is the dispersion medium and the other represents the sum of disperse phase nanodrops. Experimental estimation of the adequacy of this approach showed that the model can be used to solve the thermodynamics problems on microemulsion quite satisfactorily.

1.8.5. Geometrical constrains and interfacial curvature of microemulsions

Microemulsions are dynamic systems in which the interface is continuously and spontaneously fluctuating. “Spontaneous curvature” of the interfacial film governs the formation of different kind of microstructures in microemulsion systems at a specified composition of water-oil-amphiphile. The surface geometry and the intermolecular forces acting between surfactant molecules set the curvature at the interface [74, 92]. There are

also other factors like penetration of oil into the interfacial layer, adsorption of cosurfactant etc. that can modify the curvature of the interface.

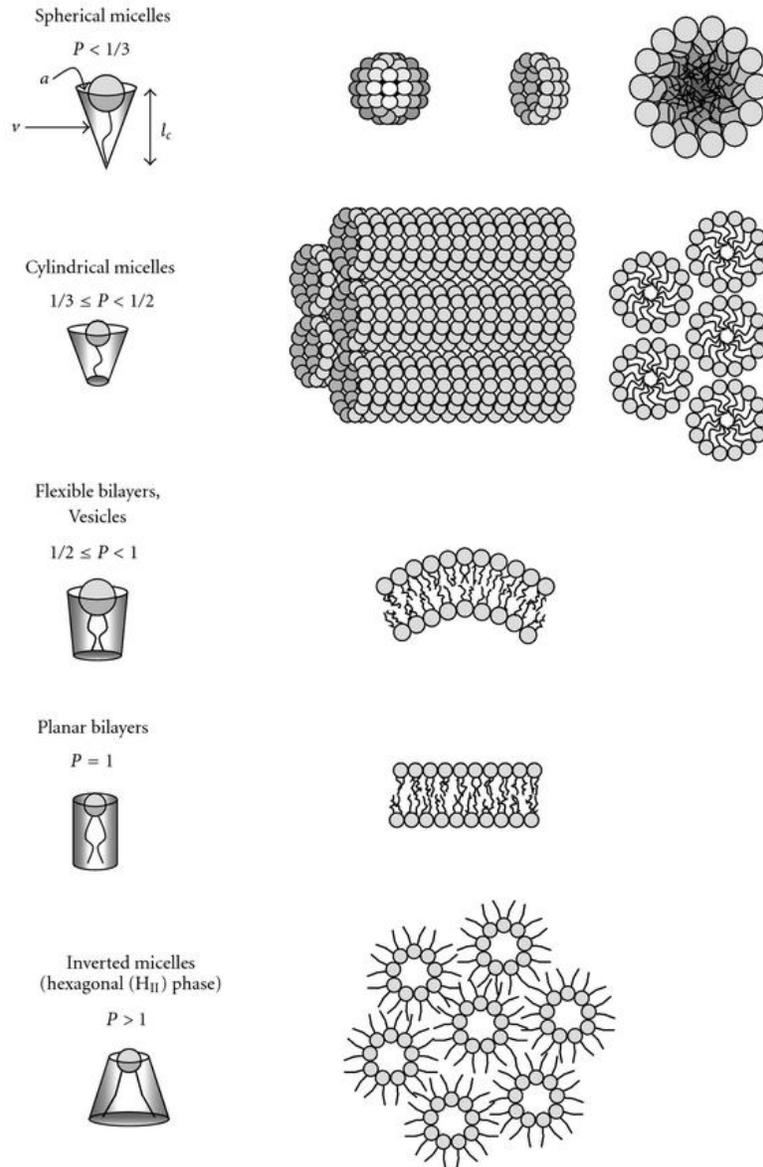


Figure 6. Correlation between packing parameter “P” and structure of self-assembled systems.

In a surfactant monolayer, a repulsive hydrophilic force between the head groups of the surfactants exists, and this repulsive force is balanced by the attractive hydrophobic interaction acting at the oil and water interface, steric repulsive forces between the tails of

the surfactants and force due to the penetration of oil into the interface [93]. . A useful concept in determining the interfacial property, is the “packing parameter” (P) introduced by Israelachvilli et al. [74]. P can be calculated as $P = v/(a_0 l_c)$ where, v is the volume and l_c is the length of the hydrophobic tail and a_0 is the area of cross section of the surfactant head group. For surfactants with $P \sim 1/3$, globular structure can be predicted. With $P \sim 1/2$ and 1, cylindrical and planer layers, respectively can be predicted. Figure. 6 represents correlation between packing parameter “P” and structure of self-assembled systems. Although P provides with an idea of the possible structure of the formulation, it should be noted that P depends on many factors, viz., penetration of oil into the interface, cosurfactant, temperature, electrolyte etc.

For a mixed surfactant systems, the effective packing parameter (P_{eff}) can be expressed according to the following relation as obtained by Evans and Ninham [94]:

$$P_{\text{eff}} = [(xv/al)_A + (xv/al)_B]/(x_A + x_B) \quad (3)$$

where, x_A and x_B are the mole fractions of surfactant A and B present at the oil/water interface, respectively.

The interfacial curvature and the spontaneous radius of curvature can be obtained for a surfactant in the following manner [95-97]: Consider a surfactant film that can stretch and bend. The surface tension (γ) is the first derivative of the film free energy (G_f) with respect to area, i.e.

$$\gamma = (\partial G_f)/(\partial A) \quad (4)$$

The area expansion modulus K_a is given by,

$$K_a = [(\partial^2 G_f)/(\partial A^2)_n] \frac{A}{2} \quad (5)$$

Where, n is the number of surfactant molecules in the film. When the area of the film is changed, the surfactants are equilibrated between the film and bulk.

For a curved surface, the curvature at each point is described by the two principal radii of curvature R_1 and R_2 . The mean radius of curvature (H) is given by,

$$H = \frac{1}{2} (1/R_1 + 1/R_2) \quad (6)$$

For spheres, $R_1 = R_2 = R$ and $H = 1/R$. For cylinders, $R_1 = R$, and $R_2 = \infty$ and $H = 1/2 R$. To assign a sign to the radius of curvature, it is customary to put positive sign for surfaces curved toward oil and negative to surfaces curved toward the polar solvent.

The free energy of the film depends upon the curvature of the film. The free energy per unit area (g_f) is given by,

$$g_f = G_f/2\pi RL \quad (7)$$

where, L is the length of the cylinder.

For a highly curved surface ($R \rightarrow 0$), g_f reaches a high value. Since g_f cannot arbitrarily reach any small value, the condition for minimum gives,

$$\partial g_f / \partial (1/R) = 0 \quad (8)$$

This corresponds to $H_0 = 1/2 R_0$, where H_0 is the “spontaneous curvature” of the film.

The bending rigidity (or the bending elastic modulus) κ of the film is given by,

$$\kappa = \partial^2 g_f / \partial^2 (1/R) \quad (9)$$

The saddle-play modulus $\bar{\kappa}$ can be obtained by considering a saddle-like deformation of the planar interface (i.e. $1/R_1 = -1/R_2$)

$$\bar{\kappa} = -1/2 \partial^2 g_f / \partial^2 (1/R) \quad (10)$$

The area expansion modulus is very large and the area per surfactant molecule remains constant as the film bends. g_f can be expanded to get the form,

$$g_f = \gamma + 2\kappa (H-H_0)^2 + \bar{\kappa} K \quad (11)$$

where, $K=1/R_1R_2$, called the Gaussian curvature.

The curvature free energy thus can be obtained as,

$$G_f = \int (g_f - \gamma) dA = \int (2\kappa (H-H_0)^2 + \bar{\kappa} K) dA \quad (12)$$

Many physicochemical properties of a microemulsion depend on the value of H_0 . It is strongly influenced by the nature of the surfactant and also, on the composition of the polar and apolar phases. Oil molecules penetrate into the hydrocarbon chain of the surfactant film which imposes more curvature towards the polar side. The longer is the hydrocarbon chain length of the oil, smaller is the effect of penetration into the hydrocarbon moiety and hence, less is the effect on curvature. Increasing temperature makes the surfactant chain more coiled and hence, H_0 is increased. For ionic surfactant,

the addition of electrolyte can alter H_0 . The higher the electrolyte concentration, the more easily the film curves toward water and consequently, H_0 is decreased.

Temperature has a strong effect on altering the surfactant curvature for nonionic surfactant derived microemulsion system. As temperature is increased, water becomes poor solvent for the ethylene oxide monomers and hence, water penetration into the palisade layer is decreased at elevated temperature resulting in a decrease in H_0 . This explains the strong temperature dependence of the phase equilibrium for systems stabilized by nonionic surfactant.

The spontaneous curvature can be tuned by altering the head group and chain length of the surfactant, temperature, nature of the oil, added electrolyte and temperature. The bending elasticity (κ) depends upon many factors and short chain cosurfactant, oil penetration etc. make the film more flexible.

1.8.6. The hydrophilic lipophilic balance (HLB) of surfactants

Attempts have been made to rationalize surfactant behavior in terms of the hydrophile–lipophile balance (HLB) [32] which can be a useful guide to the selection of surfactant for the formulation. Ionic surfactants, for example, sodium dodecyl sulfate, which possesses HLBs greater than 20, often requires the presence of a cosurfactant to reduce the effective HLB to a value within the range required for microemulsion formation. It must be noted, though, that microemulsions are only obtained under certain carefully defined conditions, and the HLB of the surfactant can only be used as a starting point in the selection of components that will form a microemulsion. Earlier, Griffin [98] proposed to calculate the HLB of a surfactant from its chemical structure and to match that number with the HLB of the oil phase. The system employs certain empirical formulae to calculate the HLB number within a range of 0 to 20. Hydrophilic surfactants that possess high water solubility and generally act as good solubilizing agents, detergents, and stabilizers for O/W emulsions lie at the higher end of the scale. Whereas, surfactants with low water solubility, act as solubilizers of water in oils and are good W/O emulsion stabilizers at the lower end of the scale (Figure 7). The effectiveness of a given surfactant in stabilizing a particular emulsion system depends on the balance between the HLBs of the surfactant and the oil phase involved. Although, the HLB system proposed by Griffin has been useful in most of the general applications by guiding

the chemist to a choice of surfactant most suited to individual needs, others have suggested HLB numbers could be calculated based upon polar and non-polar group contribution [99]. In the past, Griffin introduced a semi-empirical scale (HLB number based on the stability of emulsion), but his original method for determining HLB number was a long and laborious experimental procedure [100]. It has been reported that the hydrophilic-lipophilic (H/L) property [which is defined by the size and water solubility of the surfactant polar head (the hydrophile) relative to the size and oil solubility of the hydrocarbon chain (the lipophile)] of a pure nonionic surfactant for a water/surfactant/oil system is not affected by the change in the water/oil ratio and/or surfactant concentration. A systematic investigation on the H/L property for mixed nonionic surfactants/oil/water system was reported by Kunieda et al. [101, 102].

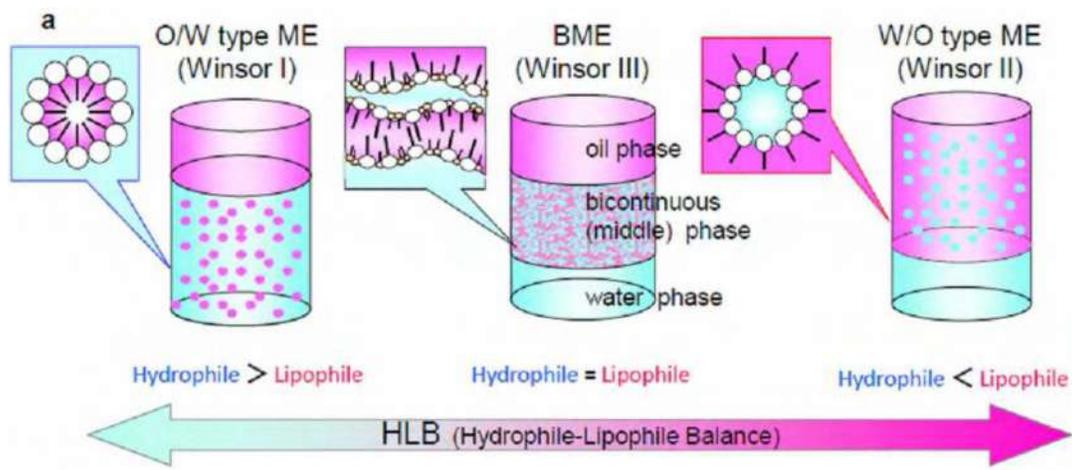


Figure 7. Different types of microemulsion systems as a function of HLB

Further, they explained HLB system on the basis of the phase equilibrium in a series of water/surfactant(s)/oil systems using different types of surfactants, and oils (hydrocarbon and polar) [103].

HLB of the mixed surfactant systems at the mixed compositions (i.e., HLB_{mix}) has been evaluated using the concept of Fu et al. [104]

$$\text{HLB}_{\text{mix}} = (m_A \text{HLB}_A + m_B \text{HLB}_B) / (m_A + m_B) \quad (13)$$

where, m_A and m_B are the mass of surfactant A and surfactant B in the mixture, respectively. HLB_A and HLB_B are the hydrophilic-lipophilic balance of surfactant A and surfactant B, respectively.

1.8.7. Effect of mixed surfactants

In colloid and surface chemistry, there is a continuing interest in research on the supramolecular surfactant assemblies that include micelles, microemulsions, liquid crystals, monolayers, vesicles, etc., with mixed surfactants containing either combination of anionic/cationic or anionic/nonionic or cationic/nonionic or nonionic/nonionic surfactants and have been discussed in detail by numerous pioneering authors [43-45, 105-108].

When surfactants are added together in water in different proportions, several physicochemical properties of the mixed system compared to those of the single surfactant system, are changed due to the fact that there is a net interaction between the amphiphiles, i.e. due to non-ideal mixing. It is well known that many amphiphilic self-assemblies and interfaces, biological or synthetic-based, consist of surfactant mixtures. The molecular structure of the surfactant (head group of different sizes and hydrocarbon tails with different chain lengths), cosurfactant with different lipophilicities, the presence of additives and co-solvents (viz. salt and polyethylene glycols etc.) and experimental variables (pH, temperature) can be manipulated in order to induce changes in interfacial activity and in intra- and inter-aggregate forces. The mixed system almost invariably yields enhanced interfacial properties (e.g. decreased CMC with higher surface activity) with respect to the individual surfactants, in what is termed *synergism* [109-114].

Mixed surfactant was found superior to the relevant single ones mainly due to the reduction in nonionic surfactant partition and/or sorption as well as the high solubilization capacity of the mixture. Decreasing loss of surfactant due to sorption and the greater apparent solubilization of the mixture will reduce the volumes of surfactants needed and thus the capital expenditure and operation cost [115]. The interaction between surfactants in mixtures can produce marked interfacial effects due to change in adsorption as well as in the charge density of the surface. In most cases, when different types of surfactants are purposely mixed, what is sought is synergism, i.e. the condition when the properties of the mixture are better than those attainable with the individual components

by themselves. Surfactant mixtures of practical interest include like-charge surfactants, for instance mixtures of anionic surfactants, or mixtures of cationic surfactants, but the more common case involves mixture of ionic and nonionic surfactants [116, 117]. The most popular advantage to ionic/nonionic surfactant mixtures is the fact that they result in temperature insensitive microemulsions [118]. Generally, ionic and nonionic surfactants behave oppositely with increasing temperature. Ionic surfactants show a hydrophilic shift with increasing temperature, while nonionic surfactants exhibit a lipophilic shift. Therefore, when two surfactants are mixed together in a particular ratio, these two effects will cancel each other, and result in formation of a temperature-insensitive microemulsion. Temperature-insensitive microemulsions having a large solubilization capacity, are very important not only because of their applications in different industrial fields, but also for basic studies in the surfactant science field. Earlier, Kunieda et al. [70] and Binks et al. [119] reported temperature-insensitive microemulsion in single water/sucrose monoalkanoate/hexanol/decane and mixed AOT/*n*-dodecyl pentaoxyethylene glycol ether (C₁₂E₅)/oil microemulsion, respectively. Very recently, Rio et al. [120] and Kundu et al. [72, 73] formulated temperature-insensitive microemulsion for mixed ionic/nonionic [(Aerosol-OT/cyclic ketal alkyl ethoxylate) and (CPC/Brij-58 or Brij-78 and SDS/Brij-58 or Brij-78)] surfactant systems in either hydrocarbon (Hp or Dc or isooctane) or polar lipophilic (IPM) oils, respectively. Mixtures of oppositely charged surfactants (i.e., anionic-cationic which also known as catanionic surfactant mixtures) usually exhibit large synergistic effects (i.e., mix non-ideally). Mixing of oppositely charged surfactants reduces the monomer surfactant concentration in the solution (i.e., increase the surface activity). On the other hand, due to absence of electrostatic attractive interactions in mixture of like-charged surfactants, the effects (if any) is not expected to be as large as for a mixture of oppositely charged surfactants [121]. Mixtures of nonionic surfactants tend to behave ideally [122]. This means, no synergistic effect is to be expected in terms of the physicochemical properties (viz. solubilization behavior, cloud point etc.). A typical feature of the adsorption of ionic (anionic or cationic)-nonionic surfactant mixture is synergism or anti-synergism (antagonism) at the oil/water interface. For example, the adsorption of one surfactant is either enhanced or retarded by the addition of a small amount of the other (second)

surfactant. In many applications, surfactant mixtures often give rise to enhanced overall performance over single component systems [123-125]. Mixed surfactants could be employed over a wide range of temperature, salinity, and hardness conditions than the individual surfactants [126, 127]. Consequently, surfactant mixtures are employed in a wide variety of practical applications such as surfactant enhanced aquifer remediation (SEAR), enhanced oil recovery (EOR), drilling mud formulation, detergency, and waste water treatment, to name just a few [128].

1.8.8. Solubilization in microemulsions

The term “solubilization” was first defined by McBain and Hutchinson [129]. According to them, solubilization is the increase in the solubility of an insoluble substance in a given medium. Nagarajan [130] defined the phenomenon of solubilization as an increase in the solubility of solvophobic substances in a solvent medium caused by the presence of amphiphilic aggregates.

A unique feature of reverse micelles/microemulsion systems is their ability to solubilize a wide class of ionic, polar, apolar and amphiphilic substances. The existence of multiple domains in reverse micelles (e.g. apolar bulk solvent, the oriented alkyl chains of the surfactant, and the hydrophilic head group region of the reverse micelles) help to solubilize such a wide range of substances. Ionic and polar substances are hosted in the micellar core and apolar substances are solubilized in the bulk apolar solvent. Whereas amphiphilic substances are partitioned between the bulk apolar solvent and the domain comprising the alkyl chains and the surfactant polar heads, i.e. the palisade layer [131]. Earlier, Maitra and Patanjali [132] suggested that the surfactant monolayer of w/o microemulsion droplet can be used well as a model for biological membranes for studies of solubilization of extra-membraneous components from the solubilization study of cholesterol in the monomolecular hydrophobic shell of AOT reverse micellar droplet. Further, Silber et al. [133] described the methodologies that can be employed to obtain distribution constants of the solute between the surrounding solvent and the micellar interface. Solubilization of water in reverse micelles or w/o microemulsion systems has been found to be dependent on various factors such as the rigidity of the interfacial film, which in turn depends upon the size of the polar head group and hydrocarbon moiety of

the surfactant, the composition, the type of oils, the presence of electrolyte, the nature and valence of the counter ion, the temperature, etc. [134]. Kon-No et al. [135] first reported on the solubilization behavior of reverse micellar systems using surfactants such as dodecylammonium carboxylate, butyldodecyl dimethylammonium bromide, polyoxyethylene nonylphenyl ether, and sodium bis(2-ethylhexyl) sulfosuccinate (AOT) in organic solvents at different temperatures in both absence and presence of electrolytes of different charge types. Modification of the interface by blending of surfactants brings about considerable changes in the elastic rigidity of the interfacial film. Earlier studies with RMs involving more than one surfactant using solubilization, identified significant modification of the physicochemical properties of the interface and consequently, of the water structure in reverse micellar or w/o microemulsion systems in comparison to the corresponding single surfactant systems. These findings summarize that the effects of surfactant blending on solubilization and also, on other physical properties, are a direct consequence of mixing and physicochemical interactions in the interfacial film [136]. Earlier, Li et al. [137] investigated the influence of two typical additives, long chain organic molecule, bis(2-ethylhexyl) phosphoric acid (HDEHP) and inorganic electrolyte (NaCl) on the water solubilization capacity of AOT and NaDEHP in *n*-heptane solution. The effects of the variables (such as, additives, water content and temperature) on the water solubilization capacity and also, on structure of the oil/water interface were also been examined by measuring the electrical conductivity of these systems. Paul and Mitra [79] reported the solubilization of water and its mechanism, microstructure in absence or presence of additives of different types in mixed RMs with anionic surfactant (AOT) and nonionic surfactants (Brijs, Spans, Tweens, Igepal CO 520), a double chain cationic surfactant (DDAB)–nonionic surfactants (Brijs, Spans, Igepal CO 520), and nonionic (Igepal CO 520)–nonionics (Brijs, Spans) in oils of different chemical structures and physical properties (isopropyl myristate, isobutyl benzene, cyclohexane). Synergism in water solubilization was observed in most of these systems and depended upon nonionic surfactant type, composition, additive and its content and oil. Results were compared with conventional linear hydrocarbons and also, reported that chemical structures of the oils play a decisive role to influence the above parameters. Further, Mitra and Paul [83] reported the effect of NaCl and temperature on the water solubilization behavior of mixed

AOT and nonionic surfactants (Brij-30, Brij-35, Brij-52, Brij-56, Brij-58, Brij-76, Tween-20, Tween-40, Span-20, Span-40, Span-60, Span-80) reverse micellar systems in IPM oil. Liu et al. [138] reported on the solubilization of water and/or aqueous NaCl solution in mixed reverse micellar systems formed with anionic surfactant (AOT) and nonionic surfactants (Brij-30, 52, 56 and 58) in cyclohexane, n-hexane, n-heptane, n-octane and iso-octane oils.

In a recent study, Das et al. [136] showed that mixed AOT/polyoxyethylene (5) nonylphenyl ether (Igepal-520) at different proportions, cyclohexane (Cy) systems exhibit a considerable synergism in the water solubilization capacity; where solubilization capacity initially increased with increasing Igepal content to pass through a maximum and beyond which it decreased. Very recently, Kundu and Paul further reported the solubilization of water in mixed RMs comprising AOT and nonionic surfactants (viz. Tween-85, Tween-80, Span-85) at different compositions of X_{nonionic} in polar lipophilic oils of different chemical structures: viz., ethyl oleate (EO), isopropyl myristate (IPM) and isopropyl palmitate (IPP) at 303 K [81].

1.8.9. State of water in the water pool of reverse micelles or w/o microemulsion systems

Typical water-in-oil (w/o) microemulsions or reverse micelles (RMs) consist of nanoscopic water pools dispersed in a nonpolar solvent confined by surfactant monolayer. The water molecules solubilized in the interior of the water pool have properties different from those of bulk water [139]. This makes the systems potentially useful for various technological applications [140] and biologically important systems [[141, 142]. The physicochemical properties of the confined water has been found to be strongly dependent on the chemical nature of the dispersant phase (oil), surfactant, cosurfactant and also on the hydration level of the w/o microemulsions ($\omega = [\text{surfactant}]/[\text{water}]$) [143-145].

State of water in the water pool in AOT based reverse micellar systems have been investigated by several workers [143, 146-150] using different techniques like NMR, ESR, FT-IR, Raman, fluorescence and near infrared spectroscopy, and differential

scanning calorimetry (DSC). According to these reports, mainly four types of water are present in reverse micelle; free water (dispersed among the long hydrocarbon chain of surfactant molecules), anion bound (the hydration site of head groups of the surfactant molecules), bulk like and cation bounded. The nature of solubilized water is strongly dependent on ω . In contrast to AOT (anionic surfactant), report on the state of solubilized water in CTAB (cationic surfactant) stabilized system is scarce [151].

Water induced alterations in the structure of reverse micelles and w/o microemulsion are reported in literature [152, 153]. The solubilization of water in surfactant aggregates has been described in three steps: (i) hydration of the headgroup, (ii) swelling of the microemulsion droplets and (iii) phase separation. All these steps have been reported to be endothermic and gain in entropy has been found to be the driving force for solubilization [154]. Several authors have investigated the energetic state of water in reverse micelles from calorimetric measurements. [155, 156]. Very recently, nature of confined water in mixed RMs (viz. anionic/nonionic, nonionic/nonionic and cationic/cationic systems) has been explored by several authors [136, 145, 157-159].

1.9. Characterization of microemulsions

Microemulsions are technologically important complex fluids. In many applications, they are required to accommodate functional additives such as drugs, polymers, and nanoparticles, which increase the complexity of the systems further. Due to their complexity, namely different types of structures and components involved in these systems, as well as the limitations associated with each technique, the characterization of microemulsions is rather a difficult task. Multiple complementary techniques are required in order to understand and also to manipulate microemulsion behavior. Recent advances in analytical techniques as well as theoretical models have allowed observation of the nanoscale morphology of different microemulsion forms of increasing complexity at ever greater resolution [4]. At the same time, there is increasing interest in the study of dynamic processes within microemulsions using scattering techniques as well as techniques such as fluorescence correlation spectroscopy and ultrafast IR spectroscopy. Some of these techniques, starting from phase behavior to Electron microscopy are presented, in brief, to identify and characterize microemulsions in the following section [17].

Phase behavior of microemulsions

Phase studies are inevitable for the basic understanding of general phase behavior and kinetics of the structural changes of a system. This is not only of fundamental interest but also is very important for industrial and technological processes. Phase diagrams for microemulsions are quite complex since there are at least three components; water, oil and surfactant. These structured fluids have a readily deformable surfactant interface, which bend either towards water or oil or both. Formulation of microemulsion phases can be difficult since microemulsions often coexist with other phases such as excess oil and/or water, and are often too close to lyotropic liquid crystalline phases. A map of the locations of different phases in composition space is known as a “phase diagram” of microemulsions [160]. A pictorial representation of “phase diagram” (as a model) considering different phases in composition (of water, surfactant and oil mixtures) has been depicted in Fig. 8.

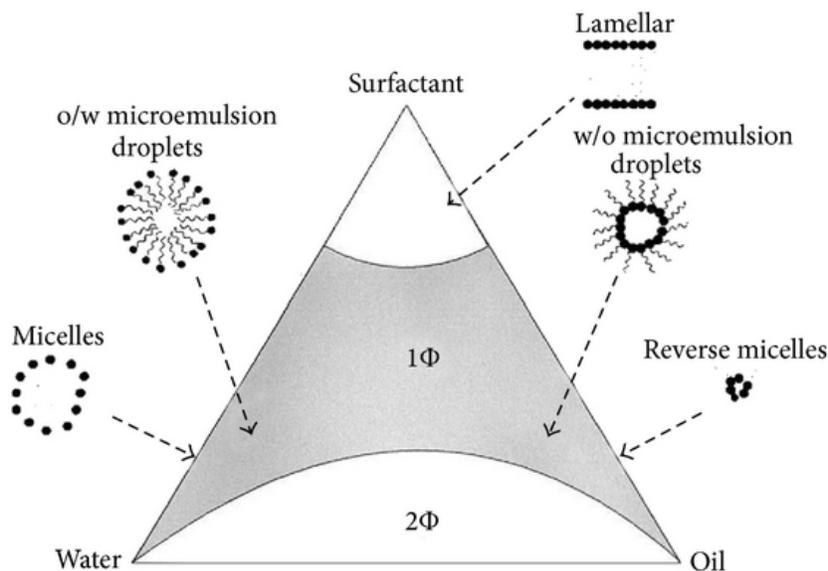


Figure 8. Pictorial representation of “phase diagram” of water, surfactant and oil mixtures.

The phase behavior of microemulsions depends on chemical structures of oils and surfactants, temperature, pressure and additives such as salt and polymers etc.. The “phase behavior” is essential in the study of surfactant systems. Earlier, Moulik and

coworkers [161-164] carried out extensive studies on phase behavior of systems containing surfactant, cosurfactant, oil and water using a three dimensional (Gibbs triangle) or tetrahedral representation. The ingredients used were Brij-92 [polyoxyethylene (2) oleyl ether], Brij-52 [polyoxyethylene (2) cetyl ether], Brij-30 [polyoxyethylene (4) lauryl ether], and Tween-20 [polyoxyethylene sorbitan monolaurate] as surfactants, and ricebran, isopropyl myristate (IPM), eucalyptus, coconut as oils. Phase volumes of the heterogeneous combinations were estimated to understand the mixing efficiency of the combinations. The effect of temperature on these volumes of multiphasic compositions was also investigated. In addition, the effect of additives of different types (viz. sodium chloride, bile salts and urea) on the physicochemical characteristics of these systems was examined. In tune with these studies, Paul and his coworker [165-169] reported phase characteristics of plant oils (saffola, eucalyptus, and clove oils) derived microemulsions. Further, Sjoblom et al. [170] reviewed the progress in understanding of the microemulsion structure on a molecular level as well as from extensive experimental studies of phase diagrams of both ionic and nonionic surfactants. In the contribution of Hellweg [171], new developments in the investigation as well as understanding of complicated phase behavior and the fascinating microstructures in microemulsion forming systems, were outlined. Very recently, several authors reported the phase diagrams of the multicomponent microemulsion systems comprising four or five components, single or mixed surfactant(s), cosurfactant, oil and water at different physicochemical conditions. [167, 172-182]. Actually, classical phase studies accomplish key importance for the understanding of microemulsions, especially when combined with refined structural investigations. Latest studies of this type yield an improved understanding of the solubilisation of triglycerides, a topic that had been addressed for a long time and where the solubilisation performance of typical detergents is far from being satisfied. In these studies, triglycerides of various chain lengths were compared systematically with respect to their phase behaviour [183]. An interesting extension far from normally employed nonionic microemulsions was shown to occur for catanionic surfactants, which typically form unilamellar vesicles under water-rich conditions. For a ternary surfactant system comprising octylammonium octanoate /octane/water, it was reported by combination of a careful phase study complemented by means of

conductivity, light scattering and SANS measurements, that at low water content W/O microemulsions are formed, where the sphere-cylinder transition and the branching of rod-like aggregates depend on the concentration of surfactant, the surfactant/water ratio, and temperature [184].

1.9.1. The Schulman's cosurfactant titration at the oil/water interface (Dilution method)

It is considered that in the formation of water-in-oil (w/o) microemulsion using a blend of surfactant/cosurfactant (amphiphiles), all the surfactant molecules reside at the interface and the cosurfactant molecules are distributed between the bulk oil and the interface depending upon their solubility in water. At fixed water to surfactant composition, a threshold amount of cosurfactant is required for the formation of stable microemulsion, and the size of the dispersed droplets in the dispersion is controlled by the cosurfactant composition. Although direct determination of cosurfactant distribution between the interfacial plane and the bulk oil is difficult [185], reports are available in literature using techniques, like SANS, SAXS and DLS [186, 187], conductivity [188], interfacial tension [189]. To understand chemical reactivity of a single or mixed species either inside the water pool or at the interface of a quaternary w/o microemulsion, the detailed knowledge on (i) interfacial composition such as relative population of surfactant and cosurfactant at the oil/water interface, (ii) the distribution of cosurfactant between the interface and bulk oil phase vis-à-vis the thermodynamics of this transfer process of cosurfactant, (iii) the number and the size of the droplets and (iv) physicochemical characteristics of the entrapped water, are essential. These parameters are strongly influenced by the type and alkyl chain length of oil and the amphiphiles (surfactant or cosurfactant) [188]. All these parameters [except (iv), which can be determined from Fourier transform infrared spectroscopy and FTIR measurements] [145], can be evaluated (without using sophisticated instruments) from the dilution method which is a pioneering work of Bowcott and Schulman [190]. This simple but elegant method is accomplished by adding oil at a constant water and surfactant level to destabilize an otherwise stable w/o microemulsion and then restabilizing it by adding a requisite amount of cosurfactant

(alcohol). For these reasons, the dilution method (which is commonly represents the Schulman's cosurfactant titration of the oil/water interface) has been widely used by a number of workers to estimate the parameters involved in the transfer of alcohol from the bulk oil to the interface [72, 73, 173, 191-205]. The method provides an understanding of the interfacial compositions of surfactant and cosurfactant as well as distribution of the cosurfactant between the interface and oil, and can quantitatively account for the thermodynamic stability of microemulsion. The mathematical model based on the dilution method and the evaluation of corresponding parameters. has been discussed in details in subsequent chapters.

Furthermore, dilution method has its own background in the development of interfacial science research for w/o microemulsions. During 1982 to 1987, reports on exploring the dilution method were due to Birdi et al. for water/SDS/pentanol/benzene microemulsion [192], Singh et al. [206] followed by Kumar et al. for water/CTAB/2-ethyl-1-hexanol/pentane or hexane or heptane microemulsions, respectively [193] and Verhoecku et al. [207]. Pithapurwala and Shah [208] affirmed modified Schulman-Bowcott model for the evaluation of interfacial composition of oil-external microemulsion formed with sodium stearate, pentanol, brine, and linear hydrocarbons (with $>C_{10}$, viz. decane, dodecane and hexadecane) as oils. Moreover, it was reported that the molecular packing was highest at the optimal salinity which corresponded to maximization of molar ratio of alcohol to surfactant at the oil/water interface. Later on, Singh et al. [194] investigated the influence of chain length of alkanes (pentane to heptane and benzene) as oil and amine (n-alkylamines and cyclohexylamine) as cosurfactant on water solubilization behavior of cationic microemulsions (CTAB and CPC) from dilution experiments. Gu. et al. [209] performed calorimetric investigation on the partition of n-pentanol (Pn) between external oil phase (heptane, Hp) and the interfacial layer of the w/o microemulsion, sodium dodecyl benzenesulfonate (DDBS)/Pn/Hp/water. The results showed fine changes in the structure of water-in-oil emulsion and the microemulsion droplets. Further, the alcohol/surfactant mole ratio in the interfacial layer of the droplets, and also, the standard thermodynamic functions of alcohol transition from the external phase to the interface were derived from calorimetric data. During analysis of these results, a criticism on the basics of dilution method or the relationships used in the dilution method was put

forwarded by him. It was reported that the calorimetric investigation adopted by Gu and coworkers provides an improved results compared to the results obtained from dilution method in 1998. However, in the following year, Moulik et al. [210] investigated two w/o microemulsion systems; water/cetylpyridinium chloride (CPC)/alkanol (1-butanol, 2-butanol, 2-methyl-1-butanol, 1-pentanol and 1-hexanol)/alkane (C_6 and C_7) and same microemulsion system (as adopted by Gu et al. [209]) at various temperatures by the dilution method, in order to collect additional data for the sake of comparison and interpretation. According to the authors, the dilution method was found to be sound and useful for the understanding of the interfacial compositions of surfactant and cosurfactant as well as the distribution of the cosurfactant between the interface and bulk oil phase. Further, it was demonstrated that the equations involved in both the methods were, in fact, identical and that the criticism of Gu et al. [209] was incorrect. Later, a series of papers on w/o microemulsion systems have been reported by employing the dilution method. Digout et al. evaluated thermodynamic properties and structural characteristics of w/o microemulsions comprising water/CPC/alkanols (C_4 - C_6)/alkanes (C_8 – C_{10}) by the dilution method [195]. In this vein, Hait and Moulik [196] introduced a polar amphiphilic (biocompatible) oil, isopropyl myristate (IPM) for the formulation of w/o microemulsions based on surfactant of different charge types, CPC, cetyltrimethylammonium bromide (CTAB) and SDS with 1-butanol as cosurfactant along with the evaluation of structural parameters at different physicochemical environments and the results were analyzed using the dilution method. Further, Bayrak [211] reported stable microemulsion system using nonionic surfactant Triton X-100 and Triton X-405 with the variation of cosurfactant chain length (C_5 OH and C_7 OH) and oil topology (hexane, heptane, octane, decane and benzene) in 2004. As dilution method proposed by Bowcott and Schulman [190] is a simple and inexpensive method which is accomplished by dilution with oil and subsequent titration with cosurfactant up to the onset of microemulsion formation, doubts are often expressed on the reliability of data obtained. In the same year, Palazzo et al. [212] published a paper entitled, “Does the Schulman’s titration of microemulsions really provide meaningful parameters?.” The interfacial compositions of CTAB/n-hexane/1-pentanol/water w/o microemulsion system were measured using the dilution method and found satisfactory agreement with high accuracy

with those obtained by using the pulsed gradient spin-echo NMR (PGSE-NMR) technique. They further pointed out that this method has applications in scattering and diffusion studies, because it provides extrapolation to single-particle properties by reducing inter-particle interactions of the microemulsions without changing its composition. Further, the same system with high concentration of Pn was investigated to underline its influence on phase equilibria and mesophase structure using the dilution method and PGSE-NMR technique [213]. It is worthy to mention that Abuin et al. employed UV-Visible spectroscopy as a tool for titration experiment involved in the dilution method for characterization of various microemulsion systems in 2004 [214]. In the following years, Zheng et al. extended the field of the dilution experiment for characterization of Gemini surfactant based microemulsion, C_{12} -s- C_{12} or C_{12} - OE_x - C_{12} /n-hexanol/n-heptane (wherein s and x signify the number of spacer (CH_2) and oxyethylene group (OE_x), respectively) for the first time [198, 199]. In 2006, the applicability of the dilution method on mixed cationic-nonionic surfactant microemulsions, CTAB/Brij-58/1-butanol (1-pentanol)/heptane (decane) was first reported by Paul and coworkers [173]. Subsequently, Paul et al. investigated water (or, aqueous NaCl)/oil (decane and dodecane) microemulsions stabilized by anionic (SDS), cationic (CPC) and nonionic [polyoxyethylene (23) lauryl ether, Brij-35] surfactants and 1-pentanol (Pn) as cosurfactant [200]. During the period 2006-2007, a series of papers were reported by Moulik et al. on the investigation of interfacial composition, thermodynamic properties and structural parameters of w/o microemulsions stabilized by anionic and cationic surfactants (alkyltrimethylammonium halide or alkylammonium bromide and its mono-, di-, and trihydroxyethylated head group analogues) and linear chain alkanols (viz. C_4OH to C_9OH) as cosurfactants using heptane, isooctane and isopropyl myristate (IPM) as oils by the dilution method [197, 203, 204]. Wang et al. [215] investigated the effect of cosurfactant of different types with linear and branched chains (viz., n-butanol, n-pentanol, iso-pentanol, n-hexanol, n-octanol) on the formation of diesel oil microemulsions, water/cetyltrimethylammonium chloride (CTAC)/alkanol(s)/diesel oil. The interfacial composition and thermodynamic properties of these microemulsions were investigated by the dilution method. It is interesting to note that under identical physicochemical conditions, n-octanol is more suitable cosurfactant than the others in

forming w/o diesel oil microemulsions. In 2009 and onwards, another group led by Panda and his coworkers [201, 202] investigated formation of w/o microemulsions stabilized by cationic (C_n TAB, where n stands for 10, 14, 16), nonionic (Tween-20, sorbitan polyalkanoates of different alkyl chain lengths) surfactants, 1-butanol and 1-pentanol as cosurfactants and heptane as oil by the dilution method. Since 2006 Paul and his coworkers published a series of papers on interfacial surfactant/cosurfactant compositions, structural and thermodynamic parameters of mixed cationic or anionic-nonionic surfactant microemulsions at different physicochemical environments by employing the dilution method [72, 73, 173, 200, 216]. During a decade, the formulation of microemulsions has been pursued with an ionic liquid (IL) as a substitute of water or oil or as an additive (aqueous), because of their proposed environmentally-benign nature with many unique and attractive properties. The objective of these studies was to combine a nanostructure of a microemulsion with the unique properties the ILs [217-221]. The first report on the investigation on the formation of w/o microemulsions involving surfactant-like IL, 1-alkyl-3-methylimidazolium bromides/alcohol/alkane/water (brine) by the dilution method is due to Chai et al. [222]. Subsequently, a series of papers were published on the investigation of IL-based microemulsion systems by the dilution method by Chai et al. [223], Moulik et al. [180], Panda et al. [224], Kar et al. [216], and Wang et al. [225].

1.9.2. Electrical conductivity

Electrical conductivity is a structure-sensitive property. Nevertheless, the results obtained from conductivity study do not provide a straightforward picture of the microstructure of microemulsions, but transition from water continuous to oil continuous microemulsion can easily be obtained from such measurements, since water continuous formulation (o/w microemulsion) usually shows higher conductance than the oil-continuous formulations (w/o microemulsion) [4]. The low conductance in dilute w/o microemulsion has been explained on the basis of charge fluctuation model [226, 227]. Further, for the w/o microemulsion systems, transition from discrete droplet structure to connected droplet or bicontinuous structure can be envisaged from sharp increase in conductance value (100-1000 times increase) with increasing volume fraction of the polar solvent or temperature.

Such phenomenon is called “conductance percolation”. The concept of conductance percolation is governed by scaling laws [160].

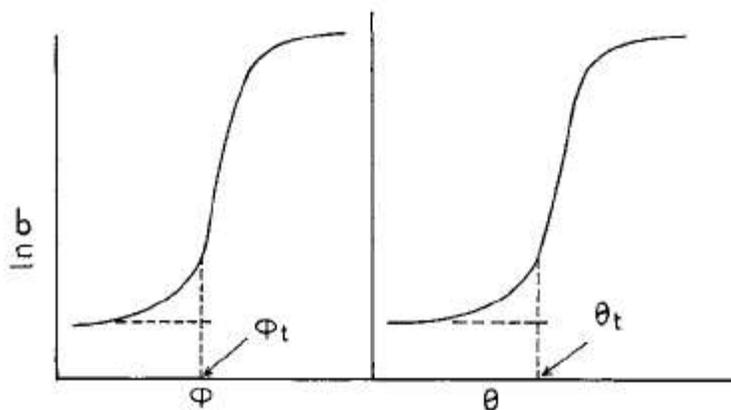


Figure 9. Typical volume and temperature percolation diagrams. The procedure for getting Φ_t and θ_t are indicated by arrow heads in the diagrams [160].

Two types of percolation phenomenon have been recognized, viz. “static percolation” [228, 229] in which a connected droplet network can be assumed; “dynamic percolation” [230, 231] in which droplets can approach their neighbors by diffusion and transfer charge to augment sharp rise in conductance. Such a conductance manifestation can occur after a threshold dispersant concentration at a constant temperature (called the volume-induced percolation) as well as after a threshold temperature at a constant dispersant concentration (called the temperature-induced percolation).

The enhancement in conductance can be attributed to two probable mechanisms, namely the “hopping” of ions from droplet to droplet beyond a threshold volume fraction of the dispersed phase is reached [232, 233] and/or by exchange of droplet contents during droplet collision known as “transient-fusion-mass transfer-fission” mechanism [137, 234-236]. Mays [237] suggested that the “transient-fusion-mass transfer-fission” process plays the major role in conductance percolation than the hopping mechanism. Over the past decade, a number of studies were carried out on the effects of experimental conditions on the electrical conductivity of single and mixed surfactant reverse micelles based on hydrocarbon and polar lipophilic oils in absence and presence of additives of different physicochemical properties by several researchers [81, 191, 238-249].

Bumajdad et al. [112, 250] measured the electrical conductivity of D₂O-in-n-heptane microemulsions stabilized by cationic/nonionic surfactant mixtures (DDAB, and either the C₇E₇ non-ionic surfactants, or polymeric nonionic surfactants of the type PEO-PPO-PEO, Pluronic®) as a function of D₂O content, surfactant concentration, and surfactant mixture composition.

Liu et al. [138, 251, 252] reported that that the molecular volume as well as configuration of solvent molecules has significant effect on the conducting properties of AOT/Brij's/linear or cyclic hydrocarbon oil(s). Mitra and Paul [253-256] published a series of papers on the effects of water content, micelle concentration, content of nonionic surfactant on the temperature-induced percolation of conductance of AOT + Brij-56 or Brij-58 mixed RMs in IPM (a polar lipophilic oil) in absence and presence of additives of various types with different physical parameters or interfacial properties. Moreover, Paul and Maitra investigated [79] the conductance behavior of mixed RMs comprising anionic surfactant (AOT) and nonionic surfactants (Brij's, Spans, Tweens, Igepal CO 520), cationic surfactant (DDAB)–nonionic surfactants (Brij's, Spans, Igepal CO 520), and nonionic (Igepal CO 520)–nonionics (Brij's, Spans) in oils of different chemical structures and physical properties (isopropyl myristate, isobutyl benzene, cyclohexane) focusing on the influences of water content (ω), content of nonionics (X_{nonionic}), concentration of electrolyte ([NaCl] or [NaBr]), and oil.

The effect of temperature on conductance has three distinct stages (pre-percolation, percolation and post-percolation). Interfacial deformation, fusion, mass transfer, and fission models were considered by different authors to rationalize the clustering process for percolation of conductance in terms of activation energy, $E_p/\text{kJ mol}^{-1}$. In general, E_p depends on two different contributions: the electrostatic interactions among the charged droplets and an attractive interaction resulting in the interdigitation of the surfactant tail and the solvent molecule, whose effect should depend on the distance between the particle surfaces [191, 247].

Although, it is known that percolation is clearly related to rigidity of the surfactant film, there is no single consistent theoretical model to predict the influence of additives, so possibility of developing a simulation tool become quite interesting. Artificial Neural Networks [ANNs] are a complete mathematical tool for data analysis which try to

reproduce artificially the human ability of taking decisions simulating the human brain's basic unit, the neuron, and the interconnections between the neurons that allow them to work together and save experience's information [257, 258]. Mejuto and coworkers published a series of papers in order to predict the percolation threshold of AOT-based microemulsion systems in presence of different inorganic (salts) and organic additives (organic molecules) by using ANNs architectures. ANNs were implemented for the prediction of temperature induced percolation threshold (T_p) for AOT/isooctane/water microemulsions in presence of different electrolytes [259]. A perceptron multilayer ANN with five entrance variables (ω value of the microemulsion, additive concentration, molecular weight of the additive, atomic radii and ionic radii of the salt components) was used. All the electrolytes resulted an increase in the temperature percolation threshold (T_p). The results revealed a clear and logical trend within the chloride series, which was rated by increasing effect on T_p in the order: $\text{HCl} < \text{LiCl} < \text{NaCl} = \text{KCl} < \text{RbCl} < \text{CsCl}$, the effect of NH_4Cl was similar to that of NaCl . By contrast, no clear trends was emerged among the various salts sharing a common cation; sodium salts. Whereas, divalent cations as Ca^{2+} in CaCl_2 showed a strong effect on T_p . The best ANN architecture consists in five input neurons, two middle layers (with eleven and seven neurons, respectively) and one output neuron. In continuation of above study, Mejuto and coworkers reported on the impact of small organic molecules (ureas and thioureas as additives instead of salts) upon electrical percolation of AOT/isooctane/water microemulsions using ANNs [260]. In this report, different possible entrance variables (viz. critical volume of the molecules, molecular weight, water solubility, logP and concentration of additives) of ureas and thioureas as additives, were assayed. Finally, three variables, viz. additive concentration, logP and ω value were used for the best prediction of T_p . It was suggested that the new ANNs is simpler than that of previous one developed for the salt as additives. Further an attempt was made by Mejuto and groups to obtain a model to predict the influence of a large family of molecules (n-alkyl-acids) on T_p of AOT/isooctane/water microemulsions by employing ANNs [261]. In particular, different ANNs architectures were assayed to predict T_p in presence of n-alkyl acids with a chain length between 0 and 24 carbons, using a multilayer perceptron with five easy-acquired entrance variables (number of carbons, logP, length of the hydrocarbon chain,

pK_a and acid concentration). Very recently, Mejuto and co-worker [262] reported a series of models, based on ANNs, of the temperature induced percolative behaviour of AOT/isooctane/water microemulsions in the presence of crown ethers as additives. Input variables, related to the chemical structure of crown ethers and their packing at the surfactant film, were selected. As a result, a model was chosen with a good forecast capability for percolation threshold of such microemulsions. In sum, ANNs have been found as an useful tool in order to predict percolation temperature of microemulsion systems, as long as error in predictions fits perfectly in the range of experimental error while determining T_p. Despite these achievements, authors concluded that design of a better and less specific model to predict the influence of different kinds of additives in a generous way, still remains far away.

1.9.3. Viscosity measurement

The viscosity of a solution can give first hand information on its internal consistency; in case of macromolecular solutions and colloidal dispersions, an understanding of the overall geometry of the dispersed entities can as well as be obtained. In the field of application, fluidity of a medium plays an important role. For localized applications, low fluidity is wanted; whereas for solubilization, spreading and reaction study, it is advantageous to have high fluidity. The knowledge of colloidal dispersions (e.g., micelles or microemulsions) thus enjoys both fundamental and application importance.

Microemulsions have varied flow behaviors, for example, lamellar (Newtonian) and non-lamellar (non-Newtonian). Low viscous microemulsions show Newtonian behavior. The Winsor-III and the bicontinuous types are usually non-Newtonian in nature and they can show plasticity [263]. The viscous properties of microemulsions depend on the type, shape and number density of aggregates present, as well as the interactions between these aggregates. The phenomenon of percolation in microemulsion is associated with droplet clustering and fusion, i.e. internal structure changes and hence, it is reflected in viscosity. A pronounced similarity in the behavior of self-diffusion, specific conductivity and viscosity of sodium bis(2-ethylhexyl) sulfosuccinate (AOT)/isooctane/water microemulsion was reported by Eicke et al. [264]. The increase in viscosity with temperature has been attributed to the phenomenon of increased clustering of the droplets [265]. The structural inversion from w/o to o/w type of microemulsion is reported from

viscosity measurement [266]. Paul et al. [267] critically reviewed the viscosity behaviors of microemulsion systems with reference to internal structure, data correlation, flow patterns, additive influence etc. from the view point of applications (viz. nanoparticle synthesis, reaction medium etc.). Several authors reported that viscosity measurements can contribute significantly in understanding of the inter-micellar interaction in single as well as mixed surfactant microemulsion systems [52, 113, 158, 181, 268-272].

1.9.4. Light scattering techniques

Among the light scattering techniques, dynamic light scattering (DLS), also known as photon correlation spectroscopy, can be used to analyze droplet size of microemulsion via determination of hydrodynamic radius, which can be extracted from measurements of the diffusion constants of diluted dispersed phase (droplets) undergoing Brownian motion [4]. This technique provides the determination of z-average diffusion coefficients (D). If interparticle interaction is assumed to be absent in a system, the hydrodynamic radius of particles (droplets) (d_h) can be obtained from the Stokes-Einstein equation:

$$D = k_B T / 6\pi\eta d_h \quad (14)$$

where, k_B is Boltzmann constant, T is absolute temperature, η is the viscosity of the medium. The DLS technique is useful to characterize size and size distribution of microemulsion droplets, as it monitors the collective diffusive motion in colloidal structured systems, provided simple diffusion is the sole mechanism responsible for the variation of the scattered intensity [[269, 273]. Polydispersity index (PDI) is another important parameter for evaluation of measurement from DLS experiment. The ratio SE/d_h , where SE is the standard error in d_h , is called PDI [274]. For a mono-dispersed sample, the PDI value is taken to be less than 0.08; whereas the value ranges from 0.08-0.7 is considered as a mid-range polydispersity [249]. Several authors have significantly contributed to the understanding of various interactions in the microemulsion droplet core by measuring the droplet size [248, 249, 269, 275-278].

The interaction between droplets can be investigated by employing Static Light Scattering (SLS) technique, where the intensity of scattered light is generally measured at various angles for different concentrations of microemulsion droplets. At sufficiently low concentrations, the Rayleigh approximation is used provided the particles are small enough [279]. Warisnoicharoen et al. [280] investigated the structure of dilute 3-

component nonionic oil-in-water microemulsions formulated with either a polyoxyethylene surfactant ($C_{18:1}E_{10}$ or $C_{12}E_{10}$) or the alkylamine-N-oxide surfactant, DDAO ($C_{12}AO$), and a triglyceride or an ethyl ester as oil using static light-scattering technique.

Earlier, Liu et al. [138, 251, 252] reported the droplet size of reverse micelles formed by AOT-Brij mixed surfactants in hydrocarbon oils. Very recently, Das et al. [136], Fanun et al. [41] and Kundu et al. [81, 82] also measured the droplet diameter of mixed anionic or cationic or nonionic/nonionic microemulsion systems stabilized in hydrocarbons and polar lipophilic oils.

1.9.5. Neutron and X-ray scattering techniques

In small angle neutron scattering (SANS), neutrons from a reactor source are scattered by the atomic nuclei of the sample. An advantage of the use of neutrons is that neutrons are non-destructive compare to X-rays, and hence, radiation damage rarely occurs in a neutron based experiment. On the other hand, the relatively slow data acquisition times and requirement of a powerful neutron source for neutron scattering experiments limits their applicability in the study of dynamic phenomena [4]. SANS provides relevant information about structure of microemulsions [268, 281-284]. Normal hydrogen and deuterium have significantly different scattering lengths. Thus scattering contrast between heavy water and hydrocarbon is very high. By varying the contrast and even matching the contrast between different components of a mixture, selective portions can be highlighted. By matching the scattering length densities of water and oil, structure of both droplet-type and bicontinuous microemulsions can be established [285, 286]. Radiation wavelength of X-rays (1-10 Å) is smaller than the typical structural length scale in microemulsion. Thus, small angle scattering with X-rays can be very useful to determine the size and shapes of microemulsion droplets from the magnitude and angular dependence of the scattered intensity [181, 248, 287]. Using synchrotron radiation sources, information about a wide range of systems can be obtained with this technique, including those systems in which the surfactant molecules are poor X-ray scatterers [288].

Earlier, Bumajdad and his coworkers [289-291] summarized the effects of surfactant blending on microstructural properties (e.g., size and shape) as a direct consequence of

mixing and physicochemical interactions in the interfacial films using SANS technique. The structure and surfactant film composition of water-in-*n*-heptane microemulsions stabilized by DDAB/C₁₂E₅ mixture were studied by Giustini et al. [292] [using SANS technique. In another study, Bumajdad et al. [293] also reported the structure of and film properties of a zwitterionic surfactant-alcohol stabilized microemulsion system by SANS technique. Very recently, the physicochemical behavior of the mixed surfactant system consisting of a ionic surfactant AOT, and the two-tailed cyclic ketal alkyl ethoxylate (2-tridecyl, 2-ethyl-1,3-dioxolan-4-yl) methoxy]-*O'*-methoxy poly(ethylene glycol)], or CK-2,13, in water/isooctane microemulsion systems, was investigated by SANS to understand the arrangement of the two surfactants at the interface *vis-à-vis* the behavior and properties of the microemulsion systems to enable applications [281]. Kljajic et al. [181] also studied the structural aspects of water-in-heptane microemulsions stabilized by mixed AOT/sodium bis(amyl) sulfosuccinate (DAS) using small-angle X-ray scattering (SAXS) technique. Fanun [271] also reported the size, shape, and internal structure of colloidal particles using SAXS technique for understanding of the microstructure parameters (i.e. periodicity, and correlation length) of the water + propylene glycol/mixed nonionic surfactants/peppermint oil + ethanol and water/sucrose laurate/ethoxylated mono-di-glyceride/R (+)-limonene U-type microemulsions.

1.9.6 Spectroscopic probing techniques

Several spectroscopic techniques have been used to study different aspects of structures and properties of microemulsions. The absorption and steady-state emission spectroscopy of probe molecules solubilized in a microemulsion system can probe the polarity of the microemulsion at their solvation location [295]. Chemiluminescence techniques have also been employed to study transitions between polar and non-polar environments in microemulsion systems. Time-resolved emission spectroscopy provides the information about the dynamics and rotation relaxation of solvent in microemulsions [295-297]. In particular, fluorescence lifetime measurement is a highly sensitive method where the lifetime of a fluorophore can alter in response to changes in the conformational state of the probe molecules or in response to the interaction with local environment in microemulsion systems [298]. The steady-state anisotropy or polarized fluorescence study provides a simple means of monitoring the processes, in which the microstructure

of the microemulsion is affected in some way [298]. Further, the anisotropy is considered as an index of the microviscosity or rigidity in the microenvironment of the probe [299].

In addition, fluorescence correlation spectroscopy (FCS), which may be considered as a miniaturization of DLS, measures the tiny spontaneous fluctuations in fluorescence intensity of molecules in a very small volume (spot), and quantifies it by temporarily auto-correlating the recorded intensity signal to obtain the variation in local concentration of fluorescent species and hence, their diffusion coefficient [300]. This technique is an excellent tool for measuring molecular diffusion and size of microemulsion droplets under extremely dilute conditions. In recent experiments, FCS technique has been shown to be applicable to microemulsion systems, where for the w/o AOT system from the diffusion times hydrodynamic radii were determined which compared well to the values obtained in parallel by SANS [301].

Earlier, absorption and emission spectroscopic studies of fluorescein dye in water/AOT/heptane microemulsion media (w/o type) were reported by Biswas et al. [302]. It was reported that the spectral behavior of a fluorophore (fluorescein) can help to identify the threshold composition between bound and free water in the microwater pool of water/AOT/heptane (w/o) microemulsion medium. Moulik and coworker estimated the pH of the oil/water interface and the interior of the water pool for water/AOT/heptane or decane microemulsions in absence and presence of butanol (cosurfactant) by the absorption and emission characteristics of probe molecules (7-Hydroxycoumarin and 1-Hydroxypyrene-3,6,8-trisulfonate) [303]. Paul and coworker investigated [304] on the characteristic features of the interface of water/AOT/Brij (Brij-30 or Brij-35 or Brij-56 or Brij-58 or Brij-76 or Brij-78)/isooctane mixed reverse micelles with the help of spectrophotometric studies using 7-hydroxycoumarin (HCM) as the fluorophore. Absorbance study showed that the HCM molecule resides in an identical pH environment for both AOT/isooctane and AOT/Brij/isooctane systems. However, based on the fluorescence data, authors concluded that with decreasing chain length of the hydrophobic moiety of the nonionic surfactants, the interface of mixed reverse micelles becomes continuously tinny. Recently, Gao and coworker [305] reported the micropolarities of bmimBF₄/TX-100/toluene, ionic liquid (IL)/oil (O) microemulsions by

UV-Visible spectroscopy using methyl orange (MO) and methylene blue (MB) as absorption probes. The results indicated that the polarity of the IL/O microemulsion increased only before the IL pools are formed, whereas a relatively fixed polar microenvironment was obtained in the IL pools of the microemulsions. Mehta et al. [191] probed the polarity and hydrogen bond interactions formed by the polar solvent in the micelle interior, for water/Brij 96/butanol/ethyl oleate microemulsion systems by absorption spectroscopy. Das and coworker [306] reported that the steady-state fluorescence spectroscopic studies of w/o mixed surfactant microemulsions (water/CTAB+Brij-30 or Brij-92 or Tween-20 or Tween-80/n-hexanol/isooctane) using 8-anilino-1-naphthalenesulphonic acid (ANS) as probe. It was reported that the interface of w/o mixed surfactant microemulsion revealed more microviscous and hydrophobic than the pure CTAB, irrespective of the composition of nonionic surfactants and varying alcohol content. The incorporation of ruthenium complex ($[\text{Ru}(\text{bpy})_3]^{2+}$) within microemulsions formed from anionic (AOT) and cationic surfactant (CTAB) was investigated as a function of water content by Birnbaum and coworker [307] using steady-state and time-resolved emission spectroscopy. Recently, Mitra and coworker [136, 145, 158] employed the picosecond resolved fluorescence spectroscopy to study the relaxation dynamics of water in the solvation shell of the microemulsion involving a variety of single and mixed surfactant system microemulsions, AOT/Brij-30, Tween 80/butyl lactate and AOT/Igepal-520, Igepal-210/Igepal-630. The rotational anisotropy of the probe was also investigated to ascertain its geometrical restriction of in microenvironment. Bhattacharyya and coworkers [308] reported the excitation wavelength dependence of the solvation dynamics and anisotropy decay in neat ionic liquid, 1-pentyl-3-methyl-imidazolium tetra-fluoroborate ($[\text{pmim}][\text{BF}_4]$) and ionic liquid containing microemulsion, $\text{pmim}][\text{BF}_4]/\text{Triton X-100}/\text{benzene}$ using time-resolved fluorescence spectroscopy (femtosecond up-conversion). The deuterium isotope effect on the femtosecond solvation dynamics in this system was also reported. [309]. Levinger et al. [146] critically reviewed the ultrafast solvation dynamics in reverse micelles and emphasized that the confinement, rather than the specific interaction with surfactants, is an important factor in determining the impact of the reverse micellar microenvironment on the photophysical processes.

1.9.6 Nuclear magnetic resonance (NMR)

This experimental technique provides an important information about the microstructure of microemulsions. Molecular self-diffusion coefficients of each component (viz. water, oil and surfactant) can be determined within the purview of same experiment and information can be obtained by with diffusion coefficients [159, 268, 310-321]. Proton magnetic resonance has proven to be a useful technique for identifying the structure of water solubilized in reverse micelles. Addition of water to reverse micelles does not significantly affect the chemical shift of other protons, except H₂O. The water proton magnetic resonance exhibits a single peak, indicating the rapid exchange between water protons at various states [147, 322]. The observed chemical shift results from the weighted average of different water species.

Recently, El Seoud and coworkers studied solubilization of formamide and 1,2,3-propanetriol (PT), and also aqueous solution of formamide and PT in reverse aggregates of AOT in heptane or isooctane by ¹H NMR spectroscopy [323, 324]. A review article focusing a variety of NMR methods applied to different surfactant aggregates is available in literature [325]. Spin relaxation and self diffusion experiments yielded both structural and dynamical information.

Generally, radioactive labeling technique is employed to obtain information on the mobility of the components of microemulsions. Earlier, this technique came out to be time consuming and use of labeled molecules in a multicomponent system was sought to be impractical [326]. But, the Fourier transform pulsed-gradient spin-echo (FT-PGSE) NMR technique, in which magnetic field gradients were applied to the sample, allowed simultaneous and rapid determination of the self-diffusion coefficients (in the range of 10⁻⁹ to 10⁻¹² m²s⁻¹), of many components [327, 328]. For an o/w droplet structure, the surfactant and oil diffuse as droplets and hence, possesses the same diffusion coefficient (in the order of 10⁻¹¹ m²s⁻¹), which in turn is lower than that of water (in the order of 10⁻⁹ m²s⁻¹). For a w/o droplet structure, a reverse phenomenon was observed and water possesses a lower self-diffusion coefficient in comparison to the continuous oil phase. In bicontinuous microemulsions, the diffusion coefficients of both water and oil are high (of the order 10⁻⁹ m²s⁻¹) and that of surfactant lies in between the values of non-associated surfactant molecules and droplet-type structure (of the order of 10⁻¹⁰ m²s⁻¹).

Hydrodynamic radius of microemulsion droplets can also be measured from self-diffusion data. The diffusion coefficients of oil and water are slightly reduced than the pure solvents due to the obstruction imposed by the opposite domain.

Earlier, the structure and surfactant film composition of water-in-*n*-heptane microemulsions stabilized by DDAB/C₁₂E₅ mixture was studied by Bumajdad et al. [290] and Giustini et al. [292] using pulsed-field gradient NMR (PFG-NMR). Li et al. [148] also studied the microstructure of mixed reverse micelles stabilized by surfactants of AOT and/or NaDEHP by means of proton nuclear magnetic resonance (¹H NMR) measurement. The chemical shift in ¹H NMR of water solubilized in these reverse micelles was changed concomitantly with water content (ω_0 , the number of solubilized water molecules per surfactant molecule) and relative content of surfactants (AOT and NaDEHP). Fanun [270, 294, 329, 330] also characterized mixed nonionic surfactant, sucrose laurate /ethoxylated mono-diglyceride microemulsion systems using PGSE-NMR. Very recently, Wolf et al. [331] reported PFG-NMR self-diffusion measurements in the single phase channels of a microemulsion system comprising anionic surfactant, magnesium dodecyl sulfate [Mg(DS)₂] and lipophilic nonionic co-surfactant, iso-tridecyl-triethyleneglycolether IT 3 (C₁₃E₃) mixture. In subsequent year, Bumajdad et al. [159] investigated the structure of solubilized water in water-in-*n*-heptane aggregates by mixing single and double tailed surfactants namely, didodecyldimethylammonium chloride/dodecyltrimethylammonium chloride (DDAC/DTAC) or didodecyldimethylammonium bromide/dodecyltrimethyl ammonium bromide (DDAB/DTAB) by ¹H NMR technique.

1.9.7 Fourier transform infrared spectroscopy (FTIR) measurements

The knowledge about hydration of surfactants in w/o microemulsions or reverse micelles is helpful for understanding of the dynamics of different physicochemical processes operative within the confined environment (i.e, local interactions in the vicinity of water molecules in w/o microemulsion). Further, it is also helpful and prospective for applications in biological and chemical reactions occurring in w/o microemulsions or reverse micelles [133]. In order to get a clear understanding of various interactions in the droplet core, including the type of H-bonding which is operative within the water pool, an excellent and non-invasive technique viz., Fourier transform infrared spectroscopy

(FTIR) has been introduced. Several authors significantly contributed to the understanding of the water dynamics in single and mixed surfactant derived w/o microemulsion systems by studying the state of water using FTIR method [144, 145, 147, 148, 159, 191, 332-336]. The characteristics of the water molecules confined inside the water pool depend strongly on both water content and the nature or type of the surfactant head group [136]. A detail observation on the dynamics and nature of encapsulated water in AOT reverse micelles with the large variation in water content, was reported by Piletic et al. [334] using linear and nonlinear infrared spectroscopy.

Zhou et al. [147] reported on the characteristic features of the solubilized water by employing FTIR technique, and the results were explained on the basis of the models that depict the water present in “layers” of different structures. For example, in the two-layer model [337, 338], water is present in two layers: the first contains water molecules that interact strongly with the surfactant head-group, and known as hydration or bound water, which possesses different physical properties (viz. organization, mobility, microviscosity, conductivity, etc.) from those of bulk water [339, 340]. The second type possesses physical properties similar to those in bulk water and hence, called (bulk-like). In the three-layer model [341], the water located at the interface is considered to be of two types, trapped water located between the chains of the surfactant and water that solvates the head-groups [342] and a four-layer model has also been advanced [322, 334, 343]. The suggested four types of water are as follows: W_{bound} (water molecules tightly bound to the surfactant head-group); $W_{\text{intermediate}}$ (distorted H-bonded water species); bulk-like water, $W_{\text{bulk-like}}$; interfacial water, $W_{\text{interfacial}}$, (lies between hydrophobic interfacial tails, which is unfavourable environment for water). This can be water in-transit during the breakdown and fusion of the droplet, which is a well-known phenomenon in microemulsion. Earlier, Correa and coworkers investigated the states of solubilized formamide and PT in AOT/Hp or isooctane based nonaqueous RMs by FTIR spectroscopy [323, 324]. Further, Gonzalez-Blanco and Velazquez [344] investigated the effect of addition of two different poly (vinylpyrrolidone) on the structure of AOT/isooctane w/o microemulsion using FTIR. FTIR technique was also applied to water-in-scCO₂ microemulsion stabilized by a mixture of fluorinated surfactants (one of which was fluorinated AOT-analogue surfactant) by studying the stretching and bending

bands of water and S=O stretching band of the surfactant over the wide range of water/CO₂ ratios. It was reported that the number of water molecules in CO₂ as dissolved, was associated with the core, or at the interface as a function of water content in the system. [345]. Very recently, Bumajdad et al. [159] reported on the state of solubilized water in w/o microemulsions stabilized by mixtures of single- and double-tail quaternary ammonium cationic surfactants, namely (DDAC/DTAC) or (DDAB/DTAB) by employing two noninvasive techniques, FT-IR and ¹HNMR with HOD probing. The results indicated that water appears to be present as a single nano-phase (or one pseudo-phase), rather than coexisting of structurally different water layers, and the properties of such one-pseudo-phase changed continuously as a result of increasing water content (ω). Further, no significant effect was found to affect the state of solubilized water on account of changing counter-ion (Br⁻ or Cl⁻), in spite of the known difference in the dissociation of these counter-ions from micellar aggregates. Very recently, Mitra and coworkers [346] characterized the state of water in a variety of single and mixed surfactant w/o microemulsion/reverse micelles (for example, AOT/Brij-30, Tween 80/butyl lactate, AOT/Igepal-520, Igepal-210/Igepal-630, TX-100/lecithin) by FTIR technique. They found three different types of water molecules in these systems, and their relative content changes with the interfacial composition as well as total water content in the system. However, Hayes et al. [281] demonstrated that an increase in the content of a two-tailed cyclic ketal alkyl ethoxylate (CK-2,13) of AOT based mixed surfactant w/o microemulsion system, led to an increase in water molecules localized near the Na⁺ counter ion of AOT from the analysis of the -OH stretching region of the FTIR spectra. It was suggested that the water molecules of hydration for the ethoxylate group reside near AOT's counter ion, resulting in increased dissociation of the counter ion, and hence, increased the hydrophilicity for AOT. Very recently, Correa and coworkers reported [157] the effect of nonionic surfactant, tri-n-octyl phosphine oxide (TOPO) on the interface of a novel w/o mixed microemulsion/reverse micelles, water/AOT/TOPO/n-heptane by FTIR measurements. FTIR experiments were performed by monitoring monodeuterated water frequency in TOPO blends and exhibited bound and “bulklike” water structure even at very low water content. On the other hand, the water structure depends on the water content for mixed systems (AOT/TOPO). Furthermore, ultrafast

vibrational spectroscopies are powerful tools for exploring both vibrational energy relaxation (VER) and molecular motion. Recently, Levinger et al. critically reviewed the application of ultrafast IR spectroscopies to explore the structure, dynamics, and energy relaxation properties of w/o microemulsion/reverse micelles [146]. Mittleman and coworkers (27–29, 79) demonstrated application of IR radiation to the study of w/o microemulsions or reverse micelles. They used ultrashort pulses to generate terahertz radiation to interrogate the micellar samples [347, 348].

1.9.8 Electron Microscopy

Electron microscopy can provide straightforward structural information of microemulsions. Images showing clear evidence of the microstructure have been obtained [96]. Both droplet and bicontinuous structures of microemulsions can be seen through “freeze fracture” technique [349-353]. Another technique, Cryo scanning electron microscopy (Cryo-SEM) is a powerful method for visualizing the structure of microemulsions. Recently, Koetz and his coworkers [354, 355] investigated the structure of the bicontinuous microemulsion by cryo-high resolution scanning electron microscopy. Further, Fanun [329] characterized biocompatible microemulsions comprising mixed surfactants (sucrose laurate/ethoxylated mono -di-glyceride) and peppermint oil by cryogenic-transmission electron microscopy (Cryo-TEM) and droplet dimensions of these systems were measured. Recently, Wolf et al. [356, 357] also reported the nanostructures of a novel microemulsion system comprising silicone oil or decane, water and a surfactant mixture of an anionic [calcium dodecyl sulfate Ca(DS₂)] and a nonionic surfactant (iso-tridecyl-triethyleneglycolether, abbreviated as IT 3) by Cryo-TEM and freeze-fracture transmission electron microscopy (FF-TEM) imaging.

1.10. Application of microemulsions

1.10.1. Single surfactant microemulsions

The outstanding properties of microemulsions, such as high capacity to solubilize water and oil, low interfacial tension, large interfacial area, spontaneous formation and fine microstructures render them excellent candidates for a variety of applications, which have been documented in several review articles and books [14, 28, 29, 140, 358-360]. However, most important and promising applications, as described in literature, are

summarized in order to demonstrate the significance and potential of microemulsion systems.

Nanoparticles and nanomaterials/nanocomposites

Over and above three decades ago, Boutonnet et al. [361] first reported that metallic nanoparticles (Pt, Pd, Rh, Ir) could be obtained by simple mixing of two w/o microemulsions, one containing a salt, or a metal complex and the other containing a reducing agent, such as boron hydride, or hydrazine. The microemulsion systems were water/CTAB/octanol and water/C₁₂E₅/hexane or hexadecane. In recent years, several authors presented review of the literature in the field of nanoparticle synthesis and characterization of several metals in the inverse microemulsion systems [362-366]. More recently, the ability to synthesize nanoparticles in water/supercritical fluid microemulsions was realized [367, 368]. This method promises to be a highly useful route for controlled nanoparticle synthesis due to the added control variables afforded by tuneability of the solvent quality (density) through pressure and temperature. The evolution of the microemulsion technique for nanoparticle synthesis was reviewed by Lopez-Quintela with special emphasis on the mechanism of control of the particle size, viz. the control by employing proper microemulsions and also, by the surfactant adsorption (capping). The kinetics of the particle formation, the possibility of the preparation of the particle formation, as well as coating core-shell and 'onion-like' structures with a precise size control, and the use of microemulsions to produce fine ceramics and finally their use in the preparation of super-lattices were addressed [369]. In a review, Eastoe et al. [370] described synthesis of nanoparticles in microemulsions, which is an area of considerable current interest. A wide variety of materials has been synthesized by employing w/o microemulsions for more than two decades. Control parameters were elucidated for influencing both nanoparticle concentration and morphology, allowing for tailored syntheses with various applications. Recently, a novel and straightforward approach of metal (Pt, Pd and Rh) and metal oxide (cerium (IV) oxide with cubic type crystalline structure) nanoparticle synthesis was reported by Solans et al. [371] by nonionic surfactant-based oil-in-water (o/w) microemulsion reaction method. The ability of amphiphilic compounds to self-assemble into well-defined structures can be taken advantage of the synthesis of inorganic materials with nanometer dimensions. The

principle, which is biomimetic in character, was discussed with special attention on three areas: microemulsion-based synthesis of nanoparticles, preparation of mesoporous materials from surfactant templates, and surfactant-mediated crystallization [372]. The synthesis of Cu–Ni nanoparticles in w/o microemulsions of SDS/*n*-butanol/*n*-heptane/water at 70 °C was reported by Feng et al. The results indicated that the composition and size of alloy nanoparticles depend on ω (the mole ratio of H₂O to SDS), the method of addition of Cu²⁺ and Ni²⁺ and the mole ratio of Cu²⁺ and Ni²⁺ in the initial precursor solution [373]. Wen and coworkers synthesized monodisperse Co–Ni–Cu amorphous alloys nanoparticles by the reduction of CuSO₄·5H₂O, NiCl₂·6H₂O and CoCl₂·6H₂O with KBH₄ in water/sodium oleate/hexane microemulsion system at room temperature [374]. Ahmed and coworkers first reported the formation of bimetallic Cu–Ni nanoparticles of varying composition (CuNi₃, CuNi, Cu₃Ni) by a microemulsion route using water/CTAB/1-butanol/isooctane systems and hydrazine/NaOH as the precipitating agent followed by reduction in hydrogen atmosphere [375]. Colloidal dispersions of silver (Ag) particles by the photoreduction of silver perchlorate (AgClO₄) in water/AOT/benzene water-in-oil (w/o) microemulsions by Harada and his coworkers [376]. Recently, Chaudhuri and Paria [377] reported an in-depth review of synthesis mechanism and applications of core/shell nanoparticles by microemulsion synthesis media. Sanchez-Dominguez et al. [378] reviewed the synthesis of inorganic nanoparticles [metallic (Pt, Pd, Rh, Ag), single metal oxides (CeO₂, ZrO₂, TiO₂, Fe₂O₃), mixed and doped metal oxides (Ce_{0.5}Zr_{0.5}O₂, Ce_{0.99}Eu_{0.01}O₂, Zr_{0.99}Eu_{0.01}O₂, and Fe₂Mn_{0.5}Zn_{0.5}O₄), semiconductors (PbS, CdS, Ag₂S, ZnS, CdSe, PbSe, Ag₂Se), fluorides (CaF₂, YF₃, NdF₃, PrF₃), phosphates (CePO₄, HoPO₄), and chromates (BaCrO₄ and PbCrO₄)] using oil-in-water (O/W) microemulsions as confined reaction media. Recently, Goshen and Magdassi [379] in a review report, presented the methods used to produce organic nanomaterials from microemulsions, and also, offered a perspective on the possibilities of particle design that can be achieved by various techniques. Tojo and his coworkers reviewed a series of papers on computer simulation study on the synthesis of nanoparticles in microemulsion [380–384]. Furthermore, numerous nanostructured materials, ranging from metallic catalysts [385–388] to semiconductor quantum dots [389, 390] to various ceramic materials [391–393],

silica and gold coated nanoparticles [394, 395], latexes and polymer composites [396, 397], double-layered nanoparticles [398], bimetallic nanoparticles [399] and even superconducting materials [400, 401], have been synthesized and characterized in reverse micelles. In a review, Lo'pez-Quintela and his coworkers [402] showed the use of microemulsions for the preparation of nanoparticles, and also as interesting organic reaction media. Recently, in a tutorial review Ganguli et al. discussed several aspects of microemulsions, for example, their stability, versatility and flexibility towards the synthesis of nanocrystalline materials which would be of interest to a cross-section of researchers working on colloids and interface science, nanoscience and materials chemistry. Authors concluded that the field has grown considerably from the initial synthesis of spherical metal nanoparticles in the 1980s to the highly complex and multifunctional nanostructures of today through the microemulsion route [403].

Biotechnology

Recently, interest on microemulsions is being focused for various applications in biotechnology, viz., enzymatic reactions, immobilization of proteins and bioseparation. Enzymatic oxidation of *oleuropein*, the most abundant olive phenolic compound, in the restricted aqueous environment of olive oil based microemulsion composed of lecithin and 1-propanol was reported by Papadimitriou et al. [404]. Xenakis and his coworkers also reported a series of papers on lipase containing microemulsions [405-410]. Kunz and his coworkers [411] also reported the activity of the enzyme *horse radish peroxidase (HRP)* in single surfactant based reverse microemulsions, composed of sodium dodecylsulfate (SDS), n-dodecane, aqueous buffer, and alcohols of the homologous series 1-butanol to 1-octanol. Sawada and Ueda [412] also investigated the activity of proteases α -chymotrypsin and subtilisin in Tween-85/isopropyl alcohol/n-hexane/water and TX-100/cyclohexane/water RMs. It was reported that the activity of enzymes in the Tween-85 RMs was similar to the aqueous systems but TX-100 RMs did not show any enzyme activity.

Drug delivery and pharmaceuticals

Solubilization capacity, dissolution efficiency, rate and extent of solute delivery are dependent on the microstructure of microemulsions. Recently, Fanun [413] reported an in-depth review on the prospective use of microemulsion as delivery systems. In the field of

drug carriers, microemulsion media have been found to be a good proposition, and can be applied to a wide variety of dosage forms including oral, topical, ocular, parenteral, periodontal, buccal and nasal formulations [414]. Further, it can be noted that microemulsion systems have applications in cancer therapy [415]. Recently, Hegde et al. [416] and Fawzia et al. [417] reviewed the prospective application of microemulsion in ocular drug delivery systems.

Miscellaneous

From the extensive review report of Paul and Moulik [14], Moulik and Rakshit [28], Stubenrauch [399, 418-420], Friberg et al. [421], Paul and Moulik [422], and De and Maitra [423], some applications of microemulsion systems, have been mentioned here in brief. Microemulsions can function as a liquid membrane. They have been found to be efficient in the extraction of heavy metals (e.g., Hg) involving oleic acid from contaminated water, and used as fuels, lubricants, cutting oils and corrosion inhibitors for several decades. Paint formulations using microemulsions have shown higher scrub resistance, better color intensity and more stain resistance than those prepared by emulsions. Due to their characteristic properties, microemulsions are promising systems for detergency purposes over traditionally-used organic solvents, as they can solubilize polar (e.g., salt, pigment, protein) and non-polar soil components (e.g., grease, oil). In many cosmetic applications such as skin care products, emulsions are widely used with water as the continuous phase. 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. The unique properties of microemulsions have been utilized to produce microemulsion-gel glasses and microporous media with high surface area. Microemulsions are reported to be used as decontamination media for chemical weapons and toxic industrial chemicals [424], and petroleum-processing technologies [425]. Due to varied consistencies and microstructures, microemulsions have been considered as useful reaction media for a variety of chemical reactions. The major types of reactions studied in microemulsions comprise formation of inorganic particles (nanoparticles), polymerization [426], photochemical [427], electrochemical [428] and organic synthesis. The review article of Holmberg [429] and Garcia-Rio et al. [430] demonstrated that microemulsions could be a

useful for (i) overcoming reactant incompatibility, (ii) speeding up reactions of one polar and one apolar reactant (microemulsion catalysis), and (iii) inducing regioselectivity in organic reactions.

1.10.2. Mixed surfactant microemulsions

Nanoparticle synthesis

Recently, Bumajdad et al. [431] showed that mixing of di-n-didodecyldimethylammonium bromide (DDAB) with small amounts of the non-ionic Brij-35 [polyoxyethylene (23) dodecyl ether, C₁₂E₂₃], gives rise to microemulsions offering an excellent environment for prospective synthesis of nanoparticles. They argued as follows. The optimized DDAB/Brij-35 microemulsions have the advantages of both low thermal sensitivity and stability toward added inorganic salt type and concentration. The positive head-group charge of the double-chain cationic surfactant ensures bulk solubility of the inorganic metal cation, whereas the long polyethylene oxide chain of the non-ionic surfactant facilitates increased steric stability. In another study, pure ceria powders, CeO₂, were synthesized in Hp-microemulsified aqueous solution of CeCl₃ or Ce(NO₃)₃ stabilized by AOT, DDAB, or DDAB/Brij-35 surfactant mixtures by Bumajdad et al. [432]. Also, Hada et al. [433], Chaing [434] and Bumajdad et al. [435] used novel water-in-oil microemulsion systems stabilized by mixed surfactants (anionic or cationic/nonionic) for the synthesis of titania (TiO₂), gold (Au) and iron oxide-hydroxide [α -Fe₂O₃; Fe(OH)₃] nanoparticles, respectively. Morphology of CdS nanocrystals synthesized in mixed AOT and zwitterionic phospholipid, L-alpha-phosphatidylcholine (lecithin) in isooctane microemulsion was reported by Simmons et al. [436]. In contrast, conventional spherical CdS quantum dots were also obtained from water-in-oil, AOT microemulsion system. Bagwe et al. [437] reported the effects of intermicellar exchange rate on absorption spectra and particle size of silver (Ag) nanoparticles synthesized in AOT/Hp RMs, and the rate was varied by changing the organic solvent (Dc, cyclohexane, Cy), surfactant (SDS, NP-5 and DTAB) and organic additives (benzyl alcohol and toluene). An interesting and potentially useful effect was observed by the addition of a small amount of a nonionic surfactant (NP-5) that particle size significantly reduces. Yunxia et al. [438] investigated water solubilization capacity and the properties of confined water molecules in the pool of an environmental friendly mixed surfactant microemulsions composed of

Span-80, Tween-60, 1-butanol, isooctane and used as nanoreactors to synthesize iron nanoparticles, which can be used in environmental contaminants remediation. The properties of the synthetic iron nanoparticles were characterized and analyzed. In another study, Chiang et al. [439] demonstrated that mixed AOT/Span-80/isooctane reverse micelles are good candidates to be used as nanoreactors for formation of shape-controlled high-quality colloidal nanocrystals and nanowires under mild conditions. Manipulation of the rate of nucleation and subsequent growth of Au in the mixed reverse micelles induce drastic changes in the particle shape and structure. Further, they demonstrated that control of the nucleation and growth kinetics of Au in the mixed reverse micelles can be used to vary the shapes of the resulting particles from a nearly spherical morphology to cylinders, trigons and cubics. Stubenrauch and coworkers [440] synthesized platinum (Pt), bismuth (Bi), and lead (Pb) nanoparticles by using w/o mixed AOT/SDS/1-butanol/*n*-decane/water microemulsions in presence of the salt (either the metal precursor [H_2PtCl_6 , $\text{Bi}(\text{NO}_3)_3$, or $\text{Pb}(\text{NO}_3)_2$] or the reducing agent [NaBH_4]) as templates. The size and the structure of the resulting nanoparticles were found to depend on the size and structure of the templating microemulsion.

Enzyme activity and drug delivery

Shioi et al. [441] reported the enzyme activity of *α -chymotrypsin* (CT) in RMs composed of C_iE_j and/or AOT using an oil-soluble substrate, 2-naphthylacetate and compared the activity in C_iE_j /AOT stabilized RMs with the AOT stabilized RMs. The activity of CT in mixed RMs remained almost unchanged after one week, whereas in the single system, the activity decreased substantially with time. Das et al. [442] reported the significant enhancement in performance of interfacially active enzymes, *Chromobacterium viscosum* (CV) lipase and horseradish peroxidase (HRP) in mixed reverse micelles of CTAB and imidazolium-based amphiphiles having varying alkyl chains. In another report [306], they investigated on the modification of the anisotropic interface of cationic w/o microemulsions by the addition of different types of nonionic surfactants and thus influence the catalytic efficiency of the surface-active enzymes. The activity of CV-lipase was estimated in several mixed reverse micelles prepared from CTAB and Brij-30 or Brij-92 or Tween-20 or Tween-80/water/*n*-hexanol/isooctane at different physicochemical environments, and concluded that lipase activity in these systems

improved maximum up to ~200% with increasing content of non-ionic surfactants compared to that in pure CTAB RMs. Chen and Liao [443] studied the stability of *yeast alcohol dehydrogenase* (YADH) in AOT/Brij-30 mixed reverse micelles. They found that the activity of YADH in AOT/Brij-30 mixed reverse micelles was affected by the hydrophobic and electrostatic interactions between enzyme and surfactants, the reverse micellar droplet size, and the quantum of bound water molecules. From investigation on the hydrodynamic diameter of mixed reverse micelles and its distribution via dynamic light scattering, they suggested that the structure of mixed reverse micelles and the stability of YADH were determined by four important factors, which include the surface charge density, bound water, reverse micellar size, and the entrapment of water by hydrophilic-hydrophilic interaction between AOT and Brij-30. An optimal reverse micellar size and the decrease of the other two factors (i.e., the hydrophobic and electrostatic interactions between enzyme and surfactants, and the quantum of bound water molecules) would lead to the enhancement of enzyme activity. Earlier, Hossain et al. [444] and Hayashi et al. [445] showed that the activity of *Chromobacterium viscosum* lipase entrapped in AOT/Tween-85/isooctane RMs by the addition of olive oil as a water-insoluble substrate and short chain methoxypolyethylene glycols (MPEGs). Fan et al. [446] also showed an enhancement in the activity of *papain* in mixed AOT or TTAB/Tween-80/isooctane RMs. Recently, Hemavathi et al. [A.B. Hemavathi, H.U. Hebbar, K.S.M.S. Raghavarao, Separation and Purification Technol. 71 (2010) 263] reported that mixed AOT/Tween-20 or Tween-80 or Tween-85 or TX-100/isooctane RMs can be used for the extraction and primary purification of β -glucosidase from the aqueous extract of barley (*Hordeum vulgare*). Liu et al. [[447, 448] reported the influence of structure and composition of mixed AOT/Tween-85 stabilized in IPM on transdermal delivery potential of a lipophilic model drug, *Cyclosporin A* (*CysA*). Further, a potentially improved skin bioavailability of *CysA* in these systems was designed. Recently, Yanyu et al. [449] investigated the influence of the structure and the composition of water/AOT/Tween-85/IPM microemulsion system on transdermal delivery of 5-fluorouracil (5-FU). Recently, Kunz and his coworkers [450] also reported the activity of the enzyme *horse radish peroxidase* (*HRP*) in mixed surfactant reverse microemulsions, composed of a mixture of anionic, SDS, and cationic, DTAB (known as, catanionic

microemulsion), n-hexanol, citrate buffer, n-dodecane. Under the perspective of potential pharmaceutical applications, Kalaitzaki et al. [451] formulated new surfactant-rich biocompatible microemulsions based on single and mixed surfactant(isopropyl palmitate/Triton X-100/water + propylene glycol, Miglyol 818/Triton X-100/water + propylene glycol and isopropyl palmitate/Triton X-100 + Span 20/water + propylene glycol) and used as novel carriers of methylxanthine drugs (e.g., *theophylline* and *theobromine*) after characterization of their structures. Recently, Moghimipour et al. [174] formulated and characterized microemulsion systems by mixing of appropriate amount of two non-ionic surfactants, Tween-80 and Span-80, propylene glycol, PG (cosurfactant) and oil phase comprising Labrafac PG – transcitol P as a topical delivery system of naproxen for relief of symptoms of rheumatoid arthritis, osteoarthritis and treatment of dysmenorrhea. Chaladze et al. [452] used mixed surfactants, Brij-30 and AOT reverse micelles as mobile phase in *high-performance liquid chromatography* (HPLC).

Mehta et al. [453] also exploited the added degree of compositional freedom provided by mixed surfactants AOT/lecithin in isooctane reverse microemulsion to demonstrate that a small amount of added lecithin significantly enhances the solubility of organodiselenides over that in single AOT reverse microemulsion alone. The information obtained from these experiments was used to design a novel synthetic route for preparing 4-chloro-2-(naphthalen-2-ylselanyl) pyrimidine in reverse microemulsion.

1.10.3. Ionic liquid based microemulsions and their applications

Formation and characterization of Ionic liquid based microemulsions

In this short introduction, recent developments in the formation, characterization and application of IL-based self-assembled systems with special emphasize on microemulsions has been dealt briefly [454]. The chemistry of room temperature ionic liquid based microemulsions (RTIL-mEs) is at an incredibly exciting stage of development. No longer are mere curiosities, RTIL-mEs are beginning to be used as solvents for a wide range of synthetic procedures. The advent of systems that are easy to handle allows those without specialist knowledge in the field to use them for the first time. Ionic liquids have also been used as additives in microemulsion formulation. A number of reactions (e.g., Diels-Alder Reaction, aminolysis, Matsuda-Heck reaction etc.) have been investigated so far to show the potential of the ionic liquid based

microemulsions [220, 455, 456]. The retention of catalytic activity in IL-based microemulsions is due to the entrapment of enzyme molecules into aqueous microdroplets formed in w/IL microemulsions, indicating that these IL-based reaction systems provide a protective environment for the enzymes. In recent years, great attention has been paid to IL-based microemulsions due to their potential application prospects in biology, pharmaceutical, catalysis and material synthesis, which have been discussed latter. In addition, ILs are not only promising candidate for the formulation of high temperature stable colloidal systems by an appropriate choice of ingredients, also low temperature stable microemulsions can be gained [457]. This is one of the advantages of IL based microemulsions over conventional aqueous microemulsions.

Recent developments in the formulation, characterization and possible applications of IL-based self-assembled systems in general and microemulsion/reverse micelle in particular, have been summarized by different research groups, and thus, an excellent overview of the relevant literature is presented below [218, 454, 458-464]. Recently, studies on the formation and characterization of self-assembled systems (viz. micelles, microemulsions etc.) in presence of different types of ILs (as replacement of surfactant or polar component or oil or additive) have been reported from the viewpoints of academic and applied aspects [218, 454, 458-463, 465-469].

Amphiphilic ionic liquids that are comprised of a hydrophilic imidazolium head group and a hydrophobic tail, are good surfactant candidates for forming micelles and microemulsions. In recent studies, Galgano and El Seoud [470, 471] evaluated the micellar properties of the surface active ionic liquid (SAIL) 1-hexadecyl-3-methylimidazolium chloride, $C_{16}MeImCl$ and compared to those of two series of cationic surfactants that carry a pertinent structural moiety; 1-hexadecylpyridinium chloride, $C_{16}PyCl$ (a heterocyclic ring), and benzyl (3-hexadecanoylaminoethyl)dimethylammonium chloride, $C_{15}AEtBzMe_2Cl$ (benzyl moiety and a hydrogen-bond forming amide group). They concluded that the structural versatility of SAILs, with practically unlimited combinations of counter-ions and substituted imidazolium rings, offers exciting possibilities for applications, because the interactions (for example, electrostatic and hydrophobic) at the interfacial region can be “fine-tuned”

according to need by a judicious combination of the head-cation (nature of the substituent introduced) and the counter-ion (charge density, hydration).

In comparison with traditional surfactant-based microemulsions, IL-based microemulsions also reveal several advantages. First, the strong attraction between the imidazolium group and counter ion of the ILs at the fluid/fluid interface prevents its leakage into the conjugated water solution. Secondly, large imidazolium head group shows a higher capacity for solutes than the tert-ammonium cationic system. Thirdly, the imidazolium head group is strongly attractive, via the aromatic ring of penicillin, strong π - π interaction. Finally, the versatile structures of ionic liquids provide a distinctive platform for exploring the hydrophilic-lipophilic equilibrium in IL-based microemulsions/reverse micelles, which play a key role for optimizing the partitioning behavior in microemulsions. Therefore, long chain ionic liquids (e.g., 1,3-dialkylimidazolium chlorides or bromides or tetrafluoroborates) are reported to be used as surfactants for formulation of the microemulsion systems [218]. Some of these reports are summarized here. The phase behaviors of three long-chained imidazolium ionic liquids, C_{12} mimBr (1-dodecyl-3-methylimidazolium bromide), C_{14} mimBr (1-tetradecyl-3-methylimidazolium bromide) and C_{16} mimBr (1-hexadecyl-3-methylimidazolium bromide), with p-xylene and water were investigated by Li et al. [472]. Zech et al. [473] formulated microemulsions with 1-hexadecyl-3-methylimidazolium chloride ($[C_{16}mim][Cl]$) as surfactant, decanol as cosurfactant, dodecane as continuous oil phase and RTILs (ethylammonium nitrate (EAN) and 1-butyl-3-methylimidazolium tetrafluoroborate ($[bmim][BF_4]$) as polar microenvironment and also, characterized the systems by employing electrical conductivity, DLS and SAXS studies. Also, Safavi et al. [474] formulated a microemulsion comprising imidazolium ILs, 1-octyl-3-methylimidazolium chloride $[omim][Cl]$, as a surfactant, a hydrophobic IL as a substitute for traditional organic solvent, 1-bmimPF₆ and water at 25°C.

Recently, Lü et al. [475] attributed to the unique role of the ionic liquid (bmimBF₄), which is capable of modifying the physicochemical properties of water/AOT/decane (Dc) microemulsions by measuring the critical concentrations and the critical temperatures. Liu et al. [476] showed that the concentration of a model IL, bmimBF₄ can act as an effective interfacial control parameter for tuning the formation of microemulsions. Gao

and his coworkers [477, 478] studied the effect of water on the microstructure of [bmim][BF₄]/TX-100/benzene or triethylamine microemulsion by phase behavior, DLS, UV-Vis, FTIR and ¹H NMR studies. Rojas et al. [354] investigated the influence of the ionic liquid (ethyl-methylimidazolium hexylsulfate) on the structure formation in the optically clear phase region in water/toluene/pentanol mixtures in presence of the cationic surfactant CTAB by conductivity, DLS, ¹H NMR and cryo-SEM techniques. Gao et al. [479] studied the effect of water on [bmim][BF₄]/TX-100/benzene microemulsion. It was reported that the addition of small amount of water to such IL-based microemulsion contributed to the stability of microemulsion and thus, increased the amount of solubilized [bmim][BF₄] in the microemulsion. In another contribution, they showed that the addition of water decreased the droplet size of [bmim][BF₄]-in-cyclohexane microemulsion [278]. The role of small amounts of water in the 1-butyl-3-methylimidazolium bis 2-ethylhexyl sulfosuccinate ([bmim][AOT]) based [bmim][BF₄]-in-benzene reverse microemulsions were also emphasized by Bai et al. [480]. Recently, Wei et al. [481, 482] also studied water solubilization, volume-induced and temperature-induced percolation of conductance behavior of AOT-based microemulsions in presence of ILs. In another study, they investigated the effects of ionic liquid, [bmim][BF₄] on the physicochemical properties (e.g., polarity, conductivity, viscosity, and droplet size) of nonionic surfactant based water-TX-100-hexanol-cyclohexane microemulsion [483]. Very recently, Paul and Panda [224] reported the understanding of the physicochemical properties of pseudo-ternary microemulsion system comprising aqueous solution of 1-butyl-3-methyl imidazolium methanesulfonate, [bmim][MS], polyoxyethylene (20) sorbitan monolaurate (Tween-20), 1-pentanol (Pn) and n-heptane (Hp) by employing phase study, method of dilution, viscosity, DLS, conductivity and spectroscopic probing techniques. Seth et al. [484, 485] also reported the interaction of water with room temperature ionic liquid (RTIL) [bmim][PF₆] in [bmim][PF₆]/TX-100/water ternary microemulsions by solvent and rotational relaxation of coumarin 153 (C-153), coumarin 151 (C-151) and coumarin 490 (C-490). A review, in the form of a book chapter, on solvent dynamics and rotational relaxation processes in IL-based microemulsions is available in literature [464].

While the studies mentioned above involve water as one of the component, water-free IL-based microemulsions are also studied by many groups [218, 305, 477, 486-495]. In the first report on the formation of IL-in-oil microemulsions, Gao et al. [486] prepared [C₄mim][BF₄]/TX-100/cyclohexane microemulsion and also, characterized by employing phase behavior, conductivity measurement, dynamic light scattering measurement, freeze-fracturing electron microscopy and UV-Vis technique. Eastoe et al. [487] further investigated size and shape of the same microemulsion by small-angle neutron scattering (SANS) measurement. They observed regular swelling behavior of microemulsion with addition of the IL, which indicates that the volume of dispersed nanodomains is proportional to the amount of IL added [487]. Several other reports on similar system are found in literature. In these investigations, [C₄mim][BF₄], TX-100 and toluene [488], *o*-xylene [489], or benzene [490] were used as the polar phase, surfactant and oil phase respectively. The water-free IL-based microemulsions with charged surfactants are rather scarce [470, 473, 491, 496-499]. Falcone et al. [491] used cationic surfactant, benzyl-n-hexadecyldimethylammonium chloride (BHDC) for the formulations of [C₄mim][BF₄]/BHDC/benzene and [C₄mim][TF₂N]/BHDC/benzene microemulsions and compared their behavior with [C₄mim][BF₄]/TX-100/benzene and [C₄mim][TF₂N]/TX-100/benzene microemulsions. With multinuclear NMR study on the behavior of [C₄mim][BF₄] in [C₄mim][BF₄]/BHDC/benzene and [C₄mim][BF₄]/TX-100/benzene microemulsions, they concluded that the structure and behavior of entrapped ILs in the microemulsions depend strongly on the surfactants used [496]. Rabe and Koetz [500] investigated the characteristic behavior 1-ethyl-3-methylimidazolium-ethylsulfate (EMIM-EtOSO₃) or 1-ethyl-3-methylimidazolium-hexylsulfate (EMIM-HexOSO₃)/CTAB/pentanol/toluene IL/o microemulsions by conductometric titrations, DLS, rheological measurements, and Cryo-Scanning Electron Microscopy. Recently, Blach et al. [501] investigated the behavior of two ionic liquids (ILs) with high electron donor ability such as 1-butyl-3-methylimidazolium trifluoromethanesulfonate (bmimTfO) and 1-butyl-3-methylimidazolium trifluoroacetate (bmimTfA) entrapped in anionic, AOT/chlorobenzene and cationic, BHDC/chlorobenzene reverse micelles (RMs) using DLS and FT-IR spectroscopy. In a recent study, Kunz and his coworkers [497] reported that use of ionic surfactants in combination with ILs is better for preparation of the

microemulsions with high temperature stability and temperature insensitivity. They explored thermal stability of EAN/[C₁₆mim][Cl]/dodecane microemulsions at ambient pressure, which exhibited stability over the temperature range 30⁰C to 150⁰C. Harrar et al. [221] reported a detailed investigation of nonaqueous 1-ethyl-3-methyl-imidazolium-ethylsulfate ([emim][etSO₄])/limonene/polyethylene glycol tert-octylphenyl ether (Triton X-114 or TX-114) microemulsions as a function of ionic liquid (IL) content and temperature. These systems were characterized by phase diagrams, conductivity measurements, and small angle X-ray scattering (SAXS) techniques. Rojas et al. [502] also formulated *N,N'*-Alkylimidazolium Alkylsulfate ([Emim][EtSO₄])/1-butyl-3-methylimidazolium dodecylsulfate ([Bmim][DodSO₄])/toluene microemulsion and also, characterized the systems with conductivity measurement, DLS and SAXS techniques. Sarkar and his coworkers [S. Mandal, S. Ghosh, C. Banerjee, J. Kuchlyan, D. Banik, N. Sarkar, J. Phys. Chem. B 117 (2013)3221] reported the formulation of a novel ionic liquid-in-oil (IL/O) mixed microemulsion where the polar core of the ionic liquid, 1-ethyl-3-methylimidazolium n-butylsulfate ([C₂mim][C₄SO₄]), is stabilized by a mixture of two nontoxic nonionic surfactants, polyoxyethylene sorbitan monooleate (Tween-80) and sorbitan laurate (Span-20), in a biocompatible oil, isopropyl myristate (IPM). The formation of the microemulsion droplets was confirmed from the dynamic light scattering (DLS) and phase behaviour study. Very recently, Rao et al. [465] presented facile methods to adjust the structural parameters of microemulsions using different hydrophobic ionic liquids (ILs) (for example, [C₂mim][Tf₂N], [C₄mim][Tf₂N], [C₆mim][Tf₂N], [C₄mim][PF₆] and [C₄mim][BF₄]) as additives (polar phase). They characterized ILs/[C₄mim][AOT]/benzene ternary system by carrying out phase behavior study, dynamic light scattering (DLS) and ¹H NMR measurements. Apart from these reports, Sarkar and his coworkers have published a good number of publications on characterization of nonaqueous ionic liquid containing microemulsions [296, 503-509]. Microemulsions with magnetic properties were formed by employing a magnetic room temperature ionic liquid, MRTIL, (1-butyl-3-methylimidazolium tetrachloroferrate, [bmim][FeCl₄]) as polar phase, a mixture of ionic (SDS, AOT and [C₁₆mimCl]) and non-ionic (C_iE_j where i and j represent hydrocarbon chains and POE chains, respectively) surfactants and decanol as a cosurfactant, and also, microstructure of these

microemulsions were characterized by SANS and electric conductivity. These systems showed structurally the same as that of normal microemulsions but the magnetic properties were shown by the incorporation of [bmim][FeCl₄] into the system formulations [510]. Zech et al. [511] demonstrated that biodiesel, which gained more and more attention in recent years resulting from the fact that it is made of renewable resources, can replace conventional oils as nonpolar phase in nonaqueous microemulsions containing the RTIL, ethylammonium nitrate as polar phase. They studied the thermal stability and microstructure of these systems by conductivity and SAXS measurements, in addition to the phase diagram and the viscosity of the microemulsions. They concluded that these high temperature stable, nonaqueous, free of crude oil based organic solvent microemulsions highlight an efficient way towards the formulation of environmentally compatible microemulsions, and open a wide field of potential applications.

Recently, Wang et al. [512] reported the successful formulation of microemulsions with vegetable oil (castor oil) as the continuous phase, RTIL 1-butyl-3-methyl-imidazolium tetrafluoroborate as the polar phase, TritonX-100 as the surfactant, and 1-butanol as the cosurfactant. A pseudo-ternary phase diagram, DLS data, UV-Vis spectra, and kinematic viscosity measurements were employed to characterize and analyze the phase behavior and microstructure of the vegetable oil-based IL microemulsions. Further, they proposed that this vegetable oil-based IL microemulsion have tremendous potential as renewable biolubricant base-stocks. Li et al. [478] also formulated a novel IL microemulsion, consisting of 1-butyl-3-methylimidazolium tetrafluoroborate (bmimBF₄) and nonionic surfactant (TX-100) in triethylamine (TEA) which was used either as an organic solvent or a Lewis base. The unique solubilization behavior of water in this system revealed the possibility of using TEA-microemulsion as a template to prepare metal hydroxides as well as metal oxides, which is not possible using traditional microemulsions.

Recently, Kunz and his coworkers [497, 513] formulated high temperature stable microemulsions by using the room-temperature ionic liquid ethylammonium nitrate (EAN) as polar phase, dodecane as continuous phase and 1-hexadecyl-3-methyl imidazolium chloride ([C₁₆mim][Cl]), an IL that exhibits surfactant properties, and decanol as cosurfactant at ambient temperature. They were able to obtain thermal

stability ranging from 30⁰C up to 150⁰C. These high temperature microemulsions are, therefore, predestined for high temperature applications such as reaction media, lubricant formulations and size controlled nanoparticle synthesis. Apart from this, Rao et al. [514] demonstrated the wide range of thermal stability of [C₆mim][TF₂N]/N,N-dimethylethanolammonium 1,4-bis(2-ethylhexyl) sulfosuccinate (DAAOT)/IPM microemulsions by carrying out phase behavior study, dynamic light scattering and ¹H NMR measurements and also, by using coumarin-480 (C-480) as a fluorescent probe.

Harrar et al. [221, 457] presented a detailed investigation of nonaqueous TX-100 or TX-114/limonene/1-ethyl-3-methylimidazolium ethylsulfate ([emim][etSO₄]) microemulsions. Different microstructures were identified, and the systems containing high amounts of ionic liquid showed remarkably large temperature stability down to -10⁰C or -35⁰C, depending on the surfactant used. Prospective use of these newly introduced low-temperature stable microemulsions, for example in extraction processes, formulation of lubricants, or as reaction media for water-sensible reactions, was envisaged.

First report, on IL-in-IL microemulsions (IL/IL) was reported by Cheng et al. [515] composed of hydrophobic IL [bmim][PF₆] as apolar phase and hydrophilic protic IL, propylammonium formate (PAF) as polar phase stabilized by an anionic surfactant, AOT. Mukherjee et al. [180] formulated unique IL-in-IL microemulsions with two alkyltriphenylphosphonium cation based ILs, in which triisobutyl(methyl)phosphonium tosylate (IL 1) as polar phase, IPM as oil phase, trihexyl(tetradecyl)phosphonium bis-2,4,4-(trimethylpentyl)phosphinate (IL 2) as surfactant and isopropanol as cosurfactant and also, characterized by phase diagram, dilution method and DLS technique. These ILs were studied against *Sarcoma-180* cell lines and proficient anti-cancer activity of IL 1 and moderate activity of IL 2 were evidenced. Good temperature stability up to 353 K was obtained for these microemulsions. Further, two studies have demonstrated the microemulsification of RTIL in compressed or supercritical CO₂ [494, 516]. These new CO₂-ionic liquid systems might possess certain advantages, especially when water sensitive compounds are involved.

Applications of ionic liquid based microemulsions

IL-based microemulsions have been extensively investigated in varied fields of drug delivery, material synthesis, enzymatic reaction, polymerization, biocatalysis, organic synthesis, protein extraction and capillary electrophoresis. In a review article, the applications of IL-based microemulsions in the synthesis of nano-materials, biocatalysis, and organic reactions are summarized [517]. Apart from this, an attempt has been made to present a brief review of the applications of this special type of microemulsions in the following paragraphs.

One important application of ionic liquid (IL)-based non-aqueous microemulsions is drug dissolution. Drug delivery using such self-assembled systems is yet to fully achieve its potential for a large number of drugs, which are insoluble or sparingly soluble in water. These limitations demand the need for alternative solvents that can be used as a polar core in microemulsions for the solubilization of sparingly soluble drug molecules. Considering these aspects, ILs could be a good candidate because they are capable of dissolution of various poorly soluble compounds including drug molecules [518]. Pharmaceutical industries have posed challenges in the topical and transdermal administration of drugs which are poorly soluble or insoluble in water and most of organic solvents. In an approach to overcome these limitations, ionic liquid-in-oil (IL/o) microemulsions (mEs) were employed by Moniruzzaman et al. [519] to increase the solubility of a sparingly soluble drug and to enhance its topical and transdermal delivery. The formulation of microemulsions was composed of a blend of nonionic surfactants, Tween-80 and Span-20, IPM as an oil phase, and IL $[C_1mim][[(CH_3O)_2PO_2]$ (dimethylimidazolium dimethylphosphate) as a pseudo phase. Among various weight ratios of Tween-80 to Span-20 investigated in the microemulsion systems, the ratio 3:2 showed an excellent solubility and also, enhanced skin permeation effect for acyclovir (ACV) as a model sparingly soluble drug. On the basis of these results, they proposed that IL-assisted nonaqueous microemulsion could serve as a versatile and efficient nano-delivery system for insoluble or sparingly soluble drug molecules that require solubilizing agents for delivery. Microemulsions with high solubility of ACV, excellent formulation stability and enhanced permeation to the *Yucatan micropig* (YMP) porcine skin, were obtained from a blend of surfactant composed of 3:2 weight ratio of Tween-80

to Span-20. Finally, it was concluded that IL/O microemulsions create a new opportunity for the controlled delivery of sparingly soluble drugs that have problems of administration by other routes. In continuation, Moniruzzaman et al. [520] reported a novel IL-in-oil(IL/O) microemulsion which was able to dissolve pharmaceuticals that are insoluble or sparingly soluble in water and most of pharmaceutical grade organic liquids. Towards this approach, the nanometer-sized ionic liquid droplets in IPM were formed with a blend of nonionic surfactants, Tween-80, and Span-20. In order to explore the use of newly developed microemulsion as a potential drug carrier, they investigated the solubility of some drug molecules (e.g., acyclovir, methotrexate and 1-[(5-(p-nitrophenyl) furfurylidene) amino] hydantoin sodium) that are insoluble or sparingly soluble in most of the conventional solvents. In another study, Moniruzzaman et al. [521] reported solubility studies indicating a high degree of solubilization of such drugs in IL microemulsions. They concluded that these microemulsions formed with ILs having unique physical, chemical and biological properties, which may offer novel opportunities to develop a potential drug delivery carrier for poorly soluble drugs molecules. They also reported the first successful application of a novel IL-assisted non-aqueous microemulsion stabilized by a blend of two nontoxic surfactants, Tween-80, and Span-20 for transdermal delivery of acyclovir, which is insoluble or sparingly soluble in water and most common organic liquids

In another study, Moniruzzaman et al. [522] explored the use of water-in-ionic liquid microemulsions composed of anionic surfactant, AOT/hydrophobic IL [C₈mim][Tf₂N] (1-octyl-3-methyl imidazolium bis(trifluoromethylsulfonyl)amide)/water/1-hexanol as the reaction medium for the enzymatic oxidation of pyrogallol catalyzed by *horseradish peroxidase* (HRP). The results demonstrated that the rate of HRP-catalyzed reactions in IL microemulsions was increased significantly compared with that obtained in conventional oil microemulsions. Therefore, they concluded that a water-in-ionic liquid microemulsion might be a very promising system for performing enzymatic reactions with HRP in ILs media. According to them, the findings will be of value for the development of ILs as a medium for the HRP-catalyzed oxidation of a variety of organic compounds such as phenols, biphenols, anilines, benzidines, and related heteroaromatic compounds. Further, they formulated aqueous microemulsion droplets in a hydrophobic

ionic liquid, 1-octyl-3-methyl imidazolium bis (trifluoromethyl sulfonyl) amide), [C₈mim][Tf₂N] stabilized by a mixture of anionic surfactant; AOT and 1-hexanol as cosurfactant, to overcome the insolubility of enzymes in most of the ILs, and the catalytic activity of one of the enzymes studied (*Pseudomonas cepacia* lipase or lipase PS) became higher than in microemulsions of AOT in isooctane [523]. Zhou et al. [524] studied the catalytic activity of two fungal oxidases, lignin peroxidase and laccase for the oxidation of o-phenylenediamine, in the TX-100 stabilized water-in-[bmim][PF₆] microemulsion. In such a medium, both lignin peroxidase and laccase were catalytically active. The laccase-catalyzed oxidation of 2,6-dimethoxyphenol in the water-in-[bmim][PF₆] microemulsion was studied. The laccase hosted in the microemulsion exhibited a catalytic activity which could be regulated by the composition of the interfacial membrane [525].

Zheng and coworkers [526] synthesized the hollow silica spheres in benzene/TX-100/[bmim][BF₄] microemulsion. For comparison, a traditional aqueous microemulsion system was used to replace the nonaqueous IL template, and no hollow silica spheres were formed. This indicates that [bmim][BF₄] plays an important role in the formation of the hollow structure of silica spheres. Furthermore, Zhao and coworkers [527] synthesized silica products with two different morphologies using nonaqueous TX-100/benzene/[bmim][BF₄] microemulsion droplets as templates. By adjusting the reaction conditions, ellipsoidal nanoparticles were formed under acidic conditions, while hollow silica spheres were obtained under alkaline conditions. Li et al. [528] used the water-in-IL microemulsion to prepare the tetragonal ZrO₂ nanoparticles. For comparison, ZrO₂ particles synthesized by water-in-oil microemulsion were assembled after calcinations. The results indicated that the IL, bmimPF₆ plays an important role in preventing the congregation of the product. Also, Zhang and coworkers [529] synthesized the bimetallic palladium/gold nanoparticles in the IL-based microemulsion. The palladium and gold precursors were dissolved in dispersive and continuous phase of microemulsion (water/TX-100/[bmim][PF₆]), respectively. Harada and his coworkers [530, 531] also synthesized metal particles of silver (Ag) by the photoreduction of silver nitrate (AgNO₃) or silver perchlorate (AgClO₄) in water-in-ionic liquid (IL) microemulsions consisting of nonionic surfactant, Tween-20 or Triton X-100, water and

ionic liquid, 1-octyl-3-methylimidazolium hexafluorophosphate ([OMIm][PF₆]) or -butyl-3-methylimidazolium tetrafluoroborate ([BMIm][BF₄]) or 1-octyl-3-methylimidazolium tetrafluoroborate ([OMIm][BF₄]). In another study, they synthesized Ag particles in water/Tween-20/[BMIm][BF₄] or [OMIm][BF₄] microemulsions mixed with a high-pressure (25 MPa) CO₂. They concluded that in the process of Ag particle formation, the water droplet size under high-pressure of CO₂ was more effectively regulated than that under ambient air, and thereby, preventing Ag particles from aggregation and precipitation. [532].

There are some limits on conducting polymerization reaction in conventional microemulsions, for example, the solubility limitations for apolar solutes remain. This limitation can be overcome by IL-based microemulsion due to the combined advantages of both IL and microemulsion. Surfactants based on imidazolium ILs, including polymerizable surfactant ILs, were synthesized by Yan and Texter [533]. These ILs were used to stabilize polymerizable microemulsions, which were useful for producing polymer nanoparticles, gels, and open-cell porous materials. Wang and coworkers [534] conducted the co-polymerization of styrene and acrylonitrile in IL based microemulsion under reverse atom transfer radical polymerization using 2,2'-azobis(isobutyronitrile) (AIBN) as initiator, FeCl₃·6H₂O/succinic acid (SA) as complex catalyst, cetyltrimethylammonium bromide (CTAB) as surfactant and [bmim][PF₆] as IL. The copolymers of styrene and acrylonitrile (SAN) with predetermined molecular weights and narrow molecular weight distribution were obtained. Zhang and coworkers [535] studied the electropolymerization behavior of pyrrole in water-in-[bmim][PF₆], bicontinuous, [bmim][PF₆]-in-water microemulsions. It was demonstrated that the water-in-[bmim][PF₆] microemulsion represents as an optimal medium with fastest polymerization rate. Chen et al. [536] used methyl methacrylate (MMA)/1-dodecyl-3-methylimidazolium bromide/[bmim][BF₄] microemulsions for free radical and atom transfer radical polymerizations. Polymers with reproducible size, well controlled molecular weight and low polydispersity could be produced. After the polymerization process, the remaining components could be recycled and reused. Guo and coworkers [537] synthesized the PANI core decorated with TiO₂ (PANI/TiO₂) nanocomposite particles in a microemulsion consisting of deionized water as the continuous aqueous phase and an oil

solution (aniline) and hydrophobic IL, [bmim][PF₆] as the dispersed phase in the presence of anatase TiO₂ nanoparticles. Further, Yan et al. [538] reported the formation of proton conducting membranes by surfactant stabilized protic IL (PIL) nanodomains dispersed in a polymerizable oil, a mixture of styrene and acrylonitrile.

In a series of studies, Huang and his coworkers [524, 525, 539] formulated single TX-100 and mixed AOT/TX-100 water-in-IL microemulsion stabilized in 1-butyl-3-methylimidazolium hexafluorophosphate ([BMIM][PF₆]) and subsequently, investigated lipase catalyzed hydrolysis of lignin peroxidase (LiP), biomacromolecule laccase, and 4-nitrophenyl butyrate (*p*-NPB) in these systems. Cheng and coworkers [540] used IL-in-water microemulsion as a pseudo-stationary phase (PSP) for the detection of a large number of acidic compounds in capillary electrophoresis (CE). A fast and an efficient separation of eight phenolic acids was achieved by using [bmim][PF₆] as oil drops, Tween-20 as the surfactant, and borate as the background electrolyte (BGE). The detection efficiency of the analytes by using IL-in-water microemulsion is much higher than that by using oil-in-water microemulsion electrokinetic chromatography (MEEKC).

The Diels-Alder Reaction (DAR) between N-ethylmaleimide and 2,3-dimethyl-1,3-butadiene was studied in water/AOT/isooctane microemulsion in presence of 1-butyl-3-methylimidazolium tetrafluoroborate (IL) [455]. The apparent second-order rate constants were determined by spectrophotometry in microemulsion. The effect of solvent on the DAR rate was investigated and interpreted. The experimental results showed that the reaction rate in the microemulsion with IL was enhanced, and it was faster compared to pure isooctane and generic AOT microemulsion as well. Selective extraction of hemoglobin was achieved by using water/AOT/[bmim][PF₆] microemulsion system from complex biological sample matrices [541]. Gayet and coworkers [456] formulated a IL-in-oil microemulsion comprising benzylpyridinium bis(trifluoromethanesulfonyl)imide ([BnPyr]NTf₂), TX-100 and toluene, and performed the Matsuda-Heck reaction between methoxybenzene diazotate and 2,3-dihydrofuran in this media. The reaction yield in IL-in-oil microemulsion was twice higher than that in neat ILs. Consequently, after the formation of IL microemulsion, not only the reaction efficiency was significantly improved, but also the consumption of IL was reduced. The results provided a basis for

designing nonaqueous IL microemulsion microreactor, and also, envisaged that this reaction medium might have a good prospect for applications in biocatalysis and nanomaterials synthesis. Zhang et al. [542] synthesized Pd nanoparticles in situ in H₂O/TX-100/[bmim][PF₆] microemulsion. TX-100 served as both reductant and stabilizer of the nanoparticles. It was reported that microemulsion containing Pd nanoparticles represents a very efficient catalytic medium for the ligand-free Heck reaction. Garcia-Rio and his coworkers analyzed the properties of the interface of ionic liquid-in-oil microemulsions by absorption solvatochromic shifts, ¹H NMR and kinetic measurements in order to investigate the properties of the ionic liquid within the restricted geometry provided by microemulsions and the interactions of the ionic liquid with the interface. They performed a quantitative kinetic study in ionic liquid microemulsions and found that the rate constant for aminolysis of nitrophenyl laurate at the interface of [bmim][BF₄]/TX100/cyclohexane, IL/O microemulsions is between two and four times higher than in water/TX100/cyclohexane, W/O microemulsions [220]. Xia et al. [543] studied for the first time an environmentally-friendly, enzyme-promoted procedure for the Henry (nitroaldol) reaction, which is considered as one of the most powerful and atom economical C–C bond-formation reactions. water/TX-100/[Bmim][PF₆] microemulsion was used as reaction medium. The report revealed that amino acylase from *Aspergillus oryzae* showed better catalytic activity for the addition reactions of nitromethane with a series of aromatic aldehydes, and a highest yield of 90% was obtained.

1.11. Advantages and disadvantages

It can be noted that that use of microemulsions as templates possess both advantages and disadvantages. Because of the ease of preparation of microemulsion, drugs that are thermo-labile are easily incorporated without the risk of degradation [544]. In drug delivery, microemulsion ultimately increases the surface area of drugs, which improves their solubilization and permeation behaviors. The rate of penetration of drug is much faster in microemulsion systems than other drug delivery vehicles, with controlled drug release rates, slow degradation, and target specificity [544]. Microemulsions have a higher solubilization capacity for hydrophilic and hydrophobic compounds compare to simple micellar solutions. Because of their thermodynamic stability, microemulsions are

more favorable than regular emulsions, since microemulsions can be prepared with very little energy input and have a long shelf life [545]. Microemulsions possess some disadvantages as well. Many experimental conditions, such as temperature and pH, influence the stability of microemulsions as well. The effects of these factors must be examined for each potential formulation. Further, formation of microemulsions generally requires large amounts of surfactant(s) and/or cosurfactant(s). All of these are generally irritating at high concentrations [544]. Although various reports on microemulsions for synthetic drug carrier systems decisively made for clinical use, are available in literature, not all of them have pharmaceutical acceptance. Each drug delivery system has to go through in vivo and biocompatibility studies so as to reduce its toxic effects. Further, high concentration of surfactant lowers the biocompatibility. In view of these aspects, there is an increasing need for development of microemulsions with low surfactant concentration and also, with naturally derived surfactant having low toxicity [27, 546].

References

References are given in BIBLIOGRAPHY under Chapter I (pp. 212-239).