

## Chapter two

---

### Literature review

#### Formation and phase behaviour of microemulsion:

##### 2.1-Types of microemulsion

The formation of oil-or water-swollen microemulsion depends on the packing ratio, property of surfactant, oil phase, temperature, chain length, type, and nature of cosurfactant.

##### 2.1.1-Packing ratio

The hydrophilic lipophilic balance (HLB) of surfactant determines the type of microemulsion through its influence on molecular packing and film curvature.

##### 2.1.2-Properties of surfactant, oil phase, and temperature

Type of surfactant also determines type of microemulsion formed. Surfactant contains hydrophilic head group, and lipophilic tail group. The oil component influences curvature by its ability to penetrate and hence swells the tail group region of the surfactant monolayer. Short-chain oils such as alkanes penetrate the lipophilic group region largely than long-chain alkanes, swelling of this region to a great extent results in an increased negative curvature. Temperature is extremely important in determining the effective head group size of non-ionic surfactants. Winsor studied the effect of temperature on the type of microemulsion formed. For the giving amount of components in ternary system with non-ionic surfactant, oil, and water, at relatively low temperature, type I system (an O/W with excess Oil) is formed. At intermediate temperature, type III system (microemulsion (Bicontinues) with excess of both oil and water ) is present. At relatively higher temperature, type II (W/O microemulsion with excess water) system exists (Winsor, 1954, 1968).

### **2.1.3-Chain length, type, and nature of cosurfactant**

Alcohols are widely used as cosurfactant in microemulsion. Addition of shorter chain cosurfactant (e.g., ethyl alcohol) gives positive curvature effect, as alcohol swells the head region more than the tail region favouring the formation of O/W type of system, while longer chain cosurfactant (e.g., cetyl alcohol) favors W/O type by alcohol swelling more in tail region than head region.

### **2.1.4-Alcohol concentration**

Increasing the concentration of low molecular weight alcohol as a cosurfactant leads to the phase transition from W/O to bicontinuous and ultimately to O/W type microemulsion. Exactly opposite phase transition is noticed to case of high molecular weight alcohol.

### **2.1.5-Surfactant hydrophobic chain length**

The increase in length of hydrophobic chain of the surfactant shows the change of O/Wmicroemulsion to W/O via bicontinuous phase.

### **Phase behavior**

(Yaghmur, Aserin and Garti, 2002) investigated the phase phase behavior of systems based on Tweens (ethoxylated sorbitan esters), was compared with non-food-grade systems based on C<sub>18:1</sub>E<sub>10</sub> (Brij 96v). Short-chain alcohol (ethanol in food-grade systems) together with polyols (glycerol and propylene glycol) when added to a three component system (oil–surfactant–water) Alcohols and polyols destabilize the liquid crystalline phase and extend the isotropic region to higher surfactant concentrations. The total monophasic area, A<sub>T</sub>, at R(+)-limonene/ethanol of 1/1 (w/w) and aqueous phase of water/PG of 1/1 (w/w), was 73 and 64% of the total area of the phase diagram for Brij 96v and Tween 60, respectively. The transition from a W/O microemulsion into an O/W microemulsion happens gradually, and continuously without any phase separation. The total monophasic area depends also on the type of the oil, on the

composition of the polar and apolar phases, and on the nature of the polyol. The results are discussed surfactant oil and surfactant cosolvent compatibility and the participation of the polyol at the interface. The difference in temperature sensitivity of PG-based and Gly-based microemulsions.

**(Ceglie, DAS and Lindman, 2004)** investigated the effect of oil on the microscopic structure having 5–16 carbon atoms and aromatic hydrocarbons with different substituents were used as oil. Oil penetration is dependent on chain length of the oil and surfactant.

**(Fanun and Salah Al-Diyn, 2006)** investigated the phase behavior of the system water/sucrose laurate/ethoxylated mono-di-glycerides/caprylic-capric triglyceride as function of temperature and oil content, they found that at low temperatures the mixed nonionic surfactants are soluble in water and two phases are observed, at high temperatures the mixed surfactants are soluble in oil and another two phases are observed and at low oil contents a one phase region is observed, this region extends for the range of temperatures from 7°C to 95 °C.

**(Fanun and Salah Al-Diyn, 2006)** investigated the phase behavior of the systems water/sucrose laurate/ethoxylated mono-di-glyceride/oil as function of temperature and the weight ratio of EMDG in the mixed surfactants. The oils were R(+)-limonene, isopropylmyristate, and caprylic-capric triglyceride, they found that, the phase inversion temperature (PIT) decreases and the efficiency of the mixed surfactants increase as the weight ratio of the EMDG in the mixed surfactants increases. R(+)-limonene gave lower phase inversion temperatures and higher efficiencies compared to isopropylmyristate, and caprylic-capric triglyceride. The solubilization capacity of the system water/sucrose laurate/oil increased upon the addition of ethoxylated mono-di- glyceride which stabilize the surfactant layer and increase the interfacial area.

**(Fanun, 2008)** investigated the pseudoternary phase behavior of the water/sucrose laurate/ethoxylated mono

the water+sodium chloride/sucrose laurate/ ethoxylated mono-di-glyceride/ peppermint oil/isopropylmyristate microemulsions at mixing ratios of both surfactants and oil equal-di-glyceride/R(+)-limonene system for different surfactants mixing ratios (w/w) at 25 °C, it was found that for surfactants mixing ratio (w/w) equals unity, the area of the one phase microemulsion region reaches its maximum.

**(Fanun, 2008)** studied the water + propylene glycol/sucrose esters/benzaldehyde + ethanol systems to determine the one phase microemulsion regions at 27°C, 37°C and 45°C, It was found that minor changes in the surfactant structure suffice to provoke a considerable change in the total monophasic area of the system and a one phase microemulsion region extending from the oil-rich region to the water-rich corner was observed in systems based on sucrose laurate and sucrose myristate at 27 °C.

**(Fanun, 2009)** studied unity and studied the properties of water + propylene glycol/sugar surfactant/peppermint oil + ethanol using electrical conductivity, it was found in all studies the same result; the electrical conductivity increases as the water volume fraction increases.

**(Fanun, 2009)** studied the systems studied were water/sucrose laurate/ethoxylated mono-di-glyceride/isopropylmyristate/peppermint oil. The solubilization capacity of water in the oils is dependent on the surfactants and oils mixing ratios (w/w). The transport properties (electrical conductivity and dynamic viscosity) were studied as function of water volume fraction. It was found that increasing the weight ratio of peppermint oil in the mixed oils improved the water solubilization capacity in the microemulsions. The molar ratios of mixed surfactants play an

important role in determining the maximum water solubilization, this study reveals that the electrical conductivities increase with the increase water volume fraction.

**(Fanun, 2010)** investigated a combination of electrical conductivity, dynamic viscosity, dynamic light scattering and small angle X-ray scattering methods was used to study the properties of the water + propylene glycol/mixed nonionic surfactants/ peppermint oil + ethanol U-type microemulsions which can be diluted with any amount of water. The surfactants were sucrose laurate and ethoxylated mono-di-glyceride. The mixing ratios (w/w) of the mixed surfactants and peppermint oil/ethanol equal unity and that of water/propylene glycol equals to two. The electrical conductivity and periodicity of the microemulsions increases with the aqueous phase content while the dynamic viscosity decreases. The variations in the values of the correlation length with the aqueous phase contents indicate the onset of structural transitions. Structural transitions from the water-in-oil to a bicontinuous phase then inversion to oil-in-water occurs in the system.

### **Volumetric and Diffusion properties**

**(Fanun, Shakarnah, et al, 2011)** studied sol-gel encaged  $[(C_8H_{17})_3NCH_3][RhCl_4]$  catalyses the double bond isomerization in the flavoring agent 4-allylanisole in aqueous microemulsions. In order to provide optimal composition of the reaction medium water/n-propanol/surfactant/4-allylanisole micellar systems were formulated. The surfactants were sodium dodecyl sulfate, cetyltrimethyl ammonium bromide, sucrose monolaurate, and polyethylene glycol (7) glyceryl cocoate. The ratio (w/w) of n-propanol/surfactant equals 2/1. The micellar densities increase with the increase in the water volume fraction. Ultrasonic velocities increase with the increase in water volume fraction up to 0.8 then decrease. Ultrasonic velocities increase with temperature

for water volume fractions below 0.8 and decrease for water volume fractions above 0.8. Quantitative analysis of the volumetric parameters enabled the characterization of structural transition along the micellar phase. The particle hydrodynamic diameter of the oil-in-water systems was determined as function of temperature. The particle hydrodynamic diameter of nonionic surfactants it increases.

### **Drug Solubilization**

(Nandi, Bari, and Joshi, 2003) studied effect of alkanols and cyclodextrins on the phase behavior of an isopropyl myristate microemulsion system and to examine the solubility of model drugs. Triangular phase diagrams were developed for the microemulsion systems using the water titration method, and the solubility values of progesterone and indomethacin were determined using a conventional shake flask method. The water assimilation capacities were determined to evaluate the effective microemulsion formation in different systems. The alkanols showed higher microemulsion formation rates at higher concentrations. A correlation between the carbon numbers of the alkanol and water assimilation capacity in the microemulsions studied was observed; isobutanol and isopentanol produced the best results. The addition of cyclodextrins showed no effect or had a negative effect on the microemulsion formation based on the type of cyclodextrin used. In conclusion, microemulsion systems improve the solubility of progesterone and indomethacin. But the two types of cyclodextrins studied affected isopropyl myristate based microemulsion systems negatively and did not improve the solubilization of 2 model drugs.

(Taha, 2009) studied indomethacin (IND) self-nanoemulsifying drug delivery formulation (SNEDDF) have been prepared to enhance its dissolution which in turn could provide a better chance for IND oral absorption. IND SNEDDF have been prepared using different concentrations of castor oil as a solvent for IND, Cremophor RH 40 (Cr-40) as surfactant and

Capmul MCM-C8 (Ca-8) as co-surfactant. Droplets size and turbidity of IND SNEDDFs were measured. Ternary phase diagram was constructed to identify the self nanoemulsifying region after evaluation of IND SNEDDFs by the visual observation. The present study revealed that the SNEDDFs increased IND dissolution rate and has the potential to enhance its bioavailability without interaction or incompatibility between the ingredients.