

ABSTRACT

Physicochemical studies on surfactant mixtures under varied composition, concentration and surfactant types have been investigated since substantial time period. Interfacial and aggregation behavior of surfactant in the form of monolayer, bilayer, micelle and gels are worthy to be carried out in view of potential applications as well as understanding their fundamental properties. Oppositely charged surfactants, through electrostatic interaction in aqueous medium, can form ion pair amphiphile (IPA). Besides the IPA, cationic surfactant can form a variety of aggregates depending on the concentration and molar ratio of the surfactants constituting the mixture as well as other environmental conditions. Oppositely charged surfactants form a variety of aggregates that can be investigated with reference to the above perspectives.

Ionic surfactants are also capable to form water insoluble species upon interaction with oppositely charged metal ions (usually bivalent or trivalent) or radicals. Metallosurfactants, prepared by mixing stoichiometric amount of anionic surfactant and metal ions, can form insoluble monolayer as well as bilayer entities, similar to the phospholipids. Hence, metallosurfactants are worthy to investigate in the form of monolayer and bilayer in combination with lipids to generate membrane mimetic systems.

Interfacial and micellization behavior of *N*-dodecyl derivatives of amino-malonate, -aspartate and -glutamate, sodium salt ($C_{12}AAS$)Na₂ in combination with HTAB have been investigated by surface tension, conductance, UV-vis absorption/emission spectroscopy, dynamic light scattering and viscosity studies. Critical micelle concentration (*CMC*) values of the surfactant mixtures were significantly lower than the predicted values, indicating strong synergistic interaction. Surface excess, limiting molecular area, surface pressure at the *CMC* and Gibbs free energy indicate spontaneity of micellization processes, compared to the pure components. *CMC* values were also determined from the sigmoidal variation in the micellar polarity (evaluated from pyrene UV-vis absorbance/emission spectra) with surfactant concentration. Aggregation number (*n*), determined by the static fluorescence quenching method, increased with decreasing mole fraction of the amino acid based surfactants $\alpha_{(C_{12}AAS)_2Na_2}$ because of the

dominance of HTAB in micelle. Micellar size increased with decreasing $\alpha_{(C_{12}AAS)_2Na_2}$, leading to the formation of larger and complex aggregates. Micelles comprising 20 - 40 mole% $(C_{12}AAS)Na_2$ were highly viscous, in consonance with their sizes. Some of the mixed surfactant systems showed unusual viscosity (shear thickening increased viscosity with increasing temperature). Such mixed surfactant systems are considered to have potentials in gel-based drug delivery and nanoparticle synthesis.

In a theoretical approach, studies on micellar structure and composition of aforementioned oppositely charged surfactants were carried out. Results suggest synergistic interaction in aqueous medium, governed by the structural parameters as well as of the mixture composition. Different parameters, viz., theoretical values of *CMC* and its comparison with the earlier reported values, mole fraction of surfactants at the micellar phase (X), at the interface (X^σ), interaction parameters at bulk/interface (β^R/β^σ), ideality/non-ideality of the mixing processes and activity coefficient (f) of individual component were evaluated, using Rubingh, Rosen, Motomora and Sarmoria-Puvvada-Blankschtein (SPB) models. *CMC* values significantly deviated from the theoretically calculated values indicating strong synergistic interaction. With increasing $\alpha_{(C_{12}AAS)_2M_2}$, negative magnitude of the (β^R/β^σ) values gradually decreased, assisted by hydrophobic interactions in the mixed micelles. With increasing $\alpha_{(C_{12}AAS)_2M_2}$, decline in micellar mole fraction of HTAB (X_2) was not significant and the values were higher than those compared with $(C_{12}AAS)Na_2$ at all stoichiometries, due to the dominance of HTAB in the micelle. Micellar mole fraction values at the ideal state of $(C_{12}AAS)Na_2$ (X_1^{ideal}) differed from X_1 , indicating non ideality in mixed micellization process. Free energy of micellization (ΔG_m) values were more negative than the free energy of micellization for ideal mixing (ΔG_m^{ideal}) indicating spontaneity of micellization processes. With increasing $\alpha_{(C_{12}AAS)_2M_2}$, enthalpy of micellization (ΔH_m) and entropy of micellization (ΔS_m) values gradually increased indicating exothermicity of micellization processes. Different physicochemical parameters of mixed micelles were correlated with the variation in the spacer length between the two carboxylate groups of $(C_{12}AAS)Na_2$.

Another part of the dissertation includes physicochemical investigation on the gels formed by $C_{12}MalNa_2$, $C_{12}AspNa_2$ and $C_{12}GluNa_2$ in combination with HTAB at different ratio. In case of *N*-dodecyl amino malonate, there is only one carbon atom in between the two carboxylate groups. In case of aspartate and glutamate the number of carbon atoms, between two carboxylate moieties, are two and three respectively. The sequential increase in the number of carbon atoms, which act as spacer between the two carboxylate moieties, favor micellization due to enhanced hydrophobicity. $(C_{12}AAS)Na_2$ -HTAB mixed systems exhibited different phases, viz., gel, viscous, precipitate and clear fluid as established through ternary phase diagram. While moving from $C_{12}MalNa_2$ to $C_{12}AspNa_2$ to $C_{12}GluNa_2$, relative proportion of gel and viscous phases gradually decreased. Internal structure and liquid crystalline behavior of gels were investigated by combined polarisation optical microscopy and fluorescence microscopy. Porous and flower like surface morphologies were identified by field emission scanning electron microscopy. Phase transitions along with the associated weight loss of the surfactant aggregates were found to be dependent on surfactant composition, established by thermogravimetric analysis. Thermotropic behaviour of the aggregates were investigated by differential scanning calorimetric studies. The entropy of transition from solid-to-liquid crystal-to-isotropic liquid for surfactant aggregates increased systematically with increasing proportion of $(C_{12}AAS)Na_2$. Gels comprising lower proportion of $(C_{12}AAS)Na_2$ (< 40 mols %) were more viscous. Gels with higher proportion of $(C_{12}AAS)Na_2$ resulted insignificant irritation on mouse skin, suggesting its possible application as vehicle for topical drug delivery. Surfactant mixtures also exhibited antibacterial effects on *Staphylococcus aureus*, a potent causative agent of skin and soft tissue infections.

As fourth part of the work, dicarboxylic amino acid based metallosurfactants were synthesized by stoichiometric mixing of $(C_{12}AAS)Na_2$ with bivalent metal salts $CaCl_2$, $MnCl_2$ and $CdCl_2$. Water insoluble metallosurfactants $(C_{12}AAS)_2M_2$ coacervates formed were isolated by solvent extraction technique using chloroform. Metallosurfactants formed layered structure as observed by X-ray diffraction studies. Thermal phase transition and associated weight loss of the synthesized compounds were studied

by thermogravimetric analysis. Monomolecular films of the metallosurfactants in combination with soy phosphatidylcholine (SPC) and cholesterol were investigated using Langmuir surface balance with intention to substitute naturally occurring phospholipids. With increasing mole fraction of metallosurfactants ($\alpha_{(C_{12}AAS)_2M_2}$), mean molecular area gradually increased, indicating reorganization of molecular packing at air-water interface, whereby collapse pressure did not change significantly. In case of 20 and 60 mole% $(C_{12}AAS)_2M_2$, positive deviations were recorded, indicative of chain mis-match among the components of mixed monolayer. Negative deviation from the ideal values signifies associative interaction and vice versa. Spontaneity of mixing of the components at air-water interface were established for all the combinations from negative Gibbs free energy changes. Dynamic surface elasticity, examined by surface rheology studies, initially increased rapidly in the surface pressure range 0 to 1.5 mN/m, after which the slope of surface elasticity vs. surface pressure profiles decreased indicating formation of relatively rigid monolayers. Brewster angle microscopic (BAM) studies suggested two dimensional phase transition (gaseous state to liquid expanded to liquid condensed state) upon compression of the monolayer at air-water interface. BAM images demonstrated homogeneous and more condensed structure of surface layer and confirmed miscibility of the components. Metallosurfactants in combination with SPC and cholesterol could form stable hybrid vesicles. Hydrodynamic diameter, zeta potential and polydispersity index values of vesicles, measured by dynamic light scattering studies, were monitored as function of time to check its stability; particles were found to be stable upto 100 days. Size, surface morphology and bilayer thickness were investigated by transmission electron microscopic studies that were comparable with the dynamic light scattering studies. Thermodynamic parameters associated with the chain melting of hybrid vesicles were investigated by differential scanning calorimetry studies. Cytotoxicity of the vesicles was assessed by MTT and cell viability studies. *In vitro* cytotoxicity studies revealed that hybrid vesicles could act as promising vehicles for drugs with controlled and sustained release.