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THE SURFACE PHYSICOCHEMICAL PROPERTIES OF DRUG-SURFACTANT AND POLYMER-SURFACTANT SYSTEMS

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ABSTRACT

In this study, three cephalosporin drugs namely cefadroxyl monohydrate (CFM), cephalexin monohydrate (CLM) and cephradine monohydrate (CDM) were used as antibiotic drug molecules; bovine serum albumin (BSA) and sodium alginate (SA) were the biopolymers as well as hexadecyltrimethylammonium bromide (CTAB), a cationic and sodium dodecyl sulfate (SDS), an anionic surfactant were used as surfactants. The physicochemical parameters such as critical micelle concentration (*CMC*), maximum adsorption of surfactant (Γ_{max}), minimum surface area per head group of surfactant (A_{min}), surface pressure at *CMC* (Π_{cmc}), free energy of adsorption (ΔG^0_{ad}) and packing parameter (*P*) for drug-surfactant and polymer-surfactant systems were determined surface tensiometrically. The *CMC* values obtained from surface tension measurements indicated the interactions between drugs and surfactant as well as polymer and surfactants. The values of packing parameter (*P*) obtained from surface tension measurement revealed that micelles formed for cephalosporins – CTAB, SA – CTAB, SA-SDS and BSA-SDS systems were spherical in shape whereas micelles were nonspherical for BSA – CTAB system.

Keywords: *Surfactants, cephalosporin, surface area, surface excess, micelles, packing parameter*

INTRODUCTION

Surfactants play a vital role in pharmaceutical formulations because of their extensive use as emulsifier, disintegrating agents, solubility enhancer and diluents (Lo, 2003 and Nerurkar *et al*., 1997). Drug - surfactant system increases bioavailability and facilitate the control of drug uptake, minimizes drug degradation and loss (Allen *et al*.,1995 and Jones and Leroux, 1999). Polymer-surfactant mixed systems are used in formulations such as paints, coatings, detergents, cosmetic products, pharmaceutical products and foodstuffs in order to achieve better performance and longer durability (Loh *et al.*, 2004). When drug or polymer is added to surfactant, the resultant solution exhibits properties different from the individual surfactant solution. This is due to the formation of complex structures upon their association. The surface physicochemical properties of both ionic and nonionic pure surfactants have been studied by a number of authors (Collaghan *et al.*, 1993 and Huang *et al*., 1999). Different methods such as Conductometric, surface tensiometry, microcalorimetry, fluorescence spectroscopy, viscometry etc. have been utilized for such study (Ghosh and Banerjee, 2002 and Winnik *et al*., 2000). Though studies on drug-surfactant as well as polymer surfactant systems have been continued up till now (Huang *et al*., 1999; Ghosh and Banerjee, 2002; Winnik *et al*., 2000 and Akhtar *et al*., 2008), a literature survey revealed that very little attention has been paid to study the surface parameters of cephalosporins –CTAB, SA-surfactant as well as BSA-surfactant systems surface tensiometrically. In this study, some surface physicochemical parameters such as critical micelle concentration (*CMC*), maximum adsorption of surfactant (Γ_{max}), minimum surface area per head group of surfactant (A_{min}), surface pressure at *CMC* (Π_{cmc}), free energy of adsorption (ΔG^0_{ad}) and packing parameter (*P*) for drug-surfactant and polymer-surfactant systems have been determined.

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MATERIALS AND METHODS

CFM, CDM and CLM were collected from Drug International Pharmaceutical Ltd. SA (Aldrich, USA), BSA (Merck, Germany), CTAB (Aldrich, USA) and SDS (BDH, England) were used. All the drugs, polymers and surfactants were used without any further treatment.

Surface tensions of the drug-surfactant or polymer-surfactant systems in aqueous medium were measured using a surface tension meter (Kruss K9, Germany). The accuracy of the surface tension measurements was within ± 0.1 mN/m. Firstly 50 ml of drug / polymer solution of a particular concentration was taken in a specific glass vessel adjustable for the tensiometer and then concentrated surfactant solution was gradually added to the drug/polymer solution. Then the surface tension values were recorded at each addition after thorough mixing and allowing 10 to15 minutes for the attainment of equilibration. The critical micelle concentration (*CMC*) was obtained from the break point of γ versus log ($c_{surfactant}$) plot.

RESULTS AND DISCUSSION

Figure 1 is a typical representation of the plots of γ versus log ($C_{surfactant}$) which shows a sharp break point. The surfactant concentration corresponding to the break point was taken as the *CMC* of the systems (Collaghan *et al*, 1993).

The maximum adsorption amount of surfactants or surface excess (Γ_{max}) at *CMC* had been evaluated with the help of Gibbs adsorption equation (Osborne-Lee *et al.*, 1985 and Rosen, 2004):

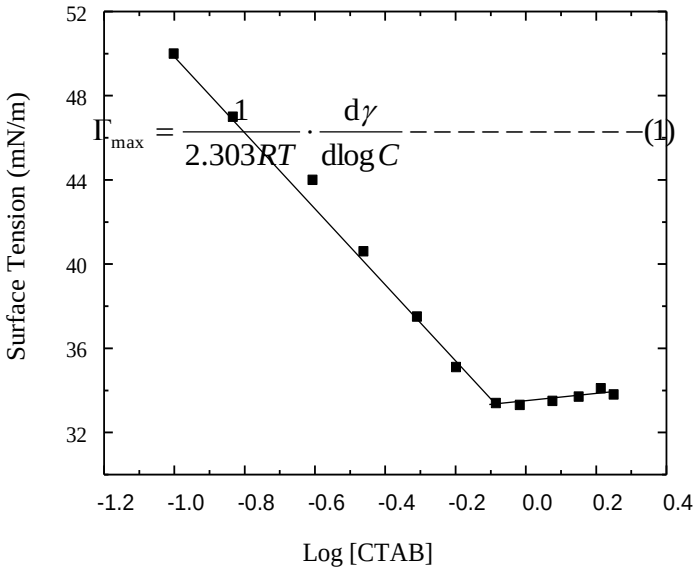

Figure 1. Surface tension (γ) versus log [CTAB] plot of CFM- CTAB system at 297.7K.

The slope of the linear portion of γ - log$C_{surfactant}$ plot was taken as equal to $d\gamma / \log C$ to calculate Γ_{max}.
The total minimum area per surfactant molecule (A_{min}) was calculated using the following equation:

Where N_A is the avogadro's number and Γ_{max} is in mol m^{-2}.
The standard free energy of adsorption for the drug – surfactant and polymer-surfactant systems was calculated using the following equations (Rosen, 2004; Ghosh and Moulik, 1998; Moulik and Ghosh, 1997)

$$A_{\min} = \frac{10^{18}}{N_A.\Gamma_{\max}} \text{ ---------- (7)}$$

$$\Delta G^0{}_{ad} = \Delta G^0{}_m - \left[\frac{\pi_{cmc}}{\Gamma_{\max}}\right] \text{ ---------- (8)}$$

Where Π_{cmc}, surface pressure at *CMC*, equals to the difference between γ values of drug/polymer-surfactant system and pure drug/polymer solution in water.

The nature of the packing of surfactant molecules in micelles and their structural geometry was determined following the procedure of Israelachvili (1991) in terms of packing parameter (*P*) as defined by the relation

$$P = \frac{V}{A_{\min}.l_c} \text{ ---------- (9)}$$

Where l_c is the maximum effective length of the hydrophobic chain of surfactant molecule, A_{min} is the surface area of the head group and *V* is the volume of the hydrophobic chain being considered to be fluid and incompressible.

Both l_c and *V* for a saturated hydrocarbon chain with C_n number of carbon atoms were obtained from the following proposed formulas of Tanford (1980):

$l_c \equiv (0.154 + 0.1265\ C_n)$ nm ---------- (10)

$V = (0.0274 + 0.0269 C_n)\ nm^3$ ----------(11)

The shape and category of surfactant micelles can be predicted from the magnitude of *P*.

The surface physicochemical parameters such as critical micelle concentration (*CMC*), maximum adsorption of surfactant (Γ_{max}), minimum surface area per head group of surfactant (A_{min}), surface pressure at *CMC* (Π_{cmc}), free energy of adsorption (ΔG^0_{ad}) and packing parameter (*P*) for cephalosporins – CTAB, SA-surfactant and BSA-surfactant systems are summarized in Tables 1, 2 and 3 respectively. The *CMC* values for cephalosporins-CTAB systems in water obtained from surface tension measurement are

Table 1. Surface physicochemical parameters for cephalosporins-CTAB system containing 1 mM drug solution

Systems	*CMC* (mmol.L^{-1})	$10^6\Gamma_{max}$ (mol m^{-2})	A_{min} (nm^2 molecule $^{-1}$)	Π_{cmc}	ΔG^0_{ad} kJmol $^{-1}$.K^{-1}	*P*	
CFM-CTAB	0.8235	1.669	0.9948	33.41	-56.92	0.21	
CLM-CTAB	0.6325	1.921	0.8643	31.41	-56.26	0.24	
CDM-CTAB	0.4446	2.261	0.7343	32.32	-52.20	0.29	

lower in magnitude compared to that of pure CTAB (Akhtar *et al.*, 2008). The *CMC* values follow the order: $CMC_{CFM\text{-}CTAB} > CMC_{CLM\text{-}CTAB} > CMC_{CDM\text{-}CTAB}$. The lowest *CMC* values of CDM-surfactant systems are due to the presence of cyclohexadienyl group in the structure of CDM. The possibility of conformational change of cyclohexadienyl group in CDM enhances the micellization of ionic surfactant whereas the presence of rigid benzene ring in the structure of CLM lowers the micellization of CLM-surfactant systems. The lowest micellization of CFM-surfactant system is due to the presence of 4-hydroxy phenyl group where hydroxyl (-OH) group is known to break down the normal hydrogen bonded structure of bulk water and thereby decreasing micellization. Though the *CMC* values obtained

from conductance and surface tension measurements are not exactly the same, the trend of the change of *CMC* values for three cephalosporins-CTAB systems is similar. Such method-dependent *CMC* values have been reported earlier by others (Ghosh and Banerjee, 2002). A_{min} values provide information about the packing and orientation of the surfactant molecules in the micelles. A_{min} value is the highest for CFM-CTAB and the lowest for CDM-CTAB systems. The A_{min} values indicate that CDM molecules are more tightly whereas CFM molecules are loosely packed in the micelles. The values of surface pressures (π_{cmc}) and free energy of adsorption, $\Delta G^0_{ad,}$ for three drugs-CTAB systems are almost the same which indicate that the micellelization process follows the same fashion in all three cases. The shape and category of surfactant micelles can be predicted from the magnitude of *P*. For spherical micelles, $P \leq 0.333$; for nonspherical shape, $0.333 < P < 0.5$; for vesicles and bilayers, $0.5 < P < 1$(Ray *et al*., 2007). The values of *P* for three cephalosporin-CTAB systems indicate that micelles formed are spherical in shape.

Table 2. Surface physicochemical parameters for SA-surfactant systems.

System	$c_{SA}CMC$ (mmol.L^{-1})	$104\times\Gamma_{max}$ (mmol.L^{-1})	A_{min} (mol m^{-2})	Π_{cmc} (nm^2 molecule^{-1})	*P*	
SA-CTAB	0.0001	0.91	20.01	8.30	35.32	0.025
SA-SDS	0.0010	3.92	21.61	7.68	46.9	0.028
SA-SDS	0.0050	3.63	25.51	6.51	47.26	0.033
SA-SDS	0.0098	3.39	36.70	4.52	46.86	0.047

The *CMC* values for SA-CTAB and SA-SDS systems in water obtained from surface tension measurement are found to be lower in magnitude compared to that of pure SDS (Akhtar *et al*., 2008). The *CMC* values for SA-SDS systems decrease with increasing concentration of SA. The values of τ_{max} increase with increase of concentration of SA. A_{min} values for SA-SDS systems are observed to decrease with increase of concentration of SA which indicates that SA molecules are more tightly packed. Thus the closeness the SA molecules in the micelle increase with increase of SA concentration. The higher values of A_{min} for SA-CTAB system containing 0.0001% SA indicate the looser packing of the CTAB molecules in the micelle. Surface pressures (π_{cmc}) for SA-SDS systems are almost the same over the concentrations being used and the value is comparatively lower in case of SA-CTAB system. The values of *P* in this study indicate that spherical micelles are formed for both SA-CTAB and SA-SDS systems.

Table 3. Surface physicochemical parameters for BSA-surfactant systems.

System	c_{BSA} % (w/v)	*CMC* (mmol.L^{-1})	$10^6\times\Gamma_{max}$ (mol m^{-2})	A_{min} (nm^2 molecule -1)	*P*
BSA-CTAB	0.05	1.31	3.69	0.45	0.47
BSA-CTAB	0.11	1.52	3.84	0.43	0.48
BSA-CTAB	0.21	1.81	4.03	0.41	0.50
BSA-SDS	0.11	5.89	2.37	0.70	0.30
BSA-SDS	0.22	5.62	1.86	0.89	0.24

The values of τ_{max} increase for BSA-CTAB system and decrease for BSA-SDS system with increase of concentrations of BSA. A_{min} values for BSA-SDS systems are observed to increase with increase of concentration of BSA which indicates that BSA molecules are loosely packed in the BDS-SDS micelles. Thus the closeness the BSA molecules in the micelle increase with decrease of BSA

concentration. The higher values of A_{min} for BSA-CTAB system containing 0.0001% BSA indicate relatively tight packing of the CTAB molecules in the micelle. The values of *P* in this study indicate that nonspherical micelles are formed for BSA-CTAB system whereas spherical micelles are formed in case of BSA-SDS system.

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