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Interfacial and Thermodynamic Properties of Amphiphile Sodium di-2-ethylhexylsulfosuccinate – Diphenlhydramen Drug System

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Abstract

Interfacial and thermodynamic properties Γ_{max}, A_{min}, π_{cmc} , ΔG°_{ads}, ΔG°_{m}, ΔH°_{m}, and ΔS°_{m} of individual sodium octyl sulfosuccinate (AOT) surfactant and their mixture with (DPH) drug at two concentrations (0.001 and 0.0001 M) have been calculated. The calculation was performed using the surface tension at temperature range 293-323 K with the variation of surfactant concentration to determine the cmc of all systems studied. The variation of critical micelle concentration (cmc) with concentration of DPH drug and the temperature was used to calculate the parameters above. The results indicate that the cmc of AOT Decrease when the DPH was added and when the temperature increased at the whole temperature studied. The results obtained for interfacial properties show that Γ_{max} decrease with the addition of DPH. The results of thermodynamic properties indicate that the micellization and adsorption at interface are spontaneous and the ΔG°_{ads} are more negative than ΔG°_{m} at all temperatures which reveal that micelle formation is less spontaneous than adsorption or surface adsorption is more preferable than micellization.

Keywords: AOT, DPH, critical micelle concentration, interfacial properties

1. Introduction

Surfactants were used as transporter of drug molecules to target organs because of; a) their ability to solubilize many water-insoluble drugs and thus increase their bioavailability, b) retention in the body (particularly in the blood) providing gradual accumulation in the target organ [1-3].The amphiphile Sodium di-2-ethylhexylsulfosuccinate commonly known as Aerosol orange T (AOT) is a versatile anionic surfactant having two alkyl chains as tails. It is widely used in chemical, biological, and pharmaceutical and medicinal preparations applications [4]. Diphenhydramine hydrochloride (DPH)(2-(diphenylmethoxy)- N, N-dimethylethylamine hydrochloride) is pharmacologically drug employed as an effective antihistaminic and it holds a two phenyl group as well as a tiny alkylamine chain having a terminal nitrogen particle, [5, 6].To our knowledge, research on the adsorption properties of surfactant and drug mixtures was done exhaustively earlier [7-10]; but, the work concerning the adsorption properties of AOT with drug mixtures is rare, such as the interactions of Ibuprofen (IBF), 2-(4-isobutylphenyl) propionic acid drug with AOT study [11], in which tensiometric, fluorimetric, and calorimetric measurements were used in order to investigate this system as a possible model drug delivery system for IBF.Physicochemical properties and mixed micellization behavior of the solutions of each mixed amphiphilic phenothiazine drug promazine hydrochloride (PMZ)[11] and an amphiphilic antidepressant drug amitriptyline hydrochloride (AMT)[12] with the anionic surfactant sodium bis(2-ethylhexyl)sulfosuccinate (AOT) was determined using conductometry at different compositions and temperatures in aqueous as well as aqueous electrolyte (25 mmolkg-1 NaCl) solutions. In the present work the behavior of AOT as anionic surfactant in aqueous and in two concentrations of DPH drug solutions was studied using surface tension measurements at four temperatures in the range (20-50)

2. Experimental

2.1- Materials

The anionic surfactant Dioctyl sodium sulfosuccinate (AOT) was obtained from Fluka, Switzerland, 98.5%, and used as received. Diphenhydramine (DPH) is a poorly water-soluble drug and its structure shown in Figure 1. The solution of individual surfactant and its mixtures with drug

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were prepared in deionized water (sp. conductivity = least 30 minutes for equilibrium before measuring the surface tension. The solutions of surfactant that have different concentration and percentage of mixture were prepared by diluting certain amounts of stock solution in 50 ml volumetric flask with the deionized water.

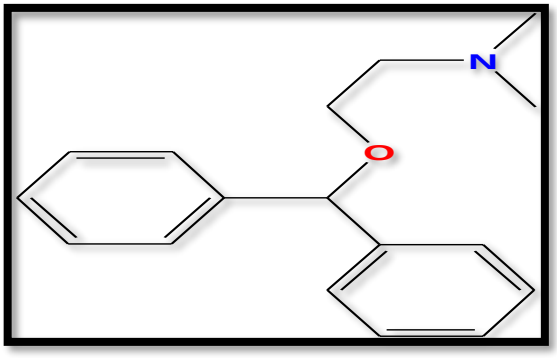

Fig. 1. Schematic diagram showing (a)

2.2 Methods

Tensiometric measurements were taken with a du Nouy tensiometer (model DST 30 M, Surface and Electro Optics (SEO) Company- Korea) using a platinum ring detachment method. For each set of experiments, the ring was cleaned by immersed in 5M HNO_3 solution. Each measurement was repeated three times to ensure the reproducibility of the results. The determined surface tension (γ) values were accurate within 0.1 mN m^{-1}. The cmc magnitude was determined corresponding to the intersection of the lines of the pre- and post- micelle regions of the concentration in the plots of γ vs. natural logarithm of surfactant concentration.

3. Results and Discussion

The cmc for the surfactant solution was determined using figure 2 which shows the variation of surface tension (γ) of AOT surfactant solutions in water and in DPH solutions (0.001 and 0.0001M) as a function of nature logarithm surfactant concentration at the four temperatures 293, 303, 313, and 323 K. The cmc values obtained for individual AOT are1.95, 1.47, 1.34, and 1.33 mM at temperatures 293, 303, 313, 323 K respectively, which are in the range of the results previously reported [10-13]. When the DFH was added the cmc values obtained for AOT/DFH (10^{-4}M) system at 293 K are 0.3 mM, while for AOT/DFH (10^{-3}M) system are 0.06 mM. These values and all the values of cmc obtained at different temperatures are listed in Table 1.

Table 1. Interfacial and thermodynamic parameters for AOT surfactant and AOT + DFH ($10^{-3}$and 10^{-4}) M drug systems at different Temperatures

system	(K)	cmc/ST (mM)	cmc/CT (mM)	? cmc mN/m	Γ_{max} 10^{-6} mol/m2	A_{min} A^2/molecule	S2/S1	ΔG^o_{ad} kJ/mol	ΔG^o_m kJ/mol	ΔH^o_m kJ/mol	ΔS^o_m J/mol.K
AOT	293	1.95	1.5	40.66	1.253	132	0.71	-43.8	-11.35	3.67	162
	303	1.47	1.48	39.52	1.220	136	0.77	-44.05	-11.33	5.62	163
	313	1.34	1.29	39.521	1.070	155	0.88	-47.67	-10.74	5.46	169
	323	1.33	1.2	38.36	0.903	184	0.87	-53.8	-11.32	7.87	190
AOT+ DPH (10^{-4}M)	293	0.3	0.7	43.22	0.98	169	0.622	-61.6	-17.52	6.64	82.45
	303	0.28	0.6	44.18	0.78	212	0.812	-72.47	-15.83	6.166	72.59
	313	0.25	0.35	45.29	0.84	197	0.517	-74.71	-20.31	8.21	91.11
	323	0.24	0.25	45.38	0.86	193	0.533	-71.74	-21.30	8.68	92.80
AOT+ DPH (10^{-3}M)	293	0.06	0.06	40.64	1.53	108	0.20	-56.42	-29.86	11.56	141
	303	0.05	0.05	40.31	0.89	186	0.085	-117.7	-33.83	13.15	155
	313	0.048	0.045	41.85	0.69	240	0.093	-135.3	-35	13.97	156
	323	0.045	0.040	41.91	0.53	312	0.116	-150.8	-39	14.67	166

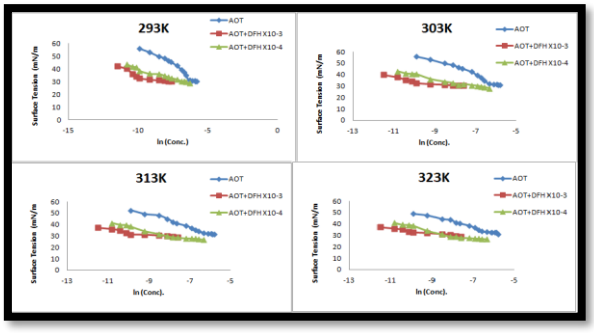

Figure 2 which shows the variation of surface tension (γ) of AOT surfactant solutions in water and in DPH solutions (0.001 and 0.0001M)

The results of Table 1 show that when DPH drug was added to the AOT solution, the cmc values decreased and the magnitude more increase as the concentration of DFH drug increased from 10^{-3} to 10^{-4} M. This means that;

1) the inonic surfactant causes a larger effect on the solubilization of the drug, thus delaying micellization [14].

2) the increase in the values of cmc indicates that in the formation of the mixed micelle, drug molecules are penetrating into the micelle formed by AOT. The penetration of drug molecules depends on the nature and polarity of the micellar core [6].

3) the long hydrophobic chain of DPH is quite rigid, and hence, we would expect some difficulty in packing these chains into a spherical micelle like a conventional surfactant, and the micelles it does form will be at high surfactant concentrations [8].

The values of cmc of AOT/ DFH mixtures dicreased with temperature increased as expected, which may be due to an increase in hydrophbicity caused dy the dsteruction of hydrogen dond between water molecules and hydrophilic groups . [15].

3.1-Interfacial properties

The surfactant species from the bulk to the surface. This is evident thermodynamically because it is more energy-friendly to be adsorbed at the air / water interface than to remain dissolved in the bulk solution**.**

Γmax is calculated from the Gibbs equation:(equation 1)$\Gamma_{max} = -1/nRT\ [d\gamma/dlnC]$ ---------(1)

The minimum area occupied by surfactant molecule, A_{min}, was computed from surface excess concentration using equation 2:

$$A_{min} = 1/N_a\ \Gamma_{max} \quad \text{----------(2)}$$

where ($d\gamma/dlnc$) is the slope of γ *vs* (ln C) plot below the cmc region, R is the universal gas constant (R = 8.314 J K^{-1} mol^{-1}), T is the temperature, N_A is Avogadro's number, and n is the number of chemical species.

The calculated parameters for AOT surfactant in aqueous solution and in the two concentration of DPH are listed in Table (1). The results of this table show that the Γ_{max} decrease and A_{min} increase in presence of DFH, this decrease in Γ_{max} or increase in A_{min} may be due to [12];

1) Drug molecule interaction with the head of surfactant,

2) The occurrence of drug molecules at the air/water interface behind the surfactant molecules. Hence, the presence of DPH molecules around hydrophilic head of amphiphile will enhance repulsions among them at the interface and will consequence in decrease in Γ_{max}.

3.2-Thermodynamic micellization

Thermodynamic parameters of micellization (ΔG°_m, ΔH°_m , and ΔS°_m) were calculated from the temperature dependence of the cmc from the following equations :

$$\Delta G^\circ_m = RT \ln X_{cmc} \text{----------(3)}$$

$$\Delta H^\circ_m = -RT^2 (\partial \ln X_{cmc} / \partial T) \quad \text{---------- (4)}$$

$$\Delta G^\circ_m = \Delta H^\circ_m - T\Delta S^\circ_m \quad \text{----------(5)}$$

π_{cmc} is calculated from the equation;

$\pi_{cmc} = \gamma_o - \gamma_{cmc}$.

Where γ_o is the surface tension of pure solvent and γ_{cmc} is the surface tension at the cmc. ΔG°_{ad} at the air/water interface is calculated from the relation:

$$\Delta G^\circ_{ad} = \Delta G^\circ_m - (\Pi_{cmc}/\Gamma_{max}) \quad \text{- - - - - - - (6)}$$

Where X_{cmc} is the cmc of surfactant in mole fraction unit and ($\partial \ln X_{cmc} / \partial T$) was evaluated from the slope of the plot of $\ln X_{cmc}$ versus temperature. $\Delta G^\circ m$ values are negative and the magnitude of these adverse values increases (in negative value) with growing concentration of drugs, which means that this method (micellization) is spontaneous in this direction. The increasing of ΔG°_m value with the addition of DFH indicates micellization to be less spontaneous thermodynamically (Table1).

Positive values of the enthalpy of micellization indicate the enothermic nature of the micellization process which inecrease at all drug concentrations with temperature. Nusselder and Engberts [16] have suggested that for positive ΔH°_m values, the London-dispersion forces play a major role in the micellar process. The positive values of standard entropy of micelle formation ΔS°_m are due to the melting of "flickering cluster" around hydrocarbon tails of the surfactant monomer and the increased randomness of the hydrocarbon chains in the micelle core [17]. Further, with the addition of DPH drug, entropy of the system is found to increase. This is due to the fact that the head groupis more than hydrated than the hydrophobic tail (18-19)

Table 1 show $\Delta G^\circ m$ values are negative and the magnitude of these adverse values increases (in negative value) with growing concentration of drugs, which means that this method (micellization) is spontaneous in this direction that ΔG°_{ad} values are negative signifying that the adsorption processes are spontaneous. Also the ΔG°_{ad} values are more than ΔG°_m for all system studied indicating that surface adsorption is more preferable than micellization which is

mean that adsorption is a primary and favorable process compared to micelle formation, which is a secondary and less favorable process.(20)

4. Conclusions

The foremost conclusions that can be drawn from the above resultsmay be expressed as following:

1- The micellar behavior of individual AOT surfactant and AOT / DPH drug systems are investigated and the cmc values obtained of binary mixtures(AOT +DPH) is highly less than cmc of individual surfactant which indicate a good attractive interaction between the two molecules.

2- The negative $\Delta G°_m$ and positive $\Delta S°_m$confirm the thermodynamic spontaneously of micellization and the $\Delta G°_{ad}$ values are > $\Delta G°_m$(in negative value) for all system studied indicating that micellization is less preferable than adsorption at interface.

3- The Γ_{max} decrease and A_{min} increase in presence of, DPH thus, the presence of drug moleculesin contact with hydrophilic head of surfactant will promote repulsions between them which will lead to Γ_{max} decrease.

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References

[1] Apensu Dey, Victoria Sandre, Daniel Gerrard Marangoni, and Soumen Ghosh, The Interaction Between a Non-Steroidal Anti-Inflammatory Drug (Ibuprofen)and Anionic Surfactant AOT and Effect of Salt (NaI) and Hydrotrope (4-4-4), J. Phys. Chem. B, Just Accepted Manuscript • DOI: 10.1021/acs.jpcb.8b00687 • Publication Date (Web): 07 Mar 2018.Downloaded from http://pubs.acs.org on March 8, 2018.

[2] Mall, S.; Buckton, G.; Rawlins, D.A. Dissolution behavior of sulphonamides into sodium dodecylsulphate Micelles: A thermodynamic approach. J. Pharm. Sci. 1996, 85, 75–78.

[3] Rub, M. A.; Asiri, A. M.; Naqvi, A. Z.; Rahman, M. M.; Khan, S. B.; Kabir-ud-Din Mixed micellization between amphiphilic drug promethazinehydrochloride and cationic surfactant (conventional as well as gemini). J. Mol. Liquids 2013, 177, 19-25.

[4] Amitabha Chakraborty, Subrata Chakraborty, and Swapan K. Saha, Temperature Dependant Micellization of AOT in Aqueous Medium: Effect of the Nature of Counterions, Journal of Dispersion Science and Technology, 28:984–989, 2007.

[5] Goodman-Hillman, A., Rall, T., Nier, A., Taylor, P., 1996. The Pharmacological Basis of Therapeutics. McGraw-Hill, New York.

[6] Akram M. El-Didamony, Moftah A. Moustafa , Spectrophotometric determination of diphenhydramine hydrochloride in pharmaceutical preparations and biological fluids via ion-pair formation, Arabian Journal of Chemistry (2010) 3, 265–270.

[7] Anirudh Srivastava, Hiromasa Uchiyama, YuheiWada Yuta Hatanaka, Yoshiyuki Shirakawa, Kazunori Kadota, Yuichi Tozuka, Mixed micelles of the antihistaminic cationic drug diphenhydramine hydrochloride with anionic and non-ionic surfactants show improved solubility, drug release and cytotoxicity of ethenzamide, Journal of Molecular Liquids 277 (2019) 349–359.

[8] Srivastava A., Liu C., Lv J., Deb D.K. W. Qiao, Enhanced intercellular release of anticancer drug by using nano-sized catanionic vesicles of doxorubicin hydrochloride and gemini surfactants, J. Mol. Liq. 259 (2018) 398–410.

[9] Fujimori M., Kadota K., Tozuka Y.,Mixed micelle systemproduced by interaction between transglycosylated stevia and an ionic surfactant improves dissolution profile of mefenamic acid, J. Pharm. Sci. 106 (2017) 1117–1123.

[10] A. Srivastava, C. Liu, H. Fang, J. Lv,W. Qiao, Interaction and binding efficiency of cationic drug chlorpheniramine maleate–anionic amino acid Gemini surfactants mixture as media for the synthesis of silver nanoparticles, Colloids Surf. A Physicochem. Eng. Asp. 529 (2017) 686–695.

[11] Farah Khan, Malik Abdul Rub, Naved Azum, Dileep Kumar, Abdullah M. Asiri, Interaction of an Amphiphilic Drug and Sodium Bis(2-ethylhexyl)sulfosuccinate at Low Concentrations in the Absence and Presence of Sodium Chloride, J Solution Chem (2015) 44:1937–1961 DOI 10.1007/s10953-015-0386-1.

[12] RUB Malik Abdul, ASIRI Abdullah M, KUMAR Dileep, AZUM Naved, KHAN Farah. Temperature Dependant Mixed Micellization Behavior of a Drug-AOT Mixture in an Aqueous Medium[J].Acta Phys. -Chim. Sin., 2014, 30(4): 699-707.

[13] Ban A, Inaam HA, Sameer HK, Micelle Formation and Adsorption of Individual and Mixed Nonionic Surfactant (Tween20+ Tween 80) System in Water, Research Journal of Pharmaceutical, Biological and Chemical Sciences , 2018; 9(3): 702- 708.

[14] Chauhan MS, Deepika K, Syal VK, Jyoti J, Study of Micellar Behavior of SDS and CTAB in Aqueous Media Containing Furosemide—A Cardiovascular Drug, J Solution Chem, 2010; 39: 622–638.

[15] Becher, p. In Nonionic surfactants :Sckick ,M.J.ED.,Marcel Dekker,New Yourk ,1967:ch.5.

[16] Nusselder J J, Engberts J B, Toward a better understanding of the driving force for micelle formation and micellar growth, J. Colloid Interface Sci. , 1992; 148: 353.

[17] Shrivastava A, Ghosh KK, Micellization of Cetyl Triphenyl Phosphonium Bromide Surfactant in Binary Aqueous Solvents, J. Surf. Deterg. , 2008; 11: 287-292.

[18] Del Rio,J..; prirto,G.Sarmiento, F.; Mosquera, thermodynamics of ionization of N-octyltrirthylamonium bromide in different media ,Langmuir ,11,1511,1995.

[19] Ayaat M. N, Sameer H. k. thermodyanamic of adsorption of TX-100 and SLES Surfactant on Air-Liquid and Solid –Liquid Intreface .Thesis, University of Baghdad 2014.

[20] Molina-Bolívar JA, Aguiar J, Peula-García JM, Ruiz CC. Surface activity, micelle formation, and growth of n-octyl-β-D-thioglucopyranoside in aqueous solutions at different temperatures. The Journal of Physical Chemistry B. 2004 Aug 26;108(34):12813-12820