

# Mixed Micellization Study of Adiphenine Hydrochloride with 1-Decyl-3-Methylimidazolium Chloride

Abbul B. Khan, Neeraj Dohare, Rajan Patel

**Abstract**—The mixed micellization of adiphenine hydrochloride (ADP) with 1-decyl-3-methylimidazolium chloride ( $C_{10}mim.Cl$ ), was investigated at different mole fractions and temperatures by surface tension measurements. The synergistic behavior (i.e., non-ideal behavior) for binary mixtures was explained by the deviation of critical micelle concentration ( $cmc$ ) from ideal critical micelle concentration ( $cmc^*$ ), micellar mole fraction ( $X_i^m$ ) from ideal micellar mole fraction ( $X_i^{ideal}$ ), the values of interaction parameter ( $\beta$ ) and activity coefficients ( $f_i$ ) (for both mixed micelles and mixed monolayer). The excess free energy ( $\Delta G_{ex}$ ) for the ADP-  $C_{10}mim.Cl$  binary mixtures explain the stability of mixed micelles in comparison to micelles of pure ADP and  $C_{10}mim.Cl$ . Interfacial parameters, i.e., Gibbs surface excess ( $\Gamma_{max}$ ), minimum head group area at air/ water interface ( $A_{min}$ ), and free energy of micellization ( $\Delta G_m^0$ ) were also evaluated for the systems.

**Keywords**—Adiphenine hydrochloride, Critical micelle concentration, Interaction parameter, Activity coefficient.

## I. INTRODUCTION

THE study of mixed amphiphile systems has become a subject of a giant concern of research in the previous decade, that show different surface and colloidal properties from their pure individual components [1]–[4]. The mixed amphiphile binary system has an important property i.e. synergism, due to their nonideal mixing that exploit their application in industrial preparations and pharmaceutical formulations [5]. The poor bioavailability of approximately 20–30% of pharmaceutical compounds is also an important concern of research because of their low solubility [6], [7], specifically in pharmaceuticals. There are several approaches have been described in the literature for increasing the drugs solubility such as the use of co solvents, surfactants, liposome formulations or complexing agents [8]–[10] as well as the formation of emulsions and solid dispersions [11], [12].

Adiphenine hydrochloride (ADP) is an anticholinergic that used in treating various conditions, e.g., Parkinson's disease,

gastrointestinal and respiratory disorders. Besides its use in several diseases it also has several side effects i.e., increased heart rate being one of them and if taken in significant amounts, a toxic reaction may take place in the body [13].

Ionic liquids (ILs) are a class of salts composed of organic cation, and an appropriate anion exists in a molten state at room temperature, and because of their unique physicochemical properties [14]–[16], they have generated massive scientific importance [17], [18]. Currently, ILs behave as green surface active agents and can be overcome over conventional surfactants, and its imidazole ring resembles its structure with many biologically important molecules such as the amino acid histidine that have an imidazole side chain and play an significant role in the structure and binding functions of hemoglobin. Consequently, a huge number of applications of ILs have been proposed in catalysis [19], electrochemistry [20], chemical separation [21], [22] and as a novel solvent in organic synthesis [23], [24]. Besides these unique properties, they also have the prominent role in miscellaneous industrial applications, where high surface areas, modification of the inter-facial activity or stability of colloidal systems are required.

As of the literature, the mixed micellar systems of drug-cationic surfactant [25]–[29] and surfactant-IL [30]–[32] have been widely studied, but the mixture of drug- IL [33], [34] have been less frequently examined. Up to our knowledge, no one has studied the thermodynamic of mixed micellization of ADP- $C_{10}mim.Cl$  binary mixtures. Therefore, keeping all these points in mind, herein, we have been investigating the mixed micellization and interfacial properties for ADP- $C_{10}mim.Cl$  binary mixtures at different mole fraction and temperatures by surface tension measurements.

## II. MATERIAL AND METHODS

### A. Chemicals

The amphiphilic drug adiphenine hydrochloride (ADP) ( $\geq 98\%$ , Sigma, USA) was used without further purification and 1-decyl-3-methylimidazolium chloride, Sigma Aldrich,  $\geq 97\%$  (CAS no. 171058-18-7) were used as received except vacuum drying. Their aqueous stock solutions of different mole fraction were prepared in doubly distilled water.

### B. Experimental Set Up

A Surface tension was measured by Delta-Pi Langmuir microtensiometer (Kibron, Helsinki, Finland) based on the Wilhelmy method and utilizing a small diameter (0.51 mm)

Abbul B. Khan is with the Biophysical Chemistry Laboratory, Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia (Central University), New Delhi-110025, India (phone: +91-9650536078; e-mail: bashar.khan2009@gmail.com).

Neeraj Dohare is also with the Biophysical Chemistry Laboratory, Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia (Central University), New Delhi-110025, India (e-mail: n.dohare.150887@gmail.com).

Rajan Patel is an assistant professor in the Biophysical Chemistry Laboratory, Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia (Central University), New Delhi-110025, India (e-mail: rajanpatelpcy@gmail.com).

special alloy wire. The temperature of the measurement cell was controlled by Grant GD120 water thermostat with temperature stability of  $\pm 0.02^\circ\text{C}$ . The wire used in the measurement was cleaned by red hot burning from butane gas through blazer. Different mole fractions of binary systems were prepared from stock solutions of different concentrations of ADP and  $\text{C}_{10}\text{mim.Cl}$ . The surface tension ( $\gamma$ ) at each mole fraction was measured by successive addition of concentrated solution of the mixture in pure water at a definite temperature. In order to determine the values of  $\text{cmc}$ , two linear fits were used for each of the isotherms. The first line was fitted to the interval of concentration characterized by a linear decrease of the surface tension and the second one to the region of concentration with nearly constant surface tension. The  $\text{cmc}$  were determined from the break point of the surface tension vs  $\log C$  curves and accuracy of the individual surface tension reading is approximately  $\pm 0.01 \text{ mNm}^{-1}$ .

### III. RESULTS AND DISCUSSION

The adsorption of amphiphilic molecules at the air/water interface and micellization are affected by its structure and adjacent micro environmental conditions. Moreover, the effect of these two factors on the two phenomena is generally not equal.

#### A. Variation of $\text{cmc}$

Fig. 1 shows the variation of  $\text{cmc}$  with the increase in the mole fraction of ADP at different temperatures. From Fig. 1, it was found that the  $\text{cmc}$  value increases almost linearly with the increase in the mole fraction of ADP. In addition, for the binary mixtures, slight increase in  $\text{cmc}$  was observed with increasing temperature where as for pure drug  $\text{cmc}$  value slightly decreases at 313 K. It is general consideration that  $\text{cmc}$  of ionic amphiphiles, first decreases at low temperatures

while increases at higher temperatures [35] while in case of non-ionic surfactants, the  $\text{cmc}$  decreases with increasing the temperature [36]. Moreover for ionic systems, continuous increase in  $\text{cmc}$  with temperature is also reported in some cases [37], [38]. However, in case of pure ADP, the  $\text{cmc}$  values first increase with temperature and then decreases at the higher temperature [35]. This is because below  $T_{\text{max}}$  (temperature at which  $\text{cmc}$  value is maximized), thermal solubility predominates over dehydration and  $\text{cmc}$  of pure ADP increases while above  $T_{\text{max}}$ , the high temperature dehydrates micelles more and this factor outweighs the solubility factor. Hence,  $\text{cmc}$  again decreases.

#### B. Interfacial Parameters

An effective measure of the adsorption at the air/water interface is (surface excess,  $\Gamma_{\text{max}}$ ) calculated by the Gibb's adsorption equation [39]:

$$\Gamma_{\text{max}} = -\frac{1}{2.303nRT} \left( \frac{\partial \gamma}{\partial \log C} \right) \quad (1)$$

and the minimum area per molecule,  $A_{\text{min}}$ , by the following equation [40]:

$$A_{\text{min}} = \frac{10^{20}}{N_A \Gamma_{\text{max}}} \quad (2)$$

where  $R$ ,  $T$ , and  $N_A$  are gas constant, temperature (in Kelvin), and Avogadro's numbers respectively.  $n$  is introduced to allow for simultaneous adsorption of cation and anion. The value of  $n$  is used as 2 for ADP and  $\text{C}_{10}\text{mim.Cl}$ . The values of  $\Gamma_{\text{max}}$  and  $A_{\text{min}}$  for mixtures are based upon  $n=3$  with the understanding that they merely indicate changes with the change in the nature of the mole fractions of components of the binary mixture.

TABLE I  
VARIOUS PHYSICO-CHEMICAL PROPERTIES FOR BINARY MIXED SYSTEMS AT DIFFERENT TEMPERATURES

$a_1$	$\Gamma_{\text{max}} \cdot 10^7 (\text{mol} \cdot \text{m}^{-2})$	$A_{\text{min}} (\text{\AA}^2)$	$\gamma_{\text{cmc}} (\text{mN} \cdot \text{m}^{-1})$	$\Pi (\text{mN} \cdot \text{m}^{-1})$	$pC_{20}$	$G_{\text{min}} (\text{kJ} \cdot \text{mol}^{-1})$
298 K						
0	28.92	57.41	45.73	27.07	1.72	15.81
0.1	22.87	72.59	37.87	34.93	1.87	16.56
0.3	20.23	82.07	38.48	34.32	1.86	19.02
0.5	16.59	100.07	37.55	35.25	1.97	22.63
0.7	16.10	103.12	40.75	32.05	1.78	25.31
0.9	16.46	100.89	45.30	27.50	1.49	27.53
1	16.88	98.37	48.80	24.00	1.52	28.91
308 K						
0	26.30	63.13	36.85	35.05	1.82	14.01
0.1	17.75	93.55	35.86	36.04	1.92	20.20
0.3	18.83	88.16	37.21	34.69	1.84	19.76
0.5	14.87	111.69	36.29	35.61	1.99	24.41
0.7	15.44	107.52	37.42	34.48	1.79	24.23
0.9	15.11	109.85	52.48	19.42	1.15	34.72
1	16.15	102.80	48.86	23.04	1.49	30.25
318 K						
0	23.49	70.67	37.14	33.86	1.93	15.81
0.1	16.51	100.59	36.76	34.24	2.02	22.27
0.3	17.92	92.63	38.06	32.94	1.85	21.23
0.5	11.99	138.48	36.29	34.71	2.19	30.27
0.7	14.73	112.74	38.87	32.13	1.82	26.39
0.9	14.33	115.89	41.58	29.42	1.57	29.02
1	15.09	110.00	49.19	21.81	1.42	32.59

The  $\Gamma_{max}$  value (Table I) is maximum for pure C<sub>10</sub>mim.Cl (i.e.,  $\alpha_1=0$ ) at all temperatures and gradually increases with the increase in the mole fraction of ADP, while decreases with the increase in temperature. The  $A_{min}$  values (Table I) follow the expected opposite trend of  $\Gamma_{max}$ .

The values of  $pC_{20}$  (Table I), which are given by (3) ( $C_{20}$  is being the concentration required to reduce the surface tension of solvent by 20 mN.m<sup>-1</sup>) [39], increase with the increase in  $\alpha_1$ ,

$$pC_{20} = -\log_{10} C_{20} \quad (3)$$

The greater the value of  $pC_{20}$ , the lower is the concentration needed to reduce the value by 20 mN.m<sup>-1</sup>. This result reveals that the system is more surface active.

### C. Interaction between Molecules in Mixed Adsorbed Film and Micelle

To explore the properties of ideal or non-ideal behavior of mixed micelles of ADP-C<sub>10</sub>mim.Cl the pseudo phase model was applied, according to that micelles are considered to be a macroscopic phase in equilibrium with a solution containing corresponding monomers. The ideal  $cmc$  is related to individual  $cmc$ 's by (4) [41]:

$$\frac{1}{cmc^*} = \frac{\alpha_1}{cmc_1} + \frac{(1-\alpha_1)}{cmc_2} \quad (4)$$

where  $\alpha_1$ ,  $cmc^*$ ,  $cmc_1$ , and  $cmc_2$  are the mole fraction of ADP in the bulk, ideal  $cmc$  of mixture,  $cmc$  of ADP, and  $cmc$  of C<sub>10</sub>mim.Cl, respectively. The experimentally obtained  $cmc$  and  $cmc^*$  values for binary mixtures of the ADP and C<sub>10</sub>mim.Cl are plotted as a function of the mole fractions of ADP ( $\alpha_1$ ) at different temperatures are given in Table II.

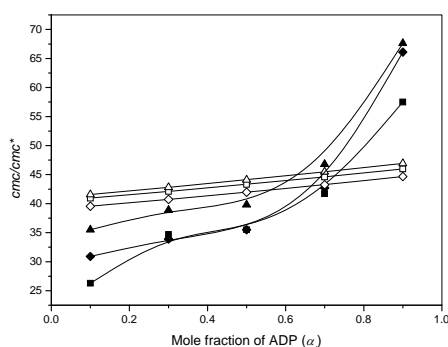


Fig. 1 Plot of  $cmc$  and  $cmc^*$  for different mole fractions of ADP at different temperatures

A comparison of experimental  $cmc$  and  $cmc^*$  values for the ADP-C<sub>10</sub>mim.Cl binary mixtures shows that at all temperatures  $cmc^*$  is lower than the  $cmc$  upto  $\alpha_1=0.7$  and then the results are reverse, and the deviation is decreases with the increase in mole fraction of ADP from  $\alpha_1=0.1$  to 0.7 and then again increases at 0.9. This reveals that with the increase in  $\alpha_1$ , non-ideality increases because the rigid structure of ADP

produced steric hindrance, although the presence of these components of binary systems decreases the repulsion.

A quantitative interpretation of micellar mole fraction can be calculated iteratively from the following equation with the help of the Rubingh's procedure, which based on regular solution theory (RST) [42]

$$\frac{(X_1^m)^2 \ln(cmc\alpha_1 / cmc_1 X_1^m)}{(1 - X_1^m)^2 \ln\{cmc(1 - \alpha_1) / cmc_2(1 - X_1^m)\}} = 1 \quad (5)$$

The micellar mole fraction ( $X_1^m$ ) values obtained from the above equation are used for the calculation of the interaction parameter ( $\beta^m$ ) by:

$$\beta^m = \frac{\ln(cmc\alpha_1 / cmc_1 X_1^m)}{(1 - X_1^m)^2} \quad (6)$$

The mixed micelle formation, due to the attractive and repulsive interactions are indicated by negative and positive  $\beta^m$  values, respectively, while a value close to zero refers to an ideal behavior [41].

The  $X_1^m$  value increases with the increase in the mole fraction of ADP ( $\alpha_1$ ) from 0.1 to 0.7 at all temperatures but its value decreases at 308 K and again increases at 318 K (Table II).

The above procedure not only characterizes  $\beta^m$  of the mixed micelles but also explains the deviation from ideality. The negative values of  $\beta^m$  mean that the attractive interaction between ADP and C<sub>10</sub>mim.Cl is stronger than the individual components.

Table II reveals that  $\beta^m$  value is maximum, for all mole fractions at 298 K that steeply decreases with the increase in  $\alpha_1$  from 0.1 to 0.7. On increase in the temperature from 298 K to 308 K there is a decrease to be observed in the magnitude of  $\beta^m$  value at all mole fractions while on further increase in temperature from 308 K to 318 K, at all  $\alpha_1$  values of ADP from 0.1 to 0.7 the  $\beta^m$  steeply decreases.

The activity coefficients ( $f_i^m$ ) in the mixed micelles, according to the RST, are calculated by:

$$f_1^m = \exp\{\beta^m(1 - X_1^m)^2\} \quad (7)$$

$$f_2^m = \exp\{\beta^m(X_1^m)^2\} \quad (8)$$

The values of  $f_1^m$  and  $f_2^m$ , calculated by using (7) & (8) are, in all cases less than unity, indicating non-ideality.

The excess free energy of mixing,  $\Delta G_{ex}$ , can be calculated using  $X_i^m$  and  $f_i^m$  by [43]:

$$\Delta G_{ex} = RT[X_1^m \ln f_1^m + X_2^m \ln f_2^m] \quad (9)$$

All the negative  $\Delta G_{ex}$  values show that the ADP- C<sub>10</sub>mim.Cl mixed micelles are more stable than the micelles of pure components, but the magnitude of  $\Delta G_{ex}$  values follow almost the same trend as of  $X_1^m$  values as reported in Table II. In addition, at all temperatures with the increasing in  $\alpha_1$  value the magnitude of  $\Delta G_{ex}$  is decreases.

The nature and the composition of the adsorbed monolayer can be evaluated by the extrapolated form of the mixed micellar RST. The molecules prefer to adsorb at the air/water interface rather than to be aggregate, due to large and rigid hydrophobic portion [44].

Analogous to (5) for mixed micelles, the values of  $X_I^\sigma$  and  $\beta^\sigma$  can be calculated at a constant  $\gamma$  value by [45]:

$$\frac{(X_I^\sigma)^2 \ln(\text{conc } \alpha_1 / \text{conc}_1 X_I^\sigma)}{(1 - X_I^\sigma)^2 \ln\{\text{conc}(1 - \alpha_1) / \text{conc}_2(1 - X_I^\sigma)\}} = 1 \quad (10)$$

where  $\text{conc}$ ,  $\text{conc}_1$ , and  $\text{conc}_2$ , are the concentrations in mixed monolayers, ADP and  $\text{C}_{10}\text{mim.Cl}$ , respectively, at a definite surface tension (in our case,  $\gamma = (\gamma_{\text{cmc}} + 5) \text{ mNm}^{-1}$ ).

Other surface parameters were also calculated by using:

$$\beta^\sigma = \frac{\ln(\text{conc } \alpha_1 / \text{conc}_1 X_I^\sigma)}{(1 - X_I^\sigma)^2} \quad (11)$$

$$f_1^\sigma = \exp\{\beta^\sigma(1 - X_I^\sigma)^2\} \quad (12)$$

$$f_2^\sigma = \exp\{\beta^\sigma(X_I^\sigma)^2\} \quad (13)$$

where  $f_1^\sigma$ ,  $f_2^\sigma$ ,  $\beta^\sigma$ , and  $X_I^\sigma$  are activity coefficients of the two components, interaction parameter in mixed monolayer, and mole fraction of ADP in the mixed monolayer, respectively. As shown in Table III, the  $X_I^\sigma$  and  $\beta^\sigma$  follow the almost same trend as of  $X_I^m$  and  $\beta^m$  values.

In ideal state, the micellar mole fraction was calculated by [46]:

$$X_1^{\text{ideal}} = \frac{\alpha_1 \text{cmc}_2}{\alpha_1 \text{cmc}_2 + (1 - \alpha_1) \text{cmc}_1} \quad (14)$$

TABLE II  
VARIOUS INTERACTION PARAMETERS IN MIXED MICELLE FOR BINARY MIXED SYSTEMS AT DIFFERENT TEMPERATURES

Mole fraction of ADP ( $\alpha_1$ )	$X_I^{\text{ideal}}$	$X_I^m$	$\beta^m$	$f_1^m$	$f_2^m$	$\Delta G_{\text{ex}}$ (kJmol <sup>-1</sup> )
298 K						
0.1	0.088	0.271	-2.96	0.21	0.80	-1.45
0.3	0.270	0.334	-0.91	0.67	0.90	-0.50
0.5	0.464	0.474	-0.80	0.80	0.84	-0.49
0.7	0.669	0.649	-0.30	0.96	0.88	-0.17
308 K						
0.1	0.087	0.184	-1.36	0.40	0.95	-0.52
0.3	0.269	0.306	-0.47	0.80	0.96	-0.25
0.5	0.462	0.469	-0.41	0.89	0.91	-0.26
0.7	0.667	0.676	0.13	1.01	1.06	0.07
318 K						
0.1	0.087	0.219	-1.91	0.31	0.91	-0.86
0.3	0.269	0.331	-0.87	0.68	0.91	-0.51
0.5	0.462	0.472	-0.67	0.83	0.86	-0.44
0.7	0.667	0.663	-0.06	0.99	0.97	-0.04

TABLE III  
VARIOUS INTERACTION PARAMETERS AT AIR-WATER INTERFACE FOR BINARY MIXED SYSTEMS AT DIFFERENT TEMPERATURES

Mole fraction of ADP ( $\alpha_1$ )	$X_I^\sigma$	$\beta^\sigma$	$f_1^\sigma$	$f_2^\sigma$
298 K				
0.1	0.157	-1.33	0.39	0.97
0.3	0.261	-0.43	0.79	0.97
0.5	0.447	-1.74	0.59	0.71
0.7	0.600	-0.22	0.96	0.92
308 K				
0.1	0.075	-0.50	0.65	0.99
0.3	0.133	0.38	1.33	1.00
0.5	0.407	-1.98	0.50	0.72
0.7	0.519	-0.77	0.84	0.82
318 K				
0.1	0.279	-3.82	0.14	0.74
0.3	0.289	-0.92	0.63	0.93
0.5	0.455	-2.85	0.43	0.55
0.7	0.573	-0.75	0.87	0.78

The deviation of  $X_I^m$  from the corresponding  $X_I^{\text{ideal}}$  values also enlightens nonideality in the mixed micelles. The  $X_I^m$  close to  $X_I^{\text{ideal}}$  values be a sign of ideal mixing, and higher  $X_I^m$  than the corresponding  $X_I^{\text{ideal}}$  points out that the mixed micelles are rich in ADP, while higher  $X_I^m$  than corresponding  $X_I^{\text{ideal}}$  indicates that mixed micelles are rich in  $\text{C}_{10}\text{mim.Cl}$ . From Table II it is clear that generally at all mole fractions the  $X_I^m$  value is higher than the corresponding  $X_I^{\text{ideal}}$  values. In addition, it is also clear that at all temperature there is no significant change to be observed.

#### IV. CONCLUSIONS

Herein, an attempt has been made to exploit the role of alkyl imidazolium IL ( $\text{C}_{10}\text{mim.Cl}$ ), in the mixed micellization with amphiphilic drug, ADP at different temperatures by using tensiometry. The results reveals that the  $\text{C}_{10}\text{mim.Cl}$  form mixed micelles with ADP, which shows the synergistic interaction (i.e., non-ideal behavior) of ADP- $\text{C}_{10}\text{mim.Cl}$  binary mixtures, explained based on RST by the deviations in  $\text{cmc}$  from  $\text{cmc}^*$  and  $X_I$  from  $X_I^{\text{ideal}}$  values. The extent of interaction explained by the deviation of  $\text{cmc}$  from  $\text{cmc}^*$ , i.e.,  $\text{cmc}^*$  is lower than the  $\text{cmc}$  upto  $\alpha_1=0.7$  and then the results are reverse. In addition, the variation of  $X_I$  and  $X_I^{\text{ideal}}$  explains that at all mole fractions the  $X_I^m$  value is higher than the corresponding  $X_I^{\text{ideal}}$  values which indicate that the mixed micelles are rich in ADP. Moreover, the values of  $\beta$ ,  $f_1$  and  $f_2$ , also confirm the synergistic interaction. The negative  $\Delta G_{\text{ex}}$  values support that ADP- $\text{C}_{10}\text{mim.Cl}$  mixed micelles are more stable than the micelle of  $\text{C}_{10}\text{mim.Cl}$  and ADP, a trend also supported by the  $X$  and  $\beta$  values.

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