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# Modulation of Aggregation Behaviour of Amphiphlic Drug and Surfactant Mixture under the Influence of Neutral Polymer

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The interaction of non-ionic surfactant, Triton X-114 (TX-114) with amphiphilic drug *i.e.*, imipramine hydrochloride (IMP) has been investigated by surface tension measurement in the absence and presence of hydroxypropyl methylcellulose (HPMC) polymer. In the presence of the HPMC the plots of surface tension *versus* concentration of TX-114 + IMP mixed system show interesting features (*i.e.*, two break points). The two break points attributed to the occurrence of two kind of aggregation process. In the presence of HPMC, the first break is close to that in pure water, can be regarded as critical aggregation concentration (*cac*), whereas second one is 2-3 times higher than the first one and can be attributed to the polymer bound micelles. The interfacial and bulk behavior was investigated using various theoretical models of Clint, Rosen, Rubingh *etc*. Synergism was observed in all binary combinations in the micelle and at the interface with or without the HPMC. Various thermodynamic parameters have been calculated with the help of regular solution theory (RST) and pseudo phase model for micellization.

**Keywords: Imipramine hydrochloride, Hydroxypropyl methylcellulose, Critical aggregation concentration, Critical micelle concentration.**

## INTRODUCTION

It is well recognized that surfactant and polymer mixtures are increasingly being used in wide range of domestic, industrial and technological applications to improve its characteristics and these properties cannot be achieved by using polymer or surfactant alone[1-5]. The mixtures are in general aqueous-based; polymers are added to the systems to control rheology, stability and to manipulate surface adsorption. Due to this very important and useful behavior polymer/ surfactant systems has greatly stimulated the interest in such systems and now the understanding of polymer/surfactant interactions is considered the most important issue in surfactant science. Though many research papers on individual surfactants, mixed polymer/surfactant material has been performed [6-11], but the interaction among surfactants/amphiphilic drugs mixed micelle with or without neutral polymers need detail exploration. The electrostatic force of interactions are very weak in neutral polymer/amphiphilic systems and other forces like hydrophobic, dipolar considered to be present in such systems and in some other systems, hydrophobic forces may be the main interactive forces which make the system more convoluted. The complex nature of these interactions and the desire to understand them has led to a wealth of research on the subject, both experimental and theoretical. Different scientists have performed various experiments on polymer surfactant mixtures about their behaviour and quite a lot of data and explanation about it exists[12-14], but their surface properties have been significantly unavailable.

The association of surfactant and polymer chain can be imagined like a necklace[15], where the surfactants are just as pearls joined to a hydrophobic centre. Actually, the interaction between an ionic amphiphile and non-ionic polymer depends upon the nature of the polymer and amphiphile. It has also been suggested that the interactions between the polymer and polar surfactant group are important. In all cases, the adsorption of complex polymer/amphiphile aggregate structures occurs at the air/solution interface. Therefore, changes in the nature of binding of amphiphile to the polymer, even when it occurs in a single-phase region, are generally evaluated by the surface tension studies.

Recently, we observed that not only pure micelles show strong interactions with the neutral polymer, but mixed micelles also have significant interactions with polymers[16], which are also affected by the variation in the mole fractions of the binary mixture. A mixed micellar system has received wide attention for several decades to obtain desired performance. In particular, their properties such as surface activity, wetting, adsorption,

solubilization, emulsification, suspension, dispersion and so forth, are often better than that of single substances. Mixed systems of conventional surfactants have been studied extensively to develop better functions or to make clear the nature of interaction between them[17-21].

The tricyclic antidepressant drugs are a family of structurally similar compounds possessing an almost planar tricyclic ring system with a short hydrocarbon chain carrying a terminal, charged nitrogen atom. It has been shown that these drugs form aggregates (or micelles) of approximately 6-12 monomers. Tricyclic antidepressant, imipramine hydrochloride (IMP), a first generation antidepressant drug, suffers from several drawbacks like anticholinergic, cardiovascular and antiarrythymic side effects. To reduce these side effects, the antidepressants are used with a drug carrier. Generally, surfactants are considered as good carriers as they form micelles and can solubilize drugs in their core. As imipramine hydrochloride molecules themselves possess capacity of self-aggregation in aqueous medium, it is worthwhile to study mixed micellization involving this drug and surfactants. A nonionic surfactant is used for solubilization of a variety of hydrophobic drugs. Mouritsen and Jorgensen[22] have shown that drugs insert into membranes and affect the organization of lipids. Computer simulations indicated that partitioned drugs accumulate heterogeneously in the membranes. This accumulation may cause a localized high concentration. Such a high concentration may change the drug's biological activity due to decreased ability to pass through biological barriers and may prove fatal. Therefore, it is important to have knowledge of the effect of surfactants on the micellization tendency of drugs, as surfactants form mixed micelles with drugs. Hence, keeping all points in mind, we have studied the effect of non-ionic surfactants (TX-114) on the micellization of amphiphilic drugs (imipramine-hydrochloride). Also, the effect of polymer (0.1 w/v % HPMC) seen on the process of micellization. To the best of our knowledge, we have not seen in literature such type of detailed study of micellization of drugs with the surfactants (TX-114) in the presence of HPMC used in the present study.

## EXPERIMENTAL

TX-114, imipramine hydrochloride and hydroxypropyl methyl cellulose (HPMC), all from Sigma, Germany were used as received. Double distilled water having a specific conductance of 1-3μ Scmc$^{-1}$ was used for the preparation of all solutions. All reference and stock solution were prepared by mass with an accuracy of ± 0.001 mg.

The surface tension measurements were carried out with Attension Tensiometer (Sigma 701) using a platinum ring at constant temperature (25 ± 0.1 °C). Solutions were contained by a double-walled Pyrex vessel thermostatted at 25 ± 0.1 °C. Attension Tensiometer operates on the Du Nouy principle, in which a platinum-iridium ring is suspended from a torsion balance and the force (in mN/m) necessary to pull the ring free from the surface film is measured. Surface tension value was taken when stable reading was obtained for a given surfactant concentration, as indicated by at least three consecutive measurements having nearly the same value. The average of a series of consistent readings for each sample was then corrected to account for the tensiometer configuration, yielding a corrected surface tension value.

## RESULTS AND DISCUSSION

**Surface activity:** The high surface tension of water is due to strong hydrogen bonding among the water molecules, leading to enhanced cohesive force, which resists the separation of a water column into two. When a surfactant is added in water, the surfactant molecules first populate at the air/water interface in order to avoid the highly energetically unfavorable interaction of water with the hydrophobic tail of the surfactant and the surfactant head groups are buried in the aqueous environment while the tails remain in the air phase. This, in turn, hinders the intermolecular hydrogen-bonding present on the surface of a pure aqueous phase and surface tension starts decreasing. The decrease in the surface tension (γ) value continues until the air/water interface is saturated with surfactant monomers. Beyond this saturation, the added surfactants assemble among themselves to form aggregates to ensure a hydrophilic periphery, hiding the hydrophobic tail within a cage to avoid water. The γ value, therefore, does not change (beyond $\gamma_{cmc}$) after reaching a certain concentration of surfactant. This concentration of surfactant is called the critical micelle concentration (cmc) and is obtained from the break point in the γ *versus* log[surfactant] profile (Fig. 1). The constant value of surface tension at the cmc is called $\gamma_{cmc}$ and is a measure of the efficacy of the surfactant to populate the air/water interface in the form of a monolayer prior to micellization.

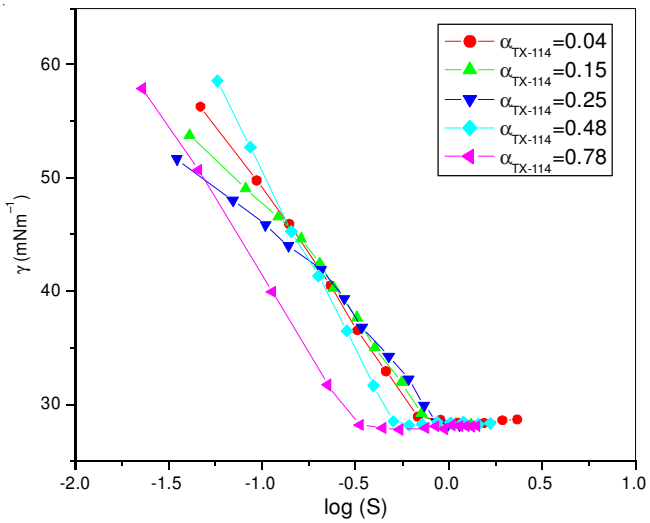



Fig. 1. Representative plots of surface tension *vs*. log [total surfactant concentration] at 25 ºC

The maximum surface excess values, at the air water interface, which comprises the surfactant concentration at the saturated surface and the average minimum surface area, were calculated using Gibbs adsorption isotherm[23-25], Eqns. 1 and 2

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

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

where R = 8.314 Jmol$^{-1}$ K$^{-1}$; $N_A$ is Avogadro number. Eqn. (1)

assumes that the mixture is a pseudo binary mixture with a concentration C of surfactant. The $\Gamma_{max}$ value is called the adsorption effectiveness and describes the adsorption tendency of surfactant molecules at the interface. The adsorption effectiveness is an important factor determining vital properties concerning foaming[26], wetting emulsification[27], solubilization[28], drug delivery[29] and biological activities[30].

The higher the, steeper is the approach to cmc and higher is the surface activity values of surface excess. So, TX-114 is the more surface active than that of imipramine hydrochloride. Table-1 shows that the TX-114 has less $A_{min}$, implying greater number density of TX-114 monomer at interface. The lower C value for TX-114 also indicates its enhanced surface activity. In the presence of polymer, $\Gamma_{max}$ values decreases for both the amphiphiles, so surface activity of both TX-114 and imipramine hydrochloride decreases with HPMC. These results also confirmed by the higher values of $A_{min}$ and C of both amphiphiles.

The molecular interaction parameters for mixed monolayers for two different amphiphiles at an interface were evaluated using the Rosen model[31]. Rosen model is used to evaluate the composition of the adsorbed monolayer formed by the two amphiphiles in the mixed system in the region of premicellar concentration. The interfacial mole fraction of the amphiphile at the mixed adsorbed film can be calculated iteratively form Rosen model solving the equation

$$\frac{[X^{\sigma 2}_1 \ln(C_{mix}\alpha_1 / C_1 X^{\sigma}_1)]}{(1-X^{\sigma}_1)^2 \ln[C_{mix}(1-\alpha_1)/C_2(1-X^{\sigma}_1)]} = 1 \quad (3)$$

where $C_{mix}$, $C_1$ and $C_2$ are the concentrations of the mixture, pure amphiphile 1 and 2, respectively, at a fixed $\gamma$ value, $\alpha_1$ is the stiochiometric mole fraction of surfactant (TX-114) in the solution. The $X^{\sigma}_1$ value was then used to evaluate the interaction parameter ($\beta^{\sigma}$) at the air/solution interface using

$$\beta^{\sigma} = [\ln(C_{mix}\ \alpha_1 / C_1 X^{\sigma}_1)]/(1-X^{\sigma}_1)^2 \quad (4)$$

The $\beta^{\sigma}$ and $X^{\sigma}_1$ values of the mixture are presented in Table-1. The negative value of $\beta^{\sigma}$ indicates synergistic interaction. Higher value of $X^{\sigma}_1$ compared to $\alpha_1$ indicated propensity of TX-114 to preferentially populate the interface as compared to the imipramine hydrochloride.

**Micellar interaction parameters:** For ideal mixtures, where the individual components are non-interacting, cmc of a mixture can be predicted using the Clint model[32,33], where the ideal cmc of a mixed surfactant solution ($cmc_{ideal}$) is given by

$$\frac{1}{cmc_{ideal}} = \sum_i^n \left(\frac{\alpha_i}{cmc_i}\right) \quad (5)$$

where $\alpha_i$ is the stoichiometric mole fraction of the ith component in the mixture and $cmc_i$ is the critical micellar concentration of the pure ith component under the similar experimental condition. The model is useful for comparison between ideal and nonideal mixtures. A lower experimental value of observed cmc ($cmc_{exp}$) for the mixture as reported in Table-2 signifies synergistic interaction among the components in the mixture. It will be seen that in all surfactant mixture the cmc value is lower than that of single imipramine hydrochloride. The cmc values of binary mixtures decrease gradually with increasing mole fraction of the TX-114 in solution, indicating the formation of mixed micelle due to a hydrophobic effect between ionic and nonionic amphiphilic hydrophobic chains. The nonionic surfactant molecules insert into the micelle of imipramine hydrochloride and the electrostatic repulsion between ionic head groups of imipramine hydrochloride is weakened. As a result, aggregation of imipramine hydrochloride molecules is advantageous. Analysis of the cmc as a function of net mole fraction $\alpha_1$ of component 1 (TX-114) in the mixed surfactant systems in terms of micellar composition ($X_1$) at the cmc, has been made in the light of Rubingh's equation[34]:

$$\frac{[X^2_1 \ln(cmc_{exp}\alpha_1 / cmc_1 X_1)]}{(1-X_1)^2 \ln[cmc_{exp}(1-\alpha_1)/cmc_2(1-X_1)]} = 1 \quad (6)$$

Based on regular solution theory, where $cmc_1$, $cmc_2$ and $cmc_{exp}$ denote the cmc values of the surfactants 1, 2 and mixed

TABLE-1
VARIOUS PHYSICOCHEMICAL PROPERTIES OF TX-114 + IMP MIXTURES AT THE INTERFACE IN THE ABSENCE AND PRESENCE OF HPMC AT 25 ºC

| $\alpha_{TX-114}$ | $C^{\sigma}$ (mM) | $X^{\sigma}_1$ | $\beta^{\sigma}$ | $f_1^{\sigma}$ | $f_2^{\sigma}$ | $\Gamma_{max}$ $10^7$ (mol $m^{-2}$) | $A_{min}$ (nm) | $\Pi$ |
|---|---|---|---|---|---|---|---|---|
| TX-114 + IMP | | | | | | | | |
| 0.0 | 37.200 | – | – | – | – | 7.90 | 210 | 23 |
| 0.04 | 0.105 | 0.68 | -11.47 | 0.308 | 0.0049 | 13.22 | 125 | 42 |
| 0.15 | 0.091 | 0.83 | -6.77 | 0.822 | 0.0094 | 9.26 | 179 | 42 |
| 0.25 | 0.067 | 0.9 | -7.19 | 0.930 | 0.0029 | 8.71 | 190 | 42 |
| 0.48 | 0.011 | 0.74 | -15.24 | 0.356 | 0.0002 | 18.54 | 89 | 42 |
| 0.78 | 0.020 | 0.89 | -10.90 | 0.876 | 0.0001 | 15.22 | 109 | 42 |
| 1.0 | 0.020 | – | – | – | – | 30.41 | 55 | 42 |
| TX-114 + IMP + HPMC | | | | | | | | |
| 0.0 | 0.479 | – | – | – | – | 2.64 | 630 | 24 |
| 0.04 | 0.105 | 0.57 | -17.57 | 0.038 | 0.0033 | 3.18 | 522 | 32 |
| 0.15 | 0.219 | 0.65 | -10.81 | 0.265 | 0.0103 | 1.61 | 1033 | 32 |
| 0.25 | 0.093 | 0.65 | -13.63 | 0.188 | 0.0031 | 2.16 | 768 | 35 |
| 0.48 | 0.059 | 0.68 | -14.82 | 0.219 | 0.0010 | 3.43 | 483 | 36 |
| 0.78 | 0.022 | 0.67 | -18.40 | 0.134 | 0.0002 | 5.73 | 289 | 36 |
| 1.0 | 0.190 | – | – | – | – | 1.29 | 129 | 27 |

TABLE-2
VARIOUS PHYSICOCHEMICAL PROPERTIES OF TX-114 + IMP MIXTURES OF BULK AT 25 ºC

| $\alpha_{TX-114}$ | $cmc_{exp}$ (mM) | $cmc_{ideal}$ (mM) | β | $X_1$ | $X_1^{ideal}$ | $f_1$ | $f_2$ |
|---|---|---|---|---|---|---|---|
| 0.0 | 47.20 | – | – | – | – | – | – |
| 0.04 | 1.16 | 5.89 | -8.29 | 0.61 | 0.88 | 0.283 | 0.045 |
| 0.15 | 1.08 | 1.73 | -4.55 | 0.77 | 0.96 | 0.785 | 0.067 |
| 0.25 | 0.84 | 1.05 | -3.72 | 0.85 | 0.98 | 0.919 | 0.067 |
| 0.48 | 0.50 | 0.55 | -3.27 | 0.92 | 0.99 | 0.979 | 0.062 |
| 0.78 | 0.31 | 0.34 | -4.87 | 0.93 | 0.99 | 0.976 | 0.014 |
| 1.0 | 0.34 | – | – | – | – | – | – |

system respectively. The ideal mole fraction ($X_1^{ideal}$) of TX-114 can be calculated to eqn. (7):

$$X_1^{ideal} = \frac{\alpha_1 cmc_2}{\alpha_1 cmc_2 + \alpha_1 cmc_1} \quad (7)$$

It is clear from the Table-2 that, $X_1$ is lower than that of $X_1^{ideal}$. This suggest a higher contribution of the IMP component to the mixed micelles than the ideal one and positive interaction in the mixed micellar phase. The interaction parameter, β, of mixed micelle formation given by

$$\beta = [In\ (cmc_{exp}\ \alpha_1/cmc_1X_1)/(1-X_1)^2 \quad (8)$$

β is an indicator not only of the degree of interaction between the two surfactants but also accounts for the deviation from ideality. A negative value of β implies an attractive interaction; the more negative its value, the greater the interaction. The values thus obtained for the binary amphiphilic system are presented in Table-2. The results show that β, although not constant, is negative throughout the concentration range with an average value of -4.94, suggesting strong synergism in the system. β is related to the activity coefficients of the surfactants within the micelle by

$$f_1 = \exp\ [\beta(1-X_1)^2] \quad (9)$$

$$f_1 = \exp\ [\beta(X_1)^2] \quad (10)$$

The $f_1$, $f_2$ values are less than unity, suggesting nonideality of mixed systems under investigation.

The surface tension plots of pure TX-114/IMP and their mixtures with HPMC are shown in Figs. 1 and 2, respectively. Obviously, the curves differ from each other. There are two distinct break points in the surface tension isotherm with HPMC and can be attributed to the occurrence of two kinds of aggregation processes. In the presence of polymer, the first break is close to that in pure water, can be regarded as the critical aggregation concentration (cac), whereas the second break is at least 2-3 times higher than first one and can be attributed to the polymer bound micelles (cmc). The two values of two-aggregation process for TX-114 + IMP + HPMC mixtures were calculated are listed in Table-3. The cac is understood to be the point at which the polymer and amphiphile to form mixed aggregates in the bulk. The aggregate take the form of amphiphile micelles associated with the polymer molecules, in a necklace formation (**Scheme-I**). In the case of amphiphile/nonionic polymer mixtures, significant interactions occur only after the concentration reaches its cac value. The free surfactant molecules continue to bind the polymer through adsorption until the state of saturation is reaches. It is believed that non-ionic polymer will change into a polyelectrolyte-like

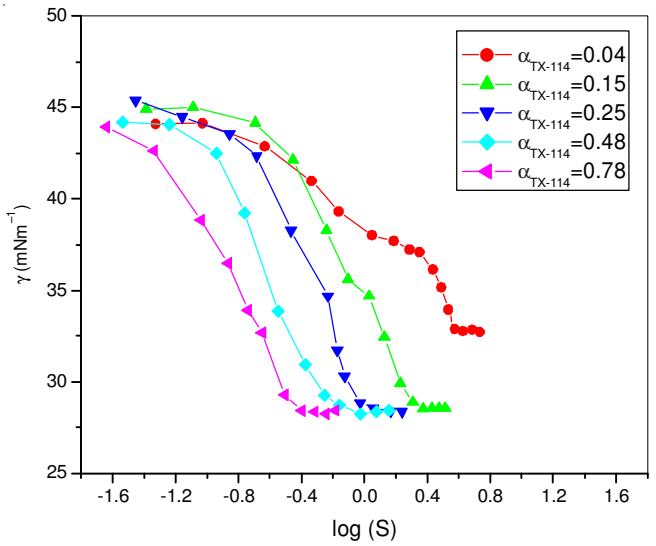
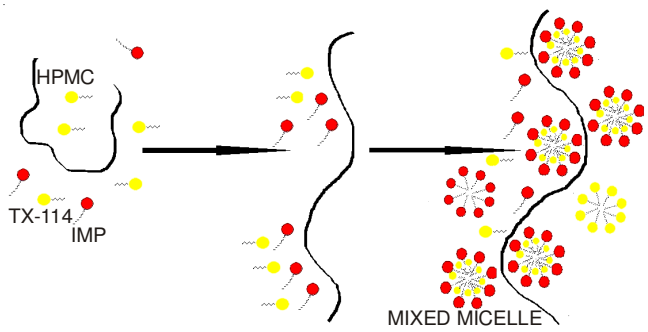



Fig. 2. Representative plots of surface tension *vs.* log [total surfactant concentration] in the presence of 0.1 wt. % HPMCat 25 ºC




**Scheme-I:** Scematic diagram describing the binding interactions between TX-114+IMP mixed system and HPMC chain

polymer when ionic amphiphile molecules are adsorbed onto the polymer *via* its hydrophobic tail. The electrostatic repulsions between ionic heads of the amphiphile molecules tend to change the way the polymer chains align with respect to other. HPMC is found to interact with both anionic and cationic surfactants as compared to the other nonionic polymers, interaction of which generally depends on the conditions of the interacting environment[35-37]. HPMC has an amphiphilic behavior and shows a considerable surface activity. It is already mentioned in previous text that the non-ionic micelles insert into IMP. IMP monomers aggregates on to the polymer chain as shown in the **Scheme-I**. In the presence of HPMC (0.1 w/v %) cac decreases. A decrease in the cac value is mainly credited to the interactions between the polymer and surfactant and this phenomenon is generally observed up to a great extent in

TABLE-3
VARIOUS PHYSICO-CHEMICAL PROPERTIES OF TX-114 + IMP MIXTURES AT BULK IN THE PRESENCE OF HPMC AT 25 ºC

| $\alpha_{TX-114}$ | $cac_{exp}$ (mM) | $cac_{ideal}$ (mM) | $cmc_{exp}$ (mM) | β | $X_1$ | $X_1^{ideal}$ | $f_1$ | $f_2$ |
|---|---|---|---|---|---|---|---|---|
| 0.0 | 25.30 | – | 66.07 | – | – | – | – | – |
| 0.04 | 1.04 | 3.05 | 3.71 | -5.81 | 0.64 | 0.88 | 0.471 | 0.092 |
| 0.15 | 0.78 | 0.89 | 2.34 | -2.59 | 0.88 | 0.97 | 0.963 | 0.134 |
| 0.25 | 0.42 | 0.54 | 1.44 | -3.86 | 0.84 | 0.98 | 0.905 | 0.065 |
| 0.48 | 0.23 | 0.29 | 0.95 | -4.96 | 0.87 | 0.99 | 0.919 | 0.023 |
| 0.78 | 0.15 | 0.18 | 0.39 | -5.97 | 0.9 | 0.99 | 0.942 | 0.008 |
| 1.00 | 0.13 | – | – | – | – | – | – | – |

polyelectrolyte's and oppositely charged surfactants[38]. The interaction between the two entities up to a certain extent which is mainly due to the presence of hydrophobic and nonpolar/ionic portions in these molecules rather than the strong electrostatic interaction between the polyelectrolytes and oppositely charged surfactants[39]. Furthermore, hydrophobicity of both HPMC and amphiphiles also plays an important role in the interaction causing the cac to decrease like in polyelectrolytes and oppositely charged surfactants systems.

A pseudophase thermodynamic model can be applied to evaluate the no ideality at cac in the presence of HPMC, since the variation of cac is expected to be similar to that in the case of pure water. For the present TX-114 + IMP + HPMC ternary system, ideal behavior is expected, since the interaction between the monomers in the mixed micelles are considered to be similar, as in the case of homomicelles and the activity coefficients should be taken as unity. A comparison between ideal cac ($cac^*$) and experimental cac ($cac_{exp}$) values shows that ideal mixing behavior. Inspection of β values in Table-3 show that the β value in the presence of HPMC are negative and slightly lower than ($\beta_{av}$ = -4.584) in the absence of HPMC. This enforces the idea of decreasing synergism in the mixed systems in the presence of HPMC.

**Thermodynamics of micellization and interfacial adsorption phenomena:** Considering the negligible degree of counterion dissociation of surfactants, the standard free energy of micellization ($\Delta G_m$) is calculated from regular solution theory using[40]

$$\Delta G_m = RT \ln X_{cmc/cac} \quad (11)$$

where $X_{cmc/cac}$ is the cmc or cac of the mixture in mole fraction unit. The $\Delta G_m$ values (Table-4) reveal that all the binary systems have considerable spontaneity of micellization with and without HPMC. The standard free energy of micellization is translated into the standard free energy of adsorption at air water interface using the eqn[41, 42].

$$\Delta G_{ad} = \Delta G_m - \pi/\Gamma_{max} \quad (12)$$

where π is surface pressure at cmc. The magnitude of $\Delta G_{ad}$ is more than the $\Delta G_m$ showing that the latter to be less spontaneous due to the hydrophobicity of surfactants, which lead them toward air/water interface. From this, it is concluded that the micelle formation secondary and less spontaneous compared to adsorption. The adsorption tendency of TX-114 + IMP mixed system is higher in the presence of HPMC due to strong interaction between imipramine hydrochloride and hydroxypropyl methyl cellulose.

The synergism in the mixed adsorbed monolayer formation can also be quantified in terms of another thermodynamic quantity, known as free energy ($G_{min}$)

$$G_{min} = A_{min}\gamma_{cmc}N_A \quad (13)$$

where, $\gamma_{cmc}$ being the surface tension of the surfactant system at equilibrium. $G_{min}$ not only contains contribution of $A_{min}$ but also, $\gamma_{cmc}$ which affects mixed monolayer formation, hence synergism. It may be defined as work needed to make a surface area per mole or free energy change accompanied by transition from the bulk phase to the surface phase of solution. The lower the value of free energy, the more thermodynamically a stable surface is formed or the surface activity is attained, which is a measure of evaluation of synergism. Since the obtained values

TABLE-4
VARIOUS THERMODYNAMIC PARAMETERS OF TX-114 + IMP MIXTURES IN THE ABSENCE AND PRESENCE OF HPMC AT 25 ºC

| $\alpha_{TX-114}$ | $\Delta G_m$ (kJ/mol) | $\Delta G_{ad}$ (kJ/mol) | $G_{min}$ (kJ/mol) | $\Delta G_{ex}$ (kJ/mol) |
|---|---|---|---|---|
| TX-114 + IMP | | | | |
| 0 | -34.63 | -63.73 | 5.95 | – |
| 0.04 | -43.81 | -75.57 | 2.12 | -4.97 |
| 0.15 | -43.98 | -89.34 | 3.02 | -2.03 |
| 0.25 | -44.61 | -92.84 | 3.21 | -1.19 |
| 0.48 | -45.88 | -68.53 | 1.51 | -0.61 |
| 0.78 | -47.06 | -74.65 | 1.84 | -0.79 |
| 1 | -47.44 | -61.25 | 0.92 | – |
| TX-114 + IMP + HPMC | | | | |
| 0 | -36.17 | -127.19 | 17.44 | – |
| 0.04 | -44.08 | -144.77 | 11.96 | -3.37 |
| 0.15 | -44.79 | -243.98 | 23.65 | -0.68 |
| 0.25 | -46.32 | -208.25 | 16.19 | -1.30 |
| 0.48 | -47.82 | -152.62 | 9.89 | -1.41 |
| 0.78 | -48.88 | -111.63 | 5.93 | -1.35 |
| 1 | -49.09 | -70.05 | 3.34 | – |

are lower in magnitude (Table-4), it can be inferred that thermodynamically stable surfaces are formed with synergistic interaction.

The excess free energy of micellization, $\Delta G_{ex}$

$$\Delta G_{ex} = [X_1 \ln f_1 + (1-X_1) \ln f_2]RT \quad (14)$$

The negative values suggest that the mixed micelles formed are more thermodynamically stable than the micelles formed from individual surfactants.

## Conclusion

Mixed micellization study of TX-114 + imipramine hydrochloride in the absence and presence of neutral polymer (HPMC), has been studied using surface tensiometry. The cmc/cac values of binary mixtures are less than the ideal values obtained by the use of Clint equation. The interaction parameters in micelle as well as at interface are negative, indicating synergistic interaction. Hydrophobicity plays an important role in the interaction as revealed by the comparative interaction of nonionic polymers with imipramine hydrochloride. The magnitude of $\Delta G_{ad}$ is more than the $\Delta G_m$ showing that the latter to be less spontaneous due to the hydrophobicity of surfactants, which lead them toward air/water interface. From this, it is concluded that the micelle formation secondary and less spontaneous compared to adsorption. The adsorption tendency of TX-114 + imipramine hydrochloride mixed system is higher in the presence of HPMC due to strong interaction between imipramine hydrochloride and hydroxypropyl methyl cellulose.

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