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Study of micellar behaviour of SDS and CTAB in aqueous medium containing Trammadol Hydrochloride - A narcotic analgesic drug

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ABSTRACT

Conductance and Viscosity studies of anionic surfactant SDS (Sodium dodecyl sulfate) and cationic surfactant CTAB (Cetyltrimethylammonium bromide) have been carried out in aqueous solutions of Trammadol Hydrochloride (0.001 and 0.01M) in the temperature range 20 – 40°C. From conductance measurements, the critical miceller concentration (CMC's) of SDS and CTAB has been determined in the above said aqueous Trammadol Hydrochloride solutions. From CMC data, various thermodynamic parameters viz. standard enthalpy change for micellization (ΔH^o_m), standard entropy change for micellization (ΔS^o_m) and standard free energy change for micellization (ΔG^o_m) have been evaluated. The work has also been extended to include the viscosity studies of SDS and CTAB in aqueous solutions of drug in order to calculate relative viscosity (η_r). All these parameters have been discussed in terms of drug – drug, drug – solvent and drug – surfactant interactions as a consequence of various electrostatic and hydrophobic interactions.

KEYWORDS

CMC;
Thermodynamic parameters;
Drug;
Surfactants.

INTRODUCTION

Drug molecules[1] are chemical entities characterized by the presence of different groups such as polar (hydrophilic) and non-polar (hydrophobic) groups which are responsible for their therapeutic value. The drug action thus can be considered as being governed by the nature of interactions that drug molecules undergo in solution depending on the functional groups. A systematic knowledge of solution behaviour[2-5] of drug thus can be of great significance to understand their physiological action. Surfactants are amphiphilic molecules consisting of polar (hydrophilic) and non-polar (hydrophobic) parts. These molecules are found to be of commercial importance as their amphiphilic structure is responsible for concentrating at interfaces or undergoing aggregation i.e. micellization. This micellization or association phenomena occurs as a result of delicate balance between various repulsive and attractive forces of species present in the solution. Some insights into these complicated processes may be obtained from studies such as micellization behaviour of surfactants in the presence of drug. Incidently there exist only a few studies[6] as demonstrating the effect of drug on

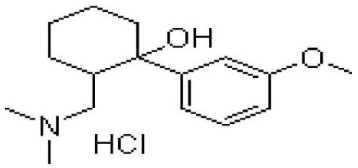
micellization of surfactant.

It is therefore, proposed to investigate the effect of Trammadol Hydrochloride, a narcotic-analgesic drug on micellization of an anionic surfactant Sodium dodecyl sulfate (SDS) and cationic surfactant Cetyltrimethylammonium bromide (CTAB) in aqueous solutions of furosemide covering a wide range of experimental condition i.e. temperature (20 – 40°C) at two different aqueous solutions of Trammadol Hydrochloride i.e., 0.001M and 0.01M. As our main tool, we have used conductometric studies. Precise viscosity measurements were also carried out to support the information obtained from the conductometric studies in probing the structural changes in different types of solution systems[2-8]. However, it is important to mention that this part of the study was carried out only at five different temperatures in the above listed aqueous solutions of Trammadol Hydrochloride (TM). Tramadol hydrochloride[7] is a centrally-acting synthetic opioid analgesic medicine which is used in relieving moderate to severe pain. It works by affecting chemicals in the brain and nervous system which are involved in the sensation of pain. Therefore by optimizing its concentration there is scope of improvement of its pharmacokinetics.

EXPERIMENTAL

Ordinary tap water of conductivity range 3 - 5 X 10^{-6} S cm^{-1} at 25°C was distilled with the help double distillation unit. The water so obtained has conductance value ≈1-4 X 10^{-7} S cm^{-1} at 25°C and pH in the range 6.5 - 7.0. Water of these specifications was used for all experiments.

Sodium dodecyl sulfate (SDS) (Biochemical grade from BDH) were used as received. Cetyltrimethylammoniumbromide (CTAB) (AR grade and purity > 99%) was also obtained from s.d. Fine - Chem..Ltd. Drug used is Trammadol hydrochloride (+/-) cis-2-((Dimethylamino) methyl)-1-(3-methoxyphenyl) cyclohexanol hydrochloride. It is supplied by Cipla Ltd in capsules dosage form and is used as such. The drug has the following structure:



Conductance measurement were carried out with a calibrated digital conductivity meter (CON 150, Merck). These were carried out in a Harco supplied water thermostat having temperature maintaining accuracy of ±0.05°C. Specific conductance (κ) of TM solution at concentration (0.001M and 0.01M) in case of SDS and 0.001M in case of CTAB have been measured at five different temperatures i.e. 20,25,30,35 and 40°C with the help of conductivity meter.

Viscosity measurements were carried out with a jacketed Ostwald viscometer supplied by Harco limited. The precision achieved in viscosity measurement was ± 0.01%. The viscosities of SDS (0.001M and 0.01M) and CTAB (0.001M) have been measured in aqueous Tramadol hydrochloride solutions at different temperatures i.e. 20-40°C.

DISCUSSION

Conductance studies

Micellization behaviour of SDS and CTAB has been traced to interpret drug-surfactant interactions. The dependence of κ on concentration of surfactants (SDS and CTAB) in aqueous solution of (TM) has been presented in Figure 1-3. It is clear from these graphs that, κ increases almost linearly with [SDS] and [CTAB] with definite break points. κ is also measured at higher concentration of drug i.e. 0.01 M in SDS, where no break points are observed Figure 3.

The break points were quite significant as observed in Figure 1,2, therefore critical micellar concentrations (CMC) were evaluated for SDS as well as for CTAB. The CMC values in case of SDS, a negatively charged surfactant, are found in the range (5- 6 mM), which are much lower than the CMC of aqueous SDS solution (8 mM). However, a contrasting behaviour has been obtained in case of CTAB, a positively charged surfactant (with CMC=0.9 mM in water) for which the CMC values are drastically increased in the presence of TM (6.0- 7.0 mM). It has been found in literature[10] that maximum solubility of TM solution is observed in aqueous-micellar solutions of cationic surfactants, because

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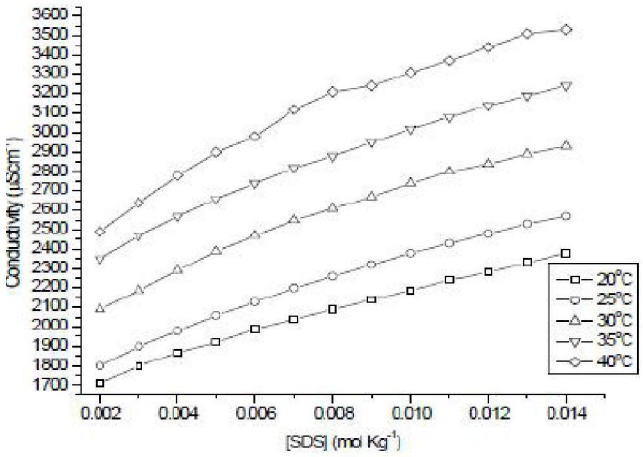

Figure 1 : Specific conductance as a function of [SDS] in 0.001M aqueous solution of furosemide at different temperatures

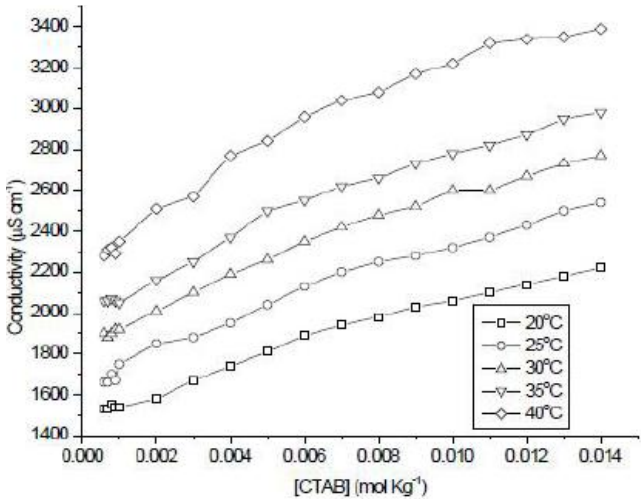

Figure 2 : Specific conductance as a function of [CTAB] in 0.001M aqueous solution of furosemide at different temperatures

of formation and solubilization of ion-pairs between TM and surfactant cations. Further, the solubilisation of this drug is highly specific to type of surfactant molecules which further affect the solubilization of drug and thus delaying micellization as shown by much higher CMC values of CTAB in the presence of drug. However, micellization of SDS in the presence of TM solution seems to be facilitated as it has least tendency for solubilisation of the drug and thus the process of micellization is achieved at a lower concentration[8]. varun

Thermodynamics of micellization of SDS and CTAB in aqueous solutions of Trammadol Hydrochloride

In order to derive further information about drug-

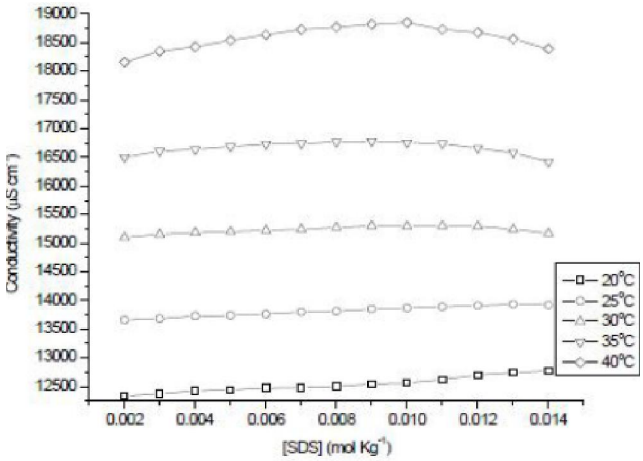

Figure 3 : Specific conductance as a function of [SDS] in 0.01M aqueous solution of Tramadol Hydrochloride at different temperatures

surfactant interactions from these experimental data, various thermodynamic parameters of micellization have been calculated and examined. The standard free energy change for micellization is given by[9,10] varun.

$$\Delta G^{o}_{m} = RT \ln (X_{CMC}) \quad (1)$$

where X_{CMC} was calculated as: X_{CMC} = CMC mol dm^{-3} of surfactant / (CMC of Surfactant + concentration of drug + 55.6). R is gas constant and T is temperature in Kelvin.

The standard enthalpy change for micellization, ΔH^{o}_{m} is obtained through a classical van't Hoff type relation given by[11].

$$\Delta H^{o}_{m} = -RT^{2} [d \ln X_{CMC} / dT] \quad (2)$$

where d ln X_{CMC} / dT is the slope of straight line obtained by plotting ln X_{CMC} against T

The standard entropy change for micellization, ΔS^{o}_{m} for SDS and CTAB was determined from eqn.[9,11].

$$\Delta G^{o}_{m} = \Delta H^{o}_{m} - T \Delta S^{o}_{m} \quad (3)$$

The negative values of ΔH^{o}_{m} and ΔG^{o}_{m} and positive values of ΔS^{o}_{m} values are indicative of drug – surfactant interactions. Figure 4-5 however, represent the dependence of these thermodynamic parameters as a function of temperature in Kelvin. The decrease in the values of these parameters with increase in temperature reflect the decrease of hydrophilic hydration of surfactant head group as well as the hydrophilic part of drug, which further facilitates the interaction of charged part of surfactants and drug electrostatically to each other in case of CTAB and for SDS they interact hydrophobically and favour micellization as anionic sur-

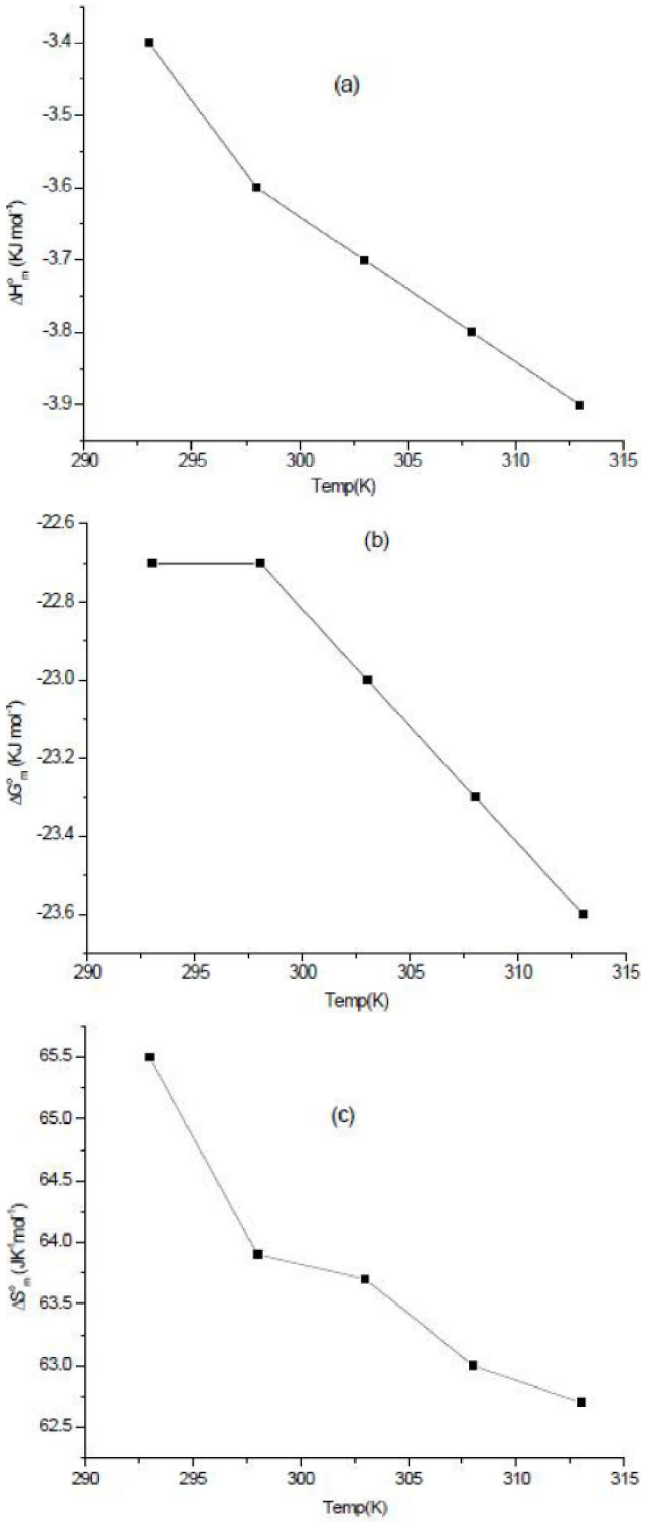

Figure 4 : Variation of thermodynamic parameters a) ΔH^{o}_{m} (kJ mol^{-1}), b) ΔG^{o}_{m} (kJ mol^{-1}), c) ΔS^{o}_{m} (JK^{-1} mol^{-1}) of SDS as a function of temperature in 0.001M aqueous solution of Tramadol Hydrochloride

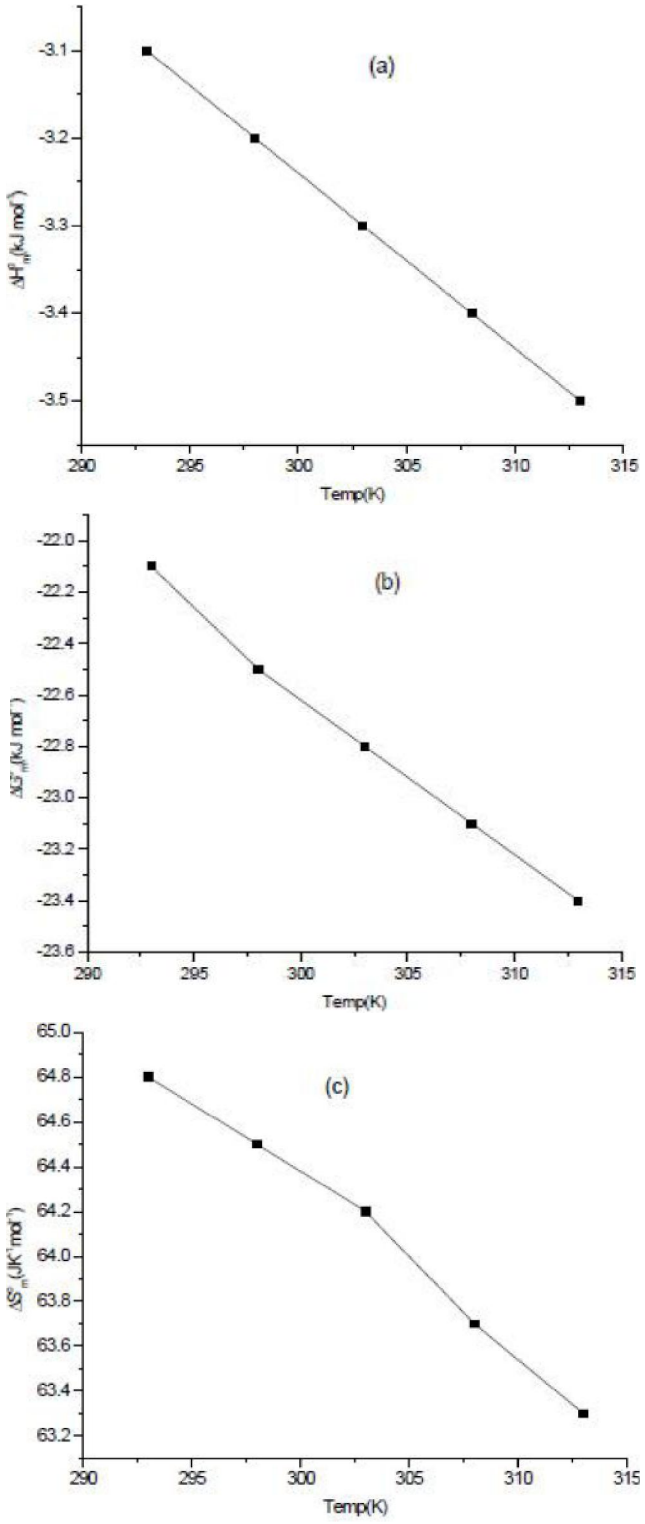

Figure 5 : Variation of thermodynamic parameters a) ΔH^{o}_{m} (kJ mol^{-1}), b) ΔG^{o}_{m} (kJ mol^{-1}), c) ΔS^{o}_{m} (JK^{-1} mol^{-1}) of CTAB as a function of temperature in 0.001M aqueous solution of Tramadol Hydrochloride

factants are known for stronger hydrophobic interactions as compared to cationic surfactant.[12,13].

Viscosity studies

The present study was further extended to include

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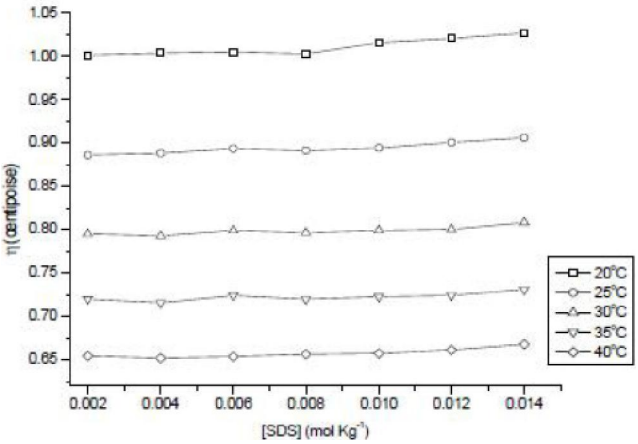

Figure 6 : Viscosity as a function of [SDS] in 0.001M aqueous solution of Tramadol Hydrochloride at different temperatures

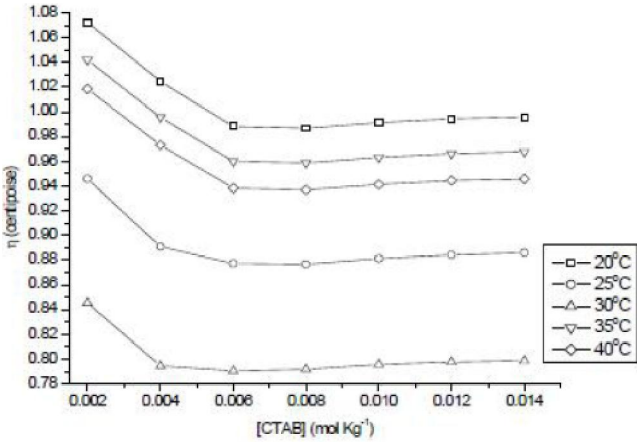

Figure 7 : Viscosity as a function of [CTAB] in 0.001M aqueous solution of Tramadol Hydrochloride at different temperatures

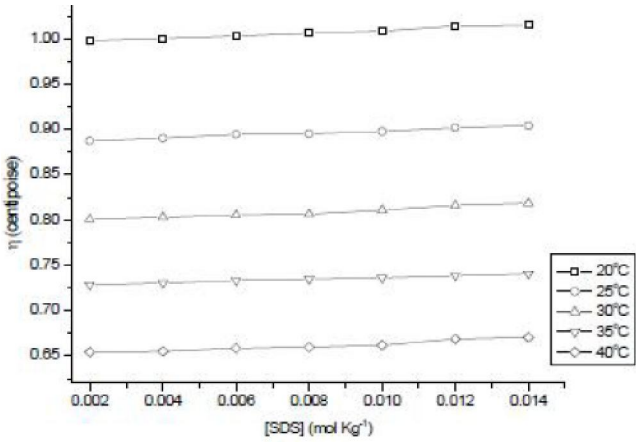

Figure 8 : Viscosity as a function of [SDS] in 0.01M aqueous solution of Tramadol Hydrochloride at different temperatures

the viscosity measurements of SDS and CTAB in aqueous solutions of furosemide. The concentration dependence of viscosity, η of SDS and CTAB has been presented in Figure 6-8.

TABLE 1 : CMC x10^3 values for SDS and CTAB in 0.001M aqueous solution of TM

CMC X 10^3		
T (K)	**SDS**	**CTAB**
293	5	6.4
298	6	6.5
303	6	6.6
308	6.3	6.8
313	6.4	7.0

It is clear from these figures that η changes almost linearly with [SDS] whereas a non-linear part is observed in case of CTAB upto 6mM. These observations are also supported by conductivity studies. Also the relative viscosity i.e. $\eta_r = \eta/\eta_o$, gives an idea about the structural changes in the solvent system showing almost similar behaviour as in case of η.

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