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ORIGINAL ARTICLE

Micellization, interaction and thermodynamic study of butylated hydroxyanisole (synthetic antioxidant) and sodium dodecyl sulfate in aqueous-ethanol solution at 25, 30 and 35 °C

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Abstract Surfactants are found to enhance the diffusion significantly depending on hydrophobic/hydrophilic group lengths and the structure of the surfactant molecule. Aggregation properties of sodium dodecyl sulfate (SDS) in the presence of butylated hydroxyanisole (synthetic antioxidant), at a range of temperatures (25, 30 and 35 °C) have been measured by the conductometric study in aqueous-ethanolic composite solution. The experimental data of aqueous-ethanolic solutions as a function of SDS concentration ranging from 1 to 14 mM dm^{-3} show the presence of inflexion points indicating micellization and interaction mechanisms. Effect of temperature was also observed in increasing the CMC (Critical Micelle Concentration) in the narrow composition. From the CMC values as a function of temperature, various thermodynamic parameters have been evaluated viz: (a) the standard enthalpy change (ΔH°_{m}), (b) standard entropy change (ΔS°_{m}), and (c) standard Gibbs energy change (ΔG°_{m}). The results showed that the presence of alcohol, as well as the composition of water + ethanol may have effect on thermodynamic parameters. The variation in these parameters with the concentration of surfactant or with the change in temperature suggests the manifestation of hydrophobic interactions in the studied system.
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1. Introduction

The knowledge of molecular mechanism of drug–membrane interaction is not only of theoretical significance, but also of potential practical implications (Xu et al., 2002). Biomembranes play vital functions besides structural roles like, control of the passage of selected compounds thus maintaining the biochemical integrity of cytosol; communication, allowing

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the exchange of information between the extra and intracellular phase; biochemical-active surface, due to occurrence of associated interactive processes studying the molecular events occurring on biomembrane, as well as the multiple interactions with bioactive compounds such as drugs which are of paramount importance to enhance our knowledge. Surfactants have been of tremendous scientific importance because of their many promising applications in detergents, cosmetics, material fabrication, and drug delivery etc. (Herbette et al., 1991; Seydel et al., 1994; Lee et al., 2009). The main property of surfactant systems is that their aggregation phenomena arise from various non-covalent interactions (such as ππ stacking, H-bonding, van der Waals interactions) operating at the molecular level (Rosen, 2004; Xu et al., 2010). The solubility of an organic compound, which is insoluble or sparingly soluble in water, is enhanced by the addition of surfactants in aqueous solution (McBain and Hutchinson, 1955; Elworthy et al., 1968). A number of investigations have been carried out to understand the phenomenon of solubilization by surfactant solutions (Ceraulo et al., 2006; Mugesh et al., 2001; Craig, 1934; Palma et al., 2003). One of the main interest concerns the extent to which a particular compound can be solubilized in a given surfactant solution at a specified concentration. The other important aspect is to know the regions where the solubilizate molecules are located within the micelles.

However, butylated hydroxyanisole (BHA) is a synthetic antioxidant available in the form of two isomeric organic compounds (Fig. 1), 2-*tert*-butyl-4-hydroxyanisole and 3-*tert*-butyl-4-hydroxyanisole. BHA is primarily used as an antioxidant and preservative in food, food packaging, and animal feed, cosmetics, rubber, and petroleum products (Sacchez-Gallego et al., 2011; Hamid et al., 2010). BHA is also commonly employed in medicines as additive, such as isotretinoin, lovastatin, and simvastatin, among others which made us to think over their aggregation behavior. 2-*tert*-Butyl-4-hydroxyanisole (a) form has been undertaken for the same studies after observing its physical properties such as insolubility in water, freely soluble in ethanol, methanol, propylene glycol, soluble in fats and oils etc. Knowledge of interactions involving surfactants is important to understand how they function in the biological system. The complete characterization of any binding interaction requires a quantification of affinity, number of binding sites and the thermodynamics. The force that drives thermodynamic data, specifically enthalpy change (ΔH°_{m}) and Gibbs free energy change (ΔG°_{m}), reveals the complex formation and mechanism of action at the molecular level. Considering the eminent industrial and biological importance of surfactant and BHA, the present work was undertaken with the primary aim of studying the inflexion point with aggregation behavior of the SDS with varying aqueous alcoholic (Ethanol) compositions at different temperatures.

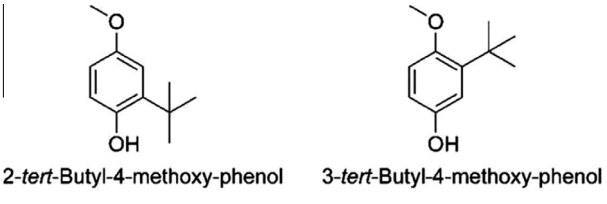
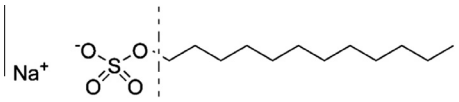


Figure 1 Structure of isomeric forms of BHA.

2. Experimental

2.1. Apparatus and material

Ordinary tap water of conductivity $(3–5)\times10^{-6}$ S cm^{-1} at 25 °C was distilled with the help of a Double distillation unit (Harco make). The water so obtained had a conductivity of $\approx(1–4)\times10^{-7}$ S cm^{-1} at 25 °C and pH in the range 6.5–7.0.



SDS (Sodium dodecyl sulfate)

Figure 2 Structural representation of head and tail portions of SDS.

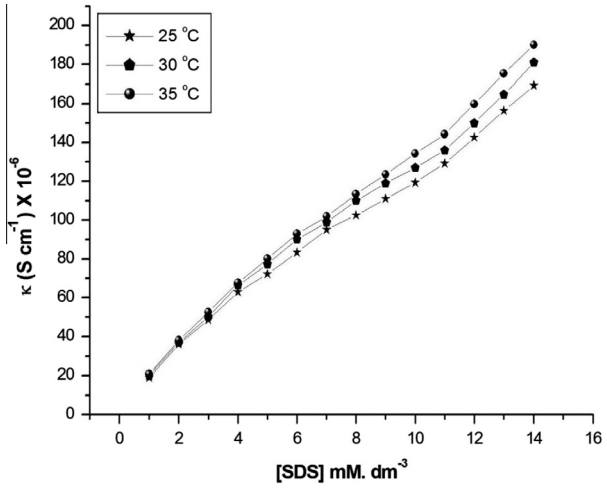


Figure 3 Specific conductivity as a function of [SDS] in 0.03 mol dm^{-3} solution at different temperatures in 100% ethanol composition.

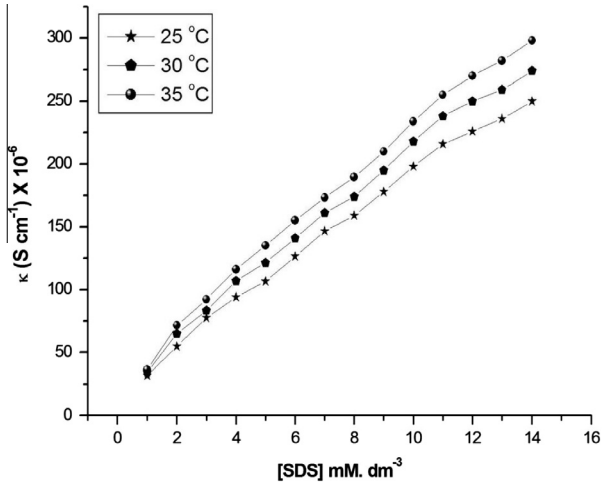


Figure 4 Specific conductivity as a function of [SDS] in 0.03 mol dm^{-3} solution at different temperatures in 40% ethanol composition.

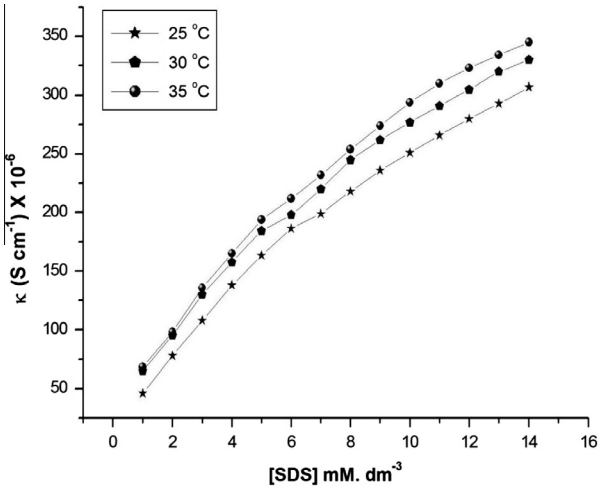


Figure 5 Specific conductivity as a function of [SDS] in 0.03 mol dm^{-3} solution at different temperatures in pure water.

Water thus purified was used for all experiments. Sodium dodecyl sulfate (SDS) (Fig. 2) and butylated hydroxyanisole (AR grade and purity >99%) were obtained from Merck Chemicals Ltd. Conductometric measurements were carried out with a calibrated digital conductivity meter (Cyber Scan CON 510, Merck). These were performed in a high precision water thermostat (Harco Make) having a temperature control accuracy of ±0.05 °C. The specific conductivities (κ) of BHA (concentration 0.03 mol dm^{-3}) solutions at a concentration range of 1–14 mM dm^{-3} of SDS have been measured at three different temperatures (i.e. 25, 30 and 35 °C).

3. Result and discussion

3.1. Conductivity study; determination of CMC

The aggregation behavior of SDS has been evaluated to understand BHA–SDS interactions. Specific conductance (κ) was found to be concentration dependent on SDS (anionic surfactant) in aqueous ethanolic solution of butylated hydroxyanisole. Definite inflexion points were obtained suggesting that κ is concentration and temperature dependent, which increases with the amount of SDS added as well as with the rise in temperature (Figs. 3–5). From these break/inflexion points on the plots, critical micellar concentrations (CMC) were evaluated for SDS as reported in Table 1. The micellization caused by SDS in pure aqueous solution with butylated hydroxyanisole was found to be lower in comparison to its standard value (8 mM dm^{-3}). This is due to the presence of a bulkier moiety as *ter*-butyl substitution at position-2 and moreover hydroxy group at position-1 contributing eminently (Fig. 6) for better interaction and therefore causing micellization much earlier. Lowering of repulsion between the surfactant head group and also the hydrophobic nature of CH_3^+ of BHA must have provided surface for the micellization. Thus, the extra hydrophobicity offered by BHA seems to reduce CMC values of SDS. However, an increase in CMC with raising temperature could be related to the increase of thermal motion of such hydrophilic (ethanol + water) groups and their solubility which favors micellization.

3.2. Thermodynamic study

In order to attain further information regarding antioxidant–surfactant interactions from these experimental data, various thermodynamic parameters of micellization have been calculated and examined. The standard Gibbs free energy change for micellization is given by Eq. (1) (Abuin et al., 1997; Ruso et al., 1999).

$$\Delta G_m^\circ = RT\ln(X_{CMC}) \quad (1)$$

where the mole fraction at which the CMC occurs is X_{CMC} = {CMC of surfactant/(CMC of surfactant + concentration of drug + 55.55)} with concentrations in units of mM dm^{-3}, R is the gas constant, and T is temperature in kelvin. The standard enthalpy change for micellization, ΔH_m° is obtained through Eq. (2) (Del et al., 1995)

Table 1 Thermodynamic parameter data – CMC, ΔH_m°, ΔG_m°, and ΔS_m° values of different compositions at three different temperatures.

% Composition (ethanol + water)	Temperature (°C)	CMC (10^3)	ΔH_m° (kJ mol^{-1})	ΔG_m° (kJ mol^{-1})	ΔS_m° (kJ mol^{-1} K^{-1})
100	25	5.5	−0.10393	−0.38760	0.01134
	30	6.6	−0.14965	−0.42725	0.00925
	35	7.0	−0.20369	−0.48450	0.00802
80	25	6.5	−0.03637	−1.88185	0.07381
	30	6.7	−0.05238	−2.25066	0.07327
	35	7.0	−0.07129	−2.61303	0.07262
60	25	7.3	−0.03637	−1.85773	0.07285
	30	7.5	−0.05238	−2.22253	0.07233
	35	7.9	−0.07129	−2.57784	0.07161
40	25	5.7	−0.04157	−1.90915	0.07470
	30	5.9	−0.05986	−2.28238	0.07408
	35	6.2	−0.08148	−2.64834	0.07333
20	25	6.4	−0.08834	−1.88507	0.07187
	30	6.6	−0.12720	−2.25441	0.07090
	35	7.6	−0.17314	−2.58910	0.06902
0 (H_2O)	25	6.0	−0.05716	−1.89849	0.07365
	30	6.4	−0.08231	−2.26209	0.07265
	35	6.7	−0.11203	−2.62577	0.07182

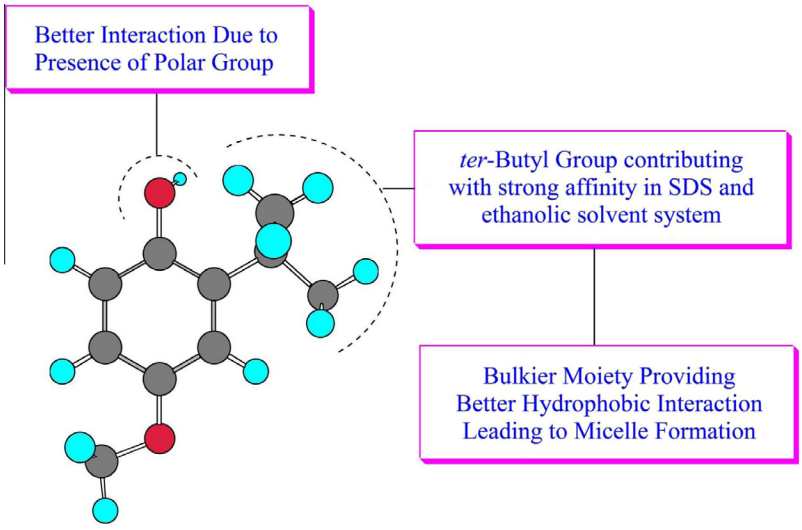


Figure 6 Overview of different substitutions of BHA.

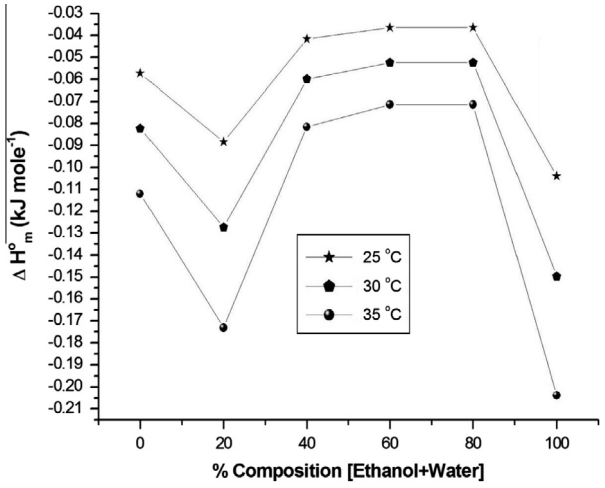


Figure 7 ΔH_m° (kJ mol^{-1}) of SDS as a function of temperature in % composition [ethanol + water].

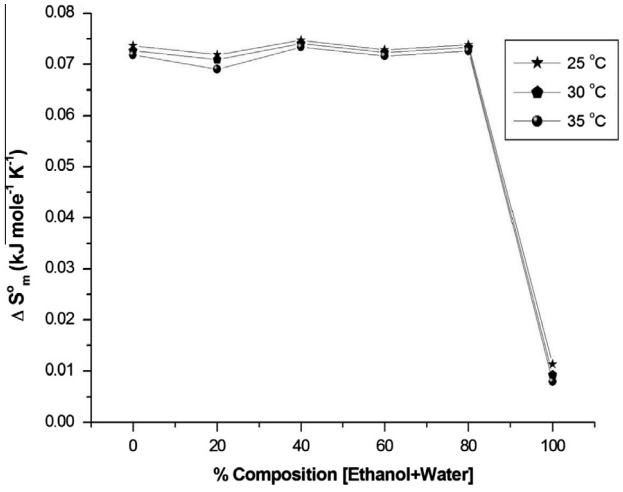


Figure 8 ΔS_m° (kJ mol^{-1} K^{-1}) of SDS as a function of temperature in % composition [ethanol + water].

$$\Delta H_m^\circ = -RT^2[d\ln(X_{CMC})/dT] \quad (2)$$

where $d\ln(X_{CMC})/dT$ is the slope of the straight line obtained by plotting ln X_{CMC} against temperature. The standard entropy changes ΔS_m°, were determined from Eq. (3) (Chauhan et al., 2007)

$$\Delta G_m^\circ = \Delta H_m^\circ - T\Delta S_m^\circ \quad (3)$$

The negative values of ΔH_m° and ΔG_m° and positive values of ΔS_m° are indicative of BHA–surfactant interactions as presented in Table 1. Negative values of ΔH_m° (Fig. 7) showed that the process of solubilization of BHA and the interaction with SDS is exothermic within the system, thus suggesting strong interactions between BHA and SDS. These interactions were found to be maximum at 20% ethanol, showing minima and at 100% ethanol (min. value), as shown in Fig. 7. This is due to BHA getting solubilized in SDS and located near the outer surface of micelle where the negatively charged head group of

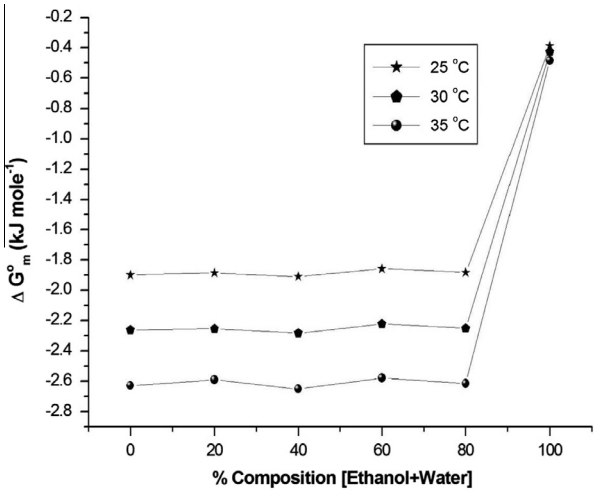


Figure 9 ΔG_m° (kJ mol^{-1}) of SDS as a function of temperature in % composition [ethanol + water].

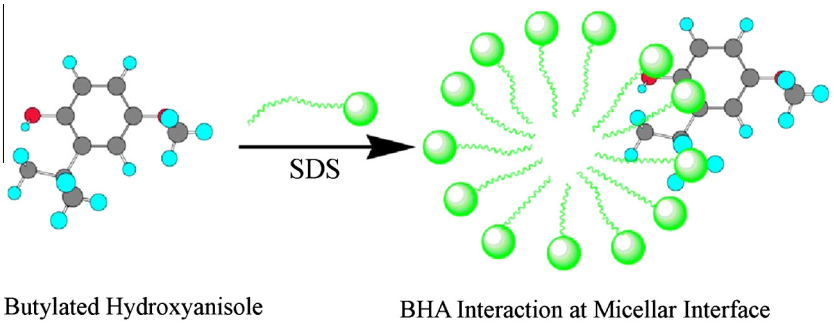


Figure 10 Proposed hypothetical model of BHA interaction.

surfactant and polar/bulkier group of BHA exist. However, the presence of ethanol component can interact by dipole–dipole or ion–dipole interactions (Dubey, 2011), whereas in water; polar groups are hydrated, the intermolecular aggregation of drug molecules through their hydrophobic parts is expected to occur in a way analogous to micellization, favoring their limited aqueous solubilization and this aggregating tendency is affected with the addition of non-aqueous components (Sharma et al., 2008). It is because of the presence of ethanol with small hydrophobic group accommodated in water structure substitutionally while larger hydrocarbon groups stays interstitially in solvent system, leading to enhancement of structure (BHA–Surfactant) (Chauhan et al., 2007). Positive ΔS°_{m} values indicated that entropy is dominating over the micellization process within the system (Fig. 8). This observation can be explained as a re-organization of water molecules at the micellar solubilization of ethanol. Such an effect would indeed cause a smaller decrease in entropy and enthalpy which is in good agreement with the observed values of ΔH°_{m} and ΔS°_{m} as reported in Table 1. A decrease in entropy with an increase in temperature is because of weakening of intermolecular bonds with temperature. However water is caging around non-polar solutes, a distorted structure is formed which enabled the maintenance of hydrogen bonds that water cannot form with the hydrophilic core (Vassili et al., 2001). So, in this process of rearrangement, entropy decreases due to the exothermic character of the process.

It has been observed that ΔG°_{m} values (Gibbs free energy) are negative and the magnitude remains practically constant over the entire ethanol composition range (Fig. 9) but for pure ethanol higher values has been observed. This observation indicated that BHA is solubilized preferentially in the micellar aggregates. A decrease in the magnitude of ΔG°_{m} with an increase in temperature clearly reveals that hydrophobic effects decrease with an increase in temperature which in turn shows the penetration of these solubilizates into the micelle becomes less favorable at higher temperatures. From the calculated thermodynamic parameters it has been depicted that BHA resides in the outer surface or interface of the micelle as shown in Fig. 10.

4. Conclusion

It can be concluded from the conductivity and thermodynamic results that the mixture formed in different compositions of BHA and SDS is an ideal system, shown through the variation in aggregation behavior and other obtained values. Micellar interactions of SDS in aqueous-ethanol solutions of BHA by conductometric and thermodynamic analysis provided valuable information regarding structural changes in the constituent molecules of BHA as well as surfactant which are further characterized by hydrophobic interaction as well as hydrophobic hydration. The decrease in CMC in the presence of BHA is due to the establishment of additional hydrophobic interactions between hydrophobic parts of surfactant and BHA. The calculated thermodynamic parameter $|T\Delta S^{\circ}_{m}|$ was found larger than $|\Delta H^{\circ}_{m}|$ suggesting micellization is entropy driven. Moreover, negative enthalpy (ΔH°_{m}) and Gibbs free energy (ΔG°_{m}) values indicated that the system is feasible and is of exothermic nature while positive ΔS°_{m} values interpret that the driving force for micellization is entropic i.e. the tendency of hydrophobic group of surfactant to transfer from solvent system to the interior of micelle.

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