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Interaction between antidepressant drug and anionic surfactant in low concentration range in aqueous/salt/urea solution: A conductometric and fluorometric study

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ABSTRACT

Aqueous/salt/urea micellar solutions of amphiphilic antidepressant drug amitriptyline hydrochloride (AMT) and anionic surfactant sodium dodecylbenzenesulfonate (SDBS) have been examined by conductivity and fluorescence measurements at different temperatures and composition. From the conductometric study, values of critical micelle concentration (*cmc*) of drug have been evaluated and analyzed in terms of effect of surfactant on the hydrophobic nature of AMT–SDBS complex. The values of critical micelle concentration (*cmc*) and other aggregation parameters, micellar mole fraction (X_1) and interaction parameters (β) were obtained and discussed in detail. In mixtures of AMT and SDBS, the synergistic interactions in mixed micelles formation increases with the raise in mole fraction of surfactant in absence and attendance of salt/urea. Thermodynamic parameters of the mixtures in aqueous as well as in salt/urea solution have been evaluated by means of a pseudo-phase model. The effect of NaCl shows the salting-out effect, which promotes aggregate formation of AMT and SDBS as well as their mixed systems at lower concentration relative to aqueous solution. The micelle aggregation number (N_{agg}) of drug increases with the raise in surfactant mole fraction in mixtures. N_{agg} value of individual and mixed amphiphiles rises in the presence of electrolyte while reduces in the occurrence of urea.

1. Introduction

The mixtures of amphiphiles are well accounted in the literature, being of key significance with the intention of advance their aggregation and convenient applications [1–3]. Surfactants are comprehensively employed in our on a daily basis life along with also in a range of industrial progressions for example textiles, paints, oil, pharmaceuticals etc. [4,6]. In the mixture of amphiphiles if one of the constituent is an amphiphilic drug in that case the mixture decreases the side effects and enhances the drug's effectiveness [5,6]. The amphiphilic drugs such as phenothiazine and benzodiazepine tranquillizers, analgesics, non-steroidal anti-inflammatory and tricyclic antidepressants have strong tendency to self-associate like surfactants [7–9]. Among these drugs, tricyclic antidepressants (TCA's) have been keystones of antidepressive therapy for over three decades.

The selected TCA's such as amitriptyline hydrochloride (AMT) are the most widely used tricyclic antidepressants in the mental health care (Scheme 1). AMT consist of a rigid hydrophobic ring as well as an alkylamine portion which turns out to be protonated at low pHs and deprotonated at elevated pHs. Employing of TCAs is one of the approaches for the cure of mental disorder. On the other hand, TCAs have facing many unwanted side effects such as anticholinergic, cardiovascular and antihistamine effects [10]. Other than this, TCAs provoke phospholipidosis, that is to say, the unnecessary intracellular gathering of phospholipids [11]. Cationic amine group of AMT interact with the anionic group of phosphate oxygen of the lipids reduces the amphiphilic nature of lipids and may change the physicochemical properties of the lipids obtain in the body. To decrease these unwanted effects, TCAs are usually employed with carriers such as surfactant.

Surfactants form micelles, principally in aqueous/nonaqueous solutions, by means of hydrophobic and hydrophilic interactions takes place inside the similar molecule [12–15]. In the present study we have used anionic surfactant sodium dodecylbenzenesulfonate (SDBS). SDBS have several uses like, it perform as an appropriate template for the preparation of nanoparticles, bio-friendly because it desorbs a lot of dangerous organic materials from soil and advances the effectiveness of soil [16,17]. This surfactant is kind, fewer irritating to skin and also have antimicrobial property, so they will improve the access of drugs through skin. Therefore, the examination of interfacial properties of this surfactant and their interactions with bio-active materials such as drugs, proteins, enzymes, amino acids and polymers are highly significant to study to enhance their utilizes in industries.

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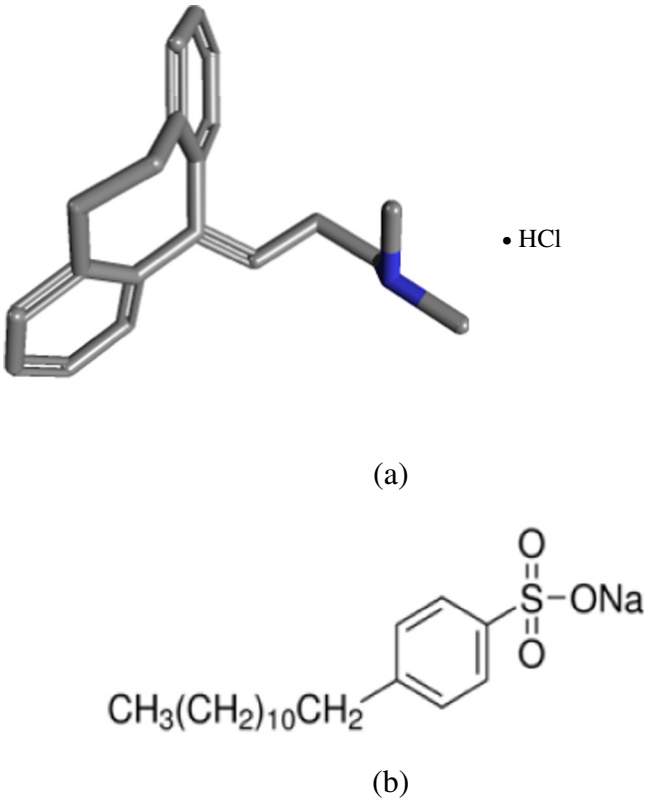

Scheme 1. Molecular structure of (a) AMT and (b) SDBS.

Rub et al. have examined the interactions among some cationic as well as anionic drug with ionic/nonionic surfactants for example gemini surfactant, sodium dodecylsulphate (SDS), Triton X-100, dioctylsulphosuccinate sodium salt (AOT), hydrotropes and bile salts and the oppositely charged drug-surfactant mixed system were achieved to be greatly synergistic [14,18–23]. Therefore, in extension to our prior study concerning drug and surfactant mixed systems we have explored this time cationic amphiphilic drug AMT and anionic surfactant SDBS mixtures possessing different head groups both in occurrence and absence of salt/urea. Up to now, the majority of the earlier works reports regarding catanionic mixed systems containing oppositely charged surfactants only and catanionic drug-surfactant mixtures remain unexplored. The study of mixed AMT–SDBS micelles in aqueous as well as in salt/urea medium may prove valuable in pharmaceutical study for drug delivery systems since both the compounds are biocompatible and pharmaceutically good enough. However, up to present, there are only very limited reports about the electrolyte/urea effect on the micellization/mixed micellization behavior of amphiphiles mixtures in aqueous solution [24,25].

The propose of this study is to examine the physicochemical properties of amphiphilic antidepressant drug AMT and SDBS together with their mixed systems in aqueous as well as in the presence of NaCl/urea with complete highlighting on the outcome of temperature by the conductometric technique that offers information about comparative characterization of amphiphilic mixtures. Therefore aggregation is significantly influenced by temperature and hydrogen bonding ability of the solutions. The analysis has been done through established theories of Clint, Rubingh, Motomura as well as Rodenas for the quantification of the interaction and thermodynamic properties (Gibbs free energy (ΔG_m^0), enthalpy (ΔH_m^0) and entropy (ΔS_m^0)). The degree of dissociation (g) and excess free energy of micellization (ΔG_{ex}) have also been evaluated and disused in detail. To the best of our information there is no statement that clarifies the aggregation of AMT drug with SDBS together with spectroscopic and thermodynamic study. Fluorescence study has supplied information regarding polarity and aggregation number of the pure amphiphiles and their mixtures in different ratio in absence and presence of salt/urea.

2. Experimental

2.1. Materials

Amitriptyline hydrochloride, AMT (≥0.98 in mass fraction, Sigma, USA), sodium dodecylbenzenesulfonate, SDBS (0.99 in mass fraction, Fluka, Switzerland), NaCl (0.98 in mass fraction, BDH, England), urea (0.99 in mass fraction, Sigma, Germany), pyrene (0.98 in mass fraction, Aldrich, Germany) and cetylpyridinium chloride, CPC (0.98 in mass fraction, Merck, Germany) were used as received. All chemicals were employed as received without further purification. Double-distilled water with specific conductivity 1–2 μS cm^{-1} was employed to prepare the solutions of the AMT and SDBS in the absence/attendance of NaCl/urea.

2.2. Methods

2.2.1. Conductivity measurements

The conductivity measurements were performed with a digital conductivity meter (model 4510, Jenway, UK) having a cell constant of cell is 1.026 cm^{-1}. Alternating current (AC) was supplied for conductivity measurements. Temperature of the solution was sustained by way of flowing water through the solution under observation. The temperature error was reduced to ±0.2 K. The instrument was standardized with potassium chloride (KCl) solutions of the right concentration range. The conductivity of solvent was measured first, subsequently, a set quantity of the stock solution of AMT were dropped to H_2O or in attendance of fixed concentration of the SDBS/(SDBS + 50 mmol·kg^{-1} NaCl)/(SDBS + 300 mmol·kg^{-1} urea) solution via a micropipette and attains the conductance of solution. Akin process was duplicated after each addition of solution. When specific conductivity (κ) versus AMT concentration of the solution was plotted, two straight lines having dissimilar slopes were attained. The intercept of these lines was considered as *cmc*. The standard uncertainties on *cmc* are near about to 2%.

2.2.2. Fluorescence measurements

The fluorescence probe solutions, pyrene, were prepared in ethanol and stored in clean amber glass vials at ~277.15 K. The solutions of pure compounds and their mixtures were freshly prepared in pure aqueous/salt/urea above their respective *cmc* value. The micellar aggregation number (N_{agg}) of pure compounds and their mixtures at various compositions were find out by means of fluorescence measurements (Hitachi F-7000 fluorescence spectrometer) having excitation as well as emission slit widths 2.5 nm at 298.15 K. Pyrene was employed as probe and cetylpyridinium chloride (CPC) was utilized as quencher. Excitation was performing at 335 nm, and emission was noted within the range 350–450 nm. For the determination of N_{agg} concentration of pure components and their mixtures were taken above their respective *cmc* value.

3. Results and discussion

3.1. Mixed micellization

The conductivity measurement of AMT and SDBS solution mixtures in different ratio was measured at various temperatures (293.15, 298.15, 303.15, 308.15, and 313.15 K) in attendance and absence of salt/urea. The specific conductivity versus concentration of amphiphiles of some selected system is given in Fig. 1 for determination of critical micelle concentration (*cmc*). Both components (AMT and SDBS) used in current study consist opposite charge therefore support the mixed micellization at much lower concentration in compare to components