Journal of Molecular Liquids xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Journal of Molecular Liquids

journal homepage: www.elsevier.com/locate/molliq

Micellization behavior of the amphiphilic drug promethazine hydrochloride with 1-decyl-3-methylimidazolium chloride and its thermodynamic characteristics

Abbul Bashar Khan [a], Maroof Ali [b], Neeraj Dohare [a], Prashant Singh [c], Rajan Patel [a,*]

[a] Biophysical Chemistry Laboratory, Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia (A Central University), New Delhi 110025, India
[b] Department of Chemistry, Aligarh Muslim University, Aligarh, Uttar Pradesh 202002, India
[c] Department of Chemistry, A. R. S. D. College, University of Delhi, Delhi 110021, India

ARTICLE INFO

Article history:
Received 14 May 2014
Received in revised form 3 July 2014
Accepted 16 July 2014
Available online xxxx

Keywords:
Promethazine
Ionic liquids
Synergism
Thermodynamic parameters
Mixed micelle

ABSTRACT

The micellization behavior of promethazine hydrochloride (PMT) with 1-decyl-3-methylimidazolium hydrochloride, $[C_{10}mim]$ [Cl], at different temperatures was investigated by using electrical conductivity. The system thermodynamic properties were also studied by calculating various thermodynamic parameters (viz., the standard Gibbs energy change, ΔG°_m, the standard enthalpy change, ΔH°_m, the standard entropy change, ΔS°_m), that favor the micellization in binary mixtures of PMT–$[C_{10}mim]$[Cl] compared with the pure counterparts, at two mole fractions of PMT. The synergistic interaction is examined using Regular Solution Theory for PMT–$[C_{10}mim]$ [Cl] binary mixtures, through the interaction parameter (β) and activity coefficient (f_1 and f_2) values. The synergism is also revealed in the deviations in the critical micelle concentration (*cmc*) from the ideal critical micelle concentration (cmc^*) and micellar mole fraction (X_1) from ideal micellar mole fraction (X_1^{ideal}) values. The value of excess free energy (ΔG_{ex}) for $\alpha_1 = 0.6$ at 308 K favor the better condition for the formation of the most stable and compact mixed micelles.

1. Introduction

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 [1–3], they have generated massive scientific importance [4,5]. Consequently, a huge number of applications of ILs have been proposed in catalysis [6], electrochemistry [7], chemical separation [8,9] and as a novel solvent in organic synthesis [10,11]. 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.

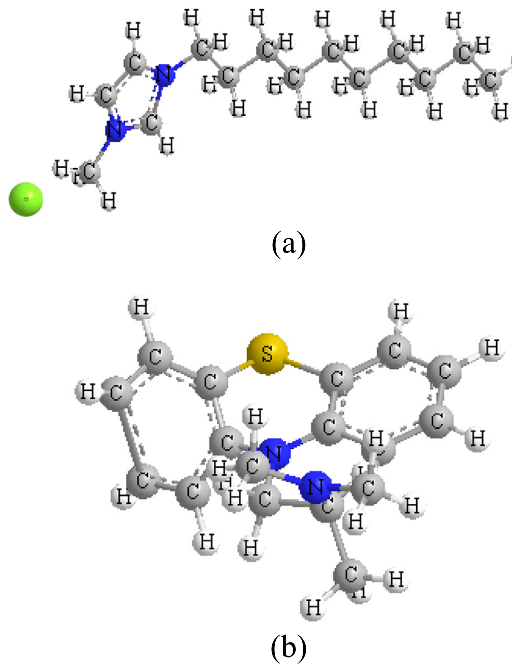
A typical imidazolium IL analyzed through the structure activity relationship (SAR), guide the assumption that ILs may acquire surface active properties similar to surfactants and would allow the ILs to form micelles in aqueous solution [12–16]. As shown in Scheme 1(a), the anion or cation of IL consists of a charged hydrophilic head group and a hydrophobic 'tail' domain, suggesting that ILs have properties analogous to amphiphiles. In addition, the self-assemblies of amphiphiles in a solvent medium have many potential applications such as nanomaterial synthesis [17], drug delivery [18,19], separation process, pharmaceutical formulation, and other dispersant technologies [20].

Generally, surfactants are believed to be as good carriers as they form micelles and can solubilized drugs in their core. An extensive literature, related to the surfactant self-assemblies in imidazolium based room temperature ILs (RTILs) [6] has reported the formation of micelles by anionic and nonionic surfactants in 1-butyl-3-methylimidazolium chloride [Bmim][Cl] and hexafluorophosphate [Bmim][PF_6]. In addition the aggregation behavior of anionic SDS, cationic CTAB, nonionic Brij, Triton *X*-100 and Tween 20 in 1-ethyl-3-methylimidazolium bis (trifluoromethylsulfonyl) imide [Emim] [T*f*2N] by using a solvatochromic probe technique have also been studied [7]. Recently, the temperature dependent self-assembly of Brij surfactant in [Bmim] [BF_4] have been reported [9] and also the effect on aggregation behavior of imidazolium based ionic liquids are studied [21,22].

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. These ILs are also able to combine with active pharmaceutical ingredients (APIs), and such IL–API compounds, offer new and improved properties like stability, solubility, permeability and drug delivery, as compared to the corresponding solid pharmaceutical forms. It is also

* Corresponding author. Tel.: +91 8860634100; fax: +91 11 26983409.
E-mail addresses: rpatel@jmi.ac.in, rajanpatelpcy@gmail.com (R. Patel).

http://dx.doi.org/10.1016/j.molliq.2014.07.021
0167-7322/



Scheme 1. Ball and stick models of (a) 1-decyl-3-methylimidazolium chloride and (b) promethazine hydrochloride.

supposed to be a third generation of ILs [23]. In addition, the micelles play an important role as drug carriers by reducing the adverse side effects of drugs in such a way that the contact of the drug with inactive species such as enzymes presents in the biological fluid is minimized.

Various drugs, particularly the local anesthetic, tranquilizing, antidepressant and antibiotic actions, are amphiphilic in nature, and the tricyclic antidepressant drugs belong to a family of structurally similar compounds possessing an almost planar tricyclic ring system with a short hydrocarbon chain carrying a terminal, charged nitrogen atom (Scheme 1(b)). Recently, researchers found the phase separation (clouding) phenomena of some tricyclic amphiphilic drugs [24,25], and conclude that like ionic surfactants, these amphiphilic drugs undergo pH, concentration, and temperature dependent phase separation in addition the thermodynamic parameters also evaluated at the cloud point [26,27].

The mixed micellization study of the drug-surfactant system, in various compositions and temperature range, have been reported by several workers [28–32] and enough literature also available for the surfactant micellization [30–33] and its thermodynamic study with various ILs [34–37]. But no one have reported the micellization of amphiphilic phenothiazine drug with IL up to our knowledge except our previous work in which we reported the mixed micellization behavior of amitriptyline hydrochloride (AMT) with 1-methyl-3-octylimidazolium hydrochloride, [C8mim][Cl], at different temperatures [38]. Therefore, in the present study, we have chosen [C_{10}mim][Cl] with PMT, to study the micellization and its thermodynamics behavior. This will help the understanding of the role that imadozolium based ILs contribute to their application in the related pharmaceutical industries in the future. The formation of the mixed micelles is expected because of the amphiphilic character of PMT and [C_{10}mim][Cl], therefore, to explore the above idea we have done the conductivity measurements at different temperatures and compositions of PMT and [C_{10}mim][Cl].

2. Experimental

2.1. Chemicals

In the present manuscript, promethazine hydrochloride, Sigma Aldrich, ≥95.5% (CAS no. 58-33-3) and 1-decyl-3-methylimidazolium chloride, Sigma Aldrich, ≥97% (CAS no. 171058-18-7) were used as received except vacuum drying. Deionized water was used to prepare the various solutions. The purity (Supplementary Table: ST-1) of the used chemicals was determined through HPLC. In addition, the water content in the samples was determined by Karl Fischer method (Supplementary Table: ST-1) using Karl Fisher Titrator with Model no. MA-101-13 from Company SPECTRALAB, India and Magnetic stirrer speed 48 rpm and the solvent used was methanol (HPLC grade).

2.2. Procedure

A Labindia Pico^{+} conductivity bridge having a cell constant 1.02 was used to measure the conductance of the samples after proper mixing. The specific conductance of doubly distilled water is 1.82 μS/cm, and the temperature in all the experiments was maintained by circulating water from an electronically controlled water bath (Julabo, Germany) with a temperature stability of ±0.01 K. The conductivity was measured after every addition of pure PMT, [C_{10}mim][Cl] and binary mixture of both of specific mole fractions in the aqueous solution and then specific conductance plotted against the molar concentration of that particular component. The reproducibility of conductance measurements was estimated to be ±0.5%.

3. Results and discussion

Amphiphiles in aqueous solution behave as simple electrolyte and follow the Onsager equation at its low concentrations; above a certain concentration, the behavior deviates from the Onsager equation, and the conductivity decreases markedly. The representative plot of specific conductivity, κ, as a function of molar concentration of pure PMT, [C_{10}mim][Cl] and their mixed systems, at 298 K is shown in Fig. 1. As shown in Fig. 1, with the rise in the electrical conductivity, the slope is gradually decreased at a particular temperature, and the break point in the plot originates from the inception of micellization.

The micellization and energetic adsorption are typically discussed in terms of different forces like hydrophobic interaction, dispersion, an attraction between hydrocarbon chains, and the electrostatic and van der Waals interactions between the head groups of PMT and [C_{10}mim][Cl]. By using the conductivity data herein, we discussed the effect of temperature on *cmc*, mixed micellization and thermodynamics of micellization of an amphiphilic drug with the alkyl imidazolium chloride. The critical micelle concentration (*cmc*) values have been found in good agreement with the literature values for PMT [39] and [C_{10}mim][Cl] [40]. There are two opposing forces that govern the micellar phenomenon, i.e., (1) van

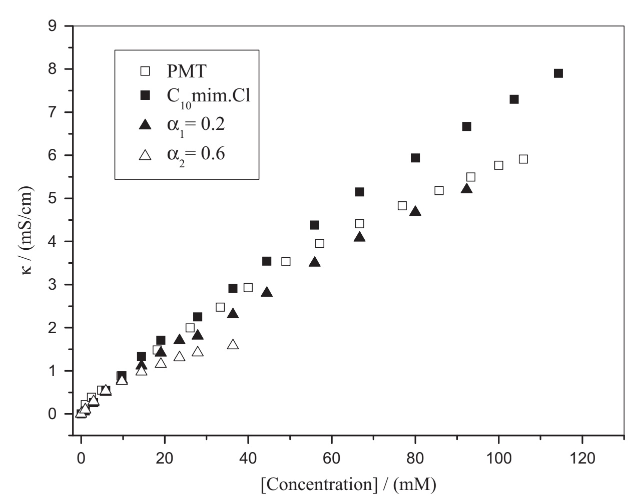


Fig. 1. Plot of specific conductivity, κ vs. [concentration] at 298 K for pure (□), pure [C_{10}mim. Cl] (■) and mixed systems (a) $\alpha_1 = 0.2$ (▲) and (b) $\alpha_1 = 0.6$ (Δ).

Please cite this article as: A.B. Khan, et al., Journal of Molecular Liquids (2014), http://dx.doi.org/10.1016/j.molliq.2014.07.021