



Synthesis, self-assembly and micellization characteristics of choline alkanolate ionic liquids in association with a star block copolymer

Pooja Patidar^a, Anita Bahadur^a, Kamalesh Prasad^b, Sanjay Tiwari^{c,*}, Vinod K. Aswal^d, Pratap Bahadur^e

^a Department of Zoology, PT Sarvajani College of Science, Surat 395001, India

^b Natural Products & Green Chemistry Division, Central Salt and Marine Chemicals Research Institute, Bhavnagar 364002, India

^c Uka Tarsadia University, Maliba Pharmacy College, Gopal-Vidyanagar Campus, Surat 394350, India

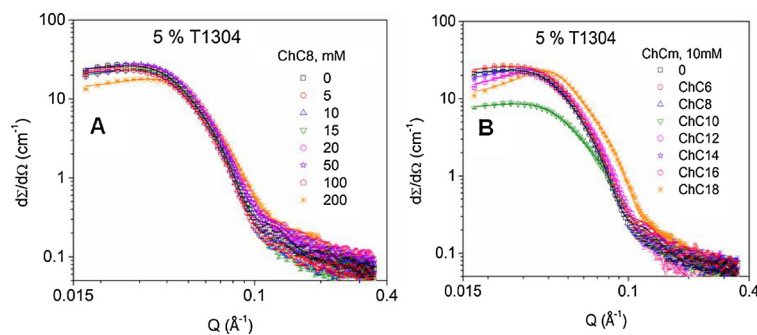
^d Solid State Physics Division, Bhabha Atomic Research Centre, Mumbai 400085, India

^e Department of Chemistry, Veer Narmad South Gujarat University, Surat 395007, India



GRAPHICAL ABSTRACT

Small angle neutron scattering profile of T1304 micelles in the presence of choline carboxylates.



ARTICLE INFO

Keywords:

Surface active ionic liquid
Self-assembly
Star block copolymer
Micelles
Drug solubilization
Biocompatibility
Aggregation number

ABSTRACT

Herein, alkyl chain dependent self-assembly of choline carboxylate ionic liquids (ILs) and their effect on micellar characteristics of a star block copolymer (Tetronic® T1304) are reported. The ILs showed good aqueous solubility (low Kraft point) and formed spherical micelles. Small angle neutron scattering (SANS) analyses revealed a reduction in the critical micelle concentration (CMC) and elevation in the aggregation number (N_{agg}) upon increasing alkyl chain length of ILs. More importantly, ILs demonstrated good biocompatibility in murine erythrocytes and A549 cells, irrespective of the chain length.

Furthermore, the effect of IL addition on micellar behaviour of T1304 was examined through thermal and scattering studies. We observed alkyl chain dependent increase in the cloud point (CP), critical micellization temperature (CMT), micelle size (R_h , R_c , R_{hs}) and N_{agg} . In association with T1304, long chain ILs ($n = C_{12}$ – C_{18}) formed charged mixed micelles with a lower N_{agg} which showed enhanced solubilization of quercetin, a hydrophobic drug. Mixed micelles, composed with such biocompatible ILs, can further be tuned to explore their drug delivery applications.

* Corresponding author.

E-mail address: tiwarisanju@gmail.com (S. Tiwari).

<https://doi.org/10.1016/j.colsurfa.2018.08.002>

Received 27 June 2018; Received in revised form 2 August 2018; Accepted 2 August 2018

Available online 03 August 2018

0927-7757/ © 2018 Elsevier B.V. All rights reserved.

1. Introduction

Remarkable physical characteristics (melting point < 100 °C) of ionic liquids (ILs) prompt their utilization in contemporary research. With their high thermal and chemical stability, polarity, low inflammability and recyclability, ILs are considered ‘green solvents’ [1,2]. Assorted anion-cation combinations enable ILs to work as “designer solvent” for task-specific applications in extraction and catalysis [3,4]. Recently, ILs have attracted significant attention for their possible applications in life sciences, biotechnology and medicine, typically as a component in drug synthesis and formulation of colloidal delivery systems [5]. As a result, the focus has now shifted towards developing biodegradable ILs, originating from biomaterials [6,7].

Choline, a trimethylethanolammonium cation, is a water-soluble component present in the vitamin B-complex. Further to its role in maintaining the cellular physiology, it acts as precursor for acetylcholine and membrane phospholipids [8]. Combination of choline with a variety of component organic anions has been exploited to produce biocompatible and biodegradable ILs. X-ray scattering and molecular dynamics studies have shown strong hydrogen bonding between cations and anions in ILs [9]. Application of choline based ILs as “green solvents” and catalyst in organic transformations has recently been reviewed [10]. Our group widely reported the solubilisation behaviour of ILs and their role in selective extraction of high molecular weight biomolecules [11–15].

Toxicity of ILs has been evaluated on microorganisms, aquatic organisms and specific cell lines. Studies on cholinium-based ILs on marine bacteria have ruled out their explicit safety. ILs can be cytotoxic depending upon the anion (cholinium or imidazolium) and alkyl chains [16]. Rengstl et al. [17] examined the effect of choline carboxylates on biological membranes. The study showed higher toxicity upon increasing the alkyl chain length [17]. Short chain carboxylates do not penetrate through cell membranes whereas penetration is significant for alkyl chain ≥ 8 [18].

Polyoxyethylene-based non-ionic surfactants and hydrophilic polymers show clouding phenomenon in aqueous medium [19]. Studies have illustrated the effect of IL incorporation on clouding behaviour and micellar characteristics of non-ionic surfactants and block copolymers. There are reports on the aggregation of surfactants in water-IL mixed systems wherein the latter are shown to attune the surfactant behaviour [20,21]. Pillai et al. [20] and Parmar et al. [22] have analysed the effect of ILs on the physicochemical properties of star block and triblock copolymers, respectively, through scattering, thermal and NMR analyses [20,22]. Depending upon alkyl chain, ILs acted as cosolvents or cosurfactants. Long alkyl chain ILs promoted the formation of mixed micelles with a decreased hydrodynamic diameter (D_h). Moreover, incorporation of ILs is accompanied with a reduction in the core radii and aggregation number block co-polymeric micelles [23]. Reddy and Venkatesu [24] demonstrated the ability of ILs (1-butyl-3-methylimidazolium) and anions (SCN^- , BF_4^- , I^- , Cl^-) in modulating the CMT of a triblock copolymer. Reduction in CMT was owed to the collective influence of charge, size of IL anion and weak ion-ion pair interactions within IL [24]. Another study shows a concentration-dependent ability of ILs to decrease the CMT of an aqueous triblock

polymer solution. Though micellization and change in CMT were contributed by both cation and anion, anion played a dominant role. This occurred through polymer dehydration, derived from a balanced interaction of polymer-water, polymer-IL and IL-water units [25].

In this study, we report aggregation behaviour of some choline carboxylate based ILs in water using neutron scattering studies. Further, we have studied the effect of ILs on micellization behaviour of a branched star block copolymer (Tetronic® T1304), an aspect unexplored so far in our knowledge. The interaction between ILs and T1304 was exploited to modulate the properties of resulting micelles. Biocompatibility of ILs was determined by hemolysis and MTT assays. Finally, the effect of IL incorporation into T1304 micelles was investigated upon the solubilisation of quercetin (QN), a model hydrophobic drug.

2. Experimental

2.1. Materials

Choline bicarbonate was purchased from Sigma Aldrich, USA. Analytical grade caproic acid, caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, isopropyl alcohol and dimethyl sulfoxide were purchased from S.D. Fine Chemicals, Mumbai, India. The polymeric surfactant (Tetronic® T1304) was received as gift from BASF, Germany. Dulbecco modified eagle medium (DMEM), L-glutamine, Pen/Strep solution, Triton X100, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and fetal bovine serum (FBS) were purchased from Hi Media Ltd., India. All other reagents were of analytical grade and used as received.

The samples for all measurements were prepared using deionized water from a Millipore Milli-Q system. SANS study samples were prepared using deuterated water (99.1% pure).

2.2. Methods

2.2.1. Synthesis of choline alkanooates and characterization

Choline carboxylates (ChCm) with $m = 6$ (caproate), 8 (caprylate), 10 (caprate), 12 (laurate), 14 (myristate), 16 (palmitate), 18 (stearate) were synthesized according to the method described elsewhere, with slight modifications (Fig. 1) [26]. Briefly, the corresponding acids were added into choline bicarbonate (80 wt% in water), in an equimolar ratio (1:1), under continuous stirring and an inert atmosphere. After complete addition of acid, the reaction mixture was refluxed at 60 °C (12 h) under nitrogen atmosphere. Finally, the synthesized product was washed with ethyl acetate in order to remove unreacted starting materials. The ILs thus obtained were dried under reduced pressure and stored in closed glass vials. Their structure was confirmed by proton NMR (Bruker Avance II 500 MHz, Germany). The sample (≈ 15 mg) was dissolved in deuterated water prior to spectrum acquisition.

Characteristic proton NMR spectra of the synthesized ILs are shown in supporting information (Figs. S1–S3). For a typical choline caproate sample, the chemical shifts were observed as δ/ppm (D_2O); 0.74 (t, 3H, $-\text{C}-\text{CH}_3$), 1.16 (m, 4H, $-\text{CH}_2-$), 1.42 (m, 2H, $-\text{CH}_2-$), 2.03 (t, 2H, $-\text{CH}_2-$), 3.07 (s, 9H, $-\text{N}-\text{CH}_3$), 3.37 (d, 2H, $-\text{CH}_2-\text{N}-$), 3.90 (d, 2H,

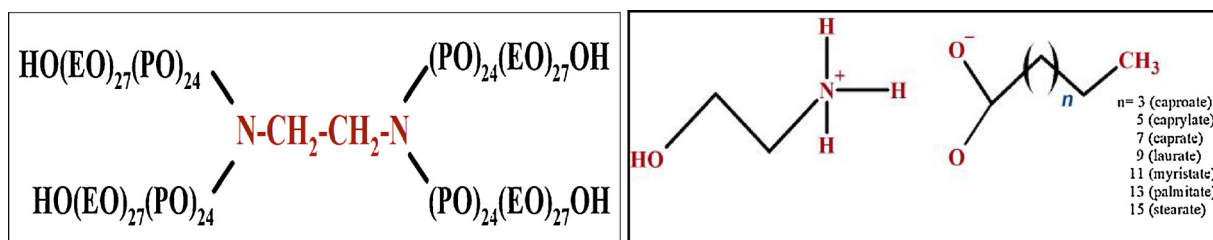


Fig. 1. Structure of Tetronic® T1304 and choline based ionic liquids.

Download English Version:

<https://daneshyari.com/en/article/6977247>

Download Persian Version:

<https://daneshyari.com/article/6977247>

[Daneshyari.com](https://daneshyari.com)