Chemical Physics Letters 665 (2016) 14–21

Contents lists available at ScienceDirect

Chemical Physics Letters

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

Research paper

# Influence of trehalose on the interaction of curcumin with surface active ionic liquid micelle and its vesicular aggregate composed of a non-ionic surfactant sorbitan stearate

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ARTICLE INFO

*Article history:*
Received 4 August 2016
In final form 8 October 2016
Available online 17 October 2016

*Keywords:*
SAIL
[$C_{16}$mim]Cl
Span 60
Trehalose and curcumin

ABSTRACT

The present investigation unravels the effect of trehalose on 1-hexadecyl-3-methylimidazolium chloride ([$C_{16}$mim]Cl), a cationic surface active ionic liquid (SAIL) micelle and SAIL ([$C_{16}$mim]Cl)-nonionic surfactant (Sorbitan Stearate, Span 60) based vesicles. The influence of trehalose on size and morphology of the aggregates has been investigated using dynamic light scattering (DLS) and transmission electron microscopic (TEM) measurements. Besides, we have studied the dynamic properties of curcumin inside these aggregates using fluorescence spectroscopic based techniques. The results revealed that trehalose molecules play crucial role in modulation of the photophysical properties of curcumin in these organized assemblies.



## 1. Introduction

The self-organised surfactant assemblies (micelles and vesicles) and their transition is of great interest due to their potential applications in drug delivery, nanomaterial synthesis, etc. [1,2]. Moreover, the surfactants forming micelles and vesicles can provide suitable microenvironments to protect the guest molecules from the interaction of water [3,4]. So far, to understand the structural transition of surfactant assemblies of micelle to vesicles, several methods are reported; but mixing of different surfactants is one of easiest and effective procedure [5,6]. The structural aspects of surfactant vesicles are similar to liposomes (phospholipids forming vesicles). The biological, chemical or industrial application of surfactant forming vesicles increases substantially because of their biodegradability, easy preparation procedure, high stability and low cost of surfactants. In recent times, researchers are interested to investigate photophysical and dynamical phenomena of various fluorophores in nanoaggregates formed by another type of amphiphilic molecules, room temperature ionic liquids (RTILs) [7,8]. The ionic liquids which contain long alkyl chain and a charged hydrophilic head group in either of their cationic or anionic moiety exhibits aggregation behaviours and these RTILs are termed as Surface active ionic liquids (SAILs). In aqueous solution, the aggregation phenomenon of imidazolium moiety containing RTILs has been investigated extensively [9,10]. There are several reports related to the photophysical and dynamical phenomena of various fluorophores in room temperature ionic liquids [11–13].

Considering the unique features of SAILs and nanoaggregates, in this article, we have characterised SAIL (1-hexadecyl-3-methylimidazolium chloride ([$C_{16}$mim]Cl))-nonionic surfactant, (sorbitan stearate (Span 60)) mixed vesicles. Further, to extend the applicability of surfactant based nanoaggregates, we have also investigated the effect of sugar (trehalose) on the $C_{16}$mimCl micelle and $C_{16}$mimCl-Span 60 mixed vesicles. Recently, Kumar et al. have investigated the effect of agarose on cationic and anionic SAIL medium [14]. It is reported that agarose interacts with the SAIL to a significant extent due to ion-dipole and hydrogen bonding interaction. Moreover, some molecular dynamics simulation and few experimental studies indicate that sugar molecules directly interact with the phospholipid forming bilayer [15,16]. It was suggested that sugar molecules associated with the bilayer via hydrogen bonding interaction with the phosphate groups and consequently replaces water molecules at the membrane surface. Therefore, the sugar molecules intercalated into the head groups of lipid membrane and increased its area. Hence, we have been interested to investigate the morphology and interaction of SAIL forming nonlipidic vesicular systems with sugar molecules. There are some literatures where vesicular drug delivery of curcumin has been investigated [17,18]. Therefore, we have been motivated to monitor the stability and photophysical aspects of potent anticancer drug curcumin in this type of self assembled systems.

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http://dx.doi.org/10.1016/j.cplett.2016.10.026
0009-2614/

Curcumin, a natural polyphenolic yellow-orange pigment, has widely been used as a food ingredient and also in medicinal applications [19,20]. But its medicinal application is restricted because of poor solubility in aqueous medium [21]. Therefore, to increase the applicability of curcumin in aqueous medium by encapsulation, various self-organized supramolecular assemblies (micelles, vesicles, cyclodextrin, proteins, etc.) has been formulated [22,23].

In solution, curcumin molecule generally exists in keto and enol tautomeric form in ground state due to formation of six-membered chelate ring via intramolecular hydrogen bond (Scheme 1) [24]. It undergoes excited state intramolecular proton transfer (ESIPT) process upon photoexcitation [25–27]. Besides ESIPT, curcumin molecules also involved in another nonradiative phenomenon (solvation dynamics) in excited state [28]. The encapsulation of curcumin into the hydrophobic microenvironments of various supramolecular nanoaggregates formed by amphiphilic molecules increases its stability as well as modulates the solvent-dependent ESIPT dynamics [29,30].

In this article, we have investigated the stability and photophysical properties of curcumin in trehalose intercalated SAILs containing micelle and vesicle aggregates. The formation of vesicular aggregates has been characterized by DLS and TEM measurements. We have also shown that the rigid, stable and restricted microenvironments provided by $C_{16}$mimCl-Span60 based vesicles in combination with the trehalose molecules are more effective to modulate the photophysics of curcumin than $C_{16}$mimCl micelles. Therefore, our present study may reveal some interesting aspects towards the effect of trehalose on the SAIL forming aggregates.

## 2. Experimental section

### 2.1. Materials and method

Curcumin (purity ~80%) and Sorbitan Stearate Span 60 were purchased from Sigma-Aldrich. Using high purity curcumin (⩾98.5%), Petrich et al. have pointed that the presence of other curcuminoids (~20%) negligibly influence the photophysical properties of curcumin molecule [29]. Trehalose obtained from SRL (India) All these chemicals were used as received. 1-Hexadecyl-3-methylimidazolium chloride ([$C_{16}$mim]Cl) was obtained from Kanto Chemicals (98% purity). Double distilled Milli-Q water was used for the preparation of solutions.

The chemical structures of curcumin, [$C_{16}$mim]Cl, Span-60, trehalose are given in Scheme 1.

### 2.2. Preparation of solutions

To prepare [$C_{16}$mim]Cl-Span 60 vesicular solution with different concentration of Span 60, initially, 0.02 M [$C_{16}$mim]Cl micellar solution was prepared in a volumetric flask. Then, required amount (volume) of the stock solution was taken in different separate glass vials. Afterwards, required amounts of Span 60 were added into each glass vial in order to vary the Span 60 content in terms of R values (R = Span 60/[$C_{16}$mim]Cl molar ratio = (Conc. Span 60)/(Conc. of [$C_{16}$mim]Cl) from 0 to 0.9. The solution mixtures were then sonicated using an ultrasonic probe sonicator (Oscar Ultrasonic) for 15 min at 298 K to obtain the vesicular solutions.

### 2.3. Dynamic Light Scattering (DLS) measurements

Nano ZS instrument having 4 mW He-Ne laser ($\lambda$ = 632.8 nm) was used for Dynamic light scattering (DLS) measurements. In this instrument, the detector angle is fixed at 173°.

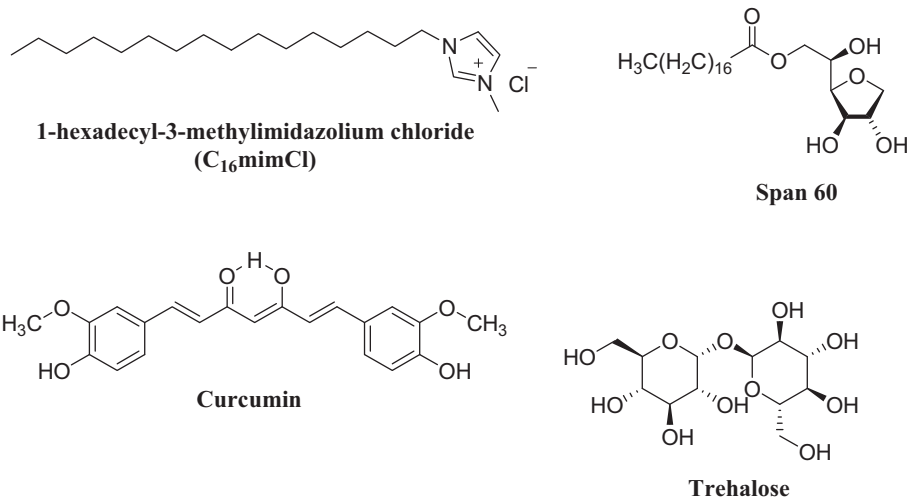
### 2.4. Transmission Electron Microscopy measurements

Transmission electron microscopy (TEM) analysis was performed by using the JEOL model JEM 2010 transmission electron microscope at an operating voltage of 200 kV. TEM images of the vesicles were taken by staining them with 0.5 wt% of uranyl acetate.

### 2.5. Steady-state and time-resolved fluorescence studies

The absorption and emission spectra of curcumin were monitored using Shimadzu (model number UV-2450) spectrophotometer and a Hitachi (model number F-7000) spectrofluorimeter, respectively.

We have used time correlated single photon counting (TCSPC) picosecond spectrometer to record the time resolved decay of fluorophores in solution. Generally, picosecond diode lasers (IBH, UK, Nanoled) of 408 nm were used as the excitation source and the emission decays were collected in magic angle (54.7°) polarization by Hamamatsu microchannel plate photomultiplier tube (MCP PMT) (3809U). The instrument response function of TCSPC set up is ~100 ps. During the analysis of time resolved decays, we have




**Scheme 1.** Structure of the different chemicals used in the experiments.