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Reactivity of a lipophilic ingredient solubilized in anionic or cationic surfactant micelles

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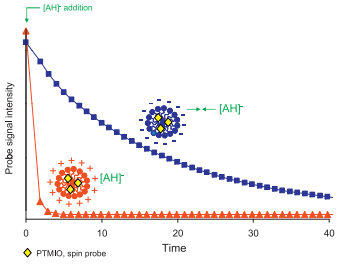
HIGHLIGHTS

- The location of a lipophilic spin probe was measured in surfactant solutions.
- The probe partitioned between micelle and aqueous environments.
- The probe in anionic micelles decreased its reactivity with the anionic reactant.
- The probe in cationic micelles increased its reactivity with the anionic reactant.

GRAPHICAL ABSTRACT



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ABSTRACT

The aim of this work was to investigate the location and reactivity of a lipophilic spin probe, 4-phenyl-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl nitroxide (PTMIO) in anionic (sodium dodecyl sulfate, SDS) or cationic (dodecyl trimethylammonium bromide, DTAB) surfactant micelles. The analysis of electron paramagnetic resonance (EPR) spectra of PTMIO in micellar systems showed that probe molecules partitioned between two populations: a more mobile fraction in the aqueous phase and a less mobile fraction in the micelle. The fraction of PTMIO incorporated in surfactant micelles increased with surfactant concentration. The rate of the reduction of the nitroxide group of PTMIO by the negatively charged, water-soluble ascorbate decreased when the probe was solubilized in anionic SDS micelles and increased when it was solubilized in cationic DTAB micelles. Thus, both the surface charge as well as the solubilization capacity of the micelles controlled the reactivity of the lipophilic molecule.

1. Introduction

A wide range of lipophilic ingredients (*e.g.*, flavors, pigments, vitamins, drugs, antimicrobials or phytochemicals) are added to food, beverage, pharmaceutical and cosmetic products to produce a desired functionality. Various formulation strategies are used to disperse lipophilic ingredients into aqueous media including emulsions, nanoemulsions and solid lipid nanoparticles [1–4]. Emulsion-based delivery systems often contain appreciable amounts of non-adsorbed emulsifiers in the aqueous phase surrounding the dispersed lipid particles. Non-adsorbed surfactant molecules form micelles when their concentration exceeds a particular level know as the critical micelle concentration (CMC). Surfactant micelles consist of a hydrophilic shell and a hydrophobic core that are capable of incorporating lipophilic molecules [5–7]. Consequently, it is possible for any encapsulated lipophilic component within an emulsion-based delivery system to partition between the non-polar regions of the lipid droplets and the surfactant micelles [8–10]. Surfactant micelles may, therefore, play an important role in the solubilization and localization of lipophilic ingredients in multiphase systems. Accordingly, surfactant micelles have been described as acting as a separate phase from water, which constitutes the basis of the pseudophase model [11].

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Depending on their molecular structure and polarity, lipophilic ingredients can partition to various locations within the micellar structure, from the external hydrophilic layer to the internal hydrophobic core [12,13]. When the lipophilic ingredient is amphiphilic, it can also form mixed micelles or co-micelles with the solubilizing surfactant molecules [7,10]. The extent of the solubilization of lipophilic molecules within surfactant micelles and their physical location within the micelle structure has previously been assessed by various techniques. The *semi*equilibrium dialysis technique is based on a physical separation of the lipophilic compounds, either in a free state or bound to surfactant micelles, followed by a quantitative determination of the compounds in each side of the dialysis membrane [14,15]. UV–visible and fluorescence spectroscopy have been used to detect changes in the electromagnetic spectrum of the lipophilic compound following solubilization within surfactant micelles (*e.g.*, changes in peak intensity or position) [12,16]. Measurements of the diffusion properties of radioactive probes have been used to determine the location of lipophilic components in micelle systems. For example, ^{14}C-labeled phenol in 3H-labeled surfactant solutions was used to determine the degree of partitioning of phenol into surfactant micelles [12]. Other labeled compounds (*e.g.*, spin probes) have also been used as model lipophilic ingredients to investigate their solubilization in surfactant micelles and the physical properties of the solubilizing micelles.

Ottaviani et al. and Baglioni et al. [17–23] performed a series of electron paramagnetic resonance (EPR) and electron spin echo modulation (ESEM) studies to investigate the solubilization and localization of nitroxide probes with various structures and polarities in anionic, non-ionic or cationic surfactant micelles and premicellar solutions. These studies demonstrated that the incorporation of amphiphilic or lipophilic spin probes within surfactant micelles led to a decrease of the global hyperfine splitting constant, which indicated a decrease in the average polarity of the environment in which the probe molecules were located. By studying doxyl-stearic acid spin probes with nitroxide groups located on various carbons of the aliphatic chain in surfactant micelles, information pertaining to the location of the spin probes within the micelle structure (*i.e.*, external hydrophilic layer vs. internal hydrophobic core) were also obtained. Finally, the phenomenon of micellar encapsulation of molecules with low hydrophilicity has also been investigated by mathematical modeling (*e.g.* Monte Carlo simulation) [24] or molecular-thermodynamic modeling [6]. In the latter study, the simulation results were in good agreement with the solubilization of ibuprofen in surfactant micelles measured experimentally.

A number of the lipophilic ingredients used in food, pharmaceutical or cosmetic applications are chemically labile and can be easily damaged during processing and storage. When these compounds are solubilized in surfactant micelles, the physical and chemical microenvironment may influence their reactivity. The chemical degradation of citral was shown to occur more slowly when it was encapsulated within micelles rather than in pure water [25]. The electrostatic charge of the surfactants has been shown to control to a large extent the reactivity of the solubilized lipophilic ingredients with water-soluble reactants, as demonstrated by the early work of Bunton and Romsted [26–28]. More recently, the encapsulation of curcumin in anionic surfactant micelles at neutral pH protected curcumin from alkaline hydrolysis through the electrostatic repulsion of OH^- ions [16,29]. Similarly, a recent study showed that the incorporation of phthalic acid within cationic surfactant micelles promoted its oxidation by the negatively charged permanganate ion [13].

In the present work, we used the spin probe 4-phenyl-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl nitroxide (PTMIO) as a model lipophilic ingredient. PTMIO is largely hydrophobic,

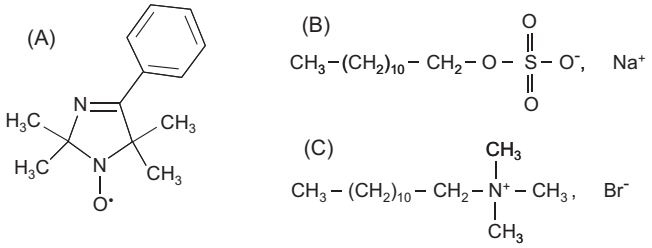

Fig. 1. Chemical structures of PTMIO (A), SDS (B) and DTAB (C).

compound (partition coefficient: log*P* value = 2.5, molecular weight: 217 g mol^{-1}; data given by the supplier) that is structurally similar to lipophilic ingredients (*e.g.*, limonene) found in foods and pharmaceutical applications. PTMIO has an unpaired electron, which makes it detectable by EPR. The aim of this study was to investigate the effect of surfactant charge on the reactivity of PTMIO in anionic or cationic surfactant micellar systems. The results are discussed according to the distribution of PTMIO molecules between the aqueous and micelle environments. This work, therefore, provides insight regarding the ability of surfactant micelles to solubilize a model lipophilic component, and the subsequent location and reactivity of that solubilized component.

2. Materials and methods

2.1. Materials

The radical spin probe PTMIO was purchased from Enzo Life Sciences (Plymouth Meeting, PA, USA). Dodecyl trimethylammonium bromide (DTAB), sodium L-ascorbate and sodium phosphate dibasic heptahydrate were obtained from the Sigma Chemical Company (St. Louis, MO, USA). Sodium dodecyl sulfate (SDS) was obtained from Fisher Scientific (Pittsburgh, PA, USA). Ferric chloride hexahydrate was obtained from Mallinckrodt Chemicals (Phillipsburg, NJ, USA). Sodium phosphate monobasic monohydrate was obtained from EMD Chemicals (Merck KGaA, Darmstadt, Germany). The chemical structures of PTMIO, SDS and DTAB are presented in Fig. 1. Their molecular weights are 217.3 g mol^{-1}, 288.38 g mol^{-1} and 308.34 g mol^{-1}, respectively.

2.2. Methods

2.2.1. Incorporation of PTMIO in aqueous surfactants solutions

PTMIO (200 μM) was added to phosphate buffer (100 mM, pH 7.0), stirred for 45 min, then centrifuged (2000 × *g*, 5 min, 20 °C) to remove any insoluble material. The concentration of PTMIO in the supernatant was measured by spectrophotometry (absorbance at 243 nm) as 177.1 ± 4.7 μM (n = 3). Aliquots of this PTMIO stock solution were added to surfactant solutions (0–30 g L^{-1}, SDS or DTAB). The solutions were gently stirred overnight at room temperature and then for 15 min at 50 °C.

2.2.2. Determination of the CMC of surfactants

The surface tension of SDS or DTAB solutions in phosphate buffer containing 177.1 ± 4.7 μM of PTMIO was determined using a drop shape analysis instrument (DSA100, Krüss, Hamburg, Germany) at 25 °C. Stable pendant droplets were generated after discarding the first five droplets to exhaust air bubbles. The equilibrium time for each droplet was 15 s. Droplet shape was analyzed from top to bottom and surface tension was calculated accordingly. Surfactant concentrations ranged between 0 and 15 g L^{-1}. Four surface tension measurements were performed for each concentration.