Tuning the position of head groups by surfactant design in mixed micelles of cationic and carbohydrate surfactants

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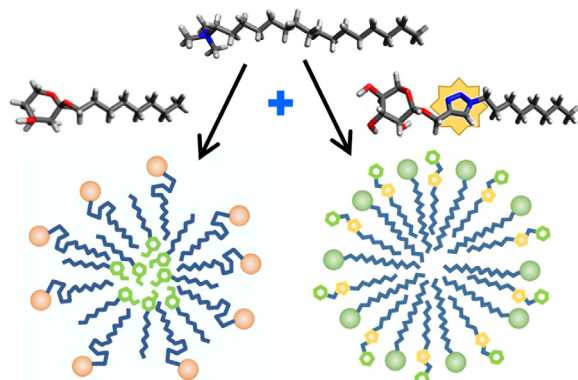
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Hypothesis: Emerging applications of carbohydrate/cationic surfactant mixtures require not only synergistic mixing, but also accessible sugar headgroups at the exterior of micelles. A previous study showed that the glucoside headgroups of octyl-β-ᴅ-glucopyranoside aggregate at the interior of mixed micelles with equimolar cetyltrimethylammonium bromide rather than mixing with trimethylammonium groups at the corona. The current study tests the hypothesis that structural characteristics of the surfactants (the relative lengths of the alkyl tails and the type of linker) can be tuned to shift the carbohydrate groups to micelle surfaces.

Experiments: The structural arrangement of 30 mM equimolar mixed micelle solutions in D_2O is investigated using NMR. The dynamics in different regions are probed using ^1H spin-lattice (T_1) and spin-spin (T_2) relaxation measurements, and relative positioning by nuclear Overhauser effect spectroscopy (NOESY). Additional micellar properties are determined using solvatochromic fluorescent probes.

Findings: Matching surfactant alkyl tail lengths is found ineffective at "pushing out" the carbohydrate headgroups due to a large mismatch in interactions between the headgroups and D_2O. However, inserting a novel polar triazole group between the carbohydrate head group and the hydrophobic tail (e.g. in *n*-octyl-β-ᴅ-xylopyranoside) using click chemistry is able to "pull out" the carbohydrate, thus giving accessible sugar moieties at the surface of mixed micelles.

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1. Introduction

In recent years, carbohydrate-based surfactants (or sugar surfactants) have drawn attention in the interfacial science community due to their environmentally friendly properties including being derived from renewable sources [1–4], low toxicity [5–8] and biodegradability [9,10]. Accordingly, sugar surfactants have tremendous potential for food [11], biorefining [12] and pharmaceutical applications [13]. Despite these advantages, the application of these carbohydrate surfactants is often limited by their weakly hydrated non-ionic head groups which aggregate due to strong intermolecular interactions [14]. These inter-headgroup interactions lead to high Krafft temperatures [15], slow lateral diffusion in micelles [16], and permit the formation of only limited types of lyotropic phases at room temperature [17], which constrain their applications.

Limitations in interfacial properties are often addressed by mixing sugar surfactants with other ionic or nonionic surfactants [18,19]. Mixtures of cationic and carbohydrate surfactants have been investigated extensively due to favorable synergistic effects such as decreased critical micelle concentration (cmc), surface tension and Krafft temperature; and increased colloidal stability relative to individual surfactants [20–22]. In addition to classic interfacial applications, carbohydrate surfactants find emerging application as templates for ordered mesoporous materials [23–25]. However, many carbohydrate surfactants such as *n*-octyl-β-d-glucopyranoside (C8G1) favor lamellar phases and are difficult to use to template stable mesophases such as the columnar hexagonal phase [25]. This problem can also be overcome by adding cationic surfactant to combat strong hydrogen binding among carbohydrate headgroups to favor the formation of hexagonal and cubic phases [26,27].

Although mixing with cationic surfactants solves problems related to strong clustering of sugar surfactants, obtaining a favorable, accessible orientation of the carbohydrate head group is not guaranteed. Having accessible carbohydrate head groups is crucial in several applications including molecular imprinting [28]. In order to create molecular imprinted sites in mixed surfactant-templated metal oxides, it is necessary to have the carbohydrate head group located slightly outside of the corona region of mixed micelles in order to interact with metal oxide precursors to create binding sites. For this and other mixed surfactant applications, a detailed understanding of the nature of the interactions between the headgroups in mixed micelles is needed.

Previous studies of mixed micelles, including recent studies of carbohydrate/cationic mixtures, focused primarily on bulk thermodynamic measurements [29–31]. Nonideal mixing in these measurements is most often modeled by regular solution theory (RST) [32,33]. According to RST, the interaction energy parameter β describes the interaction between the ionic and non-ionic surfactants in mixed micelles [34,35] where more negative values of β signify more favorable interaction between the two surfactants [18,36]. These bulk measurements provide insights into the favorability of mixing, but no direct information regarding the spatial arrangement of headgroups in the micelles.

Our previous study showed by NMR that when monosaccharide surfactants such as *n*-octyl-β-d-glucopyranoside (C8G1) or *n*-octyl-β-d-xylopyranoside are mixed with cetyltrimethylammonium bromide (C16TAB), the carbohydrate head groups aggregate into clusters within the micelles, most likely near the core of the mixed micelle [37]. This makes the carbohydrate head totally inaccessible for molecular imprinting. To make the glucose or xylose headgroup accessible we design the molecular structure of the surfactants according to two hypotheses: first, that matching the cationic and carbohydrate surfactant tail lengths can "push out" the sugar headgroup to the exterior of the mixed micelle. The second hypothesis is that matching the interaction forces of carbohydrate and cationic head groups with the polar medium can be used to "pull out" the sugar head group. To test the latter, a novel carbohydrate surfactant with a triazole linker between the carbohydrate head group and the hydrophobic alkyl chain will be used to replace one with a simple glycosidic linkage. The triazole linker is a feature of surfactants recently synthesized in our group [38,39] and is expected to provide dipolar interactions between the carbohydrate head and cationic surfactants or the surrounding polar medium. However, such surfactant mixtures have not yet been investigated.

Here, the relative position of sugar head groups in cationic-carbohydrate mixed micellar systems is investigated using NMR as a function of structural parameters selected with the intention of moving the sugar headgroups out of the core of the micelle. NMR techniques allow for direct measurements of the proximity of nuclei in mixed micelles, and therefore of their structural arrangement [40–43]. Additional micellar properties (cmc and aggregation number) are studied using fluorescence spectroscopy. The carbohydrate surfactant *n*-dodecyl-β-d-glucopyranoside (C12G1) is mixed with cationic surfactants of varying tail chain length including cetyltrimethylammonium bromide (C16TAB), dodecyltrimethylammonium bromide (C12TAB), and decyltrimethylammonium bromide (C10TAB). The accessibility of the sugar head is also studied in the case of the new triazole-containing carbohydrate surfactant *n*-octyl-β-d-triazole-xylopyranoside (C8XT1) mixed with C16TAB. Direct insights into the arrangement of sugar headgroups within the mixed micelles are gained by studying molecular-level interactions using NMR relaxation parameters T_2 (spin-spin relaxation) and T_1 (spin-lattice relaxation), and most importantly, NOESY (nuclear Overhauser enhancement spectroscopy). The results will show that the 3D arrangement of headgroups within mixed micelles can be successfully manipulated by molecular design of the surfactants.

2. Materials and methods

Cetyltrimethylammonium bromide (C16TAB), dodecyltrimethylammonium bromide (C12TAB) and decyltrimethylammonium bromide (C10TAB) (all technical grade, Acros Organics), *n*-dodecyl-β-d-glucopyranoside (C12G1) (99+%, Affymetrix), pyrene (Sigma-Aldrich) and hexadecylpyridinium chloride (C16PyCl, Sigma-Aldrich) were used as received. *n*-Octyl-β-d-triazole-xylopyranoside (C8XT1) was synthesized using click chemistry according to the procedure described by Oldham et al. [44]. All of the NMR samples were prepared by dissolving surfactant mixtures at 30 mM total concentration in D_2O (100 atom% D, Fischer Scientific).

NMR experiments were conducted using a 400 MHz Varian Inova NMR spectrometer at a fixed temperature of 50 °C maintained by a variable temperature (VT) controller. One-dimensional ¹H NMR spectra were acquired using the Varian *s2pul* pulse sequence with 32 scans and 3 s delay (d_1) between pulse sequences for each sample. Spin-lattice relaxation (T_1) measurements were performed using the INVREC (inversion recovery) pulse sequence with 15 s delay (d_1) between pulse sequences. Spin-spin relaxation (T_2) measurements were performed using the CPMGT2 (Carr-Purcell-Meiboom-Gill [45,46]) pulse sequence with a 40 s delay (d_1) between pulse sequences. Nuclear Overhauser effect spectroscopy (NOESY) was performed using standard NOESY pulse sequence with 'Z' filter [47] (to remove artifacts due to the through-bond magnetization transfer mechanism). Unless otherwise indicated, a mixing time of 600 ms was chosen to match the shortest T_1 value among all protons to observe every possible NOE correlation. A delay of 3 s (d_1) between pulse sequences