Effect of pH and counterion choice on the chiral separation of binaphthyl derivatives by L-undecyl-leucine surfactants

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Introduction
Amino acid based surfactants are used in micellar electrokinetic chromatography (MEKC) in order to separate chiral analytes and study the mechanisms for chiral recognition (1-5). In previous studies, Shamsi et al. separated amino, catonic and neutral enantiomers using undecyl-leucine-valine surfactant mixtures. Billiot et al. achieved the separation of 12 analytes using 18 types of amino acid surfactant mixtures, and Agnew-Heard et al. used N-Undecyleryl-1-valinate to separate neutral, acidic, and basic compounds (1, 3, 7). Other studies have investigated the effects of such factors as the number of amino acid molecules in each surfactant, amino acid order, and the number of chiral centers in each surfactant (7-17) on chiral selectivity. Some studies have also examined the effects of steric factors, polydispersity levels, solution temperature, and the depth of penetration of analytes into the micellar core (7, 18-22) have on enantiomeric recognition.

For this study, the nature of chiral interactions in the amino acid based surfactant L-undecyl-leucine (und-Leu) will be investigated through the analysis of performance of arginine and sodium counterions. Arginine was chosen for this study because it has a cationic side chain which is susceptible to predictable changes in ionization state when solution pH is changed.

Methods

Chemicals

Lecine amino acid, L-Arginine, D-Arginine, and racemic mixtures of binapthyl (BOH) and binaphthalophosphol (BNP) were purchased from Sigma-Aldrich (St. Louis, MO). L-Leucine surfactants were synthesized from N-hydroxysuccinimide ester of undecylenic acid according to a previously published procedure (29). The structures of these surfactants, analytes, and arginine are provided in Fig.1.

The single amino acid surfactant of sodium N-undecyl-L-leucine (SUL) was studied at a 50 mM concentration (29). The structure of this monomeric amino acid surfactant is provided in Fig. 1. The pH levels of the samples were varied with the use of an NaOH buffer and concentrated HCl.

Capillary electrophoresis procedure

Solutions of und-Leu with both a sodium and arginine counterion were used to chirally separate BNP and BOH enantiomers. Chiral separations were performed using a Hewlett-Packard (HP) 3D CE model 8710A. The fused silica capillary [effective length of 45 cm (to detection window), 30-µm i.d., with a total length of 56 cm] was purchased from Agilent Technologies (Lake Jackson, TX) and mounted in an HP capillary cartridge. The temperature of the capillary was constant at 25°C throughout this experiment.

For this experiment, buffer solutions und-Leu and the counterion were made with four different pH’s (7, 8, 9, 10, and 11) and these pH solutions were each made into eight different concentrations (15, 20, 25, 30, 35, 40, 45, and 50 mM). Solutions of 50 mM Leu-L-leucine with arginine and sodium were prepared in a 5 mM sodium borate buffer and pH was adjusted to values of 7-11 with the use of NaOH and HCl. These solutions were diluted to concentrations ranging from 15 to 50 mM and were filtered through a 0.45-µm syringe before use. A new capillary was conditioned for 30 min with 1 M NaOH, followed by 10 min with triply distilled water. The capillary was then flushed with buffer for 3 min prior to injection of the sample. Analyte standards were prepared in 1:1 methanol–water at 0.1 mg/mL. Samples were injected for 5 s at 10 bar pressure. Separations were performed at +30 kV, with UV detection at 230 nm.

Results and discussion

As can be seen in Figure 2, when arginine is used as the counterion for the separation of BNP, the enantiomeric separations increase as a function of solution concentration from 2.15 µm to 30.4 µm where the resolution begins to level off. Also shown in the inset in Figure 2 is the effect of pH on the enantiomeric resolution of BNP as a function of pH. The results show a nearly linear relationship between pH and chiral recognition ability, as the pH increases the enantiomeric resolution of BNP decreases.

For the analysis of BNP, chiral separation may be required to be robust in magnitude when either sodium or arginine counterions are used with sodium possibly being a slightly better performing counterion (see Fig. 3). In looking at the effect of und-Leu concentration on the enantiomeric separation of BOH, no predictable associations may be said to occur though there are some noticeable patterns. For und-Leu-Na, the maximum resolution (Rsep 3.24) occurred at pH 11 and at a 2.5 mM concentration of the buffer while for und-Leu-Arg, the maximum resolution (Rsep 5.13) occurred at pH 7 and at 2 mg/mL und-Leu. These results indicate that at pH 7-9, optimum resolution is observed around 20-50 mM and und-Leu. Na in looking at the chiral selectivity of BHP with und-Leu-Arg, a decline in resolution from 2.5 to 0.05 occurred at pH 7 and at 2 mg/mL und-Leu. A similar decline occurs at pH 10 and 11.

As shown in Figure 3, the retention factors (k') for BOH and BNP are very similar in terms of both ion strength and trends. That said, at lower pH values, the retention factors of BOH and BNP are higher when arginine is used as a counterion as opposed to sodium. Despite this, pH increases, the differences in the retention factors between sodium and sodium and between BOH and BNP decreases. These phenomena changes in k’ and selectivity are likely due to the change in electrostatic attraction between the micelle and the counterion as a function of pH. As discussed previously, arginine has two amines with the same charge in a single ion, whereas sodium has one at pH 7. The sodium is almost 99% neutral and a, pH of 10-11, it has lost most (99%) of its charge (24). The decrease in the positive charge on the sodium causes a decrease in the overall electrostatic attraction between arginine and the negatively charged capillary. group on the und-Leu surfactant head group.

The results of this study also indicate that the use of arginine as a counterion may enhance the chiral separation of BNP in the presence of und-Leu. This finding is aligned with previous studies indicating the conformation state of an amine and may cause charged analytes to preferentially interact with amino acid heads (5). As well, it is hypothesized that the change of analyte effects locations where they interact on the micelle (22). Also, the variation of resolution with pH are important to support previous findings indicating that micelle shape is highly affected by the acidity or basicity of the environment (26). This variation of shape is thought to affect micelle’s ability to interact with analysis for reasons that surface area and stereometry are changed which may allowable certain chiral or hydrogen to hydrogen interactions. In addition, the differing shape of micelles in different pH’s may change the static qualities of the micelle and it has been documented in previous studies that static factors are crucial to the interactions that precede chiral separation (7, 15, 20-21).

Acknowledgments

Supported by National Science Foundation (NSF), Award #206966, National Science Foundation – Texas A&M University System Louis Stokes Alliance for Minority Participation (TAMUS LSAMP), Award #0752020, Welch Departmental grant, Award #4834010, Title V-STEM SOAR Award #P0331C11001572, and Texas A&M University—McNair Scholars Research program.

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