Chiral Separation of Norlaudanosoline, Laudanosoline, Laudanosine, Chlorthalidone, and Three Benzoin Derivatives Using Amino Acid Based Molecular Micelles

Fereshteh Haddadian Billiot* and **Eugene J. Billiot**
Department of Physical and Life Sciences, Texas A&M University–Corpus Christi, Corpus Christi, TX, 78412

Yuen Kwun Ng and **Isiah M. Warner**
Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803

Abstract

In this study, 18 polymeric single amino acid and dipeptide surfactants are examined, and their performances, in terms of enantioselectivity, are compared for norlaudanosoline, laudanosoline, laudanosine, chlorthalidone, benzoin, benzoin methyl, and benzoin ethyl enantiomers. Several aspects of amino acid-based polymeric surfactants including comparison of single amino acid versus dipeptide, amino acid order, steric effect, and effect of the position of the chiral center of dipeptide surfactants on the chiral selectivity of these optically active compounds are discussed.

Introduction

Polymeric surfactants have certain advantages over conventional micelles as pseudostationary phases in electrokinetic chromatography (EKC) (1). Polymeric surfactants do not have a critical micelle concentration (CMC). Therefore, the optimum polymer concentration for resolution of some enantiomers may occur below the CMC of the corresponding monomers. In addition, the dynamic equilibrium between the monomer and micelle is eliminated, resulting in faster mass transfer rate of the enantiomers. These inherent advantages have led to the development of a variety of different polymeric pseudostationary phases for use in EKC (2–10). Several studies reported by Billiot et al. have examined the use of polymeric dipeptide chiral surfactants (PDCSs) in chiral separation using EKC (11–17). In one study, the effect of amino acid order and polarity of PDCS on the chiral resolution of binaphthyl derivatives were examined (11,12). In addition, these authors also investigated the role of the depth of penetration of the analyte into the micellar core of the PDCS on chiral separations (13). Next, the effect of steric factors, number, and position of chiral centers on chiral resolution (14) were investigated. The goal of this paper was to further investigate the role of the mentioned parameters on chiral recognition of a different group of chiral analytes.

* Author to whom correspondence should be addressed.

Experimental

Chemicals

Single amino acids, dipeptides, and racemic mixtures of the chiral analytes were purchased from Sigma (St. Louis, MO). The structures of the chiral analytes examined in this study are provided in Figure 1. Surfactant monomers were synthesized from the *N*-hydroxysuccinimide ester of undecylenic acid, according to the procedure previously reported (18). The six single chiral center dipeptide surfactants examined in this study were sodium *N*-undecanoyl (L,L) glycyl-alaninate (SUGA), sodium *N*-undecanoyl L-alanyl-glycinate (SUAG), sodium *N*-undecanoyl L-glycyl-valinate (SUGV), sodium *N*-undecanoyl L-valyl-glycinate (SUVG), sodium *N*-undecanoyl L-glycyl-leucinate (SUGL), and sodium *N*-undecanoyl L-leucyl-glycinate (SULG). The nine double chiral center dipeptide surfactants used in this study were sodium *N*-undecanoyl (L,L) alanyl-alaninate (SUAA), sodium *N*-undecanoyl (L,L) alanyl-valinate (SUAV), sodium *N*-undecanoyl (L,L) alanyl-leucinate (SUAL), sodium *N*-undecanoyl (L,L) valyl-alaninate (SUVA), sodium *N*-undecanoyl (L,L) valyl-valinate (SUVV), sodium *N*-undecanoyl (L,L) valyl-leucinate (SUVL), sodium *N*-undecanoyl (L,L) leucyl-alaninate (SULA), sodium *N*-undecanoyl (L,L) leucyl-valinate (SULV), and sodium *N*-undecanoyl (L,L) leucyl-leucinate (SULL). In addition, three single amino acid surfactants, sodium *N*-undecanoyl L-alaninate (SUA), sodium *N*-undecanoyl L-valinate (SUV), and sodium *N*-undecanoyl L-leucinate (SUL), were studied. A 100mM sodium salt solution of the monomer was then polymerized using ^{60}Co-g radiation. After polymerization, proton NMR spectroscopy was used to confirm polymerization. NMR spectra were recorded on a Bruker ARX 300 MHz spectrometer and the data were processed with Bruker XWINNMR software (Bruker Co., Billerica, MA) operating

on a Silicon Graphics Indigo workstation (Silicon Graphics Inc., Mountain View, CA). Solutions of surfactants were prepared in H_2O, and the signal disappeared at approximately 4 ppm, indicating that polymerization was complete. The structure of monomeric units of the surfactants is illustrated in Figure 2.

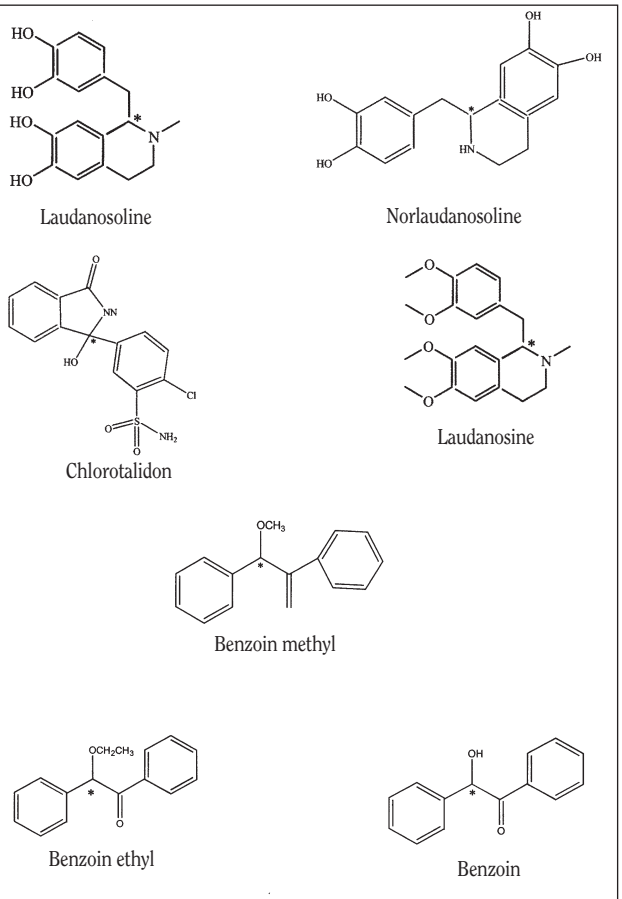
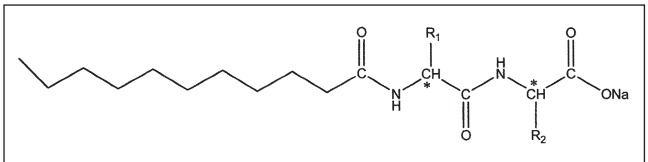


Figure 1. Structure of chiral analytes. Chiral centers (*).



R1	R2	Surfactant
CH_3	—	SUA
$CH(CH_3)_2$	—	SUV
$CH_2CH(CH_3)_2$	—	SUL
H	CH_3	SUGA
H	$CH(CH_3)_2$	SUGV
H	$CH_2CH(CH_3)_2$	SUGL
CH_3	H	SUAG
CH_3	CH_3	SUAA
CH_3	$CH(CH_3)_2$	SUAV
CH_3	$CH_2CH(CH_3)_2$	SUAL
$CH(CH_3)_2$	H	SUVG
$CH(CH_3)_2$	CH_3	SUVA
$CH(CH_3)_2$	$CH(CH_3)_2$	SUVV
$CH(CH_3)_2$	$CH_2CH(CH_3)_2$	SUVL
$CH_2CH(CH_3)_2$	H	SULG
$CH_2CH(CH_3)_2$	CH_3	SULA
$CH_2CH(CH_3)_2$	$CH(CH_3)_2$	SULV
$CH_2CH(CH_3)_2$	$CH_2CH(CH_3)_2$	SULL

Figure 2. Structure of monomeric unit of amino acid based surfactants. Chiral centers (*).

Capillary electrophoresis procedure

The EKC separations were performed using a Hewlett-Packard (HP) 3D CE model #G1600AX. The fused silica capillary [effective length of 55 cm (to detection window), 50-µm i.d., with a total length of 63.5 cm] was purchased from Polymicro Technologies (Phoenix, AZ) and mounted in an HP capillary cartridge. The cartridge temperature was maintained at 12°C for the separation of all analytes examined in this study. The running background electrolytes, which contained 30mM sodium phosphate were prepared in triply distilled water and pH adjusted to 7. All solutions were filtered through a 0.45-µm membrane filter before use.

A new capillary was conditioned for 30 min with 1N NaOH at 60°C, followed by 10 min with triply distilled water. The capillary was then flushed with buffer for 2 min prior to injection of the sample. All analyte standard solutions were prepared in 1:1 methanol–water at 0.3–0.5 mg/mL. Samples were injected for 5 s at 10 mbar pressure. Separations were performed at + 30 kV, with UV detection at 220 nm.

Results and Discussion

This study was designed to examine the effect of steric hindrance, number and location of chiral centers, size and location of amino acid side chain, and amino acid order of 18 PDCSs on chiral selectivity of seven chiral analytes. For the purpose of this manuscript, analytes examined in this study are classified in two groups: Group I includes norlaudanosoline, laudanosoline, laudanosine, and chlorthalidone, and group II analytes include benzoin, benzoin methyl, and benzoin ethyl. The optimum chiral selectivity for group I compounds was determined to be between the 6 and 10mM equivalent monomer concentrations (EMC) of the polymeric surfactants, and optimum selectivity of the group II analytes was achieved at approximately 50mM EMC.

Single amino acid versus dipeptide surfactants

The single amino acid surfactants examined in this study all possess one chiral center with two carbonyls and one amide moiety, but the dipeptide surfactants contain two chiral centers, three carbonyls and two amide moieties in their polar heads (Figure 2). The differences in polar heads of these two classes of surfactants indicate that dipeptides provide more hydrogen bonding sites and more possible chiral interaction sites, as compared with the single amino acid surfactants. In this section, the chiral selectivity of group I and II analytes is discussed using three polymeric single amino acid chiral surfactants, SUA, SUV, and SUL, three PDCSs, SUAA, SUVV, and SULL, as chiral pseudostationary phases (CPSP).

Group I analytes

As observed in Figure 3, all three single amino acid surfactants examined in this study resolved the enantiomers of norlaudanosoline. Polymers of SUV and SUL provided α values of 1.136 and 1.127 for the enantiomers of this analyte. These values are significantly higher than the α values obtained with their dipeptide counterparts, poly SUVV (α = 1.063) and poly SULL (α = 1.081). However, note that the dipeptide surfactant poly SUAA

provided a chiral selectivity of 1.114, and an α value of 1.098 was obtained using poly SUA. Among these six single amino acid and dipeptide surfactants, the single amino acid surfactant (poly SUV) provided the best chiral selectivity for the enantiomers of norlaudanosoline.

Laudanosoline has a very similar structure to norlaudanosoline. As shown in Figure 1, the only difference in the structure of these two analytes is that norlaudanosoline has a secondary amine and laudanosoline has a tertiary amine. The single amino acid surfactants poly SUV and poly SUL provided α values of 1.052 and 1.057, respectively, for the enantiomers of laudanosoline. Similar to norlaudanosoline, these values are higher than the α values provided by poly SUVV (α = 1.014) and poly SULL (α = 1.041). However, the dipeptide surfactant poly SUAA provided better chiral selectivity (α = 1.097) as compared with the single amino acid surfactant poly SUA (α = 1.060).

The next analyte examined, laudanosine, also has a structure similar to norlaudanosoline and laudanosoline. The difference in the structure of laudanosine and laudanosoline is that the hydroxyl groups of laudanosine are methylated (Figure 1A). Methylation of the hydroxyl groups of laudanosine result in a more hydrophobic and sterically hindered compound. Poly SUA is the only single amino acid surfactant that provided some chiral selectivity for enantiomers of this analyte. Although the polymers of the single amino acid surfactants SUV and SUL did not resolve the enantiomers of laudanosine, a chiral selectivity of 1.040 and 1.107, respectively, was obtained using the dipeptide surfactants poly SUVV and poly SULL.

Chlorthalidone, which is also one of the group I analytes examined in this study, is structurally very different from the other three analytes in this group. However, similar to laudanosine and laudanosoline, the dipeptide surfactants provided better chiral selectivity for the enantiomers of chlorthalidone. As shown in Figure 3, the single amino acid surfactants poly SUA, poly SUV, and poly SUL provided α values of 1.124, 1.094, and 1.077, respectively. Note that the α values of the dipeptide surfactants for these amino acids [poly SUAA (α = 1.128), poly SUVV (α = 1.156), and poly SULL (α = 1.107)] were always similar to or higher than that of the single amino acid counterpart.

Group II analytes

The group II analytes examined in this study are benzoin derivatives. All of the single amino acid surfactants (poly SUA, poly SUV, and poly SUL) and the dipeptide surfactants (poly SUAA, poly SUVV, and poly SULL) provide some chiral recognition for the enantiomers of the benzoin derivatives examined in this study. As shown in Figure 4, among these surfactants, poly SULL provided the highest chiral selectivity for enantiomers of benzoin and benzoin methyl with α values of 1.060 and 1.042, respectively. These α values were higher than the 4 α values obtained with the single amino acid surfactant poly SUL. In addition, among these six single amino acid and dipeptide surfactants, the highest chiral selectivity (α = 1.030) was achieved for enantiomers of benzoin ethyl when poly SUVV was used as the CPSP.

Examination of the α values shown in Figures 3 and 4 indicate that, with the exception of norlaudanosoline, in which the single amino acid surfactant poly SUV provided a higher α value than the corresponding dipeptide (poly SUVV), PDCSs provide lower α values compared with their single amino acid counterparts.

Effect of amino acid order on chiral recognition

Billiot et al. demonstrated that the amino acid order of a PDCS

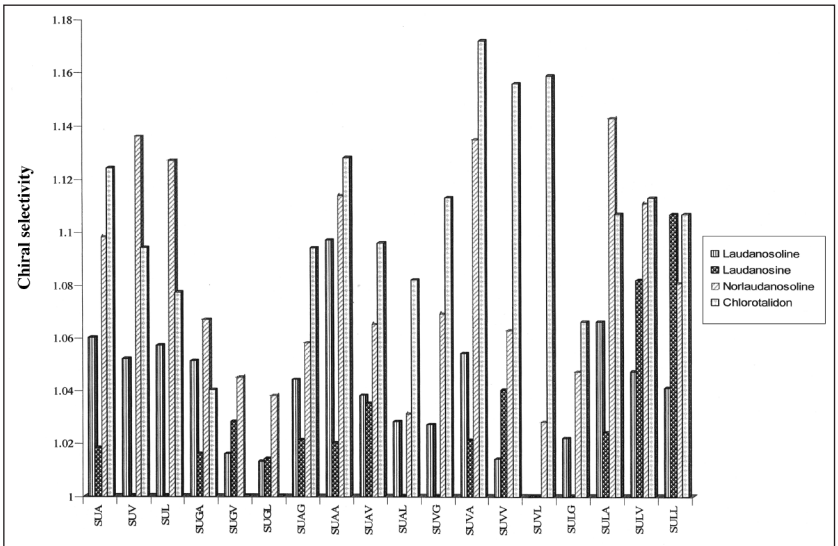


Figure 3. Chiral selectivity of norlaudanosoline, laudanosoline, laudanosine, and chlorthalidone: +30 kV applied voltage; 215 nm UV detection; sample concentration, 0.1 mg/mL; surfactant concentrations, 6–10mM of EMC; and average standard deviation ±0.002, calculated from enantiomers migration time.

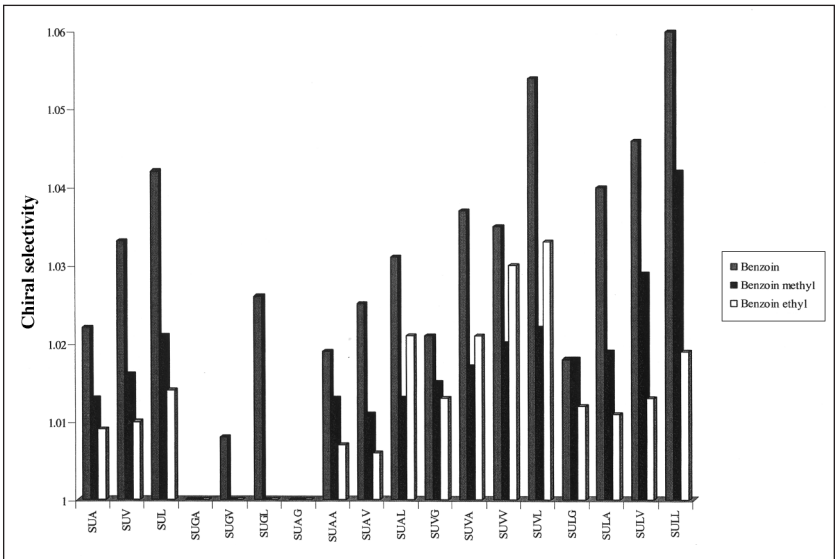


Figure 4. Chiral selectivity of benzoin derivatives. Applied voltage, +30 kV; UV detection, 215 nm; sample concentration, 0.1 mg/mL; surfactant concentrations, 50mM of EMC; and average standard deviation, ± 0.001, calculated from enantiomers migration time.

has a significant effect on the performance of the PDCS in terms of chiral recognition (11). In that study, the authors compared the chiral recognition ability of poly SULV and poly SUVL. Baseline resolution of (±)-1,1'-bi-2-naphthol, and (±)-1,1'-binaphthyl-2,2'-dihydrogen phosphate enantiomers was obtained using poly SULV, though no hint of chiral recognition of these enantiomers was obtained using poly SUVL. Note that the difference in the two surfactant polar heads is that in SULV, the larger amino acid, leucine, is located at the N-terminal position and valine is located at C-terminal position. However, in SUVL, the position of the amino acids was reversed; valine is the N-terminal amino acid and leucine is the C-terminal amino acid. A similar approach is used in this study. The chiral selectivity of group I and II analytes with polymers of SUAV, SUAL, and SUVL was compared with that of poly SUVA, poly SULA, and poly SULV, respectively.

Group I analytes

As observed in Figure 3, better chiral selectivity was observed for enantiomers of norlaudanosoline when the larger of the amino acids were located in the N-terminal position of the PDCS. An α value of 1.143 was obtained for the enantiomers of this analyte using poly SULA, with the larger of the amino acid at the N-terminal position, compared with poly SUAL, which resolved the enantiomers of norlaudanosoline with an α value of 1.031. Similarly, poly SUAV and poly SUVL provided selectivity factors of 1.065 and 1.028, respectively, though selectivity factors of 1.135 and 1.111 were obtained with poly SUVA and poly SULV, respectively. The same trend was observed when comparing the chiral selectivity of laudanosoline and laudanosine. For example, using poly SULV as the CPSP, chiral selectivities of 1.047 and 1.082 were obtained for the enantiomers of laudanosoline and laudanosine, respectively. However, poly SUVL did not show any hint of chiral recognition for enantiomers of these analytes. It should be noted that there was one exception. Poly SUAV with the larger of the amino acid at the C-terminal position provided better chiral selectivity for the enantiomers of laudanosine as compared with poly SUVA.

An examination of the effect of the order of the amino acids on chiral selectivity of chlorthalidone indicated that the amino acid order has little effect. As seen in Figure 3, an α value of 1.107 was observed with poly SULA, though poly SUAL had an α of 1.082. However, poly SUVL provided a higher chiral selectivity factor than SULV. Poly SUVL provided an α value of 1.159, and poly SULV resulted in an α value of 1.113 for the enantiomers of chlorthalidone. In contrast, poly SUVA (α = 1.172) is a better CPSP for the enantiomers of this optically active analyte than poly SUAV (α = 1.096).

Group II analytes

No consistent trend with regard to amino acid order was observed with group II enantiomers. Benzoin enantiomers were better separated with poly SUVL (α = 1.054) than poly SULV (α = 1.046). In contrast, poly SULA provided an α value of 1.040, though a chiral selectivity of 1.031 was obtained using poly SUAL. Similar to the enantiomers of benzoin, poly SUVL provided a greater α value (1.033) for the enantiomers of benzoin ethyl compared with poly SULV (α = 1.013). However the chiral selectivity of these enantiomers was higher with poly SUAL (1.021) compared with poly SULA (1.011). Benzoin methyl, the other chiral analyte in group II, was separated better with poly SULV (α = 1.029) than poly SUVL (α = 1.022).

The results of this study suggest that, among the analytes examined in group I, with the exception of chlorthalidone, the amino acid order of the PDCS does play a major role in chiral selectivity of these sterically hindered enantiomers. Billiot et al. proposed a model to explain the interaction of sterically hindered chiral enantiomers with PDCSs (12). According to that model, when the larger of the amino acids of the PDCS is located at the C-terminal position, this may limit access of bulky analytes to the N-terminal chiral center of the PDCS, thus potentially decreasing its chiral selectivity. The reason that the enantiomers of the group II analytes examined in this study do not follow any observable trend with regard to the order of amino acids is possibly attributable to the less sterically hindered structure of these analytes as compared with group I analytes.

Effect of steric factors on chiral selectivity

The effect of steric factors on chiral selectivity is examined by varying the size of the R-group in the C- or the N-terminal position (or both) of dipeptide surfactants. It should be noted that the size of the R-group increases from alanine to valine to leucine. Therefore, the C-terminal amino acid of SUAV (with valine at the C-terminal position) is more sterically hindered than that of SUAA (with alanine in the C-terminal position).

Group I analytes

The chiral selectivity of laudanosoline enantiomers decreases when the N-terminal amino acid of the PDCS with two chiral centers is held constant and the size of the C-terminal amino acids increases. As observed in Figure 3, increasing the steric hindrance of a PDCS in the series SUAA (α = 1.097), SUAV (α = 1.038), and SUAL (α = 1.028) resulted in a decline in chiral selectivity of the laudanosoline enantiomers. An even greater decline in selectivity of this analyte was observed with polymers of SUVA, SUVV, and SUVL. Similarly, the selectivity factor of these enantiomers decreased from poly SULA (α = 1.066), to poly SULV (α = 1.047), to poly SULL (α = 1.041). However, no trend for the chiral selectivity of laudanosoline enantiomers was observed when the size of the C-terminal amino acid of the PDCS was held constant and the size of the N-terminal amino acid was increased. It should be noted that the chiral selectivity of laudanosoline enantiomers was favored by the less sterically hindered dipeptide surfactant poly SUAA (α = 1.097).

Similar to the enantiomers of laudanosoline, the chiral selectivity of norlaudanosoline enantiomers decreased when the size of the C-terminal amino acid of the PDCS increased and the size of the N-terminal was held constant. There was one exception: when the size of the C-terminal amino acid of the PDCS was held constant and the size of the N-terminal amino acid increased, the chiral selectivity of these enantiomers also increased. The exception was observed with poly SUAL and poly SUVL. An α value of 1.031 was obtained with poly SUAL, which was slightly larger than the α value obtained with poly SUVL (1.028). Of these surfactants, poly SULA provided the greatest chiral selectivity for the enantiomers of norlaudanosoline.

The effect of steric factors on chiral recognition was different

for laudanosine than what was observed for norlaudanosoline and laudanosoline. No significant difference in the chiral selectivity of laudanosine was observed for the polymers of SUAA (α = 1.020), SUVA (α = 1.021), and SULA (α = 1.024). In contrast, the chiral selectivity of laudanosine increased in the series poly SUAV (α = 1.035), poly SUVV (α = 1.040), and poly SULV (α = 1.082). Although poly SUAL and poly SUVL did not provide any chiral selectivity for the enantiomers of laudanosine, an α value of 1.107 was obtained for these enantiomers with poly SULL. It should be pointed out that laudanosine enantiomers do not follow any definite trends with respect to steric factors. However, poly SULL, with the most sterically hindered polar head, provided the best chiral selectivity for these enantiomers.

In the case of chlorthalidone, a decrease in chiral selectivity was observed from SUAA (α = 1.128) to SUAV (α = 1.096) and SUAL (α = 1.082). However, poly SULV provided an α value of 1.113. This value is higher than the chiral selectivity values obtained with poly SULA (α = 1.107) and poly SULL (α = 1.107). Similarly, no trend was observed when the size of the N-terminal amino acid of the PDCS was held constant and the size of the C-terminal amino acid increased. It is interesting to note that the greatest chiral selectivity of these enantiomers was achieved when the valine was located at the N-terminal position. Polymers of SUVA, SUVV, and SUVL provided α values of 1.172, 1.156, and 1.159, respectively. These values were among the highest α values obtained for these enantiomers.

Group II analytes

An examination of the effect of steric factors on the chiral selectivity of benzoin and benzoin methyl indicates that when the size of the C-terminal amino acid was held constant and the size of the N-terminal amino acid increased, the chiral selectivity of these enantiomers increased. For example, as shown in Figure 4, the α values for the enantiomers of benzoin increased from poly SUAA (α = 1.019) to poly SUVA (α = 1.037) and poly SULA (α = 1.040). Interestingly, a similar trend was observed when the size of the N-terminal amino acid was held constant and the size of the C-terminal amino acid was increased. Poly SULL, the PDCS which has the largest amino acid at both the C- and N-terminal position, provided α values of 1.060 and 1.042 for the enantiomers of benzoin and benzoin methyl, respectively. It should be mentioned that these are the highest values among the α values shown in Figure 4, for the enantiomers of these analytes. Therefore, it can be concluded that, for the surfactants examined in this study, the chiral selectivity of benzoin and benzoin methyl enantiomers is favored by an increase in steric factors in the polar head group of the PDCS.

Similar to benzoin and benzoin methyl, higher α values for the enantiomers of benzoin ethyl were achieved when the size of the N-terminal amino acid of the PDCS was held constant and the size of the C-terminal amino acid was increased. Note that the α values increased in the series of poly SULA (α = 1.011), poly SULV (α = 1.013), and poly SULL (α = 1.019). However, no trend was observed when the size of the C-terminal amino acids was held constant and the size of the N-terminal amino acid increased. The best chiral selectivity of these enantiomers was achieved using polymers of SUVV (α = 1.030) and SUVL (α = 1.033).

Effect of the position of the chiral center of polymeric dipeptide surfactants on chiral selectivity

The effect of the position of the chiral center on chiral selectivity of group I and II analytes was examined using six single chiral center PDCSs: poly SUAG, poly SUVG, poly SULG, poly SUGA, poly SUGV, and poly SUGL. In three of these surfactants (poly SUAG, poly SUVG, and poly SULG), the chiral center is located at the N-terminal position of the PDCS. In the other three surfactants (poly SUGA, poly SUGV, and poly SUGL), the chiral center is located at the C-terminal position.

Group I analytes

As shown in Figure 3, all six single chiral center PDCSs (SUGA, SUGV, SUGL, SUAG, SUVG, and SULG) provided some chiral selectivity for the enantiomers of norlaudanosoline. Polymers of SUGV and SUGL, with the chiral centers located at the C-terminal position, provided chiral selectivities of 1.045 and 1.038, respectively. However, poly SUVG and poly SULG, with the chiral center located at the N-terminal position, separated enatiomers of norlaudanosoline with α values of 1.069 and 1.047, respectively. Consequently, it can reasonably be concluded that the enantiomers of this analyte interact with both the C- and N-terminal amino acids of the PDCS. Similar results were observed for the enantiomers of laudanosoline.

In the case of laudanosine, poly SUGV and poly SUGL, PDCSs with chiral centers at C-terminal position, provided selectivity values of 1.028 and 1.014, respectively, though no chiral selectivity of these enantiomers was obtained using poly SUVG and poly SULG (with chiral centers at the N-terminal position). However, α values of 1.016 and 1.021 were obtained using poly SUGA and poly SUAG, respectively.

Similar to laudanosine, both poly SUAG and poly SUGA provided some chiral selectivities for enantiomers of chlorthalidone. However, poly SUVG and poly SULG provided α values of 1.113 and 1.066, respectively, for enantiomers of chlorthalidone, though no chiral recognition of these enantiomers was observed using SUGV and SUGL.

The reason that poly SUVG and poly SULG do not provide chiral selectivity for enantiomers of laudanosine and chlorthalidone is not clear. However, because both poly SUAG and poly SUGA provide some chiral selectivity for enantiomers of these two analytes it can be assumed that these enantiomers interact with both chiral centers of the PDCS.

Group II analytes

From the enantioselectivity data shown in Figure 4, it can reasonably be concluded that benzoin methyl and benzoin ethyl interacted preferentially with the N-terminal amino acid of single chiral center PDCSs. Poly SUVG and poly SULG provided selectivity factors of 1.015 and 1.018 for enantiomers of methyl benzoin, respectively. In addition, the enantiomers of ethyl benzoin were separated with selectivity values of 1.013 and 1.011, respectively, using poly SUVG and poly SULG. However, no chiral selectivity of the enantiomers of these analytes was achieved with the polymers of SUGV and SUGL. The reason that neither poly SUAG nor poly SUGA were able to enantiomerically resolve the optical isomers of these two analytes was possibly the small size of the polar head of these surfactants. As noted previously, the enan-

tiomeric separation of the benzoin derivatives examined in this study appear to be favored by an increase in steric factors.

In contrast to benzoin methyl and benzoin ethyl, examination of the data suggests that the enantiomers of benzoin interact with both amino acids of the polymeric dipeptide surfactants examined in this study. Poly SUGL, with the chiral center at the C-terminal position, and poly SULG, with the chiral center at the N-terminal position, separated the enantiomers of benzoin with chiral selectivities of 1.026 and 1.018, respectively. In addition, polymers of SUVG and SUGV provided α values of 1.021 and 1.008, respectively, for enantiomers of this chiral analyte. This difference in the preferential interaction site of benzoin compared with benzoin methyl and benzoin ethyl may be attributable to the hydrophobicity of these analytes. Benzoin is more hydrophilic than benzoin methyl and ethyl. Therefore, benzoin interacts closer to the surface of the micelle while the other two chiral analytes (benzoin ethyl and benzoin methyl) penetrate deeper into the micellar core of the PDCS and interact preferentially with the N-terminal amino acid.

It should be mentioned that the preferential site of interaction in neutral enantiomers depends upon the hydrophobicity and steric hindrance of the analyte. Benzoin, which is more hydrophilic than benzoin methyl and benzoin ethyl, interacts with both C- and N-terminal amino acid, but the latter two enantiomers interact preferentially with the N-terminal amino acid. Enantiomers in group I interact with both C- and N-terminal amino acids. This is possibly caused by the steric hindrance in these analytes and the fact that the micellar core of the polymer is rigid. Rigidity of the micellar core of the polymeric surfactants does not allow enantiomers of the highly hydrophobic and sterically hindered analytes to penetrate too deeply into the micelle core.

Conclusion

Polymeric dipeptide chiral surfactants provided better chiral separation for six out of seven analytes examined in this study, compared with single amino acid surfactants. In addition, analyzing the chiral selectivity values indicated that steric factors of the PDCS are important in their performance in the chiral separation of six out of seven enantiomers examined in this study. Results of this study suggest that PDCSs, with the most sterically hindered environment (i.e., SULL and SUVL), provided the highest chiral selectivity for group II analytes. In contrast, poly SULA and poly SUVA, with the least stericlly hindered amino acid (alanine) at C-terminal, provided the best chiral separations for enantiomers of laudanosoline, norlaudanosoline, and chlorthalidone. Moreover, the position of the chiral center of a PDCS plays an important role in chiral selectivity of the analytes examined in this study.

Thus for the analytes examined in this study, the results suggest that chiral selectors with more sterically hindered environments provide better chiral selectivity for less sterically hindered analytes. Conversely, chiral selectors with less sterically hindered environments provide better chiral selectivity for analytes with sterically hindered chiral centers.

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