Combined use of cyclofructans and an amino acid ester-based ionic liquid for the enantioseparation of huperzine A and coumarin derivatives in CE

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Abstract

Cyclofructans (CFs) and their derivatives have recently been proven to be efficient chiral selectors (CSs) for the enantioseparation of several analytes in CE, HPLC, and GC. In this study, the chiral separation ability of a number of native and derivatized CFs was examined in CE. Particularly, six different CFs, with different derivatization groups and cavity sizes (native CF-6 and CF-7, isopropyl cyclofructan-6 (IPCF-6), IPCF-7, sulfated cyclofructan-6 (SCF-6), and SCF-7) were used as CSs for the enantioseparation of huperzine A, warfarin, and coumachlor. Almost all of the examined CFs, except for SCF-6-8-7, demonstrated relatively low and sometimes no chiral separation ability for huperzine A. In an effort to improve both resolution and efficiency, the chiral liquid ionic D-Alanine tert butyl ester lactate (D-AlaC4Lac) was added into the BGE. In most of the cases, the combination of CF with D-AlaC4Lac resulted in an improvement in peak efficiency and/or resolution. When CF-6 was utilized with D-AlaC4Lac, a resolution of 1.4 was obtained, while the use of IPCF-6/D-AlaC4Lac provided a baseline enantioseparation. Although the combination of SCF-7 and 40 mM D-AlaC4Lac did not affect resolution, it dramatically increased peak efficiency from 24 000 to 117 000. In the case of warfarin and coumachlor, IPCF-6 and IPCF-7 proved to be the most effective CSs. It is, therefore, concluded that the size of the cavity and the CF derivatization are the key parameters for the chiral separation capability. It is also clear from this study that D-AlaC4Lac is necessary for improved peak efficiencies and resolutions. The method was then validated by estimating the run-to-run and batch-to-batch repeatability of the method, at the optimum conditions. Finally, by estimating the uncertainty of measurements, the particular method could be suggested for the routine analysis of pharmaceutical compounds.

Experimental and Methods

Separation Conditions

- Agilent CE System equipped with UV-Vi detector (230 nm, 214nm).
- Fused-silica capillary column (l=55.5 cm, I=30.0 cm).
- A new capillary was washed with H2O (5 min), 1 M NaOH (60 min), H2O (10 min), BGE (30 min).
- BGE: i) Tris/Borate, ii) 4 nM Ammonium Acetate in H2O/MeOH (95:5), pH = 4.0, iii) 4 mM Ammonium Acetate in H2O/MeOH (80:20), pH = 4.0

Chiral Selectors and analytes

Use of native CF-6

- No chiral separation of Hup.A

Use of IPCF-6

- Greater enantioselectivity than CF-6

Use of IPCF-6 and D-AlaC4Lac

- Isopropyl groups provide more interaction sites for the enantioseparation

Addition of D-AlaC4Lac

- Addition of IL in the BGE caused increase of Rs

Synergistic effect

Conclusions

- Cyclofructans demonstrated low enantioselectivity in CE.
- Sulphated CFs demonstrated the greater enantioselectivity towards huperzine A probably due to the electrostatic interactions, however poor peak efficiency was observed.
- The addition of the chiral liquid D-AlaC4Lac in the BGE increased, in the most cases, the resolution and peak efficiency.
- A synergistic effect between D-AlaC4Lac and CFs probably takes place during the enantioseparation.
- Warfarin and coumachlor enantiomers were partially separated when IPCFs were used, while no enantioseparation was performed when SCFs were used. Therefore, the enantioseparation mechanism, in these cases, differs from that observed for huperzine A.
- The run-to-run and batch-to-batch reproducibility were evaluated and it can be concluded that the use of SCF-7 and the chiral liquid, can provide excellent reproducibility for the enantioseparation of huperzine A.

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References