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Synthesis and Characterization of Water-Soluble Carboxymethyl-Cyclodextrin Polymer as Capillary Electrophoresis Chiral Selector

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Abstract: The water-soluble carboxymethyl-cyclodextrin polymer (CM-CD polymer) was synthesized and used as capillary electrophoresis chiral selector. Verrapamil and thiopentorusodium were well separated using CM-CD polymer as chiral selector.

Keywords: Carboxymethyl-cyclodextrin polymer, capillary electrophoresis, chiral selector.

Cyclodextrin (CD) and its water-soluble derivatives have been used as chiral selectors in capillary electrophoresis successfully. Among them, the water-soluble CD polymer performs intramolecular synergistic effect in CE chiral separation and the carboxymethyl-CD (CM-CD) migrates in the opposite direction of the electroosmotic flow because of its negative charge in water. It is interesting to synthesize carboxymethyl-CD polymer (CM-CD polymer), which has properties of both the neutral CD polymer and the negative charged carboxymethyl group, and use it as CE chiral selector in separating drug enantiomers.

Synthesis and application of CD-polymer in capillary electrophoresis

CD-polymer was synthesized according to the literature[1]. Carboxymethyl-CD polymer was synthesized analogous to the procedures described in literature [2].

CD polymer (5g, 1.47mmol) was dissolved in 70mL water, KOH (4.15g, 74mmol) was added with stirring to dissolve thoroughly. The mixture was heated at 70℃and sodium chloroacetate (7.2g, 61.8mmol) was added. The temperature was kept at 90℃ for 3.5h. After cooling, the pH was adjusted to 5~6 by concentrated sulfuric acid. The anhydrous ethanol was added to precipitate inorganic salts. After filtering, the filtrate was concentrated and anhydrous methyl alcohol was added to precipitate the products. The product was collected and purified by the method described in ref. [3]. The products were dissolved in little water, and then precipitated by adding organic solvents again to remove the inorganic salts from products. Repeating the operation three times, then the products was collected and dried in vacum. Yield 70%

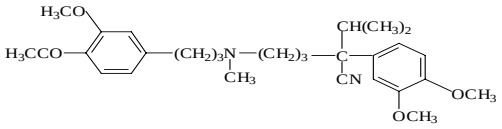
The CM-CD polymer was used as chiral selector in CE to separate chiral drugs of

Verrapamil (**a**) and thiopentorusodium (**b**). Their electrophoregrams were shown in **Figure** (0.5% carboxymethyl-CD polymer, 30mmol • L^{-1} Tris, pH 5.5, 4 respectively).

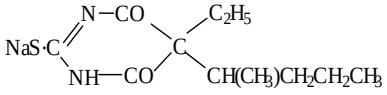
Experiments were carried out on CAPEL 103 CE SYSTEM (Lumex instruments, Russia) and on a Chrom & Spec CE Software system (Russia). Uncoated fused capillary of 46.5cm (effective length 38 cm) with 50 μm I.D. (Yongnian optical fiber factory, Hebei, China). All samples were injected by pressure on 503 mbar and detected by measuring the UV-absorbance at 254 nm. Separations were performed at room temperature applying a voltage of 14kV.

The results showed that the CM-CD polymer is a good CE chiral selector. Verrapamil was well-separated using CM-CD polymer as chiral selector, while it can not be separated with caboxymethyl-CD and CD polymer respectively. The thiopentorusodium was also well separated with CM-CD polymer as CE chiral selector. It is probable that the CM-CD polymer has the properties of CD polymer and the carboxymethyl-CD. So it improved the inclusion interaction to the guest by the intramolecular synergistic effect of CD polymer and migrated in the opposite direction of the electroosmic flow because of negative charge of the carboxymethyl group.

Figure Eletrophoregrams



(a)



(b)

Conclusion

The carboxymethyl-CD polymer was synthesized and used as CE chiral selector successfully. Verrapamil and thiopentorusodium were well separated using carboxymethy-CD polymer as chiral selector.

Referances

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