Chinese Chemical Letters Vol. 10, No. 10, pp. 831–832, 1999

Carboxymethyl-β-Cyclodextrin for Chiral Separation of Basic Drugs by Capillary Electrophoresis

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Abstract: Four basic drugs were separated by capillary electrophoresis (CE) using carboxymethyl-β-cyclodextrin (CM-β-CD) as chiral selector. The effects of CM-β-CD concentration, applied voltage, operation temperature were investigated. Under the selected conditions, norephedrine, ofloxacin, terbutaline and chlorpheniramine were enantiomerally baseline-separated using H_3PO_4-triethanolamine buffer at pH 3 containing 10, 5.5, 2, 2mmol/L CM-β-CD respectively.

Keywords: Capillary electrophoresis, chiral separation, carboxymethyl-β-cyclodextrin, basic drugs.

The separation of chiral compounds is of key importance in different areas of research, *e.g.*, pharmaceutical, biological, environmental *etc.*. Capillary electrophoresis (CE) is a powerful technique for chiral separation. The general merits of CE such as impressive peak efficiency, rapidity of analysis, small volumes and low costs are the most important factors contributing to the successful development of this technique[1,2]. Currently cyclodextrins(CDs) are the most commonly used chiral resolving agents in CE. Enantiomeric separation is based on the difference in inclusion-complex formation constants between a pair of enantiomers and CD. Neutral CDs (native α–,β–,and γ - cyclodextrin,CD, hydroxypropyl-, and methylated-β-CD) have been used successfully to separate a number of ionic chiral drugs, but they can not be used to separate neutral enantiomers. Therefore, charged CDs, both strong and weak electrolytes, have been introduced to analyze both neutral and ionic enantiomers. At the present time, anionic CD-derivatives are more commonly used as chiral selectors in CE than cationic ones. The affinity of the analyte for the CD, chiral selector is due to hydrophobic interactions between the analyte and the CD-cavity and hydrogen bonding of the analyte to OH-groups or other introduced functionalities on the CD-ring, this affinity is the first step towards chiral recognition. Introduced charges on the CD itself enable additional electrostatic interaction between the analyte and the chiral selector which increases the stability of analyte-CD complexs and can have a big influence on the resolution of the enantiomers[3].

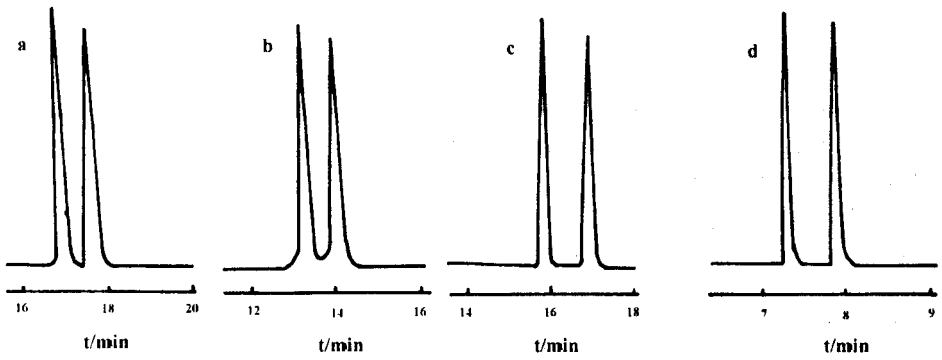
In this paper, carboxymethyl-β-cyclodextrin (CM-β -CD) was used as chiral selector for CE enantiomeric separation. The separation of four basic drugs was studied. The influences of CM-β-CD concentration, applied voltage, operation temperature were

investigated.

All the separations were carried out on a BioFocus 2000 CE System (BioRad, USA). The detection wavelength was set at 214 nm. The separations were carried out in a 50μm I.D. untreated fused-silica capillary (total length 40 cm,effective length 35 cm). Injection mode, hydrodynamic. The running buffer was composed of 100 mmol/L H_3PO_4 and the buffer pH was adjusted to pH 3 by triethanolamine. CM-β-CD was synthesized in our laboratory. All reagents were of analytical-reagent grade.

It should be regarded as gratifying that baseline separation of basic drugs such as norephedrine, ofloxacin, terbutaline and chlorpheniramine can be achieved using CM-β-CD, anionic CD-derivative as chiral selector under the conditions of 100mmol/L H_3PO_4-triethanolamine buffer at pH 3 containing 10, 5.5, 2, 2mmol/L CM-β-CD respectively, the results were showed in **Figure 1**. It was also found that migration time decreased with the increasing of applied voltage and low temperature was favorable to enantiomeric separation. For the migration time of the four basic drugs, the relative standard deviations (n=3) RSD%<5. The experimental results showed that CM-β-CD was a better chiral selector than β-CD and it possessed a higher solubility in water, therefore CM-β-CD has great potential to be used to separate other enantiomers by optimizing the conditions of CE.

Figure 1. Chiral separation of basic drugs



CE conditions: background electrolyte, 100mmol/LH_3PO_4-triethanolamine buffer, pH=3, applied voltage, 20KV, column temp., 20℃. (a) norephedrine, 10mmol/L[CM-β-CD] (b) ofloxacin, 5.5mmol/L [CM-β-CD] (c) terbutaline (d) chlorpheniramine (c,d) 2mmol/L[CM-β-CD]

Acknowledgment

This work was financially supported by the Natural Science Foundation of Zhejiang Province.

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Received 12 April 1999