Chinese Chemical Letters Vol. 13, No. 12, pp 1203 – 1204, 2002 1203
http://www.imm.ac.cn/journal/ccl.html

Effect of Micelle Composition on Acidic Drugs Separation Behavior by Micellar Electrokinetic Capillary Chromatography

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Abstract: Micellar electrokinetic capillary chromatography (MECC) separation of four acidic drugs similar in structure was studied. Both anionic surfactant sodium dodecyl sulfate (SDS) and nonionic surfactant Tween 20 were used to form single micelles and mixed micelles as pseudostationary phases. The effects of the composition of micellar solution on retention behaviors were studied. The results indicate that there is markedly different selectivity among SDS, Tween 20 and the mixed micelles systems.

Keywords: Micelle, electrokinetic chromatography, acidic drug.

Micellar electrokinetic capillary chromatography (MECC) is a branch of capillary electrophoretic techniques, in which surfactant micelles are added to the electrolyte solution as pseudostationary phase. Separation in MECC is based on electrophoretic mobilities of the analytes when partitioned into micelles[1]. In this work, four acidic drugs similar in structure with aryl carboxylic acid were separated by MECC. The effects of type of surfactant, such as anionic surfactant SDS, nonionic surfactant Tween 20 and mixtures of both, and the effect of addition of ethanol as organic modifier[2] on the retention time and selectivity were investigated. The uses of nonionic surfactant micelles and mixed micelle as the pseudostationary phases of MECC to separate ionic compounds are relatively new and unexploited areas[3].

The separations were performed on Waters Quanta 4000 capillary electrophoresis system with UV detector monitoring at 254 nm. A 50 μm I.D.× 47 cm (39 cm to detector) uncoated fused-silica capillary was used. The mixture of four acidic drugs, ketoprofen, naproxen, sulindac, and indometacin was used as the test sample.

Figure 1 shows the separation of the test sample in MECC system. As seen in **Figure 1a** and **b**, excellent resolutions for all four solutes are achieved in both SDS- and Tween 20-MECC systems. However, the elution order of solutes is exactly reversed from one system to another. Under selected pH conditions, all solutes that are negatively charged tend to the anode. In SDS-MECC system, the micelles carry many negative charges and move more slowly than the solutes to the cathode under the influence of electroosmosis flow (EOF), so the more the analyte is solubilized into the

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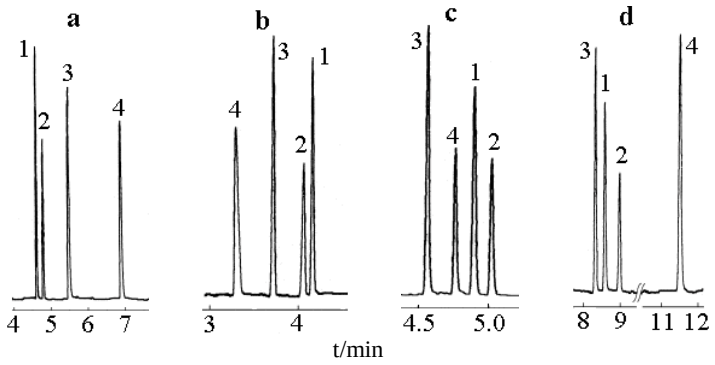
micelles, the more slowly it elutes. In Tween 20-MECC system, the micelles are electrically neutral and move accordingly with EOF, and their mobility is faster than that of the solutes, so the more the analyte is solubilized into the micelles, the faster it elutes. Hence, there are reverse elution orders between SDS system and Tween 20 system. In mixed SDS-Tween 20-MECC system, the elution order of analytes is determined by the contributions of SDS and Tween 20 micelles, and the varying selectivity was achieved by changing the ratio of micelle composition as seen in **Figure 1c**.

In this work, the effect of ethanol as organic modifier added to SDS-MECC system on the separation was also investigated. The results indicated that ethanol exerted a strong effect not only on retention time but also on selectivity. With increasing ethanol concentration (from 0% to 15%, Vol./Vol.), the retention time increased in general, but the change of sulindac was the least and so its elution order varied from the third to the first gradually as seen in **Figure 1a** and **d**. With the addition of ethanol, increased in the viscosity of the buffer and decreased in the zeta-potential of the silica wall which led to the decrease in EOF, so that the retention time of the solutes got longer. The influence on elution order may be explained by that the solubility of the hydrophobic sulindac increased very much in the aqueous buffer because of the addition of ethanol.

Figure 1 Separation of four acidic drugs by MECC



Operating conditions: running solution, (a) 30 mmol/L SDS, (b) 30 mmol/L Tween20, (c) 30 mmol/L SDS – 20 mmol/L Tween20 or (d) 50 mmol/L SDS and 15% (v/v) ethanol in 20 mmol/L NaH_2PO_4 – 10 mmol/L Na_2HPO_4 buffer (pH 6.6); applied voltage, 18 kV; temperature, 35°C. Peaks identification: 1. ketoprofen, 2. naproxen, 3. sulindac, 4. indometacin.

In conclusion, this work clearly showed that changing the composition of micellar solution offers a simple and useful method for the control of the separation behaviors in MECC.

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Received 1 April, 2002