

Enantioselective Supercritical Fluid Chromatography using Daicel's Immobilized Polysaccharide-based columns

Geoffrey Cox
Chiral Technologies, Inc., West Chester, PA

The new generation of immobilized polysaccharide chiral stationary phases (CSPs) bring new horizons to supercritical fluid chromatography (SFC). Selection of solvents giving high solubility as well as new selectivity is possible due to the stability of these CSPs to a wide range of organic solvents.

The past few years have seen the increasing use of SFC in the analysis and purification of small molecules, especially within the pharmaceutical industry. The choice of mobile phase modifier in enantioselective SFC has hitherto been limited due to the solvent incompatibility of the previous generation of coated polysaccharide phases. The completion of the range of Daicel's immobilized phases (the "Platinum Series") by the introduction of CHIRALPAK® IC™ now allows SFC methods to be developed using the most appropriate solvent for dissolution of the sample and optimization of the separation selectivity.

Experimental

Columns packed with 5 micron CHIRALPAK IA™, CHIRALPAK IB™ and CHIRALPAK IC, all 4.6 x 250 mm (Daicel Chemical Industries, Ltd) were used throughout. A flow rate of 5 ml/min with back pressure of 150 bar at 35°C were used. A Berger Minigram SFC system fitted with autosampler and diode array detector was employed.

Results

The majority of enantioselective SFC separations are carried out using methanol or 2-propanol as organic modifier in the mobile phase. During the development of preparative SFC methods, however, it is frequently found that the sample solubility in the modifier is insufficiently high and the sample either crystallizes from the feed solution before or during the separation. Equally, where the selectivity using the conventional modifiers is insufficient either for the analytical application or the preparative separation, the use of alternative modifiers for selectivity optimization becomes desirable.

The recently introduced immobilized polysaccharide-based CSPs solve these problems by allowing the use of any organic solvent as mobile phase modifier. Figure 1 shows the separation of the enantiomers of benzoin ethyl ether on CHIRALPAK IA using methanol, 2-propanol and ethyl acetate as modifier.

CHIRALPAK is a registered trademark and IA, IB and IC are Trademarks of Daicel Corporation

Ethyl acetate in this case shows a much improved selectivity over the alcohol modifiers. It should be noted that aprotic solvents such as ethyl acetate appear to be somewhat weaker in elution power in SFC than in HPLC; often an alcohol modifier at low concentration has to be added to increase the solvent strength sufficiently to allow elution of the solutes. A typical case is shown in Figure 2, where the separation of the enantiomers of mephensin is shown using CHIRALPAK IC with 18% methylene chloride and 2% ethanol in CO₂ as mobile phase.

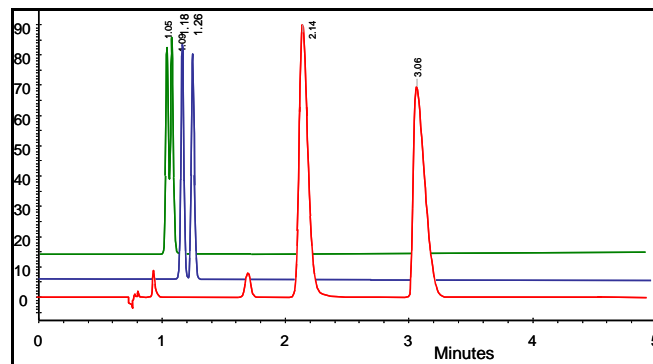


Figure 1. Separation of benzoin ethyl ether enantiomers on CHIRALPAK IA with 20% methanol (green), 20% 2-propanol (blue) and 30% ethyl acetate (red) as modifiers in CO₂.

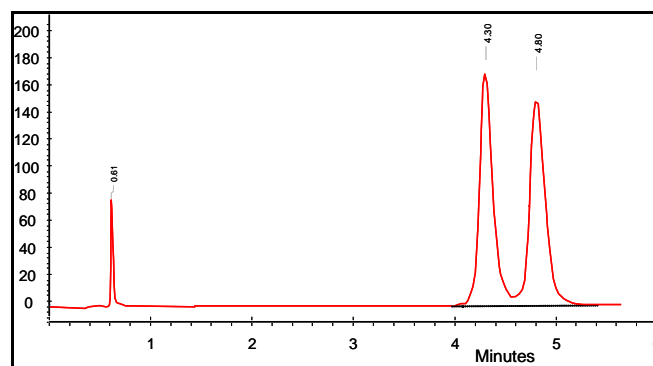


Figure 2. Separation of mephensin enantiomers using CHIRALPAK IC with 18% dichloromethane and 2% ethanol in CO₂.

Conclusions

By virtue of their unique stability, the new Platinum Series range of immobilized polysaccharide chiral columns allows the use of new SFC mobile phase modifiers to enhance solubility and to optimize selectivity in both analytical and preparative separations.