Highly sulphonated cyclodextrins for chiral analysis

Application Note

Pharmaceutical

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Abstract

Capillary electrophoresis is ideally suited to the analysis of chiral solutes where the ease of method development and greatly reduced costs makes it an attractive alternative to liquid chromatography. The use of highly sulphonated cyclodextrins has been described together with their more generic application to separate a range of analytes. Highly sulphonated cyclodextrins have an associated high current which must be controlled in order that Joule heating does not unduly deteriorate the separation. This Application Note describes the use of highly sulphonated cyclodextrins for the analysis of chiral analytes. By using small 25 µm id capillaries with an extended pathlength of 125 µm id the Joule heating can be controlled while enhancing sensitivity.

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Experimental

All experiments were performed using the Agilent Capillary Electrophoresis system equipped with diode array detection and the Agilent ChemStation software. Heptakis (6-sulfato)-ß-cyclodextrin was supplied by Regis Technologies, Inc. Illinois, USA. The small bore capillary was quickly and easily flushed using a high pressure of 8 to 12 bar. Negative polarity is employed since the enantiomers are carried towards the detection end by their interaction with the cyclodextrins.

Figure 1 shows the generic applicability of the cyclodextrins by applying one method and set of conditions to a range of chiral solutes. The excellent control of Joule heating is demonstrated by the linearity of Ohm's Law plot, V vs I, (figure 2). This conforms almost perfectly to theoretical expectations. The stability of thermostatting is further demonstrated by the reproducibility of the peak migration times of the clenbuterol enantiomers at 0.30 % (peak 1) and 0.31 % (peak 2) for n=8 (figure 3). The linearity of detection was also determined over the range 0.03 to 5 mg/mL with r^2 = 0.999 while the concentration limit of detection at a signal to noise ratio of ca. 2.5 was 30 µg/mL (figure 3).

Equipment

- Agilent Capillary Electrophoresis system
- Agilent ChemStation
- Extended light path capillaries

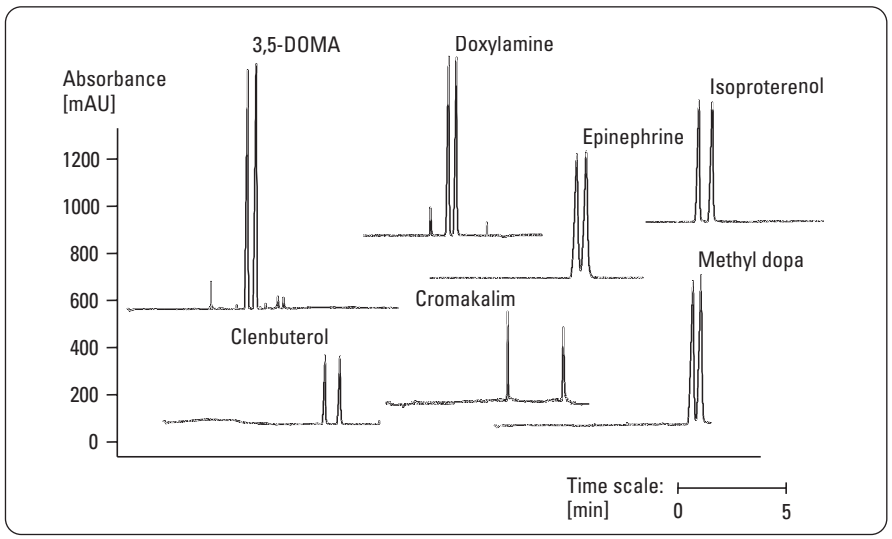

Figure 1
Separation of several drugs using a single method.

Chromatographic conditions

Capillary:	Effective length 40 cm, total length 48.5 cm, internal diameter 25 µm, BF 5 (Agilent part number G1600-60132)
Buffer:	25 mM phosphate/TEA pH 3.3, 5 % (w/v), Heptakis sulpho-ß-cyclodextrin
Detection:	195/10 nm
Injection:	500 mbar x s
Voltage:	30 kV
Temperature:	25 °C

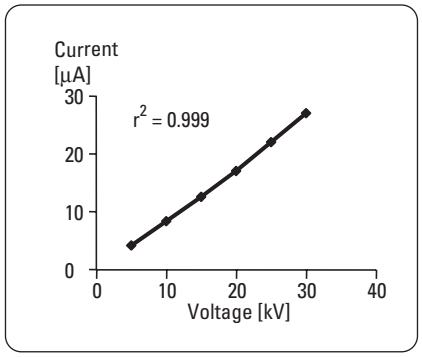

Figure 2
Ohm's law plot for separation conditions.

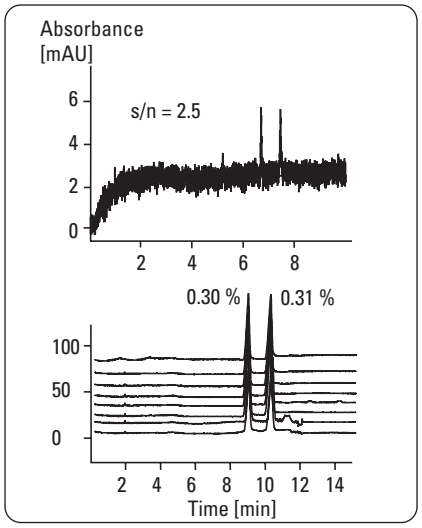

Figure 3
Clenbuterol: Migration time reproducibility and sensitivity.

Conclusion

The use of highly sulphonated cyclodextrins in conjunction with 25 µm id extended light path capillaries provides a reproducible and sensitive method for separating chiral compounds. This combination also provides a method development versatility in choice of temperature and cyclodextrin concentration which is not easily achieved with wider bore capillaries.

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