SEPARATION OF DISOPYRAMIDE ON **DAICEL'S NEWEST IMMOBILIZED CHIRAL STATIONARY PHASE CHIRALPAK® IJ**

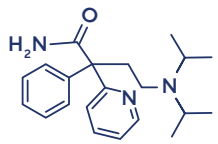
APPLICATION NOTE

INTRODUCTION

For the past two decades, Daicel Corporation has been expanding its catalog of chiral stationary phases (CSPs) with the introduction of more chemically resilient immobilized versions of its coated polysaccharide phases. The newest immobilized phase being introduced is CHIRALPAK® IJ, the immobilized version of CHIRALCEL® OJ. CHIRALPAK® IJ is a cellulose polymer derivatized with tris(4-methylphenylbenzoate) moieties. Because coated phases like CHIRALCEL® OJ are susceptible to degradation from incompatible mobile phases, the immobilized CHIRALPAK® IJ offers more flexibility for screening and method development conditions.

For molecules exhibiting either no resolution or poor resolution on corresponding coated phases, the use of the immobilized counterpart, and an expanded range of solvents, allows for an increased probability of success. Disopyramide is one such example presented in this application note. Disopyramide is an antiarrhythmic medication used under the trade names Norpace and Rythmodan, which was previously not separated on CHIRALCEL® OJ under normal phase conditions. Now with the ability of the immobilized CHIRALPAK® IJ to withstand dichloromethane (DCM), a baseline resolution can be achieved.

ANTIARRHYTHMIC MEDICATION



DISOPYRAMIDE

EXPERIMENTAL

CHROMATOGRAPHIC CONDITIONS FOR THE SCREENING OF DISOPYRAMIDE

CHIRALCEL® OJ-H (5 µm) - (4.6 mm I.D. X 150 mm)	
MOBILE PHASE	n-Hex/EtOH/DEA = 95:5:0.1 v/v/v n-Hex/IPA/DEA = 95:5:0.1 v/v/v
FLOW RATE	1.0 ml/min
DETECTION	UV, 225 nm, ref 450 nm
TEMPERATURE	25°C
SAMPLE	1.0 mg/ml in EtOH
INJECT. VOL.	5.0 µl

CHIRALPAK® IJ (5 µm) - (4.6 mm I.D. X 150 mm)	
MOBILE PHASE	n-Hex/DCM/DEA = 90:10:0.1 v/v/v n-Hex/EtOAc/DEA = 90:10:0.1 v/v/v n-Hex/THF/DEA = 90:10:0.1 v/v/v n-Hex/MtBE/DEA = 90:10:0.1 v/v/v
FLOW RATE	1.0 ml/min
DETECTION	UV, 280 nm, ref 450 nm
TEMPERATURE	25°C
SAMPLE	1.0 mg/ml in EtOH
INJECT. VOL.	5.0 µl

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EXPERIMENTAL CONTINUED

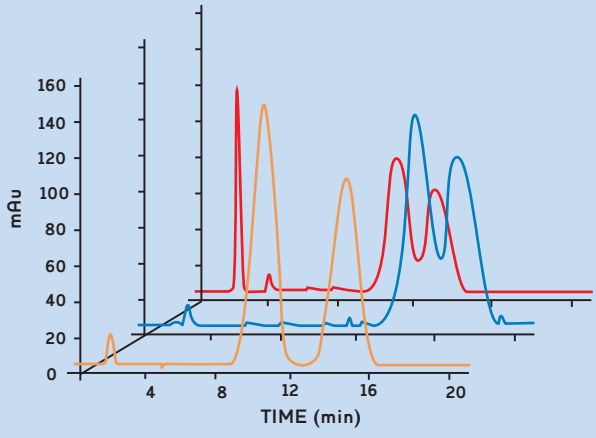
CHROMATOGRAPHIC CONDITIONS FOR THE OPTIMIZATION OF DISOPYRAMIDE

CHIRALCEL® OJ-H (5 µm) - (4.6 mm I.D. X 150 mm)	
MOBILE PHASE	n-Hex/EtOH/EDA = 99:1:0.1 v/v/v n-Hex/IPA/EDA = 99:1:0.1 v/v/v
FLOW RATE	1.0 ml/min
DETECTION	UV, 225 nm, ref 450 nm
TEMPERATURE	25°C
SAMPLE	1.0 mg/ml in EtOH
INJECT. VOL.	5.0 µl

CHIRALPAK® IJ (5 µm) - (4.6 mm I.D. X 150 mm)	
MOBILE PHASE	n-Hex/DCM/EDA = 93:7:0.1 v/v/v
FLOW RATE	1.0 ml/min
DETECTION	UV, 280 nm, ref 450 nm
TEMPERATURE	25°C
SAMPLE	1.0 mg/ml in EtOH
INJECT. VOL.	5.0 µl

FIGURE 1:

BASELINE SEPARATION OF DISOPYRAMIDE



— CHIRALPAK® IJ with n-Hex/DCM/EDA = 93:7:0.1 v/v/v
— CHIRALCEL® OJ-H with n-Hex/EtOH/DEA = 99/1/0.1 v/v/v
— CHIRALCEL® OJ-H with n-Hex/IPA/DEA = 99/1/0.1 v/v/v

DISCUSSION

Disopyramide screened on the conditions in the table above (Chromatographic Conditions for the Screening of Disopyramide) which yielded partial separations on CHIRALCEL® OJ-H for both n-Hex/EtOH and n-Hex/IPA conditions, as well as a near baseline resolution on CHIRALPAK® IJ with n-Hex/DCM. Because of some peak shape issues, the basic additive was optimized from DEA to EDA, yielding more symmetrical peak shape and less tailing. The optimization of both normal phase conditions (n-Hex/EtOH and n-Hex/IPA) on CHIRALCEL® OJ-H was unsuccessful in producing a baseline separation, whereas the optimization of the extended range conditions (n-Hex/DCM) on CHIRALPAK® IJ achieved a robust, quantifiable baseline separation. This previously unreported chiral separation will allow for the accurate assessment of this important medication's purity post-manufacturing.

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