SEPARATION OF THE ENANTIOMERS OF (+/-) Δ⁸-THC AND (+/-) Δ⁹-THC

APPLICATION NOTE

INTRODUCTION

Potency testing of cannabis and its related products often centers on the amount of THC and CBD that are present, but there are an additional 14 cannabinoids that need to be identified and quantified for an accurate assessment. Of those 14, there is a particularly troublesome pair of cannabinoids to separate, Δ⁸ -THC and Δ⁹ -THC. The placement of a double bond around the C9 of the fused-cyclohexene ring is the only distinguishing feature, making separating these structural isomers a challenge. Each structural isomer then also contains a pair of enantiomers, (+) and (-), making a challenging separation even more difficult.

Since the early 2000's, DAICEL Corporation has been expanding its catalog of chiral stationary phases (CSPs) by launching more robust immobilized versions of its coated phases. One example is CHIRALPAK® IF, the immobilized version of CHIRALPAK® AZ. CHIRALPAK® IF is an amylose polymer derivatized with tris(3-chloro-4-methylphenylcarbamate) moieties. Because coated phases like CHIRALPAK® AZ are susceptible to degradation from incompatible mobile phases, the immobilized CHIRALPAK® IF offers more flexibility under screening and method development conditions.

EXPERIMENTAL

A mixture containing four isomers, (+/-) Δ⁸ -THC and (+/-) Δ⁹ -THC, were subjected to normal phase screening conditions on the library of DAICEL Corporation's immobilized CSPs. Conditions were optimized to achieve good resolution and selectivity, as well as individual injections of each isomer to establish the elution order.

DISCUSSION

CHIRALPAK® IF showed good initial selectivity under normal phase conditions of 70:30 hexane/IPA. The method was optimized further to 95:5 hexane/IPA to increase the resolution, resulting in baseline separation for all four isomers. The quality of separation allows for this method to be used in an accurate quantitation of all four isomers. As shown in the included chromatograms, both Δ⁸ -THC isomers elute before the Δ⁹ -THC isomers. In the case of Δ⁸ -THC, the (-) elutes first, and with Δ⁹ -THC, the (-) elutes second.

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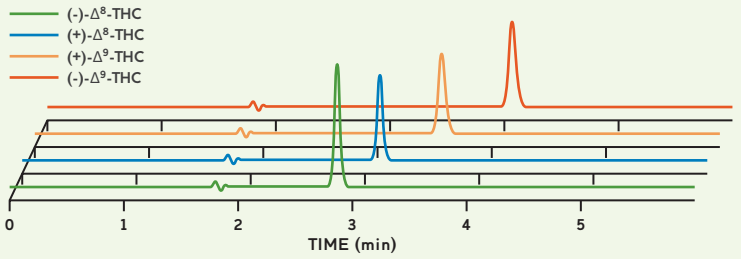
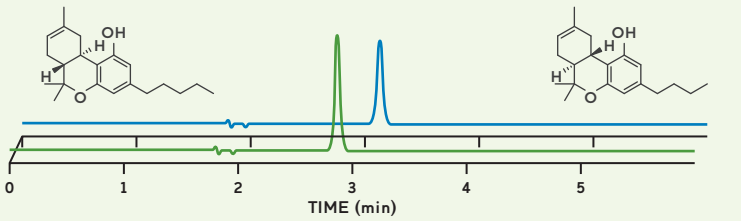
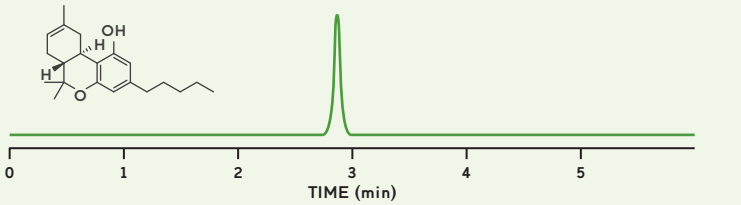
MIXTURE OF FOUR ISOMERS



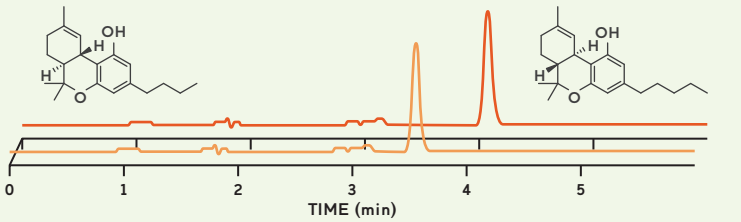
(+/-)-Δ⁸-THC



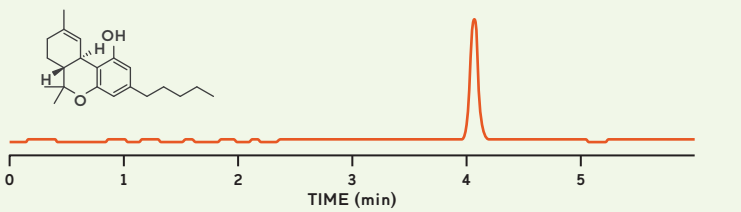
(-)-Δ⁸-THC



(+/-)-Δ⁹-THC



(-)-Δ⁹-THC



CHROMATOGRAPHIC CONDITIONS

Column: CHIRALPAK® IF-3
Column Size: 4.6 mm i.d. x 150 mm long
Mobile Phase: n-Hexane/Isopropanol (95:5) v/v
Flow rate: 1.0 mL/min.
Temperature: 25° C
Sample Mixture: 1.0 mg/ml in heptane, Single isomer: Mobile Phase
Inject. Vol.: Mixture of 4 isomers: 5.0 µl, Mixture of 2 isomers: 2.5 µl, Single isomer: 0.5 µl