K8 Delta-8-Tetrahydrocannabinol (Delta-8-THC): Increased Prevalence in Drug Seizure Cases and Impact on Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) Analysis of Biological Specimens

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Learning Overview: After attending this presentation, attendees will understand the increased prevalence of delta-8-THC in drug seizure cases and the potential impact on LC/MS/MS analysis of biological specimens for cannabinoids.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by informing toxicologists of the need to evaluate LC/MS/MS cannabinoid methods for the potential of interference of delta-8-THC with delta-9-THC.

Introduction: Delta-8-THC is a cannabinoid that is a minor constituent found naturally in the cannabis plant. Delta-8-THC is an analog of delta-9-THC and has similar effects and receptor activity, but lower potency. Recently, drug seizure exhibits submitted in Palm Beach County, FL, have contained delta-8-THC as the primary constituent or as a mixture with delta-9-THC. The first drug seizure submission was from an incident that occurred in November of 2018. From November 2018 to June 2019, delta-8-THC has been identified in a total of 12 drug seizure cases with 4 cases from May 2019. Ten of the exhibits were vape cartridges and two were food items.

Objective: Evaluate the ability of a validated LC/MS/MS blood cannabinoid quantitation method employing a biphenyl LC column to discriminate between delta-8 and delta-9-THC.

Method: A previously described LC/MS/MS blood cannabinoid quantitation method that included delta-9-THC, delta-9-hydroxy-THC, and delta-9-carboxy-THC was employed.[1] Briefly, 0.5mL of whole blood was extracted by liquid-liquid extraction with hexane:ethyl acetate (80:20). Analysis was conducted on a Shimadzu® Prominence XR LC system with a SCIEX™ 3200 Qtrap® MS/MS and a Raptor™ Biphenyl column with dimensions of 50 x 2.1mm and a 2.7µm particle size. A gradient LC program was employed with LC/MS water and LC/MS methanol, each with 0.1% formic acid. The calibration range was from 1–40ng/mL for delta-9-THC and delta-9-hydroxy-THC and 5–200ng/mL for delta-9-carboxy-THC. Stable isotope internal standards were used for all three target analytes.

Three different fortified blood samples were prepared and extracted along with the routinely used calibrators and controls to evaluate the selectivity of the method through an interference study: one fortified with delta-8-THC at 40ng/mL without internal standard; one fortified with delta-8-THC at 5ng/mL with internal standard; one fortified with delta-9-THC and delta-9-hydroxy-THC at 5ng/mL, and delta-9-carboxy-THC at 25ng/mL, as well as delta-8-THC at ng/mL with internal standard.

Results: There was no interference from a high concentration of delta-8-THC (40ng/mL) with the internal standards. Delta-8-THC did not interfere with delta-9-OH-THC or delta-9-carboxy-THC, but did interfere with delta-9-THC. Delta-8-THC produces the same precursor/product ion transitions in the same relative abundances as delta-9-THC. The retention time for delta-8-THC (4.75) was 0.03 minutes later than the average of the calibrators (4.72), but was still within the 0.1 minute acceptance window. The Multiple Reaction Monitoring (MRM) ratios were slightly higher than the average of the calibrators (36% compared to 32%), but were also within the acceptance range of +/-20%. The 5.0ng/mL delta-8-THC control was identified by the method as containing delta-9-THC at 4.7ng/mL. The mixed control containing both delta-8-THC and delta-9-THC, each at a target concentration of 5.0ng/mL, was identified by the method to contain delta-9-THC at 9.4ng/mL. No split peak or other indication of the presence of two unique compounds was observed. Unpublished reports from laboratories employing C-18 LC columns have observed a split peak with incomplete resolution of delta-8 and delta-9-THC. Drug standards for delta-8-hydroxy-THC and delta-8-carboxy-THC were not available to evaluate potential interferences for the delta-9 counterparts targeted by the method. A polar-C18 column was evaluated and demonstrated the ability to resolve delta-8- and delta-9-THC. Further work will be conducted to develop a method employing a polar-C18 column.

Conclusion: The LC/MS/MS blood cannabinoid method employing a biphenyl LC column could not discriminate between delta-8- and delta-9-THC as the compounds have identical MRM transitions and were not resolved chromatographically. Delta-8-THC may also cause interference with delta-9-THC for LC/MS/MS methods that employ a C-18 column. LC/MS/MS methods for the determination of cannabinoids should be evaluated for specificity between delta-8- and delta-9-THC and the potential impact to casework examined.

Reference(s):

1. Tiscione, N.B., Miller, R., Shan, X., Sprague, J., Yeatman, D.T. (2016) An Efficient, Robust Method for the Determination of Cannabinoids in Whole Blood by LC-MS-MS. *Journal of Analytical Toxicology*, 40: 639-648.

Delta-8-THC, Validation, LC/MS/MS

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