

Dilute-and-shoot determination of THC-COOH and THC-COOH-glucuronide in human serum by LC-MS/MS

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Background: Cannabis is widely used as a psychoactive drug for medical and recreational purposes. It is not uncommon for women to use it during pregnancy. Research has shown that first and second-hand cannabis smoking during pregnancy can result in negative health impacts on both baby and mother. 11-nor-9-carboxy-tetrahydrocannabinol (THC-COOH) and THC-COOH-glucuronide are the major metabolites that have long half-life and are detected in higher concentration after cannabis use. Therefore, they serve as biomarkers for monitoring. In this study, we developed a dilute-and-shoot method for rapid analysis of THC-COOH and THC-COOH-glucuronide in serum using LC-MS/MS. (94)

Methods: Serum samples were treated by protein precipitation using acetonitrile containing 0.1% formic acid. The supernatant was centrifuged, filtered using 0.2 µm PTFE, and further diluted with water to result in a 20-fold dilution). 10 µL of the final extract was analyzed. The LC-MS/MS analysis was carried out on a Sciex Qtrap 5500 in negative MRM mode coupled with Agilent 1260 Infinity HPLC. Separation was performed using an Eclipse Plus Phenyl-Hexyl column (4.6mm×100 mm, 5µm). Gradient elution was performed with 0.1% formic acid in water and acetonitrile at an initial flow-rate of 1000µl/min. (93)

Results: The limit of quantification (LoQ) was 1 ng/mL for both THC-COOH and THC-COOH-glucuronide. Calibration curves were established at 1 – 2000 ng/mL for THC-COOH and 1 – 1000 ng/mL for THC-COOH-Glucuronide with $R^2 > 0.999$. For both compounds, the matrix effect was between -8.7 to 8.6% (corrected with internal standard), and the extraction recovery ranged from 82.0% - 92.5%. The intra and inter-day precision CV% was less than 10%. Accuracy was observed between 86.7 to 118.5%. Spiked recovery was from 93.2% to 113.9%. No carryover was observed even after the highest calibrator. No endogenous or exogenous interference was observed. (98)

Conclusions: A fast, simple, sensitive, robust and high throughput method for the determination of THC-COOH and THC-COOH-glucuronide in serum using LC-MS/MS was developed and validated. The method achieved a low LoQ for THC-COOH-glucuronide comparing with other published methods. It meets the high sensitivity requirement for biomonitoring applications. (47).

Key words: THCCOOH; THCCOOH-glucuronide; Dilute-and-shoot; LC-MS/MS (6)