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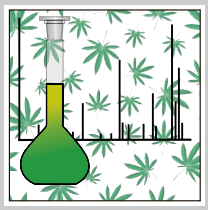

Highlights of Analytical Sciences in Switzerland

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Assessing Cannabis Consumption Frequency: Is the Quantification of Free and Glucuronidated THCCOOH in Blood the Key?

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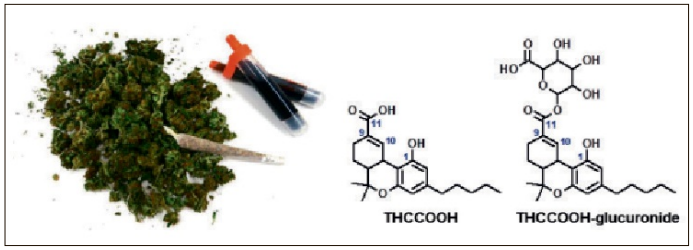
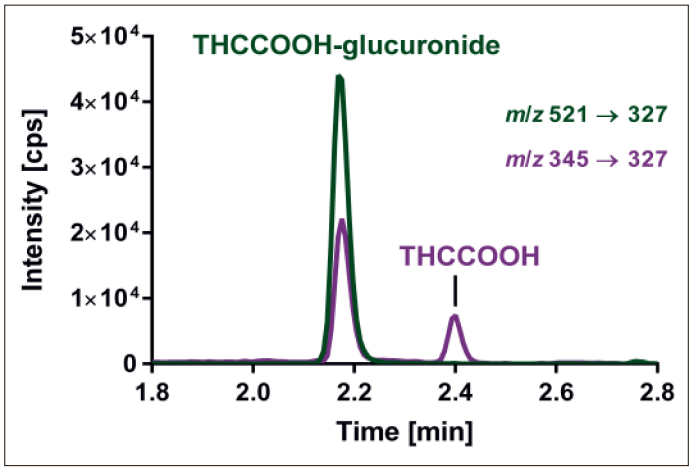
Knowledge of the consumption behavior of cannabis consumers is important in many forensic and clinical circumstances, for example for deciding on medical treatment or administrative and legal consequences, such as suspension of the driver's license. The concentration of the cannabis metabolite 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THCCOOH) serves as a diagnostic marker to distinguish between occasional and frequent smokers. In Switzerland, a THCCOOH blood level of 40 µg/L is currently used by forensic experts as decision limit for regular consumption. However, this threshold concentration was found to be correlated with a low sensitivity. Therefore, an additional and/or enhanced indicator of cannabis consumption frequency would be beneficial. Since THCCOOH in blood is extensively glucuronidated, we assume that the blood level of THCCOOH-glucuronide could serve as an additional parameter for assessing the frequency of cannabis use. To verify this assumption, we have developed a column-switching LC-MS/MS method for the simultaneous quantification of free and glucuronidated THCCOOH in whole blood.

The use of a trapping column for on-line sample enrichment and purification and an analytical column for separation and detection allows us to prepare blood samples by a simple protein precipitation step without sample preconcentration by evaporation and reconstitution. Employing two columns, each containing a different stationary phase, provides the needed selectivity to obtain excellent separation of the two analytes within a total run time of only 4.5 min. Detection of the analytes is accomplished by electrospray ionization in positive ion mode and selected reaction monitoring using a triple-stage quadrupole mass spectrometer.



11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THCCOOH) and its glucuronide conjugate are metabolites of Δ^9-tetrahydrocannabinol (THC), the major psychoactive component of cannabis. Their quantification in whole blood is of interest for interpreting cannabis consumption behavior.



Chromatogram of an authentic whole blood specimen from a cannabis consumer (THCCOOH, 97.6 µg/L; THCCOOH-glucuronide, 296 µg/L). The purple peak at 2.16 min corresponds to the THCCOOH fragment originating from in-source decay of the glucuronide.

This method was used to analyze blood samples from a controlled cannabis administration study and therefore provided the required pharmacokinetic data for investigating the suitability of free and glucuronidated THCCOOH as indicators of cannabis consumption frequency.

Column-switching chromatography combined with tandem mass spectrometry allows for simultaneous and ultra-rapid quantification of THCCOOH and THCCOOH-glucuronide in whole blood, requiring only minimal sample pre-treatment, and offers new possibilities for assessing cannabis consumption behavior.

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Reference

M. Hädener, W. Weinmann, S. Schürch, S. König, *Anal. Bioanal. Chem.* **2016**, *408*, 1953.

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