

A Q&amp;A

# Rapid Detection and Quantification of Synthetic Cannabinoids in Human Serum



Dr. Rafaela Martin  
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**T**o learn more about Rapid Detection and Quantification of Synthetic Cannabinoids in Human Serum, LCGC recently spoke with Application Chemist Dr. Rafaela Martin of Bruker Daltonics.

**Michael Swartz: Could you tell us a little about Synthetic Cannabinoids?**

**Dr. Rafaela Martin:** Synthetic cannabinoids first appeared on the recreational drug scene in 2004. The term synthetic cannabinoid refers to manmade mind altering chemicals that are available either spread on dried, shredded plant material that is smoked, or as liquid to be vaporized and inhaled in e-cigarettes and other devices. Chemically, synthetic cannabinoids are quite diverse as they include a lot of different structures like indazole and indole derivatives.

**Michael Swartz: What are the risks of synthetic cannabinoids?**

**Dr. Rafaela Martin:** In an attempt to circumvent legislation, synthetic cannabinoids are misleadingly marketed and sold via the internet or in head shops as bath salts or plant food, often in colorful packages with creative names judged by consumers to be safe and legal. Many are full agonists of the cannabinoid receptors CB1 and CB2 and therefore the psychoactive effects are similar to those of cannabis but they can be much stronger. Consumption can also lead to unpredictable side effects like high blood pressure, nausea, hallucination, psychosis, physical addiction and even life threatening conditions.

**Michael Swartz: How are synthetic cannabinoids analyzed?**

**Dr. Rafaela Martin:** To keep ahead of evolving drug laws and modern detection methods, new or slightly modified variants of synthetic cannabinoids are regularly synthesized and rapidly marketed to the recreational drug user market. Analytical methods therefore need to be regularly updated and must be capable of analyzing synthetic cannabinoids in serum at sub ng/mL concentrations. Traditional detection methods such as immunoassay don't have the required specificity, sensitivity or flexibility to cope with this growing analytical challenge; that's why we developed a targeted quantitative assay using UHPLC triple quadrupole MS.

**Michael Swartz: Can you tell us about the instrument used for the analysis of synthetic cannabinoids?**

**Dr. Rafaela Martin:** The instrument used for the analysis was an EVOQ LC Triple Quadrupole which is available in two versions. The EVOQ Qube for standard applications and the EVOQ

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Elite for the highest sensitivity applications. One key feature of this instrument is the vacuum insulated probe for heated ESI. The high efficiency ceramic heater delivers the highest heat near the probe tip and the vacuum insulation protects the UHPLC eluent from boiling inside the probe prior to nebulization. As a result, the fluid path remains cool, which is essential for protecting thermally labile compounds. Furthermore, the source housing is equipped with an active exhaust that consists of a nozzle that works like a water jet pump routing the expanded air to exhaust, minimizing the re-circulation of gasses within the source housing resulting in less contamination and maximum robustness. The 180-degree angle curved collision cell helps to maintain a compact design and small instrument footprint. Neutral particles are not focused by the electric field and can't travel around the bend, resulting in less chemical noise and a higher sensitivity.

**Michael Swartz: How are methods developed using this instrument?**

**Dr. Rafaela Martin:** There is an MRM library with several hundred compounds available, which includes optimized MRM transitions and respective collision energies that can be added to any method. If an analyte is not in the library, the analyst can use the MRM builder tool: by infusing a standard solution of the new compound the MRM builder automatically finds transitions and the optimal collision energy to allow the analyst to easily develop a targeted quantitative assay.

**Michael Swartz: How are the samples prepared?**

**Dr. Rafaela Martin:** Sample preparation consists of a two-step liquid-liquid serum extraction using hexane and ethyl acetate in a basic buffer. Deuterated internal standards are added for quantitation and to compensate for matrix effects.

**Michael Swartz: Why are you only looking for the parent compounds and not the metabolites in serum?**

**Dr. Rafaela Martin:** In serum, you look for the parent compound to prove the acute influence of drugs. Metabolites can be found mainly in urine to prove the consumption of the drug with a much wider detection window than serum. However, for synthetic cannabinoids only a limited number of metabolites are available and many are unknown, making meaningful analyses in urine difficult.

**Michael Swartz: Is the method validated?**

**Dr. Rafaela Martin:** The method has been fully validated according to GTFCh guidelines. Validation parameters included selectivity, matrix effects and recovery, limits of detection and quantitation as well as linearity, precision and accuracy. Detection limits of around 5 to 10 pg/mL could be achieved for most of the 99 analytes. The low detection limits provide the necessary evidence to show recent use of synthetic cannabinoids in forensic cases such as driving under the influence of drugs or in post mortem cases.

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