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## ACCEPTED MANUSCRIPT

# Implementation of a generic SFC-MS method for the quality control of potentially counterfeited medicinal cannabis with synthetic cannabinoids

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#### **Keywords**

SFC-MS, supercritical fluid chromatography (SFC), synthetic cannabinoids, cannabis, method validation, Quality by Design

#### **Highlights**

Fast generic SFC-MS method was developed for the quality control of cannabis samples.

The proposed method is useful in the context of counterfeit drugs tracking.

QbD strategy helped to propose a robust working area (DS) for routine analysis.

Quantitative performances were demonstrated by means of total error approach method validation.

#### **Abstract**

In this study, we describe the development of a SFC-MS method for the quality control of cannabis plants that could be potentially adulterated with synthetic cannabinoids. Considering the high number of already available synthetic cannabinoids and the high rate of development of novel structures, we aimed to develop a generic method suitable for the analysis of a large panel of substances using seventeen synthetic cannabinoids from multiple classes as model compounds. Firstly, a suitable column was chosen after a screening phase. Secondly, optimal operating conditions were obtained following a robust optimization strategy based on a design of experiments and design space methodology (DoE-DS). Finally, the quantitative performances of the method were assessed with a validation according to the total error approach. The developed method has a run time of 9.4 minutes. It uses a simple modifier

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