Suspect and non-target screening workflows to investigate the \textit{in vitro} and \textit{in vivo} metabolism of the synthetic cannabinoid 5-Cl-THJ-018

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**Introduction**
Synthetic cannabinoids cause similar effects as Δ^9- tetrahydrocannabinol. (Ab)use can lead to health hazards and fatal intoxications. Most investigated synthetic cannabinoids undergo extensive biotransformation. As a result, parent compounds cannot be detected in urine and serum which hampers forensic investigations. Limited information about biotransformation products of new synthetic cannabinoids makes detection of these compounds in biological matrices challenging.

**Experimental setup**^3^  

**Objectives**
- Identify \textit{in vitro} metabolites of 5-Cl-THJ-018 using suspect and non-target screening workflows
- Evaluate added value of different non-target screening workflows
- Identify \textit{in vivo} metabolites in an authentic urine sample of a 5-Cl-THJ-018 user using suspect screening

**Overview screening workflows**

**Results in vitro metabolism**

**Conclusions**

The synthetic cannabinoid 5-Cl-THJ-018 underwent extensive \textit{in vitro} metabolism. Predominant Phase I pathways \textit{in vitro} are \textit{oxidative reactions} (with and without dechlorination) and subsequent Phase II glucuronidation and sulfation.

The application of non-target screening workflows in parallel to suspect screening increased the number of metabolites being identified.

**Seven metabolites** were also identified in the \textit{in vivo} urine sample. All these metabolites started from the oxidative dechlorination of 5-Cl-THJ-018, followed by further oxidative reactions and/or Phase II biotransformation.

As only the dechlorinated metabolites were identified in this specific \textit{in vivo} sample, no specific biomarkers could be proposed to distinguish 5-Cl-THJ-018 use from the use of the nonhalogenated or other similar halogenated analogues.

**Suggested pathway**

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1. Chimalakona KC, Seely KA, Bratton SM, et al. (2012); Drug Metab Dispos. 40: 2174-84
2. Favretto D, Pascali JP, Tagliaro F (2013); J Chromatogr A. 1287: 84-95