Metabolism and urine analysis of the new synthetic cannabinoid MDMB-CHMICA

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Introduction and Aims

Figure: Products containing MDMB-CHMICA analysed at the Institute of Forensic Medicine:

Herbal blends: „AK47“, „Amnesia“, „GALAXY“, „Goa Party“, „Crazy Monkees 2“, „Happy New Year“, „Hausmarke Kiwi“, „Red Russian“, „Scooby Snax Potpurri“, „Spice“, „YAMA“, „5G“ (not shown), „5G Monster“ (not shown), unlabelled sachet (not shown)

Research chemicals labelled „MMB-CHMINACA“

The new synthetic cannabinoid MDMB-CHMICA (often misleadingly sold as ‘MMB-CHMINACA’) is structurally related to AB-CHMINACA and was first seized in Europe by the Hungarian police in August 2014.[1] From a clinical perspective these substances seem to be particularly problematic due to serious, sometimes life-threatening side effects. In our institute, in October 2014 the substance has been detected in several authentic serum samples and in November also in different herbal blends offered as a legal cannabis alternative. Because of the rapid spread of the drug we aimed to develop a robust method for the detection of this compound and its metabolites in urine samples.

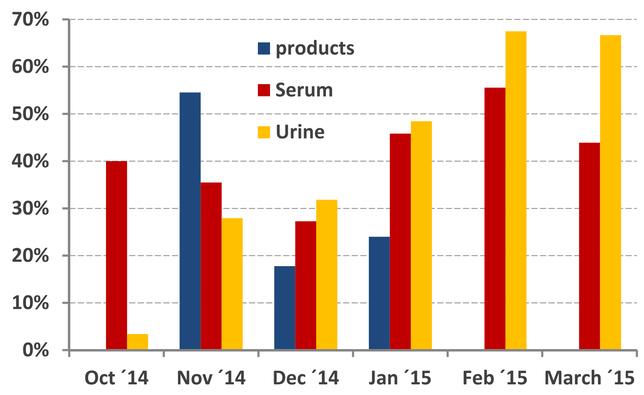

Figure: MDMB-CHMICA positives in relation to all positive samples

Methods

Mass spectrometry conditions

- QTRAP® 5500 (AB Sciex)
- Positive ionisation mode
- Multiple reaction monitoring (MRM)
- Enhanced product ion scan (EPI)
- Precursor scan (Prec)

Liquid chromatography conditions

- UHPLC Nexera X2 (Shimadzu)
- Kinetex C18 column (100 mm × 2.1 mm, 100 Å, 2.6 µm)
- Solvent A (1 % ACN, 0.1 % HCOOH, 2 mM $NH_4^+HCOO^-$)
- Solvent B (ACN with 0.1 % HCOOH, 2 mM $NH_4^+HCOO^-$)
- Post column: Isopropanol (0.2 mL/min)

Sample preparation

- Pooled human liver microsomes (pHLM)[2]
  Incubation: 1 h at 37 °C
- Urine samples (0.5 mL):
  Incubation with glucoronidase (1 h, 45 °C)
  Extraction with ACN / 10 M $NH_4^+HCOO^-$

Results and discussion

For identification of the main metabolites of MDMB-CHMICA an assay using pooled human liver microsomes was applied and the metabolic profile was compared to the profiles detected in authentic urine samples of patients who used the drug as proven by detection of MDMB-CHMICA in paired serum samples.

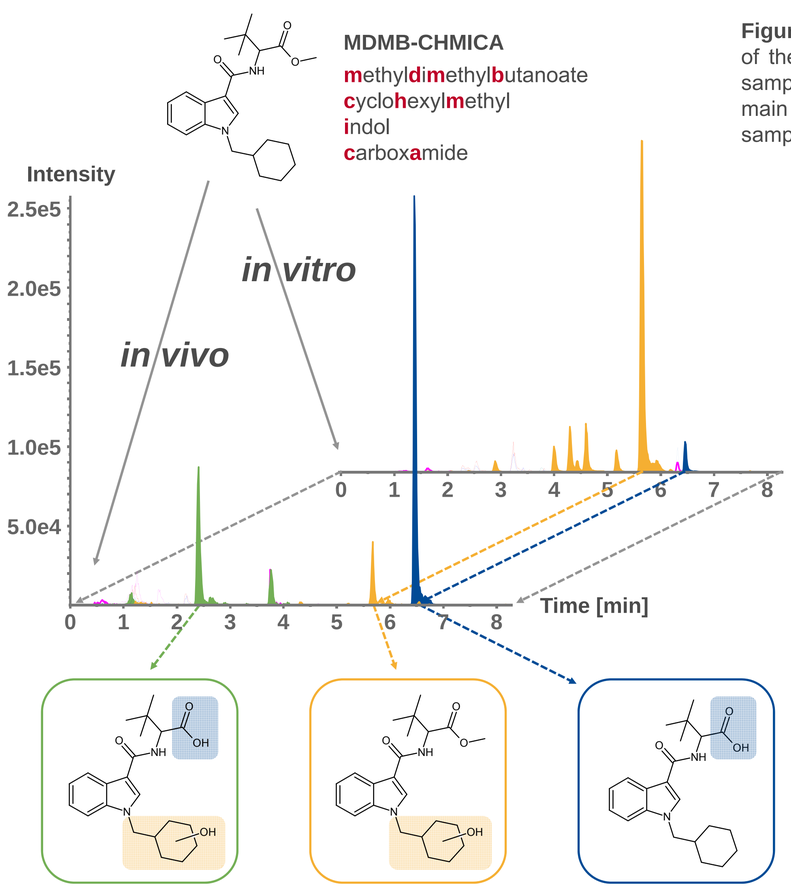

Figure: Chromatogram of the *in vitro* and *in vivo* samples and the identified main metabolites in urine samples.

Hydroxylated methyl ester cleavage product | **Cyclohexyl-methyl hydroxylated metabolite** | **Product of the methyl ester cleavage**

The corresponding ion transitions were integrated into an existing LC-MS/MS based screening method and the method was already successfully applied for the qualitative detection of the metabolites in authentic urine samples. The cyclohexyl-methyl hydroxylated metabolite is specific for MDMB-CHMICA. In contrast, the metabolites obtained after ester hydrolysis are likely to be also metabolites of the carboxamide analogue ADB-CHMICA.

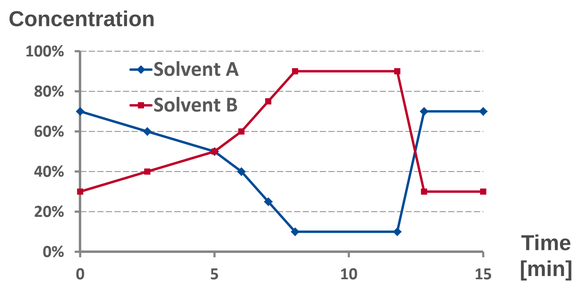

Figure: LC gradient (flow rate 0.5 mL/min) used for the metabolite identification method.

CAVE: Due to structural similarity (same nominal mass and almost identical fragment ion spectra) of MDMB-CHMICA and BB-22 there is a risk of confusion regarding the detection of these substances and their metabolites using LC-MS/MS.

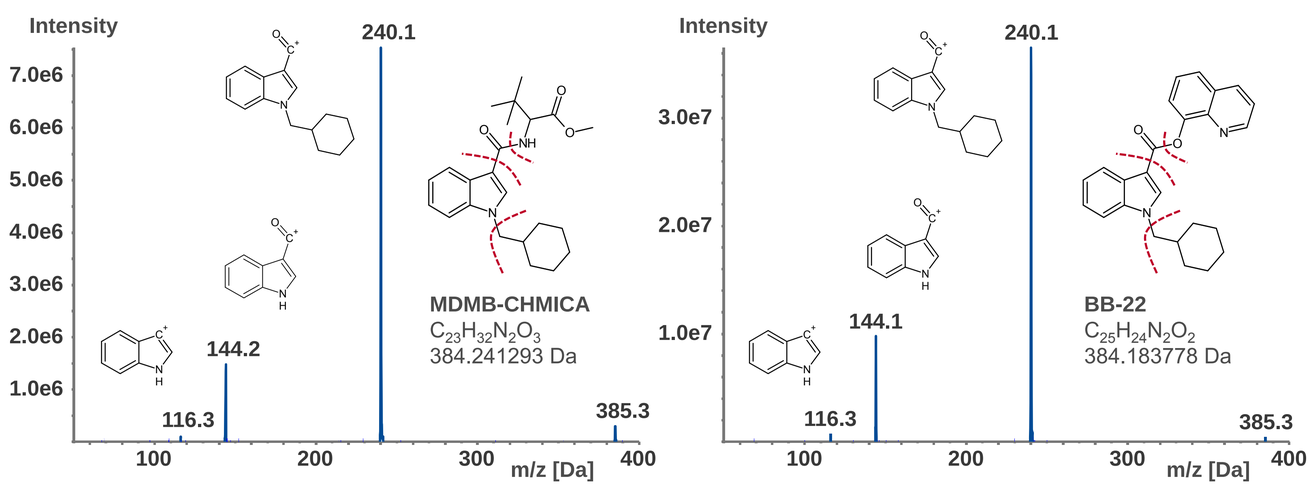

Figure: EPI spectra of MDMB-CHMICA (left) and BB-22 (right) with a CE 35 eV and CES 15 eV. Monoisotopic masses are shown for both substances.

Conclusion

Metabolism of MDMB-CHMICA is very similar to AB-CHMINACA metabolism and is dominated by ester cleavage and hydroxylation.[3] For a reliable differentiation of MDMB-CHMICA and BB-22 as well as their metabolites, reference materials or high resolution mass spectrometry are needed. Increasing knowledge on metabolism of single compounds enables more reliable prediction of metabolic profiles of new compounds.

Acknowledgement

This publication has been produced with the financial support of the European Union, the German Federal Ministry of Health and the City of Frankfurt/Main.

Bundesministerium für Gesundheit

References

[1] EDND of the EMCDDA

[2] “Mammalian Liver Microsomes, Guidelines for Use” TF000017 Rev 1.0 (BD Biosciences)

[3] Erratico *et al.*, Drug Test. Analysis (2015)

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