Comprehensive characterization of the synthetic cannabinoid NE-CHMIMO within an intoxication case

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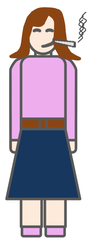
Introduction:

Synthetic cannabinoids (SC) play a significant role in the market of new psychoactive substances for many years now. The most frequent form of consumption for this class of substances is smoking of 'herbal mixtures' purchased via the Internet. In the present work the identification and structure elucidation of a new SC is described. The substance was found together with 5F-ADB [1] in a 'herbal mixture' labeled 'Jamaican Gold Extreme', which was sent to our laboratory in the context of a suspected case of intoxication. Furthermore, the *in vivo* phase I main metabolites of the new compound were investigated and the respective ion transitions were successfully integrated in an LC-MS/MS screening method for SC in urine.

Intoxication case

Method



17-year-old female: consumption of 'Jamaican Gold Extreme'

Seizure, mydriasis, vomiting, aggressiveness

Emergency room

information

Poisons Information Center Freiburg

"EU-Project"

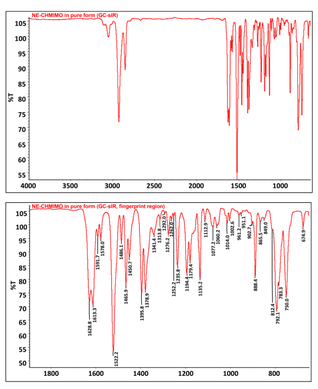
Screening for drugs of abuse using
- Immunoassays
- GC-MS
- LC-MS/MS
- LC-MS^n (Toxtyper^{TM})

Institute of Forensic Medicine Freiburg

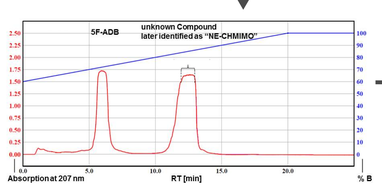
Gas chromatography solid-state infrared analysis (GC-sIR): no hit for the unknown substance

Extraction with *n*-hexane and analysis with GC-MS

5F-ADB + additional peak (no library hit)



Isolation with flash chromatography



NMR

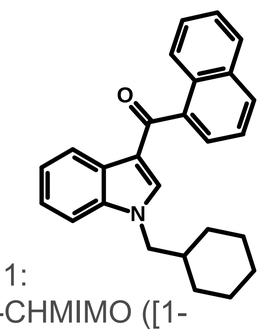


Fig 1:
NE-CHMIMO ([1-(cyclohexylmethyl)-1*H*-indol-3-yl](naphthalen-1-yl)methanone) [2]

Metabolism

Method

in vitro:

NE-CHMIMO

pooled human liver microsomes (pHLM) incubation 1h at 37°C

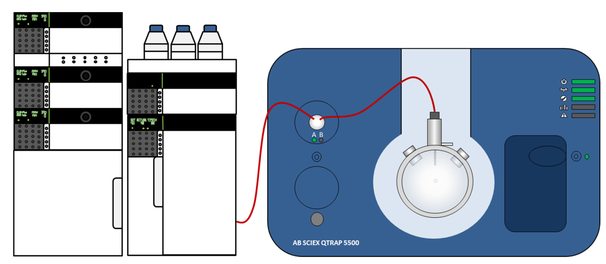
Dilution

in vivo:

Urine sample

incubation with β-glucuronidase (1h, 45 °C)

Extraction with ACN/ 10 M $NH_4^+HCOO^-$



Liquid chromatography conditions:
- UHPLC Nexera X2 (Shimadzu)
- Flow: 0.3 ml/min, gradient elution
- Kinetex® C18 column (100 mm x 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 $NH_4^+HCOO^-$)

Mass spectrometry conditions
- QTRAP® 5500 (Sciex)
- Positive ionization mode
  - Multiple reaction monitoring (MRM)
  - Enhanced product ion scan (EPI)
  - Precursor ion scan (Prec)

Results

Serum:
- 5F-ADB: ca. 15 ng/ml
- NE-CHMIMO: positive
- AB-CHMINACA: < 0.1 ng/ml
- MDMA: ca. 93 ng/ml
- MDA: ca. 15 ng/ml
- THC: 25 ng/ml
- THC-COOH: 230 ng/ml
- 11-OH-THC: 8.5 ng/ml

Herbal blend
- 5F-ADB positive
- NE-CHMIMO (see Fig. 1) positive

Urine:
- Creatinine: 200 mg/dl
- 5F-ADB: OH-pentyl-metabolite and methyl ester cleavage metabolite positive
- NE-CHMIMO metabolites (see Fig. 2) positive
- AB-CHMINACA/AMB-CHMINACA: only valine metabolite positive
- AB-FUBINACA/FUB-AMB: only valine metabolite positive
- MDMA 2,900 ng/ml
- MDA 470 ng/ml
- THC-COOH 2,900 ng/ml
- Midazolam 41 ng/ml
- α-OH-Midazolam > 1,000 ng/ml

Results

Fig 2:
NE-CHMIMO metabolism

Conclusion

The in depth analysis of a herbal mixture obtained in the context of an intoxication case enabled the characterization of a previously unknown psychoactive drug and emphasizes the high value of providing additional exhibits found at the scene to the forensic laboratory. Moreover, the extracted pure substance can be used as a reference material for updating analytical methods and to perform further studies. The combination of structural elements of JWH-018 and MDMB-CHMICA is reflected by the metabolic profile of NE-CHMIMO and shows structure-metabolism relationships to be a helpful tool for the prediction of phase I main metabolites.

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References:

[1] EMCDDA (2015) EMCDDA reporting form on the new drug 5F-ADB. Forensic Toxicology Department University Medical Center Freiburg. accessible via EDND database of the EMCDDA

[2] Angerer V, Bisel P, Moosmann B, Westphal F, Auwärter V Separation and structural characterization of the new synthetic cannabinoid JWH-018 cyclohexyl methyl derivative "NE-CHMIMO" using flash chromatography, GC-MS, IR and NMR spectroscopy. Forensic Sci Int. doi:http://dx.doi.org/10.1016/j.forsciint.2016.05.031

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