Detection of synthetic cannabinoids in human specimens

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Analytical methods for synthetic cannabinoids in human samples 2009-2012

- Blood or serum 7
- Urine 14
- Hair 2
- Oral fluid 2

- Analytical technique is mainly liquid chromatography – tandem mass spectrometry (LC-MS/MS)

Serum

- Kneisel S, Auwärter V. *Analysis of 30 synthetic cannabinoids in serum by liquid chromatography-electrospray ionization tandem mass spectrometry after liquid-liquid extraction.* **J Mass Spectrom. 2012;47:825-35.**
- 1.0 mL, liquid extraction
- LC-ESI-MS/MS (MRM), positive ionization
- Quantitative for 27 parent compounds
- LOQ 0.1 – 2.0 ng/mL
- Median concentrations found in serum below 1.0 ng/mL

Urine

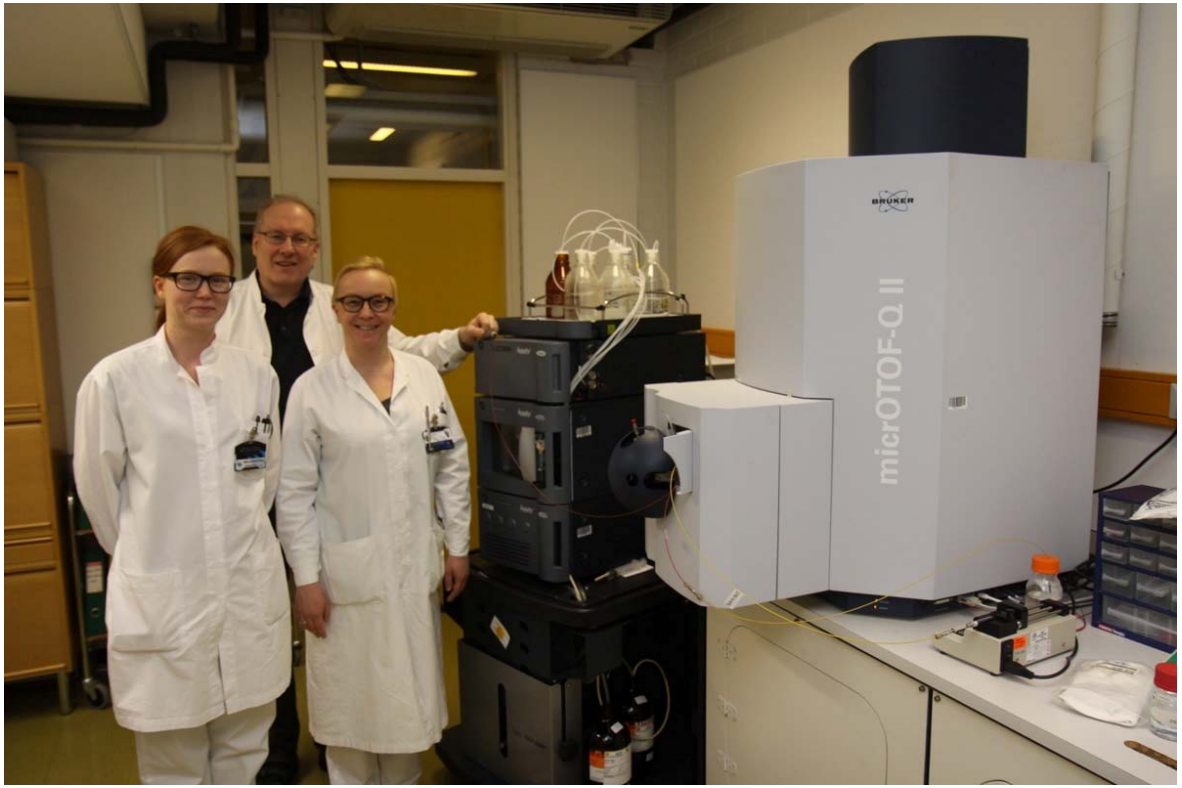
- de Jager AD, Warner JV, Henman M, Ferguson W, Hall A. *LC-MS/MS method for the quantitation of metabolites of eight commonly-used synthetic cannabinoids in human urine--an Australian perspective.* **J Chromatogr B Analyt Technol Biomed Life Sci. 2012;897:22-31.**
- 0.5 mL urine, enzyme hydrolysis, liquid extraction
- LC-ESI-MS/MS (MRM), positive ionization
- 11 metabolites representing 7 parent compounds
- Cut-off ≈ 0.1 ng/mL

Why urine?

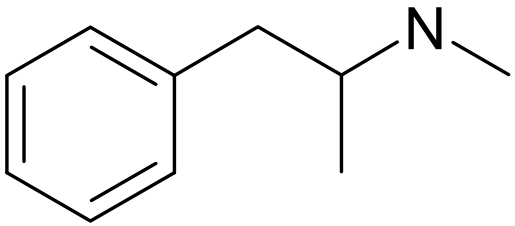
- Synthetic cannabinoids exist in urine as metabolites
  - Metabolism can be predicted
    - monohydroxylation and/or
    - carboxylation
- Longer detection window than in blood
- Higher concentrations in urine: up to several hundred ng/mL
- Synthetic cannabinoids can be incorporated into comprehensive drug testing program

Drug screening in urine by an accurate mass technique: time-of-flight MS

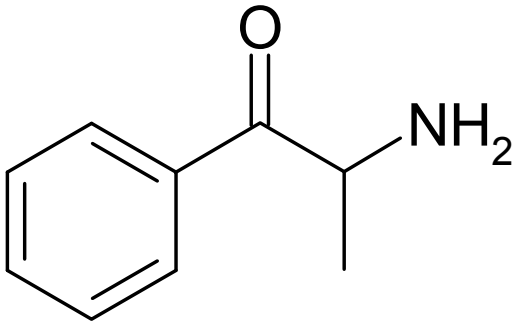
- 1.0 mL urine, enzyme hydrolysis, solid-phase extraction
- UPLC-ESI-QTOF, broadband, positive ionization



Differentiation of isobaric compounds by accurate mass



Methamphetamine MH^+ $C_{10}H_{16}N$ = 150.1
Exact mass 150.12773



Cathinone MH^+ $C_9H_{12}NO$ = 150.1
Exact mass 150.09134

ΔM = 36.4 mDa or 224 ppm

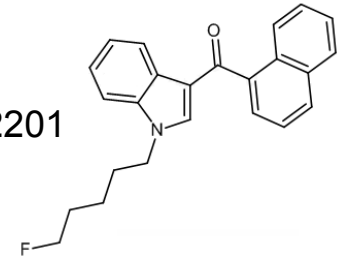
Coverage of the method: 234 compounds

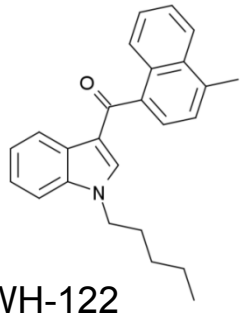
- Synthetic cannabinoids (42 parent + 21 metabolites)
- Cathinones (MDPV)
- Piperidine derivatives (2-DPMP)
- Tryptamine derivatives (5-MeO-DiPT)
- Other phenethylamine derivatives (DOB, bromodragonfly)
- Conventional drugs of abuse (cannabis, amphetamine)
- Prescription medicines, such as morphine and buprenorphine

Cut-off concentrations for synthetic cannabinoids in urine

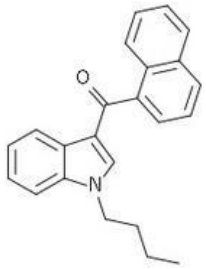
- LOD 1-100 ng/mL
  - Compounds with N: 1-60 ng/mL
  - Compounds without N: 40-100 ng/mL

AM-2201



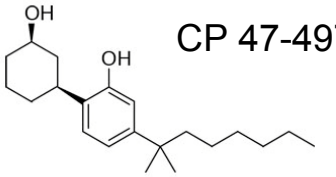


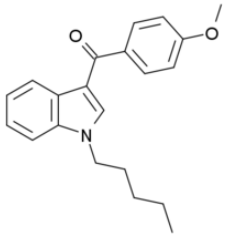
JWH-122



JWH-073

CP 47-497



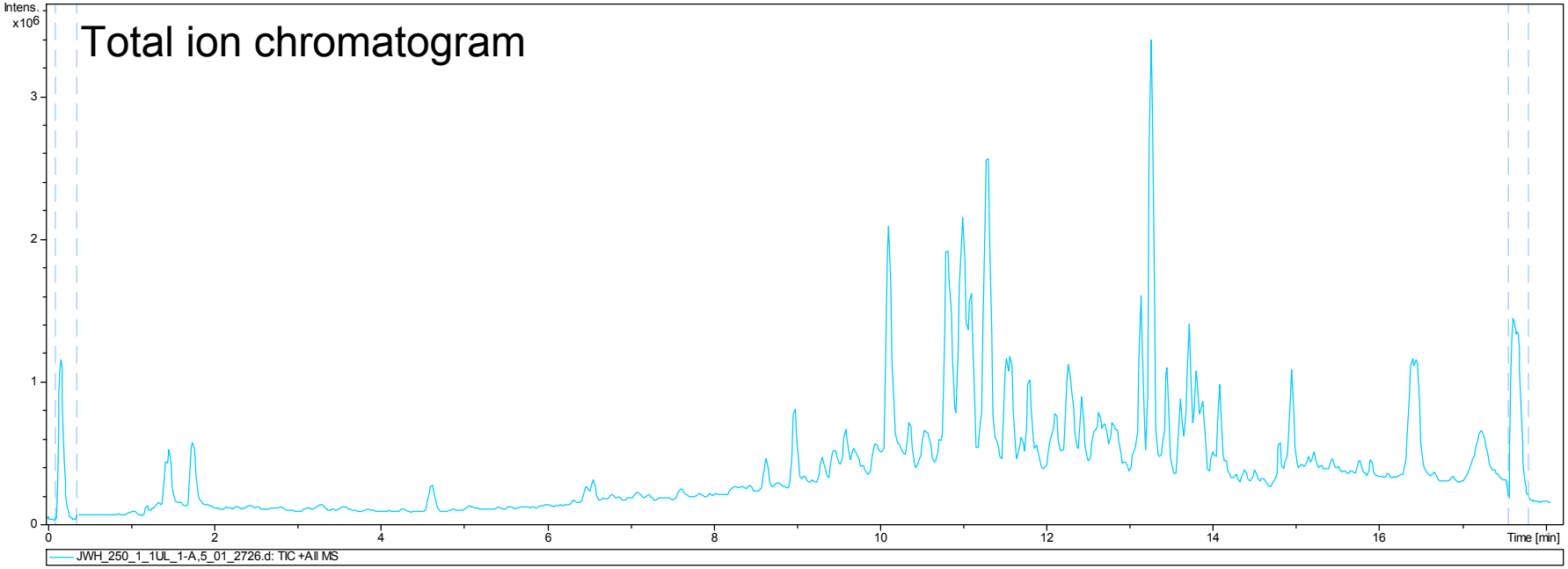


RCS-4

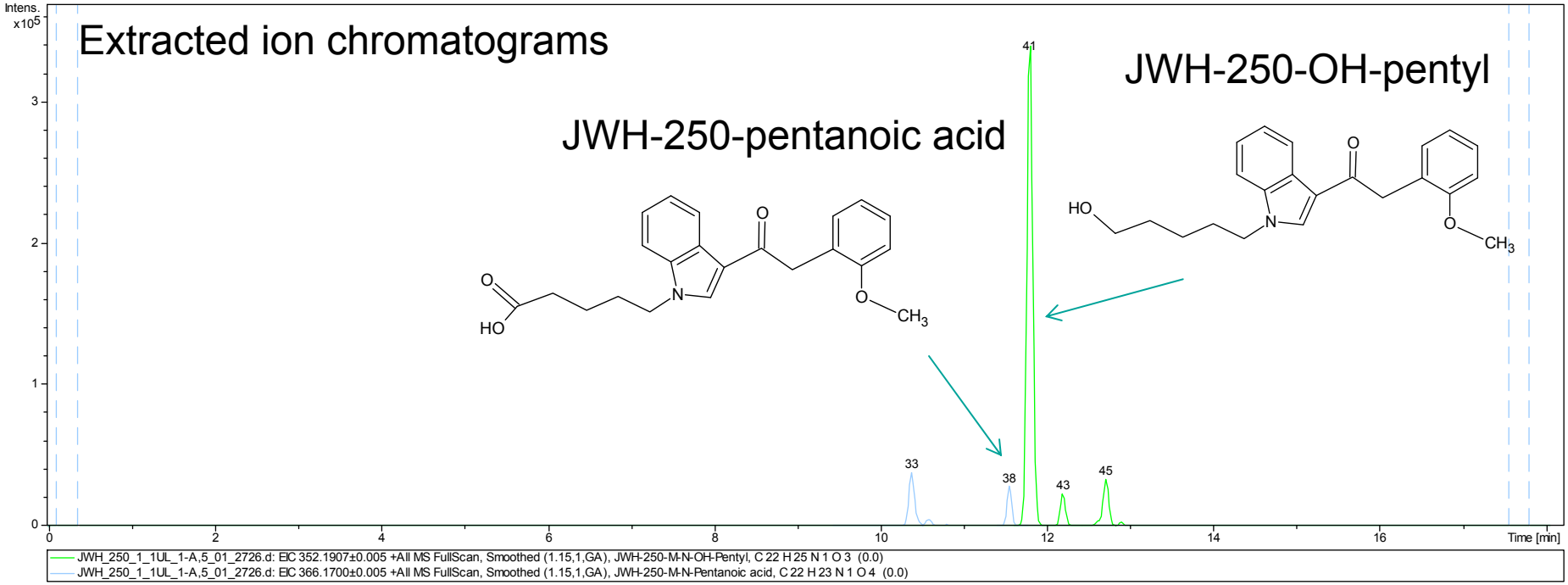
SYNTHETIC CANNABINOIDS	ng/ml
JWH-073	1,5
JWH-073-M-N-Butanoic acid	8
JWH-073-M-3-OH-Butyl	2
JWH-073-M-4-OH-Butyl	3
JWH-073-M-4-OH-Ind	6
JWH-073-M-5-OH-Ind	3,5
JWH-073-M-6-OH-Ind	3,5
JWH-073-M-7-OH-Ind	6
CP 47-497	60
HU-210	40
RCS-4	1
RCS-4-M-5-COOH-Pentyl	5
RCS-4-M-5-OH-Pentyl	3
WIN-48098	3
AM-2201	2
JWH-122	7,5
JWH-081	6
JWH-302	3
JWH-201	3

Urine sample from JWH-250 user:

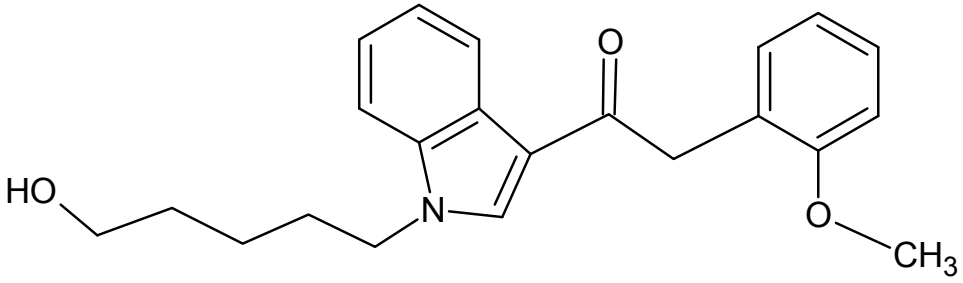
screening without reference standards

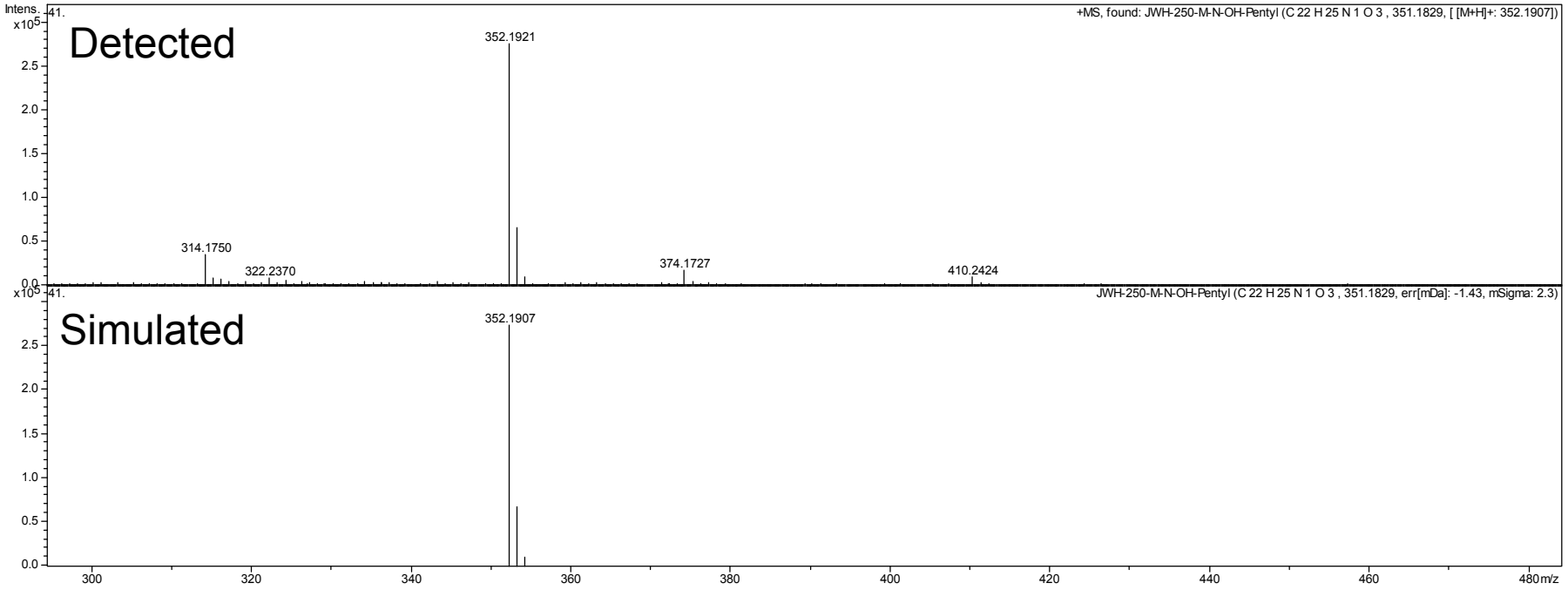


Screening: JWH-250 metabolites detected

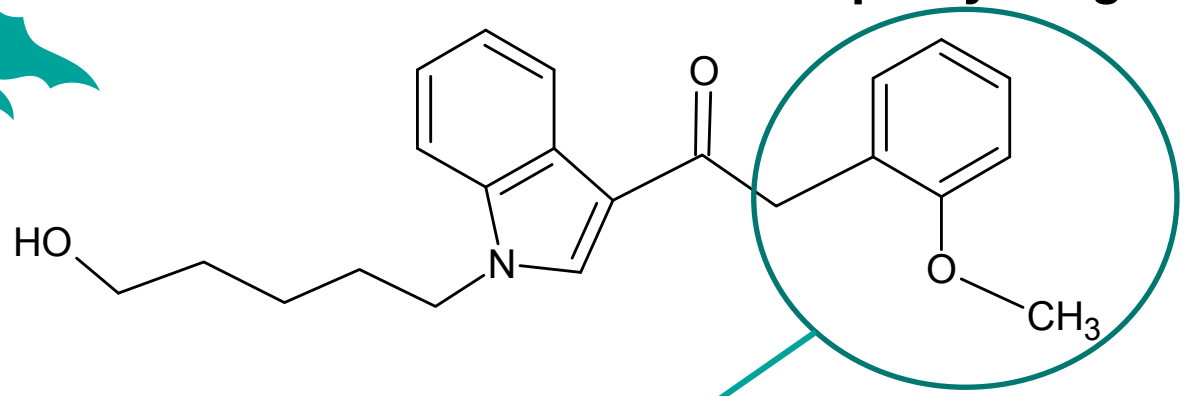


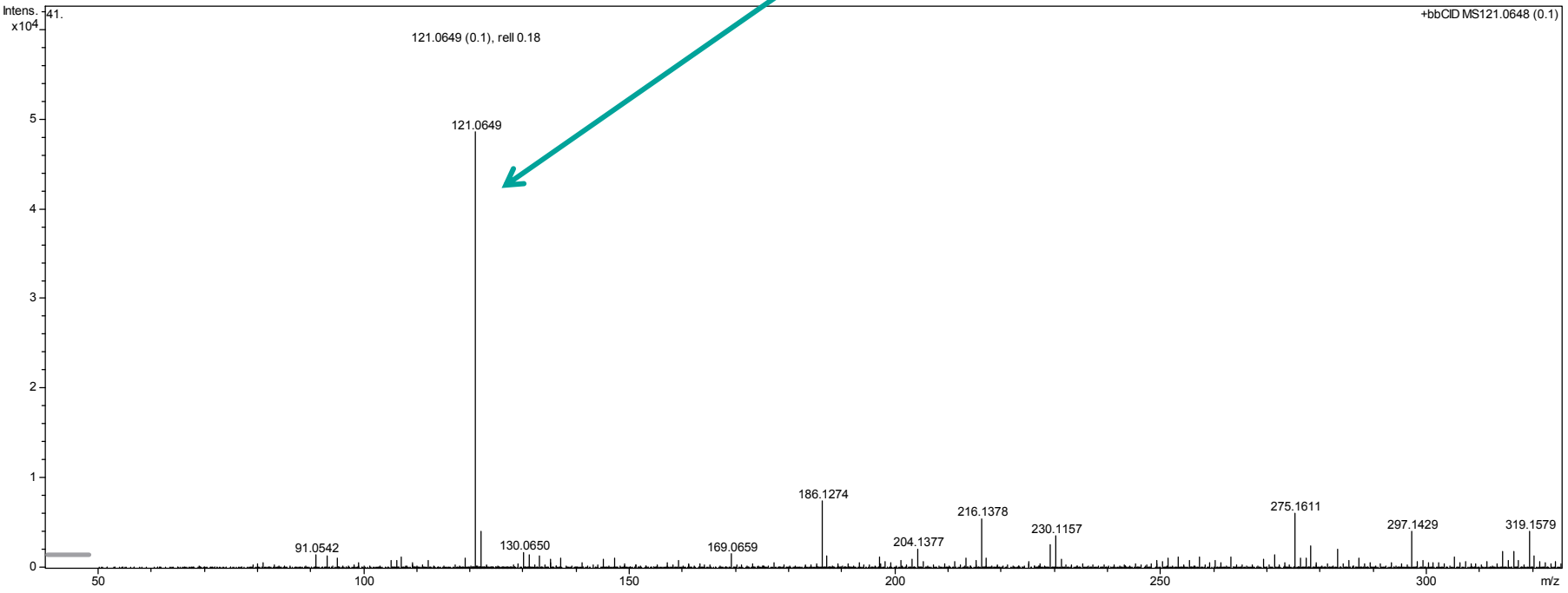
Screening: JWH-250-OH-pentyl precursor ion





Confirmation: JWH-250-OH-pentyl fragment ion





Conclusions

- Target methods for synthetic cannabinoids are mainly based on LC-MS/MS
- Parent compounds can be found in blood, serum, hair and oral fluid
- Due to low concentrations, very high sensitivity is required
- Metabolites can be found in urine in higher concentrations
- For urine screening, targeted or untargeted LC-QTOFMS is feasible