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

- 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

  - 0.5 mL urine, enzyme hydrolysis, liquid extraction
  - LC-ESI-MS/MS (MRM), positive ionization
  - 11 metabolites representing 7 parent compounds
  - Cut-off \( \approx 0.1 \) 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

\[ \text{Methamphetamine MH}^+ \text{ C}_{10}\text{H}_{16}\text{N} = 150.1 \]
Exact mass 150.12773

\[ \text{Cathinone MH}^+ \text{ C}_9\text{H}_{12}\text{NO} = 150.1 \]
Exact mass 150.09134

\[ \Delta M = 36.4 \text{ mDa or 224 ppm} \]
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

<table>
<thead>
<tr>
<th>SYNTHETIC CANNABINOIDS</th>
<th>ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>JWH-073</td>
<td>1,5</td>
</tr>
<tr>
<td>JWH-073-M-N-Butanoic acid</td>
<td>8</td>
</tr>
<tr>
<td>JWH-073-M-3-OH-Butyl</td>
<td>2</td>
</tr>
<tr>
<td>JWH-073-M-4-OH-Butyl</td>
<td>3</td>
</tr>
<tr>
<td>JWH-073-M-4-OH-Ind</td>
<td>6</td>
</tr>
<tr>
<td>JWH-073-M-5-OH-Ind</td>
<td>3,5</td>
</tr>
<tr>
<td>JWH-073-M-6-OH-Ind</td>
<td>3,5</td>
</tr>
<tr>
<td>JWH-073-M-7-OH-Ind</td>
<td>6</td>
</tr>
<tr>
<td>CP 47-497</td>
<td>60</td>
</tr>
<tr>
<td>HU-210</td>
<td>40</td>
</tr>
<tr>
<td>RCS-4</td>
<td>1</td>
</tr>
<tr>
<td>RCS-4-M-5-COOH-Pentyl</td>
<td>5</td>
</tr>
<tr>
<td>RCS-4-M-5-OH-Pentyl</td>
<td>3</td>
</tr>
<tr>
<td>WIN-48098</td>
<td>3</td>
</tr>
<tr>
<td>AM-2201</td>
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</tr>
<tr>
<td>JWH-122</td>
<td>7,5</td>
</tr>
<tr>
<td>JWH-081</td>
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<tr>
<td>JWH-302</td>
<td>3</td>
</tr>
<tr>
<td>JWH-201</td>
<td>3</td>
</tr>
</tbody>
</table>
Urine sample from JWH-250 user: screening without reference standards

Total ion chromatogram
Screening: JWH-250 metabolites detected

Extracted ion chromatograms

- JWH-250-pentanoic acid
- JWH-250-OH-pentyl
Screening: JWH-250-OH-pentyl precursor ion

-MS, found: JWH-250-M-N-OH-Pentyl (C_{22}H_{25}N_{1}O_{3}, 351.1829, [M+H]+: 352.1907)

Detected

Simulated
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