NYSAM 2019 Drugs of Abuse Update

Nicholas Nacca
University of Rochester Medical Center
38 year old male inmate of 5 years duration presented to the emergency department with altered mental status. Only past medical history is HTN and Asthma.

<table>
<thead>
<tr>
<th>Vital Signs</th>
<th>Physical Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temp: 35 degrees Celsius</td>
<td>HEENT: Pink/Moist OM, Pupils mid-ranged and sluggish</td>
</tr>
<tr>
<td>HR: 47 BMP</td>
<td>Heart/Lungs: bradycardia</td>
</tr>
<tr>
<td>BP: 139/53 mmHg</td>
<td>Abd: Soft, NT, ND</td>
</tr>
<tr>
<td>RR: 12 BMP</td>
<td>Skin: No track marks/lesions, cool and dry</td>
</tr>
<tr>
<td>02 sat: 95% RA</td>
<td>Neuro: Confused, staring off into space. Not answering all questions appropriately. Able to obey simple commands.</td>
</tr>
</tbody>
</table>
• CBC
• BMP
  – Na 139, K 3.0, Cl 102, HC03 28, BUN 38, Creatinine 0.9, Glucose 111, Ca 10.4
• LFT: AST 20, ALT 24, Alk phos 59, Lactate: 1.2 mmol/L
• UDS: negative
  – Amphetamine, Barbiturate, Bzd, Cocaine, Opiates, THC, PCP, Paroxetine, Oxycodone, Buprenorphine, Methadone
• APAP negative, ETOH negative
Case progression

• Day 0- presents to OSH with AMS
  – Urine drug screen negative
• Day 1- intubated due to respiratory failure
  – Bradycardia, hypotension, hypothermia, hypoglycemia, possible sz activity
  – Transiently on Dextrose infusion
• Day 4- Repeat urine drug screen positive for BZD only
  – Received BZD for what looked like a seizure
• Day 5- A CT Abd/Pelvis is ordered
5 packets identified on CT scan:
• 2 in the body of the stomach
• 1 in the small bowel
• 2 in the colon.
Case progression

- **Day 5**: CT abd/pelvis identifies multiple (5) opaque FB
  - Enema attempted & PEG @ 100 ml/hour
  - 2 ruptured powder-filled packets expelled per rectum
- **Day 6**: Pt transferred to academic medical center
  - On DA for bradycardia upon arrival
- **Day 7**: 2 packets removed by EGD (1 intact, 1 ruptured)
  - “Comprehensive” urine drug screen positive for THC, BZD, metoclopramide, atropine
  - Given AC and WBI started with PEG-ELS @ 500 ml/hr (stopped after residuals measured 1.2 L)
  - Episodes of hypertension and bradycardia treated with hydralazine & atropine
- **Day 8**: Troponin (0.19→0.21→0.30)
Advanced testing

• Day 6 - serum
  – Diphenhydramine, *Metoclopramide*, Scopolamine, *Midazolam*, ADB-FUBINACA (34.2 ng/mL)
  – Positive for cocaine Liquid Chromatography Quadrupole Time-of-Flight Mass Spectrometry, Negative via Liquid Chromatography Tandem Mass Spectrometry (below reference limit)

• Day 7 - urine
  – Negative for UR-144, AB-CHIMNACA, ADB-PINACA, ADBICA
    • LC-MS/MS methodology
  – Positive for MDMB-FUBINACA (metabolite of ADB-FUBINACA)

• Day 8 - plasma
  – *Metoclopramide*, *Midazolam*, ADB-FUBINACA (17.2 ng/mL)
Advanced testing

- 4 Packets sent for analysis
  - A: Phytocannabinoids
  - B: ADB-FUBINACA
  - C: ADB-FUBINACA
  - D: Phytocannabinoids

Figure 1. Chromatogram of Sample A
Case progression

- Day 9 - Pt has witness generalized seizure
- Day 10 - EEG reveals focal subclinical seizure in left temporal lobe
- Day 14 - Repeat CT scan reveals 2 radiopaque foreign bodies in the rectum
  - Passed leafy material and packaging material over 1 week period
- Day 22 - Discharged without sequelae
Discussion

ADB-FUBINACA  
(present in the above case)

AMB-FUBINACA  
(2016 NYC outbreak)

![Chemical structures of ADB-FUBINACA and AMB-FUBINACA](chart.png)

![Graphs showing body temperature and heart rate](graph.png)
Synthetic cannabinoids

• Heterogeneous group of compounds with varying clinical effects
  – Range from sedative hypnotic to sympathomimetic toxidromes

• Moving target of detection
  – There are LOTS of them!

• Not routinely screened for on urine chemical dependency
  – Some panels exist in reference labs but are not exhaustive
What are they?

John W Huffman 2009

Fig. 2 Structures of cannabimimetic indoles, pyrroles, and indenes
## Why are they different from THC?

Table 1. Binding affinities of synthetic cannabinoids determined by displacement of radioactive CP 55,940 (unless otherwise marked)

<table>
<thead>
<tr>
<th>Compound</th>
<th>CB₁ Kᵦ (nM)¹</th>
<th>CB₂ Kᵦ (nM)²</th>
<th>CB₃ Kᵦ (nM)³</th>
<th>Ref.</th>
<th>Compound</th>
<th>CB₁ Kᵦ (nM)¹</th>
<th>CB₂ Kᵦ (nM)²</th>
<th>CB₃ Kᵦ (nM)³</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HU-210</td>
<td>0.06±0.007</td>
<td>0.52±0.04</td>
<td>8.52</td>
<td>[27]</td>
<td>XLR-11</td>
<td>24±(4.6)</td>
<td>2.1±(0.6)</td>
<td>0.09</td>
<td>[112]</td>
</tr>
<tr>
<td>AM-694</td>
<td>0.08</td>
<td>1.44</td>
<td>18.00</td>
<td>[60]</td>
<td>JWH-306</td>
<td>25±1</td>
<td>82±11</td>
<td>3.28</td>
<td>[43]</td>
</tr>
<tr>
<td>ADB-FUBINACA</td>
<td>0.36</td>
<td>—</td>
<td>—</td>
<td>[10]</td>
<td>JWH-251</td>
<td>29±5</td>
<td>146±36</td>
<td>0.20</td>
<td>[43]</td>
</tr>
<tr>
<td>JWH-210</td>
<td>0.46±0.03</td>
<td>0.69±0.01</td>
<td>1.50</td>
<td>[43]</td>
<td>UR-144</td>
<td>29±(0.9)</td>
<td>4.5±(1.7)</td>
<td>0.01</td>
<td>[112]</td>
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<tr>
<td>CP 55,940</td>
<td>0.58±0.07</td>
<td>0.69±0.02</td>
<td>1.19</td>
<td>[87]</td>
<td>JWH-251</td>
<td>29±3</td>
<td>146±36</td>
<td>5.03</td>
<td>[43]</td>
</tr>
<tr>
<td>JWH-122</td>
<td>0.69±0.5</td>
<td>1.2±1.2</td>
<td>1.74</td>
<td>[41]</td>
<td>JWH-237</td>
<td>38±10</td>
<td>106±2</td>
<td>2.79</td>
<td>[43]</td>
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<tr>
<td>AM-2201</td>
<td>1</td>
<td>2.6</td>
<td>2.60</td>
<td>[59]</td>
<td>Delta9-THC</td>
<td>41±2</td>
<td>36±10</td>
<td>0.88</td>
<td>[15,87]</td>
</tr>
<tr>
<td>JWH-081</td>
<td>1.20±0.03</td>
<td>12±4±2.23</td>
<td>10.33</td>
<td>[5]</td>
<td>JWH-200</td>
<td>42±5</td>
<td>—</td>
<td>—</td>
<td>[5]</td>
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<tr>
<td>WIN 55212-2</td>
<td>1.9±0.09</td>
<td>0.28±0.16</td>
<td>0.15</td>
<td>[52,87]</td>
<td>JWH-211</td>
<td>70±0.8</td>
<td>12±0.8</td>
<td>0.17</td>
<td>[41]</td>
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<tr>
<td>CP 47,497</td>
<td>2.20±0.47</td>
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<td>—</td>
<td>[89]</td>
<td>JWH-312</td>
<td>72±7</td>
<td>91±20</td>
<td>1.26</td>
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<tr>
<td>AM-411</td>
<td>6.9</td>
<td>52</td>
<td>7.50</td>
<td>[59]</td>
<td>JWH-167</td>
<td>90±17</td>
<td>159±14</td>
<td>1.77</td>
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<tr>
<td>JWH-203</td>
<td>8.0±0.9</td>
<td>7.0±1.3</td>
<td>0.88</td>
<td>[43]</td>
<td>JWH-303</td>
<td>117±10</td>
<td>138±12</td>
<td>1.18</td>
<td>[43]</td>
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<tr>
<td>JWH-249</td>
<td>8.4±1.8</td>
<td>20±2</td>
<td>2.38</td>
<td>[43]</td>
<td>JWH-205</td>
<td>124±23</td>
<td>180±9</td>
<td>1.45</td>
<td>[43]</td>
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<tr>
<td>JWH-073</td>
<td>8.9±1.8</td>
<td>38±24</td>
<td>4.27</td>
<td>[5]</td>
<td>JWH-208</td>
<td>179±7</td>
<td>570±127</td>
<td>3.18</td>
<td>[43]</td>
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<tr>
<td>JWH-018</td>
<td>9.0±5.0</td>
<td>2.9±2.6</td>
<td>0.32</td>
<td>[5]</td>
<td>JWH-206</td>
<td>389±25</td>
<td>498±37</td>
<td>1.28</td>
<td>[43]</td>
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<tr>
<td>JWH-019</td>
<td>9.80±2.00</td>
<td>5.55±2.00</td>
<td>0.57</td>
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<td>JWH-313</td>
<td>422±19</td>
<td>365±92</td>
<td>0.86</td>
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<tr>
<td>JWH-250</td>
<td>11±2</td>
<td>33±2</td>
<td>3.00</td>
<td>[43]</td>
<td>JWH-209</td>
<td>746±49</td>
<td>1353±270</td>
<td>1.81</td>
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<td>JWH-204</td>
<td>13±1</td>
<td>25±1</td>
<td>1.92</td>
<td>[43]</td>
<td>JWH-248</td>
<td>1028±39</td>
<td>657±19</td>
<td>0.64</td>
<td>[43]</td>
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<tr>
<td>JWH-305</td>
<td>15±1.8</td>
<td>29±5</td>
<td>1.93</td>
<td>[43]</td>
<td>JWH-201</td>
<td>1064±21</td>
<td>444±14</td>
<td>0.42</td>
<td>[43]</td>
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<tr>
<td>JWH-302</td>
<td>17±2</td>
<td>89±15</td>
<td>5.24</td>
<td>[43]</td>
<td>JWH-207</td>
<td>1598±134</td>
<td>3723±10</td>
<td>2.33</td>
<td>[43]</td>
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<tr>
<td>JWH-311</td>
<td>23±2</td>
<td>39±3</td>
<td>1.70</td>
<td>[43]</td>
<td>JWH-202</td>
<td>1678±63</td>
<td>645±6</td>
<td>0.38</td>
<td>[42]</td>
</tr>
</tbody>
</table>

Gurney, Scott, Kacinko, Presley & Logan • Synthetic Cannabinoids — Pharmacology, Toxicology & Adverse Effects
**Where are they from?**

<table>
<thead>
<tr>
<th>Country of vendor</th>
<th>23-August-16</th>
<th>31-October-16</th>
<th>21-December-16</th>
<th>24-February-17</th>
<th>21-April-17</th>
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<tbody>
<tr>
<td>Australia</td>
<td>0</td>
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<td>1</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Austria</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>China</td>
<td>198</td>
<td>245</td>
<td>218</td>
<td>188</td>
<td>199</td>
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<tr>
<td>Finland</td>
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<td>2</td>
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<tr>
<td>France</td>
<td>10</td>
<td>11</td>
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<td>Germany</td>
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<td>56</td>
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<tr>
<td>Netherlands</td>
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<tr>
<td>Poland</td>
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<td>13</td>
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<td>Portugal</td>
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<td>10</td>
<td>11</td>
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<tr>
<td>Spain</td>
<td>3</td>
<td>9</td>
<td>19</td>
<td>17</td>
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<td>United Kingdom</td>
<td>34</td>
<td>130</td>
<td>66</td>
<td>45</td>
<td>46</td>
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<tr>
<td>United States</td>
<td>89</td>
<td>54</td>
<td>49</td>
<td>22</td>
<td>20</td>
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<tr>
<td>Unknown</td>
<td>19</td>
<td>18</td>
<td>18</td>
<td>20</td>
<td>36</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>396</strong></td>
<td><strong>576</strong></td>
<td><strong>440</strong></td>
<td><strong>442</strong></td>
<td><strong>460</strong></td>
</tr>
</tbody>
</table>

Figure 1. Number of synthetic cannabinoids listed for sale from Chinese vendors.

Synthetic Cannabinoids and Coagulopathy

• March 8\textsuperscript{th} 2018
  – Index case of unexplained coagulopathy associated with synthetic cannabinoid use identified in IL

• March 22\textsuperscript{nd} 2018
  – Illinois Poison Center received 4 calls of unexplained coagulopathy in patients who reported use of synthetic cannabinoids
  – “Superwarfarins” (brodifacoum) identified as the causal adulterant

• By April 11\textsuperscript{th} 2018
  – 118 cases identified in 2 geographical regions in Illinois

“Superwarfarins”

• All “warfarins” inhibit the activity of vitamin K 2,3 epoxide reductase
  – This is the enzyme that allows vitamin K to activate clotting factors II, VII, IX, X
  – The result is coagulopathy and can be measured by INR
    • Hematuria, abdominal pain, bruising, spontaneous epistaxis, ICH

• Requires long term vitamin K treatment
  – Brodifacoum can last weeks to months
CDC reports

• April 5th
  – Reported 94 patients identified
    • 89 in IL, 2 in IN, 1 ME, 1 MI, 1 WI
    • 2 fatalities both in IL

• April 23rd
  – Total of 160 patients identified in 9 states (IL, FL, IN, ME, MI, WI, PA, VA, KY)
    • 3 fatalities, 7 different synthetic cannabinoids

• November 26th
  – Total of 320 patients identified (States now include NC and WV)
    • 8 fatalities

December 21, 2018

TO: Healthcare Providers, Hospitals, Off-Campus Emergency Departments, Substance Use Disorder/Mental Health Agencies, and Local Health Departments

FROM: New York State Department of Health, New York State Office of Mental Health, New York State Office of Alcoholism and Substance Abuse Services

INFORMATIONAL MESSAGE:
Synthetic cannabinoid (SC) - related coagulopathies – 2018

For healthcare facilities/hospitals, please distribute to the Emergency Department, Director of Nursing, Medical Director, Director of Psychiatry, Director of Pharmacy, and Laboratory Service.

The CDC has also recommended checking the INR of all patients known or suspected to have used SC in the last 3 months, regardless of their presentation, due to the risk of consuming a SC product contaminated with a vitamin K-dependent antagonist.

All cases of suspected or confirmed poisonings should be reported to the Poison Control Centers in New York State. The staff can assist in determining further testing of the SC samples and/or patient biological samples. This is vital for detecting and responding to serious adverse events related to use of these products.


