Synthetic Cannabinoids and their impact on driving

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IACP Conference, Denver 2016
<table>
<thead>
<tr>
<th><strong>Cannabis</strong></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Horizontal Gaze Nystagmus (HGN)</strong></td>
<td>None</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Vertical Nystagmus (VGN)</strong></td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lack of Convergence (LOC)</strong></td>
<td>Present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pupil Size</strong></td>
<td>Dilated (Possibly normal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Reaction to Light</strong></td>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pulse</strong></td>
<td>Up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blood Pressure (BP)</strong></td>
<td>Up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Body Temperature (BT)</strong></td>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Muscle Tone (MT)</strong></td>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>General Indicators</strong></td>
<td>Marked reddening of the conjunctiva</td>
<td>Odor of marijuana</td>
<td>Marijuana debris in mouth</td>
<td>Body/eyelid tremors</td>
</tr>
<tr>
<td><strong>Usual Methods of Administration</strong></td>
<td>Smoked, oral</td>
<td></td>
<td></td>
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</tbody>
</table>
Cannabinoids

• Endocannabinoids
  – Receptors CB₁ and CB₂ (1980s)
  – Regulating appetite, nausea, mood, pain, and inflammation

• Plant cannabinoids
  – Marijuana

• Synthetic cannabinoids
  – Research labs-therapeutic applications
Cannabinoid Receptors

• CB1
  – Widely expressed in central nervous system

• CB2
  – Peripheral tissues of immune system
Binding Affinity

• How tightly a compound binds to a receptor

• Defined by Ki values
  – The lower the Ki the more tightly the compound binds

• Ki value for CB1 receptor
  – THC = 40 nM
  – AB-PINACA = 0.78 nM
  – 5F-ADB = ??
Synthetic cannabinoids

• Chemically synthesized
  – Prepared to mimic the desired effects of marijuana
• SPICE products
• Recreational use started in 2008
• Solids or oils sprayed onto herbal mixture
  – Inconsistent application
  – Ingredients vary lot to lot/manufacture
  – Not all components listed on packaging
Variation in Compounds/Concentration

• Quantitative variation **within one** package (5F-APINACA)
  • Dutchy: Average= 40 mg/g (Range: 30-52)
  • Green Crack: Average=206 mg/g (Range: 186-219)

• Quantitative variation **between** packages (5F-APINACA)
  • Dutchy: Average= 36 mg/g (Range: 30-40)
  • Green Crack: Average=219 mg/g (Range: 182-290)

Spice manufacturing

DEA
Albuquerque, New Mexico, District Office (DO) Task Force Agents

May 27, 2012
DEA Seizure – New Mexico

• 363 pounds bulk compound
  – Yields ~110,000 packets of finished product
• 36,000 finished product seized
• Over the last year, operation had shipped tens of thousands of products across the country
  – Shipped to 38 states
  – Roughly $8 M in revenue for the shops
• $597,691, 16 vehicles, and one firearm
DEA Seizure – New Mexico

• In addition to Albuquerque, drug trafficking organization was also linked to Salt Lake City, UT

• Investigation also led to seizures in SLC
  – $440,269, five weapons (including one AR-15 assault rifle), military-style body armor, and three vehicles

• Seizure in NYC -- $20,000

• Seizure in Mississippi – 50 weapons
'Spice' arrests, seizures carried out in Tucson, 2 other cities

By Caitlin Schmidt Arizona Daily Star  Updated Jul 30, 2016

U.S. Drug Enforcement Administration
It's unclear how many were arrested in Tucson or where each raid took place.
Self-Reported Reasons for Using Synthetic Cannabinoids
(N=150 Adult Residential Substance Use Disorder Treatment Patients Reporting Lifetime Synthetic Cannabinoid Use)

- Curiosity: 91%
- To Feel Good or Get High: 89%
- To Relax or Relieve Tension: 71%
- To Get High Without Having a Positive Drug Test: 71%
- Liked the Effects: 63%
- Boredom: 59%
- To Have a Good Time with Friends or to Fit In: 59%
- Anger or Frustration; To Get Away from Problems or Troubles: 48%
- To Help Deal with Pain: 39%
- To Increase or Decrease the Effects of Some Other Drugs: 32%
- Because It Is Safer Than Other Drugs: 30%
User demographics

- Military
- Probation
- Professional Athletes
- Work place drug testing
Professional Athletes

- Jan 2014: Jets Tight End Kellen Winslow arrested in Target parking lot for masturbating
  - “Winslow allegedly told police he smoked the 'Mr. Happy' and 'Funky Monkey' at his home to relax because the NFL doesn't drug test for it, and that he buys the stuff on the internet and at gas stations”

- Jan 2016: Patriots Chandler Jones hospitalized after “bad trip” on Spice

- Oct 2016: Seahawks Derrick Coleman admitted to smoking Spice prior to crash
More than 30 people fall ill in apparent mass drug overdose in New York

Police called to Bedford-Stuyvesant neighbourhood of Brooklyn after reports of victims lying on the sidewalk shaking

K2 is a form of synthetic marijuana that can cause extreme anxiety, hallucinations, vomiting, fainting and kidney failure. Photograph: William Mathis/@MathisWilliam

Associated Press

Wednesday 13 July 2016 05.40 EDT IACP Conference, Denver 2016
Video NY City

Look at these dudes.
Yo, look, they can’t even stand straight.
K2 Overdoses Surge in New York: At Least 130 Cases This Week Alone

Passing a K2 cigarette on Thursday in Brooklyn. New York City officials are concerned that use of the synthetic drug is rising, not dropping.

Christopher Lee for The New York Times
Poison Center calls

AAPCC Poison Center Synthetic Cannabinoids Exposure Calls (2010 - 2016)
Synthetic Cannabinoid Calls to U.S. Poison Centers (1/1/16-6/30/16)

PLEASE NOTE:

- These data are only representative of calls received by the poison centers and may not reflect the actual severity of the problem in the U.S. or any specific geographic location.
- As there is no mandatory reporting, there may be emergency room presentations and hospital admissions of which poison centers are unaware.
- Subject to the above bullets, these numbers are largely reflective of those users/abusers who have experienced adverse effects from the use of these products significant enough to warrant poison center or other health professional intervention; not all individuals who use/abuse such products call poison centers or visit emergency rooms.
- Nevertheless, the data are a good surrogate marker for rising use/abuse patterns and patterns of adverse medical outcomes associated with their use.
- For more information about the American Association of Poison Control Centers (AAPCC) data, please visit: http://www.aapcc.org/data-system/
Figure 3.3  Percentage of total drug reports identified as AB-PINACA, by State, 2013

Percent per State
- 1.6–2.0
- 1.0–1.5
- 0.6–0.9
- 0.1–0.5
- 0.0
- No Data

NFLIS 2014 Annual Report
Evolution of Spice in WA and AK

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Scheduling of synthetic cannabinoids

- March 1, 2011: Temporary scheduling of JWH-018, JWH-200, JWH-073, and CP-47,497
- May 16, 2013: Temporary scheduling of UR-144, XLR11, and AKB48
- February 10, 2014: Temporary scheduling of PB-22, 5F-PB-22, AB-FUBINACA, ADB-PINACA
- January 30, 2015: Temporary scheduling of AB-CHMINACA, AB-PINACA, THJ-2201
  - September 16, 2015: Temporary scheduling of ADB-CHMINACA
- February 5, 2016: Temporary scheduling of MAB-CHMINACA
- May 11, 2016: Permanent scheduling, UR-144, XLR-11, AKB48 added to Schedule 1 Controlled Substances Act
Timeline of novel compounds

• Current drug is regulated by FDA
• New drug introduced on drug market
• Increased reports to Emergency Room/calls to Poison Centers
• Compound identified in seized material

• Toxicology lab begins testing for compound
Toxicology testing for new compounds

- Reference standard must be available
- Develop an extraction
- Develop and validate analysis method for instrument

- TIME and MONEY!
Chemical structures

- THC

- Indole 3-carbonyl derivatives
  - XLR-11, UR-144

- Indazole 3-carbonylamide derivatives
  - AB-PINACA, AB-CHMINACACA, 5F-AMB
UR-144 and XLR-11

• UR-144
  – Invented by Abbott Laboratories
  – Much higher affinity for CB$_2$ receptor

• XLR-11
  – First identified in 2012
  – Closely related to UR-144
XLR-11 and UR-144 cases

- WA: June 2012 – December 2015
- WI: September 2012 – April 2016

- WA: 40 DUI/DRE cases positive
- WI: 11 DUI/DRE cases positive

- WA: 10 DRE cases only XLR-11 and/or UR-144
- WI: 2 DRE cases only XLR-11

- WA: 100% Males (mean age=24, range 19-41)
- WI: 67% Males (mean age=28, range 20-49)
<table>
<thead>
<tr>
<th></th>
<th>Cannabis</th>
<th>UR-144 and XLR-11 (N=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horizontal Gaze Nystagmus</td>
<td>None</td>
<td>42% Present (2 ≥ clues)</td>
</tr>
<tr>
<td>Vertical Nystagmus</td>
<td>None</td>
<td>17% Present</td>
</tr>
<tr>
<td>Lack of Convergence</td>
<td>Present</td>
<td>58% Present</td>
</tr>
<tr>
<td>Pupil Size</td>
<td>Dilated (Possibly normal)</td>
<td>75% Normal; 25% Dilated</td>
</tr>
<tr>
<td>Reaction to Light</td>
<td>Normal</td>
<td>50% Normal; 50% Slow</td>
</tr>
<tr>
<td>Pulse</td>
<td>Up</td>
<td>60% Normal (range 69 – 105)</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Up</td>
<td>75% Normal</td>
</tr>
<tr>
<td>Body Temperature</td>
<td>Normal</td>
<td>75% Normal (low 97.2)</td>
</tr>
<tr>
<td>Muscle Tone</td>
<td>Normal</td>
<td>50% Normal, 50% Rigid or Flaccid</td>
</tr>
</tbody>
</table>

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SFST Performance (n=12)

- WAT (≥2 clues): 6 cases
- OLS (≥2 clues): 3 cases
- Majority had slurred speech, bloodshot eyes, poor coordination

- Eyelid tremors: 6 cases
Driving Behavior

• Erratic driving
• Severe lane travel
• Collisions with stationary objects and other moving vehicles
• Inconsistent speed/stopping in traffic
• Driving in the wrong direction
WA- Case Report

- 25 yr old male
- Stopped vehicle on interstate then accelerated away; collision with median
- Seizure activity
- 6/6 HGN
- Slurred and choppy speech
- Admitted to use 15 min prior to driving
- XLR-11 present
AB-CHMINACACA & AB-PINACACA

- AB-CHMINACACA
  - First synthesized by Pfizer, 2009 patent

- AB-PINACACA
  - First identified in Japan in 2012
  - Aug 2014: DEA reports first time seized in Alabama
AB-CHMINACA/AB-PINACA

• November 2013-December 2015

• Total DUI/DRE cases
  • WA: 78
  • WI: 34

• DRE cases with one or both drugs
  • WA: 22 cases 100% male (mean age: 30 range 21-44)
  • WI: 15 cases 87% male (mean age: 30, range 20-59)
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<tr>
<th></th>
<th>Cannabis</th>
<th>AB-PINACA &amp; AB-CHMINACA (N=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horizontal Gaze Nystagmus</td>
<td>None</td>
<td>46% Present (2 ≥ clues)</td>
</tr>
<tr>
<td>Vertical Nystagmus</td>
<td>None</td>
<td>27% Present</td>
</tr>
<tr>
<td>Lack of Convergence</td>
<td>Present</td>
<td>51% Present</td>
</tr>
<tr>
<td>Pupil Size</td>
<td>Dilated (Possibly normal)</td>
<td>54% Normal; 38% Dilated, 8% Constricted</td>
</tr>
<tr>
<td>Reaction to Light</td>
<td>Normal</td>
<td>73% Normal</td>
</tr>
<tr>
<td>Pulse***</td>
<td>Up</td>
<td>43% Normal (range 51 – 120) AB-CHIM Elevated</td>
</tr>
<tr>
<td>Blood Pressure***</td>
<td>Up</td>
<td>43% Down</td>
</tr>
<tr>
<td>Body Temperature</td>
<td>Normal</td>
<td>81% Normal (low 96.4)</td>
</tr>
<tr>
<td>Muscle Tone</td>
<td>Normal</td>
<td>54% Normal, 46% Rigid or Flaccid</td>
</tr>
</tbody>
</table>
Synthetic Cannabinoids (n=37)

- Cooperative/confused
- Coordination - slow and sluggish
- Slow, slurred speech
- Blood shot eyes
- Ptosis
- Paraphernalia/synthetic material in vehicle
- Eyelid tremors - 7 cases

- Poor coordination
- Body tremors
- Sway 0-6” (0-2”)
- *Internal clock: slowed, normal, fast
- WAT: (29) ≥ 2/8 clues
- OLS: (21) ≥ 2/4 clues
- Opinion: Cannabis, Depressant
Driving Behavior/Observations

• Lane deviation
• Slumped over wheel, unconscious
  – Vehicle still running
  – In middle of road and/or at stop light
• Collisions
• Unable to maintain balance/stand, think, or formulate coherent statements
  – “Out of it”
• Majority of cases self report Spice use
CASE STUDY

• 59 year old male
• Arrested twice within 5 days
• Poor driving/asleep at the wheel
• Unsteady
• Slow slurred speech
• Bloodshot, watery eyes, ptosis; HGN and VGN, pupil size=normal
• Pulse = normal, BP = low
• WAT 6/8 clues, OLS 3/4
• Mad Hatter, WTF, and Climaxxx
• Toxicology: AB-PINACA and AB-CHMINACCA = “PRESENT”
5F-ADB

- Also known as 5F-MDMB-PINACA
- An indazole-based synthetic cannabinoid from the indazole 3-carboxamide family
- Believed to be a potent agonist of CB1 receptor
- Little research conducted on this compound
  - Physiological and toxicological properties have not been determined
- First identified in a post-mortem sample in November 2014 in Japan*
- Later identified in 10 people who died from unexplained overdoses in Japan (Sept-Dec 2014)*
Emergence of 5F-ADB in Washington

- Testing began in November 2015 (AIT Labs)
- From November 2015 – June 2016, 38 confirmed positive driving cases
- First death associated with 5F-ADB use in March 2016
  - 54 yr old male found unresponsive by wife
  - Cardiac arrest secondary to synthetic cannabinoid overdose
- 31 of the 38 driving cases were negative for any other psychoactive substance other than 5F-ADB
  - 4 had small amounts of THC-COOH (<10 ng/mL)
  - 2 had 5F-AMB
  - 1 had ADB-FUBINACA
  - 1 had 5F-PB-22
Emergence of 5F-ADB in Washington

- 38 confirmed driving cases (28 DUI’s and 10 DRE’s)
- 31 males and 7 females
- Ages ranged from 21-54 years old
- Two subjects, 1 male and 1 female, were both arrested four times in a two week span
  - Male found positive 2/4 times, while female was positive 4/4 times
- Another subject was arrested three times in a span of a few months
  - Found positive 2/3 times
- Concentrations of 5F-ADB ranged from 0.2-1.2 ng/mL

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Effects of 5F-ADB on driving patterns

Reason for stop or contact

- Intoxicated person
- Passed Out
- Collision
- Erratic Driving

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Effects of 5F-ADB on driving patterns

• 19 of 38 drivers (50%) that tested positive were found passed out at the wheel
  – 12 passed out in roadway
  – 7 passed out prior to collision

• 9 of 38 drivers (~24%) that tested positive were involved in collisions
  – 4 were involved in one car collisions
  – 3 were involved in two car collisions
  – 2 were involved in parked vehicle collisions

• All drivers were found to be highly impaired
DRE Indicators (n=10)

• HGN (≥ 2 clues): 4 cases
• VGN: 0 cases
• Lack of Convergence (LOC): 5 cases
• Pupil Size: 60% dilated
• Pulse: 60% normal (range 56-106)
• Blood Pressure: 50% elevated
• Body Temperature: 50% low
• Reaction to light: 50% normal
• Muscle tone: 2 rigid, 2 flaccid, 6 normal
SFST Performance (n=10)

• WAT (≥2 clues): 100%
• OLS (≥2 clues): 4 cases
• Majority had slurred speech, bloodshot eyes, poor coordination
• Eyelid tremors: 2 cases
Physiological effects

• Wide range of effects observed, many are similar to marijuana use, while others are far different
  – Extremely high blood pressure
  – Vomiting
  – Convulsions
  – Blank stare
  – Incoherent/unintelligible speech patterns
  – Seizures
  – Unconsciousness
Physiological effects

Eye Appearance

- Bloodshot
- Watery
- Droopy eyelids
- Constricted pupils
- Dilated pupils
Physiological effects

Speech

- Slurred
- Slow
- Raspy
- Incoherent
- Combative
- Mumbling

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Physiological effects

Coordination

- Poor
- Lethargic
- Convulsing/Shaking
- Unsteady/Stumbling
Case report #1

• 21 yr old male
• Citizen informs officer that a person is passed out while driving
• Officer observes defendant and uses patrol vehicle to stop him from crossing into oncoming traffic
• Unable to stand or follow commands
• Slurred, raspy speech
• Bloodshot, watery eyes
• Chemical smell on person
• Admits using spice for 3-4 years
• Smokes to get high
• Toxicology: 0.6 ng/mL 5F-ADB and 6.8 ng/mL ADB-FUBINACA
Case report #2

- 52 yr old male
- Arrives at ignition interlock center and is incoherent
- Police arrive to find defendant growling, yelling, and shaking violently
- Behavior is cyclic: calm to extreme rage
- Rigid muscles, argumentative, profane language
- Pupils go from constricted to dilated
- 10 prior lifetime DUI’s
- Toxicology: 1.2 ng/mL 5F-ADB and 8.8 ng/mL THC-COOH
Case report #3

- 37 yr old male
- Erratic driving, lane travel, stopped in roadway
- Contacted after being observed smoking
- Eludes police who find him a few minutes later standing against a car sleeping
- Slow reactions, blank stare, argumentative
- Heavily slurred speech
- Cyclic behavior in patrol car, calm to argumentative
- Toxicology: 1.0 ng/mL 5F-ADB
Case report #4

- 26 yr old male
- One car collision, left scene after firefighters informed defendant they were not detaining him
- Left scene with witnessed severe lane travel
- Found a few blocks away passed out at stop sign
- Dazed, confused, stumbling
- Covered in vomit and drooling on himself
- 6/6 HGN + VGN, 6/8 WAT, 3/4 OLS
- Toxicology: 0.4 ng/mL 5F-ADB
Case report #5

- 22 yr old male
- Stopped for driving across traffic at a 45° angle
- Passed out when cops contact him
- Blank stare and uncommunicative
- Unstable and frozen appearance while standing
- Physically unable to perform SFST’s due to severity of impairment
- Admitted eating “spice” 2 hrs prior
- Poison control contacted and placed on 4 hr emergency room hold
- Toxicology: 0.3 ng/mL 5F-ADB
## Summary of Indicators

<table>
<thead>
<tr>
<th></th>
<th>CANNABIS</th>
<th>XLR-11/UR-144 (n=12)</th>
<th>AB-CHMINAC A and/or AB-PINACA (n=37)</th>
<th>5F-ADB (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HGN</td>
<td>None</td>
<td>Present (42%)</td>
<td>Present (46%)</td>
<td>Present (40%)</td>
</tr>
<tr>
<td>VGN</td>
<td>None</td>
<td>Present (17%)</td>
<td>Present (27%)</td>
<td>None</td>
</tr>
<tr>
<td>LOC</td>
<td>Present</td>
<td>Present (58%)</td>
<td>Present (51%)</td>
<td>Present (50%)</td>
</tr>
<tr>
<td>Pupil Size</td>
<td>Dilated (normal)</td>
<td>Normal (dilated)</td>
<td>Normal (dilated)</td>
<td>Mostly dilated</td>
</tr>
<tr>
<td>Reaction to light</td>
<td>Normal</td>
<td>Normal (50%)</td>
<td>Normal (73%)</td>
<td>Normal (50%)</td>
</tr>
<tr>
<td>Pulse</td>
<td>Elevated</td>
<td>60% Normal 40% elevated</td>
<td>43% Normal 43% elevated</td>
<td>60% Normal 30% elevated</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Elevated</td>
<td>75% Normal 25% elevated</td>
<td>43% Normal</td>
<td>50% Elevated</td>
</tr>
<tr>
<td>Body Temp</td>
<td>Normal</td>
<td>Normal (75%)</td>
<td>Normal (81%)</td>
<td>50% Normal 50% Low</td>
</tr>
<tr>
<td>Muscle Tone</td>
<td>Normal</td>
<td>50% Normal 50% Rigid/Flaccid</td>
<td>54% Normal 46% Rigid/Flaccid</td>
<td>60% Normal 40 % Rigid/Flaccid</td>
</tr>
</tbody>
</table>
Toxicology Testing

• Approximately 50% of the cases that are submitted for synthetic cannabinoid testing have results of “None detected”
  – Drug paraphernalia often present

  – Admission by subject

  – Extreme impairment/odd behavior observed with no other drugs detected
Possible explanation for ‘none detected’

• Short half life of drug

• Time of blood draw in relation to incident

• New compound used that is not detected by testing yet

• Test method is not able to detect compound at typical ‘therapeutic’ concentrations
Testimony Limitations

• Limited clinical studies that discuss pharmacokinetics
  – How long drug lasts in body
  – How metabolized
  – Typical concentrations following ingestion

• Limited studies published regarding effects

• Tested by external laboratory?
What can you do

• Collect the solid material/packaging

• Collect blood as Step 1 of DRE examination

• Have a toxicologist explain why a drug might not be detected but that someone could still be impaired
Final Thoughts

• Conversation with laboratory regarding testing capabilities/testimony
• Facilitating testing, who pays for testing?
• Prosecution- the devil is in the details
The New York City Department of Health and Mental Hygiene is using this graphic on their social media channels to concisely educate consumers on synthetic marijuana products. Credit: The New York City Department of Health and Mental Hygiene
Excited Delirium
Questions???
Contact Information

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