Classes and Structures of Emerging Cannabimimetics and Cathinones

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Herbal Smoking Blends - SPICE

- In late 2008, THC Pharma reported the presence of JWH 018, a synthetic cannabimimetic indole in some blends
- In early 2009, analogues of CP 47,497 (another synthetic cannabinoid) were also found in some blends by the U. of Freiburg
- In early 2009, several European Countries control Herbal Blends/JWH 018/CP 47,497

Herbal Smoking Blends - SPICE

- Products quickly reformulated with new, non-controlled synthetic cannabimimetics
- Five of the synthetic cannabimimetics controlled at the Federal level in 2011
- Synthetic Drug Abuse Prevention Act of 2012

Herbal Smoking Blends - SPICE

- K2 enters market in April, 2009
- Interest booms in herbal smoking blends in 2009
- Many new products appeared, typically with JWH 018 and JWH 073
- States begin to control the blends/synthetic cannabinoids

Classes of Synthetic Cannabinoids Observed on Smoking Blends

i) 2-(3-hydroxycyclohexyl)phenol (CP 47,497)
ii) 3-(1-naphthoyl)indole (JWH 018)
iii) 3-(1-naphthoyl)pyrrole
iv) 1-(1-naphthylmethylene)indene
v) 3-phenylacetylindole or 3-benzoylindole
Structures of the Major Cannabimimetic Classes Detected

Cannabimimetics Observed Starting in 2011 – More JWH's, Introduction of Fluoroalkyls and the Beginning of Novel Materials

2011 – Introduction of Novel Materials

- Materials identified never reported in scientific or patent literature
- Initially named after the website selling it
  - RCS-4
  - RCS-8
- Made by changing/modifying known material

2011 – Introduction of Novel Materials

RCS-4

AM670

RCS-4

JWH-081
2011 – Introduction of Novel Materials
RCS-8

JWH 250
RCS-8

2012 – Introduction of Tetramethylcyclopropyl Materials

A-796,260
UR-144
SFUR-144

AKB48 – New Material in 2012

AKB48
Falls within claims of 2003 World Patent
but not given as example

2012 – Continued Introduction of New Materials

AKB48
New

2NE1
New

STS-135
New

2012 – AB001, A New Material Derived from a Combination of Known Compounds

AM1248
New

JWH1018
New
Cannabimimetics Observed Starting in 2013 – Continuation of New Materials and New Classes

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>JWH 018</td>
<td>JWH 203</td>
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<td>JWH 073</td>
<td>JWH 019</td>
<td>AB-FUBINACA</td>
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<td>JWH 081</td>
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<td>CP 47,497</td>
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<td>PB22</td>
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<tr>
<td>JWH 250</td>
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</tbody>
</table>

2013 – Introduction of Indazole Carboxamides and Derivatives

2013 – New Materials Derived From 8-Hydroxyquinoline

Designer Cathinones

Three parts of methcathinone can be modified:
- Aromatic ring
- Alkyl group
- Amine group

Designer Cathinones – Changes in the Aromatic Ring
Designer Cathinones - Changes in the Alkyl Group

\[
\text{methcathinone} \rightarrow \text{buphedrone}
\]
\[
\text{methcathinone} \rightarrow \text{pentedrone}
\]

Designer Cathinones - Changes in the Amine Group

\[
\text{methcathinone} \rightarrow \text{ethcathinone}
\]
\[
\text{methcathinone} \rightarrow \text{\( \alpha \)-PPP}
\]

Designer Cathinones - Changes in All Groups

\[
\text{methcathinone} \rightarrow \text{MDPV}
\]

Just the changes discussed in the last three slides can produce 12 different Cathinone derivatives.

Questions?

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Outline

- Novel Hallucinogens and Plant-Derived Highs
  - Emily Dye
  - Forensic Chemist
  - Special Testing and Research Laboratory
  - Drug Enforcement Administration

- Hallucinogens
  - 2C Compounds
  - NBOMe Compounds
  - DOX Compounds

- Empathogens
  - Aminoindanes
  - APDB
  - APB

- Plant-Derived Highs
  - Kratom
  - Fly Agaric Mushrooms
  - Kava Kava
  - Kanna
2C Compounds

- Psychedelic phenethylamines
- Synthesized by Alexander Shulgin
  - Published in PiHKAL
- 27 known compounds
  - Most common: 2C-C, 2C-B, and 2C-I

2C-B-FLY

- Psychedelic phenethylamine
- Synthesized by Aaron Monte

Bromo-DragonFLY

- Psychedelic phenethylamine
- Synthesized in the lab of David Nichols
- Deaths associated with misrepresentation as 2C-B-FLY

NBOMe Compounds

- Hallucinogenic phenethylamines
- Synthesized by Heim, et al.
- Isomers can be distinguished via RT and MS
NBOMe Dangers

- Compounds are highly hallucinogenic at very low dosages
  - As low as 50 µg
  - Has been seen in kilogram quantities
- Due to their potency, misjudging the dose of NBOMe series chemicals carries very real risks. A substantial dosage error could lead to undesirable or dangerous effects. If one of these compounds is in pure powder form, small breezes, accidental inhalation, or touching the eyes or mouth after handling could result in full-blown effects or dangerous overdoses. Because of these dangers, NBOMe series chemicals should be labeled clearly and handled with laboratory methods (goggles, gloves, mask) to minimize risks.

DOX Compounds

<table>
<thead>
<tr>
<th>Name</th>
<th>R</th>
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<tbody>
<tr>
<td>DOAM</td>
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<td>Br</td>
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<tr>
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<td>CH₂H₂</td>
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<td>CH₂CH₃</td>
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<tr>
<td>Aleph-2</td>
<td>SCH₂CH₃</td>
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<tr>
<td>DOF</td>
<td>F</td>
</tr>
<tr>
<td>DDF</td>
<td>C₂H₅F</td>
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<tr>
<td>DOI</td>
<td>I</td>
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<tr>
<td>Aleph-4</td>
<td>SC₃H₃</td>
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<tr>
<td>TMA-2</td>
<td>OCH₃</td>
</tr>
</tbody>
</table>

Aminoindanes

- Psychoactive empathogen
- Synthesized in the lab of David Nichols

5-APDB and 6-APDB

- Phenethylamine empathogen
- Synthesized in the lab of David Nichols
- Different color test results
- Difficult to differentiate via RT or MS, but IR is different

5-APB and 6-APB

- Phenethylamine empathogen
- Different color test results
- Difficult to differentiate via RT or MS, but IR is different
Kratom (*Mitragyna speciosa*)
- Can be found as:
  - Whole or powdered leaf
  - Resin
- Legal status:
  - No federal regulation
  - Some states have controls in place

Fly Agaric Mushrooms (*Amanita muscaria*)
- Can be found as:
  - Dried mushroom material
  - Extract
- Legal status:
  - No federal regulation
  - LA and TN have controls in place

Kava Kava (*Piper methysticum*)
- Can be found as:
  - Ground or whole leaf
  - Ground root
  - Extract
- Legal status:
  - No federal regulation
  - FDA and CDC have issued warnings

Kanna aka Channa (*Sceletium tortuosum*)
- Can be found as:
  - Ground or whole leaf
  - Extract
- Legal status:
  - No federal regulation

Thank you

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References
Overview

EU Early warning system
Fundamental shift in the drugs market
Diversity of new drugs - monitoring in action
Concerns - getting new drugs in perspective
What next?

EWS institutional partners

Risk assessment new psychoactive substances

- Formalized guidelines
- Health risks, Social risks, Organized crime
- Diffusion potential

- MBD (1998) — not controlled EU
- 4-MTA (1999) — controlled EU
- GHB (2000) — controlled UN
- Ketamine (2000) —
- PMMA (2002) — controlled EU
- 2CEP (2007) — controlled EU
- Mephedrone (2010) — controlled EU
- 4-MA (2012) — proposal for control EU
- 5-IT (2013) — risk assessment held April 2013

EWS: Triangulation of information from different sources

Internet, media, users

- Research, legal purchase, wastewater analysis, Q SAR modelling
- Forensic data/toxicology.  law enforcement, surveys, health & care

European Database on New Drugs
The challenge we face today — has it changed?

U.S. Drug Sleuths Finally Solve Mystery of the Deadly China White
New Narcotic Identified After Monthlong Quest

As Federal drug agents and California police stepped up their search for the sources of the China White, the forensic chemists turned their detection scales to a backlog of other, more routine cases. The challenge of identifying a new drug from the street comes no more than once or twice a year.

236 new drugs notified since 2005
More than 280 monitored since the EWS started

Synthetic cannabinoids, phenethylamines and cathinones most common
More diverse and obscure substances being reported
Many more substances offered for sale that have not yet been identified by chemical analysis

Fundamental shift
Gary L. Henderson, Ph.D.
Designer Drugs: Past History and Future Prospects

Future Trends
In the view of this author, it is likely that the future drugs of abuse will be syntheses rather than plant products. They will be synthesized from readily available chemicals, may be derivatives of pharmaceuticals, will be very potent, and often very selective in their action. In addition, they will be marketed very cleverly.

Substances reported via the EWS

Joint action 97/396/JHA (June 1997 – May 2005) – 30 notifications
Increasing number & quality of reports received

What is driving this?
A complex web...

Globalisation and advances in information technology, internet as:
- Communication tool
- Access to information (medicinal chemistry, patents, etc., etc)
- Global market place

Available and cheap synthetic synthesis capacity
Legally sourced often outside Europe
Limited regulation/monitoring - availability on the open market
- Differences in national laws
What is driving this?

A complex web...

Innovative marketing of products within a 'grey' regulatory zone

Changes in illicit drug market and interaction between markets
   - Gaps in availability (such as poor quality of illicit stimulants or heroin drought?)
   - Interaction between the markets in illicit drugs, 'legal highs' and medicines
   - Creation of new drug markets

Users willing experiment... and substitute

A new marketplace: monitoring the Internet

058 online shops identified selling to the EU in 2012
   Up from 514 in 2011 and 170 in 2010

Other features of the online market include:

Legal highs may not be legal!

Open market
   - Dietary supplements, lifestyle and self-medication products (e.g. phenbut, DMAA)

Developments:
   - Spam pricing, diversification, & more covert strategies

The internet and drug diffusion - Spice

- Monitoring internet may also be important for understanding trends
- 'Mexican seafood' was asking about spice back in 2006 and 'mad scientist' told him that we did not know.
- It took another 2 years to confirm the nature of the ingredients.

The emergence of synthetic cannabinoids

First CRA in a smoking mixture sold as 'Spice' was JWH-018
First detected (analytically confirmed) in Europe, Dec. 2008
Now, EWS monitors more than 70 CRA's

Risk Assessment 5-IT (5-(2-aminopropyl)indole)

Notified to EMCDDA in June 2012

Stimulant type drug (little known)

Sometimes sold as 'Benzofury' which has contained different drugs in the past (e.g. 5F-APB).

Users may think they are taking a different drug

Analytical difficulties (cf. AMT)

24 deaths in 4 MS linked to the drug
**-NBOMe compounds (1)**

Al-2-methoxybenzyl derivatives of the '2C' series of phenethylamines

- Extremely potent, active at ng level
- Binding affinities at 5-HT2A receptors Ki: 0.16–1.49 nM
- Typically detected in 'blotters' and sugar cubes

---

**Phenethylamine** | **NBOMe derivative** | **Date** | **Country**
--- | --- | --- | ---
2C-B | 2B-B-NBOMe | Dec-12 | Sweden
2C-G | 2G-CN-B-NBOMe | Jun-11 | Finland
2C-D | 2D-CN-B-NBOMe | Apr-12 | UK
2C-E | 2E-CN-B-NBOMe | Dec-12 | Poland
2C-G | 2G-CN-B-NBOMe | Dec-12 | Poland
2C-I | 2I-CN-B-NBOMe | Jun-12 | Sweden
2C-N | 2N-CN-B-NBOMe | Dec-12 | Poland

---

**Information sources – The challenges**

- Better conceptual models to understand diffusion potential
- Need to develop hospital emergency data
- Increase capacity to respond rapidly to particularly toxic products – rapid and sound assessment of properties & risks
- Identification of DIDs associated with NPS
- Evaluation of potential user and chronic toxicity in humans
- Receptor binding and mode of action studies
- Assessment of psychoactivity
- Follow – up over time important
  - Re-emergence of controlled drugs and establishment on the illicit market

---

**What next?**

- Synthetic cannabinoid co-drugs, not yet detected in Europe, e.g.

  *N. Uchihyama et al./ Forensic Science International xxx (2012) xxx–xxx*

  ![S-Fluoropenta-3-syntheticinolide (3)](image)

  S-Fluoropenta-3-syntheticinolide (3)

  C_{12}H_{10}N_{2}O_{2}: 310

---

**What next?**

- Cheaper, H. K., (2010), Opioid-cannabinoid co-drugs with enhanced analgesic and pharmacokinetic profiles, University of Kentucky, KY

  ![Codeine-Δ1-Tetrahydrocannabinol Carbonate](image)

  Codeine-Δ1-Tetrahydrocannabinol Carbonate.
Let's see!

andrew.cunningham@emcdda.europa.eu

Emerging Trends in Synthetic Drugs: Mid-Atlantic Region

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Objectives

- State Legislation
- Compound Trends
- Analytical Approaches
- Reporting Results

Mid-Atlantic Region

State Legislation

Legislation

- Virginia
  - Amendments to VA Code in March 2011, July 2012 and March 2013
  - Synthetic Cannabinoids - § 18.2-248.1:1
    - 26 Specifically Listed Compounds
    - Eleven Structural Classes
  - Schedule I - § 4.1-3446
    - 41 Specifically Listed Compounds added through legislation since July 2012

Legislation

- Synthetic Cannabinoid Definition:
  - Virginia:
    - Any substance that contains one or more cannabimimetic agents or that contains their salts, isomers, and salts of isomers
  - 'Cannabimimetic agent' is any substance within any of eleven defined structural classes or is specifically listed under § 18.2-248.1:1(A)(2)
Structural Classes

<table>
<thead>
<tr>
<th>2012</th>
<th>2013</th>
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</thead>
<tbody>
<tr>
<td>a. Cyclohexylphenols</td>
<td>f. 3-cyclopropylindoles</td>
</tr>
<tr>
<td>b. Naphthoylindoles</td>
<td>g. 3-adamantoylindoles</td>
</tr>
<tr>
<td>c. Naphthylypyrroles</td>
<td>h. N-(adamantyl)-indole-3-carboxamides</td>
</tr>
<tr>
<td>d. Naphthylmethylindenes</td>
<td>i. N-(adamantyl)-indazole-3-carboxamides</td>
</tr>
<tr>
<td>e. Phenylacetylindoles</td>
<td>3-Benzoylindoles</td>
</tr>
</tbody>
</table>

Legislation

- **Maryland**
  - 2008 Provision in Maryland law allowed for the use of Federal Controlled Dangerous Substances (CDS) Regulations
  - July 2012: Adoption of Synthetic and Drug Abuse Prevention Act of 2012
  - House Bill 1 – Effective October 1, 2013
    - Cannabimimetic Agents under Schedule I

- **Virginia** Code § 18.2-248.1:1(F)
  - “Designer Drug” (analog) clause
    - Privately compounded with intent to circumvent criminal penalties
    - Chemical changes
    - “emulate or simulate effects”

- **Pennsylvania**
  - Senate Bill No. 1006 (Enacted 2011)
    - Resembles legislation passed on Federal level
    - Synthetic cannabinoids and psychedelic phenethylamines (‘2C-’ compounds) added to Schedule I

Mid-Atlantic Region

- Compound Trends
  - Direct correlation to enacted legislation
  - Many distributors are acutely aware of legislation and adapt quickly
Compound Trends
Virginia Synthetic Cannabinoids Trends

<table>
<thead>
<tr>
<th>Compound</th>
<th>Year 1</th>
<th>Year 2</th>
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<tr>
<td>JW1-018</td>
<td>2010-2011</td>
<td></td>
</tr>
<tr>
<td>AM-2201</td>
<td>2011-2012</td>
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</tr>
</tbody>
</table>

Compound Trends

- The wave of the (near) future:

PB-22
AM-2201

5F-PB-22

Compound Trends

- AKB48, 5F-AKB48, STS-135

Compound Trends

- Mushrooms and Monkeys and Turtles, Oh My!
**Compound Trends**

- Illicit Tablets and Capsules
  - Caffeine and more Caffeine!
  - Recent Trend
    - Benzodiazepines/CyclohexylPiperidine
      - AKA: Benzocyclomine, BTCP
    - 3,4-MDMA Returns

- Blotter paper?
  - 25I-NBOMe
    - 25C-NBOMe
      - Five confirmed cases in Virginia

**Compound Trends**

- Lysergic Acid Diethylamide

- Food Items
  - Marijuana preparations
  - 4-Acetoxy-dimethyltryptamine

- Undosed plant material

**Mid-Atlantic Region**

**Analytical Approaches**
**Analytical Approaches**

- **Traditional Approach**
  - Color Tests
    - Marquis
      - 25I-NBOMe – Avocado green
    - BTCP – Indigo blue
  - GC/MS
    - R_ Comparison
      - Traditional: HP-5, HP-1 (15m x 0.25mm i.d.)
      - HP-35 (15m x 0.25mm i.d.)

- **'Novel' Approach**
  - DART-TOF
    - Efficient screening
    - Exact Mass
  - DiscovIR
    - GC/FTIR (solid state)
Reporting

- Virginia
  - Synthetic Cannabinoids
    - When a Listed Synthetic Cannabinoid is present: "0.254 gram of powder, found to contain 1-propyl-3-(1-naphthoyl)indole (JWH-018) (a synthetic cannabinoid listed in § 18.2-248.1:1).
    - When a compound within a defined structural class is present (but not specifically listed): "0.254 gram of plant material, found to contain 1-propyl-2-methyl-3-(1-naphthoyl)indole (JWH-015). This compound is a synthetic cannabinoid as defined in § 18.2-248.1:1(A)(1)(b) and is within the structural class 3-(1-naphthoyl)indole."

- Synthetic Cannabinoids (cont)
  - When a Non-Listed/Non-Structural Class Synthetic Cannabinoid may be present, but is not identified:
    - "No controlled substances or synthetic cannabinoids defined in § 18.2-248.1:1(A) were identified."

Reporting

- Maryland
  - [Name of compound]
    - [Schedule]
      - "Not a Controlled Dangerous Substance"
      - "No Controlled Dangerous Substance Detected"
  - Pennsylvania
    - Analog language:
      - Identified and scheduled substance to which it is structurally similar is indicated in results

Acknowledgements

- Maryland
  - Eileen M. Briley, Maryland State Police
  - Jessica Taylor, Maryland State Police

- Pennsylvania
  - Kristen Clemens, Cumberland County Office of the District Attorney

Questions

Emerging Trends in Synthetic Drugs: Legislation, Brands, Structures, and Approaches to Analysis in Florida

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FDLE Crime Lab - Overview

The FDLE crime lab provides timely, expert and professional examination of evidence to aid in the investigation, prosecution, and/or exclusion of criminal offenses by using scientific equipment and proven techniques.

FDLE has 7 regional laboratories offering services in the following disciplines: Chemistry, Biology, Latent Prints, Firearms, Toolmarks, Crime Scene Services, Computer Evidence Recovery, Questioned Documents, Footwear/Tire Impression, Toxicology, Trace Analysis

FDLE has over 400 forensic personnel and works on average 76,000 service requests per year

FDLE - Pensacola

- The Chemistry lab in Pensacola provides controlled substance analysis for the 1st, 2nd, and 14th judicial circuits in Florida, covering 16 counties and a population of about 1.25 million.
- The lab averages about 400 cases per month.
- The lab has 3 full time analysts, 2 part time lab assistants, and a supervisor

Top Drugs in our Region, 2011

Top Drugs in our Region, 2012

Top Drugs in our Region, 2013 to date
Designer Drugs, 2012 NW FL

- AM-2201 - 204 cases
- Methylone - 62 cases
- JWH-210 - 84 cases
- Alpha-PVP - 55 cases
- JWH-122 - 27 cases
- Pentedrone - 24 cases
- Pyrovalerone - 8 cases

Trends

- XLRn & UR-144, both emergency controlled in December 2012, have moved to #4 and #12, respectively.
- AM-2201 & JWH-210, #7 and #8 last year, respectively, have dropped out of the top twenty. Both were controlled in March 2012. AM-2201 and JWH-210 were "replaced" by XLRn and UR-144 after legislation.
- Methylone continues to climb. It was #10 last year, with 62 cases. It sits at #8 currently. 62 total last year, 30 already thru March.
- Heroin use on the rise - 0 cases in 2010, 11 in 2011, 21 in 2012, 8 through 3 months.
- PB-22 - 16 cases in 2013.

Florida Legislation - Timeline

- January 26, 2011 - The Florida Attorney General’s Office emergency scheduled six drugs that were commonly seen in "Bath Salt" samples in Florida. They were added to schedule I.
  - 3,4-Methylenedioxymethcathinone (Methylone)
  - 3,4-Methylenedioxypyrovalerone (MDPV)
  - 4-Methylmethcathinone (Mephedrone)
  - 3-Methoxymethcathinone (3-MMC)
  - 3-Fluoromethcathinone (3-FMC)
  - 4-Fluoromethcathinone (Flephedrone, 4-FMC)

- July 1, 2011 - HB1039 made the following designer cathinones permanently controlled, schedule I, FS893:
  - 3,4-Methylenedioxymethcathinone
  - Methylmethcathinone
  - Methylethcathinone
  - Methoxymethcathinone
  - Fluoromethcathinone
  - 3,4-Methylenedioxypyrovalerone (MDPV)

  Differences from emergency control legislation:
  - Addition of Methylethcathinone (MEL); Removal of isomer designations on some.
  - Removal of common names, with the exception of MDPV

- March 23, 2012 - HB1175 added approx. 90 new drugs to FS893, schedule I. These include many synthetic cannabinoids, designer cathinones, and novel hallucinogens.

  Included:
  - BZP, FPP, MPP, CPP, 12 Tryptamines, DOI, DOC, 2C-E, 2C-C, 2C-I, Butylone, Ethylone, Naphyrone, Buphedrone, 3,4-Dimethylmethcathinone, Pentylone, MDPBP, BTCP, alpha-PVP, PPP, and PBP, MPPP, 16 JWH compounds, CB-13, 25, and 52, AM-2201, AM-694, RCS-4 and 8

Florida Legislation - Timeline

- July 1, 2011 - HB1039 made the following designer cannabinoid compounds illegal, schedule I, FS893:
  - CP47,497
  - CB homologue of CP47,497
  - HU-210
  - JWH-018
  - JWH-073
  - JWH-200
  - Plant material coated with synthetic cannabinoids have reduced penalties if under 3 grams (misdemeanor). Automatic felony at any weight if in powder form.
Florida Legislation - Timeline

- December 11, 2012 - The Florida Attorney General's Office emergency scheduled 22 new chemicals:
  - Pentedrone, Fluoroamphetamine, Fluoromethamphetamine, Methoxetamine, Methiopropamine, 4-Methylbuphedrone, APB, APDB, UR-144, XLRu, 5-Chloro-UR-144, AKB48, AM-2233, STS-135, URB-597, URB-602, URB-754, 2C-D, 2C-H, 2C-N, 2C-P, and 251-NBOMe

Drug Generations - Florida

- 1st generation bath salts began in mid to late 2010 and ended shortly after the emergency rule.
  - 1st generation bath salts: Mephedrone, Methylyone, MDPV. Methylone, however, has not disappeared. It is our 8th most popular drug in our region, even after being added to schedule I. "Molly" is the slang term. Generally seen in capsule form.
  - 1st generation synthetic cannabinoids: JWH-018, JWH-073, JWH-200. These are long gone.

- 2nd generation bath salts emerged after the July 1, 2011 legislation, and ended in March 2012 (with the next legislation). They include Naphyrone, Buphedrone, alpha-PVP, Pentedrone, MPPP
  - 2nd generation synthetic cannabinoids, same time frame: JWH-250, AM-2201, JWH-210, JWH-122, JWH-081, JWH-203

- 3rd generation synthetic cannabinoids (after March 23, 2012, ending with emergency schedule 12/11/12): UR-144, XLR11; to a lesser extent, AKB48 and STS-135
  - 3rd generation bath salts: Pentedrone, Fluoroamphetamine
  - 4th generation (current) synthetic cannabinoids: PB-22 and 5-Fluoro AKB48
  - No 4th generation bath salts. Major dip in seizures/submissions after mid-2012. However, Methylone has moved in to the illicit drug market as "Molly"

Florida Legislation - Timeline

- Pending bills: S294 and H619 - Controlled Substances. They include the permanent addition of the emergency scheduled drugs from 12/11/12 to schedule I of FS893.
  - Also adds PB-22, 5-Fluoro PB-22, BB-22, and 5-Fluoro AKB48
  - Unanimously passed House and Senate; awaiting Governor's signature
PB-22 Storage

- Store cold (at least -20°C)
- PB-22 is an ester and not stable in alcohols
- Transesterification will cause major degradation peaks on GC/MS if you store in alcohol
- Try acetonitrile as the solvent

PB-22

- Mass Spectrum is dominated by the product of an alpha-cleavage at the right of the oxo-group at nominal m/z 214

![Mass Spectrum Diagram]

PB-22 Expanded View

![Expanded View Diagram]
AKB-48 / 5-Fluoro AKB-48

AKB48

\[
\text{C}_{23}\text{H}_{31}\text{N}_3\text{O}
\]

MW 365

Emergency controlled in FL, 12/31/12

AKB48 Mass Spectrum

AKB48 Mass Spectrum (standard purchased from Cayman Chemicals)

5-Fluoro AKB48

\[
\text{C}_{23}\text{H}_{30}\text{F}_3\text{N}_3\text{O}
\]

MW 383

LEGAL

5-Fluoro AKB48 Mass Spectrum

COURTESY ROSNER / TDPS
Where Do These Names Originate?

AKB48 – Japanese girl band

STS-135 – Final mission of the American Space Shuttle Program

UR-144 / XLR11

UR-144
C_{21}H_{29}NO
MW 311
Emergency Controlled in FL, 12/11/12

XLR11
AKA 5-Fluoro UR-144
C_{21}H_{28}FNO
MW 329
Emergency Controlled in FL, 12/11/12

UR-144 Mass Spectrum (Purchased from Cayman Chemicals)

XLR11 Mass Spectrum (Purchased from Cayman Chemicals)

Samples in the lab

Positive for Butylone

Samples in the lab

Positive for JWH-110
Samples in the lab

Positive for AM-2201

Samples in the Lab

Both Positive for AM-2201 and JWH-210

Samples in the lab

Positive for XLR11

Samples in the lab

Positive for AM-2201

Samples in the lab

Both Positive for AM-2201 and JWH-210

Samples in the lab

Positive for XLR11

T20 High Quality damiana not for human consumption. Legal under New Fl. Law HB/175 (eff. 3/23/12) Potpourri

Popular Brands

• Most popular brands seen in the lab:
  • WTF: Next Generation
  • Dead Man Walking
  • Super POW
  • Scooby Snax
  • OMG
  • Master Kush
  • Forget-Me-Not
  • Bird of Paradise
  • Mad Hatter
  • Lick Me All Over
  • Down2Earth ChimaXXX and Reggie

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  • Mad Hatter
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  • Down2Earth ChimaXXX and Reggie
**Preparation tips**

- Build libraries – buy standards and add them to your internal GC/MS libraries. Use free libraries like Cayman and SWGDRUG. Buy Mass Spectra of Designer Drugs by Rosner.
- Stay active – become a member of CLIC (they have an active Yahoo! Group). Use Forendex and Forendex Forums.
- Build an internal drug repository to store articles and data for easy search and retrieval.
- Read as many articles as you can get your hands on.

**Drug Standards**

- [https://www.caymanchem.com](https://www.caymanchem.com)
- [http://www.cerilliant.com](http://www.cerilliant.com)
- [http://www.lipomed.com](http://www.lipomed.com)
- [http://www.sigmaaldrich.com](http://www.sigmaaldrich.com)
- [http://www.steraloids.com](http://www.steraloids.com)
- [http://www.trc-canada.com](http://www.trc-canada.com)
- [http://www.discoverysciences.com](http://www.discoverysciences.com)

**Websites for Spectra Searching**

- Designer Drugs (Rosner website): [https://db12.designer-drugs.de/db/main.pl](https://db12.designer-drugs.de/db/main.pl)

**Analytical issues**

- To reduce analytical issues, we try to name compounds in the statutes without isomer designations, and specify that all isomers are controlled. For instance, “Fluoroamphetamine” is controlled, all isomers. So instead of having to differentiate between the 2, 3, and 4, we just obtain a MS, and compare retention time against any of the 3 isomers. If it matches, we report out Fluoroamphetamine. This cuts down on standards needing purchasing; analytical procedures to differentiate; and reporting clearly and unambiguously.
**Analytical issues**

- Those that get added in statute with isomer designation (like TFMPP) are compared with the 3-TFMPP and a remark is placed on the report that "Specific isomer not determined"

**How we report drugs**

- If a controlled substance: *Name of substance.*
- If it is emergency scheduled, we add a comment under the remarks section that: ***was emergency controlled in the state of Florida December 11, 2012.***
- If it’s a potential analog: ***, which is substantially similar to ***.**
- If we do not identify the specific isomer in statute, we add a remark that: *Specific isomer not determined.*

**Analogs**

- (2)(a) As used in this section, "controlled substance analog" means a substance which, due to its chemical structure and potential for abuse, meets the following criteria:
  1. Is substantially similar to that of a controlled substance listed in Schedule I or Schedule II of s. 893.03; and
  2. Has a stimulant, depressant, or hallucinogenic effect on the central nervous system or is represented or intended to have a stimulant, depressant, or hallucinogenic effect on the central nervous system substantially similar to or greater than that of a controlled substance listed in Schedule I or Schedule II of s. 893.03.

**Analogs**

- We only deal with prong 1 – whether it is substantially similar in chemical structure. We have a generally accepted practice in Pensacola for how to approach and determine potentially "substantially similar" compounds.

**AKB48 vs 5-Fluoro AKB48**

- AKB48
  - C23H31N3O
  - MW: 365
  - Emergency controlled in FL, 12/n/12

- 5-Fluoro AKB48
  - C23H30F3N3O
  - MW: 383
  - LEGAL

5-Fluoro AKB48, which is substantially similar to AKB48.

**Thank you!!!**

Joseph Graves
Crime Lab Analyst Supervisor, Drug Chemistry
Florida Department of Law Enforcement
Pensacola Regional Operations Center
JosephGraves@fdle.state.fl.us
Toxicological Aspects of Synthetic Drugs
Barry K. Logan, PhD, DABFT

Synthetic Drugs

2008-2012

- Benzylpiperazines (6+)
  BZP, TFMPP, m-CPP
- β-Keto amphetamines (30+)
  Ephedrine, mephedrine, methylone, methedrine...
- Phenethylamines (2C suite) (20+)
  2C-B, 2C-E, 2C-I, 2C-B, 2C-T-7, NBOMe Series...
- Pyrrolidophenones (pyrovalerones) (20+)
  α-PVP, MDPV, PPP,...

Synthetic Cannabinoids (200+)
  JWH series, AM Series, Adamantyls, Cyclopropyls...

NFLIS 2011

Table 2.3

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<th>Hallucinogens</th>
<th>Number</th>
<th>Percent</th>
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<td>AM-2201</td>
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<td>Pentazocine</td>
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<td>TFMPP (noncrystalline)</td>
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<td>Methylone (NMDA)</td>
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https://www.nflis.deadversion.usdoj.gov/

Scope: Hallucinogens & Stimulants

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Screen: Basic Extraction
El/GCMS
Confirmation: GCMS
LCTOF
LCMSMS

Scope: Synthetic Cannabinoids

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NMS Labs Synthetic Cannabinoids Screen, Blood (Forensic) Test

December 12, 2012

Tucker Cipriano smoked Spice, took mushrooms and drank alcohol in hours before a fatal baseball bat attack on his father
December 23, 2012

Bath Salts Mystery: Ex-Universal Pictures Co-Chair Breaks Silence on LAPD Beatdown

WHEN YOU NEED TO KNOW

November 9, 2012

The Times-Picayune
Greater New Orleans

25-I banned after Voodoo Fest death, Legislature to move forward on anti-drug laws

The Louisiana Department of Health and Hospitals (DHH) announced Friday it was banning the possession, manufacture and distribution of 25-I, the synthetic drug that resulted in the death of an Alabama student at last month’s Voodoo Festival in New Orleans. DHH Secretary Bruce Greiman said he, along with the Legislature and police, would continue to target the class of drugs writ large.

25-J banned after Voodoo Fest death, Legislature to move forward on anti-drug laws

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April, 2013

Los Angeles Times LOCAL

'Veep' star's stepdaughter is 'edgy and difficult': Kim Kardashian

The Los Angeles Times reported on Kim Kardashian's stepdaughter, who was described as 'edgy and difficult.'

April 2013

Bath salts overdose killed teen, sickened 4 others, medical examiner says

The Los Angeles Times reported on the overdose death of a teenager from bath salts and the serious illness of four others.

Toxicology of Synthetic Drugs

•Adverse Events
  • Intoxication/Impairment
  • Psychosis
  • Medical Crises
  • Death

Designer Stimulants and Hallucinogens
**Bath Salts**

AKA:
- Bath Bubbles
- Bath Salts
- Pond Cleaner
- Soft Drink Additive
- Burial Powder
- Glass Cleaner
- Plant Food
- Plant Vitamin
- Insecticide

---

**5-HT<sub>2A</sub> Effects**

<table>
<thead>
<tr>
<th>Effects</th>
<th>Agonists</th>
<th>Antagonists</th>
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<tr>
<td>Anxiety</td>
<td>25I-NBOMe</td>
<td>Clozapine</td>
</tr>
<tr>
<td>Appetite</td>
<td>2C-B</td>
<td>Olanzapine</td>
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<td>Sleep</td>
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<td>Thermoregulation</td>
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---

**Synthetic Stimulants Adverse Effects**

- Agitation
- Insomnia
- Mydriasis
- Myoclonus
- Tachycardia
- Hypertension
- Chest pain
- Paranoia
- Delusions/hallucinations
- Excited Delirium
  - Combative behavior
  - Hyperthermia
  - Rhabdomyolysis
  - Kidney Failure
  - Seizures
  - Death

---

**Intoxication - 25I-NBOMe**


- 18-year-old male presented to the emergency department (ED) with severe agitation and hallucinations after jumping out of a moving car. Tachycardiac (150 – 160 bpm) and hypertensive (150 – 170 mm Hg systolic and 110 mg Hg diastolic), required physical restraints and treatment with intravenous lorazepam administration.
- 0.76 ng/ml of 25I-NBOMe

---

**Intoxication - Mephedrone**


- 32 Impaired Driving arrest cases, including nine with mephedrone as the only drug present.
- Generally impaired driving, weaving, erratic, dilated pupils, poor performance, slurred speech.
- Blood concentrations ranged up to 0.74 mg/L (n=9; mean 0.21, median 0.10) although the most common value encountered is likely to lie between 0.2 and 0.3 mg/L.
### Intoxication - DMAA


- Consumed two capsules of 99.9% DMAA. Became confused, incontinent, drowsy, slurred speech, facial droop, asymmetric weakness, memory impairment, seizure. Pills were analyzed and contained only DMAA.

### Intoxication - MPHP


- A 27 year old man was admitted to hospital in an agitated state and with fractures of both feet after jumping from a window. Pronounced rhabdomyolysis and had to be treated by repeated hemodialysis. Elevated liver parameters indicated toxic liver damage.
- MPHP was found at 100 ng/ml

### Psychosis - MDPV, 4-FMC


- 23-year-old male with a prior psychiatric history, with bizarre behavior, suicidality, and hallucinations. MDPV levels of 186ng/mL and flephedrone of 346ng/mL in the serum. Agitated and complained of visual, tactile, and auditory hallucinations. He stated snakes were crawling on him and in his bed. Treated and stabilized with Lorazepam, and Droperidol.

### Psychosis - “Bath Salts”


- e.g. 31 year old male, found wandering in his neighborhood, fearful, confused, “Overheated”, sweating. Became combative. Reported seeing snakes who were threatening his life.
- Hallucinations, paranoia and agitation resolved after administration of haloperidol.
- No Toxicology confirmation.

### Medical Crises - DMAA


- 26 year old soldier in Afghanistan, takes 3 scoops of Jack3d, before exercising. Awakes with worsening headache, assymetrical dysesthesia, weakness and lack of coordination. Diagnosed with Dejerine-Roussy Thalamic stroke. 1 scoop contains 4g of DMAA.

### Medical Crises - Bath Salts?


- 39 y/o male brought to the emergency room by police. Combative and confused. Sedated for CAT scan. Elevated CK indicating renal problems. Diagnosed with acute tubular necrosis, and spent 13 days in dialysis. Admitted to recent increasing use of Bath Salt pills, and confirmed that the precipitating event had occurred immediately after such an administration.
**Death – MDPV**


- 40-year-old male who injected and snorted "bath salts" containing MDPV and subsequently became agitated, aggressive, and experienced a cardiac arrest. He was resuscitated after his initial arrest; however, he developed hyperthermia, rhabdomyolysis, coagulopathy, acidosis, anoxic brain injury, and subsequently died.
- MDPV was quantified in his serum at 82 ng/mL.

**Synthetic Cannabinoids**

AKA:

- Legal high
- 50 state legal
- Incense
- Fake Weed
- Fake Pot
- K2
- Spice

**Death – Mephedrone**


- 40-year-old male who injected and snorted "bath salts" containing MDPV and subsequently became agitated, aggressive, and experienced a cardiac arrest. He was resuscitated after his initial arrest; however, he developed hyperthermia, rhabdomyolysis, coagulopathy, acidosis, anoxic brain injury, and subsequently died.
- MDPV was quantified in his serum at 82 ng/mL.

**Death – MDPV, others**


- Commonly poly drug cases with multiple synthetic or therapeutic drugs present.
- In five cases both peripheral and heart blood were tested with an average heart to peripheral blood ratio was 1.48, with a range of 1.3 to 1.7.
- Concentrations were not correlated with outcome.
- e.g. In PM Case 1, the death was caused by injuries sustained in an auto accident; however, this decedent had a blood methylene concentration of 729 ng/mL.

**MDPV PMD**

<table>
<thead>
<tr>
<th>Toxicology Results for MDPV Overdose</th>
<th>Serum</th>
<th>Heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>MDPV</td>
<td>Methylene</td>
</tr>
<tr>
<td>Femoral Blood</td>
<td>0.4</td>
<td>0.14</td>
</tr>
<tr>
<td>Heart Blood</td>
<td>0.40</td>
<td>0.14</td>
</tr>
<tr>
<td>Liver</td>
<td>&gt; 5.0</td>
<td>0.12</td>
</tr>
<tr>
<td>Whole Blood</td>
<td>&gt; 2.0</td>
<td>0.50</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.90</td>
<td>0.50</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.94</td>
<td>0.50</td>
</tr>
<tr>
<td>Lung</td>
<td>0.90</td>
<td>0.50</td>
</tr>
<tr>
<td>Skeletal Muscle</td>
<td>0.64</td>
<td>0.50</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.64</td>
<td>0.50</td>
</tr>
<tr>
<td>Skin</td>
<td>0.04</td>
<td>0.50</td>
</tr>
<tr>
<td>Brain</td>
<td>0.36</td>
<td>0.50</td>
</tr>
<tr>
<td>Heart</td>
<td>0.36</td>
<td>0.50</td>
</tr>
<tr>
<td>Liver</td>
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<td>0.50</td>
</tr>
<tr>
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<td>Liver</td>
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<tr>
<td>Brain</td>
<td>0.12</td>
<td>0.50</td>
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Wyman et al, 2013
**Scope: Synthetic Cannabinoids**

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<tr>
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<tr>
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<td>JWH-030-9 analog</td>
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</tr>
</tbody>
</table>

**Cannabinoids Adverse Effects**

- **Major Effects**
  - Cardiovascular
    - Hypertension
    - Tachycardia
  - Gastrointestinal
    - Vomiting
  - Neurological
    - Agitation
    - Confusion
    - Hallucinations
    - Seizures

- **Other Effects**
  - Headache
  - Muscle
  - Numbness
  - Slurred speech
  - Syncope
  - Vomiting
  - Tremors
  - Drowsiness

**Texas Poison Center Networks**

**Marijuana/K2 Effects**

- Red eyes / bloodshot
- Burning of the eyes
- Xerostomia (dry mouth)
- Tachycardia
- Changes in perception/mood
- Balance and Coordination
- Hallucinations
- Sedation
- Subjective thought disruption/loss of concentration
- Impaired sense of time
- Self assessed Impairment
- Arrhythmias
- Seizures/Convulsions
- Panic Attacks
- Paranoia and Anxiety
- Sickness

**Intoxication – Syn Canns**


- 12 cases of Suspected impaired driving involving synthetic cannabinoids. Other drugs and alcohol were ruled out. Attitude of the drivers was described as cooperative and relaxed, speech was noted to be slow and slurred, and coordination was noted to be poor. Pulse and blood pressure were generally elevated. The most consistent sign noted was a marked lack of convergence in all cases where it was assessed.

- JWH-018 (n=4), 0.1-1.1ng/mL; JWH-081 (n=2) qualitative only; JWH-122 (n=3) 2.5ng/mL; JWH-210 (n=4) 0.1ng/mL; JWH-250 (n=1) 0.38ng/mL; AM-2201 (n=6) 0.43 – 4.0ng/mL.

**Psychosis – Syn Canns**


- Semi-structured interviews regarding the use and effects of JWH-018 in 15 patients with serious mental illness in a New Zealand forensic and rehabilitative service.
- Anxiety and psychotic symptoms were common after use, with 69% of users experiencing or exhibiting symptoms consistent with psychotic relapse after smoking JWH-018. Although psychological side effects were common, no one reported becoming physically unwell after using JWH-018.
- Three subjects described developing some tolerance to the product, but no one reported withdrawal symptoms.

**Medical Crises – Syn Canns**


- Three sentinel cases of AKI in patients in Wyoming.
- A case search defined as nausea, vomiting, abdominal or back pain, and AKI led to a cohort of 16 patients in 5 states.
- All had smoked products containing synthetic cannabinoids, confirmed in product samples and serum to be XLR-11.
- Five of the 16 patients required hemodialysis, and four patients received corticosteroids; none died.
- Other infectious, autoimmune, pharmacologic, or other toxic causes of AKI were not found.
Death? – Syn Canns

Anderson University basketball player Lamar Jack died after ingesting a chemical that is a key ingredient in synthetic marijuana, the county coroner said Saturday.

Anderson County Coroner Greg Shore said specialists from an accredited laboratory in Pennsylvania ran toxicology tests and analyzed blood samples that were taken when Jack was admitted to Amed Health Medical Center in Anderson. The lab testing and analysis revealed that Jack had the chemical JWH-018 in his body when he collapsed during a preseason warm-up with his team on Sept. 30. Just days later, on Oct. 4, Jack died. He was 19.

On the basis of an autopsy and the toxicology test results, Shore is ruling Jack's death accidental — caused by "acute drug toxicity with excited delirium that led to multiple organ failure."

Conclusions

- Adverse effects from both classes of drugs have been documented.
- They include intoxication, and the risks associated with cognitive and psychomotor impairment.
- Synthetic Stimulants and Hallucinogens
  - Cause suicidal and homicidal ideation
  - Induce psychosis
  - Cause excited delirium
  - Can result in serotonin syndrome
- Synthetic Cannabinoids
  - Induce psychosis
  - May be associated with Acute Kidney Injury

Questions?

www.nmslabs.com  www.forensicscienceeducation.org