Spice, K2 and Other Synthetic Cannabinoids

AADCP - Specialty Court Conference

Douglas Kramer – TASC, Inc
Herbal Incense

Sold in head shops or online as an incense product

Herbs and botanicals treated with synthetic cannabinoid chemicals

Many varieties/scents

Labeled “Not for Human Consumption”
Herbal Incense

Variety of Products Available

Spice, K2, Smoke, Yucatan, Fire, Hush, Genie
Single Use or Bulk Product

Sold Loose or in joint form
Aromatic Herbs

_Canavalia maritima, Nymphaea caerulea, Scutellaria nana, Pedicularis densiflora, Leonotis leonurus, Zornia latifolia, Nelumbo nucifera, Leonurus sibiricus... many more._
Herbal Effects

Most of the herbal components have very little psychoactive effects, although some traditional herbalists may disagree. At most, they:

- Add color and flavor
- May have mild relaxing properties
- Decrease blood pressure
- Reduce inflammation
- Induce mild euphoria

So where is the high coming from?
Intense psychoactive properties were being reported, but with little verification.

In late 2008, forensic analyses conducted in Europe identified JWH-018 as a psychoactive ingredient in many of these products.

Cannabis Overview

Used for more than 4000 years for euphoric and therapeutic effects

Most commonly abused drug in the world.

Roughly 4% of the world's adult population (162 million people) use cannabis annually, and about 0.6% (22.5 million) use it on a daily basis.
Cannabis

Contains:

>450 chemicals
>60-90 different cannabinoids

$\Delta^9$-Tetrathydrocannabinol (THC)
Main psychoactive ingredient of marijuana
Cannabis

THC content in marijuana varies – typically 2-5% in cannabis, but much higher has been found.

Marijuana users may experience stimulant, depressant, and/or hallucinogenic properties.

Most commonly used for hallucinogenic effects.

Most individuals self-titrate their THC intake.
Cannabis

Most common Medicinal Uses:

- Relief from nausea and vomiting
- Stimulation of hunger
- General analgesic effects (pain reliever)
- Lowered intraocular eye pressure
What are Cannabinoids?

Class of chemicals that have similar structure and/or activity that mimic:

- Phytocannabinoids (found in cannabis plants)
  - Natural, herbal, classical

- Endocannabinoids
  - (found in CNS and immune systems of animals)
Cannabinoid Functions

What are the Endocannabinoid functions?

Signaling molecules (Lipid messengers) that are released from cells to bind to nearby cell receptors.

Signaling is retrograde (reverse direction postsynaptic to presynaptic neurons)
Cannabinoid Receptors

At least two subtypes of Cannabinoid Receptors:

- **CB$_1$ Receptor**
  - Found throughout the peripheral and CNS systems

- **CB$_2$ Receptor**
  - Found throughout the peripheral nervous system and associated with the immune system
Concentrations of CB₁ receptors

- **Basal Ganglia**
  - Movement

- **Cerebral Cortex**
  - Higher cognitive function

- **Cerebellum**
  - Movement

- **Hypothalamus**
  - Appetite

- **Hippocampus**
  - Learning, memory, stress

- **Medulla**
  - Nausea/vomiting, chemoreceptor trigger zone (CTZ)

- **Spinal Cord**
  - Peripheral sensation including pain

References:
Synthetic Cannabinoids

Four Groups of Synthetic Cannabinoids:

- THC Analogue (classical)
- Non-classical – Cyclohexylphenyl (CP) series
- Aminoalkylindoles – (JWH compounds)
- Other – Fatty Acid Amides
Synthetic Cannabinoid Agonists

Most are full CB₁ & CB₂ receptor agonists.

Originally investigated for medicinal purposes:

- Analgesics
- Weight management
- Control of Nausea
- Smoking cessation
Cannabinoid Agonists

- THC Analogues
  - HU-210, HU-211, HU-243,
  - HU-308, HU-320, HU-331,
  - HU-336, HU-345

Raphael Mechoulam
Hebrew University
Cannabinoid Agonists

Cyclohexylphenyl (CP) Series

Pfizer Pharmaceutical

CP 47,497, CP 55,940,
CP 47,497 – (C8),
CP 50,556-1, CP 55,244
Cannabinoid Agonists

Aminoalylindoles

Over 470 analogues

John W. Huffman

Clemson University
## Synthetic Cannabinoid Agonists

<table>
<thead>
<tr>
<th>Product</th>
<th>JWH-018</th>
<th>JWH-073</th>
<th>CP 47,497</th>
<th>JWH-250</th>
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</table>

Table Data Compiled by NMS Labs
Adverse Effects

Physiological Effects
- Raised blood pressure and heart rate
- Bloodshot eyes
- Swaying
- Slurred speech

Psychological Effects
- Anxiety, Agitation
- Paranoia and Hallucinations
- Seizures and convulsions
- Short-term memory loss
- Time dilation
Adverse Effects

JWH-018 Initial Trials

Statistically significant, dose-dependent, region-specific decreases in cannabinoid binding observed in all brain regions examined following 4 and 14 days of treatment.

The pattern of CB1 receptor down-regulation was similar to that observed in adults treated with cannabinoids; however, the magnitude of down-regulation was smaller in adolescents.

This reduced compensatory response in juveniles may contribute to some acute behavioral effects, the pharmacological cross-tolerance and the long-lasting, adverse psychological consequences of cannabinoid exposure during adolescence.
A Case of Dependence

20-year old patient reported that he had smoked "Spice Gold" daily for 8 months.

He developed tolerance and rapidly increased the dose to 3g per day. He felt a continuous desire for the drug and kept on using it despite the development of persistent cognitive impairment.

Urinary drug screens were negative on admission to the hospital, as they were again on discharge.

On hospital days 4–7, he developed inner unrest, drug craving, nocturnal nightmares, profuse sweating, nausea, tremor, and headache.

His blood pressure was elevated for two days, with a maximal value of 180/90 mm Hg accompanied by a heart rate of 125/min.

The patient stated that he had experienced a similar syndrome a few weeks earlier during a phase of abstinence owing to a short supply, and that it had quickly subsided after he had started consuming "Spice" once again.
Federally Banned Cannabinoids (March 2011)

Δ9-THC

JWH-018

JWH-073

CP-47,497

Cannabicyclohexanol

JWH-200
Additional AZ Banned Cannabinoids (Feb 2011)

△9-THC

HU-210

JWH-015

JWH-019

JWH-250

JWH-398
Analysis by LC/MS/MS
Detection

- Most compounds are not detected by drug screening tests.

- Detection period roughly 24-72 hours in urine:
  - Only metabolites are detected in urine.
  - Typically JWH metabolites analyzed due to availability of standards.

- Approximately 8-48 hours in blood and oral fluid:
  - Parent drug detected.

- Advanced testing methodology utilized:
  - Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS).
Challenges

- Hundreds of potential compounds can be used in the manufacturing process of Spice products
- Limited number of banned chemicals on the books
- Moving target – Spice industry responds to the bans, Laboratories must respond in kind
- Lack of complete understanding of metabolism
- Lack of certified metabolite standards (getting better)
Promising Synthetic Cannabinoids

Δ9-THC

HU-210*

WIN 55,212

JWH-133

* Banned in AZ
Drug Development: Rimonabant

(SR141716) Antiobesity drug
Antagonist of CB1 receptor -
Possible use to mediate CB1 cannabinoid pharmacodynamics by blockade of agonists

• Decrease in heart rate (BPM)
• Reduced cannabis effects of 40-75% in single dose or multiple small dosing
• No significant cannabis withdrawal
• No clinical adverse effects
Rimonabant (cont’d)

First CB1 Receptor antagonist on the market, used in conjunction with diet and exercise for weight loss.

Other Uses:
• Assisted in smoking cessation therapy
• Addiction reduced cocaine-seeking responses by 2 of 3 most common triggers in relapse (priming and cues)
• Possible reduction of ethanol and opiate-seeking behavior
• Hypothetically could improve short-term memory (in rats)
• Blocks *psychoactive* and cardiovascular effects of THC without affecting the pharmacokinetics

FDA supported its use for obesity in 2006 but never was brought to market after failure to demonstrate safety by the manufacturer.

Benefits deemed no longer outweighing the risks – pulled in 2009
Bath Salts and Other Stimulants

17th National TASC Conference on Drugs & Crime

Douglas Kramer – TASC, Inc. - Arizona
Bath Salts

Sold in head shops, gas stations and online

Psychoactive / Dissociative

Illegal in many states

Highly addictive and dangerous

Snorted, but can be smoked, taken orally or injected
Bath Salts

4MMC, Meow-meow, MC, MTV, M-CAT, Bounce, Plant Food

$30-90 / gram - talc-like

Usually made in China / Asia

Pixie Dust, Ivory Wave, Ocean, Charge Plus, White Lightning, White Girl, Scarface, Hurricane Charlie, Vanilla Sky, Bonzai, Grow, Blue Silk, Lovey Dovey
Bath Salt Effects

- Effects last 2 - 4 hours
- Feelings of euphoria - Increased alertness
- Dilated pupils
- Slurred speech, Inability to stop talking
- Increased heart rate
- Both decreased and/or increased sexual function/desire
Negative Effects

Physical:
- CNS stimulant
- Increase BP and heart rate
- Chest pain, heart attack, stroke
- Infertility

Psychological:
- Delusions, paranoia, psychosis
- Personality disorders
- Depression when not using – as long as several weeks

After effects such as tachycardia, hypertension, and mild stimulation lasting from 6 - 8 hours
Chemical Composition

Mephedrone - 4-methylmethcathinone (4-MMC)

AKA: Meph, drone, MCAT

- Originally developed in 1929 - recently “rediscovered”
- Analogue to other controlled substances
- Sold as plant food or bath salts – not for human consumption
Chemical Composition

MDPV (3,4-methylenedioxypyrovalerone)

AKA: MDPK, Magic, Super Coke, MTV and PV

- Originally developed in the 60’s for chronic fatigue and appetite suppression.
- Abuse and dependence a problem with a compulsive desire to continuously re-dose
- Similar in structure to MDMA, but more of a stimulant
- Only has mild empathogenic or entactogenic properties
High Addiction Potential

- Abuse and dependence a problem with a compulsive desire to continuously re-dose
- Some are constantly chase that first high
- Mephedrone reduces to 4-methylephedrine - a known cardiotoxic compound
- Crushing chest pain – common redosing the cause?
Other Stimulants

Cathinone

- Found in the shrub *Catha edulis* (Khat)
- Part of the Middle East culture
- Stimulant typically extracted from chewing fresh leaves
Other Stimulants

Methcathinone

- First synthesized in 1928
- It was used in the Soviet Union during the 1930s and 1940s as an anti-depressant.
- Since the 1960s, methcathinone has been used as a recreational drug in the (former) Soviet Union.
Stimulant Structures

Mephedrone

Methcathinone

Cathinone

MDPV

MDMA
Detection

- Most compounds are not detected by drug screening tests
- Detection period roughly 24-72 hours in urine
- Analyte-specific methodologies are used
  - Gas Chromatography/Mass Spectrometry (GCMS)
  - Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS)
- Specialized Stimulants Panel should include:
  - Amphetamine / Methamphetamine
  - MDA / MDMA
  - Cathinone / Methcathinone
  - Mephedrone / MDPV
Questions and Commentary
Thank You!

Presentation: www.tascaz.org/NTASC2011

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Salvia

Active constituent - Savinorin A

Most potent naturally occurring hallucinogen

- Rapid high in 1-5 minutes
- Tapers off 5-10 minutes
- Return to “baseline” in 20-30 minutes