Update on Synthetic Drugs of Abuse

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Disclosures

• Author of Toxicology in a Box – Out of Print
• No other disclosures
Outline:

- History of Synthetic Drugs
- Synthetic Cannabinoids
- Stimulants
- Hallucinogens
- Opiates

History of Synthetic Drugs / Legal Highs
Background

- “Research Chemicals” have been available for bulk purchase over the Internet from Chinese Manufacturers for years.
- Sold as a powder, in bulk weight, and not packaged in a pill → thus “not for human consumption”.
- Some products were a manufacturing precursors to active compounds (2-CH → 2-Cl or 2-CB).
- Some products were pro-drugs converted in the human liver/kidney to active form (GBL → GHB).
- Some products are psychoactive drugs by themselves (JWH-018, MDVP, 4-MMC/4-MEC).
- Some products are non-scheduled drugs by themselves (Khat, Salvia, Kratom).

GHB Home Manufacturing Kit – Available Online in the Early 1990’s
GBL (Gamma-Hydroxybutyrate / GHB) Advertisement in High Himes Magazine

“Legal Buds” Have Been Advertised in High Times Magazine Since 1990’s
JWH-018 as a “Research Chemical”

How Many Options Are There?

LOTS!!!!
And LOTS!!!!

Where Do These Chemicals Come From?
Where to Purchase?
How Are They Manufactured?
Inert Plant Material + Proprietary Blend Secret Ingredient

SPICE / K2
Article on Wholesale Product

Synthetic Marijuana / Incense
Synthetic Cannabinoids

- “legal buds” & “herbal smoke” sold since early 2000’s.
- K2/Spice first major players late 2000’s.
- Synthetic cannabinoids first identified as active ingredients in these products in 2008.
- John W. Huffman at Clemson University first synthesized THC analogs in late 1990’s.
- Sold in “head shops” and “smoke shops”.
- Concentrations of psychoactive compounds vary per sachet (0.2-3%), as well as the binding affinity of the synthetic to the anandamide receptors in brain (can vary between 5-800x affinity).

Synthetic Cannabinoids

• Thousands of synthetic cannabinoids exist, each with different CB1 and CB2 receptor affinities and effect.

Examples:
• JWH-XX – John W. Huffman
• HU-XX – Hebrew University
• AM-XX – Alexander Makriyannis
• CP-XX – Pfizer
• AB-FUBINACA, ADB-FUBINACA, ADB-PINACA, PX-3
What You Get

- Tachycardia
- Bloodshot Eyes
- Discordination
- Dry Mucus Membranes
- Paranoia*
- Hallucinations*
- Delusions*
- Altered Time Perception*
- Psychosis*
- Tremors*
- Seizures*
- Agitation*
- Catatonia **
- MI***
- CVA***
- Death****
Severe Adverse Reactions

- Suicide
- Agitated Delirium
- Catatonia
- Autonomic Dysregulation – hypotension, bradycardia
- Acute Kidney Injury
- Acute Myocardial Infarction
- Seizure
- CVA/TIA - Stroke

Adverse Reactions - Detailed

- June 6, 2010 – D.R. – 18 year old high school athlete in Iowa smoked a synthetic cannabis product, had no history of depression, complained to a friend that he “Felt like was in Hell”, went home and shot himself in the head with a shotgun.

- 2011 Case series of STEMI with elevated troponins, and clean caths were identified in 3 teens complaining of chest pain an ED in Utah.¹

- 2012 – Four cases of oliguric renal failure (ATN) in Alabama.² Three in Casper, WY and a dozen others sickened with “back pain, nausea and vomiting” after smoking “blueberry spice”.³

1: Mir, Obafemi, et. al. MI Associated with Use of Synthetic K2, Pediatrics June 28, 2011
2: Bhanushali, ain, et al. AKI Associated with Synthetic Cannabinoids, CJASN, December 2012
3: Zuckerman, L. Wyoming Kidney Failure Outbreak Linked to “Spice” Drug, Reuters. March 5, 2012
STEMI

CVA

• 25 y/o male – JWH-018 – dysarthria, expressive aphasia, R face and arm weakness: hyperdense L MCA with clot → t-PA improved and lost to follow up.

• 19 y/o female – JWH-018 – syncope, AMS, tremors, global aphasia, right hemiplegia, sensory loss, elevated troponin: L MCA clot and infarct, punctate infarcts in R cerebral hemisphere → outside t-PA window and left with persistent R hemiparesis and expressive aphasia.

Patient A


Patient B

CVA

• 31 y/o male seizure after “Crazy Monkey” XLR-11 = multiple intraparenchymal hematomas, bilateral frontal SAH, left anterior cerebral and middle cerebral artery vasospasm.

• 25 y/o female seizure after unknown “spice” = diffuse SAHs, acute ischemic strokes bilateral cortical hemispheres and cerebellum, severe vasospasm.

• Neither had aneurysm or artery malformations.


So Why So Popular?

• Profitability – both wholesale and retail
• Doesn’t show up on conventional urine testing
• Convenience
• Perceived Safety
Diagnostic Workup and Treatment

- Supportive Care
- Reassurance and Calming Techniques
- EKG to r/o underlying arrhythmias
- Consider CIP (Cardiac Injury Panel) & BMP
- CXR to r/o barotrauma (pneumomediastinum or pneumothorax)
- Mild Benzodiazepine for Anxiety
- Physical and/or Chemical Restraints if Required (Adulterated Marijuana)

Catatonia: Brooklyn, NY

33 Overdoses of Synthetic Marijuana Product July 12, 2016
Stimulants

How Many Options Are There?

LOTS!!!
MDVP - Methylenedioxyxpyrovalerone

- Norepinephrine-Dopamine Reuptake Inhibitor*
- Developed in 1969
- Hit the Radar in 2004
- MDPK, MTV, Magic, Maddie, Super Coke, PV
- White to yellowish color, fishy odor with age
- Stimulant Effects > Empathogenic Effects
- More “speedy”, less “trippy”.
- 4-6 hour high with a comedown – total effect 10 hours
- Addictive – High Desire to Redose
- Causes Agitated Delirium – Florid Psychosis

α-PVP - α-Pyrolidinopentiophenone

- Flakka or Gravel
- “$5.00 Insanity”
- Chemically related to pyrovalerone
- Norepinephrine-Dopamine Reuptake Inhibitor*
- White to pink in color – can be injected, snorted, cheeked, vaporized
- Hit the radar in Florida in 2014
- Causes psychosis, hyperthermia, agitated delirium
- Several high profile media cases in US over the years
MDVP - Effects

- Hypertension
- Tachycardia
- Bruxism
- Diaphoresis
- Mydriasis
- Hyperthermia
- Rhabdomyolysis
- Paranoia
- Psychosis
- Delusions
- Hallucinations

Bath Salts

some product names

HYPERTENSION  IVORY SNOW  Cloud Nine  VANILLA SKY

chemical structure
dilated pupils (mydriasis)
delusions
grinding teeth (bruxism)
fishy odor

Faces, it's what's for dinner!

Bath salts are Substituted Cathinones.
Hallucinogens
Molly – Coming Soon to a College Near You!

MDMA
MDMA Identification Charts

Ecstasy In Japan 2006

For law enforcement officers use only

- MDMA
- MDA
- MDEA
- Amphetamine
- Methamphetamine
- Caffeine
- Ketamine

MDMA Testing Kits
“Molly”

- Users are insistent that it’s pure MDMA
- Think of a “catch all” term for a synthetic drug that causes more hallucinations than stimulation: Empathogenic > Stimulant Effects
- 13% of Molly seized in NY State was MDMA as per DEA
- Most “Molly” confiscated and tested proved to be cathinones
- Can be: phenethylamines (2ci, 2cb), cathinones (mephedrone, 4-MEC, 4-MEPP), “MDMA-like” 5/6-APB (Benzofury), α-PVP (Flakka), 4-FA (Flex), rarely MDMA, MDA, MDEA
- NIDA estimates 5% of 12th graders have tried MDMA (Molly)
- Often used at electric music dance parties

Molly in Syracuse

- 22 indictments in August 2011
- Investigations began spring of 2009
- 100 kg of “Molly” distributed between March 2010 through April 2011
- 25 kg of “Molly” ($525,000), 24 guns, 4 vehicles, a Bayliner boat and $100,000 seized
- “Molly” determined to be 4-MMC and 4-MEC
- Substituted Cathinones = Mephedrone

http://www.drugandalcoholdependence.com/article/50376-8716(16)00057-0/fulltext
https://www.drugabuse.gov/drugs-abuse/mdma-ecstasymolly
Wesleyan Molly

• Enrollment: 3224 students
• 0.1g = $20, 1g = $200 ($80-$100)
• 5 arrested, 5 suspended, charges dropped in 2 cases
• Analysis: AB-Fubinaca and “substance similar to MDMA” which was 6-MAPB
• Main distributor created pamphlets to distribute to students on appropriate dose and “safe” drug use
Wesleyan Molly

**AB-Fubinaca**
- Invented by Pfizer in 2009
- Hit the synth scene in 2012 in Japan
- AB-PINACA, 5F-AB-PINACA, ADBICA, etc., etc.
- “Synthetic Marijuana”
- Associated with several deaths

**6-APB**
- 6-(2-aminoproply)benzofuran
- “Benzofury”
- Phenethylamine
- Triple monoamine reuptake inhibitor and 5-HT$_{2B}$ Agonist
- “Similar” to MDA

25I-NBOMe “N-BOMB”
25I-NBOMe “N-BOMB”

- “LSD Alternative”
- Synthetized 2004 Germany Ralph Heim
- Substituted phenethylamine
- Similar to 2CI, 2CE, 2CB
- STRONG 5-HT_{2a} Receptor Agonist (16x 2C-I)

25I-NBOMe “N-BOMB”

- Tachycardia, Dilated Pupils, Tremors, ↑ WBC, Seizures, Clonus, Agitation, Hallucinations, HTN, AKI, Metabolic Acidosis
- Potent enough for Blotter Paper Hits
- Sublingual, Buccal, Nasal, Vaporized, IV
- March 2012-August 2013 19 deaths in Americans between ages 15-29 y/o*

* DEA Press Release November 15, 2015
Synthetic Opiates

Shady 80s
Synthetic Opiates

- Fentanyl – “Body Bag” brand in Philadelphia 2006 – stronger and more potent = frequent OD
- Fentanyl cut heroin has returned across US 2014
- Fentanyl cut heroin is on the rise
- Fentanyl is 50x more potent than heroin
- Carfentanil is 100x more potent than fentanyl
- Carfentanil is 10,000x more potent than morphine
- Higher doses of naloxone may be needed – 2, 5, 10 mg
- Intubate if necessary

20,000 50mcg doses
$0.28 per dose
Deadly opioid carfentanil bound for Calgary seized in Vancouver

1 kg Carfentanil Seized
Calgary, Canada
From China
August 9, 2016
1 Million Lethal Doses
U-47700

- Upjohn-47700
- Pink, Pinky, U4
- Opioid analgesic by Upjohn discovered in 1970’s
- Hits µ-opioid and κ-opioid receptors
- 80x stronger than morphine
- Considered a “research chemical”
- Reportedly found in: Ohio, Wyoming, Georgia
- Schedule 1 as of November 14, 2016
W-18

- 1984 patent on W-18 and 30 related compounds described it as 10,000x stronger than morphine
- Never tested as an opiate agonist
- Clandestine manufactures began manufacturing and selling the chemical
- Chemical begins showing up in confiscated opiates
- Canada and US move to make it a scheduled drug so manufactures begin selling newer, altered chemicals to bypass law
- W-18 not proven to have any opiate like effects in humans

Gray Death

- News media started reporting on this in May 2017
- Apparently a mixture of various synthetics
- May not show up on tests
- $10-$20 per unit/baggie
- Seen in: Georgia, Alabama, Ohio, Pennsylvania

Kroll, D. W-18 Is Not A Super-Potent Designer Opioid as Originally Believed, Forbes, July 28, 2016
Things That Make You Go Boom!

Popularity of E-Cigs

- Experimentation
- Smoking Cessation
- Perceived Safety
- Lower Costs
- Variety of Flavors
- Indoor use/use in Public
- Fashionable/Look Cool
E-Cigs/Vaping in Movies

HBO True Detective – Season 2
Robert DeNero - Heist
Dennis Quaid - Beneath the Darkness

John Cusack – Drive Hard
Johnny Depp – The Tourist
Kevin Spacey – House of Cards

Hollywood Stars E-Cigs/Vaping

Leo!
Simon
Catherine Zeta Jones

Jack!
Anatomy of E-Cig

- Lithium battery – power source
- Atomizing device/heater
- Liquid-filled cartridge – with or without nicotine

3 Main Categories

- First Gen: “Cigalikes” – resemble cigarettes
- Second Gen: eGos – larger models with refillable fluid tanks
- Third Gen: Mods – a modified version combining elements of above models
First Generation

• Single piece = disposable – 200-500 puffs
• Rechargeable with replaceable cartridges
• Can have push button or is activated with inhalation pressure sensors
• User doesn’t handle nicotine fluid
Second Generation

- Larger, more colorful units
- Larger batteries
- Atomizer and fluid tanks are separate
- Customizable
- Refillable e-liquid chamber
Third Generation: Mods

- Modified Mint tins (Altoids), Atari 2600 joystick, metal or wooden boxes, etc.
- Can have larger batteries, larger e-fluid tanks, variable voltage settings
- Changing resistance settings, adding/altering coils, adjusting voltage affects fluid atomized, cloud size, throat hit, etc.

Vapor4Life: Odd Mods


Speaking of Ghostbusters
E-Cig MP3 Player & Telephone

SuperSmoker Club

Exploding E-Cigs
Exploding E-Cigs

Exploding E-Cigs
Butane Hash Oil
Butane Hash Oil

- BHO, 710 OIL, shatter, glass, honey, bees wax, wax, hashish oil, budder, dabs
- Potent form of THC and cannabinoids extracted from plant material using pressurized butane.
- May contain up to 60-85% THC.
- Smoked in small aliquots known as “dabs” using a vaporizer or blowtorch heated water pipe.
- Water pipe may be referred to as an “OIL Rig”
Butane Hash Oil

- Can cause explosions when being manufactured/extracted.
- Sells for $10-$40 gram in Green States, $100 elsewhere.
- Reportedly no odor when vaped.
- Commercial vaporizers sold/marketed specifically for this purpose.

BHO Use
BHO Fails

BHO Aftermath