“Keeping Up With Designer Drugs”

North Carolina Foundation for Alcohol and Drug Studies
Winter School, February 2015, Greensboro, NC
Designer drug is defined as:

Drugs which are *created* to:

- To be legal - through loop hole in federal law
- To be undetectable by conventional drug testing
- To modify existing chemical structure to be structurally different than banned drugs
- To create new drugs of entirely different structure that produce similar effects to illegal recreational drugs
"Legal High" Business 2008

In Quest for ‘Legal High’ Chemists Outfox Law; WSJ

- Modified Ritalin® (methylphenidate)
- Created Nopaine (ethylphenidate)

Nopaine "is every bit as good as cocaine," says Mr. Llewellyn

When the housing market crashed in 2008, David Llewellyn's construction business went with it. Casting around for a new gig, he decided to commercialize something he'd long done as a hobby: making drugs.
The Federal Analog Act

§ 813. Treatment of controlled substance analogues

The Federal Analog Act is a section of the United States Controlled Substances Act which allowed any chemical "substantially similar" to a controlled substance listed in Schedule I or II to be treated as if it were also listed in those schedules, **but only if intended for human consumption.**
Synthetic Cannabinoids (SC)
“Herbal Incense” Spice, K2, Genie, Yucatan Fire, Spice Gold
Synthetic Cannabinoids: “Herbal Incense”

Spice, K2, Genie, Yucatan Fire, Spice Gold, Plant food

- Mixture of herbal/spice plant products sprayed with synthetic cannabinoids
  - Sold as aromatic incense, potpourri, plant food
  - Often contaminated with unidentified toxic
  - “Natural” misconception of safety

- Marketing
  - Appearance - olive green leafy material; similar to marijuana
  - Sold in variety of colors/flavors
  - $30-45 per 3Gm
Legal Potpourri

- Grenade
- Chill Spice
- Clown Loyal
- Super Kush
- Dank Herbal Potpourri
- Natural Spirits
- Red Planet Herbal Potpourri
- Super Kush

Legal in all 50 states because it's cannabinoid FREE!
Cannabinoid vs. SC

- **Phytocannabinoids**
  - Found in cannabis plant
  - THC, CBD, CBN

- **Endocannabinoids**
  - Produced within the body
  - Lipid messengers

- **Synthetic Cannabinoids: 6 chemical classes**
  - Depending on synthetic compound, can be anywhere from 4 times to over 100 times more potent than the THC in marijuana
Synthetic Cannabinoids (SC)

- Developed for research
  - JWH-018 & JWH-073
  - JWH-250, CP-47, 497
  - HU-210

- Dr. John W. Huffman, Clemson University professor, synthesized many novel cannabinoids as part of research for National Institute for Drug Abuse (NIDA) on endogenous cannabinoid receptors - but never tested on humans nor approved by FDA. “Apparently someone picked it up, I think in Europe, on the idea of doping this incense mixture with the compound and smoking it” –Dr. Huffman

There are over 100 known synthetic cannabinoids

\[ \text{JWH-018} \]

\[ \Delta^9-\text{THC} \]
The Emergence of Synthetic Cannabinoids

- **JWH-018/073** arrived early and have come and gone.
- **JWH-250** arrived a little later and has also cycled out.
- **JWH-081** was part of a second wave that has already completed its cycle.
- **JWH-122** was part of the same wave but has persisted in popularity and is part of the current scene.
- **AM-2201** was part of the same second wave and has gained in popularity, probably currently the most prevalent.
- **JWH-022** and **JWH-210** are showing signs of increasing popularity.
- Recent emergent drugs are the adamantoyl (**AM-1248**) and tetramethylcyclopropyl (**XLR-11** and **UR-144**) indoles which are ahead of the latest attempts to schedule these drug classes.

Timeline of Synthetic Cannabinoid Products

Synthetic Cannabinoids: “The Next Generation”

• New compound, URB-754: Does NOT bind to CB receptors itself, but inhibits enzyme that breaks down endocannabinoids
  – More endocannabinoid around → more binding to receptors
• AND, one “spice” sample was found to contain URB + a cathinone, which reacted with one another and together created a whole new psychoactive compound

SOURCE: Doris Payer, #CHSF2013.
Next Generation

- **AM-694**
  - 1-[(5-fluoropentyl)-1H-indol-3-yl]-(2 iodophenyl)methanone
  - Powerful agonist at receptors CB1

- **AM-2201**
  - 1-[(5-fluoropentyl)-1H-indol-3-yl]-(naphthalen-1-yl)methanone
  - New category of cannabinoids and patented in the US

- **JWH-019**
  - 1-hexyl-3-(naphthalen-1-yl)indole
  - Derivative of JWH-018

- **JWH-081**
  - 4-methoxynaphthalen-1-yl-(1-pentyldinol-3-yl)methanone

- **JWH-122**

- **JWH-200, 203, 210, 398**

- **PB-22, BB-22, 5F-PB-22**
MAM-2201
analogue of AM-2201 with variation in the position of their naphthyl group

RCS-4

XLR-11

UR-144
Synthetic Cannabinoids Identified in U.S. NFLIS Forensic Labs

19 variations reported in 2010
n=3,286

44 variations reported in 2011
n=23,688

55 variations reported in 2012
n=41,458

Updated Testing Panels

JWH 073 NBA (N-butanoic acid)
JWH 122 N5HP (N-5-Hydroxypentyl)
JWH 018 N5HP
JWH 081 N5HP
JWH 210 N5HP
JWH 203 N5HP
JWH 019 5HH
JWH 250 N5HP
AM2201 N4HP
RCS4 5HP
JWH 398 N5HP
AM694 N5HP
MAM2201 N4HP
UR 144 NPA
UR 144 N5HP
XLR 11 N4HP
November 2010 - DEA announces temporary ban listing handful of compounds

March 2011 - DEA classifies Schedule I
❌ JWH018, 073, 200
❌ CP47, 496

July 2012 – President signs Synthetic Drug Abuse Prevention Act of 2012 into law
As substances are added to Schedule I and “bans”,
How do sales continue???????
Use of E-cigarette devices to “vape” cannabis products: produces odorless vapor
THC EXTRACTION

- Butane Honey Oil
- Skuff/Kief
- Liquid Solvent
- Hash
- Bubble Wash Hash
New Cannabis Substances also produced with butane, nitrous oxide, alcohol, carbon dioxide and even cold water.

“Ear Wax Weed, Butane Hash Oil (BHO), Cannabis Oil, Honey Oil, Shatter, Wax, Bubble Hash”, et al.
Extraction process is known as “Dabbing”
“Dabbing” butane hash oil (BHO) aka “wax, shatter, honey oil” et al.

Alleged to result in a waxy product containing 70-90% THC!
"But it’s just a plant..."
(80-90% THC) Concentrates

“Green Crack” wax

“Ear Wax”

Butane Hash Oil (BHO)

“Budder”

“Shatter”
Marijuana Edible Displays
CAN YOU TELL THE DIFFERENCE?

NEITHER CAN YOUR KIDS.

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Indigenous to East Africa

- *Catha edulis* bush
- “African Salad”
- Harvested all year

Traditional use for centuries

Ingestion

- Chew
- Extracted for tincture, teas
- Crystallized and smoked

Amphetamine

Cathinone
Synthetic Stimulants

“Bath Salts”

- Synthetic stimulants (SS)
  - MDPV
  - Mephedrone (MMC, MCAT, Meow-meow)
  - Methylone
  - Complete ingredient content??

- Product labeling
  - Ivory Wave, Vanilla Sky, Purple Wave
    Ocean Burst, Cloud 9, plant food
  - Cost $20-30 per packet
  - “Not for human consumption”
    loop hole to Federal analog Act
Synthetic Stimulants

- **Production**
  - Illicit laboratories
    - × Initially China and Asia
    - × More home “grown”
  - ↑ effects vs. plant, ↑ potency, ↑ ↑ ↑ ill effects

- **Route of ingestion**
  - Snorting most common
  - Can be smoked or swallowed
Synthetic Stimulants

- **Pharmacology**
  - NE/DA reuptake inhibitor
  - Duration: 6-8hrs...24hr??

- **Effects**
  - Rush, $\uparrow$HR/BP
  - $\uparrow$energy, insomnia
  - Hallucination, psychosis
  - Violet behavior
  - Seizure, kidney failure $\rightarrow\rightarrow$ death
  - Permanent neuronal damage??
Mephedrone
(4-methylmethcathinone)

- MMC, MCAT, Meow-meow, Drone, **Plant Food**
- Synthetic derivative amphetamine/cathinone
- Jan 2010 most popular “club drug” UK
- Appearance: white powder
- According to the DEA, companies in India and China are principally responsible for manufacturing and exporting the synthetic stimulants
Pump-It Powder
Energy Boost and/or Plant Food

Pump-it Energy contains (methylhex-anamine)

Mephedrone plant food contains methylmethcathinone
Methyline has almost the same potency of MDMA, but it does not produce the same effects. It has almost an antidepressant action, pleasant and positive, but not the unique magic of MDMA.

Alexander Shulgin
“Bath Salt”
Media History Horror Stories

- October 2009, Sarah F (35) dies taking “Ivory Wave” to lose weight for her London wedding

- May 2011, Dateline NBC story of adolescent suicide after taking “bath salts”

- January 15, 2012, 34 y.o. New Orleans Woman develops severe necrotizing fascitis from IV “bath salt” abuse

- May 29, 2012, face-eating naked cannibal high on “bath salts”? killed by police in Miami, Fl. but only cannabinoids reported by toxicology??
Current ER Management

- Concerns: Lethality (ICU?), non-detectable with routine drug screens, often used or adulterated with other drugs of abuse

- Restraints, iv benzos for seizures
  - High dose iv sedatives (2+2 lorazepam/haloperidol)

- Fluids and cautious of rhabdomyolysis

- Monitor and treat morbid hyperthermia prn
Synthetic Stimulants
Bath Salts / Plant Food

- **DEA temporary ban Sept 8, 2011**
  - Scheduled I as of Oct 8, 2011
  - MDPV, Mephedrone, Methylone

- **Synthetic Drug Abuse Prevention Act of 2012**
  - Bans 31 specific compounds: 3 stimulant, 20 cannabinoid and 9 hallucinogenic compounds
  - Conviction/penalties for sale or possession-punishable for up to 20yrs in prison
Next Generation SS

- “Cosmic Blast” or naphyrone
  - Derived from pyrovalerone
  - Currently very little data on safety/toxicity
- Pentedrone
  - Related to pyrovalerone and mephedrone
  - No reliable information as yet
- 3-Flourothemethcathinone
  - 4-Fluoromethcathinone
- Jewelry Cleaner, Glass Cleaner, Glass Cleaner,.... AND
Phenethylamine psychedelics

- 2CB, 2Cl, 2CT, 2CE, Bromo-DragonFLY
- Amphetamine-like
- Trigger hallucinations/paranoia
- Marketed as Eros, Nexus, Smiles.....
New Age Psychedelics and PsychoStimulants

~ infinite number of potential analogs isomers, isosteres, or other chemical modifications
Chemicals of concern.....

- 2C-T-7  Tripstasy, Blue Mystic
- 2C-B  Nexus
- 2C-I  Smiles (also 2C-E, -I, 25-I & 25b-Nbome)
- 5-methoxy diisopropyltryptamine  Foxy, Methoxy
- alpha methyltryptamine  Spirals
- N-benxylpiperazine  BZP
- dimethyltryptamine  DMT
- bromobenzodifuranylpropylamine  Bromo-DragonFly
Bromo-DragonFLY

(1-(8-bromobenzo[1,2-b;4,5-b’]difuran-4-yl)-2-aminopropane hydrochloride)

- Extremely potent hallucinogen
- Usually sold as “plant food”
- Typically purchased over the internet
- Intense peripheral vasoconstriction
- limb ischemia, hypertension, tachycardia, agitation, and seizures

Bromo-DragonFLY is a research chemical, that is not approved for human consumption
COMMON & BRAND NAMES
2C-I-NBOMe; 25I-NBOMe; 25I; N-Bomb

**Blotters** are placed between the gums and cheek, one on top and one on the bottom lip.

The **powder** form is often snorted.
5-MeO-DMT

- *Tryptamine* family of compounds
  - Effect *neurotransmitters* such as *serotonin* (5-hydroxytryptamine) and the primary pineal hormone, *melatonin*

- Found in a number of plants and in the venom and skin of some toads
  - “Spirit vine” ayahuasca plant
  - Colorado River Toad: only true-entheogen venom

- Various ways of ingesting
  - Smoking, snorting, iv
  - Extract and brew/swallow
"New" Designer Ecstasy-Like Psychostimulants

Benzo Fury

5-APB [5-(2-aminopropyl)benzofuran]

Or,

6-APB [6-(2-aminopropyl)bensofuran]

Compare these to Ecstasy or MDMA (3,4-methylenedioxy-N-methylamphetamin)e molecule
Cocaine Paste

- Oxidado, Oxi, Rust, Pasta, Basay (2 times stronger than cocaine)

Shake-n-Bake

Methamphetamine
Explosion of Legal OTC Energy Drinks and Bar Energy Drink Cocktails
2012 Frito-Lay Cracker Jack’d Jelly Belly Extreme Sport Beans Kraft MiO Energy
Endless Possibilities

Salvia divinorum
Salvia divinorum

- Aka Diviner’s Sage, Seer’s Sage
- Indigenous to Mexico
  - Over 1000 species of Salvia worldwide
  - *Salvinorin A* is the only one that is a hallucinogen, contained in plant leaves not flowers
  - Part of mint family
- Religious tradition
  - Incarnation of Virgin Mary
Ingestion

- Traditional
  - Macerate leaf
  - Extract juice
  - Tincture

- Chewing “quid” method

- Smoke dried leaves
Pharmacology

- Kappa-opioid receptor agonist
- Partial agonist dopamine receptor (D2)

- Hallucinogen
  - Psychotomimetic, dysphoric
  - Fast onset, duration 30-60min (user experience days-weeks)
  - No activity 5-HT2A SE (site of action LSD)

Low risk dependence, low toxicity
Effects of Salvia

- Laughter, evokes childhood memories
- Sensation of motion, merging, overlapping realities
- S-A-L-V-I-A
  - S  subtle effects, relaxation
  - A  altered perception
  - L  light, colors
  - V  vivid visionary states, “encapsulation”
  - I  immaterial existence, dissociation
  - A  amnesia
Salvia: Medicinal Effects??

- Inhibits intestinal motility
- Decreases gut inflammation
- Antispasmodic properties
- No large controlled studies, however
  - University of Kansas, Med Chem Dept
Legal Status  *Salvia divinorum*

- A Drug Enforcement Administration study is still pending to determine the 8 point criteria to place Salvia on the Federal Controlled Substance Act
  - Alabama, Colorado, Delaware, Louisiana, Michigan, Missouri, Ohio and others have passed regulations restricting use
Kratom is a tropical tree indigenous to Thailand, Malaysia, and other areas of South East Asia.
Kratom Overview

- Botanical Classification
  - Genus: Mitragyna
  - Species: speciosa
  - 7-hydroxymitragynine, speciogynine, paynantheine, mitraphyl-line, & about 2 dozen others

- Common names
  - Kratom, Kakuam, Ithang, Thom, Kekum

- Description
  - Leaves contain MG (SG) and are chewed as an opiate substitute and stimulant in Thailand and South-East Asia, primarily among the working class
  - Relatively long history of human use
Produces stimulant effects at low dose
  ◦ Yohimbe-like effect
  ◦ Increased alertness, physical energy, talkative and sociable
  ◦ Similar effect as 1-2 cups of coffee

**Mu-opioid receptor agonist**
  ◦ Analgesia, cough suppression
  ◦ Euphoria
  ◦ CNS depressant \equiv sedation
  ◦ Quick onset and lasts \sim 1-3hr
  ◦ *Opioid-like full physical addiction*
Side Effects  

**Acute side effects include:**
- Nausea, constipation
- Sweating, itching
- Dry mouth, loss of appetite

**Long term use:**
- Anorexia, weight loss
- Darkening of skin, esp face
- Tolerance phenomena
- Withdrawal syndrome
  - Achy muscles, hostility, aggression
  - Emotional liability, runny nose......
Sold

- Raw or crushed leaves
- Various commercial concentrated 15X to 250x extracts

Ingestion

- Chew; extract and brew tea or tincture
- Decrease potency by heat/smoke

Potencies and strains vary

- $15 to $50 per five-gram packet
- $18 to $25 for about 50 capsules
- Doses generally 2-10 grams.
Captain Kratom: “Synthetic Vicodin”
“Dirty” cousin of morphine
- Khanka
- Desmophrine produced from codeine
- Gasoline, paint thinner, HCl, iodine...
- “Recipes” posted on web

Epidemic in Russia
- Seize rate ↑↑↑ 23-fold 2009-present

Few user’s survive 2 years
- Rotting at injection site, gangrene, amputation
- Significant and prompt jaw degeneration
Xylazine

- Used for sedation, anesthesia, and muscle relaxation in horse and cattle
- Prevalent use in Puerto Rico
- Combination use
  - Cocaine speedball
  - “Cut” heroin
- Ingestion
  - IV
  - Insufflation
- May have severe cardiac effects
Texas “Cheese Heroin”

Black Tar Heroin

PLUS

TYLENOL® PM Caplets

Extra Strength

Acetaminophen

Diphenhydramine HCl
Jenkem, aka “Ass Gas”

Human or Animal excrement fermented to methane gas said to be a ~ psychedelic?
“What’s Old is New”

**Hallucinogens**
- Psilocybin
  - “Shrums”
  - Disrupts natural functioning of SE system

**Dissociatives**
- DXM, Robo- ataxia, slurred speech
  - How many mgs of DXM are in 4oz Robitussin? 360 mg
- PCP- paranoia, aggression, hallucination

Dissociative drugs distort perceptions of sight and sound and produce feelings of detachment (dissociation) from the environment and self.
Ketamine
Dissociative

- Diverted from hospital and veterinary stock rooms abused as a dissociative/psychedelic
- Effect - depersonalization, memory loss; SA dissociative anesthetic

“K” or Special K in U.S.
“Roflcoptr” in U.K.
“What’s Old is New”
Baker’s Brew
Alcohol Without Liquid (AWOL)
Ethanol Inhalant Devices

Banned in many States
Dry Ice ‘Smoking’ Alcohol

Images from KCTV via New York Times and Nub TV via YouTube Videos
Palcohol= freeze-dried alcohol in powder form to be mixed with water

Approved by U.S. Alcohol and Tobacco tax and Trade Bureau in early 2014 but rescinded its approval on 4/21/14
Blogs, Forums, Websites

- Erowid (.org)
- Grasscity (.com)
- Psychonaut (.com)
- Shoomery (.org)
- Spice University (.org)