



New Psychoactive Substances “Designer Drugs”

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Topics

- ▶ Synthetic Cannabinoids (SC)
- ▶ Stimulants
 - *Natural* khat plant
 - *Synthetic*
 - Bath Salts/Ivory Wave
 - Psychedelic stimulants (2CE, 2CB, 2CI...)
- ▶ Salvia
- ▶ Kratom
- ▶ Other chemicals/substances

Definition

Designer drug is a term used to describe drugs which are *created* (or marketed if they already existed) in order to *get around existing laws* by:

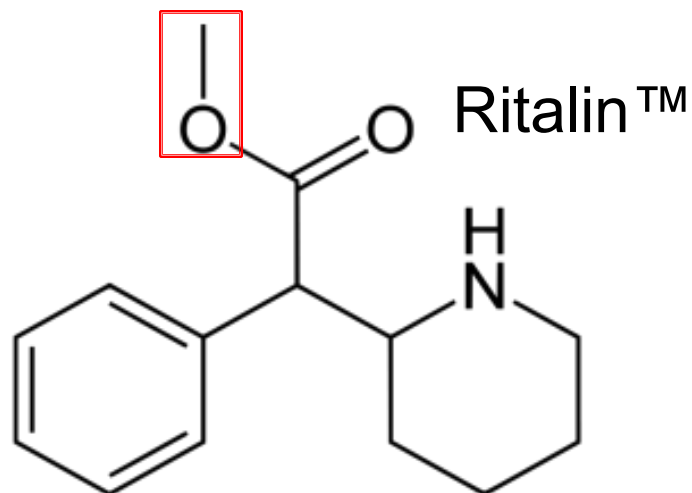
- ▶ *modifying* the molecular structures of *existing* drugs
- ▶ finding drugs with *entirely different chemical* structures that produce *similar effects* to illegal recreational drugs

"LEGAL HIGH" BUSINESS 2008

In Quest for 'Legal High' Chemists Outfox Law; WSJ

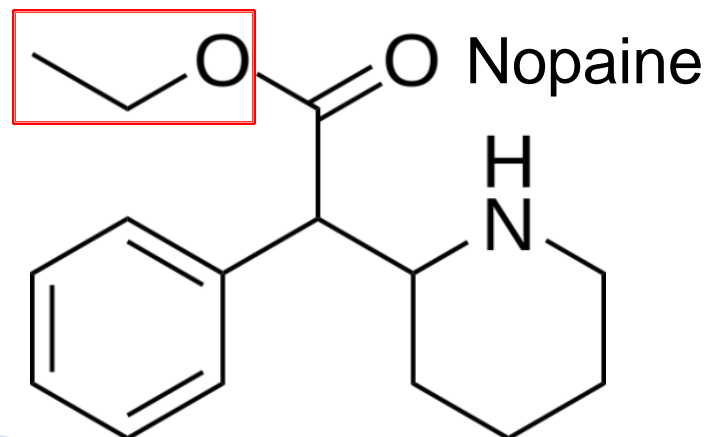
Original

- Ritalin™
- (methylphenidate)



Modified

- Nopaine
- (ethylphenidate)



Legal

- "every bit as good as cocaine" says Mr. Llewellyn

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.



**NOT FOR
HUMAN CONSUMPTION**

Synthetic Cannabinoids (SC)

“Herbal Incense” Spice, K2, Genie, Yucatan Fire, Spice Gold



“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 in appearance to marijuana, oregano
 - Sold in variety of colors/flavors
 - \$30-45 per 3Gm



Synthetic Cannabinoids (SC)

- ▶ Developed for research

- CB1 vs. CB2
- 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

**THERE ARE OVER 100
KNOWN SYNTHETIC
CANNABINOIDS**

Clarification of Terms

▶ Phytocannabinoids

- Found in cannabis plant
- THC, CBD, CBN

The endocannabinoid system is a group of neuromodulator lipids and their receptors that are involved in a variety of physiological processes including appetite, pain, mood, and memory.

▶ Endocannabinoids

- Produced within the body
- Anandamide (arachidonylethanolamine or AEA)
- 2AG (2-arachidonoyl glycerol)
- Nolandin Ether (2-arachidonoyl glyceryl ether)
- N-arachidonoyl-dopamine (NADA)
- Virodhamine (O-arachidonoyl-ethanolamine or OAE)

▶ Synthetic Cannabinoids: 7 chemical classes

- Full agonist vs. partial (↑↑potency)
- Variable duration of action



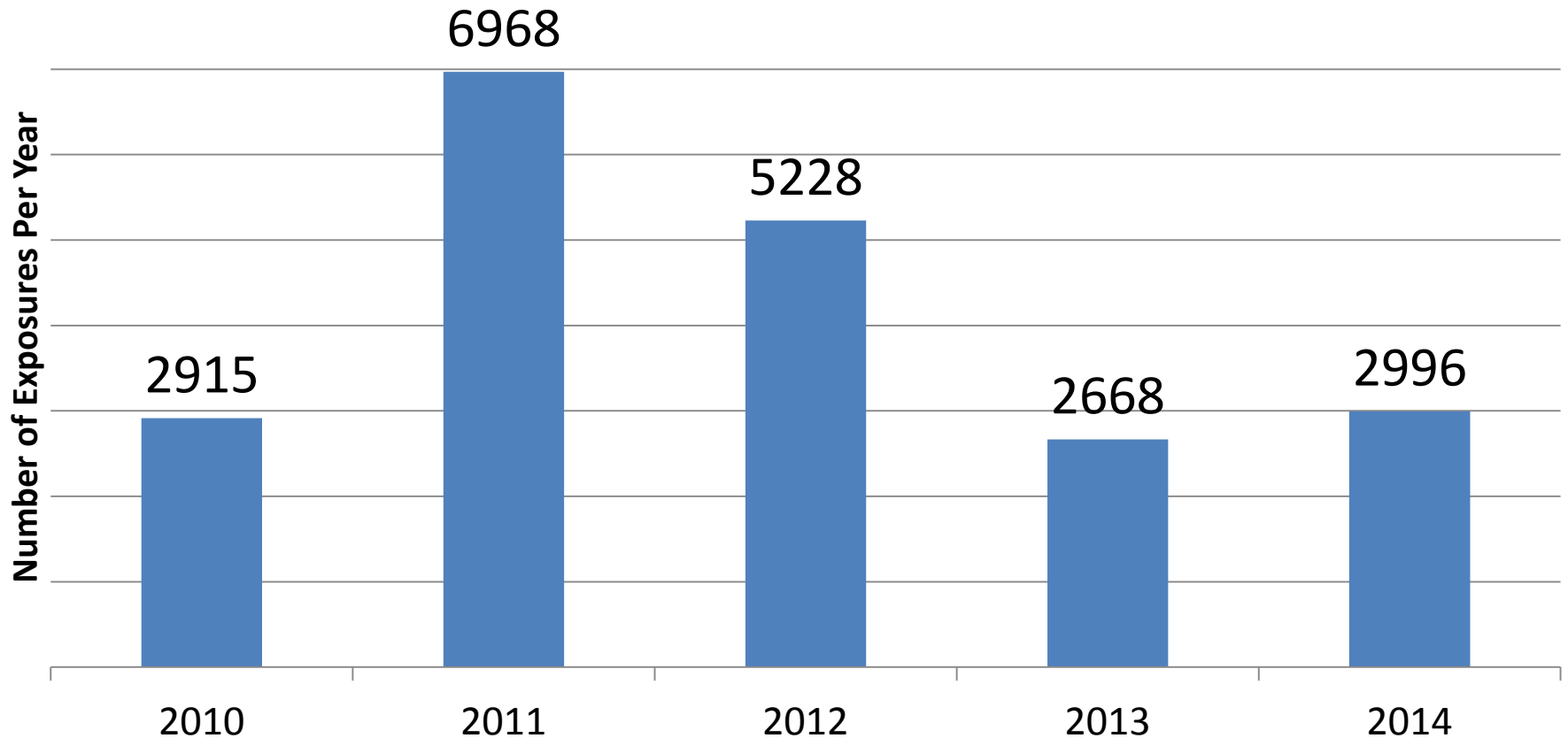
Effects

- ▶ Similar euphoric high as THC
 - More potent than THC
 - Low dose, high affinity
 - Duration 6-12hr
 - Detection times ??
- ▶ **MORE** toxic than phytocannabinoids
 - Since 2010, estimated 6,000 ER visits per year and climbing!!
 - Drug-Drug Interactions?



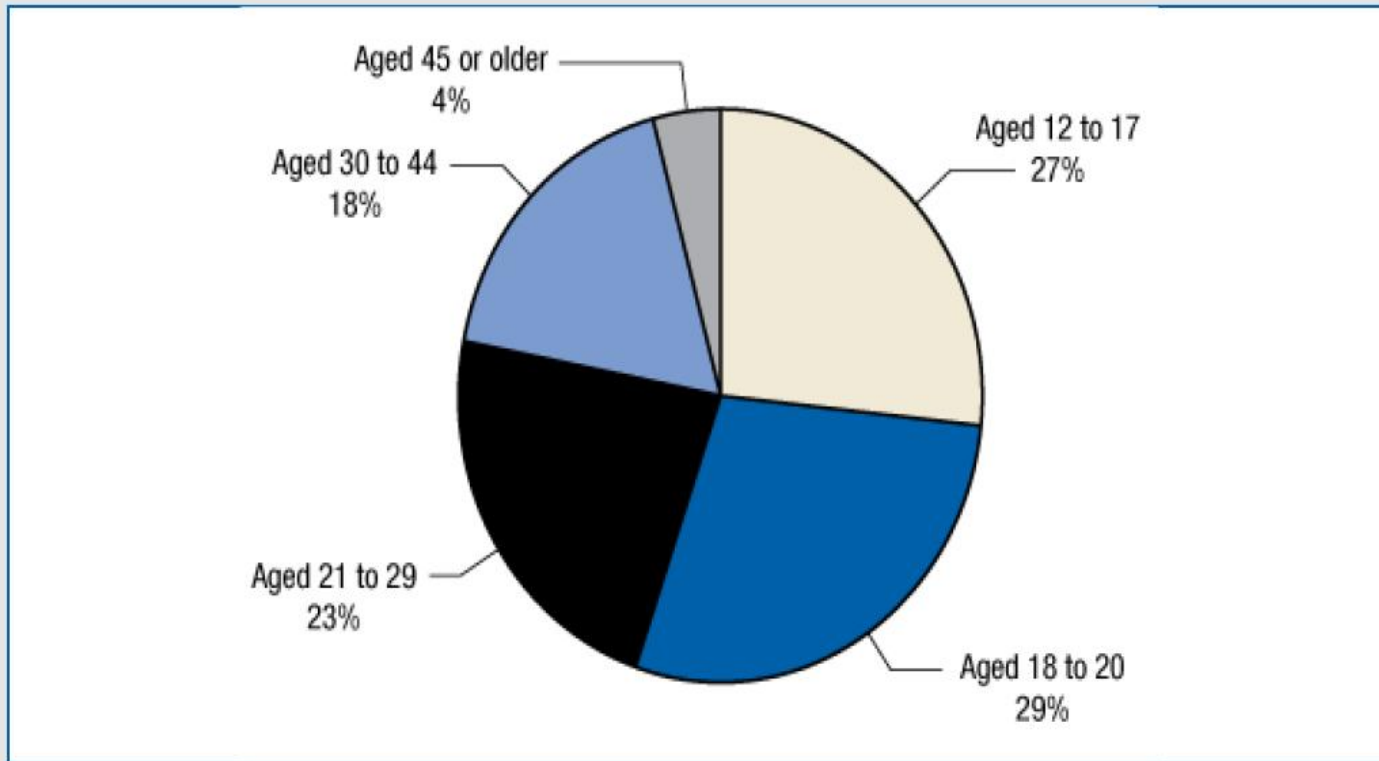
National Poison Control Data

Synthetic Marijuana Exposure Cases Per Year



(As of 10/31/14)

Figure 4. Emergency department (ED) visits involving synthetic cannabinoids, by age group*: 2011



*Percentages may not sum to 100 due to rounding.

Source: 2010 and 2011 SAMHSA Drug Abuse Warning Network (DAWN).



Legal Status



- **July 2012** – President signs Synthetic Drug Abuse Prevention Act of 2012 into law
 - Includes 15 specific molecules
- **May 2013** – DEA emergency scheduled 3 new molecules
 - **UR-144, XLR11, and AKB48**
- **February 2014** – DEA emergency scheduled 4 new molecules
 - **PB-22, 5-fluoro-PB-22, AB-FUBINACA, and ADB-PINACA**

Next Generation

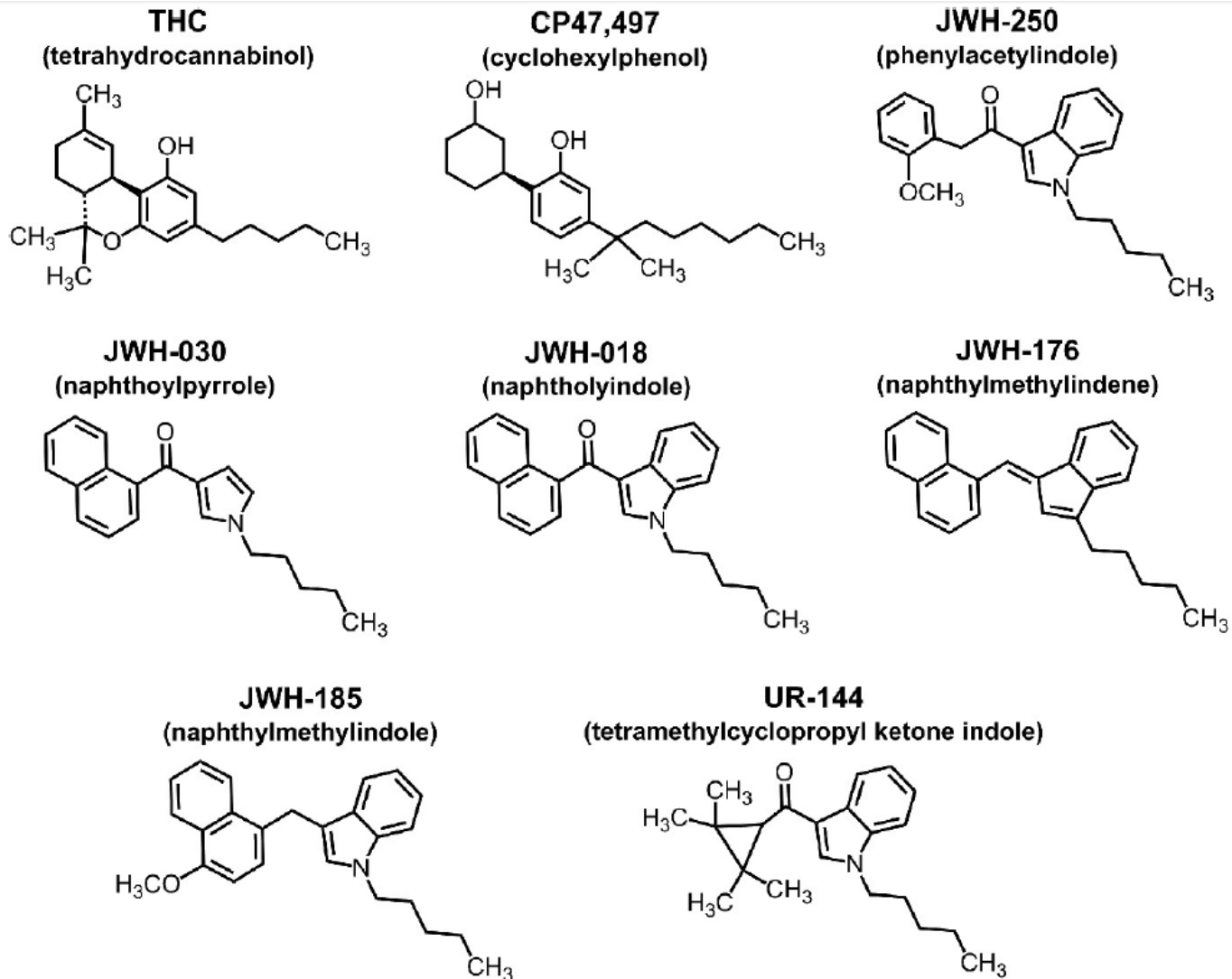


Figure 2. Chemical structures of synthetic cannabinoids found in spice NPS and their relationship to the plant-derived compound THC.

Updated Testing Panels

AM694 N5HP	AM2201 N4HP	JWH-018 N5HP	JWH-019 5HH
JWH-073 NBA	JWH-081 N5HP	JWH-122 N5HP	JWH-203 N5HP
JWH-210 N5HP	JWH-250 N5HP	JWH-398 N5HP	MAM2201 N4HP
RCS-4 N5HP	UR-144 NPA	UR-144 N5HP	XLR-11 N4HP

As substances are added to
Schedule I and “bans”,
How do sales continue???????

Legal Potpourri

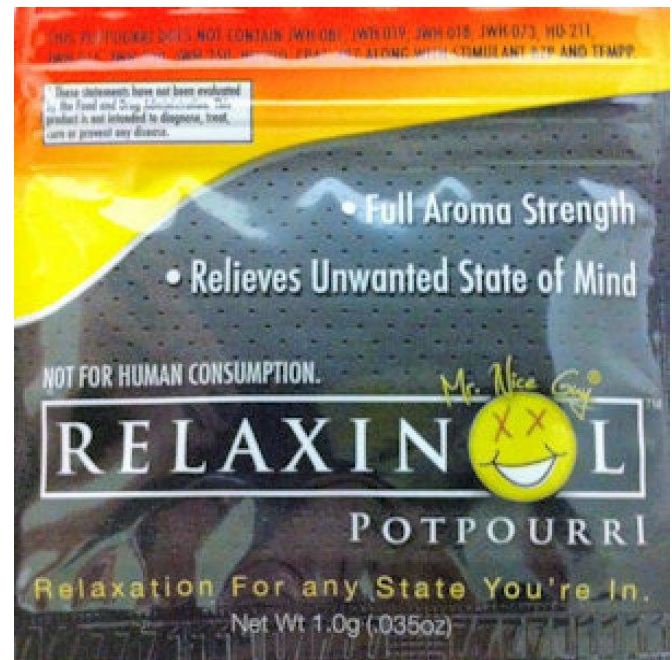


DANK

HERBAL POTPOURRI

100% Synthetic-Cannabinoid Free!

Legal in all 50 states because it's cannabinoid FREE!



RED PLANET

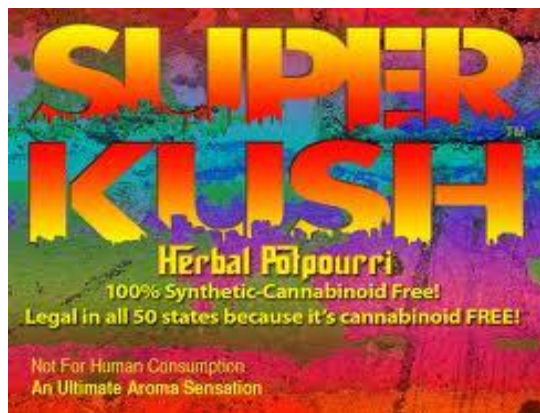
HERBAL POTPOURRI

100% Synthetic-Cannabinoid Free!

Legal in all 50 states because it's cannabinoid FREE!

Not For Human Consumption

Releases a Rich Aroma When Burned



Synthetic Stimulants

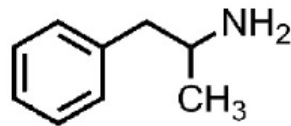
“Bath Salts”

- ▶ 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

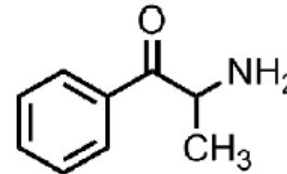


Chemical Structures

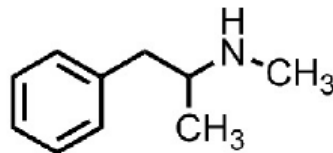
Amphetamine



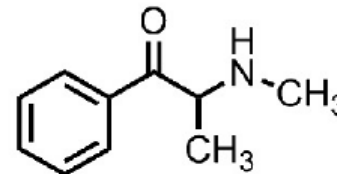
Cathinone



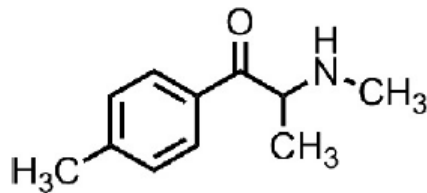
Methamphetamine



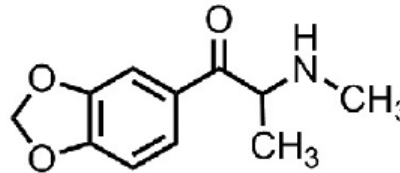
Methcathinone



Mephedrone



Methylone



MDPV

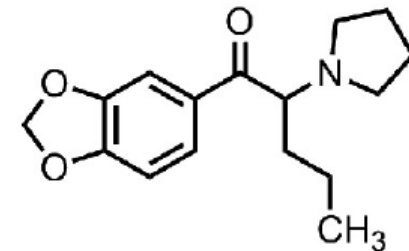


Figure 1. Chemical structures of synthetic cathinones found in bath salts NPS and their relationship to the plant-derived compound cathinone.

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

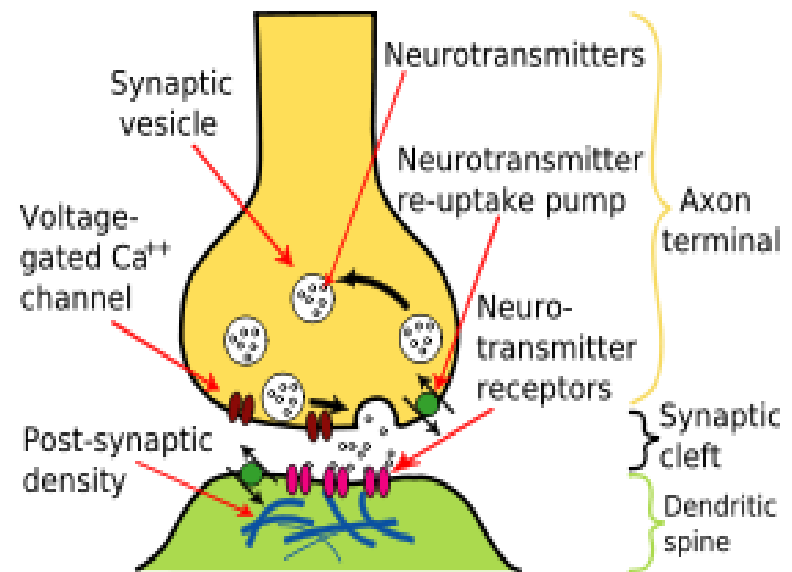
Synthetic Stimulants

▶ Pharmacology

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

▶ Effects

- Rush, ↑ HR/BP
- ↑ energy, insomnia
- Hallucination, psychosis
- Violent behavior
- Seizure, kidney failure → death
- Permanent neuronal damage?



KHAT, QUAT

Origins of MDPV, Mephedrone, Methyone, et al (aka Bath Salts)

Indigenous to East Africa

- *Catha edulis* bush
- “African Salad”
- Harvested all year
- Traditional use for centuries

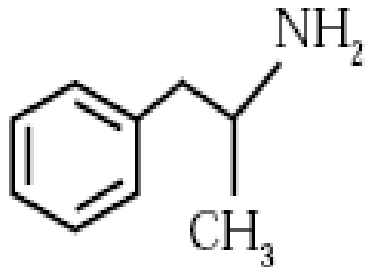


KHAT

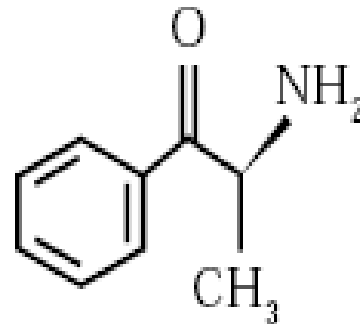
“Natural Amphetamine”



Main Constituents: cathinone and cathine



Amphetamine



Cathinone

Khat

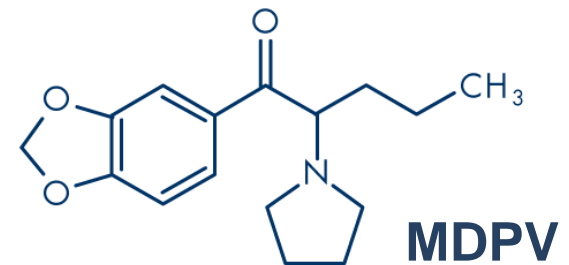
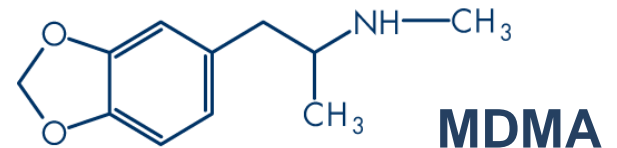
- ▶ Ingestion
 - Chew
 - Extracted for tincture, teas
 - Crystallized and smoked

- ▶ Few/no case reports psychosis, MI
 - Less likely than synthetic stimulants
 - Why?



MDPV (methylene-dioxy-pyro-valerone)

- ▶ CNS stimulant, similar to methamphetamine & MDMA (Ecstasy)
- ▶ White to light brown crumbly powder

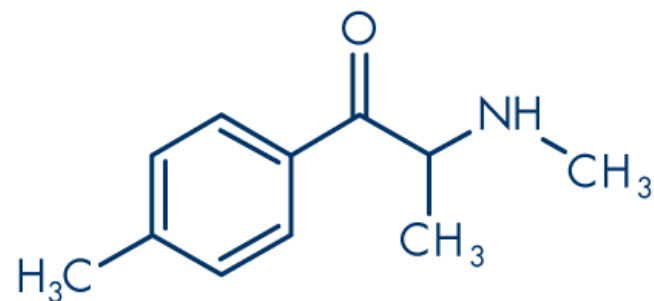


May cause seizures, panic attacks, or psychosis

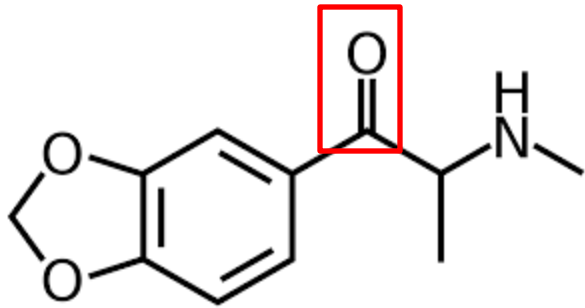
Mephedrone (4-methylmethcathinone)



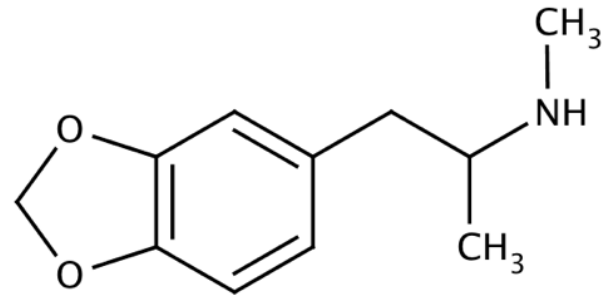
- ▶ MMC, MCAT, Meow-meow, Drone, **Plant Food**
- ▶ Synthetic derivative amphetamine/cathinone
- ▶ Jan 2010 most popular “club drug” UK
- ▶ Appearance: white powder
- ▶ According to the DEA, companies in India and China are principally responsible for manufacturing and exporting the synthetic stimulants



Methylone vs. Ecstasy



Methylone (bk-MDMA)



Ecstasy (MDMA)

“Methylone 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

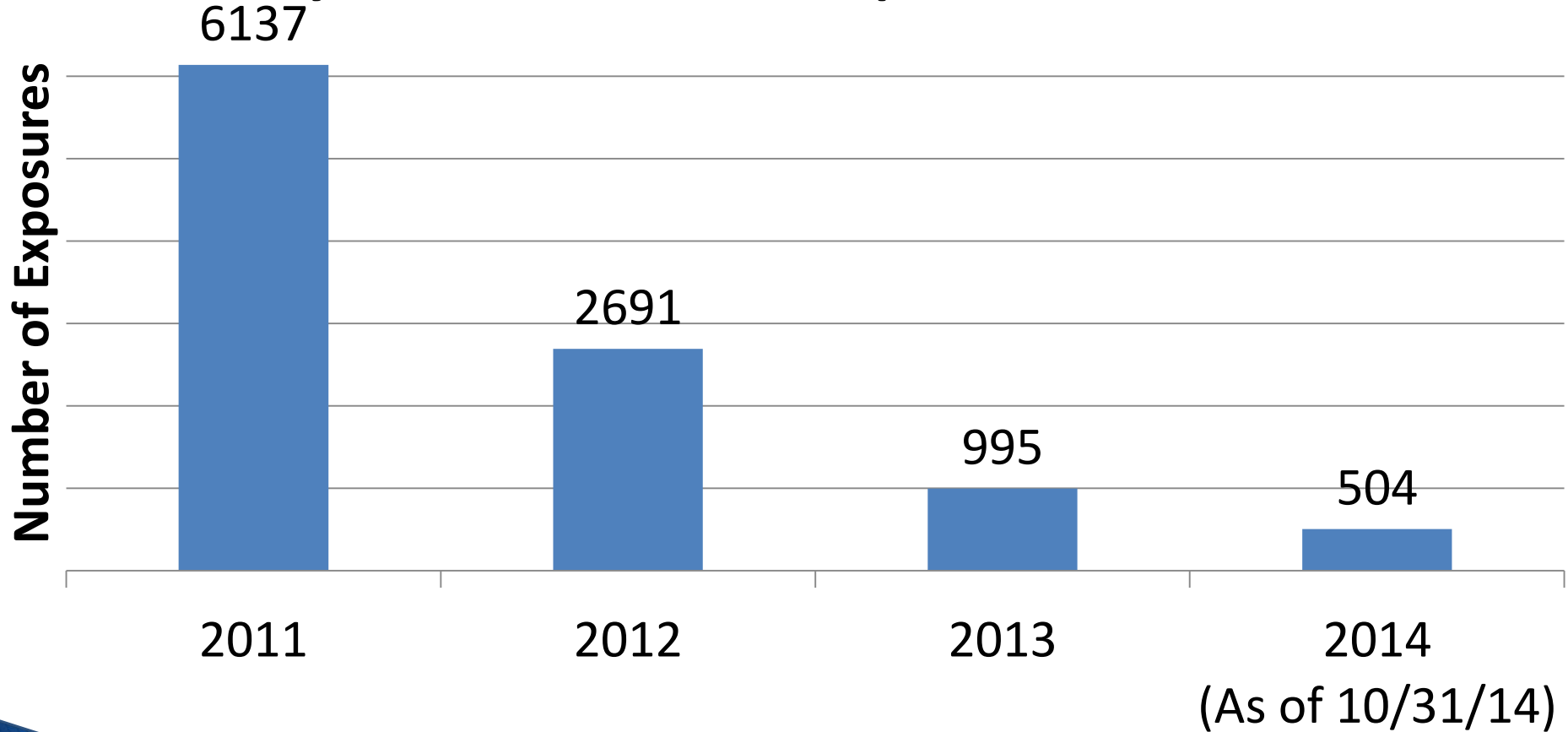
- ▶ October 2009, Sarah F (35) dies taking “Ivory Wave” to lose weight for her London wedding
- ▶ May 2011, Dateline NBC story of adolescent suicide after taking “bath salts”
- ▶ January 15, 2012, 34 y.o. New Orleans Woman develops severe necrotizing fasciitis from IV “bath salt” abuse
- ▶ May 29, 2012, 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

Poison Control Center Data

Synthetic Cathinone Exposure Per Year



Synthetic Stimulants

Bath Salts / Plant Food



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

- ▶ **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-Flouromethcathinone
4-Fluoromethcathinone
Jewelry Cleaner, Glass Cleaner....

AND



Pump-It Powder

Energy Boost and/or Plant Food



Pump-it Energy contains
(methyhex-anamine)



Mephedrone plant food contains
methylmethcathinone

Other Stimulants of Concern...

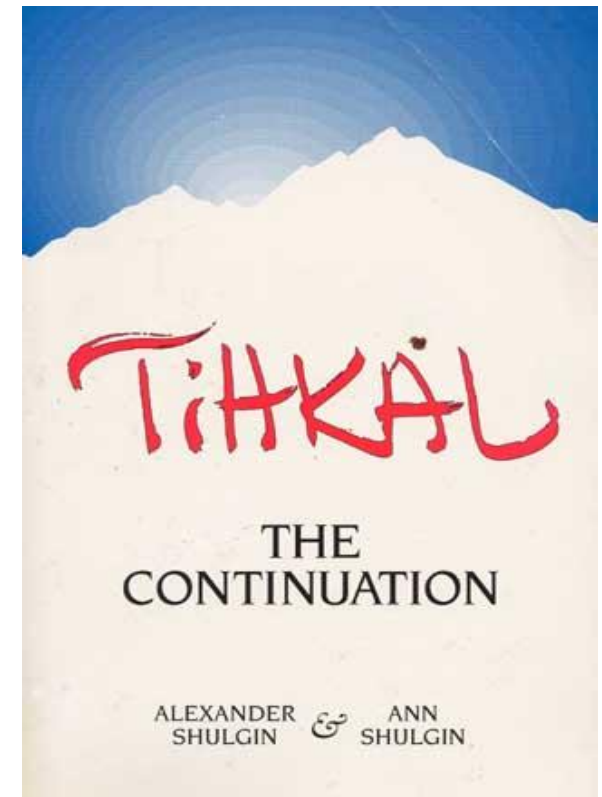
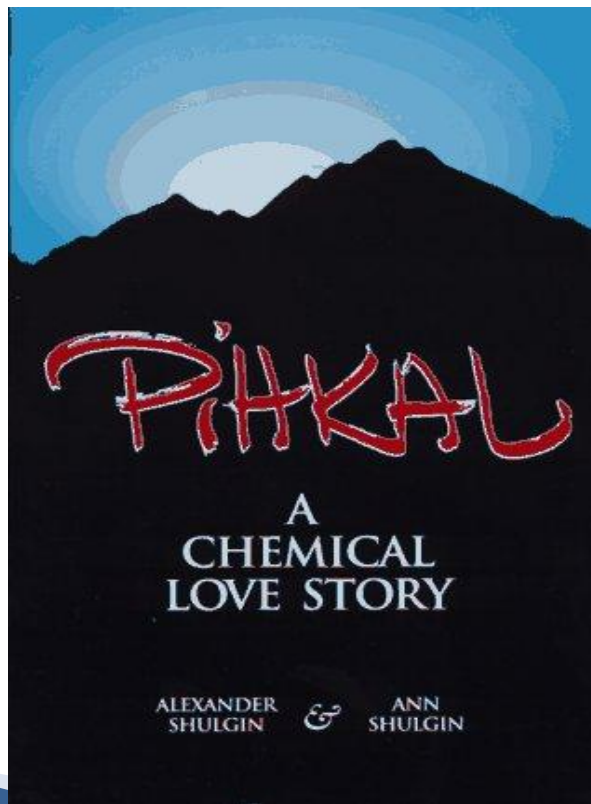
Stimulant Psychedelics

- ▶ Phenethylamine psychedelics
 - 2CB, 2CI, 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...

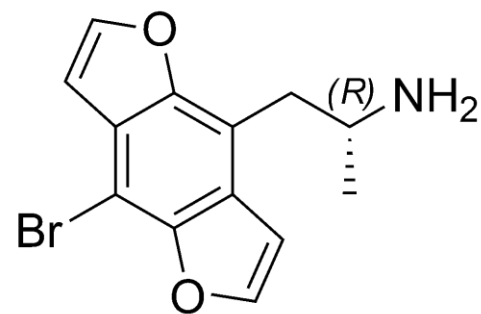
Chemical Name	Street Name
2C-T-7	Tripstasy, Blue Mystic
2C-B	Nexus
2C-I	Smiles (also 2C-E, -I, 25-I & 25b-Nbome)
5-methoxy diisopropyltryptamine	Foxy, Methoxy
Alpha methyltryptamine	Spirals
N-benxylpiperazine	BZP
Dimethyltryptamine	DMT
Bromobenzodifuranylpropylamine	Bromo-DragonFly

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



Stimulant Psychedelics

25I-NBOMe (2C-I-NBOMe)

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



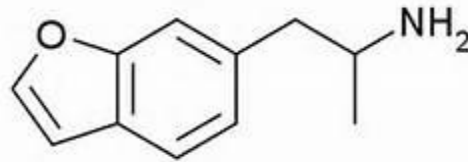
5-MeO-DMT

- ▶ *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

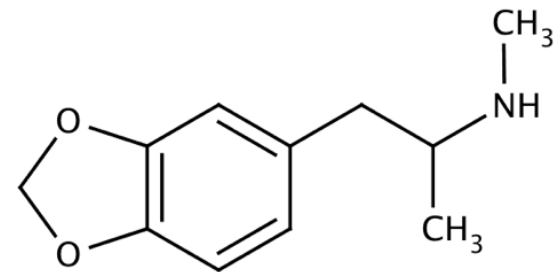


5-APB [5-(2-aminopropyl)benzofuran]



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

Compare these to Ecstasy or MDMA (3,4-methylenedioxy-N-methylamphetamine) molecule



Cocaine Paste



Cocaine Paste:
Oxidado, Oxi, Rust, Pasta, Basay

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

Insect Repellent, Natural Stain Remover, Ladybug Attractant, “Legal” Synthetic Cocaine, et al.



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-HT_{2A} 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

Subtle effects, relaxation

Altered perception

Light, colors

Vivid visionary states, “encapsulation”

Immaterial existence, dissociation

Amnnesia



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
 - Salvia is illegal in 27 States

Kratom



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

Pharmacology

- ▶ 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 Kratom

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.....



Kratom

- ▶ **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.



Mitragyna speciosa Leaves
Photo by K. Trout, Used by Erowid with Permission



Captain Kratom: “Synthetic Vicodin”



Concern over Kratom: “Legal Phyto-Vicodin?”



**Alleged 15X Concentrated
mitragynine and
7-hydroxymitragynine
extracted from Kratom leaves**

Legal Status Kratom

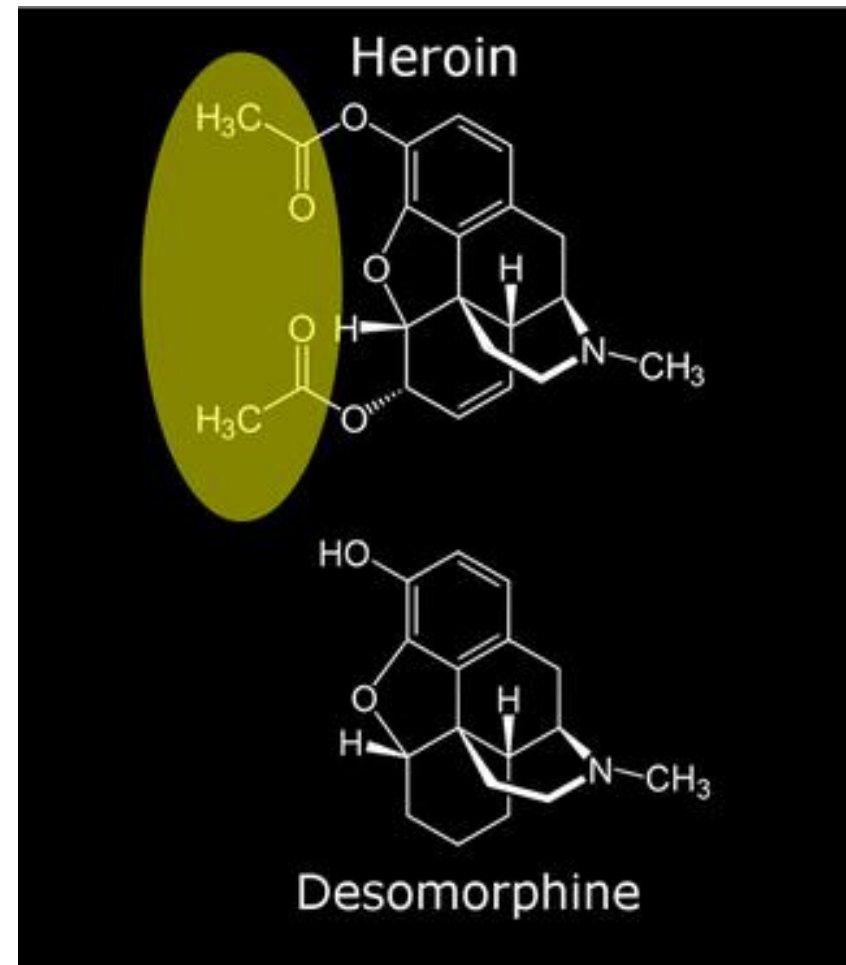


- ▶ Kratom is not controlled under the Controlled Substances Act
- ▶ **Herbal drug of abuse**



Russian Designer Krokodil

- ▶ “Dirty” cousin of morphine
 - Khanka
 - Desmorphine 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



Jenkem, aka “Ass Gas”

Human or Animal excrement fermented to methane gas said to be a ~ psychedelic?



“What’s Old is New”

▶ Hallucinogens

- Psilocybin
 - “Shrooms”
 - 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, dissociative anesthetic



“K” or Special K in U.S.
“Roflcoptr” in U.K.

“What’s Old is New”



Alcohol Without Liquid (AWOL) Ethanol Inhalant Devices



Banned in many States

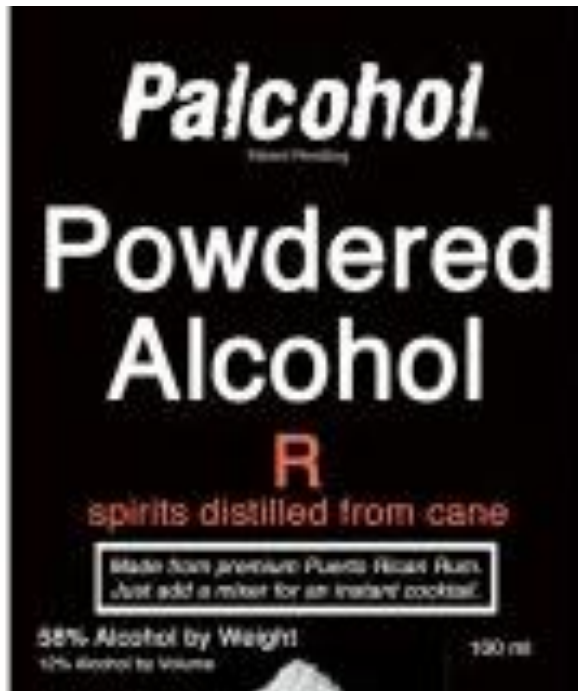
Dry Ice 'Smoking' Alcohol



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

THC Extraction Processes



THC “Hash”

Traditional Hash

- Trichomes are shaken off of the flowers onto silk screens
- Sieved through screens to create kief
- Kief is compressed to make a hash brick



Bubble Hash

- Alternative method for creating hash
- Trichomes are collected through collection of screens
- Utilize ice cold water to sieve trichomes through screens

THC “Concentrates”

- Contain **higher** percent of THC
- Use some type of solvent to extract THC
 1. CO2
 2. Butane
- Not all solvent is removed
- CO2 System \$\$\$
 - Safer
- Butane System \$
 - More Dangerous



THC “Concentrates”

Wax

- Whipping hash oil during purging process
- Easier to manipulate



Oil

- Sticky like honey
- Used in “vape pens”

THC “Concentrates”



Shatter

- Refined version of Hash Oil
- Pressure vacuum utilized
- Semi-transparent
- Yellow or amber color
- ↑ 90% THC

“Dabbing”

- Technique for consuming concentrates
- Place “dab” on heated surface
- Inhale the vapors

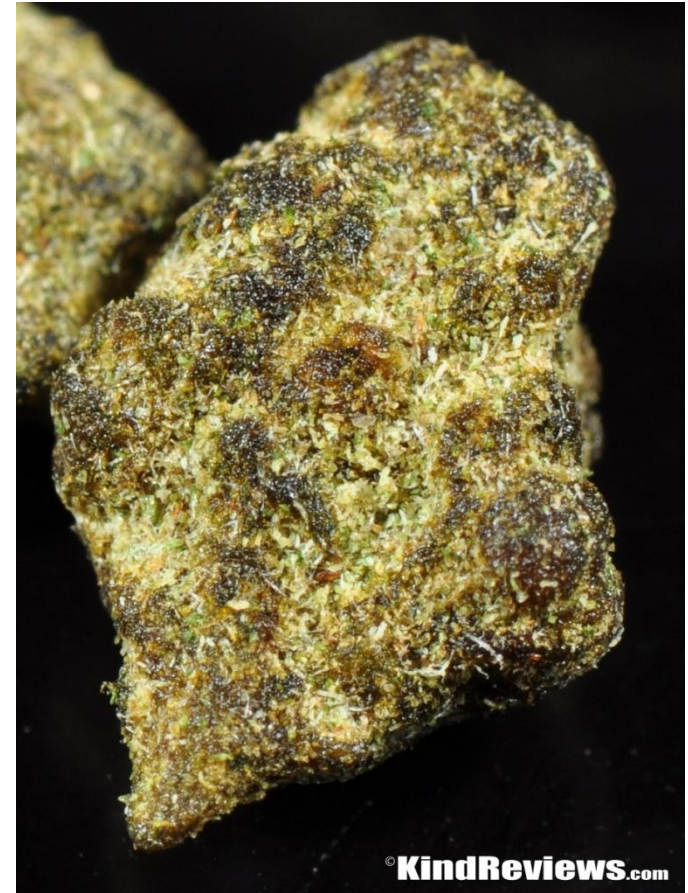


Use of E-cigarette devices to “vape” cannabis products: produces odorless vapor



Cannabis Caviar

- ▶ Marijuana dipped in oil concentrate and rolled in kief
- ▶ High potent THC concentration
- ▶ \$60 per gram
 - At dispensaries
- ▶ “Colorado Caviar”
- ▶ “Moon Bud”



Blogs, Forums, Websites

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