



Will They Turn You into a Zombie? What Clinicians Need to Know about Synthetic Drugs (2nd Edition)

TRAINER'S NAME

TRAINING DATE

TRAINING LOCATION

Training Collaborators

- South Southwest Addiction Technology Transfer Center
 - University of Texas at Austin, School of Social Work
- Pacific Southwest Addiction Technology Transfer Center
 - UCLA Integrated Substance Abuse Programs
- Centre for Addiction and Mental Health, Research Imaging Centre

Special Acknowledgements

- Dr. Volker Auwaerter, University Medical Center Freiburg, Germany
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- James Hall, Nova Southeastern University
- Dr. Barry Logan, National Medical Services Labs, Inc.
- J. Randall Webber, JRW Behavioral Health Services

Introductions

Briefly tell us:

- What is your name?
- Where do you work and what you do there?
- Who is your favorite musician or performer?
- What is one reason you decided to attend this training session?

What are we talking about?

(Insert U.S. Navy Bath Salts video)

“Tales of Bath Salts and Zombie Cannibalism”

- Bath Salts made headlines in summer 2012 when a story of possible cannibalism was reported in Miami, FL
- The Miami-Dade Medical Examiner found no traces of bath salts, LSD, or synthetic marijuana in the perpetrator's system
- The sole psychoactive substance detected was cannabis (marijuana)

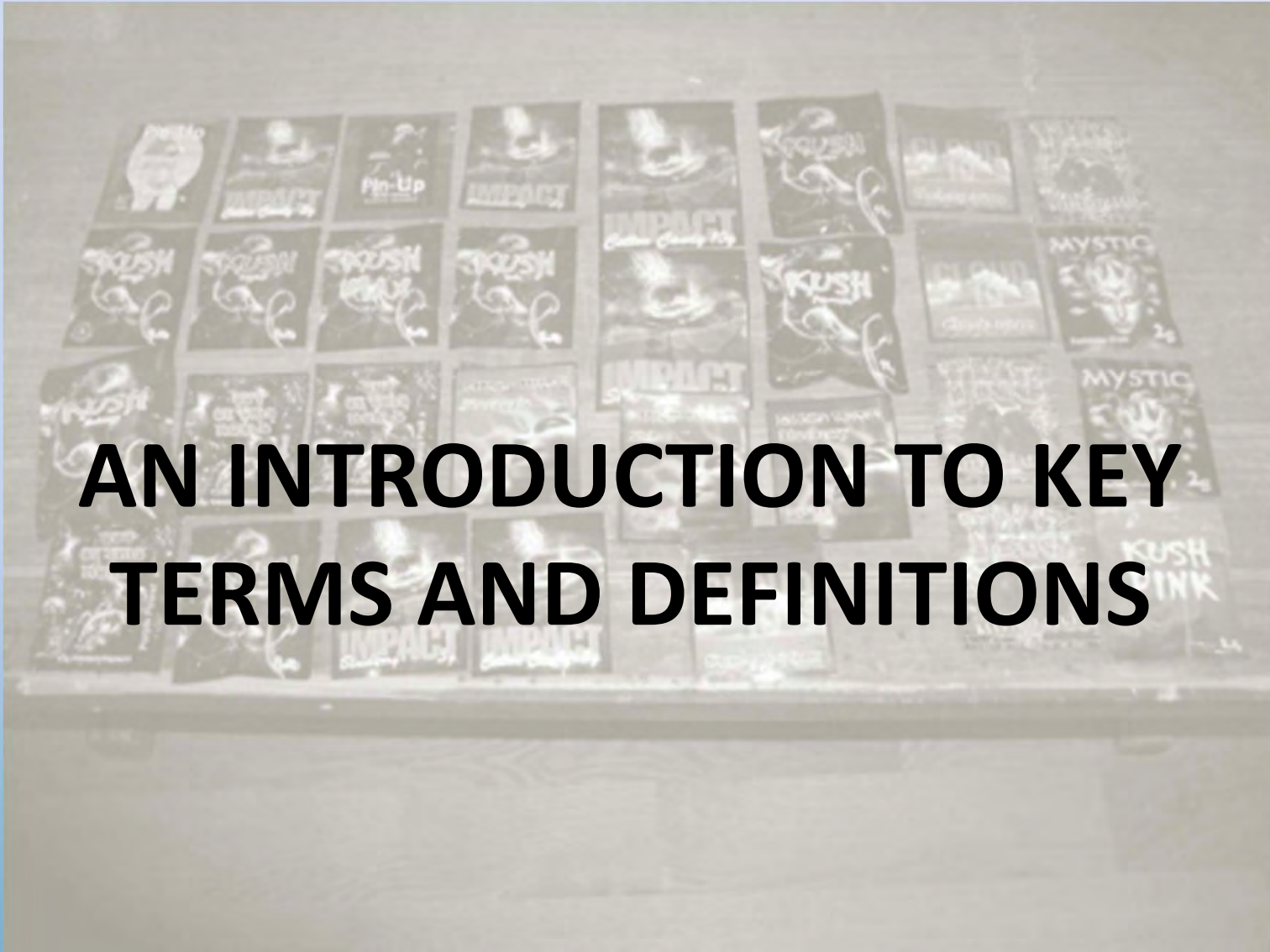
Have you heard these other media reports about “Bath Salts”?

- The man who slashed himself to remove the “wires” in his body
- The mother who left her demon-ridden 2-year-old in the middle of the highway
- The 21-year-old son of a family physician who, after snorting bath salts once, shot himself following 3 days of acute paranoia and psychosis, including hallucinations of police squad cars and helicopters lined up outside his house to take him away

Educational Objectives

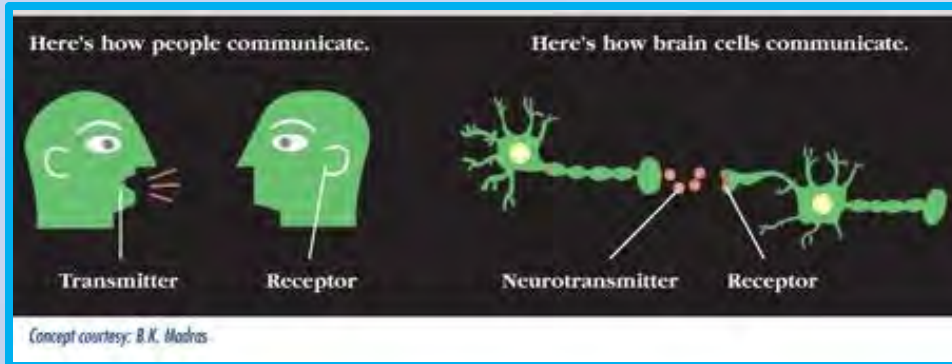
At the end of this presentation, participants will be able to:

1. Identify the key characteristics and effects of synthetic drugs, most notably synthetic cannabinoids and synthetic cathinones.
2. Explain the neurobiology of synthetic drug use, and the differential impact of synthetic drugs vs. “classic” illicit drugs, such as marijuana and cocaine.
3. Describe the current information available on the availability and patterns of synthetic drug use in the United States.
4. List at least three strategies for communicating the dangers involved with synthetic drug use.



AN INTRODUCTION TO KEY TERMS AND DEFINITIONS

How Psychoactive Substances Work



- Because of their chemical structure, alcohol and drugs have dramatic effects on neurotransmitters in CNS
- Effects on:
 - Mental processes
 - Behavior
 - Perception
 - Alertness

Commonly Used Psychoactive Substances

SUBSTANCE	EFFECTS
Alcohol (liquor, beer, wine)	euphoria, stimulation, relaxation, lower inhibitions, drowsiness
Cannabinoids (marijuana, hashish)	euphoria, relaxations, slowed reaction time, distorted perception
Opioids (heroin, opium, many pain meds)	euphoria, drowsiness, sedation
Stimulants (cocaine, methamphetamine)	exhilaration, energy
Club Drugs (MDMA/Ecstasy, GHB)	hallucinations, tactile sensitivity, lowered inhibition
Dissociative Drugs (Ketamine, PCP, DXM)	feel separated from body, delirium, impaired motor function
Hallucinogens (LSD, mushrooms, Mescaline)	hallucinations, altered perception

“Designer” Psychoactive Substances

Psychedelics

5'-substituted tryptamines

Related to: bufotenin

5-MeO-DMT 5-MeO-DALT
5-MeO-MIPT 5-MeO-MET
5-MeO-DIPT 5-MeO-DPT
5-MeO-AMT
5-MeO-AET

NBOMe series

Related to: 2C-x series

25C-NBOMe
25I-NBOMe
25D-NBOMe

2C-x series

Related to: mescaline

2C-B 2C-D
2C-I 2C-E
2C-T-7 2C-P
2C-B-FLY

4'-substituted tryptamines

Related to: psilocin

4-AcO-DMT 4-HO-DPT
4-AcO-DET 4-HO-DALT
4-HO-MIPT 4-HO-DIPT
4-MES-DMT

Ergolines

Related to: LSD, LSA

ALD-52
LA-SS-Az (LSZ)
PRO-LAD
ETH-LAD

Psychedelic amphetamines

Related to: 2C-x, amphetamine

DOB DOM
DOC DOET
DOI TMA-2
Bromo-dragonFLY

AMT
AET
MIPT
DIPT
DALT
NMT
DET
DPT

Stimulants

Cathinones

Related to: methcathinone, cathinone, amphetamine, MDMA

Mephedrone Pentedrone
Methylone Flephedrone
Butylone bk-PMMA
Benzedrone
4-MEC

Piperazines

Related to: piperazine

BZP mCPP
MBZP pFPP
DBZP MeOPP
MDBZP TFMP

5-APB
6-APB
6-ADPB
4-methylaminorex
4-ethylaminorex

Phenylalkyl-pyrrolidines

Related to: Pyrovalerone, Prolintane

MDPV α-PPP
α-PVP MDPVP
α-PBP MOPVP

MDAI
MDAT
2-AI
5-AI
Dimethocaine

Substituted amphetamines

Related to: amphetamine, methamphetamine

4-FA 3-FMA
4-FMA PMA
3-FA PMMA

Methiopropamine Ethylphenidate
Camfetamine

Cannabinoids

Functionally related to naturally occurring cannabinoids including THC

Naphthoylindoles

JWH-018 JWH-019
JWH-073 JWH-081
JWH-122 JWH-200
AM-1221
AM-2201

Phenylacetylindoles

JWH-250
JWH-251
JWH-203
RCS-8

WIN-55,212-2 AB-001
CP-47,497
CP-47,497, C8 homologue
CP-55,940
JWH-133
JWH-161 CB25
CB52

Benzoylindoles

AM-694
AM-1241
AM-2233
RCS-4

Cyclopropanoyl-indoles

UR-144
5F-UR-144
A-834,735
A-796,260

Naphthoylpyrroles

JWH-307
JWH-147
JWH-030

HU-210
HU-211
HU-331 O-1812
JWH-175

Dissociatives

Related to: ketamine, PCP

Methoxetamine
3-MeO-PCP
4-MeO-PCP
3-MeO-PCE
2-MeO-ketamine

Sedatives

Opioids

Related to: morphine, fentanyl, heroin

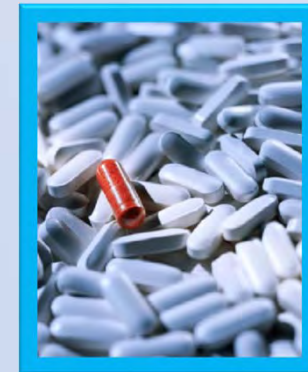
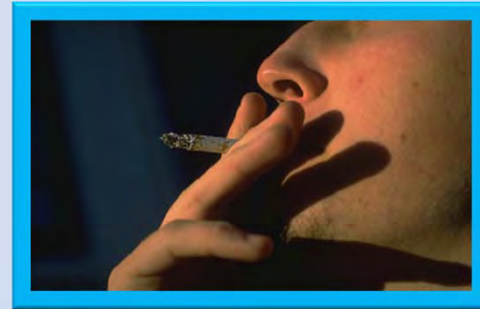
α-methylfentanyl
3-methylfentanyl
MPPP
O-desmethyltramadol
7-acetoxymitragynine
Metonitazene
AH-7921

Phenazepam

Why People Use Psychoactive Substances

Why Start?

- Experimentation
- Peer Pressure
- Medical



Why Continue?

- Relieve stress/pain
- Function better
- Have fun/relax
- Cope with mental health disorders



After repeated drug use, “deciding” to use drugs is no longer voluntary because

DRUGS CHANGE THE BRAIN!



Addiction
Risky user
Alcoholic
Substance abuse
Addict
Abuser
Substance Use Disorder (SUD)
Chemical
Dependence
Dependence

The language we use matters

Drug Addict
Abuse
Recreational user
Substance Misuse

What is a Substance Use Disorder?

- A substance use disorder (SUD) is a continuum of problematic use of substances:
 - On one end of the continuum are people who are using at risky levels. They may not be having problems yet, but are at risk of developing them if current level of use continues.
 - On the other end, SUD is a complex, chronic, relapsing brain disease characterized by compulsive, and at times, uncontrollable drug craving, seeking, and use that persist even in the face of extremely negative consequences.

Some Additional Important Terminology

- Psychological craving
- Tolerance
- Withdrawal symptoms

Psychological Craving

- Psychological craving is a strong desire or urge to use drugs. Cravings are most apparent during drug withdrawal.



Tolerance

- Tolerance is a state in which a person no longer responds to a drug as they did before, and a higher dose is required to achieve the same effect.



SOURCE: Krasnegor, N.A. (Ed.). (1978). *Behavioral Tolerance: Research and Treatment Implications*, NIDA Research Monograph 18. Rockville, MD: Department of Health, Education, and Welfare.

Withdrawal

The following symptoms may occur when substance use is reduced or discontinued:

- Tremors, chills
- Cramps
- Emotional problems
- Cognitive and attention deficits
- Hallucinations
- Convulsions
- Death



A REVIEW OF SYNTHETIC DRUGS



User Report #1 (Drug not specified)

- *“This is the worst experience I’ve ever had”*
- *“The most anxiogenic substance I’ve ever used”*
- *“Nausea, vomiting, heart pounding like I’m going to have a heart attack”*
- *“Not sure whether I just said that, thought it, or read it”*
- 2 hours later: *“Will never take this again”*

User Report #2 (Synthetic Cannabinoid)

- 3 individual “hits” from a small pipe
- “Organic” taste/no chemical odor or taste
- 5 minutes: *“Feels like cannabis”*
- 10 minutes: *“Like an intense cannabis high”*
- *“More than 3 puffs might be too much”*

“Designer” Psychoactive Substances

Two classes:

1. Stimulants: mephedrone, MPDV, piperazines, “bath salts”
2. Psychedelics: 2C-B, mescaline, DMT, etc.

Differences in users:

1. Stimulant users **similar to** other ecstasy users; (shifting to mephedrone and MPDV due to shortage of Ecstasy?)
2. Psychedelic users **started ecstasy use earlier**; were more frequent users; **used multiple substances**; had more legal, mental health, and social problems.

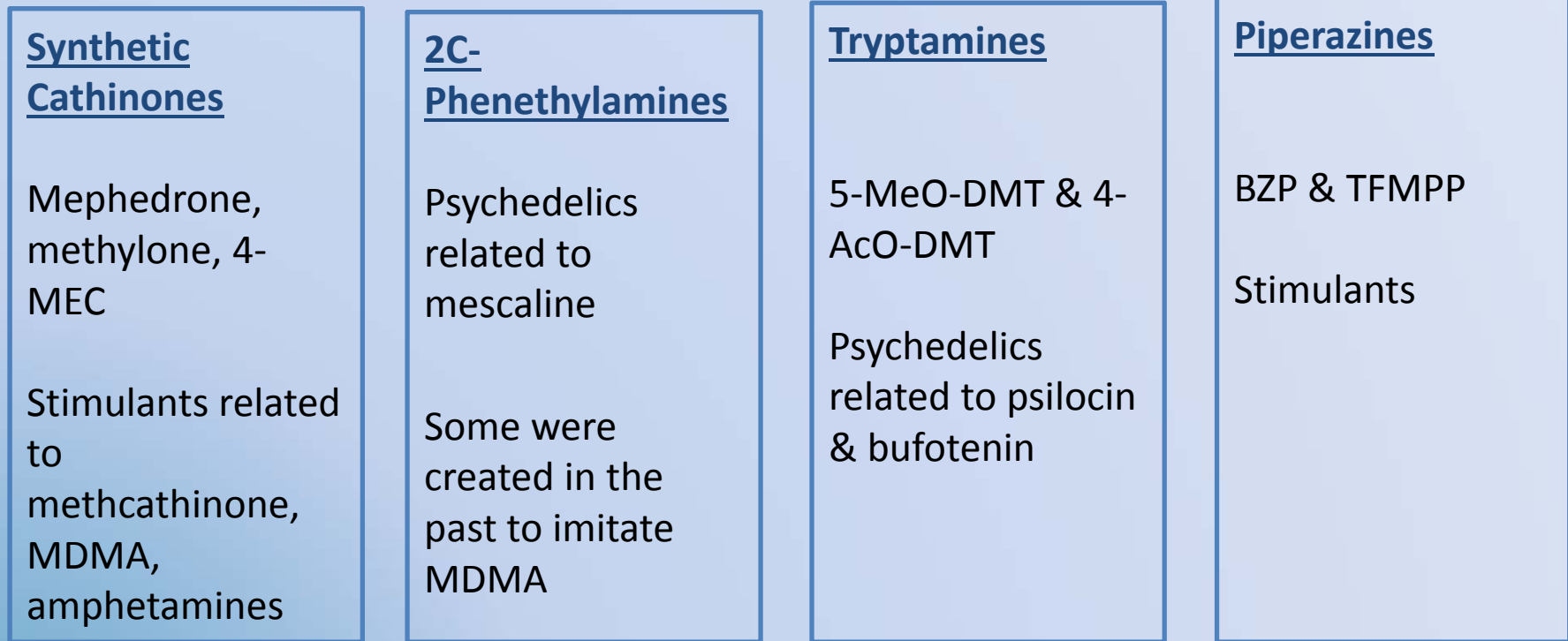
Examples of Major Synthetic Psychedelics

DRUG NAME	DESCRIPTION
2C-I	Phenethylamine, via PiHKAL; stimulant and hallucinogen Slow onset (1 hr); long duration of action (8-10 hr.)
2C-B	Phenethylamine, via PiHKAL; visuals Faster onset; shorter duration than 2C-I
5-MeO-DMT	Tryptamine; naturally occurring (toad, shamantic brews) Smoked: almost immediate, very intense, short effect (<30 min)
DMT	Tryptamine; naturally occurring Smoked: almost immediate, very intense, short effect (<20 min)

Examples of Major Synthetic Stimulants

DRUG NAME	DESCRIPTION
Mephedrone	4-methyl-methcathinone; “Miaow” Similar to cocaine and MDMA (ecstasy)
Methylone	β -MDMA: 3,4-methylenedioxy-methcathinone; “Explosion” Similar to cocaine and MDMA (ecstasy)
MDPV	3,4-methylenedioxyprovalerone; MDPV; “NRG-1” (Brandt, 2010); “Ivory Wave” Stimulant with rapid onset; 2-4 hour duration of action
BZP	1-benzyl-piperazone Similar to amphetamine 1/10 potency of <i>d</i> -methamphetamine

From the term “Bath Salts” to...



And **Dissociatives** related to ketamine and PCP and **Opioids** related to morphine, fentanyl, and heroin.



Synthetic Drugs



- Not really “Spice,” “Bath Salts,” “Incense,” or “Plant Food”
- Chemically-based; not plant derived
- Complex chemistry
- Constantly changing to “stay legal”
- Need to prove “intended to use” to convict in some areas

Synthetic Cannabinoids

Spice vs. "Spice"



≠



Synthetic Cathinones

Bath Salts vs. “Bath Salts”



≠



Marijuana (Cannabis)



- Often called pot, grass, reefer, MJ, weed,
- A mixture of the dried, shredded leaves, stems, seeds, and flowers of *Cannabis sativa*—the hemp plant
- Most commonly used drug in the U.S.
- Delta-9-tetrahydrocannabinol (THC) is the main active ingredient in marijuana
- Common effects include: euphoria, relaxation, heightened sensory perception, laughter, altered perception of time, and increased appetite
- May also produce anxiety, fear, distrust, or panic, and can lead to severe mental health problems for some users.

Synthetic Cannabinoids

- Wide variety of herbal mixtures
- Marketed as “safe” alternatives to marijuana
- Brand names include: “Spice,” “K2,” fake weed, “Yucatan Fire,” “Skunk,” “Moon Rocks,” herbal incense, “Crazy Clown,” “Herbal Madness”
- Labeled “not for human consumption”
- Contain dried, shredded plant (inert) and chemical additives that are responsible for their psychoactive effects.



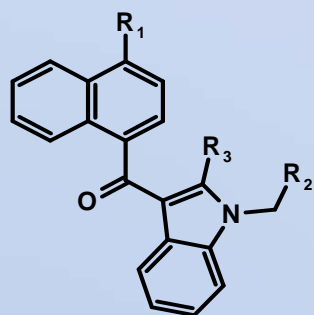
Synthetic Cannabinoids

- Mainly abused by **smoking** (alone or with marijuana); may also be prepared as an herbal infusion for **drinking**.
- Many of the active chemicals most frequently found in synthetic cannabis products have been classified by the DEA as Schedule I controlled substances, making them **illegal to buy, sell, or possess**.
- Multiple “generations” of drugs.



Synthetic Cannabinoids: The Major Compounds

a) Naphthoylindoles



JWH-018

JWH-073

Sts-135

Pb-22

JWH-081

UR-144

JWH-122

A-796,260

Urb-602

JWH-007

AM-2201

MAM-2201

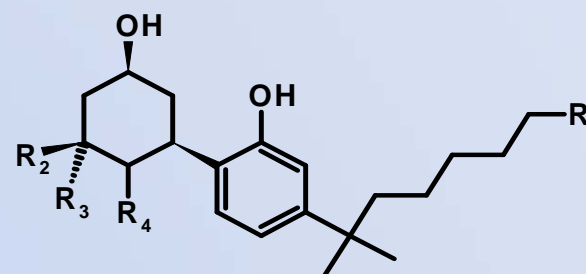
AKB48

AM-1220

XLR-11

5-Fluoropentyl-JWH-122

b) Cyclohexylphenoles



CP-47,497-C8



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



Factors Associated with Synthetic Cannabinoid Popularity

- They induce psychoactive effects
- They are readily available in retail stores and online
- The packaging is highly attractive
- They are perceived as safe drugs
- They are not easily detectable in urine and blood samples

Six States Report Cases of Kidney Damage Linked to Synthetic Cannabinoids

- Sixteen cases of kidney damage reported by CDC
 - All admitted to hospital
 - Five required hemodialysis
- Fifteen of the patients were male; ranged in age from 15 to 33, no history of kidney disease
- In early Feb 2013, UA-Birmingham reported 4 cases of previously healthy young men, whose acute kidney injury was associated with synthetic marijuana
 - Symptoms of nausea, vomiting, and abdominal pain
 - All four men recovered kidney function, and none required dialysis

Synthetic Cannabinoid Use Leads to Dangerous Symptoms in Pregnant Women

- Leads to symptoms similar to those caused by dangerous conditions known as preeclampsia and eclampsia
 - Preeclampsia is marked by high blood pressure and a high level of protein in the urine
 - Preeclampsia can lead to eclampsia, which can cause a pregnant woman to develop seizures or coma, and in rare cases is fatal

Case Example: Synthetic Cannabinoid Use among Pregnant Woman

- A woman (35 weeks pregnant) suffered a seizure and appeared agitated
 - High blood pressure and protein in urine, treated for eclampsia
 - An emergency C-section was performed (baby in distress)
- The woman screened negative for drugs, but an anonymous caller reported the woman regularly smoked “Spice Gold,” a synthetic cannabinoid.
 - Spice Gold cannot be detected with a standard urine test.
- The baby tested negative for drugs.
- The woman required psychiatric care for psychotic behavior the day after delivery.
 - *“This was not a pregnancy problem but a drug problem. Eclampsia is cured with delivery of the baby, but she did not get better after delivery.”* (Dr. Cindy Lee)

Khat



- Pronounced “cot”
- Stimulant drug derived from a shrub (*Catha edulis*) native to East Africa and southern Arabia
- Use is considered illegal, because one of its chemical constituents, cathinone, is a Schedule I drug
- Khat found in the U.S. often comes in by mail from Africa

Synthetic Cathinones

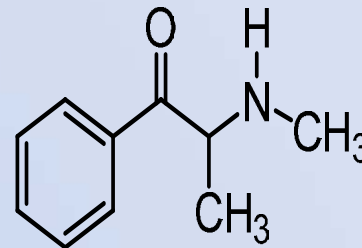
- Could be MDPV, 4-MMC, mephedrone, or methyldone
- Sold on-line with little info on ingredients, dosage, etc.
- Advertised as legal highs, legal meth, cocaine, or ecstasy
- Taken orally or by inhaling
- Serious side effects include tachycardia, hypertension, confusion or psychosis, nausea, convulsions
- Labeled “not for human consumption” to get around laws prohibiting sales or possession



Synthetic Cathinones are β -keto ('bk') Analogues of Amphetamine



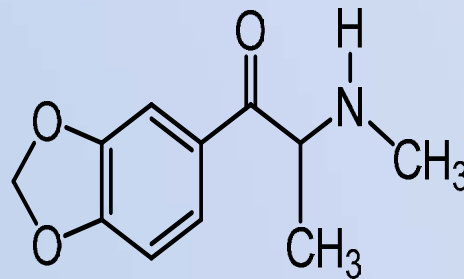
Methamphetamine



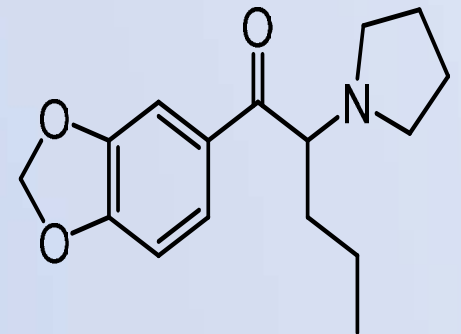
Methcathinone



4-Methylmethcathinone
(Mephedrone)



3,4-Methylenedioxy-methcathinone
(Methylone)



3,4-Methylenedioxy-pyrovalerone
(MDPV)

Sources and Continuing Availability

- A number of synthetic marijuana and bath salt products appear to **originate overseas** and are manufactured in the **absence of quality controls** and **devoid** of governmental **regulatory oversight**.
- The large profits from sales, plus the fact that these chemicals can be easily synthesized to stay one step ahead of control, indicate there is **no incentive to discontinue retail distribution** of synthetic cannabinoid products under the current statutory and regulatory scheme.

Challenges with Chromatography Screening

- Lack of availability of the reference standard for new drugs
- Variable quality of reference standards
- Lack of purity and labeled internal standards
- Chemical similarity of new drugs within a class requires great care with identification
- Sensitivity (correctly IDs the drug)



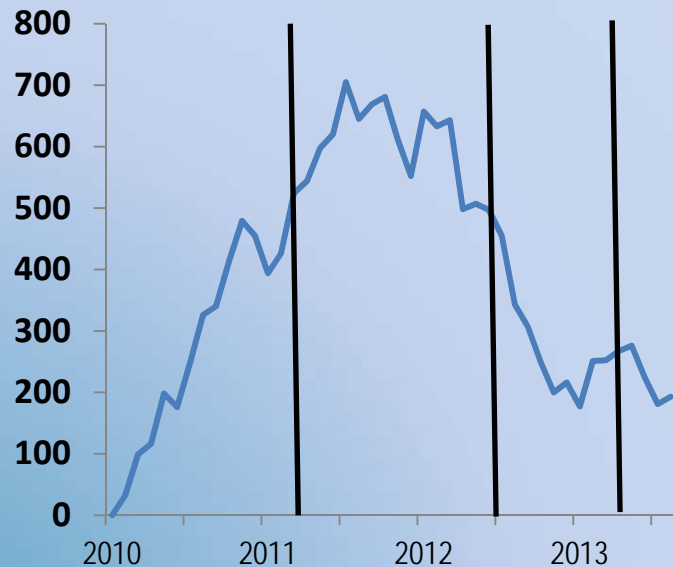
Synthetic Drug Testing Protocol – What to Consider

- Questions to consider when selecting a toxicology laboratory:
 - For which synthetic drugs should you test?
 - How many derivatives/formulations can the laboratory detect with their test?
 - Are the newest generations (4th and above such as the AM, XLR, and UR versions) detected?
 - How much does the test cost?

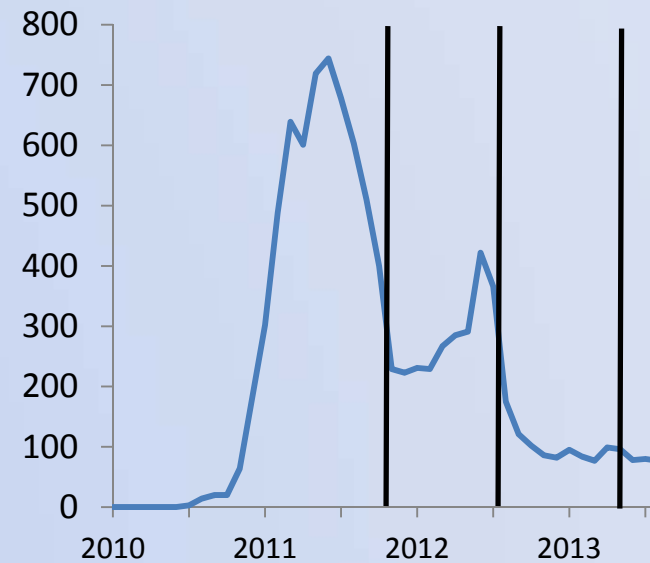


Human Exposure Calls to U.S. Poison Centers on Synthetic Cannabinoids and Cathinones and the Effect of Federal Regulations

The Effect of Federal Controls on Synthetic Cannabis Calls to Poison Centers



The Effect of Federal Controls on Synthetic Cathinone Calls to Poison Centers



SOURCE: American Association of Poison Control Centers, 2010-2013 data.

“New Zealand’s Designer Drug Law Draws Global Interest”

- The law, enacted in July 2013, represents a U-turn from the traditional approach of retroactively banning synthetic drugs
- New Zealand will attempt to regulate designer drugs, allowing their sale if they go through rigorous safety testing similar to that for pharmaceuticals
- Giving users a high wouldn't be a reason to ban them

THE EFFECTS OF SYNTHETIC DRUGS



“People high on these drugs can get very agitated and violent, exhibit psychosis, and severe behavior changes...some have been admitted to psychiatric hospitals and have experienced continued neurological and psychological effects.”

(Dr. Rick Dart, AAPCC President)

Short-Term Effects of Synthetic Cannabinoids

- Loss of control
- Lack of pain response
- Increased agitation
- Pale skin
- Seizures
- Vomiting
- Profuse sweating
- Uncontrolled spastic body movements
- Elevated blood pressure
- Elevated heart rate
- Heart palpitations

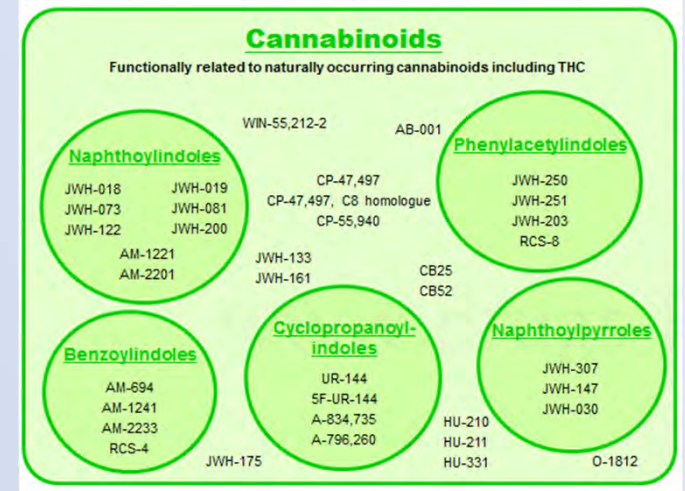
In addition to physical signs of use, users may experience severe paranoia, delusions, and hallucinations.

Cannabis vs. Synthetic Cannabinoids: Effects Seen in Clinical Cases

- Most symptoms are similar to cannabis intoxication:
 - Tachycardia
 - Reddened eyes
 - Anxiousness
 - Mild sedation
 - Hallucinations
 - Acute psychosis
 - Memory deficits
- Symptoms not typically seen after cannabis intoxication:
 - Seizures
 - Hypokalemia
 - Hypertension
 - Nausea/vomiting
 - Agitation
 - Violent behavior
 - Coma

Synthetic Cannabinoids: Other Considerations

- Unlike cannabis, synthetic cannabinoids have no therapeutic effects
 - *Example: no cannabidiol (anti-anxiety), so mood effects unpredictable*
- Packets can contain other psychoactive substances: opioids, oleamide, harmine/harmaline (MAO-Is) that can interact with the synthetic cannabinoid
- Cancer-causing potential of inhaling smoke from these compounds unknown



“A Tale of Two Cases” – Case #1

- 33 year-old male
- Employed as an imaging technician
- Stable 8-year marriage
- Previous drug use: marijuana, alcohol, tobacco
- Used “herbal incense” daily
- After 3 months of use, suddenly experienced a panic attack
- Immediately discontinued all alcohol/drug use
- Repeated episodes of anxiety still occurring after 18 months of abstinence

“A Tale of Two Cases” – Case #2

- 16 year-old female
- In treatment for alcohol dependency
- History of bi-polar disorder
- Smoked 3 “hits” of “herbal incense”
- 10 minutes later (8:00 p.m.), experienced psychotic episode
- Following observation at hospital, returned to normal (12:00 a.m.)
- Next day, no apparent after-effects

Group Discussion: Why the Discrepancy in Reported Effects?

What factors do you think played a role in the differential effects of “herbal incense” on these two users?

Clinical Symptoms of Synthetic Cathinone Use in Patients Admitted to the Emergency Department (N=236)

Agitation	82%
Combative/Violent behavior	57%
Tachycardia	56%
Hallucinations	40%
Paranoia	36%
Confusion	34%
Myoclonus/Movement disorders	19%
Hypertension	17%
Chest pain	17%
CPK elevations	9%

Effects of Mephedrone

Intended Effects:

- Euphoria
- Stimulation
- Enhanced music appreciation
- Decreased hostility
- Improved mental function
- Mild sexual stimulation

Unintended (Adverse) Effects:

- Bruxism (teeth grinding)
- Dilated pupils
- Poor concentration
- Problems focusing visually
- Poor short-term memory
- Hallucinations
- Delusions

Effects of Methylone

- Central Nervous System stimulation
- Euphoria or dysphoria
- Anxiolysis/Anxiogenesis
- Increase in sociability
- Insomnia
- Restlessness
- De-realization/
De-personalization
- Hallucinations
- Psychosis
- Tachycardia (rapid pulse)
- Hypertension (high BP)
- Hyperthermia
- Sweating
- Dilated pupils
- Nystagmus
- Trismus (inability to open the mouth)
- Bruxism (teeth grinding)
- Anorexia
- Nausea and vomiting

Synthetic Stimulants: Cognition



- Same changes in mental state as classic stimulants: impulsive acts, decision-making, judgment → can lead to risky behavior in nightlife context
- Single human study: 20 mephedrone users snorting in own homes (vs. drug-free visit, vs. controls)
 - Regardless of high vs. not: worse memory than controls, some personality differences (schizotypy, depression)
 - High caused drug-wanting, “speedy” effects, increased speed of movement, worse working memory

Bath Salts in Michigan

Case Report – MMWR, May 2011

- First report to summarize epidemiology of bath salt ED cases
- Based on 35 people who had ingested, inhaled, or injected bath salts and subsequently visited a Michigan Emergency Department (ED) between 11/13/10 and 3/31/11
- Patients presented with hypertension, tachycardia, tremors, motor automatisms, mydriasis, delusions, and paranoia
- No relationship found between route of administration and severity of illness

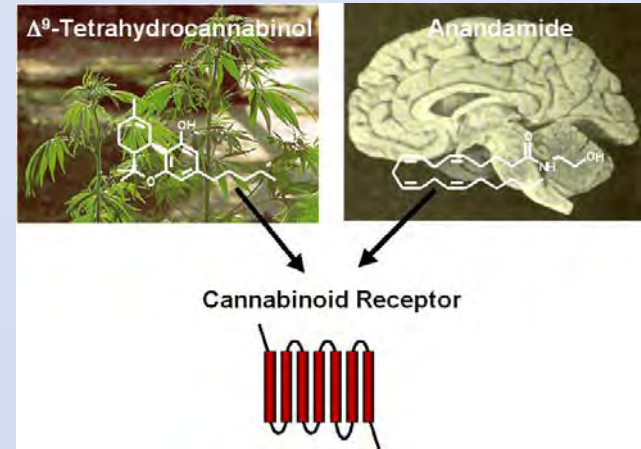
Maine Reports Serious Infections Linked with Injection of Bath Salts

- Four cases of invasive Group A streptococcal infections
- Dangerous because it can cause infections of heart and bloodstream
- Two patients developed Streptococcal Toxic Shock Syndrome
 - Can cause rapid drop in blood pressure and organ failure
- One patient developed necrotizing fasciitis, a disease that progresses quickly, destroying muscles, fat, and skin tissue



THE NEUROBIOLOGY OF SYNTHETIC DRUG USE

Cannabinoids



- Neurobiological Concerns:
 - Shown to induce dopamine release (although less directly than stimulants) → brain reward signal → potential for compulsive use/addiction
 - Shown to impact regions of the brain responsible for coordination, problem-solving, sense of time, motivation, etc. → impaired when high
 - Effects on regions underlying learning and memory → possible long-term effects
 - Possible link to psychosis and schizophrenia

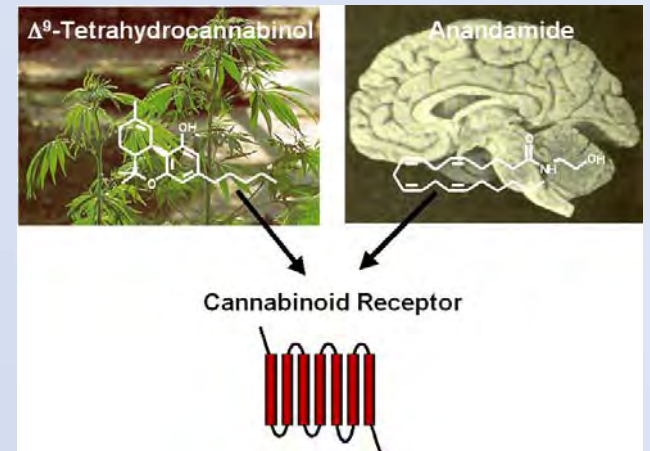
“Classic” Cannabinoids

- Endocannabinoid system (“endo” = within)

Only recently discovered, unusual, not well understood

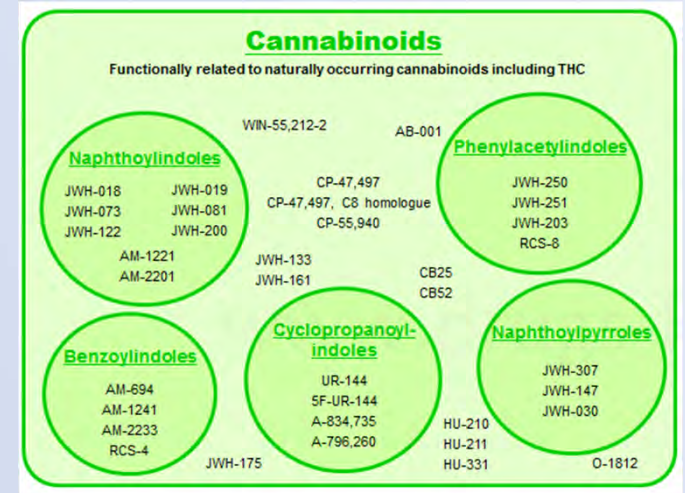
- Receptors: CB1 (brain), CB2 (immune system)
- Transmitters: Anandamide, 2-AG

- THC: binds to CB1 receptor
 - But not very well (low affinity) and not very good at inducing effects (partial agonist)
 - But unlike endocannabinoid transmitters, not degraded immediately, so CB1 activation is extended/exaggerated compared to anandamide



Synthetic Cannabinoids

- No structural similarity to THC, but same effects profile
 - Bind to CB1 and CB2 receptors
 - Same types of physical effects & impairments
 - In animals: signs of “high” similar, but at 2-14x lower dose
- The problem: Stronger & longer-lasting than THC
 - Better binding to receptors (high affinity/potency) AND each binding event has greater effect (full agonist)
 - 4x higher affinity for CB1, 10x for CB2
 - Longer half-life so effects longer lasting
 - Products of break-down (metabolites) also psychoactive
 - Together: More, more-likely, and longer-lasting adverse effects (especially if dosing is based on cannabis)



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



Contents lists available at SciVerse ScienceDirect

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journal homepage: www.elsevier.com/locate/forsciint

URB-754: A new class of designer drug and 12 synthetic cannabinoids detected in illegal products[☆]

Nahoko Uchiyama, Maiko Kawamura, Ruri Kikura-Hanajiri, Yukihiro Goda *

National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo 158-8501, Japan

Stimulants

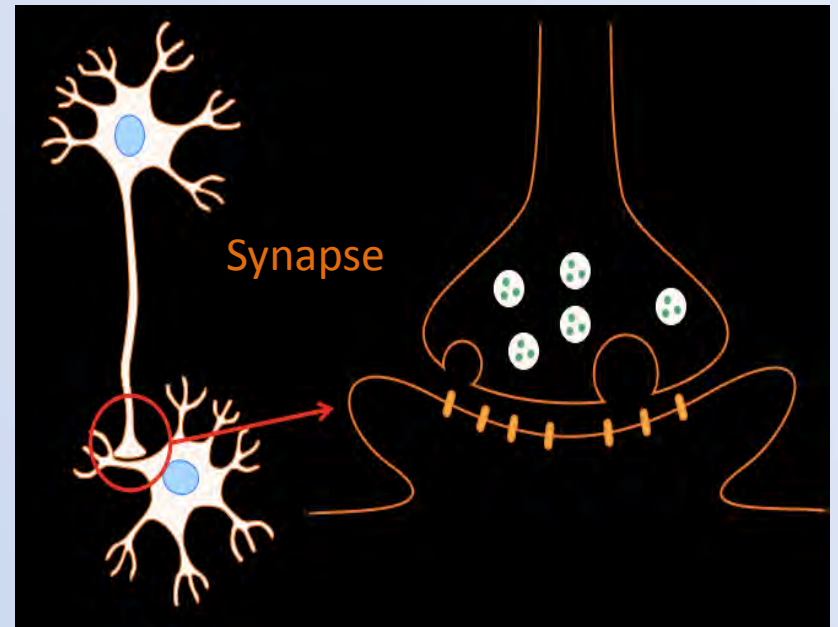
- Neurobiological Concerns
 - Addiction
 - Compulsive chase and use
 - Physical health
 - Cardio-vascular (heart rate, blood pressure, etc.)
 - Body temperature
 - Long-term brain changes
 - Mental state
 - Risky decisions, impaired judgment, impulsive acts, etc.



“Classic” Stimulants

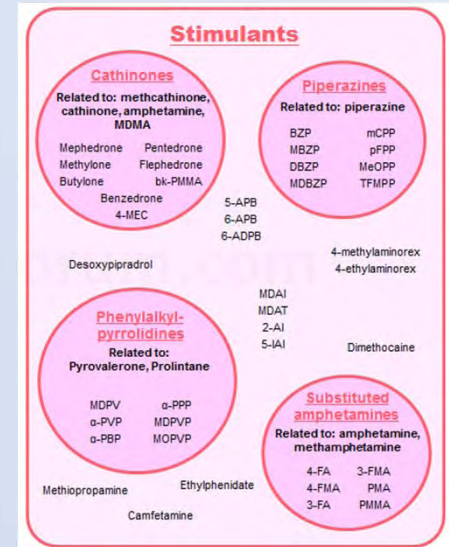
Direct action on synapse

- Amphetamine, cathinone: induce dopamine release
- Cocaine, methylphenidate (Ritalin): block dopamine removal
- MDMA: additional effects on serotonin
 - Dopamine effects less strong, so less “reward,” so animals do not self-administer as much
 - Synthetic stimulants are variations on this theme, BUT:
“Very subtle structural modifications can yield profoundly different behavioural, neurochemical, and neurotoxicological effects.”



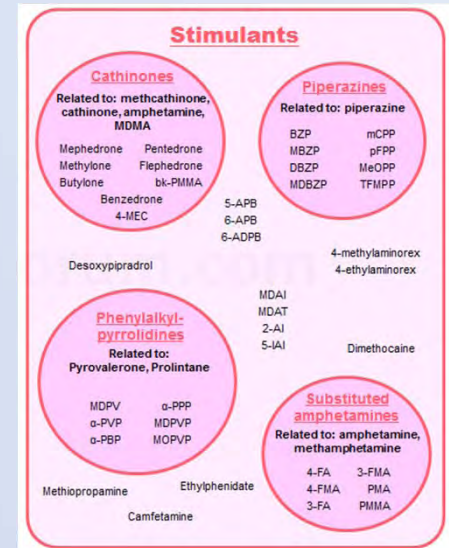
Synthetic Stimulants

- In general: dopamine ↑ and animals like/want/work for drug
 - Sign of high abuse potential
 - Recreational use can progress easily to compulsive use



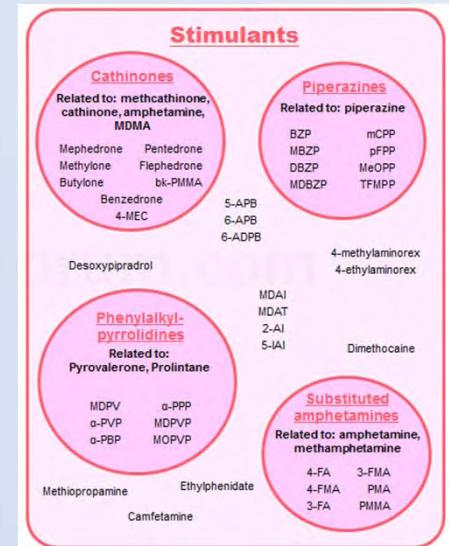
Synthetic Cathinones

- Block transporters (removal)
 - Rank at **DAT**: MDPV/pyrovalerone >> cocaine, amphetamine/MA, methcathinone, naphyrone > mephedrone, butylone, methylone, etylone, flephedrone, MDEA > cathinone, MDMA, MBDB
 - Rank at **SERT**: MDEA, MDMA, naphyrone > MBDB, cocaine, ethylone, mephedrone, butylone >> rest
 - Rank at **NET** (fight/flight): MDPV, pyrovalerone > amph/MA, methcathinone > cathinone, mephedrone, flephedrone, naphyrone > MDMA, cocaine, methylone > MDEA, butylone, ethylone, MBDB



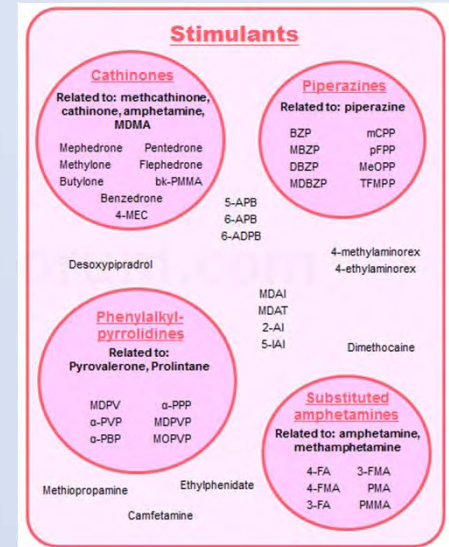
Synthetic Cathinones

- Also release
 - **Dopamine**: Amph/MA, cathinone, methcathinone, mephedrone*, flephedrone > MDMA (potency low)
 - **Serotonin**: MDMA, MDEA, MBDB, methylone, ethylone, butylone, mephedrone
 - Amph/MA, methcathinone, flephedrone only at very high concentrations
- Pyrovalerone, naphyrone, MDPV: **NO** dopamine or serotonin release, but still extremely good at blocking removal – 10x cocaine



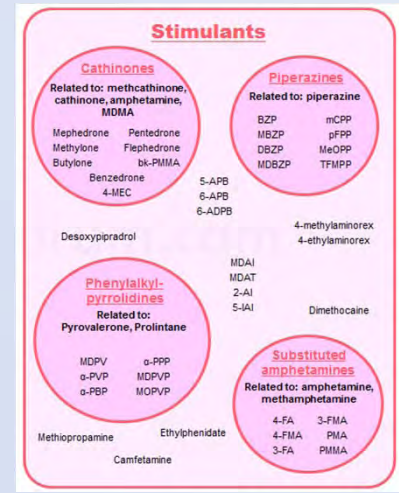
Synthetic Cathinones vs. “Classic” Stimulants

- Mephedrone originally thought to be more like MDMA than amphetamine b/c of serotonin effects, but dopamine release more like amphetamine → greater abuse liability
- In and out of brain faster than MDMA → greater potential for repeated binge use
- Effects on body temperature regulation different from MDMA: “Adverse effects cannot be extrapolated from previous observations on MDMA” (Shortall)
- MDPV: greater self-administration than even MA



Synthetic Stimulants: Physical Concerns

- Norepinephrine (fight/flight) system: hyper-active movement, body temperature regulation, cardio-vascular effects
- Especially MDPV
 - Better than cocaine (x10) at producing hyper-active movement, increased heart rate & blood pressure
 - Itself does not disrupt body temperature regulation (like MA or MDMA do), but heart rate/blood pressure **interact with room temperature** (Fantegrossi)
- Neurotoxicity (“brain damage”): some evidence for serotonin and dopamine depletion in animals
 - Mephedrone NOT toxic to dopamine cells (several reports)
 - ****BUT: Mephedrone enhances toxic effects of amph/MA and MDMA!** (Angoa-Perez) → co-administration frequent, even if accidental

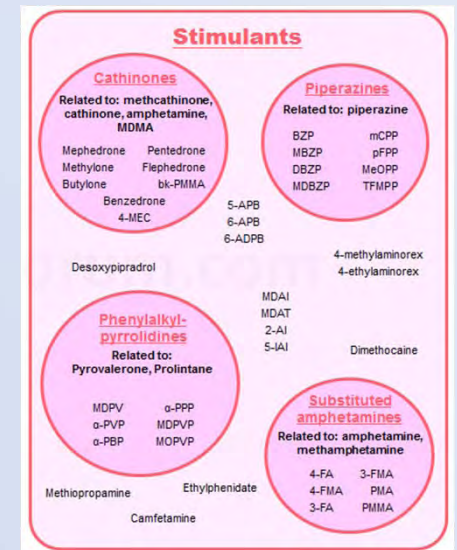


MDPV Addiction Potential

- August 2013 journal *Neuropharmacology*
- Animal self-administration
- Found to be more rewarding than methamphetamine and poses a substantial threat for compulsive use that is potentially greater than that for methamphetamine

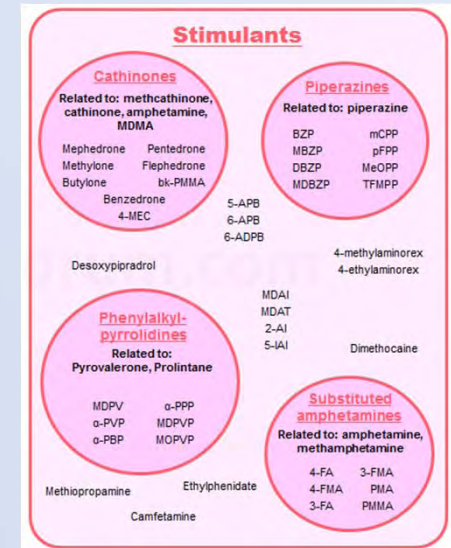
Piperazines

- BZP, TFMPP: Release dopamine and serotonin, but less than MDMA or MA
- mCPP: serotonin release; human study: no reinforcing or stimulant-like effects (unlike MA/MDMA) (Tancer)
- **BZP + TFMPP sometimes taken together because
 - Roughly adds up to to low-dose MDMA → but combination induces seizures (Baumann)



PMA/PMMA

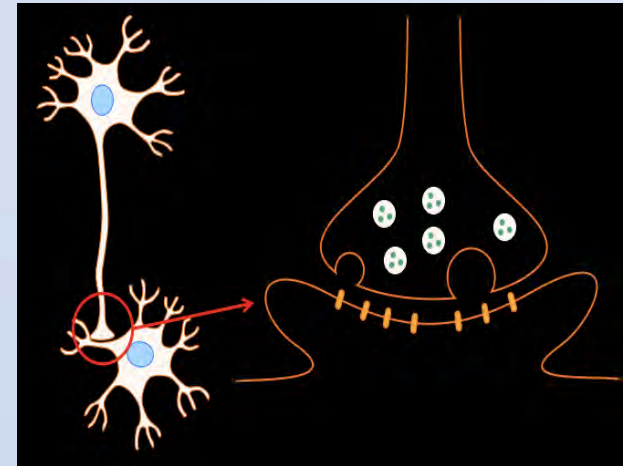
- Serotonin effects different from MDMA: **delayed peak** (risk of redose/overdose while waiting), **effects last longer**, serotonin syndrome
- Evidence for **long-term serotonin depletion** (but not as pronounced as MDMA)
- Dopamine **not affected long-term**
- ****Can interact with MAO-Is and temperature to produce unexpected effects (Stanley)**



Dissociative Anesthetics

Neurobiological Concerns

- Addiction/dependence
- Dissociation
- Mental state that mimics psychosis
- Interaction with other sedative drugs (e.g., alcohol)



“Classic” dissociatives (PCP, Ketamine)

- Block receptor in the glutamate system (NMDA)
 - Slows everything down
- Bind to brain opiate receptors
- Block removal of dopamine, serotonin, norepinephrine from the synapse (“reward”)

Synthetic Dissociatives

Methoxetamine

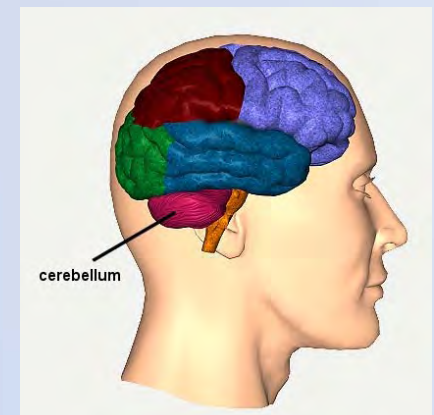
Same as classics, but additionally:

- Higher likelihood of abuse
 - Blocks more dopamine and serotonin removal from synapse (also 3-MeO-PCE)
 - Binds to & activates receptors: dopamine, serotonin, opiate systems
- Similar effects profile as ketamine, **BUT**
 - Takes longer to come on → risk of redosing
 - Side effects more severe
 - Mood disturbance/suicide attempts
 - Possibly toxic to cerebellum
 - Lasts longer → unwanted side effects

Dissociatives

Related to: ketamine, PCP

Methoxetamine
3-MeO-PCP
4-MeO-PCP
3-MeO-PCE
2-MeO-ketamine



Psychedelics

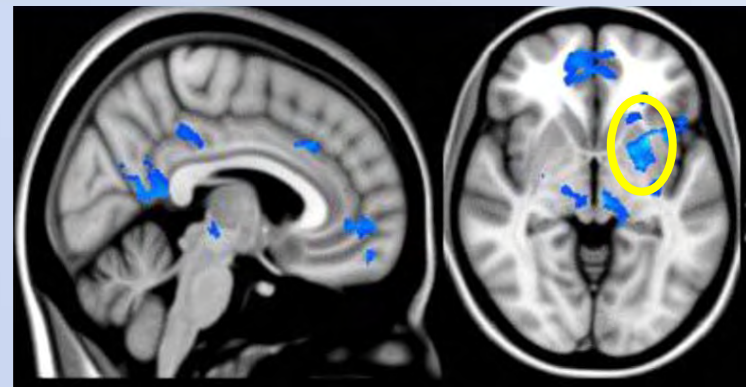
Neurobiological Concerns

- Long-term psychosis
- Unpredictable effects while high
- Low abuse potential (no “reward circuitry” dopamine component, animals won’t self-administer)

“Classic” Hallucinogens

(LSD, psilocybin, 2-cx, mescaline)

- Very few human studies, have to rely on animal “head twitch” models
- 5-HT_{2A} (sub-type of serotonin receptor) main site of action; correlation between binding and hallucinogenic properties
→ necessary & sufficient.

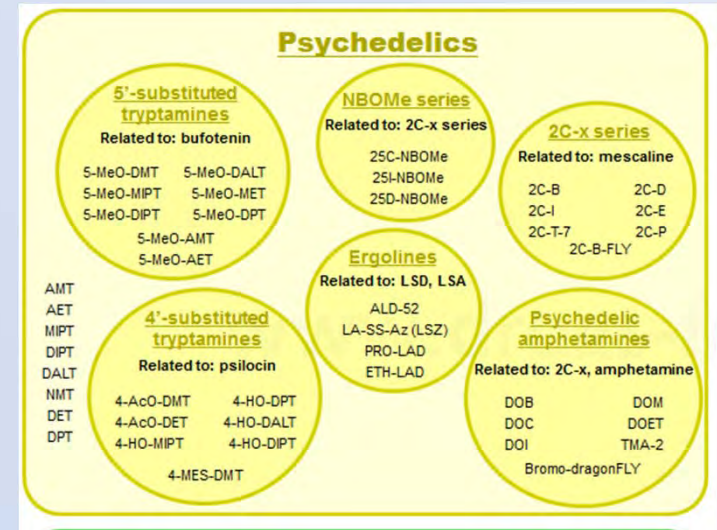


Synthetic Psychedelics

- Potency at 5-HT₂ receptors:
LSD ~ = DOI > DOB >> DOM >
5-MeO-DMT > DMT
- Can roughly rank hallucinogenic properties
- But also have additional action on serotonin system

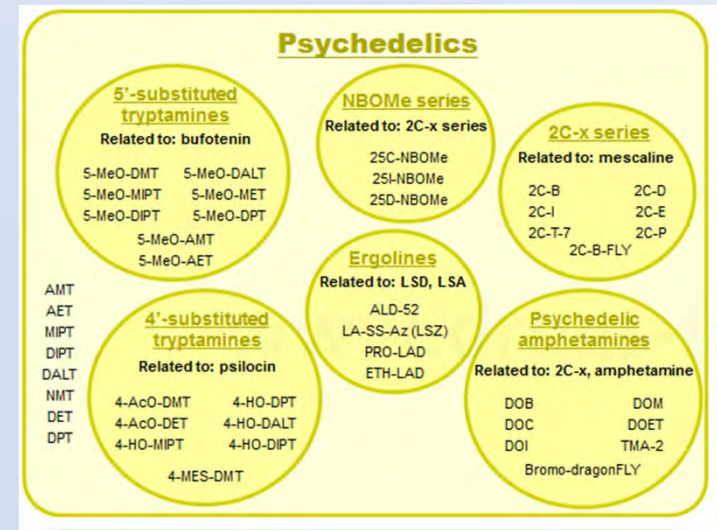
5-MeO-DIPT (Foxy)

- Blocks SERT (serotonin removal from synapse, like cocaine, SSRIs)
- Rats find it “like LSD, but not exactly”
 - Same for 2C-T-7
 - May be less intense: also activates 5-HT_{1A}, which inhibits 5-HT_{2A}
- Potential long-term effects
 - Toxic to petri-dish serotonin system (Nakagawa, Sogawa)
 - Giving it to adolescent rats → worse cognitive function as adults → serotonin system damage? (Compton)



Synthetic Psychedelics: Other Considerations

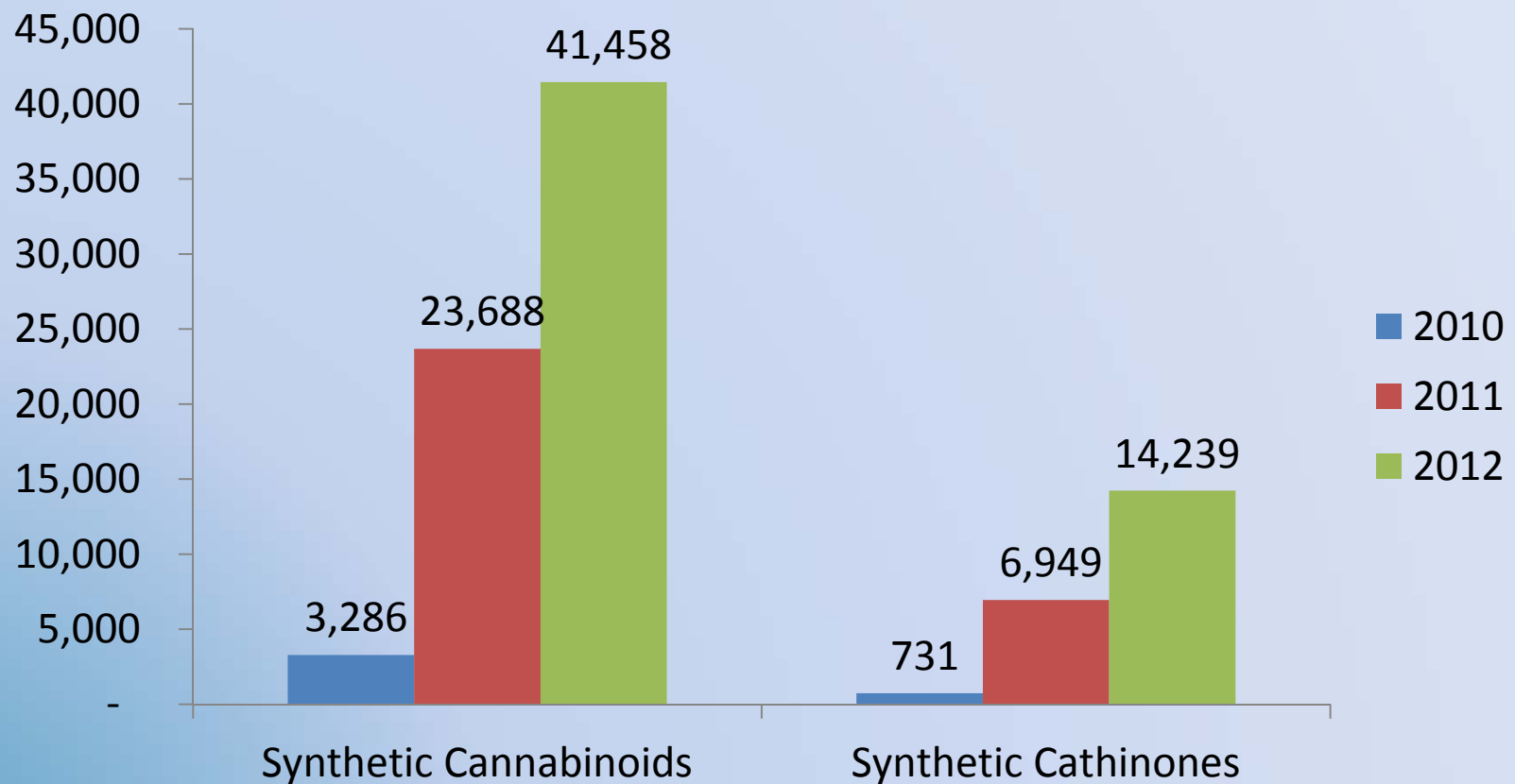
- 5-MeO-DMT interacts with MAO-Is
 - (unlike classics)
 - DMT and bufotenine (active metabolite) stay in system longer (Jiang et al.)



THE EPIDEMIOLOGY OF SYNTHETIC DRUG USE

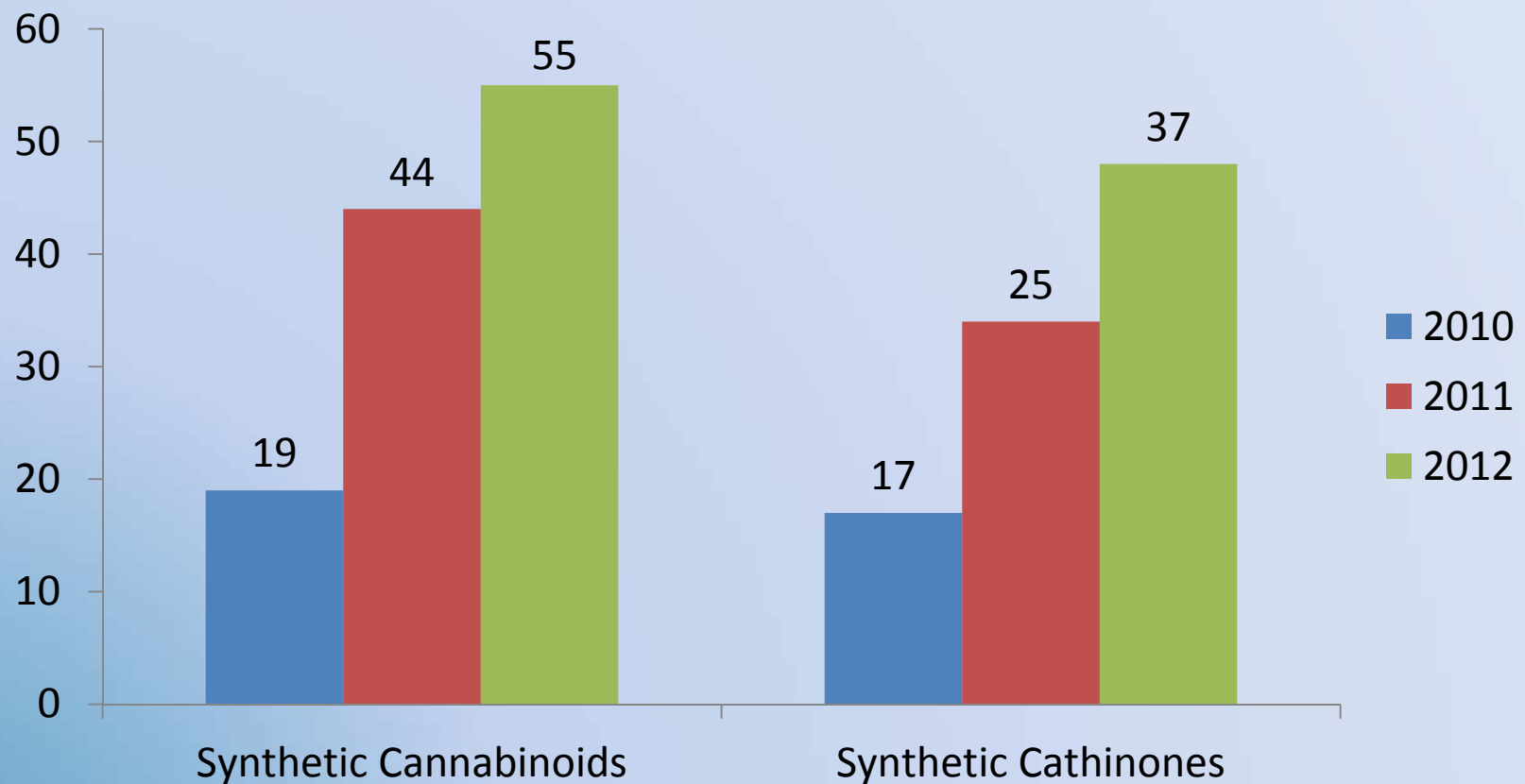


Emerging Drug Items Identified in U.S. NFLIS Forensic Labs: 2010-2012



SOURCE: U.S. DEA, Office of Diversion Control, NFLIS data, 2012.

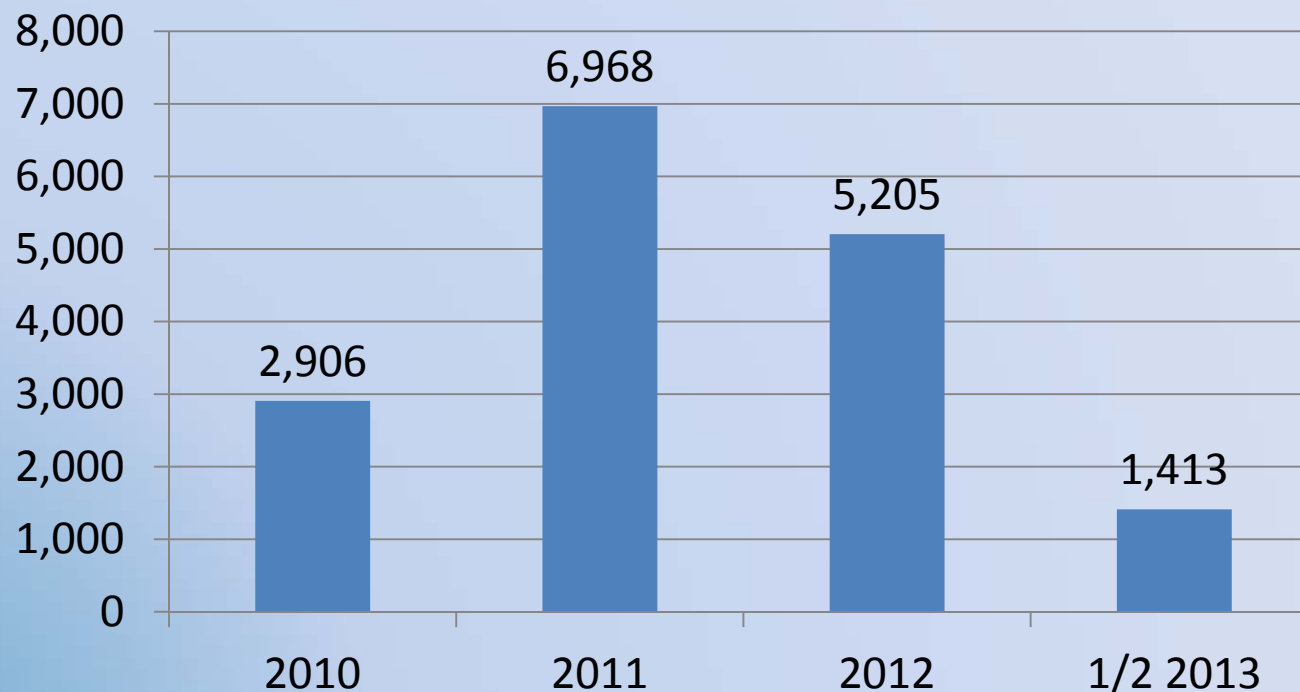
Number of Unique Types of Synthetic Drugs Identified Nationally: NFLIS (2010-2012)



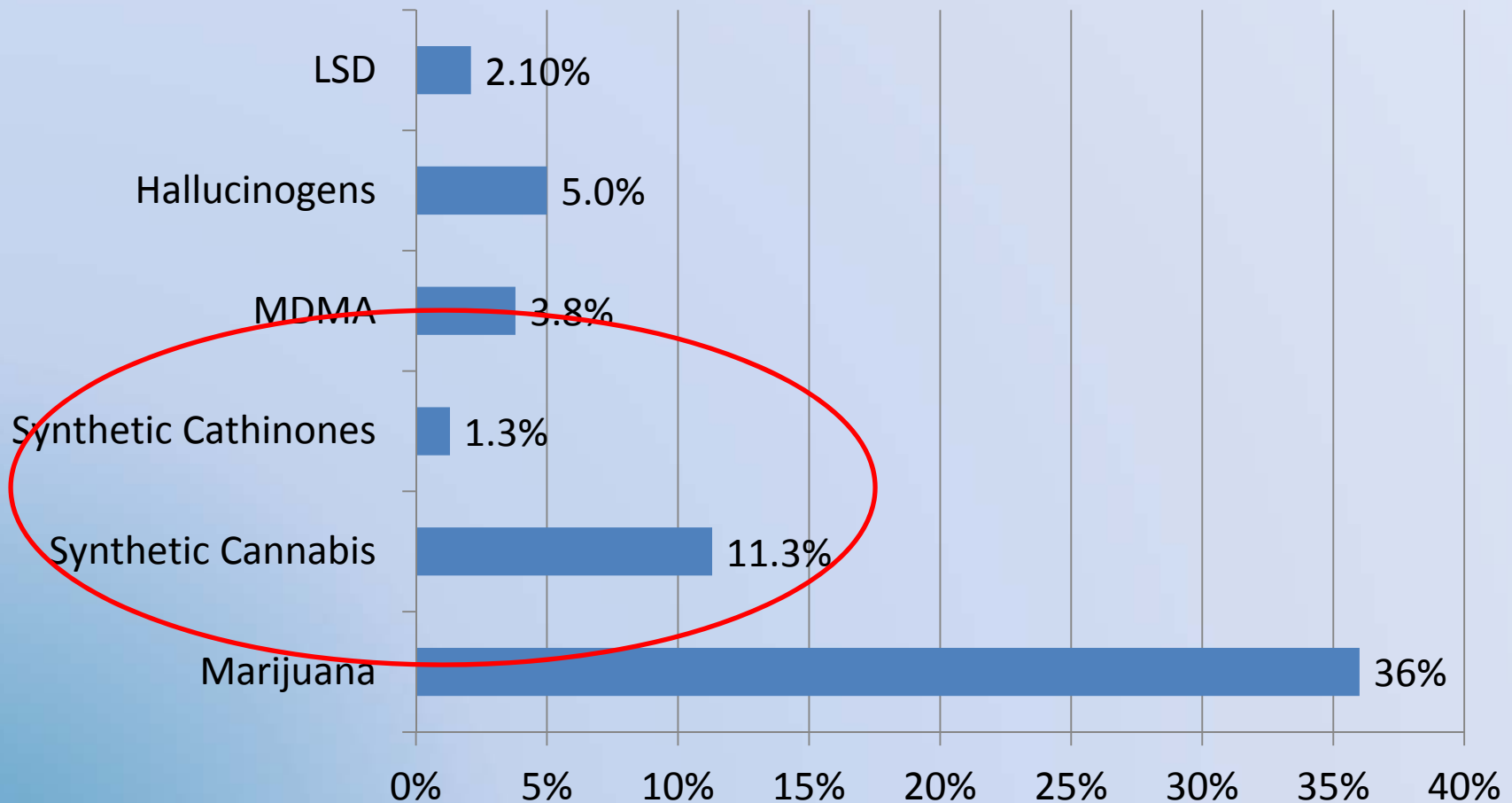
SOURCE: U.S. DEA, Office of Diversion Control, NFLIS data, 2012.

Calls Received by U.S. Poison Control Centers for Human Exposure to Synthetic Marijuana, 2010 to July 2013

There was 1 cannabinoid death in 2010 and 4 in 2011

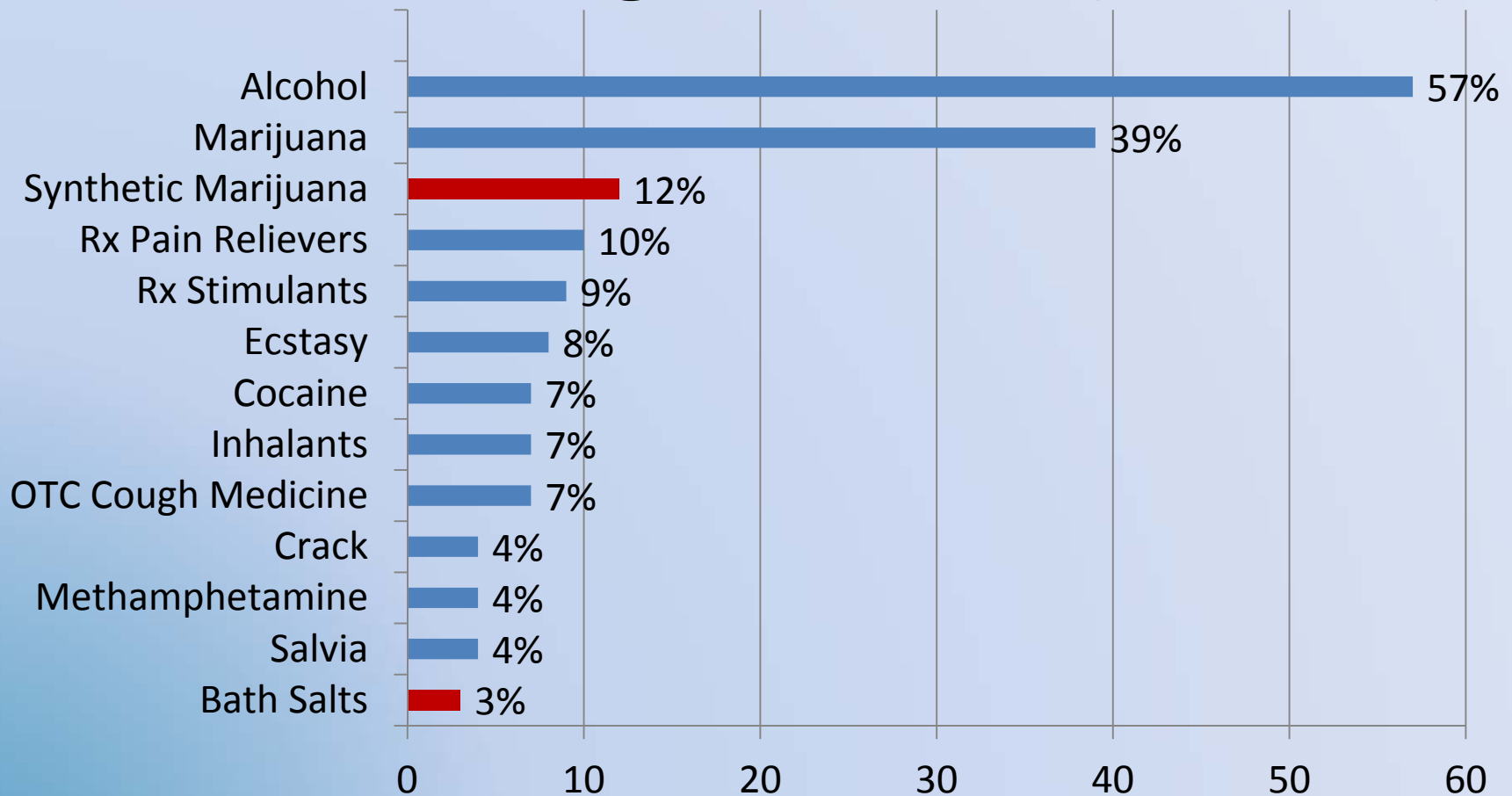


Past Year Drug Use by 12th Grade Students: MTF, 2012



SOURCE: Monitoring the Future Survey, 2012 results.

Percentage of U.S. Students (Grades 9 to 12) Reporting Past Year Alcohol and Other Drug Use, 2012 (N=3,884)



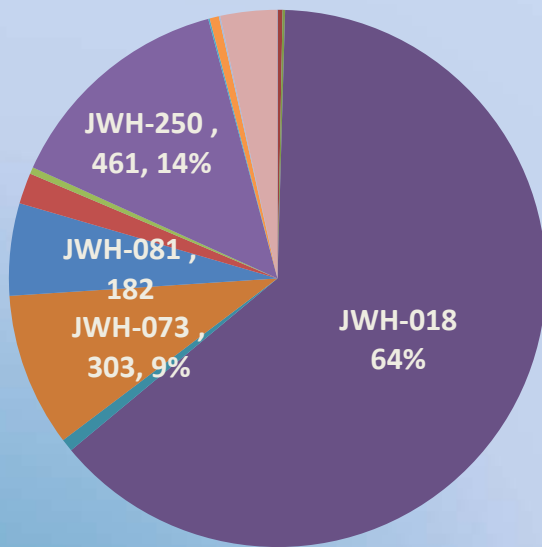
SOURCE: Adapted by CESAR from The Partnership for a Drug-Free America and the MetLife Foundation, *The Partnership Attitude Tracking Study (PATS): Teens and Parents*, 2013.

Emergency Room Visits Related to Synthetic Cannabis and Cathinones: DAWN, 2011

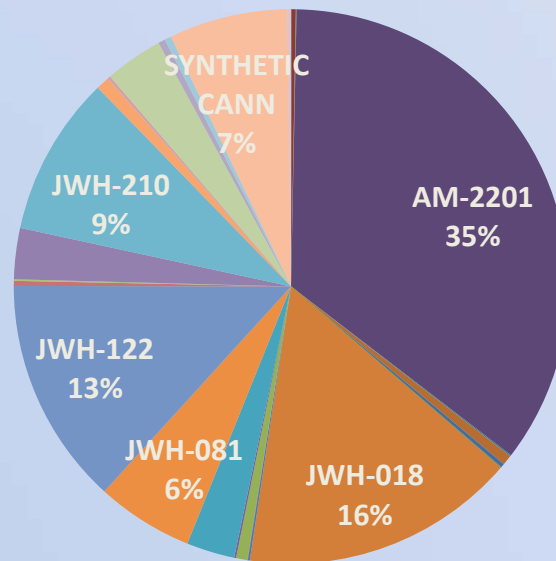
	% Male	% Under Age 21	% Sent to ICU or Sub. Abuse Treatment	% Discharged Home
Synthetic Cannabis	70%	55%	3%	78%
Synthetic Cathinones	76%	14%	12%	55%

Synthetic Cannabinoids Identified in U. S. NFLIS Forensic Labs

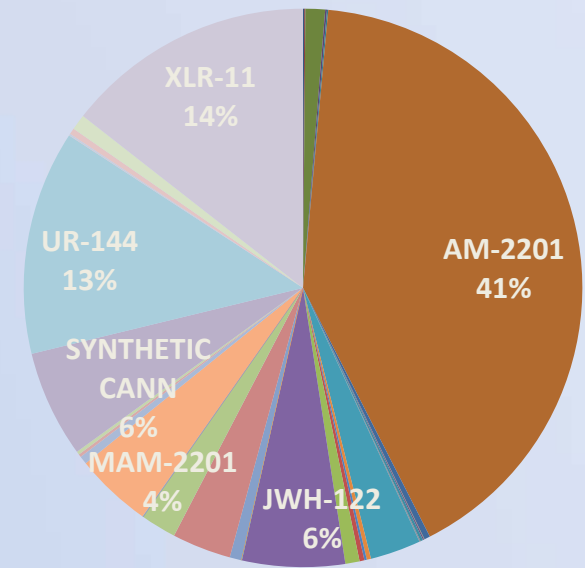
19 variations reported in 2010
n=3,286



44 variations reported in 2011
n=23,688

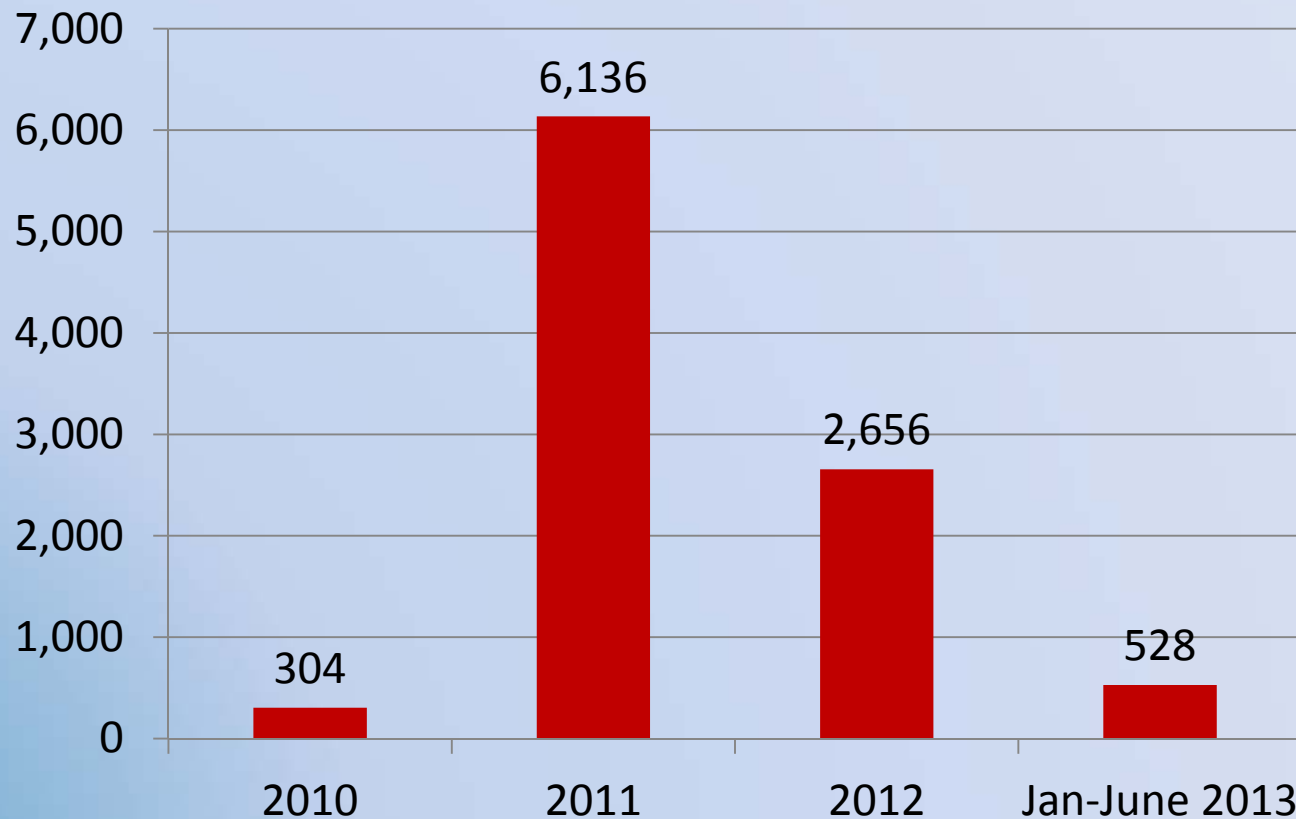


55 variations reported in 2012
n=41,458



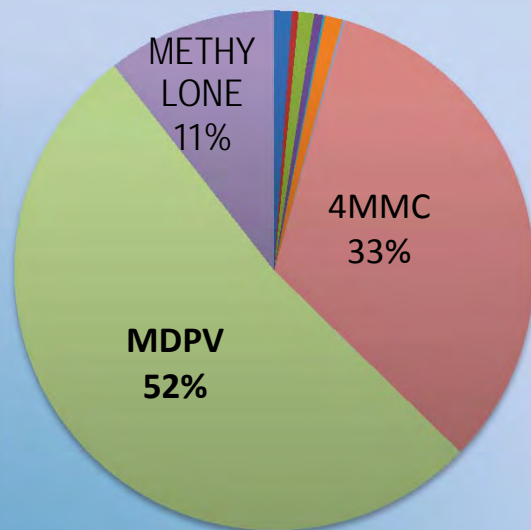
Calls Received by U.S. Poison Control Centers for Human Exposure to Synthetic Cathinones, 2010 to July 2013

There were no synthetic cathinone fatalities in 2010 but there were 18 in 2011

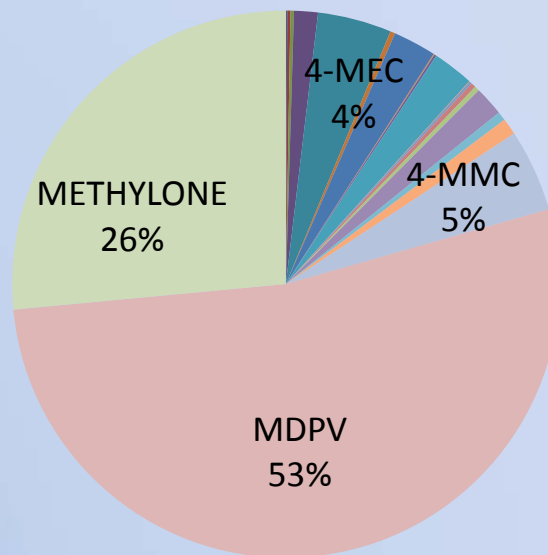


Synthetic Cathinones Identified in U.S. NFLIS Forensic Labs

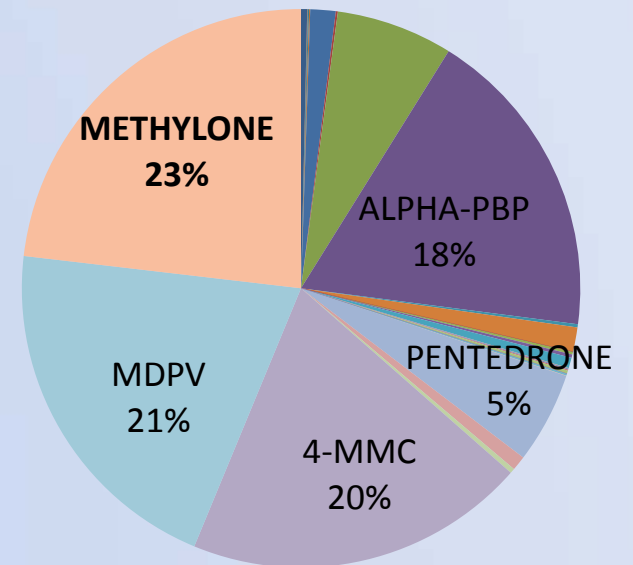
17 varieties identified in 2010
n=731



34 varieties identified in 2011
n=6,949



48 varieties identified in 2012
n=14,239



Psychedelic Drug Use and Baby Boomers

- 32 million Americans have used any psychedelic drug at least once in their lifetimes— about 17% of all American adults between the ages of 21-64.
- Overall rates of lifetime psychedelic use are roughly the same among the 'baby boomers' and younger adults
- Lifetime psychedelic drug use among baby boomers aged 50 to 64 was on par with that of younger adults aged 21-25, about 15%.
- The highest rate was among adults aged 30-34 (over 20%)
- Adults over the age of 65 largely missed the advent of psychedelic drugs in popular culture, since only 1% reported using them.

Synthetic Drug Use in Europe

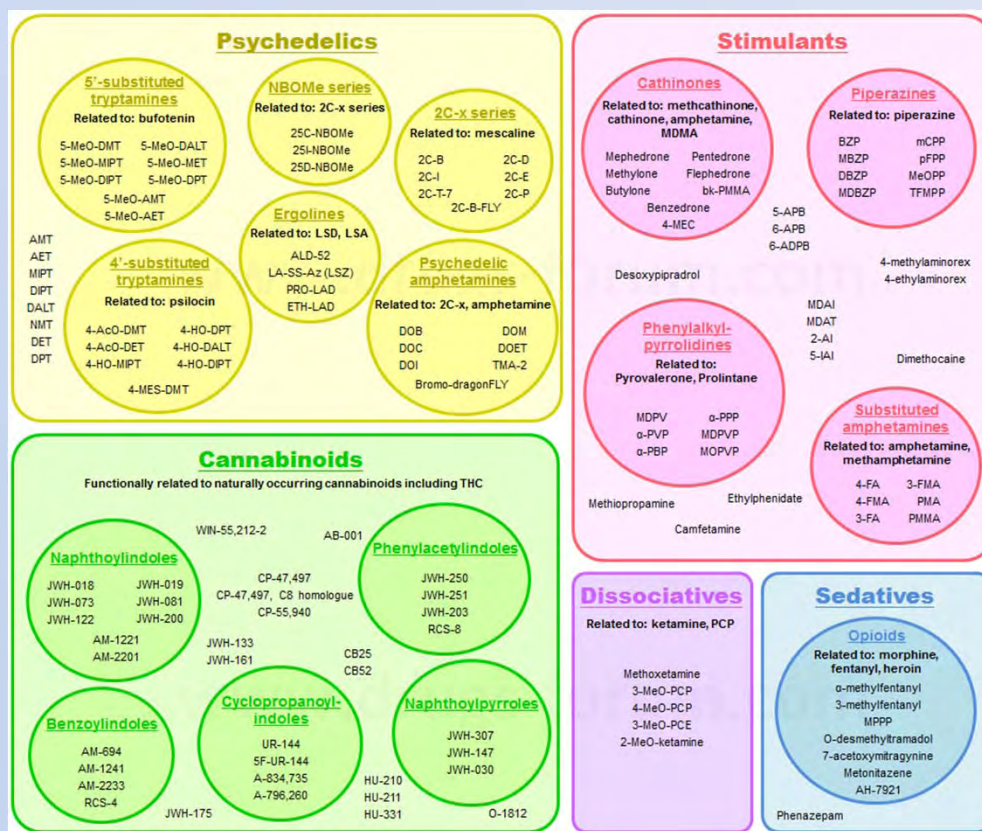
- Seventy-three (73) new psychoactive substances were officially notified for the first time in 2012 via the EU Early warning system (EWS).
- This continues the upward trend of substances reported in a single year: from 49 in 2011, 41 in 2010 and 24 in 2009.
- In 2012, the list of substances reported was dominated by 30 synthetic cannabinoids
- Over 280 new psychoactive substances are currently monitored by the EWS.



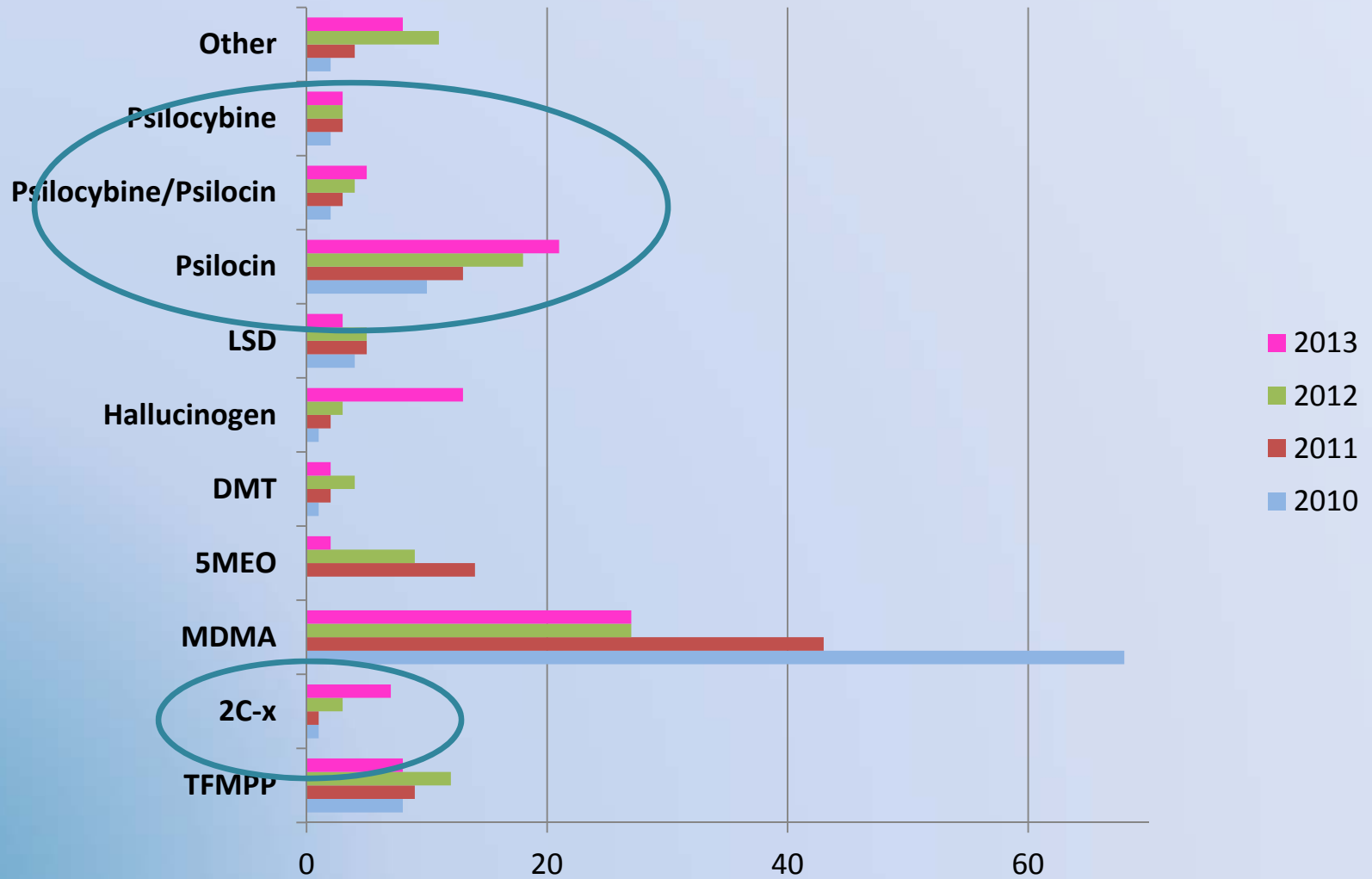
**OTHER NOTABLE SYNTHETIC
DRUGS – “NEW AND OLD”**

What will be Covered in this Section?

- MDMA/ecstasy, and Molly
- Piperazines
- 2C-Phenethylamines
- Psilocybin/Psilocin
- Dextromethorphan
- PCP
- Kratom
- Krokodil
- Benzo Fury
- Syrup/Sizzurp/Drank
- Dabs/Vapor Pens



Not Just New Drugs: Some Old Ones are Reappearing: 2010-June 2013



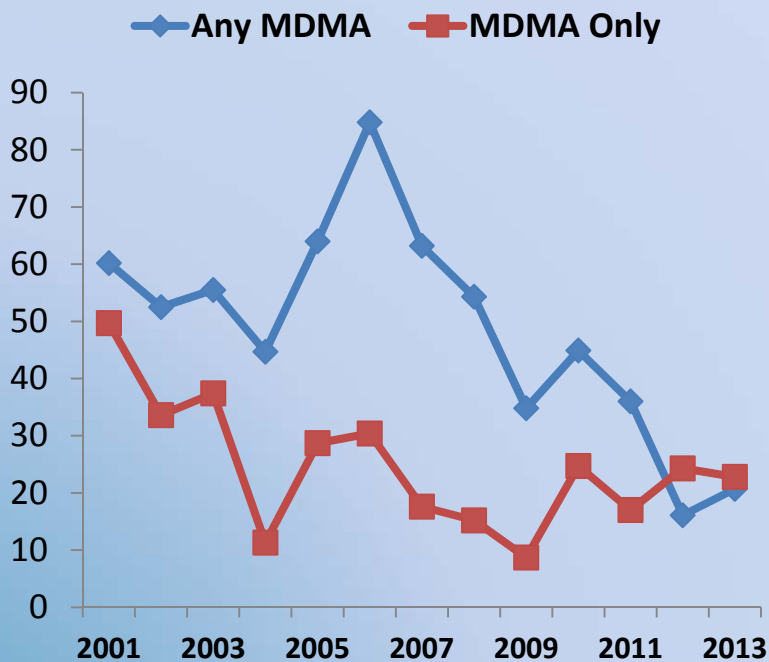
SOURCE: U.S. DEA, Office of Diversion Control, NFLIS data, 2010-2013.

MDMA (Ecstasy)

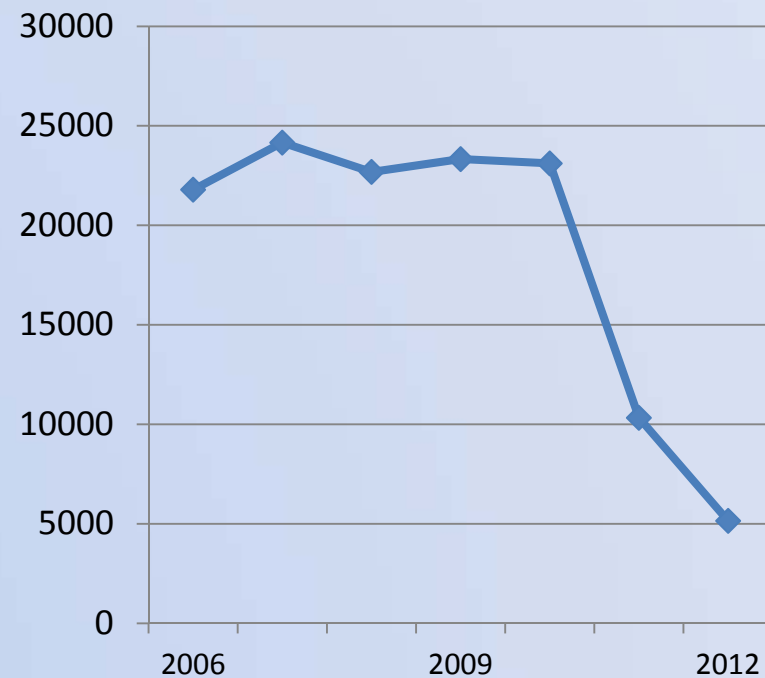
- 3, 4-methylenedioxy-methamphetamine
- Street terms: Adam, E, X, XTC, love drug, Molly
- A synthetic, psychoactive drug with both **stimulant** and **hallucinogenic** properties similar to methamphetamine and mescaline
- Adverse effects: **enhanced physical activity, sweating, lack of coordination, mental confusion, jaw clenching, hyperthermia, and agitation**

Glimpses of MDMA Situation in U.S.: 1999-2013

Results of Pill Tests Containing MDMA*



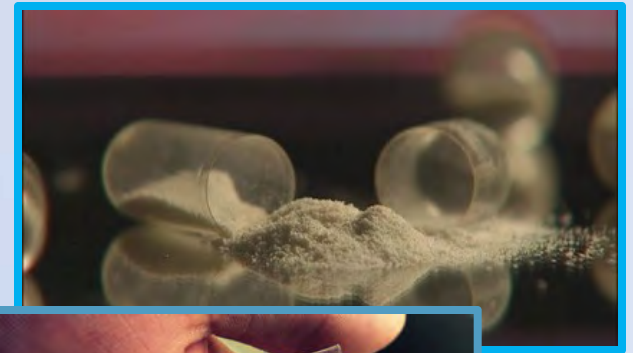
MDMA Reports: NFLIS Forensic Labs 2006-2012



SOURCES: http://www.ecstasydata.org/stats_substance_by_year.php; U.S. DEA, Office of Diversion Control, NFLIS data, 2006-2012.

What is “Molly”?

1. Ecstasy pills with little MDMA and lots of caffeine, meth, assorted drugs? OR
 2. A pure crystalline form of MDMA, most often sold as a powder filled capsule? OR
 3. Methylone? Bath salts?
- Reports of desired effects of euphoria, but also increased paranoia, agitated delirium, scary hallucinations, psychotic episodes, violent or destructive self-harm behavior, including death
 - Bottom line - Molly usually is not a pure form of MDMA, but may be a drug that can be very dangerous since its contents are unknown



Piperazines

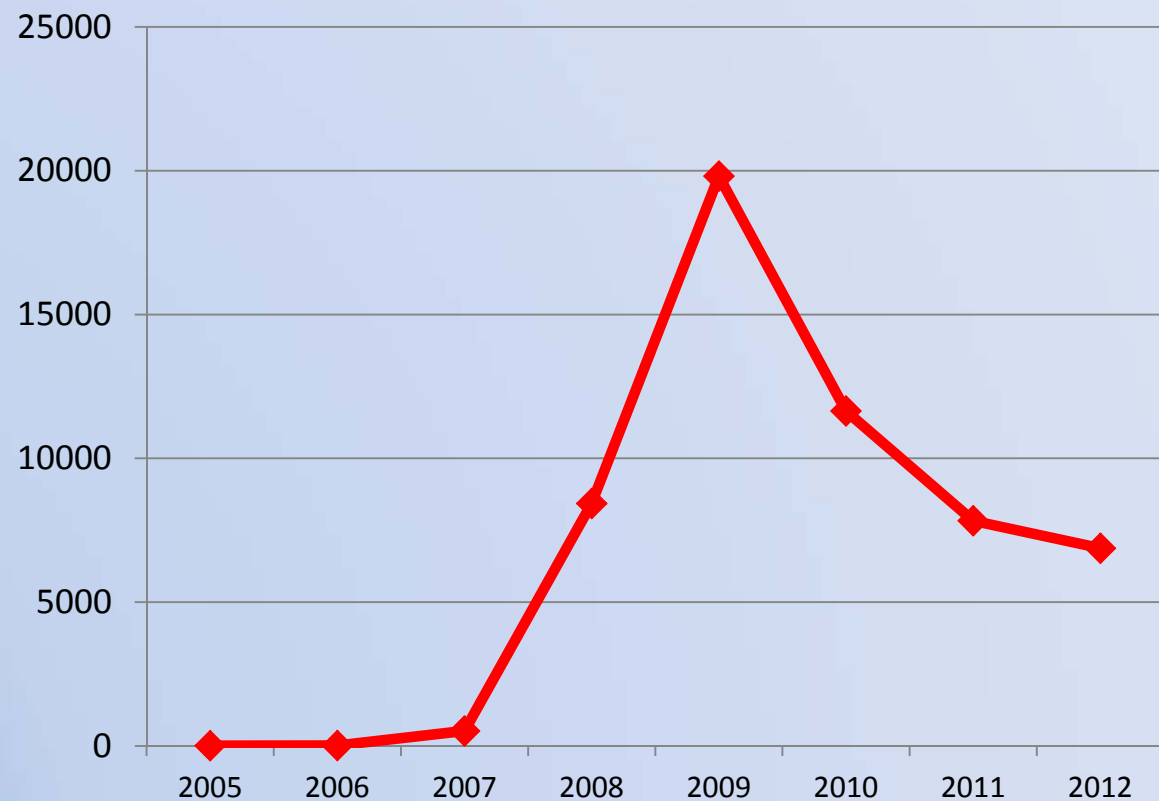
- Frenzy, Bliss, Charge, Herbal ecstasy, A2, Legal Z, Legal E.
- Mainly available over internet and sold as ecstasy pills that are “safe.”
- Two classes: (1) benzylpiperazines (BZP) and (2) phenylpiperazines (TFMPP).
- Mimics effects of ecstasy (MDMA); dangerous with seizure disorders, psychiatric illness, or coronary disease.
- Adverse events included hypertension, reduced consciousness, psychotic episode, hallucinations, tachycardia, hyperthermia, coma. Could be toxic if combined with MDMA or amphetamines.

Piperazines

TFMPP is not controlled at the federal level but is controlled by at least 10 states.

Levels of use peaked in 2009 and have declined since.

Piperazine Reports by NFLIS Labs: 2005-2012



2C-Phenethylamine

- A broad range of compounds that share a common phenylethan-2-amine structure.
- Some are naturally occurring neurotransmitters (Dopamine and Epinephrine), while others are psychoactive stimulants (Amphetamine), entactogens (MDMA), or hallucinogens (the 2C-X series of compounds).
- 2 C-X can be snorted or dissolved into a liquid and placed on blotter paper under the tongue.
- May last 6-10 hours; onset takes 15 min to 2 hours.
- Reports of seizures and renal failure.



2C-Phenethylamines

- Almost all of the 2C-phenethylamines are produced in Asia, principally China, but some small labs in the U.S. are capable of producing 2C (usually 2C-B).
- In 2011, DEA offices throughout the country began noting the increasing availability and abuse of 2C at raves and in nightclubs, particularly by teenagers and young adults.
- NFLIS labs nationwide identified 253 reports of phenethylamines in 2010, 336 in 2011, 828 in 2012, and 230 through May 2013.

Spread of 2C-Phenethylamine throughout the United States

Figure 5.1 2C-Phenethylamine Reports to NFLIS, by State, 2006

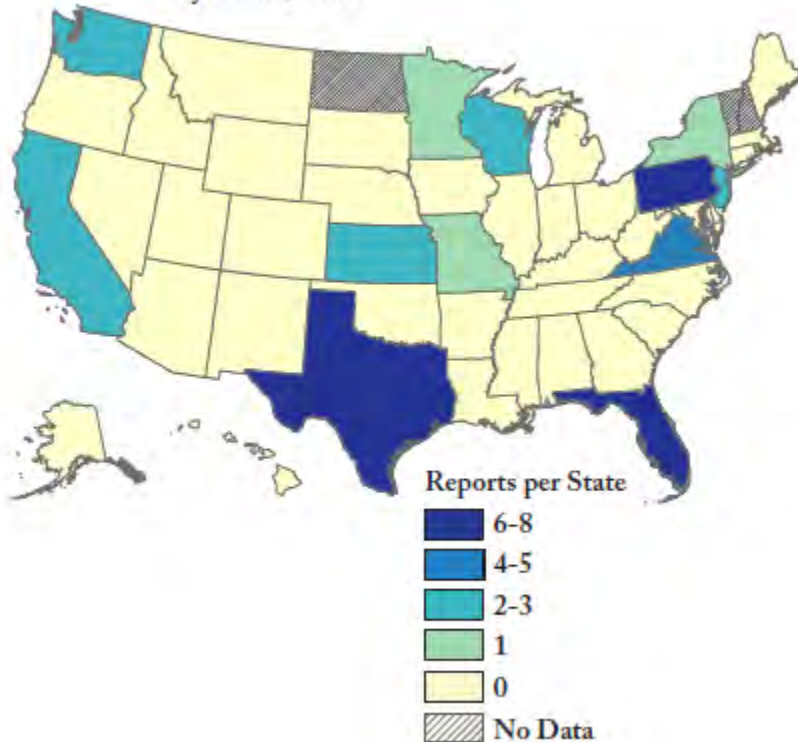
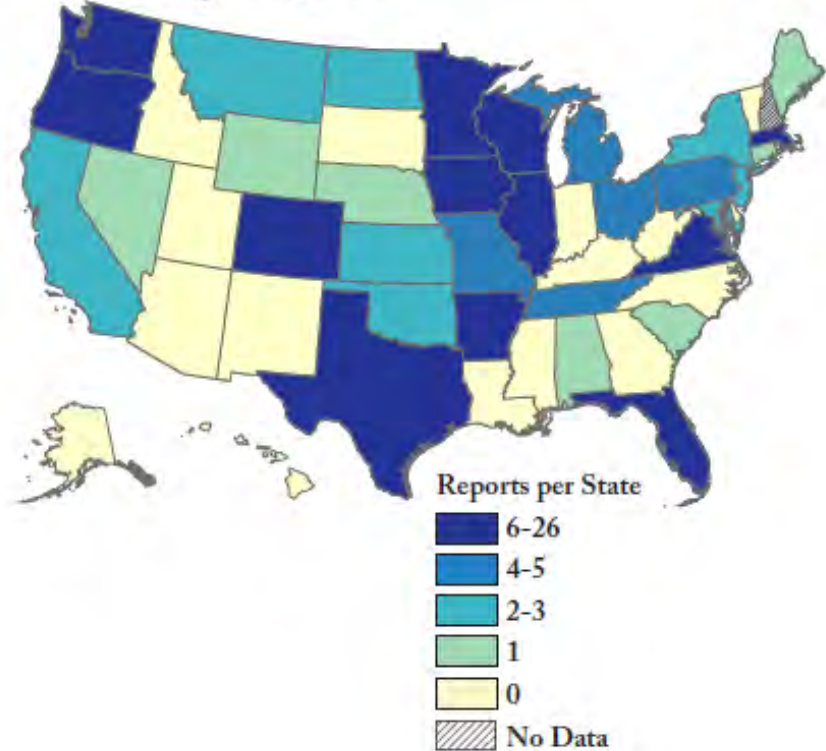


Figure 5.2 2C-Phenethylamine Reports to NFLIS, by State, 2010



SOURCE: U.S. DEA, Office of Diversion Control. (2012). *National Forensic Laboratory Information System Special Report: Emerging 2C-Phenethylamines, Piperazines, and Trypamines in NFLIS, 2006-2011.*

2C-C-NBOMe, 2C-I-NBOMe, Mescaline-NBOMe

- Analogs of the 2C-X family of phenethylamines
- Strongly active at the sub-milligram dose (a **Super Potent drug**)
- Most 25I and 25C is sold as **pure powder**
 - Weighing and handling pure high-potency chemicals such as LSD or 25I-NBOMe should be performed wearing eye protection, gloves, and a filter mask
- Perhaps the greatest risk of the wide availability of pure NBOMe powders is **confusing one white powder for another**, or simply **misunderstanding the difference** between one psychedelic or stimulant drug and another
- In 2011, 10 items of the NBOMe family were seized and identified in NFLIS forensic laboratories, as compared to 447 in 2012.

Psilocybin vs. Psilocin

- Psilocybin and psilocin are naturally occurring psychedelics with a long history of human use. Both are present in 'psychedelic' or 'magic' mushrooms.
- Psilocybin, the better known of these two chemicals, is metabolized after ingestion into psilocin, which is the primary active chemical.



What is **DXM**? **Dextromethorphan** is a psychoactive drug found in common over the counter cough medicines.



Dextromethorphan (DXM)

- Dextromethorphan's slang names include "Robo;" people refer to using DXM as "robo-tripping."
- At high doses, may produce dissociative hallucinations (distance from reality, visual effects with eyes open and closed; perceptual changes, drug liking, mystical-type experiences similar to use of psilocybin).
- Can also produce tachycardia, hypertension, agitation, ataxia, and psychosis at high doses.
- Users of DXM engage in "dose dependent" behaviors in which they try to gauge the amount of the drug they take to produce the desired effects, which they call "plateaus". Plateau is the mildest effect and the 5th plateau will guarantee a trip to the hospital.

DXM Dosage Calculator



Enter your weight in pounds:

150

Second Plateau



Cough Syrup



Powder

Strength:

2

mg/mL

Calculate DXM Needed

Quit DXM Calculator

About

You must drink between 85mL and 256mL of cough syrup to achieve your desired high!

Phencyclidine

- PCP, Angel Dust, Killer Weed
- Dissolved in embalming fluid (“Fry,” “Amp,” “Water, Water”)
- Swallowed, sniffed, smoked on joints dipped in “Fry”
- Users report out-of-body strength

A Few Other Substances to Throw in the Mix...

- Kratom – opioid-like effects
- Krokodil – cheap heroin replacement
- Salvia divinorum – hallucinogenic effects
- Methoxetamine – “legal ketamine”
- Benzo Fury (5-APB) – stimulant and hallucinogenic effects

Kratom

- Structurally similar to some hallucinogens but no hallucinogenic activity or effects
- Acts on opioid receptors
- Not scheduled in U.S.
- Seems to be a stimulant in lower doses
 - Mitragynine
- Seems to be a sedative at higher doses
 - 7 hydroxymitragynine
- Often produces a mixed effect
- Onset of effects within 5 to 10 minutes of ingestion; effects last for several hours



Krokodil

- Russian cheap replacement drug for heroin made from cooking down desomorphine with gasoline, paint thinner, alcohol, iodine, red phosphorous (match heads), etc.
- In Russia, lack of clean needles and methadone, high cost of heroin, poverty, high numbers of HIV+ individuals, etc.
- No confirmed cases of desomorphine in the U.S. since 2 were identified in 2004.
- Injuries that look like krokodil can be due to shared dirty needles, bacteria, toxic adulterants, gangrene, staph infection, MRSA.

Benzo Fury

- Active ingredient is 5-APB
- Stimulant and hallucinogenic properties
- Fairly easy to buy via the Internet, at music festivals, and in clubs - priced at around \$15 per pill.
- User-reported effects include:
 - Increased happiness, euphoria, extreme mood lift, increased self-acceptance, increased intimacy, closed-eye hallucinations, increased sexual interest



“Syrup” in Texas

- Codeine cough syrup continues to be abused.
- Cut with Karo syrup, jolly ranchers, and soft drink.
- Hip-Hop/Rap music on syrup continues to drive this phenomenon.
- Also available as a non-alcoholic soft drink pre-packaged to introduce to youth or ready to add the syrup.

New “Relaxation” Drinks: Drank and *Lean*

*Valerian
Roots*

Melatonin

Rose Hips

*“Slow Your
Roll”*

*“Slow
Motion
Potion”*



“Sizzurp” Cognac, Vodka, and Fruit Flavor

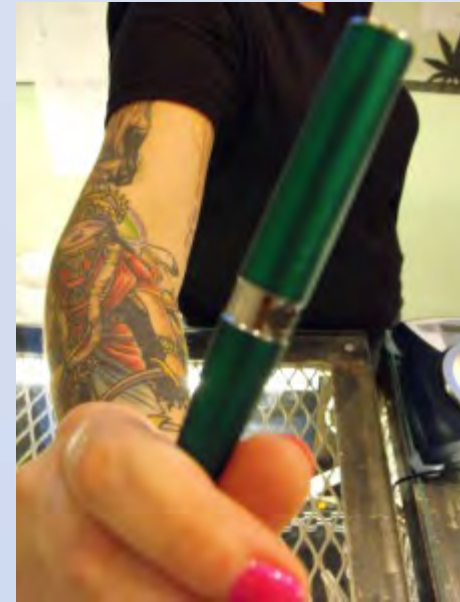


Dabs, BHO, Honey, Budder

- Dabs, shatter wax and vaporizer pens contain hash oil (“wax”). Supposedly 80%-90% THC. Different methods available on the Internet.
- Butane Honey Oil or Butane Hash Oil is a golden resin created by placing dried and ground marijuana into a special pvc filter. Butane gas is shot in through one end of the filter while the other end is placed in a bowl full of water. The filter spews out the fresh oil in to the cold water where it sinks to the bottom. The bottom is scraped and the oil is ready to use.
- Users touch the heated knife point or the pin to the Budder on the end of a pin and inhale fumes (and sit down).

Vapor Pens

- Advertised for “patients”
- Cost \$100-\$200
- Potency varies
- Higher percentage of THC
- No odor. Similar to electronic cigarettes
- Pen-style vaporizers contain 100-150 hits
- Some can be recharged and refilled





**CASE STUDIES, SAMPLE
TREATMENT PROTOCOLS AND
CONCLUDING THOUGHTS**

Case Study #1

You are a professional in a setting working with youth (e.g., counselor, educator, tutor, etc.). During your normal duties, you overhear a group of youth talking about their interest in trying a new synthetic drug they heard about from one of their older siblings.

1. What messages would you want to communicate?
2. What strategies would you use to maintain trust but also being able to point out the possible dangers from using one of these synthetic drugs?
3. What initial assessment questions would you want to ask?
4. What alternative activities would you explore to using these drugs?

Case Study #2

A nineteen year old male reports using “spice” 7-8 times along with marijuana. He stopped using spice about 45 days ago, and stopped marijuana about 30 days ago. While on these drugs, his thoughts became disorganized, and he was having grandiose ideas. Since he discontinued his use of drugs, his behavior can best be described as manic. He sleeps 4-5 hours over a two-day period, and then sleeps 22 hours straight. He is constantly moving around, sings loudly, and has delusions about becoming a rap star. He has been hospitalized three times, and the psychiatrists keep saying “he is mentally ill and his drug use probably caused the onset.”

Case Study #2, continued

1. What additional information do you need to know before figuring out a treatment plan?
2. What kind of intervention does this young man need?
3. Do you believe he has stopped using spice and marijuana altogether?
4. Where do you go from here?

Synthetic Cannabinoids – Clinical Presentation

- Persistent depression
- Memory problems (can last for several weeks)
- Blunted affect
- Difficulty focusing
- Difficulty participating in clinical until stabilized
- Users also report elevated mood, relaxation, and altered perception
- Psychotic effects, such as extreme anxiety, paranoia, and hallucinations

Sample Clinical Treatment Protocol for Synthetic Cannabinoid Users

- Direct individual to emergency room via ambulance
- Consult a regional Poison Control Center
- Acute management consists of:
 - Supportive care with the use of benzodiazepines, if needed, to control agitation and anxiety
 - Observe until resolution of abnormal vital signs, vomiting, and psychiatric symptoms

Recognizing Synthetic Cathinone Intoxication

- Present with severe sympathetic stimulation:
 - Tachycardia
 - Hypertension
 - Hyperthermia
 - Seizures
- Present with profoundly altered mental status:
 - Severe panic attacks
 - Agitation
 - Paranoia
 - Hallucinations
 - Suicidal behavior



Sample Clinical Treatment Protocol for Synthetic Cathinone Users

- Supportive care
- Aggressive sedation with benzodiazepines (for agitation, seizures, tachycardia, and hypertension)
- Significant hyperthermia may require passive or active cooling
- Lab studies including electrolytes, renal and liver function tests, cardiac markers, and creatine kinase should be considered

What do you do if someone has taken a Synthetic Drug?

- Call your local poison center at 1-800-222-1222
 - 57 poison centers around the country have experts waiting to answer your call.
 - The experts at the Center can help you decide whether someone can be treated at home, or whether he or she must go to a hospital.
- Dial 9-1-1 immediately if they:
 - Stop breathing
 - Collapse
 - Have a seizure

...or if they have taken one of these and are having physical symptoms or behaving in a way that is concerning to you

In Summary: Key Points

- Lack of information on the chemical contents, dosage levels, and consistent quality of the products is a major problem since users are taking drugs about which they know little, which makes provision of health care for adverse events more difficult.
- Despite widespread Internet availability and use among certain populations, health care providers remain largely unfamiliar with synthetic drugs and the multiple variations which have appeared recently.

In Summary: Key Points

- Research is needed to better understand the side effects and long-term consequences associated with the use of synthetic cannabinoids and synthetic cathinones.
- More toxicological identification of these new drugs, more information on the sources of them, as well as their distribution and patterns of use is needed to curtail future increases in use.

In Summary: Key Points

- We do not have human neurobiological data or long-term data, but we can extrapolate a few key points from the existing literature:
 - Synthetics vs. Classics: Neurobiological concerns hold up, plus more
 - In all cases, neurobiology predicts abuse potential
 - In general, synthetic versions are not a simple substitute for “classics” – effects tend to be more intense (including side effects), some unexpected, and some new interactions that were not a concern before

Resources for Continued Learning

- American Association of Poison Control Centers, www.aapcc.org
- Drug Enforcement Administration, www.dea.usdoj.gov
- European Monitoring Centre for Drugs and Drug Addiction, www.emcdda.europa.eu
- National Institute on Drug Abuse, www.nida.nih.gov
- Office of National Drug Control Policy, www.ondcp.org
- Pacific Southwest ATTC, www.psattc.org
- Refer to the *Synthetic Drugs Reference List***



Thank you for your time!

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<http://www.psattc.org>

http://www.attcnetwork.org/regcenters/index_southsouthwest.aspt