



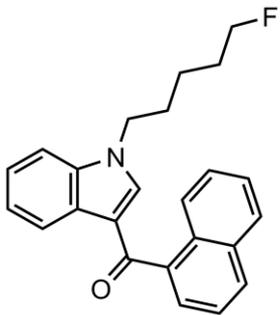
Designer Drugs
From Product Surveillance to Forensic Casework

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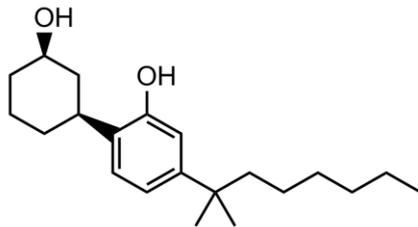
Synthetic Cannabinoids



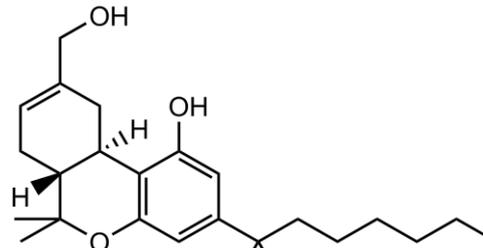
- Most were developed in legitimate research on the endocannabinoid system
 - “AM” compounds were synthesized at Northeastern University by Alexandros Makriyannis
 - “CP” compounds were synthesized by Pfizer
 - “HU” compounds were synthesized at Hebrew University.
 - “JWH” compounds were synthesized at Clemson University by John W. Huffman
 - “WIN” compounds were synthesized by Sterling-Winthrop



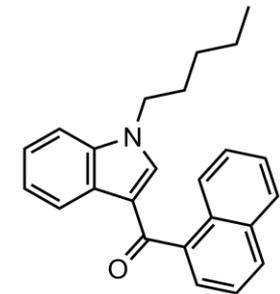
AM-2201



CP47,497



HU-210



JWH-018

- Most are *suspected* agonists at cannabinoid receptor 1 (CB₁) and cannabinoid receptor 2 (CB₂).
 - Many have not been subjected to functional assays determining activity at the receptor.

Endocannabinoid System

- Cannabinoid receptor type 1 (CB₁)
 - Central nervous system
 - Increased appetite, nausea reduction, improved mood
 - Dysphoria, vasodilation, tachycardia
 - Impaired memory/cognition, altered perception, euphoria
 - Impaired psychomotor skills

- Cannabinoid receptor type 2 (CB₂)
 - Peripheral nervous system, GI system and immune system
 - Evidence that CB₂ does exist in CNS
 - Effects
 - Inflammation reduction, pain perception reduction
 - Immunosuppression

- Many have binding affinities (K_i) greater than THC

Analyte	CB1, K_i (nm)	CB2, K_i (nm)
A796,260	945	4.6
AM-2201	1.0	2.6
CP47,497	2.2	-
HU-210	0.061	0.5
JWH-018	9.0	2.9
JWH-019	9.8	5.6
JWH-073	8.9	38
JWH-081	1.2	12.4
JWH-122	0.7	1.2
JWH-210	0.5	0.7
JWH-250	11	33
THC	41	36
UR-144	150	1.8

- Fatty acid amide hydrolase (FAAH) inhibitors
 - URB447
 - URB597
 - URB602
 - URB754
 - URB937

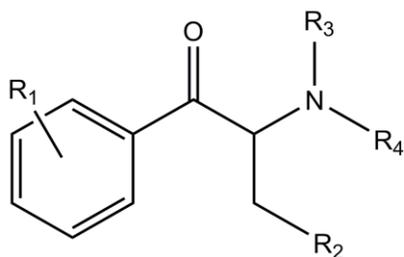
- FAAH functions at synapse to break down the endogenous cannabinoid, anandamide

- An FAAH inhibitor stops or slows down the degradation leading to accumulation of anandamide in the CNS.

- Show promise in applications for pain treatment; currently in clinical trials
 - Measurable antidepressant and analgesic effects

Substituted Cathinones

- Derivatives of cathinone
- Structural similarities
 - Phenethylamine core
 - Alkyl group attached to the α -carbon
 - Ketone group attached to the β -carbon



General Chemical Structure of Substituted Cathinones

R₁ is a hydrogen, or any combination of one or more alkyl, alkoxy, alkylendioxy, haloalkyl, or halide

R₂ is a hydrogen or any alkyl

R₃ is a hydrogen, any alkyl or incorporation in a cyclic structure

R₄ is a hydrogen, any alkyl or incorporation in a cyclic structure



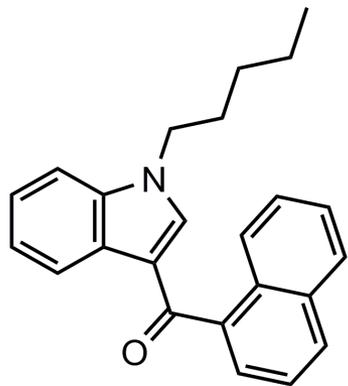
- Most are suspected to bind to catecholamine transporters and/or act as reuptake inhibitors
- Many stimulate release of norepinephrine, dopamine, and serotonin
 - Norepinephrine
 - Flight or fight response
 - Heart contractions
 - Increases blood flow to muscle and release of glucose
 - Dopamine
 - Role in “reward-driven” learning
 - Behavior and cognition, motivation, punishment, reward
 - Mood, attention, sleep
 - Serotonin
 - Feelings of well-being and happiness
 - Mood, appetite, sleep
 - Memory and learning



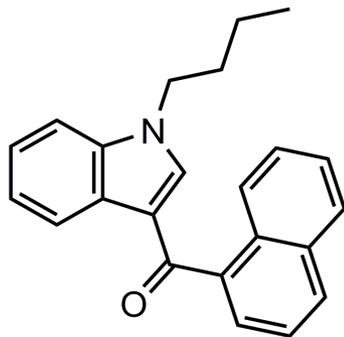
- Many have effects similar to cocaine, MDMA, amphetamine, and methamphetamine

Analyte	Mechanism of Action
Butylone	Nonselective monoamine uptake inhibitor, releases Serotonin
Ethylone	Nonselective monoamine uptake inhibitor, releases Serotonin
Flephedrone	Dopamine and Norepinephrine reuptake inhibitor, releases Dopamine
MDPV	Dopamine and Norepinephrine transporter inhibitor
Mephedrone	Nonselective monoamine uptake inhibitor, releases Serotonin
Methylone	Nonselective monoamine uptake inhibitor, releases Serotonin
Pyrovalerone	Dopamine and Norepinephrine transporter inhibitor
Naphyrone	Nonselective monoamine uptake inhibitor

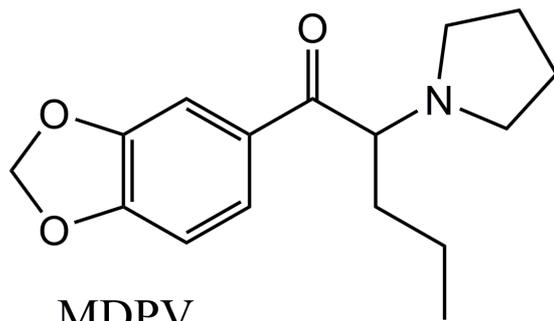
Product Analysis 1st Generation



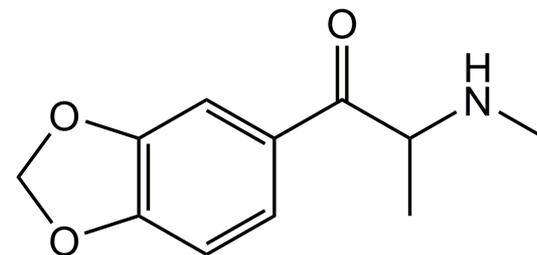
JWH-018



JWH-073



MDPV



Methylone







- DEA emergency scheduled 5 compounds in to schedule 1 of the CSA (2010-2011)

CP47,497

CP47,497-C8

JWH-018

JWH-073

JWH-200

MDPV

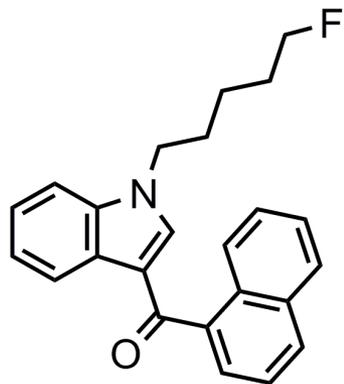
Mephedrone

Methylone

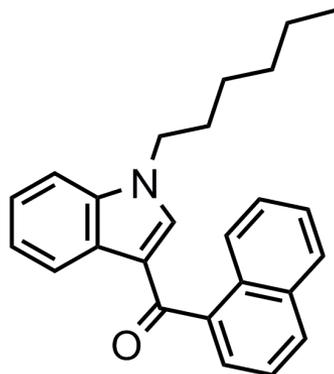
- HU-210 was already a schedule 1 compound
- Did not affect any other compounds



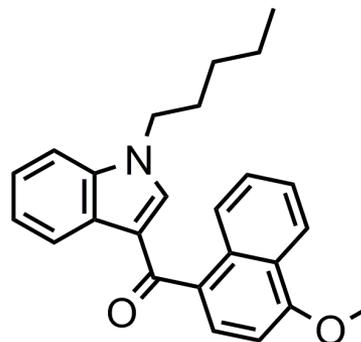
Product Analysis 2nd Generation



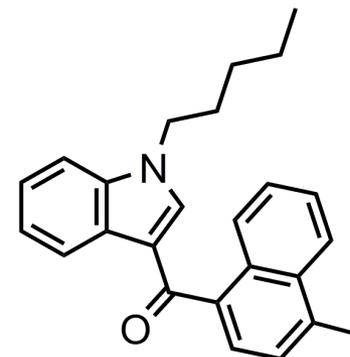
AM 2201



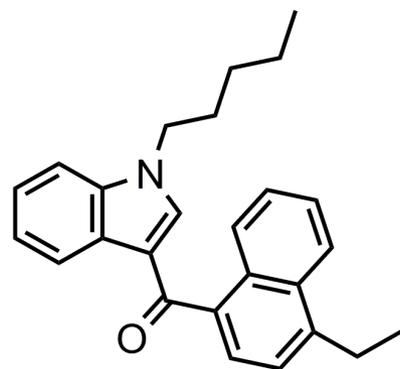
JWH 019



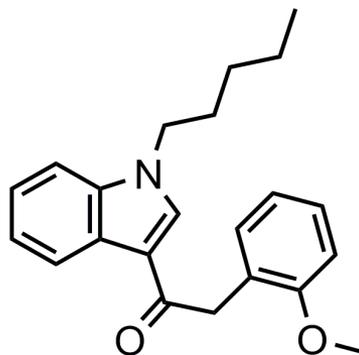
JWH 081



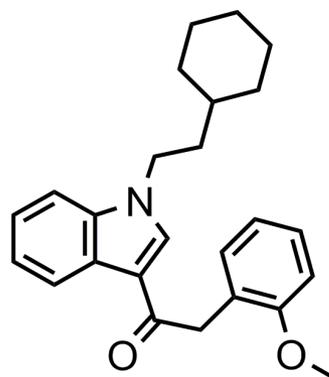
JWH 122



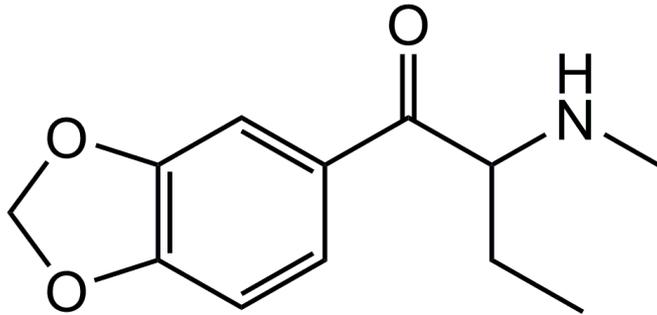
JWH 210



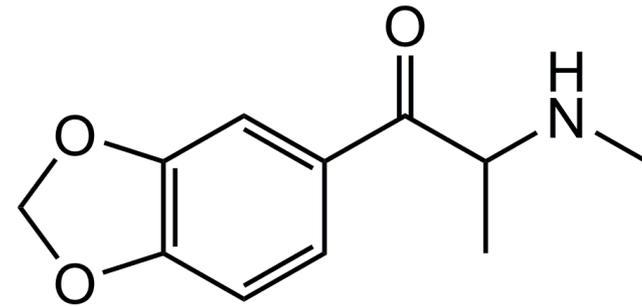
JWH 250



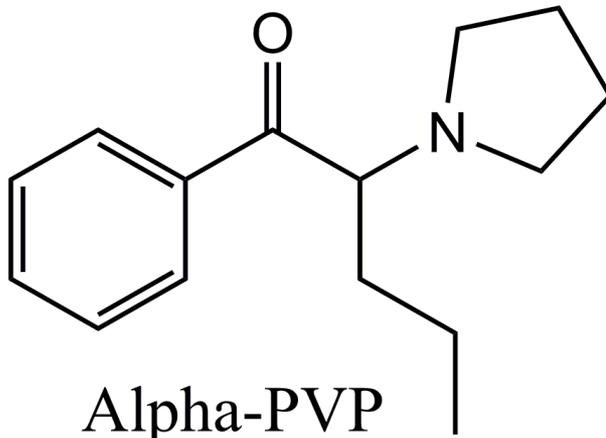
RCS 8



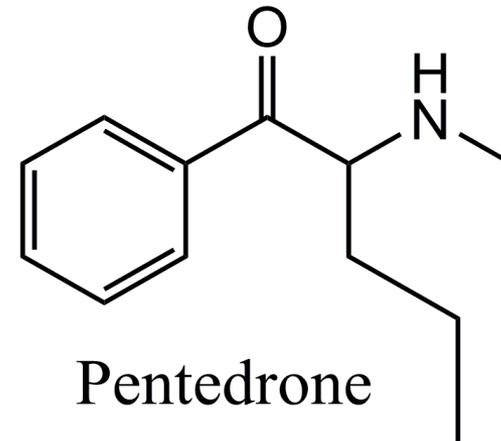
Butylone



Ethylone

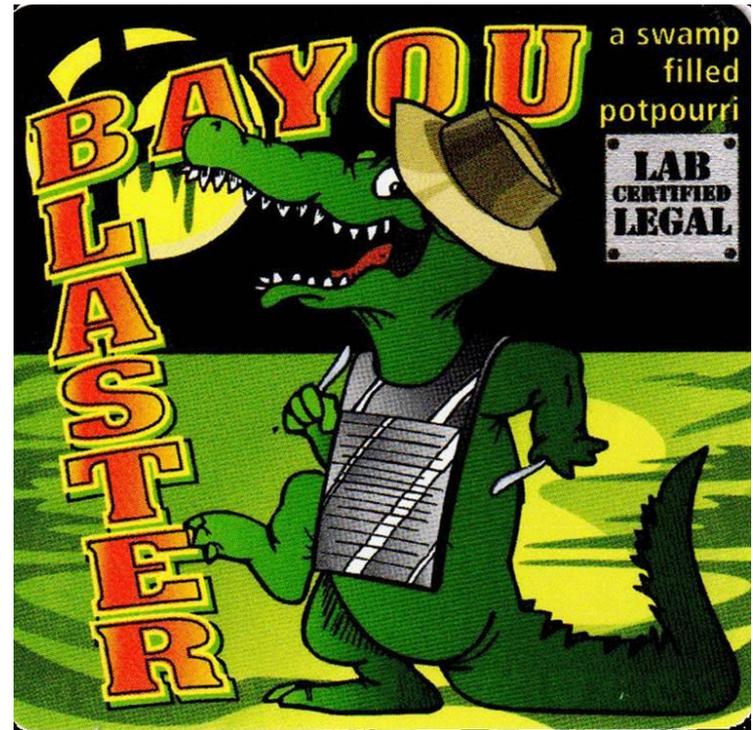


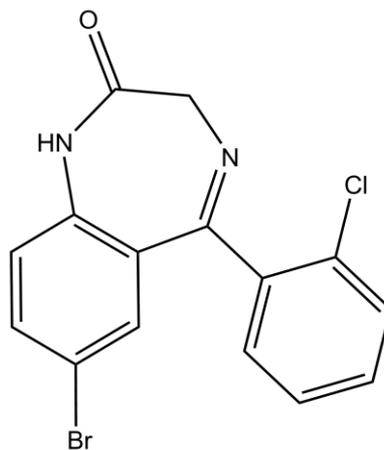
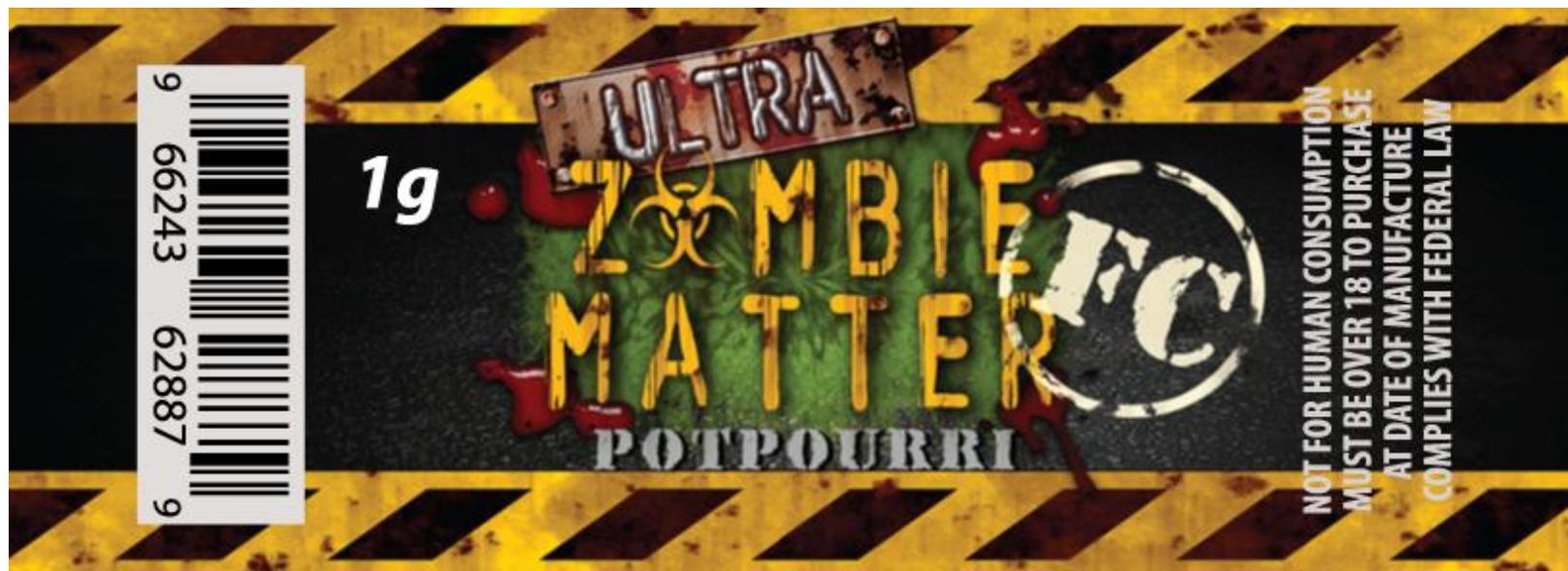
Alpha-PVP



Pentedrone







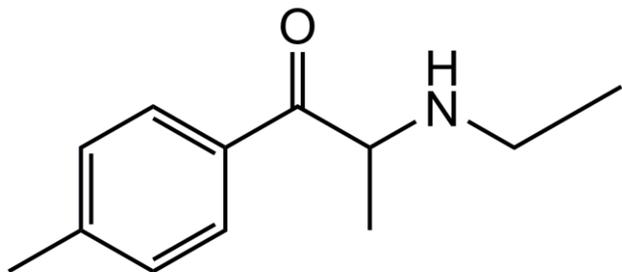
Phenazepam



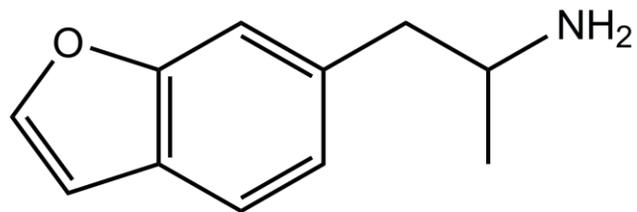
- Explicitly bans 15 cannabinoids, 2 stimulants, and 9 psychedelics (July 2012).
- Bans any CB₁ agonist by structural class
 - Includes all 1st and 2nd generation chemicals by structure
 - Must prove prove agonism by functional assay and binding affinity
- Federal analog act
 - Substantially similar in chemical structure
 - Substantially similar in pharmacological effects on the CNS



Product Analysis 3rd Generation



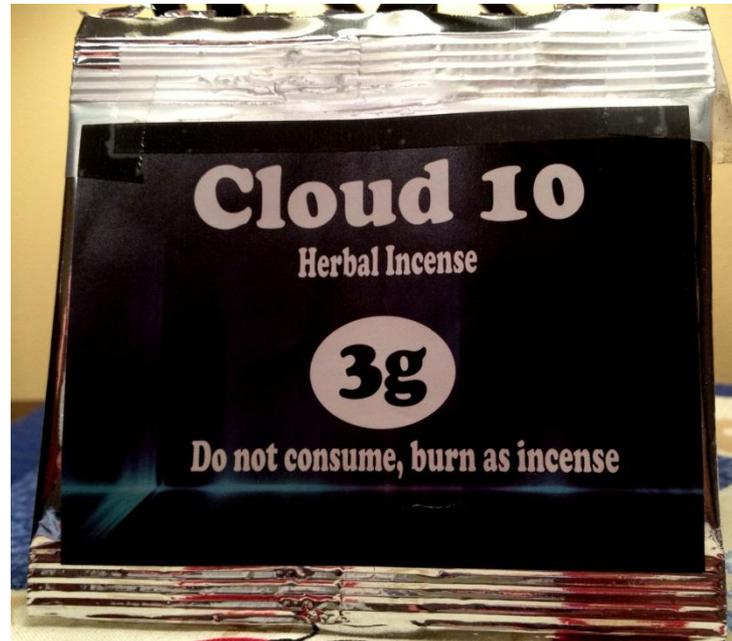
4-MEC



6-APB

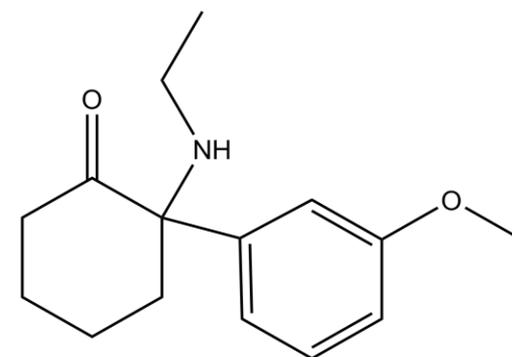






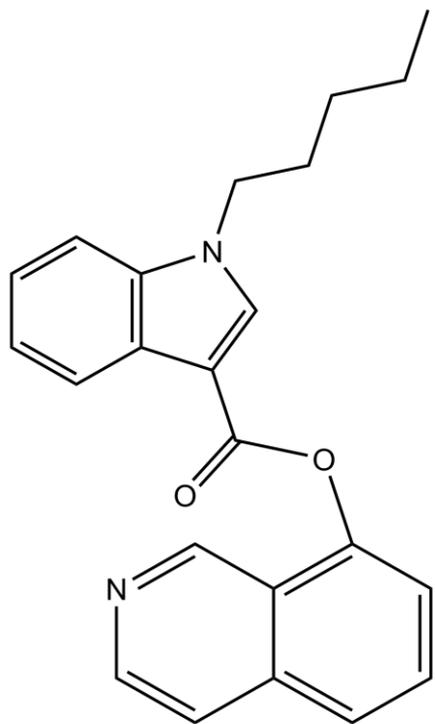




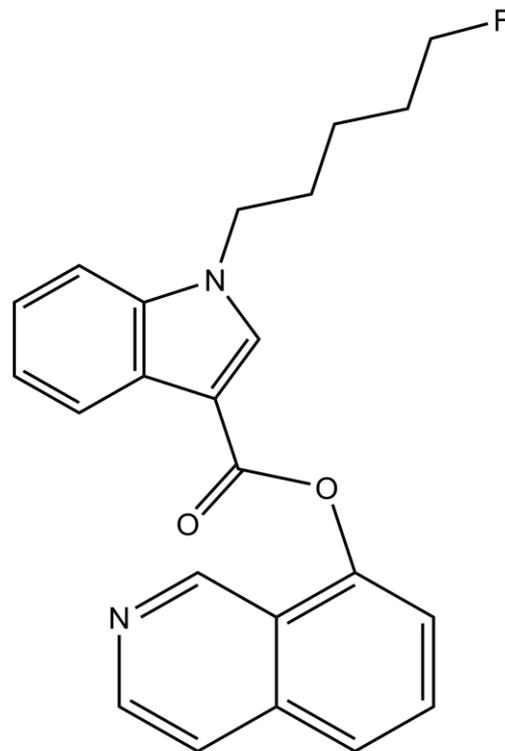


Methoxetamine

Product Analysis 4th Generation



PB-22



5F-PB-22



The cat-and-mouse games will continue.



Synthetic Cannabinoids

What are we seeing now in forensic casework?

UR-144, XLR-11, PB-22, 5F-PB-22

Still have appearances of older chemicals, but rare

Positive results from:

AZ, IN, IL, KY, LA, MI, MO, OH, TN, TX, WI

Synthetic Stimulants

What are we seeing now?

Alpha-PVP, Pentedrone, and 4-MEC

1 MDPV and 1 Methylone positive case over the last 12 months

Positive results from:

AZ, IN, IL, KY, LA, MO, OH, and PA

30+ postmortem cases in 2011-2012

1 case in 2013

5 selected cases – Suicide

AZ (1), IN (3), PA (1)

3 males, 2 females

Total age range: 25-36years

Male: 25-33 years

Female: 35-36 years

Concentrations: 68.3-1,044 ng/mL

Mean (427 ng/mL)

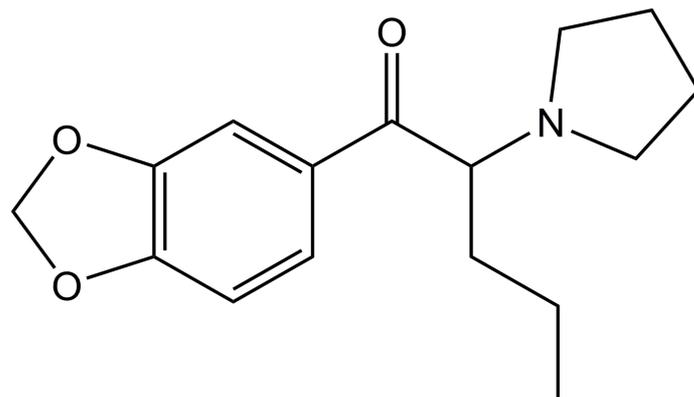
Std Dev (372 ng/mL)

Never the sole substance detected.

Other commonly detected drug classes

Ethanol, Amphetamines, Cannabinoids, Opioids

3 gun shot wounds, 2 hangings



25 year old male

Previous suicidal behavior noted

Chronic user of “bath salts” over the last 2 weeks

On a binge with a “friend”

Extreme paranoia and delusions

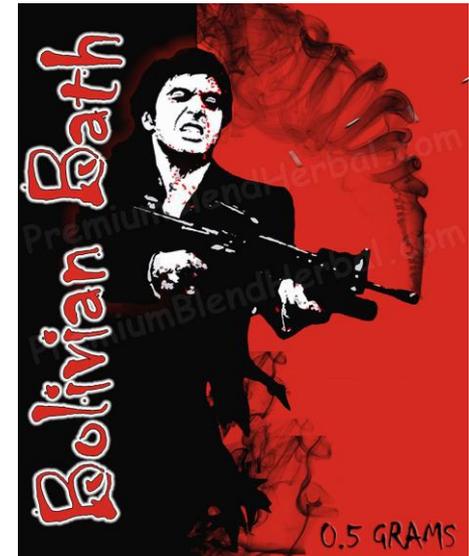
Ran away from “people trying to beat and kill him”.

Found hanged.

MDPV (472 ng/mL)

Mephedrone (<10 ng/mL)

THC-COOH



Bolivian Bath
BOLIVIAN BATH salt contains a pure, (99+%) single entity, water softening agent, designed to enhance your bath with feelings of intense euphoria, energy & focus.
NOT FOR HUMAN CONSUMPTION
MANUFACTURED IN THE USA
FOR
Pure-Bath.com

17 postmortem cases in 2012

AZ (2), CO (1), IA (1), IL (2), IN (7), KY, (1) MI (1), MO (1), OH (1)

13 males, 4 females

Total age range: 19-52 years

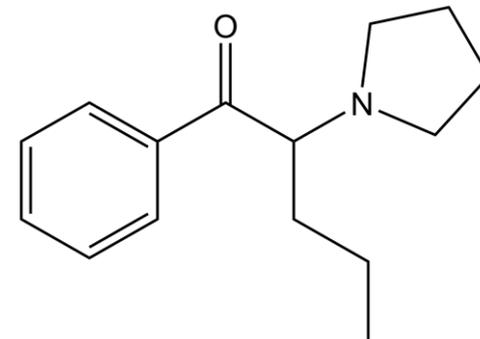
Male: 19-49 years

Female: 26-52 years

Concentrations: 5-732 ng/mL

Mean (317 ng/mL)

Std Dev (227 ng/mL)

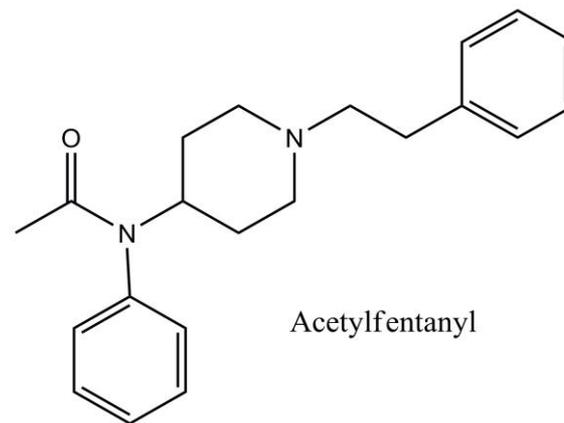
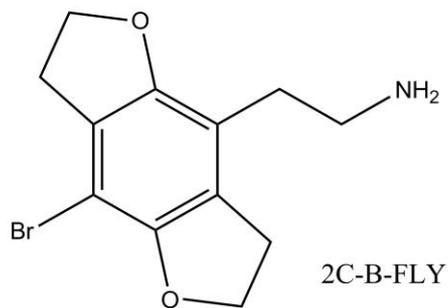
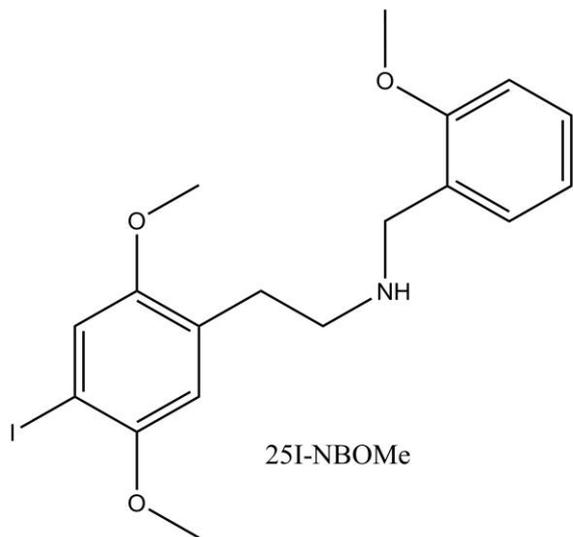
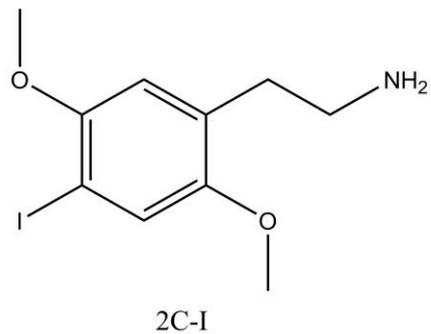
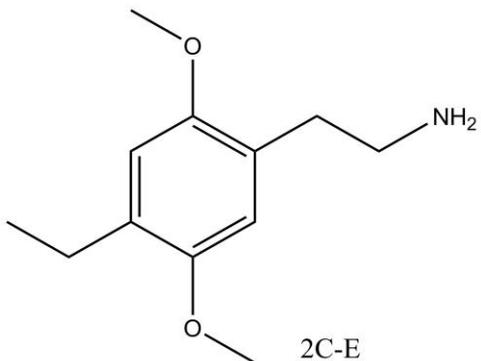


Never the sole substance detected.

Other commonly detected drug classes

Cannabinoids (7), Opioids (6), Amphetamines (5), Antidepressants (4)

Variable causes and manners of death



Thank you!

Comments? Questions?