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**SYNTHETIC DRUGS:
BATH SALTS, HERBAL INCENSE
AND MORE...**

Disclosure

- I have no possible financial or personal relationships with commercial entities (or their competitors and products) that may be referenced in this presentation.

Objectives

- Identify emerging trends in synthetic drugs of abuse
- Understand the history, development, and pharmacology of synthetic drugs
- Recognize the most common clinical manifestations of these drugs
- Apply appropriate management principles and modalities in intoxicated patients

One major caveat

- Very few street drugs are 100% pure
- Many are adulterated or contaminated
- Discussion will be over pure presentation

Shrub to Bath Salts?



Catha Edulis

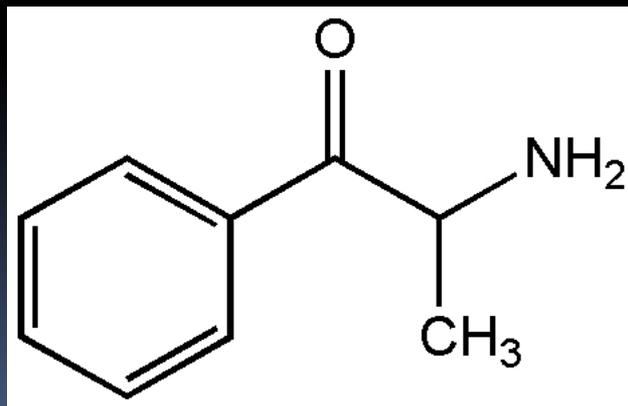


Khat plant geography



What is khat?

- Cathinone active alkaloid in khat leaves
- Chewing popular in middle east
- Produces amphetamine-like sympathomimetic symptoms

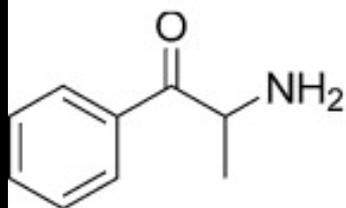


What are bath salts?

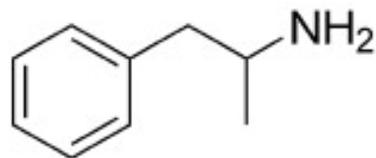
- Synthetic cathinone derivatives
- Synthesized as early as 1928 and studied for medical use
 - Methcathinone
 - Mephedrone
- Bupropion only cathinone with medical indication
- MDPV, mephedrone, buphedrone, pentedrone, methylone, 4MEC, 4MePPP, α -PVP, etc

Structures!

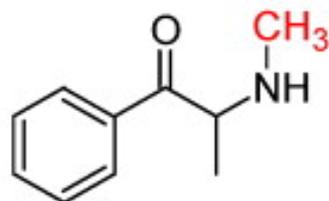
Cathinone



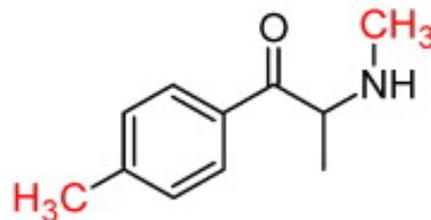
Amphetamine



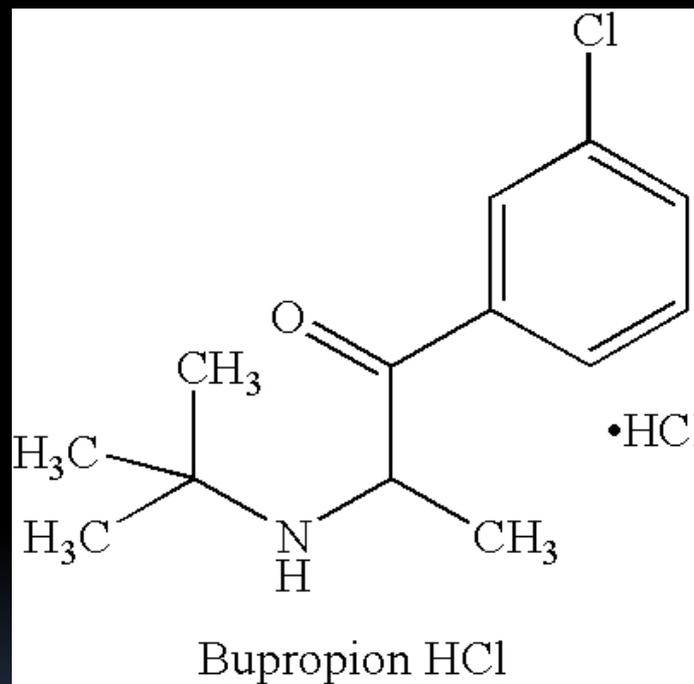
Methcathinone



Mephedrone



Source: EMCDDA (2009c).



Pharmacology

- Similar to amphetamines
 - Affect dopamine, serotonin, and norepinephrine
- Neuronal stimulation due to increased post-synaptic catecholamines
 - Increased release of catecholamines
 - Blockade of pre-synaptic uptake and storage
 - Reduced MAO activity
 - Indirect glutamate pathway stimulation
- End result: increased chemicals in the synapse causing increased effects

How supplied?

- Powder, capsules, and tablets
- Insufflation, ingestion, IV use, and rectal use
- Mephedrone: 100 – 200 mg
- MDPV: 10 – 15 mg
- Effects within 30 mins; lasts up to 7+ hours



Patient Case

- 30 yo male admits to using 1 – 2 grams of bath salts daily x 2 months
- VS: 187/93 P129 R12-16 T 98
- Presents to ED “shaky and anxious” and hallucinating
- Administered lorazepam
- Patient returns to baseline 24 hours later

Patient Case

- 26 yo male presents to ED after injecting bath salts
- Found agitated, altered, violent and combative and foaming at the mouth by EMS
- VS: 148/66 P175 T 106.3 (rectally)
- Patient intubated with RSI and aggressive cooling measures instituted
- CK peaked at 235,377 U/L (normal < 170 U/L)

Patient Case

- 40 yo male injected unknown amount of “bath salts”
- Became aggressive, uncontrollable, delusional, removed all his clothing, and violent behavior
- Tazed by police and had to be physically restrained by EMS
- VS: P 164 131/72 R24 rectal temp 105.4
- Declared brain dead 42 hours after presentation after complicated ICU stay

Clinical Manifestations

- Agitation (53.3%)
- Tachycardia (40%)
- Hypertension (20%)
- Seizures (20%)
- Palpitations (13.3%)
- Hallucinations/delusions
- Paranoia
- Renal failure?
- Cannibalism?
- Death



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Clinical Manifestations

- 45% of patients experience symptoms beyond 24 hours post exposure
- 30% have symptoms > 48 hours post exposure
- Are there adulterants present or contaminants?



Management

- Protect yourself!
 - Difficult to manage patients and unpredictable behavior
- ABCs
- No antidote
- GI decon?
- BZDs, BZDs, and more BZDs for agitation
 - DPH likely won't be effective
 - Haloperidol could be problematic

Management

- All BZDs work the same
 - Increase frequency of chloride channel opening leading to hyperpolarization
 - Only works in conjunction with GABA

	Diazepam	Midazolam	Lorazepam
Onset			
IV	Quick (min)	Quick (min)	5 – 20 min
IM	Unpredictable	5 – 10 min	20 – 30 min
Duration			
Single dose	Short	Short	Long
Repeated Doses	Long	Intermediate	Long

Management

- What if BZDs do not work?
 - No real ceiling to BZD doses
 - Respiratory depression
 - Haloperidol
 - Anticholinergic
 - QTc prolongation
 - Risk vs benefits
- Bring product into ED

Synthetic Cannabinoids



Mr. Nice

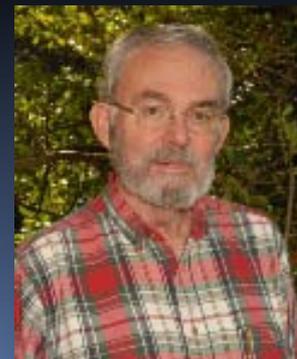


HERBAL SMOKE
ULTRA PREMIUM SMOKE BLEND
100% DRUG TEST SAFE



Where did it come from?

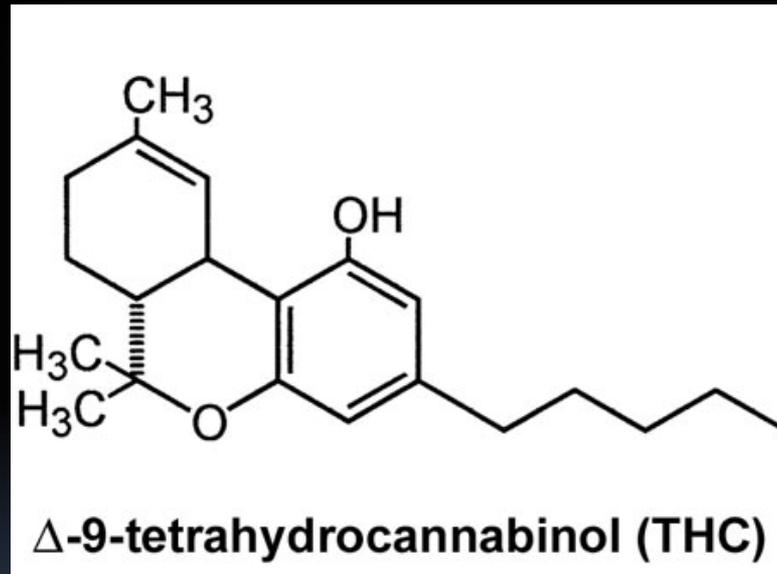
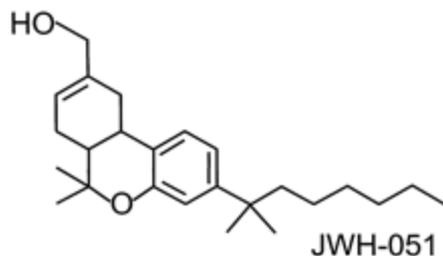
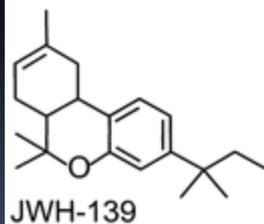
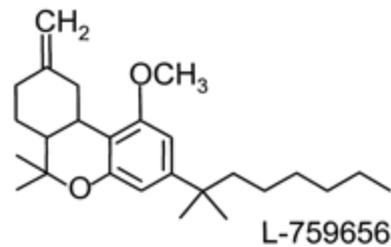
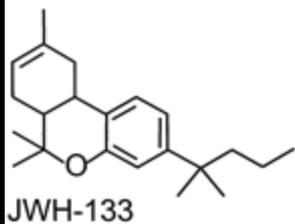
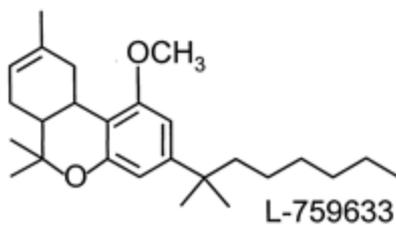
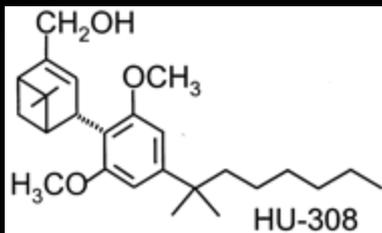
- 1960s: research into THC-like compounds
 - Analgesic and anti-inflammatory minus psychotropic effects
- Recognized as drugs of abuse in early 2000's in Europe
- Dr. JW Huffman researched THC analogues for use in cancer and AIDS patients
 - Developer of JWH compounds
 - HU-210 from Hebrew University



What are they?

- Synthetic cannabinoids which work on the CB₁ and CB₂ receptor like THC
- Marketed as herbal incense, herbal smoking blends, potpourri, etc.
 - Spice, K2, Mr. Nice Guy, Legal Funk, Tai Fun, Zen Ultra, Smoke, Chaos Mint, etc.
- Misleading packaging
 - Not for human consumption
- Commonly smoked

What's in them?



Pharmacology

- Effects likely from mixture of herbs and actual synthetic compounds
 - Baybean, Beach bean, Dwarf skullcap, red clover, vanilla, honey, wild dagga and more
- Affects CB₁ and CB₂ receptors found in CNS/PNS
 - Responsible for elevating mood, anxiety, cognition
 - Responsible for reducing inflammation induced pain
- HU-210 100-800x more potent than THC

Patient Case

- 21 yo male smoked some K2 earlier in evening
- Presents to ED tachycardic, dilated pupils and with myoclonic jerking
- Given BZDs and symptoms resolved over 8 hours

Patient Case

- 48 yo man had generalized seizure within 30 minutes of ingesting a synthetic marijuana-like product
- Initial vital signs were: pulse, 106/min; BP, 140/88 mmHg; respirations, 22/min
- GCMS confirmed substance to be JWH-018

Patient Case

- 35 yo male admits to smoking legal weed 90 minutes ago
- C/o chest pain and dizziness
- Supportive care instituted
- Patient leaves AMA

Clinical Manifestation

- Most information from case reports and case series
- Psychiatric effects predominate
 - Anxiety, paranoia, agitation, delusions, and psychosis
- Physical manifestations
 - Tachycardia, HTN, diaphoresis, seizures, and ????

Management

- Like bath salts, unpredictable
- ABCs
- GI decontamination
- No antidote
- Supportive care
 - BZDs for agitation and anxiety
- Bring product into the ED

Ecstasy-related Compounds



Ecstasy-related Compounds

- 1990s: surge in use of 3,4-methylenedioxy-N-methylamphetamine (MDMA)
- Many new derivatives available now
- Most contain little MDMA
 - Amphetamine, DXM, BZP, etc.
- Next generation includes:
 - Tryptamines
 - Phenylethylamines
 - Piperazines

Tryptamines

- Re-emerged on drug scene
- Include DMT, 5-MeO-DIPT, 5-MeO-DMT, and more
 - Yakee plant, Foxy methoxy, alpha-O, O-DMS, alpha and bufo toad secretions
- Similar to psilocybin, psilocin, and bufotenine
- Derivatives of tryptamine contain stimulant and hallucinogenic effects

Tryptamines



diisopropyltryptamine (5-Me)-DIPT)

Tryptamines

- DMT discovered in 1960s
- “Businessman’s lunch”
- DMT used in South America for spiritual and medicinal purposes
- Available in various formulations



Tryptamines

- Mechanism of action not fully elucidated
- Similar to classical hallucinogens like LSD
 - Agonists at 5-HT₂ and 5-HT_{1C}
- Presentation includes
 - Empathy
 - Euphoria
 - Visual/auditory hallucinations
 - Tachycardia/HTN
 - Confusion
 - Seizures

Tryptamines

- Management essentially supportive
- No specific antidote
- Benzodiazepines used for sympathomimetics symptoms

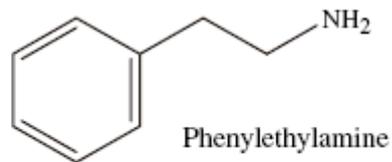
Phenylethylamines

- Newer designer analogues designated “2C” series
 - DOM: STP (Serenity, Tranquility, & Peace)
 - Mescaline: Mesc, Buttons, Cactus
 - 2C-B: Nexus, Bromo, Bees, Venus
 - 2C-T-2: Triptasy or Beautiful
 - 2C-E: Europa, Eternity
 - 2C-T-7: Blue Mystic and 7th Heaven
- Magical half-dozen

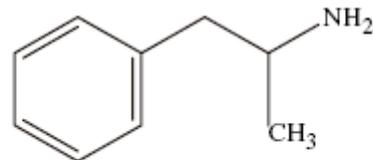
Phenylethylamines

- Exact mechanism uncertain but...
 - Direct and indirect sympathetic receptor stimulation
 - Inhibition of monoamine oxidase
 - Inhibition of reuptake by presynaptic neurons
 - Biotransformation to indolamines related to 5-HT
 - 5-HT_{2A} agonism
- Net result: hallucinogenic and stimulant activity

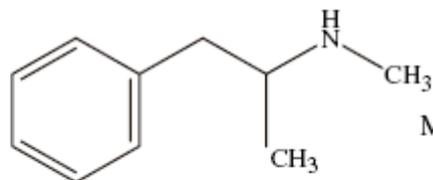
Phenylethylamines



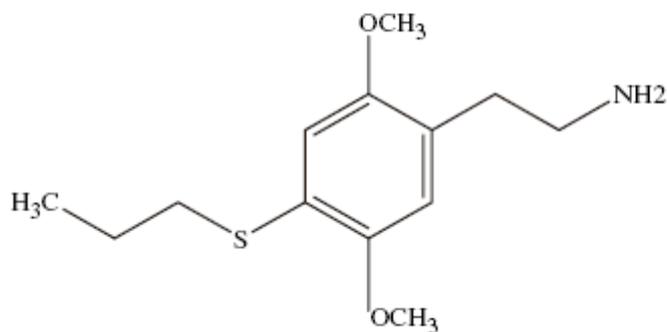
Phenylethylamine



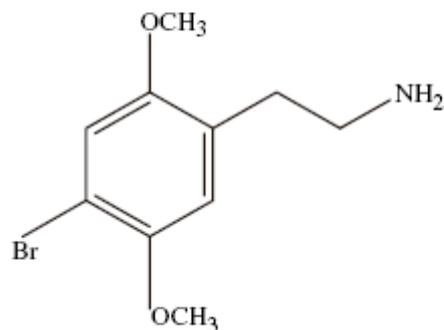
Amphetamine



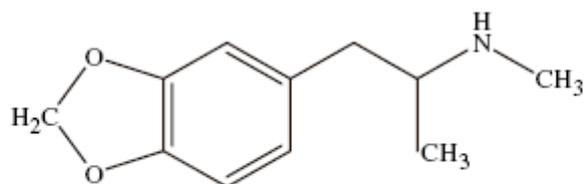
Methamphetamine



2,5-dimethoxy-4-(n)-propylthiophenethylamine (2C-T-7)



4-Bromo-2,5-methoxyphenyl-ethylamine (2CB)



3,4-Methylenedioxyamphetamine (MDMA)

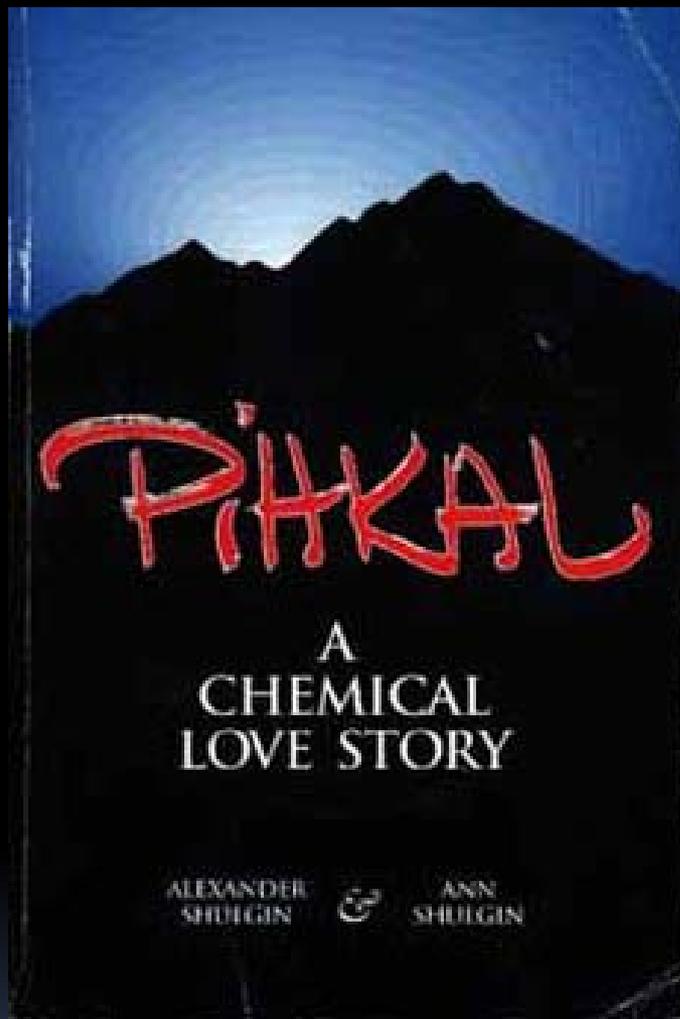
Phenylethylamines

- Hallucinations
 - Visual and auditory
- Euphoria
- Entactogen
- Tachycardia
- Paranoia
- Delirium
- Violent behavior
- Several fatalities reported with 2C-T-7
- Recently in Oklahoma
 - Death in young adult secondary to 2-CE exposure
- MAOI activity coupled with polysubstance ingestion?

Management

- Management largely supportive
- Gut decontamination indicated depending on route of administration
- Benzodiazepines as indicated for sympathomimetic symptoms

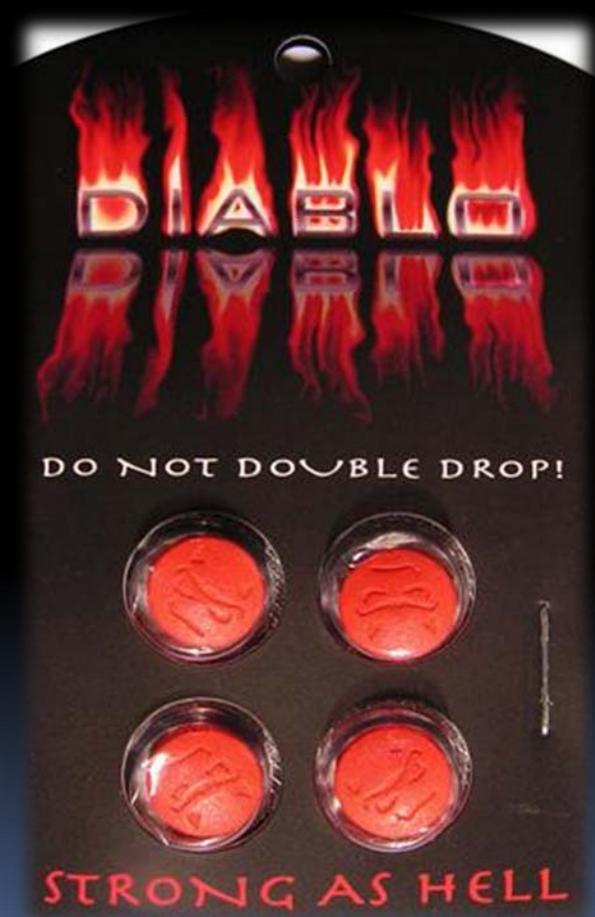
PIHKAL



http://www.erowid.org/library/books_online/pihkal/pihkal033.shtml

Piperazines

- Popular drugs of abuse marketed as “Party Pills” and “Legal Ecstasy”
- Street names include Benzo Fury, A2, Molly, MDAI, XXX Strong as Hell, and Exotic Super Strong
- Piperazines used as antihelminthic agents



Piperazines

- 1970s: potential antidepressant due to active metabolite
 - Serotonin reuptake inhibition and receptor agonism
- Due to adverse side effect profile, not pursued
 - BZP increased DA more than 5-HT → increased motor activity
- BZP schedule I drug as of 2004
 - TFMPP currently unscheduled

Pharmacology

- Increases sympathomimetic activity
 - Increased release of serotonin, norepinephrine, and dopamine
 - Inhibition of serotonin reuptake
- Net result: increased excitatory neurotransmitters in synapse

Piperazines

- BZP and TFMPP often combined due to synergistic and MDMA-like effects
- Presentation mix of stimulant and hallucinatory effects
- Deaths reported with BZP
 - 23-year-old woman developed massive brain edema and subsequent tonsillar herniation

Management

- Management largely supportive
- Benzodiazepines as indicated
- TFMPP and BZP known to be skin irritants
 - Skin decontamination
- Piperazines known to cause QTc prolongation in about a third of patients
 - EKG

Poison Control

- 24/7/365
- RNs, PharmDs, MDs
- On-call toxicologists
- Public and professional education
- 1-800-222-1222



Questions?

