Emerging Drugs of the 21st Century

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Emerging Drugs of Abuse discussion group

I don’t think we’re in Kansas anymore

Dorothy to Toto, “Wizard of Oz”

Previously "Emerging Drugs"

- 1805: Morphine
- 1837: Codeine
- 1880's: Cocaine is extracted from the coca leaf
- 1887: Amphetamine first synthesized
- 1898: Heroin is synthesized
- 1910: MDA is discovered
- 1911: MDMA is discovered
- 1937: LSD is synthesized
- 1950s: The benzodiazepines are introduced into medicine

Previously “Emerging Drugs”

- 1950s: PCP is developed by Parke-Davis
- 1960s: PCP, LSD, MDA become popular street drugs
- 1970-1980s: MDMA/”ecstasy” becomes a popular street drug

Our Agenda

- Synthetic cannabinoids (“K2/”Spice”)
- Synthetic cathinones (“Bath Salts”)
- “Drank”

How Prevalent is the Use of herbal Incense ("synthetic marijuana")?

- "Monitoring the Future" study:
  - 2011: 11.4 % of high school seniors have tried "synthetic marijuana" in the past year
  - 2012: 11.3%
  - Second most common illicit drug among adolescents
  - Only 25% of 8^{th}, 10^{th} and 12^{th} graders said that there is "great risk" in trying synthetic marijuana once or twice

Herbal Incense

- Crushed, non-psychoactive herbal/plant matter treated with one or -more synthetic cannabinoids
  - First Generation: “K2”, “Spice”, “Black Mamba”, “Red Dragon”
  - Second Generation: “K3”, “Splice”, “Apocalypse”, “Destiny”, “Cloud Ten”, “Head Trip”, house mixes
  - Third generation: ?

Current Legal Status of "first generation" Herbal Incense

- 2011: Drug Enforcement Administration (DEA) emergency scheduling authority makes five chemicals (JWH-018, -073, -200, CP-47,497, and cannabicyclohexanol) now illegal for at least one year

- DEA and the U.S. Department of Health and Human Services (DHHS) to study whether these chemicals and products should be permanently controlled.

- August 2012: All synthetic cannabinoids placed in Schedule I

Banned Herbal incense Brands

- Frequently marketed as “incense” under a variety of names:
  - K2
  - Spice/Spice Gold
  - Arctic Synergy
  - Black Mamba
  - Yucatan Fire
  - Red Dragon
  - Genie
  - Blaze
  - Red X
  - Dawn

BANNED HERBAL INCENSE PRODUCTS


12


Spice
10.11.08
NF
GOLD


HOME
spice
20.00
net wt. 3g
NOT FOR HUMAN CONSUMPTION
www.homespiceblends.com


2000
ORIGINAL
www.gomespiceblends.com


HOME spice
premium herbal incense blend
STRAWBERRY
net wt. 3g
+18 TO PURCHASE
NOT FOR HUMAN CONSUMPTION
www.homespiceblends.com
20.00

New Herbal Incense Brands

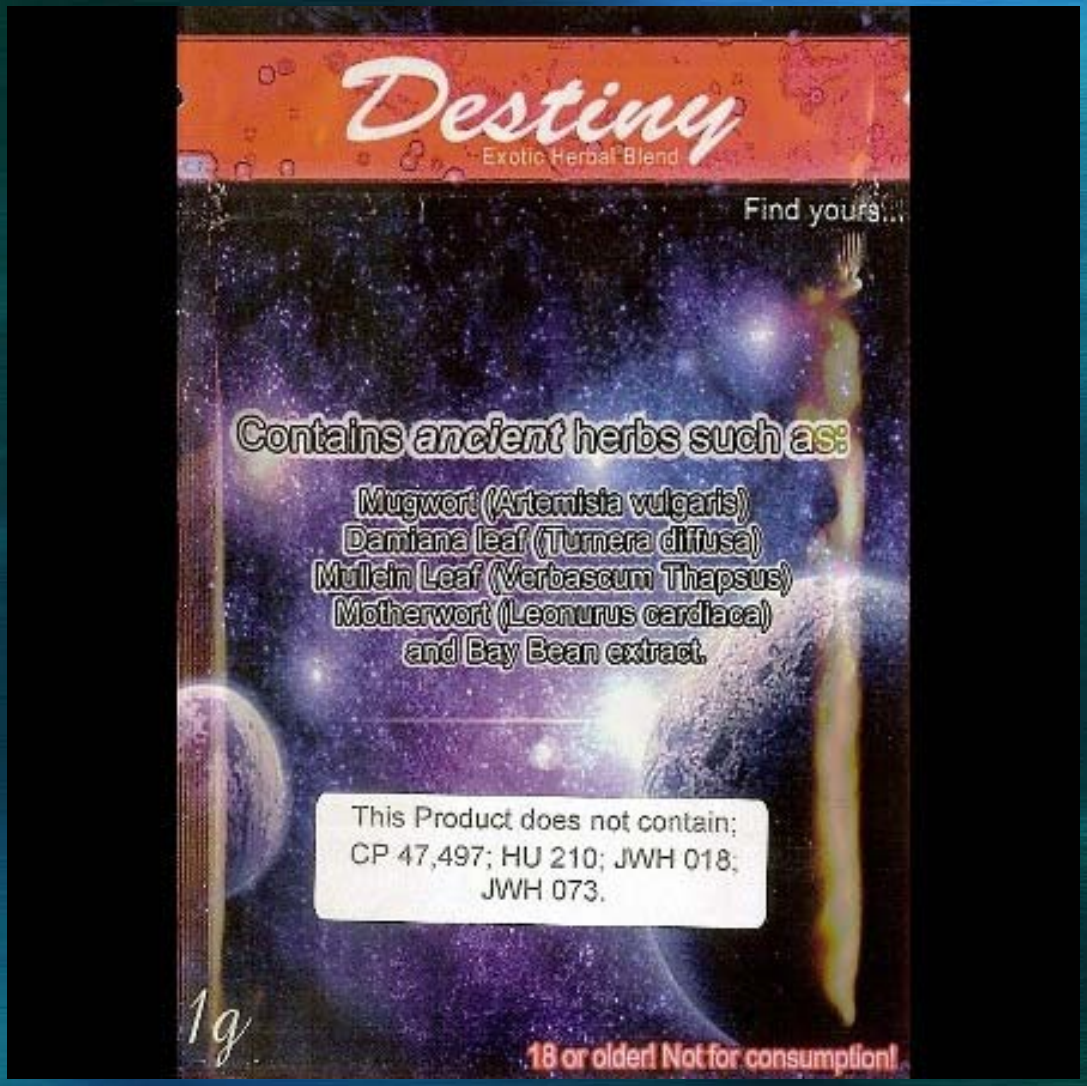
- K2
- K3
- Destiny
- Splice
- Apocalypse
- Cloud Ten
- Head Trip
- “House Blends”

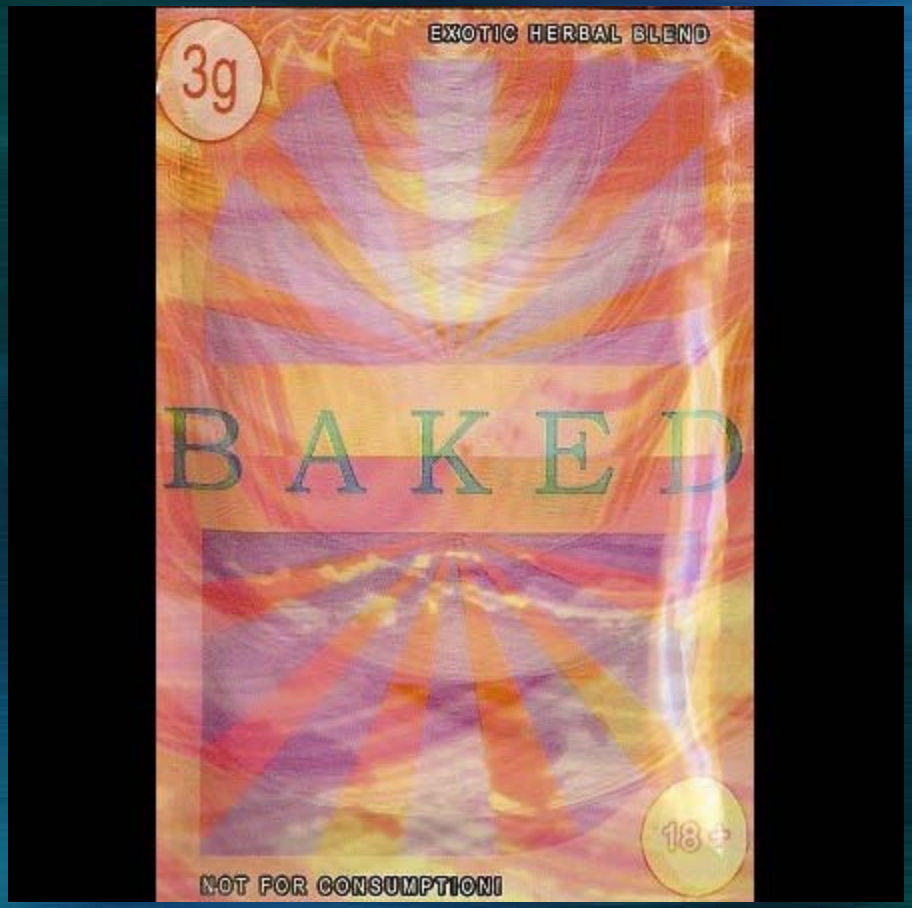
Apocalypse Flavors

- BLUEBERRY
- STRAWBERRY
- JUNGLE JUICE
- CHERRY
- **COTTON CANDY**
- COCONUT
- LEMON
- LIME.
- SPEARMINT
- **ROOT BEER**
- BANANA
- **BUBBLE GUM**
- ORANGE
- COCA COLA
- **”JOOSY FRUIT”**
- RASPBERRY
- PEACH
- APPLE
- CHOCOLATE
- GRAPE
- WATERMELON
- PINEAPPLE
- MANGO


K3
NEW & IMPROVED
XXX


Splice tm
Herbal Additive &
Extreme Herbal De-celerator


Destiny
Exotic Herbal Blend
Find yours...
Contains ancient herbs such as:
Mugwort (Artemisia vulgaris)
Damiana leaf (Turnera diffusa)
Mullein Leaf (Verbascum Thapsus)
Motherwort (Leonurus cardiaca)
and Bay Bean extract.
This Product does not contain:
CP 47,497; HU 210; JWH 018;
JWH 073.
1g
18 or older! Not for consumption!

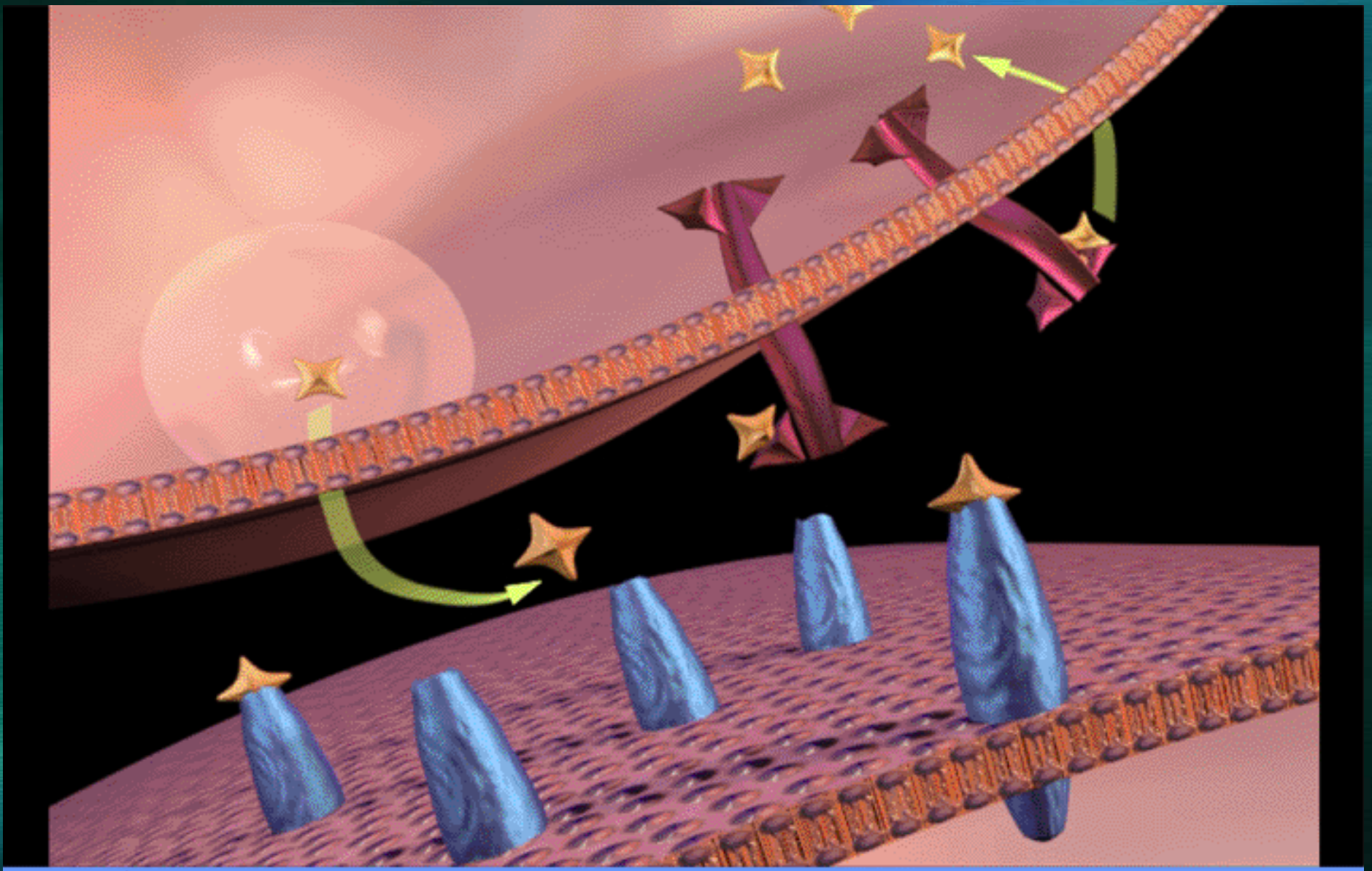

3g
EXOTIC HERBAL BLEND
BAKED
18+
NOT FOR CONSUMPTION!

Herbal incense Pharmacology

- Hundreds of synthetic cannabinoids (similar to both Δ9-THC and endogenous cannabinoids) have been created
- Potency ranges from hundreds of times *more* potent than THC to over 1000x *less* potent
- Most common psychoactive ingredient in herbal incense was JWH-018 (1-pentyl-3-[1-naphthoyl]indole)
- Synthesized in 1995 by Dr. John W. Huffman at Clemson University

Herbal incense Pharmacology

- Research supported by NIDA
- Two cannabinoid receptors in the human brain, CB_1 and CB_2
- CB_2 affects inflammatory pain and was the focus of NIDA study
- JWH-018 targets both receptors
- Huffman: “JWH-018 easiest to make outside a lab, requiring only two steps involving commercial products”
- Transferring the JWH to the botanical product involves using acetone



NIDA NATIONAL INSTITUTE ON DRUG ABUSE

www.drugabuse.gov

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Herbal Incense in the Popular Press

- Sales of “K2” products increased significantly in Chicago following news of its impending status as a controlled substance
- Following an August 2008 report on “herbal incense” in Germany, ER visits ↑ significantly
- How do we inform the public of new drugs without setting of an epidemic of use?

Herbal Incense Pharmacology: The Scientific Literature

At present, almost nothing is known about the pharmacology, toxicology and safety profile of such compounds in humans*, except the opinions of consumers in internet forums.

Mustata, C; Torrens, M; Pardo, R; Perez, C; Farre, M. (2009).

a/k/a “human guinea pigs”

- 2009-2013: Peer-reviewed papers and medical reports begin to appear in the literature

Herbal Incense: Typical Effects

- Cannabis-like intoxication
- Dreaminess
- Euphoria
- Introspective mood
- Hilarity
- Forgetfulness
- Heightened sensory perception

THESE ARE THE EFFECTS MOST COMMONLY REPORTED BY USERS

Poison Control Center/ER Data

- Data from the American Association of Poison Control Centers' "National Poison Data Center"
  - 2010: 2,874 calls
  - 2011: 3,000
  - As of July 31, 2011: 3787
  - All of 2011: 6995 (90% from hospitals)
  - 2012: "Calls continue to increase"
- Drug Abuse Warning Network (DAWN):
  - 2011: 11,406 emergency department visits involve a synthetic cannabinoid product
  - 2012: 28,531.

Herbal Incense: Other Possible Effects

- Severe anxiety (may persist after herbal incense use is discontinued)
- Panic attacks
- Dissociation (e.g., derealization)
- Racing thoughts
- Hallucinations
- Rapid pulse (tachycardia)
- Seizures (*Journal of Addiction Medicine*, Sept 2012)

User Report # 1

- 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: "Apocalypse"

- 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

Case Study 1

- 33 y.o. man
- 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 AOD use
- Repeated episodes of anxiety still occurring after 18 months of abstinence

Case Study 2

- 16 y.o. female
- In treatment for alcohol dependency
- History of bipolar disorder
- Smoked 3 “hits” of herbal incense
- 10 minutes (8:00 P.M.) later experienced psychotic episode
- Following observation at hospital, returned to normal at 12:00 A.M.
- Next day no apparent aftereffects

Why the Discrepancy in Reported Effects?

- Use of other drugs (including alcohol) with herbal incense
- Varying potency
- “Hot spots”
- Overdose
- Presence of different cannabinoids
- “Knock-offs”
- User/environmental characteristics:
  - Setting
  - Set

Why the Discrepancy in Reported Effects?

- User/environmental characteristics:
  - Set
    - Age
    - Psychological stability
    - Previous experience with psychoactive drugs
    - Immediate support system
- Sensationalism (some reports taken out of context)
- Anti- Pro-drug attitudes
- Agency funding/Visibility

Overview

- Herbal incense contains a cannabinoid closely related to THC/marijuana
- No quality control
- Manufacturing process may be associated with adverse effects
- Subjective effects most commonly resemble those of extremely powerful marijuana

Overview

- Other reported effects range from intense euphoria and pleasant hallucinations to abject terror and near-psychotic reactions
- Almost complete lack of scientific study
- 2012: Reports of seizure activity begin
- Street information is very inconsistent

Synthetic Cathinones

Khat

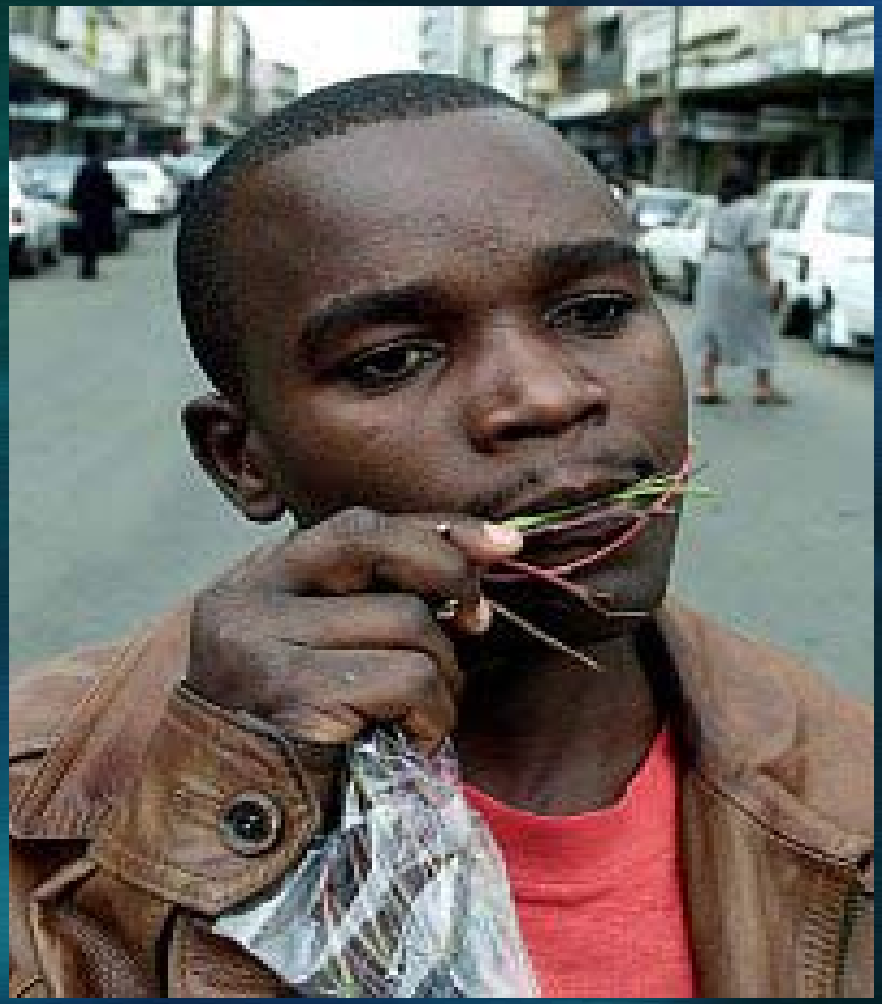
Khat

- Native to tropical East Africa and the Arabian Peninsula
- Fresh leaves/tops chewed or consumed as tea
- Stimulation and euphoria
- Part of social culture in many countries (coffee, tea, coca or khat?)


EGYPT
SAUDI ARABIA
OMAN
CHAD
ERITREA
YEMEN
SUDAN
DJIBOUTI
ETHIOPIA
CENTRAL AFRICAN REPUBLIC
SOMALIA
UGANDA
DEM. REP. OF THE CONGO
KENYA
RWANDA
BURUNDI
TANZANIA
INDIAN OCEAN

Khat cultivation in Yemen

Khat chewing



Women in Somalia Selling Khat/Quat

Khat

- Coca--------Cocaine
- Khat---------Cathinone (Schedule I)
- Cathinone: Structure similar to amphetamines
  - Euphoria
  - Anorexia
  - Stimulation
  - Dilated pupils

BATH SALTS*

* Contain schedule I substances as of October 2011

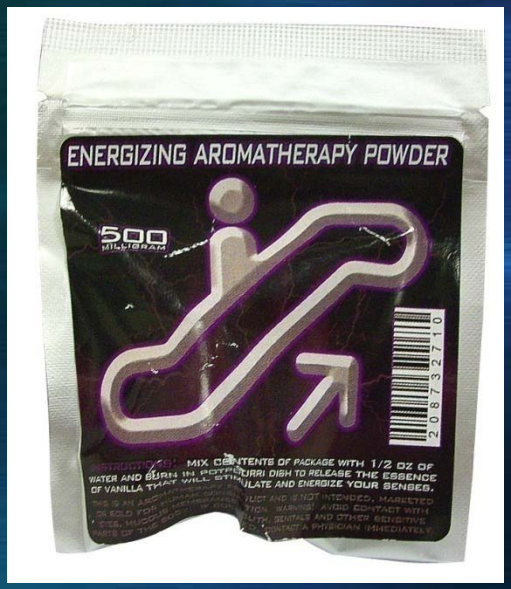
Typical Stimulant Effects

- CNS Stimulation
- Insomnia
- Decrease in appetite
- Euphoria

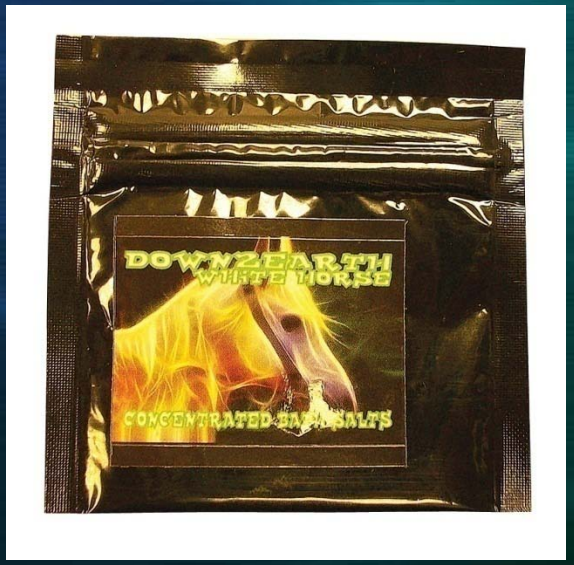
- Cardiovasular events
- Stroke
- Psychosis

“Bath Salts” A/K/A “Plant Food”

- Energizing Aromatherapy
- Down2Earth White Horse
- Kamikaze
- Ivory Wave
- Purple Wave
- Red Dove
- Blue Silk
- Vanilla Sky
- White Blizzard
- *Fake Cocaine*



Aromatherapy



Bath Salts

"White Blizzard"

Khat to Cathinone

- Khat
- Cathinone (Schedule I)
- Methcathinone (Schedule I)

Methcathinone (Schedule I)

- First synthesized in 1928
- 1930s: Used in the Soviet Union as an anti-depressant.
- 1960s: Began to be used as recreational drug in (former) Soviet Union
- More powerful than cathinone
- Effects similar to amphetamines/cocaine
- 1990s: Appeared in U.S. as “cat”
- Little current use

Possible Substances in "Bath Salts"

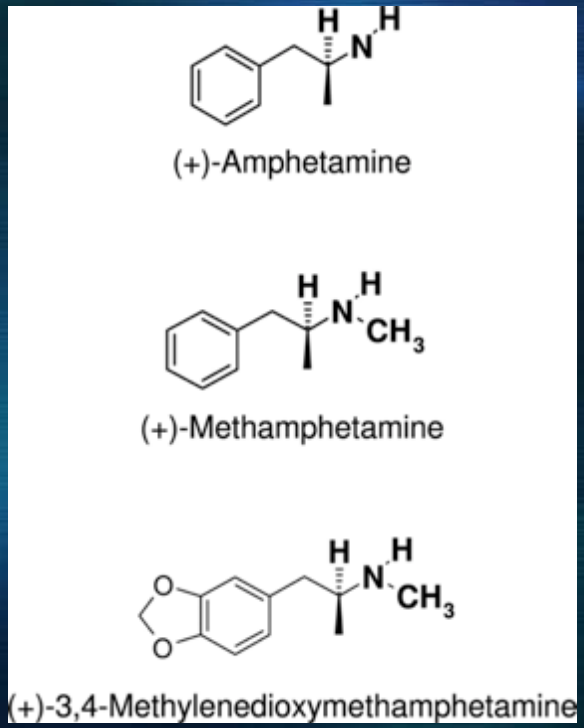
- **All related to cathinone/methcathinone**
  - **3,4 – Methylenedioxypyrovalerone (MDPV)**
  - **4 – Methylmethcathinone (Mephedrone, M-Cat, Meow, 4-MMC)**
  - **3,4 – Methylenedioxymethcathinone (Methylone, MDMC)**
  - Butylone
  - Pentedrone
  - Pentylone
  - MPPP

Possible Substances in “Bath Salts”

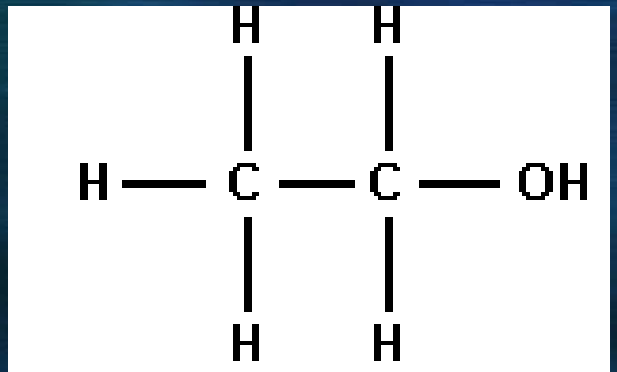
- **All related to cathinone/methcathinone**
  - **Alpha-pvp**
  - **6-apb**
  - **Ethylone**
  - **Buphedrone**
  - **4-MEC**
  - **3,4-DMMC**
  - **Isopentadrone**
  - **pyrovalerone**

Small Differences = Different Drugs

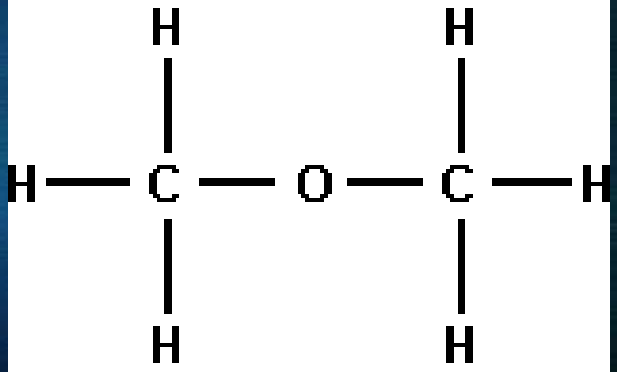
- Methamphetamine
- Methcathinone
- Methylenedioxymethamphetamine
- Methylenedioxymethcathinone



CHEMICAL ISOMERS
BOTH CHEMICALS ARE H_6C_2O,
BUT THEY ARE NOT THE SAME CHEMICAL!



ethanol



dimethyl ether

MPTP: A Cautionary Tale

- Meperidine (Demerol®) is a synthetic opiate
- MPPP is a similar substance
- MPTP can be produced during manufacture of MPPP
- MPTP is converted into MPP^+
- MPP^+ destroys dopamine cells in the substania nigra
- Leads to Parkinson-like symptoms
  - Tremor
  - Rigidity
  - Slow movements
  - Problems with walking and gait
  - (Paralysis)

M-CAT

4-Methylmethcathinone & Caffeine:

MDMA, caffeine & 4-Methylmethcathinone

4-Methylmethcathinone & Caffeine

4-Methylmethcathinone & Methylone

“Plant Food”

“Novelty Collector’s Item

Mephedrone

- (4-methylmethcathinone /(4-MMC) or 4-methylephedrone)
- Do not confuse with methadone or methylone
- Onset:
  - Oral: 15–45 minutes
  - Insufflation (nasal/“snorting): 10 minutes
  - i.v. injection (rare): 30 seconds
- Duration:
  - Oral/Nasal: 2-3 hours
  - Intravenous: 30 minutes

Mephedrone

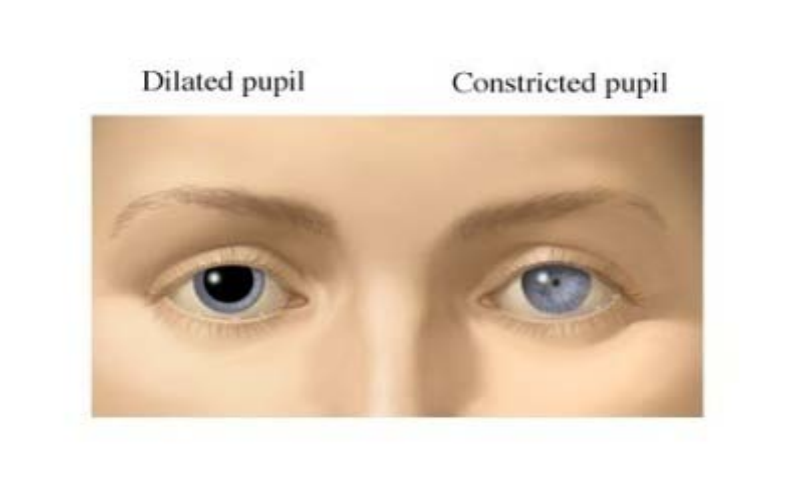
- No formal published studies effects on humans
- One animals study that could be applied to humans
- Controlled under federal analog

Mephedrone

- Intended Effects: (Similar to MDMA/"ecstasy", amphetamines and/or cocaine)
  - Euphoria
  - Stimulation
  - Enhanced music appreciation
  - Decreased hostility
  - Improved mental function
  - Mild sexual stimulation

Mephedrone

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

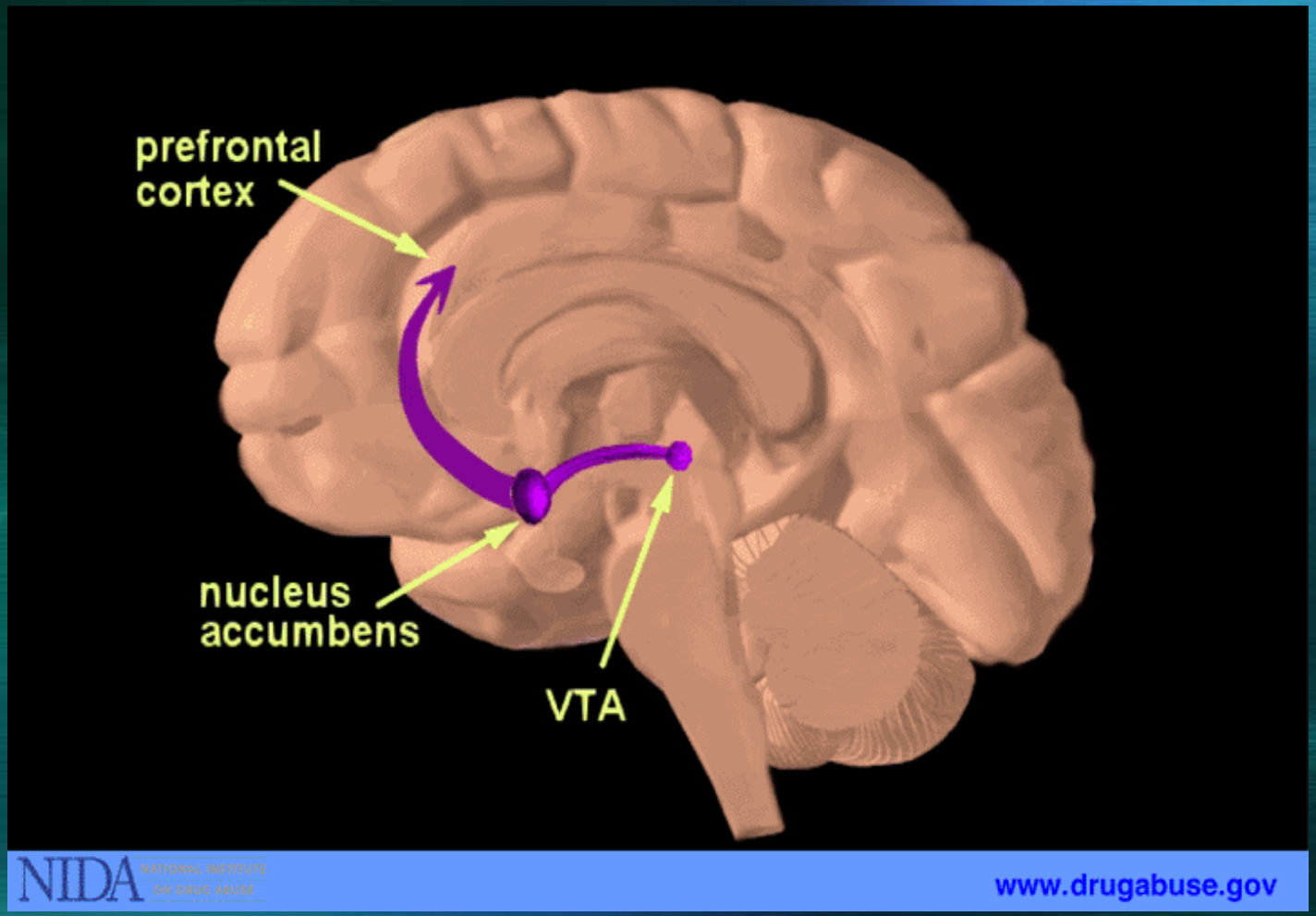


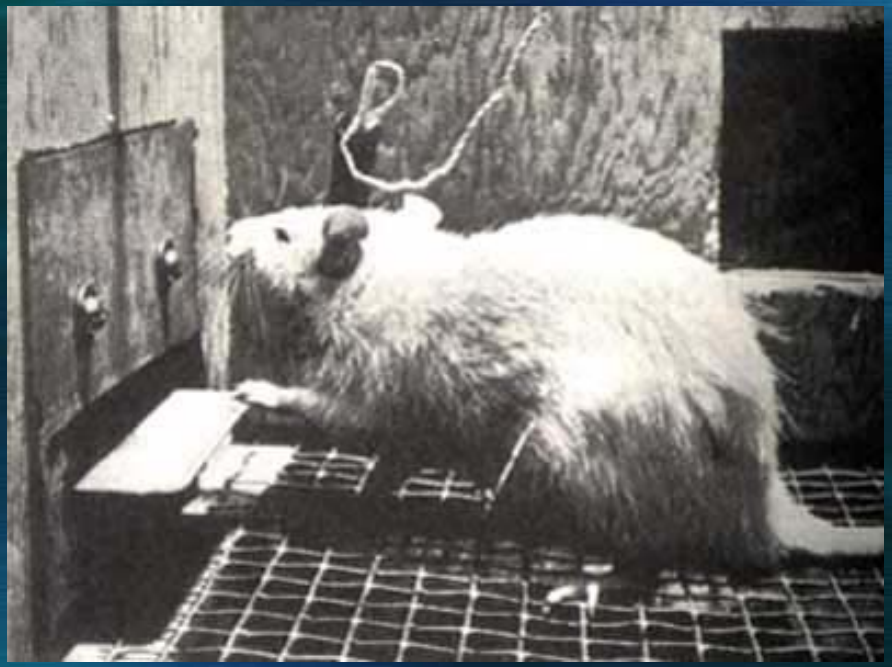
Mephedrone Research

- UK Study:
  - Users w/ previous cocaine experience:
    - Better quality and longer lasting high
    - Less addictive
- Robinson, et. al. (2012)

Mephedrone: Addiction Potential

- Dr. C.J. Malanga at University of North Carolina
- Effect of mephedrone and cocaine on intracranial self-stimulation (ICSS)


prefrontal cortex
nucleus accumbens
VTA
NIDA
www.drugabuse.gov



Intracranial Self-Stimulation

- Animal is fitted with an e electrode implanted in mesolimbic reward pathway (MRP)
- Animal allowed to stimulate MRP by bar pressing
- Results in brain stimulation reward (BSR).

Cocaine and Intracranial Self-Stimulation

- Allowing an animal already fitted for ICSS to self-administer cocaine decreases its ICSS
- Cocaine augments the pleasurable sensations produced by BSR and reduces the animal's desire to engage in ICSS
- When cocaine is available, ICSS is less desirable

Mephedrone and Intracranial Self-Stimulation

- Animals allowed to self-administer mephedrone decrease their ICSS
- Like cocaine, mephedrone makes ICSS less desirable
- Consistent with user self-reports

MDPV

- euphoria
- increased alertness, awareness and arousal
- increased energy and motivation
- mental stimulation/increased concentration
- increased sociability
- sexual stimulation/aphrodisiac effects
- Mild empathogenic properties
- diminished perception of the requirement for food and sleep

MDPV Addiction Potential

- August 2013 journal *Neuropharmacology*
- Animal self-administration
- Found to be more rewarding than methamphetamine

Methylone

- Central Nervous System Stimulation
- Euphoria or dysphoria,
- Anxiolysis or Anxiogenesis
- Increase in sociability.
- Insomnia
- Restlessness
- Derealization/depersonalization
- Hallucinations
- Psychosis

Methylone

- Tachycardia (rapid pulse)
- Hypertension (high BP)
- Hyperthermia
- Sweating
- Dilated pupils
- Nystagmus
- Trismus (inability to open the mouth)
- Bruxism (Tooth grinding)
- Anorexia
- Nausea and vomiting

Methylone

Sold as methylone

Sold as ecstasy

(Sold as M1)
Methylone, bk-MBDB

(Sold as Dragonfly Pokeball)
Methylone, Caffeine

Purple Drank

- Drank
- Syrup
- Sizzup
- Lean

Purple Drank

- Codeine/promethazine cough syrup
- Mountain Dew/Sprit
- Jolly Rancher candy*

* Connection to John Jolly?


PROMETH
WITH CODEINE
COUGH SYRUP
C

Purple Drank

- Codeine/promethazine cough syrup
- Mountain Dew/Sprit
- Jolly Rancher candy*

* Connection to John Jolly?

Purple Drank

Purple Drank

- May have originated as early as 1960s
- Popular in Texas in early 90s
- Spread through southern states, then nationwide
- Mentioned in rap and hip-hop music
- 2000: “Three Mafia” song “Sippin’ on Some Syrup”, "Rainbow Colors“ (feat. Lil’ Flip)

Pour up (Drank drank drank drank)
Head shot (Drank drank drank drank)
Sit down (Drank drank drank drank)
Stand up (Drank drank drank drank)
Pass out (Drank drank drank drank)
Wake up (Drank drank drank drank)
Faded (Drank drank drank drank)

Purple Drank

- Codeine: Opiate effect
  - Sedation
  - Pain relief
  - Euphoria
- Promethazine (Antihistamine):
  - Sedation
  - Potentiates codeine
  - May be more lethal than codeine

Purple Drank

- Sometimes (less often) hydrococone (Vicodin) cough syrup
- Cheaper “knock-off” version contains dextromethorphan (DXM)
  - Sedative in small doses
  - Dissociative anesthetic (like PCP) in high doses

Purple Drank Deaths & Arrests

- RIP
  - DJ Screw: 2000
  - Big Moe: 2007 (?)
  - Pimp C: 2007
- Busted
  - Terrence Kiel (SD Chargers)
  - John Jolly (GB Packers)
  - JaMarcus Russell (former Oakland Raiders when arrested)

Sippin Syrup

Slow your roll

PURPLE DRANK

ima grip and sip

WARNING!

THIS BEVERAGE MAY BE EXTREMELY RELAXING AND CALMING

Purple Drank

The Nutritional Supplement of Champions

Other Drugs “On the radar “

- Methoxetamine ("Mexxy")
- 4-MeO-PCP /Methoxydine
- mCPP
- Dimethocaine
- Piperazine Derivatives (e.g., BZP, TFMPP, “Plant food”)
- Tryptamine substances

THANK YOU FOR YOUR ATTENTION!

WWW.LINKEDIN.COM

EMERGING DRUGS OF ABUSE DISCUSSION GROUP