

**Part 4: Hallucinogens and Other Street Drugs**

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**AN INTRODUCTION TO KEY TERMS AND DEFINITIONS**

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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, Mescaline)	hallucinations, altered perception

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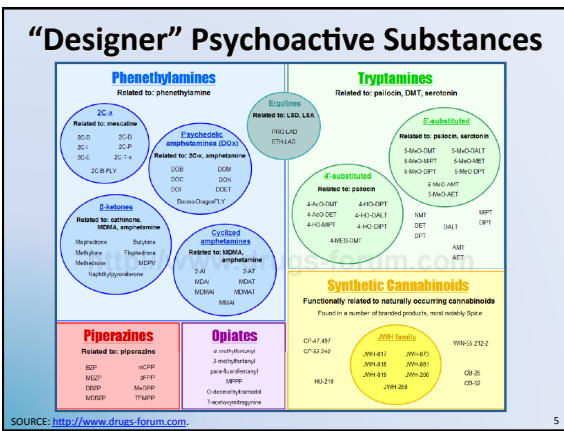
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DRUG NAME	DESCRIPTION
<b>Mephedrone</b>	4-methyl-methcathinone; “Miaow” Similar to cocaine and MDMA (ecstasy)
<b>Methylone</b>	β-MDMA: 3,4-methylenedioxy-methcathinone; “Explosion” Similar to cocaine and MDMA (ecstasy)
<b>MDPV</b>	3,4-methylenedioxyprovalerone;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

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### Examples of Major Psychedelic Drugs

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 (1 hr.); shorter duration than 2C-I
5-MeO-DMT	Tryptamine; naturally occurring (toad, shamanic brews) Smoked: almost immediate, very intense, short effect (<30 min)
DMT	Tryptamine; naturally occurring Smoked: almost immediate, very intense, short effect (<20 min)

SOURCE: Slide courtesy of R. Bruno et al., 2011, with revisions by James Hall, 2012.

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### Bath Salts

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### ***“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)

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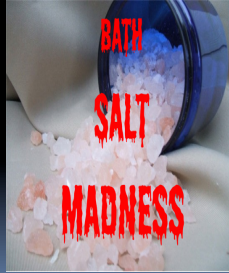
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## Methylenedioxypropylamphetamine (MDPV)

- Street names: Bath Salts, Ivory Wave, Plant Fertilizer, Plant Food, Vanilla Sky, Energy-1
- Designer drug developed to get around drug control laws



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## MDPV – “Bath Salts”

- Effects: similar to cocaine, amphetamine, or MDMA
  - Positive: mental and physical stimulation, euphoria, creativity, feelings of empathy, increased sociability and productivity, sexual arousal
  - Negative: tightened jaw muscles, grinding teeth, loss of appetite, disturbed sleep patterns, involuntary body movements, confusion, GI disturbance, muscle tension, headache, harsh comedown effects, tachycardia, hypertension, vasoconstriction, psychotic behavior, residual depression, anxiousness/paranoia

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## MDPV – “Bath Salts”

- Routes of Administration: most often insufflated (snorted), but can be smoked, injected, or ingested orally; usual amounts 5 mg or less (active ingredient)
- Duration of action: 3 to 4 hours for subjective effects, 6 to 8 hours for side effects
- Legal status: Not federally controlled, several states have banned either bath salts or chemicals used to make MDPV. Georgia has proposed a bill to ban sale of bath salts, but they have been commonly available in convenience stores and head shops

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### MDPV – “Bath Salts”

- Prevalence of use: Information is currently very limited, data is not yet reported by any national drug study programs due to relative newness of drug
- Used predominantly in youth population
- Increasingly cases are being reported of overdose on MDPV leading to death – 2 men in Pennsylvania and 1 woman in Illinois in April 2011, and 1 man in Michigan in May 2011

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### MDPV – “Bath Salts”

- Chemistry and Pharmacology
  - Related in chemical structure to MDMA and cathinone
  - MDPV administered to mice increased dopamine levels 60 minutes after administration, though not as markedly as increases induced by methamphetamine or MDMA
  - Has a “cousin” mephedrone: also found in bath salts with same effects and dangers

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### MDPV – “Bath Salts”



- Availability: Typically sold in smoke shops or convenience stores as a “bath salt” under the product names Ivory Wave or Vanilla Sky. It is marked “for novelty use only” and has no instructions on dosing. Also sold online as “Energy 1” on UK based websites or as “Plant Food”

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### MDPV – “Bath Salts”

- **Addiction Potential:** No studies have shown addiction potential as of yet, but self-report from users indicate the high is so addictive they can not stop using.
  - Intense cravings have been reported
  - Some users have sought professional help after only one month of abuse
- No information available on withdrawal or tolerance

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### MDPV – “Bath Salts”

- **Long-term effects:** Unknown – Bath salts have only come into spotlight within last 2 years, so no studies are available
- **Toxicity and overdose:**
  - Severe and life-threatening toxic effects that do not respond to conventional medical treatment
    - Usually non-responsive to sedatives
    - When users present with psychosis, psychotic state returns when sedatives and antipsychotics withheld, even after days
  - Toxic and lethal doses are unknown

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### MDPV – “Bath Salts”

- **Drug Testing**
  - Not commonly tested for in standard and extended drug screens
  - Redwood Toxicology Lab has a 2-panel urine drug screen that tests for MDPV and mephedrone, as well as an extended 14-panel screen that includes these drugs

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## 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

SOURCE: NIDA. (2011). NIDA DrugFacts: Khat. 19

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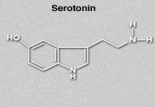
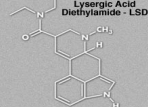
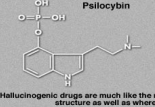
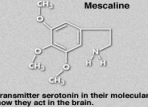
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## Serotonergic Hallucinogens

**Structure of Serotonin and Selected Hallucinogens**

<p><b>Serotonin</b></p> 	<p><b>Lysergic Acid Diethylamide - LSD</b></p> 
<p><b>Psilocybin</b></p> 	<p><b>Mescaline</b></p> 

Hallucinogenic drugs are much like the neurotransmitter serotonin in their molecular structure as well as where and how they act in the brain.

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## Serotonergic Hallucinogens

- Types:
  - Lysergic Acid Diethylamide (LSD)
  - Dimethyltryptamine (DMT)
    - Active ingredient in *Virola calophylla* and *Mimosa Hostilis* plants
  - Psilocybin (mushrooms)
  - Psilocin (active ingredient in Psilocybin)
  - Bufotenine
    - Found in animals and plants
  - Ololiuqui
  - Harmine
    - Psychedelic agent of the seeds of *Peganum harmala* plant

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## Serotonergic Hallucinogens

Drug	Botanical Source	Area Found	Other Names
Lysergic acid diethylamide (LSD)	Synthetic, but derived from the ergot fungus	Ergot native to Europe	Acid, many others
Ibogaine	Iboga plant: Tabernaemontana iboga	Africa	—
Psilocybin	Mushrooms of genus Psilocybe, Conocybe, Panaeolus, and Stropharia	Throughout the world	Teonanacatl
Dimethyltryptamine (DMT)	Viola tree: Virola calophylla and other species	South America	Yakoo, yopo
Mescaline	Peeyote cactus: Lophophora williamsii	Mexico and Southwest U.S.	Peeyote
Harmaline, Harmine	Ayahuasca vine: Banisteriopsis caapi, Banisteriopsis toebrians	South America	Yagé
Lysergic acid amide	Morning glory seeds: Rivea corymbosa, Ipomoea violacea	Throughout the world	Olooluqui

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## Serotonergic Hallucinogens

- Typically synthesized from plant products
  - Related to substances in ergot fungus
- History:
  - Entheogen use by Central and South American groups
    - Allows user to commune with God
  - LSD first discovered by Albert Hoffman in 1938 and later worked on in 1943
  - LSD originally thought to be a truth serum
  - 1950s researched as adjunct to psychotherapy
  - 1960s dramatic increase in LSD use followed by sharp declines
  - LSD made illegal in 1960s
  - Slight rise in 1990s

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## Serotonergic Hallucinogens



**LSD**



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## Pharmacokinetics

- ROA
  - Oral (absorbed within 60 minutes)
  - Transdermal
  - Typically 20-60 minutes for effects to show
- Peak & Duration
  - LSD: 8-12hrs; peaks around 3hrs
  - Psilocybin: 3-4hrs

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## Pharmacodynamics

- 5HT<sub>2A</sub> receptor agonist
  - Especially in visual/sensory cortexes
- Disruption in locus coeruleus connection to thalamus and cortex
  - Produces hallucinations
- Limited effects on dopamine release in pleasure pathway
- Actions in Rostral pathway for Serotonin
  - Rostral raphe neurons to sensory cortex
- Activates norepinephrine
  - Sympathetic nervous system

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## Effects

- Changes in visual perception
  - Hallucinations, distortions, intense visual imagery
- Mood changes
- Bizarre thoughts
- Magical thinking
- Drowsiness
- Nausea
- Dizziness
- Uterine & Visceral sensations
- Sympathomimetic
  - Pupil dilation
  - Heart rate
  - Increased blood pressure
  - Sweating
  - Increased Temperature
- Interpretation of experience influences effect ("bad or good trips")
- In some cases, long term psychotic reactions (similar to schizophrenia)
- Flashbacks
- Most deaths due to accidents, homicides, suicide, or respiratory arrest

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# Catecholaminergic Hallucinogens

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- ## Catecholaminergic Hallucinogens
- Types:
    - Mescaline
    - DOM
    - MDA
    - MDMA (ecstasy)
    - DMA
    - TMA
    - MDE
    - Myristin
    - Elemincin
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## Mescaline

- Derived from peyote cactus
- Also sold in synthetic form
- Similar in structure to norepinephrine
- Psychedelic effect comes from 5HT2A affinity
- Used for 5000 yrs or more
- Legalized for Native American church
- Mescal Button: dried part of cactus in disk form, eaten



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## Myristicin/Elemicin

- Found in Nutmeg & Mace
  - From trees of the genus Myristica
- Dose: 1-2 tsps or 5-15 grams
  - Usually in tea
- Delay of psychedelic effects
  - 2-5 hour delay
- Side Effects
  - Nausea, vomiting, tremors

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## Glutamatergic Anesthetics

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## Glutamatergic Anesthetics

- Types:
  - Phencyclidine (PCP)
  - Ketamine (Special K)
  - Dextromethorphan
- Also known as Dissociative Anesthetics
  - User experiences separation from sensory experience



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### Phencyclidine and Ketamine

- Synthesized in 1956
- Anesthetic that permits consciousness
- PCP primarily used in 1960s
- Can no longer be researched due to negative effects
- Ketamine use is increased in 1990s and early 2000s
- It can still be researched today

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### Pharmacokinetics

- Routes of Administration
  - Inhalation via smoking/sniffing
  - Oral
  - Intravenous
- Peak Effects
  - Inhalation: 5-15 minutes
  - Oral: 2 hours
- Metabolism/Excretion
  - Elimination half-life: ~18 hours (ranges from 11-51hrs)
  - Remains unmetabolized for ~2 days
  - Detectable in urine for weeks

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### Pharmacodynamics

- Selective glutamate antagonists
- Stimulates dopamine release in primary reward pathway
- Effects typically last 4-6 hours
- Confusion/Cognitive impairment may continue for 8-72hrs

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### Effects

- Euphoria
- Numbness
- Slurred Speech
- Sedative Effects
- Perceptual distortions (hallucinations rare)
- Cognitive slowing
- Analgesia
- Amnesia
- Disinhibition
- Coma or stupor at high doses
- Rapid heart rate
- Nystagmus
- Sweating

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### Effects

- Overdose/Lethal dose can produce
  - Coma
  - Convulsions
  - Respiratory arrest
  - Brain hemorrhage
  - Kidney failure
- Can cause prolonged paranoia, violence
- Can exacerbate predisposition/family history of psychosis

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### Anticholinergic Hallucinogens

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## Anticholinergic Hallucinogens

- Types:
  - Scopolamine, Atropine, Hyoscyamine
    - In BellaDonna, Datura, Mandrake root, Henbane, Deadly Nightshade
- Antagonizes muscarinic receptors
- History:
  - Used by poisoners in the Middle Ages (deadly nightshade)
  - BellaDonna gets it's name from it's ability to dilate pupils (thought to be a mark of beauty)
  - Ingestion of Datura berries has taken out entire armies
    - E.g. Marc Antony's army in 36 BC; British soldiers during Bacon's Rebellion

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## Manmade Anticholinergics

- Manmade substances also exist:
  - Benzotropine
  - Trihexylphenidyl
- These are often used as antidepressants/antipsychotics

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## Effects

- Sensation of flying
- Increased heart rate
- Dry mouth
- Constipation
- Blurred vision
- Drowsiness
- Amnesia
- Mental confusion
- Respiratory depression
- Nausea/Vomiting
- Dilated pupils
- Hallucinations
- Increased Temperature



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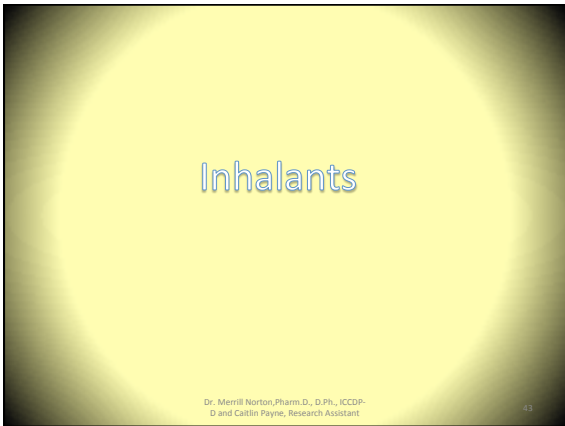
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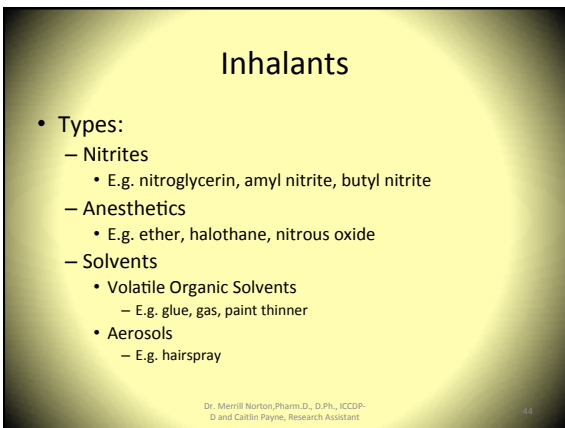
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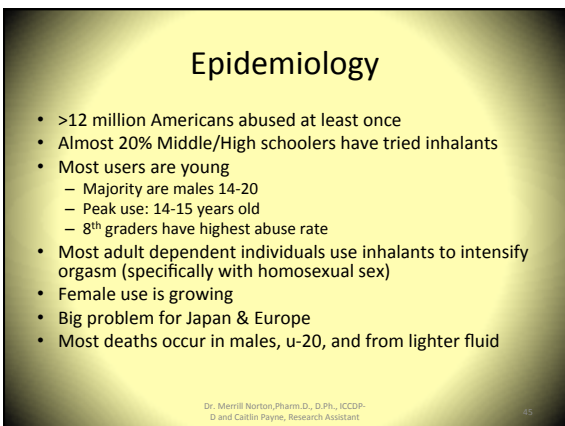
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## Nitrites

- Primarily used to enhance sex due to it's actions on the blood vessels and ability to relax smooth muscles
  - Relaxes anus for anal intercourse
  - Produces light-headedness, giddy feeling, nausea, throbbing (actions on vessels in head)
  - Relieves pain of blood vessel spasm

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## Anesthetics

- Taken for:
  - Pain relief
  - Muscle relaxation
  - Loss of consciousness
- Nitrous oxide can be toxic
  - Hypoxia: lack of oxygen

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## Solvents

- Effects:
  - Visual/auditory hallucinations
  - Ataxia
  - Decreased heart rate
  - Decreased breathing
  - Light-headedness
  - Giddiness
  - Nausea
  - Chills
  - Loss of consciousness
  - Shakiness

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## Solvents

- Toxic due to:
  - Heart failure
  - Suffocation
    - Physical object blocking airway
    - Lack of oxygen
  - Accidents
    - Lead poisoning
    - Lack of coordination/unconsciousness
    - Sprays coating the lungs

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## Suggestions for Treatment & Prevention

- Acute intoxication: give oxygen
- Make unpleasant with nausea-producing additives
- Warning labels
- Education
- Ban legal use

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## Synthetic Marijuana

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# Spice

- A Dangerous Legal High

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# Synthetic Marijuana

- 2007: “spice” “mojo” “legal weed” appeared
  - Synthetic psychoactive drug mixture of different herbals
  - Commonly labeled as incense
  - Mimics cannabinoids
  - Undetectable in urine drug screens designed to check for cannabinoids
  - Some states have banned; others have legislation pending

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# Synthetic Cannabinoids

- Street names: K2 and Spice
- Marketed as “herbal incense”; claims to be a blend of traditionally used medicinal herbs but instead is laced with synthetic cannabinoids that are not naturally in the herbs it is labeled to possess



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### Synthetic Cannabinoids (a.k.a. Spice)

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



SOURCE: NIDA. (2012). NIDA DrugFacts: Spice (Synthetic Marijuana).

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### Synthetic Cannabinoids (Spice)

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

SOURCE: NIDA. (2012). NIDA DrugFacts: Spice (Synthetic Marijuana).

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### Synthetic Cannabinoids: The Major Compounds

a) Naphthoylindoles

b) Cyclohexylphenoles

- JWH-018
- JWH-073
- JWH-398
- JWH-200
- JWH-081
- JWH-015
- JWH-122
- JWH-210
- JWH-019
- JWH-007
- AM-2201
- JWH-020
- JWH-387
- AM-1220
- JWH-412
- 5-Fluoropentyl-JWH-122

CP-47,497-C8



SOURCE: Agudelo et al. (2012). Effects of Synthetic Cannabinoids on the Blood Brain Barrier, Presented at 74<sup>th</sup> Annual CPDD.

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### 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.

SOURCE: Logan, B.K. (2012). Testing Strategies to Monitor Novel/Emerging/Designer Drug Use in At-Risk Populations, Presented at 74<sup>th</sup> Annual CPDD.

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### Timeline of Synthetic Cannabinoids and Spice Products

SOURCE: Fattore & Fratta. (2011). *Frontiers in Behavioral Neuroscience*, 5(60), 1-12.

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### Factors Associated with Spice Products' 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

SOURCE: Fattore & Fratta. (2011). *Frontiers in Behavioral Neuroscience*, 5(60), 1-12.

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## Spice

- Effects: has marijuana-like psychoactive effects in humans – decreased activity, analgesia, decreased body temperature, euphoria, anxiety, altered perception
- Does not induce “the munchies” in most users
- When used with alcohol, exacerbates hangovers and causes headaches at base of skull that last for hours

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## Spice

- Routes of Administration: smoking in pipes, bongs, or joints
- Duration of Action: the high lasts an average of 10 minutes, and no longer than 30 minutes
- Legal status: As of March 1, 2011, synthetic cannabinoids have been temporarily placed in Schedule I federally, but has been illegal on a state level in Georgia since May 2010

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## Spice



- Prevalence of use: primary abusers are youth purchasing these substances from Internet sites, gas stations, convenience stores, and smoke shops

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## Spice

- Chemistry and Pharmacology
  - The chemical structure of synthetic cannabinoids shares similarities with THC as seen on the next slide, but is not classified as a THC
  - Synthetic cannabinoids bind to the brain cannabinoid receptor CB<sub>1</sub> and peripheral receptor CB<sub>2</sub> with higher affinity than THC, suggesting it would have the same effects as THC in vivo

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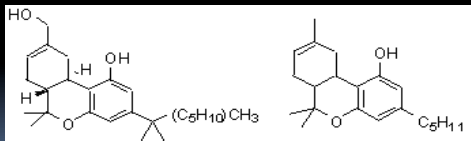
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## Spice

- Comparison of chemical structure of THC (left) and HU-210, a synthetic cannabinoid (right)



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## THE EFFECTS OF SYNTHETIC CANNABINOIDS AND SYNTHETIC CATHINONES

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*“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)

SOURCE: Dimond, D. This Spice Can Kill You. Posted 8/8/12 at 2:49 p.m. 67

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### Cannabis vs. 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

SOURCES: Hermanns-Clausen et al. (In Press). *Addiction*; Rosenbaum et al. (2012). *Journal of Medical Toxicology*; Forrester et al. (2011). *Journal of Addictive Disease*; Schneir et al. (2011). *Journal of Emergency Medicine*. 68

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### 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%

SOURCE: Spiller et al. (2011). *Clinical Toxicology*, 49, 499-505. 69

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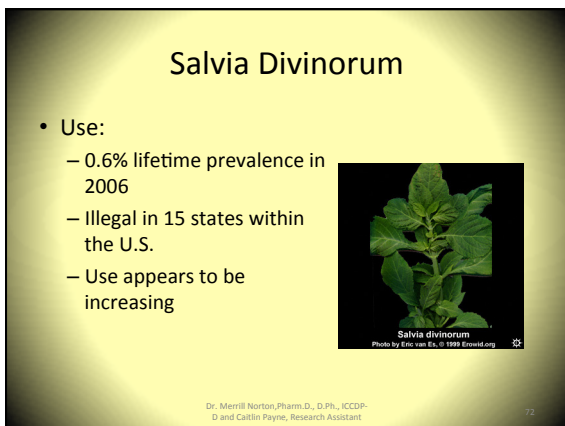
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### Pharmacokinetics

- Routes of Administration
  - Inhalation via smoking
  - Oral via tea
  - Sublingual via chewing leaves
- Onset
  - Extremely rapid
  - 5-20 minute duration

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### Pharmacodynamics & Effects

- Opioid Kappa receptor agonist
- Limited dopamine neurotransmission
- Effects
  - Changes in spatial orientation
  - Parts of the body experiencing feelings of energy or pressure sensation
  - Revisiting childhood memories
  - Cartoon-like visions
  - Feeling of supernatural contact
  - Many feel long-term insight and positive mood after taking
  - Some reported anxiety, physiological effects resembling poisoning, prolonged psychotic episodes

Dr. Merrill Norton, Pharm.D., D.Ph., ICCDP-D and Caitlin Payne, Research Assistant

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### Treatment

- No specific treatment for hallucinogens

Dr. Merrill Norton, Pharm.D., D.Ph., ICCDP-D and Caitlin Payne, Research Assistant

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## References

- Advokat, C. PhD. Drugs and Behavior Hallucinogens [PowerPoint Slides]. Retrieved from the Department of Psychology, LSU.
- MacKillop, James. PhD. (2011). Psychology 3100/5100: Addiction [PowerPoint Slides]. Retrieved from Department of Psychology, the University of Georgia.
- <http://www.erowid.org>

Dr. Merrill Norton, Pharm.D., D.Ph., ICCDP-D and Caitlin Payne, Research Assistant

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