



Thug Drugs

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Faculty

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- WV PDMP Advisory Panel Member
- CDC Grant Reviewer



Disclosures

- Consultant/Independent Contractor: Daiichi Sankyo, Clinical Pharmacists Advisory Panel, Member

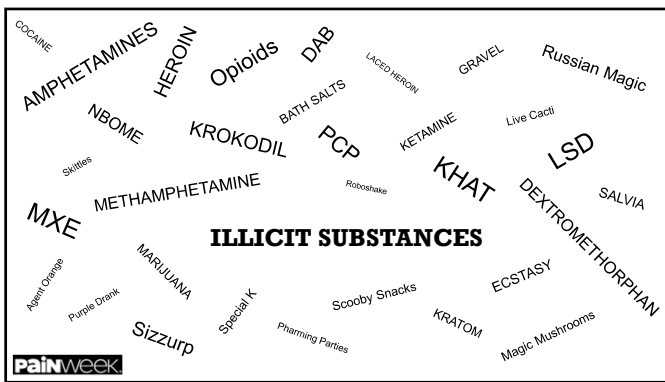
This presentation was not a part of the presenter's official duties at the WVU and does not represent the opinion of WVU



Learning Objectives

- Recognize commonly abused substances across the globe.
- Classify commonly abused substances based on each substance's mechanism(s) of action.
- Explain how to provide guidance to the lay public on the anticipated effects of commonly abused substances.





What are *illicit* substances?

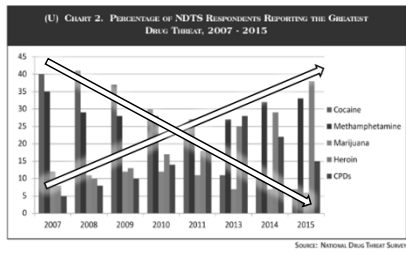
1. Schedule 1 Controlled Substances
 - Illegal to make, sell, or use
 - No accepted medical use, dangerous, & potential severe dependence
2. Any Schedule Controlled Substance utilized for unintended people/uses

Laws are not uniform among states/countries

- Heroin is LEGAL in the UK, Portugal, Canada, etc.
- Marijuana is "LEGAL" in certain US states, yet Illegal on the Federal Level

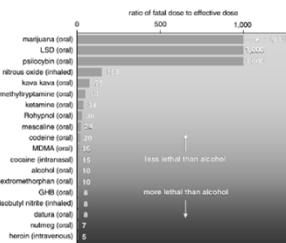


Most Abused Illicit Substances (2015)



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Illicit Therapeutic Index



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The Toxicity of Recreational Drugs. American Scientist. 2006. Volume 94, 206-208.

Word of Mouth

www.stretrx.com

Shows daily observed prices by location

Did you get a good deal? -

Submission to SAMHSA

Name of drug:

Formulation:

Price per unit: \$

Resource for addiction treatment centers by zip code (Links to SAMHSA)

Nevada

\$8	oxycodone ER tablet	Not Bad
\$9.99	gabapentin 600mg pill	Reasonable
\$10	gabapentin 600mg pill	Reasonable
\$14	gabapentin 600mg pill	Not Bad
\$12	gabapentin 600mg pill	Reasonable

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Illicits de Venn



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Illicit Substances Overview

Hallucinogens

- NBOME
- LSD
- Ketamine
- MXE
- PCP
- Psychedelic Mushrooms
- Peyote Cacti
- Ecstasy

Stimulants

- Cocaine
- Meth(amphetamine)
- KHAT
- Bath Salts & Gravel

Cannabis Products

- Marijuana Plant
- Synthetic Marijuana
- Marijuana Extracts

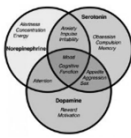
Opioid-Related Products

- Heroin
- Laced Heroin
- Krokodil
- Kratom
- Salvia
- Dextromethorphan
- Loperamide

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Increased Neurotransmitter Effects

	Serotonin (5HT)	Dopamine (DA)	Norepinephrine (NE)	Opioid
Effects	Hostility/Agitation Muscle Rigidity Shivering Goose Bumps Dilated Pupils Fever/Sweating Diarrhea Seizures Rhabdomyolysis Tachycardia	"Reward & Pleasure" Schizophrenia Muscle Twitching Amnesia Insomnia Tachycardia	"Fight or Flight" Dilated Pupils Tachycardia Dry Mouth Urinary Retention	Constricted Pupils Confusion Nausea/Vomiting Constipation Dry Mouth Urinary Retention Respiratory Depression
Structures	 <chem>CC(N)Cc1ccc(O)c1</chem>	 <chem>CC(N)Cc1ccc(O)c1</chem>	 <chem>CC(N)Cc1ccc(O)c1</chem>	 Morphine (Phenanthrine)







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Dipiro L, et al. Pharmacotherapy: A Pathophysiologic Approach, 10th Edition. McGraw-Hill Education, 2017

HALLUCINOGENS





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Hallucinogens

NBOMe	1 st 5-HT _{2A} Receptor Agonist	
LSD	Affects D/5HT/NE Receptors	
Ketamine	NMDA Antagonist, D/mu/K agonist, 5/N/D-RI, Na/Ca Channel Blockers, NO Synthase Inhibitor	
MXE	NMDA Antagonist & SSRI (5HT)	

Painweek © 2017 Stage of Abuse Resource Guide: <http://www.stageofabuse.com/2017/03/01/hallucinogens/>

Hallucinogens

PCP	NMDA Antagonist, Anti-Cholinergic, & Dopamine	
Psychedelic Mushrooms	5-HT _{1A} and 5-HT _{2A} and 5-HT _{2C} Agonist	
Peyote Cacti	5HT-2A Receptors & Dopamine	
Ecstasy (MDMA)	5HT/DA/NE	

Painweek © 2017 Stage of Abuse Resource Guide: <http://www.stageofabuse.com/2017/03/01/hallucinogens/>

STIMULANTS

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Cocaine

Nicknames

Coke, Speed, Snow, Blow, or Cocoa Puffs



Mechanism

5HT/NE/D & Na-Channel Blocker



Market

Snorted Powder "Lines" include: "Bumps" (35mg) or "Ralls" (100mg)
Cocaine HCl + Baking Soda → Crack Dime Bags: \$10 for 1/10th Gram (Smoked)



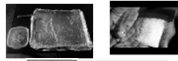
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04-2017 Drug of Abuse Resource Guide <http://www.painweek.org/2017/04/2017-drug-of-abuse-resource-guide/>
<http://www.painweek.org/2017/04/2017-drug-of-abuse-resource-guide/>

Stimulants

Meth(amphetamine)

NE & Dopamine



Khat

NE & Dopamine



Bath Salts & Gravel

Synthetic Cathinones
NE & Dopamine



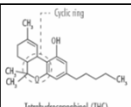
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<http://www.painweek.org/2017/04/2017-drug-of-abuse-resource-guide/>

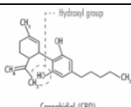
Marijuana

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Let's Dive into the WEEDS...



Tetrahydrocannabinol (THC)



Cannabidiol (CBD)

THC	CBD
<ul style="list-style-type: none"> Pain Nausea Vomiting Appetite Glaucoma Insomnia Anxiety Muscle Spasticity (Stiffness) 	<ul style="list-style-type: none"> Pain Inflammation Seizures Psychosis Depression IBS

<https://www.analyticalcannabis.com/articles/cbd-vs-thc-what-are-the-main-differences-201805>

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Marijuana



Plant → THC, CBD, etc.

Synthetic → Scooby Snax®, K2®, Spice®, Legal Funk®, etc.

Extractions → DAB, Butane Hash Oil (BHO), Hash Oil, Honey Oil, & Shatter

KD → Plant/Synthetic Marijuana, Tobacco, or BANANAS Laced with Bug Spray

types of cannabis

NSA 2017 Drug of Abuse Reference Guide <https://www.fda.gov/oc/2017/08/2017-drug-of-abuse-reference-guide>

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Cannabinoids

Adverse Effects & Interactions

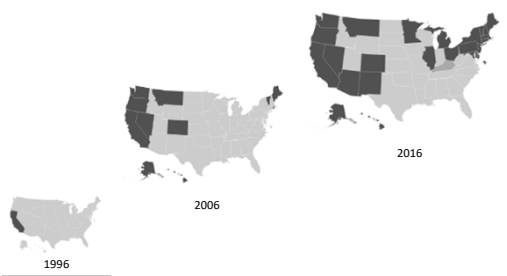
Adverse Effect	~Odds Ratio
Disorientation	5
Dizziness	5
Dry Mouth	4
Euphoria	4
Drowsiness	4
Confusion	4
Balance Issues	3
Hallucinations, Nausea, Vomiting, Diarrhea, & Fatigue	2

Cannabinoid	CYP-2C9	CYP-2C19	CYP-3A4
Δ9-THC	X		X
Δ8-THC	X		X
CBD		X	X
CBN	X		X

Copyright Department of Public Health and Environment. Monitoring Health Outcomes Related to Marijuana in Colorado, 2016. David D. et al. JGIM 2016;31(11):1413-1418. doi:10.1093/ajph/2016.31.1413. URL: http://ajph.org/ajph/article/doi/10.1093/ajph/2016.31.1413.1413-1418




“Medical” Marijuana States Timeline




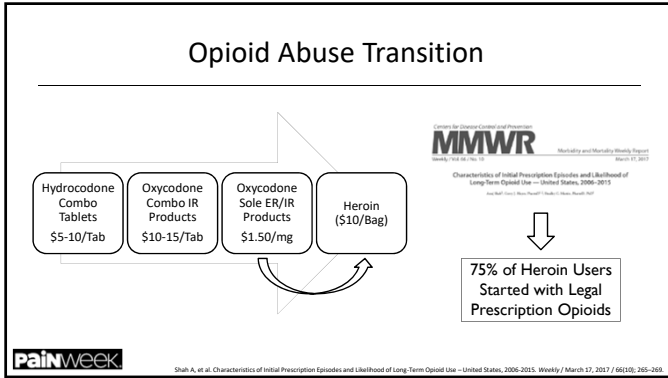
California	1996
Alaska	1998
Oregon	1998
Washington	1998
Maine	1999
Colorado	2000
Hawaii	2000
Nevada	2000
Montana	2004
Vermont	2004
Rhode Island	2006
New Mexico	2007
Michigan	2008
Arizona	2010
New Jersey	2010
Washington, DC	2010
Delaware	2011
Connecticut	2012
Massachusetts	2012
Illinois	2013
New Hampshire	2013
Maryland	2014
Minnesota	2014
New York	2014
Arkansas	2016
Florida	2016
North Dakota	2016
Ohio	2016
Pennsylvania	2016
West Virginia	2017
Oklahoma	2018

http://hibovallresource.org/2016/07/15/medical-marijuana-basis/?_ga=2.210143126.2028368723.1469395668



Opiates/Opioids





Heroin

Nicknames	Dope, H, Brown Sugar, Black Tar, Smack, & Dragon	
Mechanism	Mu Opioid Receptors	
Chemical	Di-acetyl-morphine	

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DEA 2017 Drugs of Abuse Resource Guide: <https://www.dea.gov/en/press/releases/drugs-of-abuse-guide>
<http://www.samhsa.gov/2k17/drugs-of-abuse-guide>


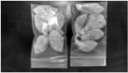
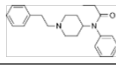

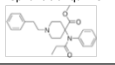

Heroin Production

1. Purification of raw opium
2. Extractions of morphine from opium
3. Morphine → Diacetylmorphine Base
4. Diacetylmorphine Base → Diacetylmorphine HCl Salt

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<http://www.arsnib.org/en/show/Phodium/Chemistry/Heroin%20mg.html>


Laced Heroin

Heroin	Fentanyl	Carfentanil
<ul style="list-style-type: none"> MME: 3 	<ul style="list-style-type: none"> MME: 100 Theraflu, Bud Ice, or Income Tax 	<ul style="list-style-type: none"> MME: 10,000 Wildnil Elephant tranquilizer
 	 	 

Remifentanyl
Sufentanyl
Afentanyl



PainWeek DEA 2017 Drugs of Abuse Resource Guide: https://www.dea.gov/multimedia-library/publications/Drug_of_Abuse.pdf

Krokodil

Nicknames	Russian Magic or Poor Man's Heroin	
Mechanism	Mu Opioid Receptors	
MME Factor	Ten (10)	
Chemical	Desomorphine (di-hydro-des-oxy-morphine) Patented in 1934 as Permonid in Switzerland	

PainWeek Miles et al. et al. The Novel Chemistry Behind Krokodil (Desomorphine): Synthesis and Mechanism of Toxicity. *Scientific Reports International* 14(1):2012-2014. <https://www.nature.com/articles/s41598-018-20120-2>

Kratom

Nicknames	Thang, Thom, & Swim	 
Mechanism	Potent K-Opioid D2 Agonist COX-2 Anti-inflammatory	
Drug Interactions	CYP450 3A4, 2D6, & 1A2 Inhibitor	
Chemical	Mitragyna Speciosa Tropical plant in coffee family Native to Southeast Asia	

PainWeek DEA 2017 Drugs of Abuse Resource Guide: https://www.dea.gov/multimedia-library/publications/Drug_of_Abuse.pdf
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5816283/>
 Rich MA et al. New Drugs of Abuse. *Pharmacotherapy* 2015; 35(12):189-197



Salvia

Nicknames Salvia Divinorum, La Maria, Magic Mint, or Diviner's Sage

Mechanism Potent K-Opioid D2 Agonist Endocannabinoid Modulator

Drug Interactions CYP450 1A1, 2C18, 2D6, & 2E1

Chemical Sage plant (Mint Family) Native to Mexico

DEA 2017 Drugs of Abuse Resource Guide: https://www.dea.gov/om/medialibrary/publications/Drug_of_Abuse.pdf
<http://www.emhda.europa.eu/html/du/index.html>
 Hoch MA et al. New Drugs of Abuse. Pharmacotherapy. 2015; 35(12):189-207

Dextromethorphan (DXM)


Nicknames Sizurg, Purple Drank, Purple Tonic, Robussin, DM* → Roboshake, Delim™ → Agent Orange, Concordia HSP → Supties

Mechanism Non-Selective Serotonin Reuptake Inhibitor, NMDA Antagonist, Opioid Sigma Agonist, & Anesthetic

Chemical D-enantiomer of levomethorphan (methyl-levorphanol)


One in 10 American teenagers have abused products with DXM

Dose (mg)	Effects
100-200	Mild Stimulation
201-400	Euphoria & Hallucinations
401-600	Distorted Vision & Coordination
601-1500	Dissociative Sedation



DEA 2017 Drugs of Abuse Resource Guide: https://www.dea.gov/om/medialibrary/publications/Drug_of_Abuse.pdf
 Clinical Pharmacology Online Database: 2018

Chirality



Samuel-L-Jackson Samuel-D-Jackson

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Opioid "Cousins"

Dextromethorphan (DXM)

CN1CC[C@H]2[C@@H]1CC[C@@H]2C(=O)O

→

CYP-2D6
O-demethylation

Dextrorphan (DXO)
 "D(+)-enantiomer" of racemorphan

CN1CC[C@H]2[C@@H]1CC[C@@H]2C(=O)O

↕

Levorphanol
 "L(-)-enantiomer" of racemorphan

CN1CC[C@H]2[C@@H]1CC[C@@H]2C(=O)O

Painweek Clinical Pharmacology Online Database, 2018

loperamide

Nicknames → Poor Man's Methadone & Imodium®

Mechanism → Peripheral Mu-Opioid Agonist

Info → 1988 Moved from C-V to OTC

Eggeston W et al. Loperamide abuse associated with cardiac dysrhythmia and death. Am J Emergency Medicine. 2016; 1-4.
 Dienken J et al. Poor man's methadone: a case report of loperamide toxicity. Am J Forensic Med Pathology. 2015;36:259-270.

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Illicit Substances Overview

<p><u>Hallucinogens</u></p> <ul style="list-style-type: none"> • NBOME • LSD • Ketamine • MXE • PCP • Psychedelic Mushrooms • Peyote Cacti • Ecstasy 	<p><u>Stimulants</u></p> <ul style="list-style-type: none"> • Cocaine • Meth(amphetamine) • KHAT • Bath Salts & Gravel <p><u>Cannabis Products</u></p> <ul style="list-style-type: none"> • Marijuana Plant • Synthetic Marijuana • Marijuana Extracts 	<p><u>Opioid-Related Products</u></p> <ul style="list-style-type: none"> • Heroin • Laced Heroin • Krokodil • Kratom • Salvia • Dextromethorphan • Loperamide
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Increased Neurotransmitter Effects

	Serotonin (5HT)	Dopamine (DA)	Norepinephrine (NE)	Opioid
Effects	Hypotility/Agitation Muscle Rigidity Shivering cool/sweaty Dilated Pupils Fever/Sweating Diarrhea Seizures Restlessness Tachycardia	"Reward & Pleasure" Schizophrenia Muscle Twitching Annesia Insomnia Tachycardia	"Fight or Flight" Dilated Pupils Tachycardia Dry Mouth Urinary Retention	Constricted Pupils Confusion Nausea/Vomiting Constipation Dry Mouth Urinary Retention Respiratory Depression
Substances	Peyote Cacti Cocaine DMM Ecstasy Kratom LSD Psychodelic Mushrooms MXE NBOMe PMA	Gravel Peyote Cacti Cocaine Ecstasy Ketamine Khat LSD Bath Salts PCP Salvia	Gravel Cocaine Ecstasy Khat LSD Bath Salts	DMM Heroin Ketamine Kratom Krokodil Salvia U-47700 W-18



Dipiro, J, et al. Pharmacotherapy: A Pathophysiologic Approach, 10th Edition, McGraw-Hill Education, 2017.
DEA 2017 Drugs of Abuse Resource Guide: https://www.dea.gov/multimedia-library/publications/drug_of_abuse.pdf

Pharming & Punchbowl Parties



DEA 2017 Drugs of Abuse Resource Guide: https://www.dea.gov/multimedia-library/publications/drug_of_abuse.pdf

Resources Concentrating on Illicit Substances



Support Groups

Alcoholics Anonymous (AA)

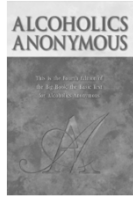
- ❖ <http://www.aa.org/>
- ❖ 212-870-3400

Narcotics Anonymous (NA)

- ❖ <http://www.na.org/>
- ❖ 1-818-773-9999

Nar Anon (Family & Friends)

- ❖ www.nar-anon.org
- ❖ 1-800-477-6291



Audience Question #1

Which of the following illicit substances is a hallucinogen?

- a) Bath Salts
- b) Khat
- c) Ketamine
- d) Carfentanyl



Audience Question #1 (ANSWER)

Which of the following illicit substances is a hallucinogen?

- a) Bath Salts
- b) Khat
- c) KETAMINE
- d) Carfentanyl



Audience Question #2

While stopped at a cross-walk on Jefferson St. in downtown Phoenix outside the Gypsy Bar at 2am, you notice a college student next to you leaning against a stop light post, shaking, with a red-toned skin color, grinding her teeth, and profusely sweating. If the student was to have ingested an illicit substance, which of the following would be the most likely of the listed substances.

- a) Kratom
- b) Scooby Snax
- c) Heroin
- d) Ecstasy



Audience Question #2 (ANSWER)

While stopped at a cross-walk on Jefferson St. in downtown Phoenix outside the Gypsy Bar at 2am, you notice a college student next to you leaning against a stop light post, shaking, with a red-toned skin color, grinding her teeth, and profusely sweating. If the student was to have ingested an illicit substance, which of the following would be the most likely of the listed substances.

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- c) Heroin
- d) ECSTASY



Audience Question #2

While stopped at a cross-walk on Las Vegas Boulevard (i.e. "The Strip") at 2am, you notice a college student next to you leaning against a stop light post, shaking, with a red-toned skin color, grinding her teeth, and profusely sweating. If she was to have ingested an illicit substance, which of the following would be the most likely of the listed substances.

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Audience Question #3

Which of the following are effects of various doses of dextromethorphan (i.e. DXM)?

- a) Cough Suppression
- b) Pain Suppression
- c) Hallucinations
- d) Euphoria
- e) All of the Above



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Audience Question #3 (ANSWER)

Which of the following are effects of various doses of dextromethorphan (i.e. DXM)?

- a) Cough Suppression
- b) Pain Suppression
- c) Hallucinations
- d) Euphoria
- e) ALL OF THE ABOVE



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Discussion



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