Not for Human Consumption:
New Drugs of Abuse and Their Detection

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Disclosures

- Courtney Kominek:
  - Consultant, Axial Healthcare
- This presentation was not a part of the presenter’s official duties at the VA and does not represent the opinion of the VA
Learning Objectives

- Explain the pharmacology and toxicology of new drugs of abuse
- Describe the desired and undesired effects of new drugs of abuse
- Select and interpret urine drug tests for new drugs of abuse

Introduction

- Multiple new drugs of abuse emerging
- Often advertised as legal highs and attempt to skirt existing legislation
- Frequently available on the Internet or at convenience stores/head shops
- May be associated with significant and life-threatening reactions
Introduction

- Krokodil: desomorphine
- Salvia
- Kratom
- Loperamide
- Synthetic cathinones: bath salts and flakka
- Synthetic cannabinoids: spice
- Piperazines

“Krokodil:” Desomorphine
“Krokodil:” Introduction

- Active substance is desomorphine
- Street names: krokodil, crocodile, zombie drug
- Synthetic mu-opioid agonist similar to heroin
- Schedule I controlled substance in Controlled Substances Act (CSA)
- Available from illicit sources


Desomorphine: History

- First synthesized in the USA in 1932 as an alternative to morphine
- Used commercially in Switzerland
- Less expensive alternative to heroin in Russia and European countries
- Reports of use in the U.S. in Missouri, Arizona, Utah, and Illinois but unconfirmed by Drug Enforcement Agency (DEA)

Desomorphine: Kitchen Chemistry

- Made in at-home laboratories with a process similar to methamphetamines
- Uses chemicals that are cheap, readily available, and highly toxic
- Requires minimal laboratory equipment
- Doses can be made in under an hour
- Made into a suspension that is injected intravenously usually without a filter


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Desomorphine: Pharmacology and Kinetics

<table>
<thead>
<tr>
<th>Desomorphine is 8-10 times more potent than morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of action: 1-2 min</td>
</tr>
<tr>
<td>Duration of action: 1-2 h</td>
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</tbody>
</table>

Desomorphine: Adverse Effects

- Adverse effects typical of opioids
- Immediate damage to blood vessels, muscles, and bones
- At injection site, tissue necrosis and gangrene
- Systemic adverse effects may include: bacteremia, osteomyelitis, meningitis, speech/motor skill impairments, liver and kidney damage, venous ulcers, and skin eschars
- Average survival from first use is estimated at 2 years


Desomorphine: Treatment

- Supportive care
- Naloxone administration
- Precautions for opioid withdrawal
- No evidence for mixed opioid agonists/antagonists but may be considered
- Screen for infectious diseases
- Patients may also need intensive psychiatric care, nutrition evaluations, and both physical and psychiatric rehabilitation

Desomorphine: Detection

- Synthetic opioid
- Not detected by opiate immunoassay
- Detected from gas chromatography-mass spectroscopy (GCMS)
- Remnants of codeine may be detected by immunoassay


Desomorphine: U.S. Case Report

- 30 yo male presenting to St. Louis, MO hospital with pain, swelling, and ulceration of left thigh
- Injecting heroin daily into arms and thighs for 7-8 years ($300/day)
- Injecting krokodil into thigh for last 6-7 months because it was cheaper
- Initially had blisters at injection sites that turned black
- After 1 month, necrotic areas peeled off leaving a necrotic ulcer
- 2 months before admission noticed increased swelling of left little finger which progressed to blisters that later turned black and auto-amputated
- While inpatient, treated with intravenous antibiotics and wound care
- Patient left against medical advice and was lost to follow-up

Salvia: History

- Hallucinogen from the plant *Salvia divinorum*, a sage plant of the mint family
- Salvinorin A is the psychoactive molecule
- Endemic to Sierra Mazatec region in Mexico
- Utilized by Mazatec Indians for hallucinogenic properties
- Traditional remedy for rheumatism, diarrhea, and migraine
- Not listed in the CSA
- Regulatory controls in several states
- Kappa opioid receptor agonist and modulates endocannabinoid system

Mahendran K et al. Salvia divinorum: an overview of the usage, misuse, and addiction processes. Asia-Pacific Psychiatry. 2015;8:23-31
Salvia: Street Names

- Magic Mint
- Sally D
- Diviner’s Sage
- Lady Sally
- Puff
- Incense Special

Salvia: Prevalence and Availability

- 1.3% among U.S. adults
- Most commonly used by young adults aged 18-25 years
- Common among recent users of lysergic acid diethylamide (LSD), ecstasy, heroin, phencyclidine (PCP), and cocaine
- Users often self-report anxiety and depression
- Grown domestically and imported
- Available online and in local shops
Salvia: Reasons for Use

- Curiosity, relaxation, getting “high,” dream-like states
- < 22 years used for fun or boredom
- > 22 years for spiritual effects


Salvia: Patterns of Use

- Tea
  — Method used by Mazatec Indians for spiritual experience
- Chew leaves
  — Absorption via buccal cavity with rapid onset of effect
- Vaporization/smoking
  — Most intense psychoactive effects
  — Similar effects to ketamine and tetrahydrocannabinol (THC)

Salvia: Pharmacokinetics

- **Absorption**
  - Buccal
  - Lungs

- **Metabolism**
  - First pass limits oral use
  - CYP2D6, CYP1A1, CYP2C19, and CYP2E1
  - UGT2B7

- **Excretion**
  - Bile
  - Urine

- **Onset**
  - Smoked and buccal: seconds-minutes

- **Duration**
  - Smoked: 30 minutes
  - Buccal: 1 hour

- **Half-life**
  - Dose related
  - 75 minutes

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Salvia: Effects

<table>
<thead>
<tr>
<th>Positive/Desired Effects</th>
<th>Negative/Undesired Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Relaxation and improved mood</td>
<td>• Loss of control</td>
</tr>
<tr>
<td>• Calmness</td>
<td>• Difficulty integrating experiences</td>
</tr>
<tr>
<td>• Psychedelic-like effects</td>
<td>• Racing thoughts</td>
</tr>
<tr>
<td>• Altered state of consciousness</td>
<td>• Tiredness, physical exhaustion</td>
</tr>
<tr>
<td>• Vivid visual hallucinations</td>
<td>• Dizziness and drowsiness</td>
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<tr>
<td>• Auditory hallucinations</td>
<td>• Irritability, anxiety, fear, panic</td>
</tr>
<tr>
<td>• Increased intrusive thoughts</td>
<td>• Psychomotor agitation</td>
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<tr>
<td>• Feelings of dissociation, depersonalization, and derealization</td>
<td>• Amnesia</td>
</tr>
<tr>
<td>• Increase in sensual and aesthetic appreciation</td>
<td>• Dysphoria</td>
</tr>
<tr>
<td>• Floating feeling</td>
<td>• Lack of motor coordination</td>
</tr>
<tr>
<td>• Increased self-confidence</td>
<td>• Profound sweating</td>
</tr>
<tr>
<td>• Increased insight</td>
<td>• Chills</td>
</tr>
<tr>
<td>• Spiritual experiences</td>
<td>• Nausea, vomiting, abdominal pain</td>
</tr>
</tbody>
</table>

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Salvia: Treatment

- Patients rarely present for treatment
- No known antidote
- Theoretical use of naloxone
  - Likely require 5-10 times the typical naloxone dose
- Supportive care
  - Benzodiazepines for agitation


Salvia: Detection

- Detected via GCMS or liquid chromatography mass spectroscopy (LCMS)
- Subject to adulteration

Mahendran R et al. Salvia divinorum: an overview of the usage, misuse, and addiction processes
Asia-Pacific Psychiatry. 2015;8:33-31
Kratom

Kratom: History

- Active compound is mitragynine, an alkaloid, found in a tropical tree native to Southeast Asia
- Opioid-like properties
- Nonprescription herbal available on the Internet and in head shops
- Typically sold as leaves, powder, extract, capsule, pellet, or gum
- Kratom can be smoked, chewed, or drank as a tea
- 10 fold increase in U.S. poison center calls from 2010-2015

Cinosi E et al. Following "the roots" of kratom: the evolution of an enhancer from a traditional use to increase work and productivity in Southeast Asia to a recreational drug in western countries. Biomed Res Internat. 2015;1-11
Kratom: Legality

- No known legitimate medical use per the DEA
- Undergoing review by DEA for possible scheduling
- Other countries have banned or limited the use of kratom
- Listed on FDA Poisonous Plant Database
- Street names include:
  - Biak-biak
  - Ketum
  - Kahum
  - Ithang
  - Thom


Kratom: Uses

- Reduce musculoskeletal pain and to increase energy, appetite, and sexual desire
- Used for the treatment of hypertension, diarrhea, and cough
- In Western countries, increasing use for self-treatment of pain and for opioid withdrawal
- Substitute for heroin

**Kratom: Pharmacology**

- **Postsynaptic α-2**
  - Adenosine-2a
  - Dopamine-2s

- **Opioid receptors**
  - Agonist

- **Serotonin receptors**


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**Kratom: Pharmacokinetics**

- **Onset:** 5-10 minutes
- **Duration:** 2-5 hours
- **Dosing**
  - 1-5 g: mild stimulant effects
  - 5-15 g: opioid-like effects
- **Inhibits CYP3A4, CYP2D6, CYP1A2**

Kratom: Adverse Effects

Effects typical of opioids
- Nausea/vomiting
- Constipation
- Respiratory depression
- Itching
- Dry mouth
- Decreased urination
- Anorexia
- Palpitation
- Dependence and withdrawal

Neurologic effects
- Hallucinations
- Psychosis
- Seizures
- Agitation

Kratom: Serious Toxicities and Fatalities

Serious toxicity is rare
- Higher doses (>15 g)
- Coingestants typically involved

Chronic, high doses (14-21 g/day x 14 days)
- Jaundice
- Pruritis
- Severe hypothyroidism

Fatalities
- "Krypton" – kratom + O-desmethyltramadol
- Pulmonary edema found on autopsies suggesting respiratory depression

References:
**Kratom: Detection**

- Not detected by opiate immunoassay
- Detected via LCMS


**Kratom: Treatment**

**Addiction**
- May respond to opioid replacement therapy

**Overdose**
- Similar to treatment of an opioid overdose
- Mixed data on the use of naloxone in animal studies
- Consider use of naloxone

Loperamide: Poor Man’s Methadone

Loperamide: Background

Available over-the-counter (OTC)

Prior to 1988 listed as Schedule V in CSA

Inhibits intestinal peristalsis
- Mu-opioid receptor agonist
- Calcium channel inhibitor
- Calmodulin inhibition
- Paracellular permeability reduction

Thought to have limited abuse potential
- Poor systemic bioavailability (0.3%)
- CNS penetration
- P-glycoprotein (p-gp) efflux

Dosing

- **Therapeutic doses:**
  - Adults and children 12 years and over
    - Caplets: 2 caplets after the first loose stool; 1 caplet after each subsequent loose stool; but no more than 4 caplets in 24 hours
    - Liquid: 30 mL (6 tsp) after the first loose stool; 15 mL (3 tsp) after each subsequent loose stool; but no more than 60 mL (12 tsp) in 24 hours

- **Abuse:**
  - Supratherapeutic doses 30-200 mg higher
  - Concomitant use of p-gp inhibitor

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Loperamide: Abuse

- **Increasing reports of abuse**
- **71% increase in reports of intentional loperamide exposures from 2011-2014**
- **Potential for abuse**
  - Accessible
  - Low cost
  - OTC
  - Lack of social stigma
  - Increasing legislation and regulations with opioids
- **Reasons for abuse**
  - Prevent opioid withdrawal
  - Euphoria

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FDA MedWatch - Loperamide (Imodium): Drug Safety Communication - Serious Heart Problems With High Doses From Abuse and Misuse

- RECOMMENDATION: Health care professionals should be aware that use of higher than recommended doses of loperamide can result in serious cardiac adverse events
  - Possible cause of unexplained cardiac events including QT interval prolongation, Torsades de Pointes or other ventricular arrhythmias, syncope, and cardiac arrest
- In cases of abuse, individuals often use other drugs together with loperamide in attempts to increase its absorption and penetration across the blood-brain barrier, inhibit loperamide metabolism, and enhance its euphoric effects
- In the 39 years from when loperamide was first approved in 1976 through 2015, FDA received reports (through FDA Adverse Event Reporting System) of 48 cases of serious heart problems associated with use of loperamide
  - Thirty-one of these cases resulted in hospitalizations, and 10 patients died. More than half of the 48 cases were reported after 2010


Loperamide: ADE

- Therapeutic doses
  - Usually mild
    - Nausea
    - Constipation
    - Drowsiness
    - Headache
  - Does not lead to withdrawal with administration of naloxone
- Serious
  - Toxic megacolon
  - Pancreatitis
  - Gastroenteritis

Loperamide: ADE

Supratherapeutic doses

- Constipation
- Opioid toxicity
  - Miosis
  - CNS depression
  - Respiratory depression
- Cardiac dysrhythmias


Loperamide: Detection

- Not detected via opiate immunoassay
- Able to be detected via GCMS/LCMS

Loperamide: Treatment

- CPR and ACLS first-line for cardiopulmonary arrest
- Treatment of ventricular dysrhythmias
- Naloxone is reasonable from animal and human data
- Report to FDA MedWatch


Bath Salts: Synthetic Cathinones
Bath Salts: Background

- Novel synthetic stimulant
- Cathinone derivatives
- Odorless, white/tan/gray powder or fine crystals
- $25-75 per 0.5 g package
- Marketed as “legal” high
- Sold in head shops, Internet, gas stations
- Labeled not for human consumption or plant food

Bath Salts: Street Names

- Bloom
- Ivory
- Wave
- Vanilla Sky
- White Lightning
- Red Dove
- Cloud 9

References:
Cathinone

- Chemical name: (S)-2-amino-1-phenyl-1-propanone
- Schedule I
- Beta-keto analog of amphetamine
- CNS stimulant
- Found in leaves of Catha edulis (Khat) plant
  - Chewing of leaves for stimulant effects popular in Middle Eastern countries
  - Must chew fresh leaves

Coppola M et al. Synthetic cathinones: chemistry, pharmacology, and toxicology of a new class of designer drugs of abuse marketed as “bath salts” or “plant food.” J Med Toxicol. 2012;8:144-149

Synthetic Cathinones

- Butylone
- Dimethylcathinone
- Ethcathinone
- Ethylone
- 3-Fluormethcathinone
- 4-Fluormethcathinone
- Mephedrone
- Methcathinone
- Methedrone
- Methylone
- Methylenedioxy-pyrovalerone (MDPV)
- Methedrone
- Methylone
- Pyrovalerone

**Bath Salts: Legality**

- Emergency scheduling of mephedrone, methylethyl, and MDPV by DEA in 2011
- Rapid alteration of existing, illegal substances, to new "legal" substances
- Synthetic Drug Abuse Prevention Act of 2012
  - Cannabinimimetic agents
  - Specified additional hallucinogenic substances

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**Bath Salts: Prevalence**

- Primarily used in young men
  - Mean age mid to late 20s
  - Ranging from teens to 40s
- Exposures reported in children as young as 6
- First reports in 2010, increasing in 2011, and peaking in 2012
- 0.9% annual prevalence in grades 8, 10, and 12
- Most samples from DEA National Forensic Laboratory Information System
  - South 57%
  - Midwest 25%
  - Northeast 16%
  - West 2%

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Bath Salts: Patterns of Use

- Frequency: daily to episodic
- Routes
  - Most often snorted or ingested orally
  - “Bombing”
  - “Keying”
  - Others
  - Users may combine or switch routes during binge
- Often used in combination with other drugs


Bath Salts: Dosing

- No data on purity
- Generally 1 mg-1g
- Redosing during a session is common
- MDPV
  - 5-30 mg per ingestion
  - > 200 mg in a session
- Mephedrone
  - Snorted: 25-75 mg
  - PO: 150-250 mg
- Commonly used with other substances to increase desired effects and decrease undesired effects

Coppola M et al. Synthetic cathinones: chemistry, pharmacology, and toxicology of a new class of designer drugs of abuse marketed as “bath salts” or “plant food.” Forensic Science International. 2012;211:144-149
Back WD. New drug abuse. Pharmather. 2015;17(2):189-197
**Bath Salts: Pharmacokinetics**

**Absorption**
- Mostly oral mucosa
- Secondary absorption from stomach and small intestines

**Distribution**
- More polarized than amphetamines
- Decreased diffusion across blood brain barrier

**Metabolism**
- Extensive phase I and phase II
- CYP2B6, CYP2C19, CYP2D6, CYP1A2

**Elimination:** urine

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**Bath Salts: Pharmacokinetics**

- **Mephedrone**
  - Snorting
    - Onset: 10-20 min
    - Duration: 1-2h
  - PO
    - Onset: 15-45 min
    - Duration: 2-4h
  - IV
    - Onset: 10-15 min
    - Duration: 30 min

- **MDPV**
  - Onset: 60-90 min
  - Duration: 6-8h

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Bath Salts: Desired Effects

- Sociability
- Energy
- Libido/sexual performance
- Capacity of work
- Euphoria
- Empathy

Coppola M et al. Synthetic cathinones: chemistry, pharmacology, and toxicology of a new class of designer drugs of abuse marketed as “bath salts” or “plant food.” Toxicol Letters. 2012;211:144-149

Bath Salts: Common Presenting Symptoms

**Physical**
- Diaphoresis
- Hyperreflexia
- Hypertension
- Hyperthermia
- Jaw tension
- Mydriasis
- Myocardial infarction
- Nausea/vomiting
- Palpitations
- Respiratory distress
- Seizures
- Tachycardia
- Hyponatremia

**Neuropsychiatric**
- Aggression
- Agitation
- Anxiety
- Combative behavior
- Dysphoria
- Hallucinations
- Insomnia
- Paranoia
- Psychosis
- Suicidal thoughts

Bath Salts: Objective Findings During Intoxication

- Decreased renal function
- Acidosis
- Elevated creatinine kinase or troponins
- ECG changes
- Leukocytosis
- Increased LFTs
- Electrolyte abnormalities


Bath Salts: Detection

- Routine toxicology tests ineffective
- May lead to false positive on methamphetamine screen
- MDPV may lead to false positive on PCP
- Samples
  - Blood, urine, stomach contents
  - Hair analysis
- Techniques
  - Gas chromatography-mass spectrometry
  - Liquid chromatography-mass spectrometry

Gershman JS et al. Synthetic cathinones ("bath salts"): legal and health care challenges. PEDIATRICS.2012;129(3):e371-e372
Cappello W et al. Synthetic cathinones: chemistry, pharmacology, and toxicology of a new class of designer drugs of abuse marketed as "bath salts" or "plant food." Toxicological Letters. 2012;211:166-169
Bath Salts: Treatment of Intoxication

- No antidote
- Mostly supportive
  - Cooling
  - Restraints
  - Fluid restriction and hypertonic saline
- Pharmacotherapy
  - Benzodiazepines
  - Antipsychotics
  - Propofol
- Education/addiction treatment

Bath Salts: Dependence and Withdrawal

- Tolerance may occur following repeated dosing
- Dependence less likely than amphetamines or cocaine
- Dependence may occur with chronic high doses
- Withdrawal syndrome
  - Depression
  - Anhedonia
  - Anxiety
  - Sleep disorders
  - Craving
Flakka

- \(\alpha\)-pyrrolidinovalerophenone (\(\alpha\)-PVP) or gravel
- Temporarily listed as Schedule I
- Similar in structure to cathinone
- Effects
  - Excitation, delirium, hyperstimulation, paranoia, hallucination
  - Kidney damage and failure
  - Aggression, self-injury, suicidal tendencies, and heart attacks also common

Wood MK et al. The dangerous new synthetic drug \(\alpha\)-PVP as the hydrated chloride salt of \(\alpha\)-pyrrolidinopentiophenone hydrochloride \& \(\alpha\)-PVP-hydrate. Acta Cryst. 2016;C72:08-31


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Synthetic Cannabinoids: Spice
Spice: Background

- Known as “fragrance,” “potpourri,” “herbal incense,” K2, Spice
- Many listed as Schedule I controlled substances
- Synthesized in lab and dissolved in solvent
- Sprayed onto plant material and allow for solvent to evaporate
- Packaged as loose leaves or rolled
- Labeled “not for human consumption”
- Available in head shops, convenience stores, Internet
- 3 g bag of K2 $30-$50

Rundhoven CB et al. Here today, gone tomorrow… and back again? J Med Toxicol. 2012;8:15-32

Spice: Use

- Smoked via various methods
- Primarily used by white males in teens and 20s
- 80% of K2 users have also used marijuana at least once

Spice: Pharmacology

- Full agonists of
  - Cannabinoid 1 (CB1) receptors located in brain
  - Cannabinoid 2 (CB2) receptors located on immune cells
- Activity at presynaptic CB1 receptors causes the release of inhibitory and excitatory neurotransmitters
- Leads to CNS effects


Spice: Pharmacokinetics

- Onset
  - Minutes to hours
  - Varies on product, amount, and route
- Duration about 1-3 h
- Metabolized by CYP2C9 and/or CYP1A2
- Excreted in the urine

Spice: Desired Effects

- Increased energy
- Focus and creativity
- Euphoria
- Dream-like state
- Relaxation and anxiolysis
- Sensory, perception, and motor alterations
- Appetite stimulation


Spice: Undesired Effects

<table>
<thead>
<tr>
<th>Common</th>
<th>Severe</th>
</tr>
</thead>
</table>
| • Anxiety  
• Agitation  
• Irritability  
• Tachycardia  
• Hallucinations  
• Nausea/vomiting  
• Hypertension  
• Confusion  
• Xerostomia  
• Acute ischemic stroke  
• Tachycardia  | • Psychosis  
• Seizures  
• Acute kidney injury  
• Palpitations  
• Hyperthermia  
• Rhabdomyolysis  
• Death  
• Suicidal ideation  |

Spice: Withdrawal Syndrome

- May last a few days
- Symptoms
  - Headaches
  - Insomnia
  - Anxiety
  - Restlessness
  - Irritability
  - Somatic pain
  - Coughing, shortness of breath
  - Nausea


Spice: Treatment

- No antidote
- Supportive care and monitoring
  - IV fluids
  - Benzodiazepines for agitation, catatonia, and severe anxiety
  - Antipsychotics for psychosis and hallucinations
  - Anti-emetics
  - Rarely is intubation needed
- Consider coingestants

Spice: Detection

- Not detected by THC immunoassay
- Rapid tests available but not widely used
- Detected via LCMS and GCMS


Piperazines
**Piperazines: Background**

- Stimulant and hallucinogenic effects
- Mimics 3,4-methylenedioxyamphetamine (MDMA, ecstasy)
- Derived from 2 main groups: 1-benzylpiperazine (BZP) and 1-phenylpiperazine
- Street name: molly, A2, Legal X, party pills
- Used in 1990s as “legal ecstasy”


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**Piperazines: Legality**

- BZP and 1-(3-trifluoromethylphenyl)piperazine (TFMPP) added to temporary list of Schedule I substances in 2002
- BZP permanently added to Schedule I 2004
- Individual states have legislation
- Nearly all piperazines are legal

Piperazines: Use

- Young adults 14–25 years
  - 18% report regular use
  - 90% report coingestion
  - Typically used orally via capsule, pill, tablet, powder form
  - Less common routes include injection, smoking, and mixing in drinks
  - Dose
    - BZP 75–250 mg
    - 1-(3-trifluoromethylphenyl)piperazine (TFMPP) 5–100 mg
  - Available on the Internet
  - $10–60 per package


Piperazines: Pharmacology

- Works to increase release of dopamine, serotonin, and norepinephrine and inhibits reuptake
- 10x weaker effects compared to amphetamines
- Lower doses: stimulant effects
- Higher doses: hallucinogenic effects

Piperazines: Pharmacokinetics

Absorption
- Rapidly absorbed

Distribution
- Multi-phase distribution
- Delayed peak effect at 75-90 minutes

Metabolism
- BZP: minimal metabolism
- TFMPP: CYP2D6, CYP1A2, CYP3A4

Elimination
- Urine
- Effects last 6-8 h


Piperazines: Effects

- Usually mild and doesn’t require medical attention
  - Agitation
  - Insomnia
  - Headache
  - Nausea
- Neuropsychiatric effects
  - Anxiety
  - Confusion
  - Paranoia
  - Short temper
  - Auditory hallucinations
  - Seizures in 1:5

Piperazines: Effects

- Cardiovascular effects often require medical attention
  - Hypertension
  - Tachycardia
  - Chest pain
  - QTc prolongation
- Others
  - Bruxism
  - Hyponatremia
  - Serotonin syndrome
  - Nephrotoxicity
  - Disseminated intravascular coagulation
  - Fatalities are uncommon


Piperazines: Treatment

- Supportive care
- ECG and electrolyte monitoring
- Agitation and seizures
  - Treat with benzodiazepines
  - Antipsychotics are not recommended
- Severe hypertension
  - IV antihypertensive or clonidine
  - Avoid selective beta-blockers

Piperazines: Detection

- No immunoassay available
- GCMS or LCMS
- BZP may produce a false positive for amphetamine immunoassay


Conclusion

- Rapidly changing molecules to avoid the law
- Difficult to detect with standard urine drug testing
- Substances not necessarily “safe” and may cause severe reactions
- Patients may seek treatment which is typically supportive care
Audience Response Question #1

BT is a 55 yo male who presents to the emergency room with signs of opioid withdrawal and necrotic lesions on his left arm. A UDS is obtained with the following results. After providing the sample, he admits to using “krokodil.” What would you expect his UDS results to be assuming this is the only substance he is using?

A. (+) Opiates
B. (+) Amphetamines
C. (+) Oxycodone
D. (-) for all substances

Audience Response Question #2

DK is a 61 yo male on tramadol 50 mg PO TID prn for chronic low back pain which provides analgesic and functional benefit. The patient states that he recently started drinking kratom tea. What would you expect an immunoassay drugs of abuse UDS panel to show?

A. (+) Opiates
B. (+) Oxycodone
C. (+) PCP
D. (-) negative for all substances
**Audience Response Question #3**

JB a 48 yo male with opioid use disorder presents to behavioral health for his appointment for renewal of buprenorphine/naloxone. The patient provides a UDS before being seen by the physician. His UDS comes back with the following results below. He denies using methamphetamines or PCP. What substances might explain the results below:

A. Bath salts
B. Salvia
C. Spice
D. Piperazines

<table>
<thead>
<tr>
<th>Substance</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>Opiates</td>
<td>Negative</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Negative</td>
</tr>
<tr>
<td>Methadone</td>
<td>Negative</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Negative</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Negative</td>
</tr>
<tr>
<td>PCP</td>
<td>Positive</td>
</tr>
<tr>
<td>THC</td>
<td>Negative</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Negative</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Positive</td>
</tr>
</tbody>
</table>

**Not for Human Consumption:**
**New Drugs of Abuse and Their Detection**

Courtney Kominek, PharmD, BCPS, CPE