ASHP Live Webinar: Coming to a Hospital Near You – Current Trends in Drug Abuse

Christopher Edwards, PharmD, BCPS
Christi Jen, PharmD, BCPS
Katelyn Dervay, PharmD, BCPS

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Wacky Tobbaccy
Synthetic Cannabinoids

Christopher J. Edwards, PharmD, BCPS
Clinical Pharmacist
Department of Emergency Medicine
University of Arizona Medical Center
Tucson, Arizona

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Objective

- **Characterize the toxidrome associated with the use of JWH-018**

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A Guy Walks into the ED…

- A 25 year old male presents to the emergency department certain that he is going to die
  - "I am going to die"
  - "This is it"
  - "I am dying"
  - "Call my mom"
  - "Who is going to take care of my cat"

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Physical Exam and Vital Signs

- Patient is anxious and restless
  - Oriented to person, place, and time
- Vitals
  - BP 134/87, HR 119, Respiratory Rate 18
  - O2 Sat 98% on room air
- Physical Exam
  - Pupils 4 mm, equal, round, reactive to light
  - Slightly dry mucous membranes
  - Otherwise unremarkable

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History of Present Illness

- No previous medical history
- No previous psychiatric history
- Patient reports taking a few "bong hits of this stuff my buddy gave me"
  - Eventually remembers the name of the substance is K2

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Background

- **Synthetic cannabinoids**
  - **Alternative to marijuana use**
  - **Frequently sold as incense products**
    - Labeled "Not for human consumption"
    - Brands include K2, Spice, Eclipse, etc…

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Background

- **Products are pharmacologically inert plants coated with synthetic cannabinoids**
- **The incense can be smoked using a pipe or rolled into a cigarette**
- **Most common synthetic cannabinoid found in these products is JWH-018**
  - **Others include CP-497, CP-47, HU-210, JWH-073, JWH-175**

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History of JWH-018

- **1995 – JWH-018 first synthesized**
- **2006 – Incense products with JWH-018 commercially available on the internet**
- **2006 –"Spice" gains popularity in Europe**
- **2009 – Several European countries move to schedule/ban synthetic cannabinoids**
- **2009 – DEA reports first appearance in US**

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Pharmacology

- THC binds to the CB1 and CB2 receptors with equal affinity
  - CB1 is responsible for psychoactive effects
  - CB2 is responsible for pain control, possibly mood and behavior disturbances
- JWH-018 has a higher affinity for the CB1 receptor than the CB2 receptor
- Users claim the experience is similar to marijuana, only more intense

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Adverse Effects

- Frequent
  - Paranoia
  - Anxiety
  - Tachycardia
  - Irritability
  - Vomiting
  - Hypokalemia
  - Mydriasis
  - Xerostoma
- Infrequent
  - Slurred Speech
  - Hypertension
  - Chest Pain
  - Hallucinations
  - Tremor
- Rare
  - Psychosis
  - Seizures

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Treatment

- Supportive Care
  - Benzos for anxiety, agitation, tachycardia, seizure
  - Antiemetics for nausea, vomiting
- Tincture of time
  - Most cases report resolution of symptoms within 2 hours post ingestion

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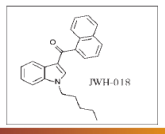
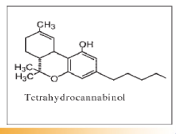
Screening for JWH-018

- Does not cross react with THC on common urinary toxicology screens
- Can be identified with thin layer chromatography, mass spectrometry





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Regulatory Status

- Classified by DEA as Schedule I substance as of March 2011
  - JWH-018 and 073, CP-47 and 497, HU-210
- Most states (45 of 50) have passed laws to prohibit the sale and possession of these products to varying degrees
  - Still available on the internet and black market

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Back to the Patient

- EKG showed sinus tachycardia
- Received lorazepam 2 mg IV x 1
  - Relieved anxiety, reduced heart rate
- Urinary toxicology screen
  - Negative for THC, opiates, barbiturates, phencyclidine, cocaine, and amphetamines
  - Positive for benzodiazapines
- BMP, CBC, and troponin all unremarkable

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Disposition

- He did not die
- 1.5 hours after presentation, the patient asked to be discharged
- Patient was released 6 hours after presentation

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Rub-a-Dub-Dub! Kitty in a Tub!

Katelyn R. Dervay, PharmD, BCPS
Pharmacotherapy Specialist – Emergency Medicine
Tampa General Hospital
Tampa, Florida

Learning Objective

- **Review the effects of new synthetic stimulants including "bath salts" and "meow meow" and be able to manage patients on these drugs.**

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- **"27 yo female is brought into the ED by police after she & her boyfriend called stating there was an assailant in their home. The couple also claimed there was a dead boy in their house and they were about to be killed"**
- **Presentation:**
  - **Tachycardiac**
  - **Diaphoretic**
  - **Paranoid**
  - **Anxious**

Labs: WNL
CT: negative
UD: negative

Porrovecchio A. ACP Hosp 2011
http://forums.penny-arcade.com/discussion/64723/requiem-for-a-chat

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What's going on here?

- **Pt admitted to hospital & managed on risperidone**
- **Improved over 24 hrs**
- **Admitted to 5-6 day binge of "Powdered Rush"**

http://forums.penny-arcade.com/discussion/64723/requiem-for-a-chat

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Synthetic Stimulants

- 3,4-methylenedioxypyrovalernove (MDPV)
  - "Bath salt"
  - "Fertilizers"
- 4-methylmethcathinone (mephedrone)
  - "meow meow"
- CNS stimulants
- Related to cathinone
  - Alkaloid found in khat plant

http://www.accessrx.com/blog/current-health-news/bath-salts-cocaine-meth-mdpv-b0124

www.synchronium.net/2010/01/05/mephedrone-cat/

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Timeline

1960's - MDPV used for treatment of chronic fatigue

1969 – Boehringer Ingelheim files patent application for MDPV

2005 – MDPV mentioned on Drugs-Forum as a recreational drug

2007 – seizure of MDPV in Germany

2008 – First US seizure of MDPV

2010 – Finland, UK, Germany, Sweden, and Australia lists MDPV as controlled substance

2010 – US market increases

2011 – State bans on MDPV and mephedrone seen (FL, LA, AL, MI, MS, NC, ND, and UT)

2011 – US DEA bans MDPV and mephedrone, classified as schedule I substance

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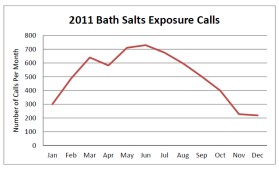
American Association of Poison Control Centers : Bath Salt Data

Year	Number of Calls
2010	304
2011	6,138
2012 As of Jan. 31, 2012	228



http://www.aapcc.org/dnn/NewsandEvents/NewsMediaResources.aspx

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Other Names

MDPV

- White Lightning
- Ivory Wave
- Loco-motion
- Vanilla Sky
- Super Coke
- Energy-1
- Scarface
- Mtv
- Magic

Mephedrone

- Meow Meow
- Meph
- Drone
- MCAT
- Plant Feeder
- Miaow
- Bubbles

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Abuse

- **Route:**
  - **Snorted**
  - **Smoked**
  - **Oral – Mephedrone**
    - Swallow capsules
    - Bombing – swallowing powder wrapped in cigarette paper
  - **Injected**
  - **Rectal**
- **Dose**
  - **50mg ($25-$50)**

http://www.ioffer.com/i/mdpv-500mg-99-9-best-quality-fertilizer-paypal-200477282

http://www.guardian.co.uk/politics/blog/2010/mar/17/mephedrone-deaths-drugs-agent

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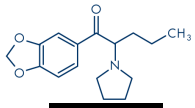
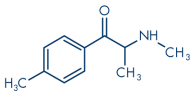
Pharmacology

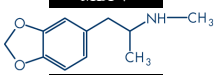
- **Dopamine-norepinephrine reuptake inhibitors**
- **Similar to methamphetamine, MDMA or cocaine**



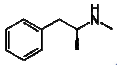
MDPV



Mephedrone



MDMA



Amphetamine

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Pharmacology

	MDPV	Mephedrone
Dose	5-20 mg	20-50 mg
Onset	20-40 min	10-20 min
Peak	3-4 hrs	45-60 min
Duration	6-8 hrs	1-2 hrs

- **Redosing common due to short effect, especially with mephedrone**

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Effects

- **Desired Effects:**
  - **Euphoria**
  - **Increased alertness**
  - **Diminished requirement for food & sleep**
  - **Hallucinations**
  - **Sexual arousal**
- **Side Effects:**
  - **Tachycardia**
  - **Hypertension**
  - **Diaphoresis**
  - **Anxiety**
  - **Agitation &Psychosis**
  - **Suicidal Ideation**
  - **Abstinence Syndrome**
  - **Nystagmus**
  - **Mydriasis**
  - **Dehydration**
  - **Stiffness/Jaw Clenching**

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Treatment

- **ABC/CAB**
- **Supportive Care**
  - **Antipsychotics**
  - **Antiaxiolytics**
    - Benzodiazapines
- **Intubation – if needed**
  - **Propofol**
  - **Benzodiazepines**
- **Physical Restraints**
  - **Avoid when possible**

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Legal Status & Future Direction

- Illegal throughout the EU
- Banned in many states in the US
- DEA issues a one year ban on Oct 21, 2011
  - Classified as schedule I substance
  - MDPV, Mephedrone & Methylone
- Chemists creating new molecules with variations of side chains
  - New molecules not regulated by DEA

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Now New Formulation! Legal High with Naphyrone

Christi Jen, PharmD, BCPS
Clinical Pharmacist – Emergency Medicine
Banner Boswell Medical Center
Sun City, Arizona

Learning Objectives

- **Familiarize with the most common formulations of naphyrone and understand its effects on users**

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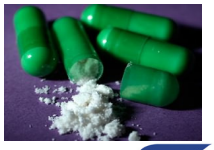
Story of SWIM

- **SWIM: Someone Who Isn't Me**
  - **Describes experience on Drugs Forum**
- **Male, 200 lbs, 5'10"**
- **Dosage: 200 mg in gel capsule**
- **Route: orally**
- **Duration: ~ 3 hours**



From: http://www.drugs-forum.com/forum/showthread.php?t=123121

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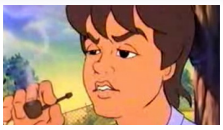
SWIM's Story Continues



Bust out his new gel capsule machine and spread the product across and weighed each capsule. Little did SWIM know that he had made a mistake measuring and the capsule had 0.21 grams instead of 0.021 grams.

From: http://www.drugs-forum.com/forum/showthread.php?t=123121

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5:30PM – SWIM ingested the capsule with a glass of water

6:30PM – Effects SWIM remembers from the night before start kicking in. Rapid heart rate, slight euphoria. Very thirsty.

7PM – SWIM notices stomach cramps/discomfort… SWIM probably has consumed about 4 bottles of water

8PM – SWIM's mood changed drastically and mindset was not normal. Felt depressed and unhappy about life. Just wanted to crawl in bed and sleep.

From: http://www.drugs-forum.com/forum/showthread.php?t=123121

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Naphyrone

- **Also known as**
  - **NRG-1, ENERGY, RAVE, O-2482**
  - **Synthetic cocaine**
  - **Glass cleaner, pond cleaner, nail polish remover**
  - **Cosmic Blast, 8 Ballz**
- **Naphthylpyrovalerone**
  - **Triple monoamine reuptake inhibitor**
  - **Structurally similar to cathinones e.g. mephedrone, MDPV, pyrovalerone**

http://webarchive.nationalarchives.gov.uk/+/http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary
http://www.talktofrank.com

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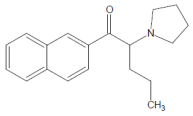
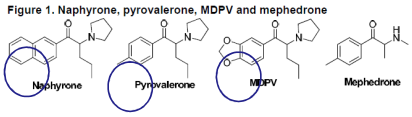


β-Naphyrone
Molecular Formula = C19H23NO
Formula Weight = 281.39202

Figure 1. Naphyrone, pyrovalerone, MDPV and mephedrone



http://webarchive.nationalarchives.gov.uk/+/http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary

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History

- **1971: pyrovalerone synthesized to treat lethargy and fatigue**
  - **Added to DEA Controlled Substance Act Schedule V in 1988**
- **2003: Meltzer and colleagues at Harvard**
  - **Studied neurotransmitter activities of pyrovalerone and other analogs e.g. naphyrone**
  - **New medications to treat cocaine abuse**
- **Mid-Late 2000's**
  - **Increased use of naphyrone combined with other materials**
    - Mephedrone
    - Butylone
    - Caffeine

http://webarchive.nationalarchives.gov.uk/+/http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary
http://www.deadiversion.usdoj.gov/schedules/orangebook/orangebook.pdf

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History of Naphyrone

- **July 2010**
  - **naphyrone added to Misuse of Drugs Act 1971 in UK**
- **April 2011**
  - **DEA requesting for information on naphyrone in addition to other synthetic cathinones**
- **October 2011: DEA Emergency Schedule**
  - **Emergency ban for 1 year**
  - **THC homologs, mephedrone homologs**

http://webarchive.nationalarchives.gov.uk/+/http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary
http://www.deadiversion.usdoj.gov/schedules/orangebook/orangebook.pdf
http://www.aapcc.org/dm/Portals/0/2010%20NPDS%20Annual%20Report.pdf

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Epidemiology

- **Prevalence**
  - **Europe: UK, France, Scotland**
  - **US: still relatively unknown**
    - Arizona, Missouri
- **Cost**
  - **£12.50/gram (UK)**
  - **$80/gram (US)**
- **Available at head/smoke shops, online**

http://webarchive.nationalarchives.gov.uk/+/http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary

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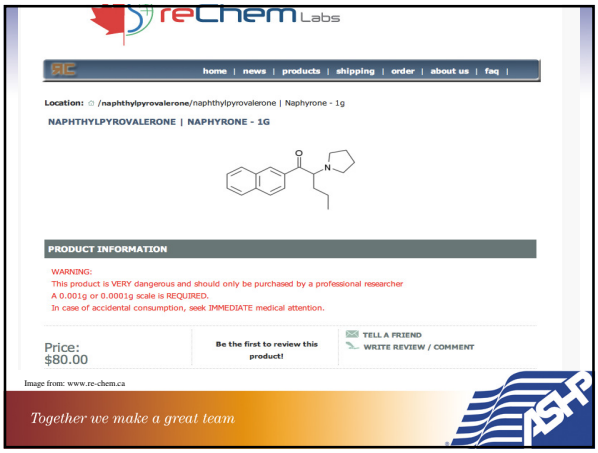

Image from: www.re-chem.ca

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How It's Done

- **Formulation: white powder**
- **Recommended dose: 0.02 grams naphyrone**
  - **Mephedrone: usual dose 5-10x higher**
- **Route of administration**
  - **Insufflation/Inhalation**
  - **Snorted**
  - **Oral ingestion**

http://webarchive.nationalarchives.gov.uk/+/http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary
http://www.talktofrank.com

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How to Use Cosmic Blast Jewelry Cleaner

1. Mix with 1 cup water
2. Add jewelry
3. Shake for 20 seconds

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Pharmacology of Naphyrone

- Mechanism of Action: *in vitro*
  - Reuptake inhibitor of dopamine (DA), serotonin (5-HT), norepinephrine (NE)
  - "Cocaine-like effect"
- Potency
  - 10x more than cocaine
- Onset and duration of action: unknown
- No available detection tests e.g. UDS

http://webarchive.nationalarchives.gov.uk/+/http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary

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Cocaine-Like Effects

- Cardiovascular:
  - Tachycardia, hypertension, QT prolongation
- Hyperthermia, diaphoresis
- Rhabdomyolysis
- Neuropsychiatric:
  - Psychosis - Euphoria - Seizures
  - Anxiety - Alertness - Coma
- Death
- Possible carcinogenesis from naphthyl moiety

http://webarchive.nationalarchives.gov.uk/+/http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary

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What are the concerns?

- Alpha and beta-isomers found in commercial products e.g. NRG-1
- Recommended doses 0.025 grams
  - Increased risk for overdose
- Still considered legal in the U.S.
- Misbranding of products
  - NRG-1 may not contain solely of naphyrone
  - Brandt et al: 13 NRG-1 products from internet
    - 1/13: naphyrone
    - Remaining 12: mixtures of illegal cathinones

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Management

- Not enough literature on naphyrone effects and management
- Not identified in urine drug screens – YET!
  - Gas chromatography (GC-MS)
- Supportive care
  - ABC/CAB
  - Hyperthermia = cooling, antipyretics
  - Benzodiazepines for agitated delirium and/or seizures
  - IV fluids for hydration and rhabdomyolysis
  - Intubation when appropriate

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What happened to SWIM?

5PM next day

- SWIM went to work but came home with bad back pain and leg pain. Feels like body aches when SWIM has a fever.
- Mindset returned to normal. Not immediately interested in redosing because of the horrible comedown experience

SUMMARY:

- SWIM feels he can't pass judgment since he dosed so incorrectly [sic]
- He felt fully recovered, but the body aches are staying with him [sic]

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