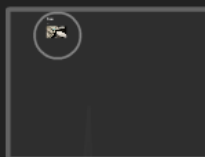




# Toxicology Trends: Keeping Us On Our A-game

*Jeanna M. Marraffa, Pharm.D., DABAT, FAAC*



Case:  
• 30-year-old male presents  
with seizure  
• PMH: Opioid addiction



Final Thoughts

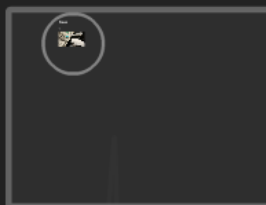


Questions?  
• [marraff@upstate.edu](mailto:marraff@upstate.edu)



# Toxicology Trends: Keeping Us On Our A-game

*Jeanna M. Marraffa, Pharm.D., DABAT, FAAC*



Case:  
- 30 year old male presents  
with syncope  
- PMH: Opioid addiction



# *Objectives*

- Describe new and emerging trends in managing acutely poisoned patients
- Discuss the toxicity of several emerging new agents of abuse
- Describe drug contaminants
- Discuss opportunities to have an impact

I have no financial disclosures



# Case

17-year-old female  
Presenting with  
fever, weight loss,  
night sweats,  
muscle pain, and  
fatigue.



**37 year old female**

- **Known heroin abuser**
- **Found unresponsive**
- **Apneic and pulseless**
- **Needle remains in Right AC**
- **4 mg naloxone with no effect**

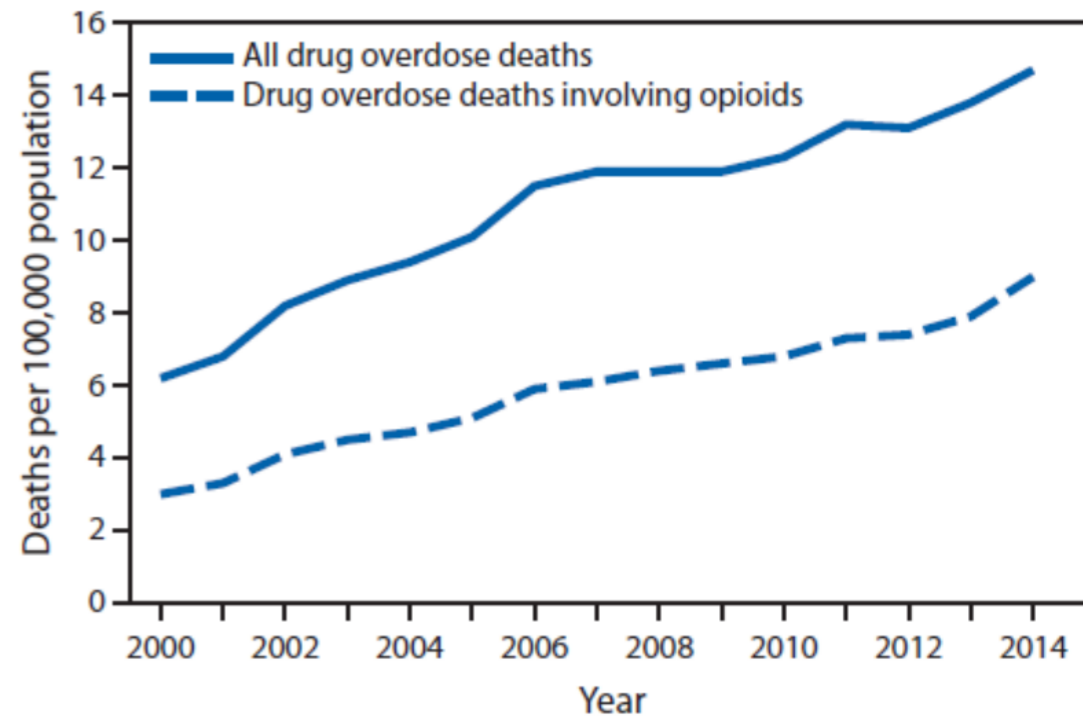
Needle remains in right eye  
- 4 mg naloxone with no effect



Drug Contaminants/Additives



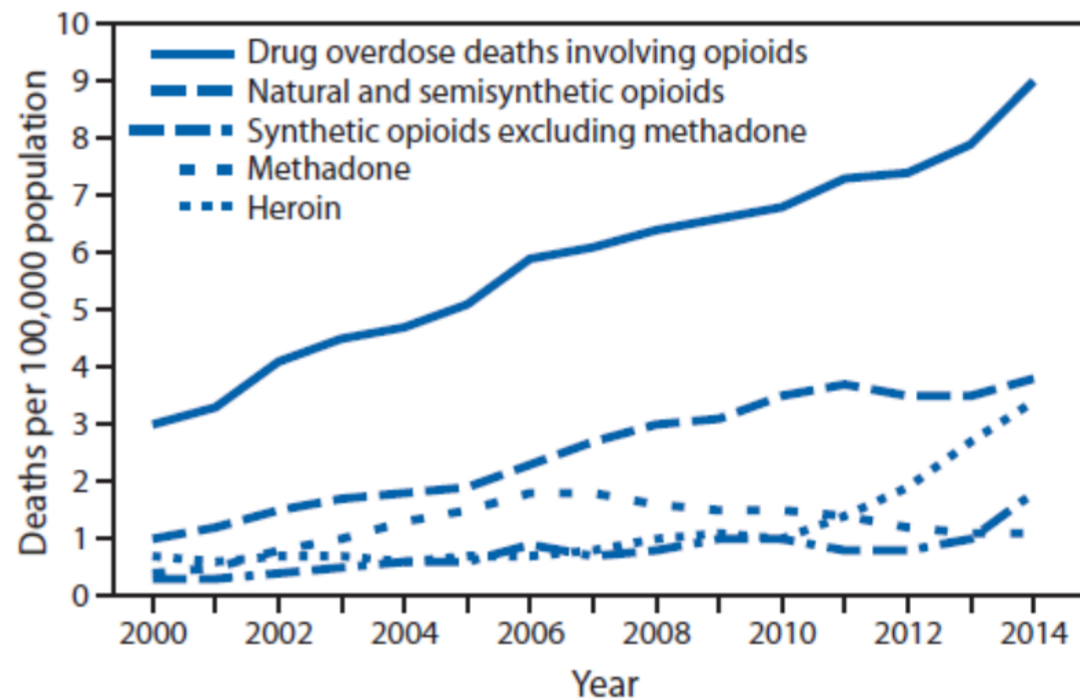
FIGURE 1. Age-adjusted rate\* of drug overdose deaths† and drug overdose deaths involving opioids§,¶ — United States, 2000–2014



Source: National Vital Statistics System, Mortality file.

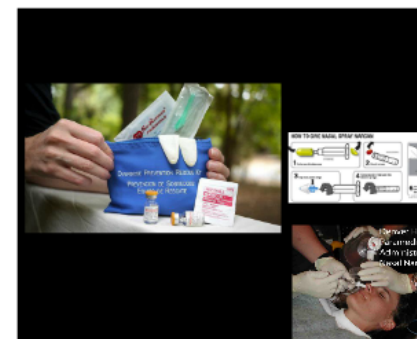
MMWR Jan 2016

FIGURE 2. Drug overdose deaths\* involving opioids,<sup>†,§</sup> by type of opioid<sup>¶</sup> — United States, 2000–2014



Source: National Vital Statistics System, Mortality file.

MMWR Jan 2016





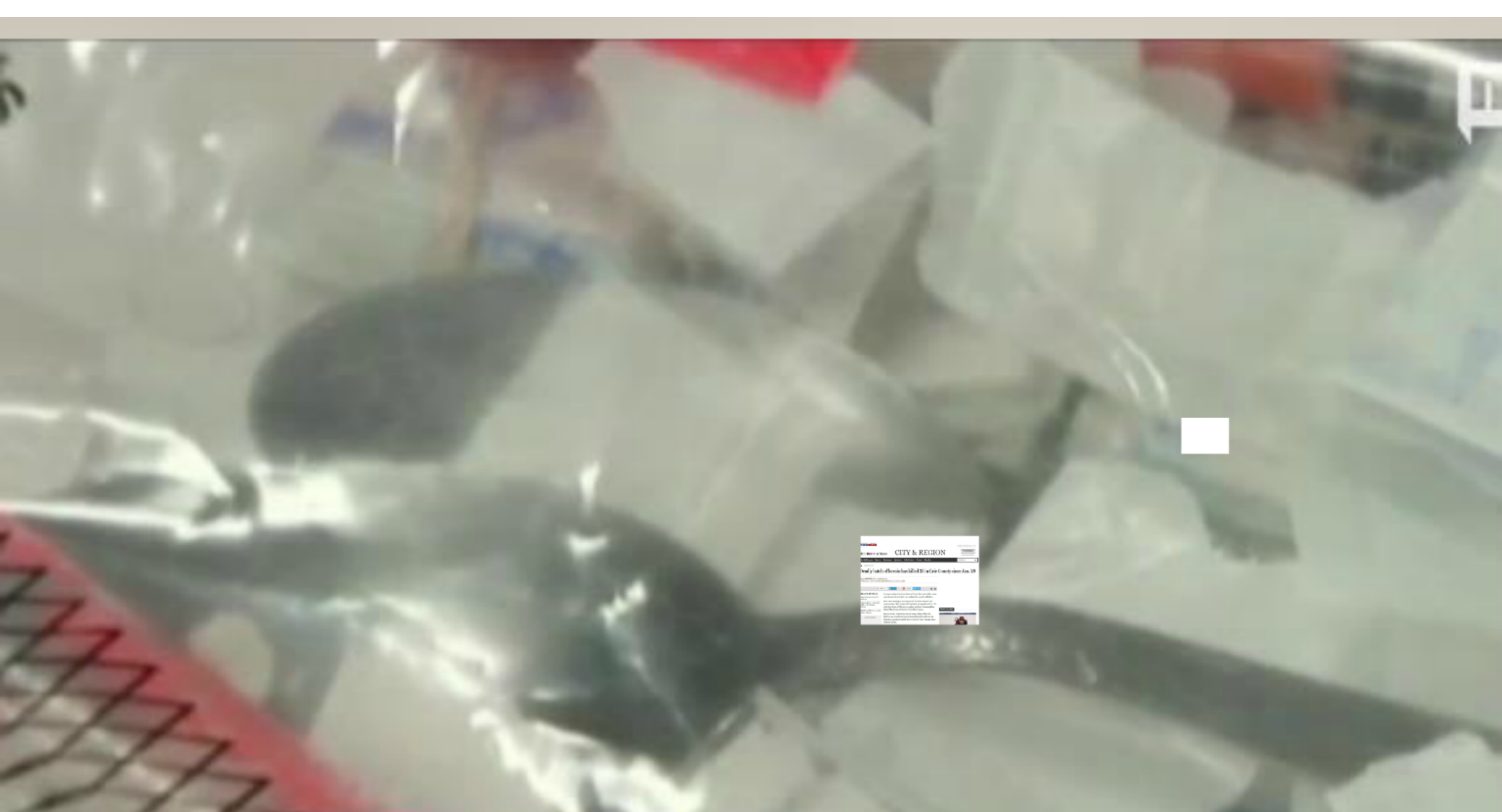




# Drug Contaminants/Adulterants







**ACTION NEWS** New This Morning

## Bad Heroin Kills 22 People in Western Pa.



5:46 17°

WPVI

BASKETBALL

CHICAGO

86

F



NBA

PHOENIX

124

P

# Deadly batch of heroin has killed 23 in Erie County since Jan. 29

by Lou Michel | News Staff Reporter

February 9, 2016 - 10:56 AM, updated February 9, 2016 at 1:15 PM

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## RELATED ARTICLES

Opioids rise to top of list for abuses

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Epidemic of heroin, opioids begs for solution

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A young couple drove from Seneca County last week to buy some supercharged heroin that was making the rounds in Buffalo.

Soon after smoking it, the 21-year-old Waterloo woman lost consciousness. Her 26-year-old boyfriend managed to call 911. It took three doses of Narcan, an opiate antidote, before Amherst Police Officer Sean D. Shaver revived the woman.

She was lucky. These days, heroin being widely sold in the Buffalo area is really fentanyl or heroin heavily laced with the laboratory-produced opioid that is 30 to 50 times stronger than ordinary heroin.

## PHOTO GALLERIES





## Everything We Know So Far About W-18, the Drug That's 10,000 Times More Powerful Than Morphine

 By Allison Ekin  
Staff Writer

February 2, 2016



Fake Oxy pills, pictured above, have led to hundreds of deaths in the past year in Alberta. Photo via [Twitter](#)

## Case:

- 30 year old male presents with syncope
- PMH: Opioid addiction





Feb 21 12 03:52p

Amcare Ambulance Service 3153393075

P.6

Name:

ID:

Patient ID:

Incident:

Age: 43 Sex:

Shock 2 50J

Impedance

HR

SpO2\*PR

822112114551

21 Feb 12

12:22:16

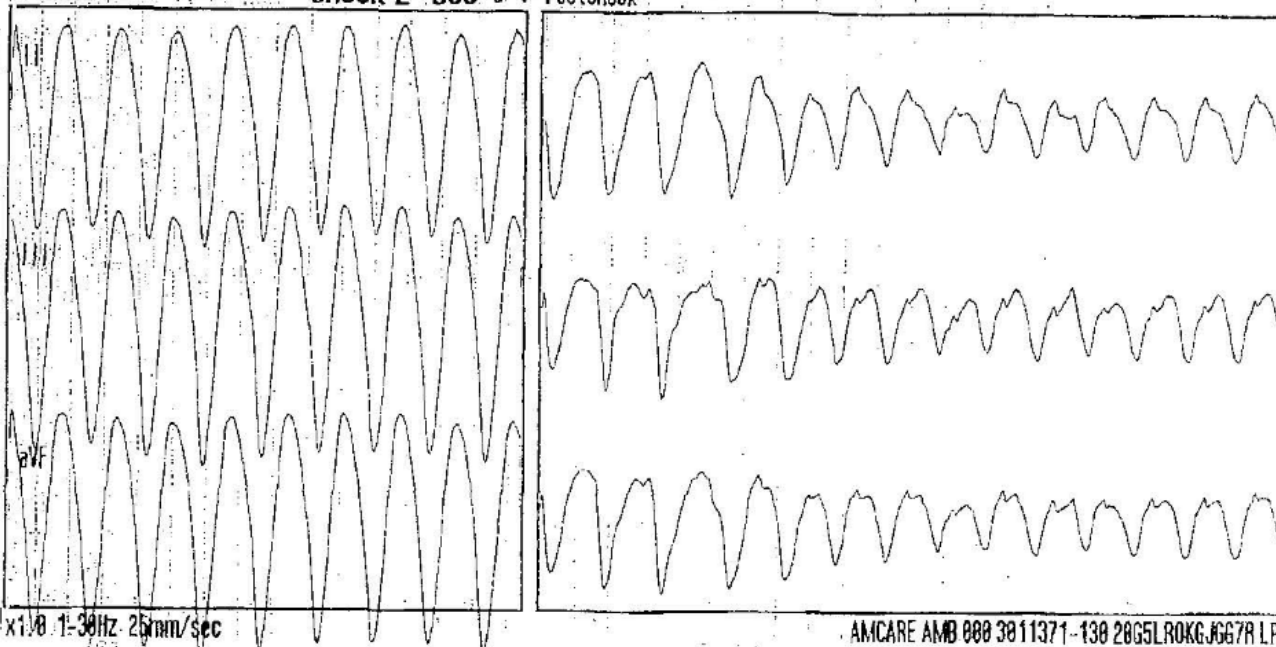
61

85

Preshock

Shock 2 50J

Postshock



(5)

- Loperamide: An Emerging Opioid Substitute ?!?!

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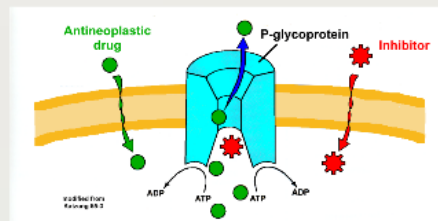
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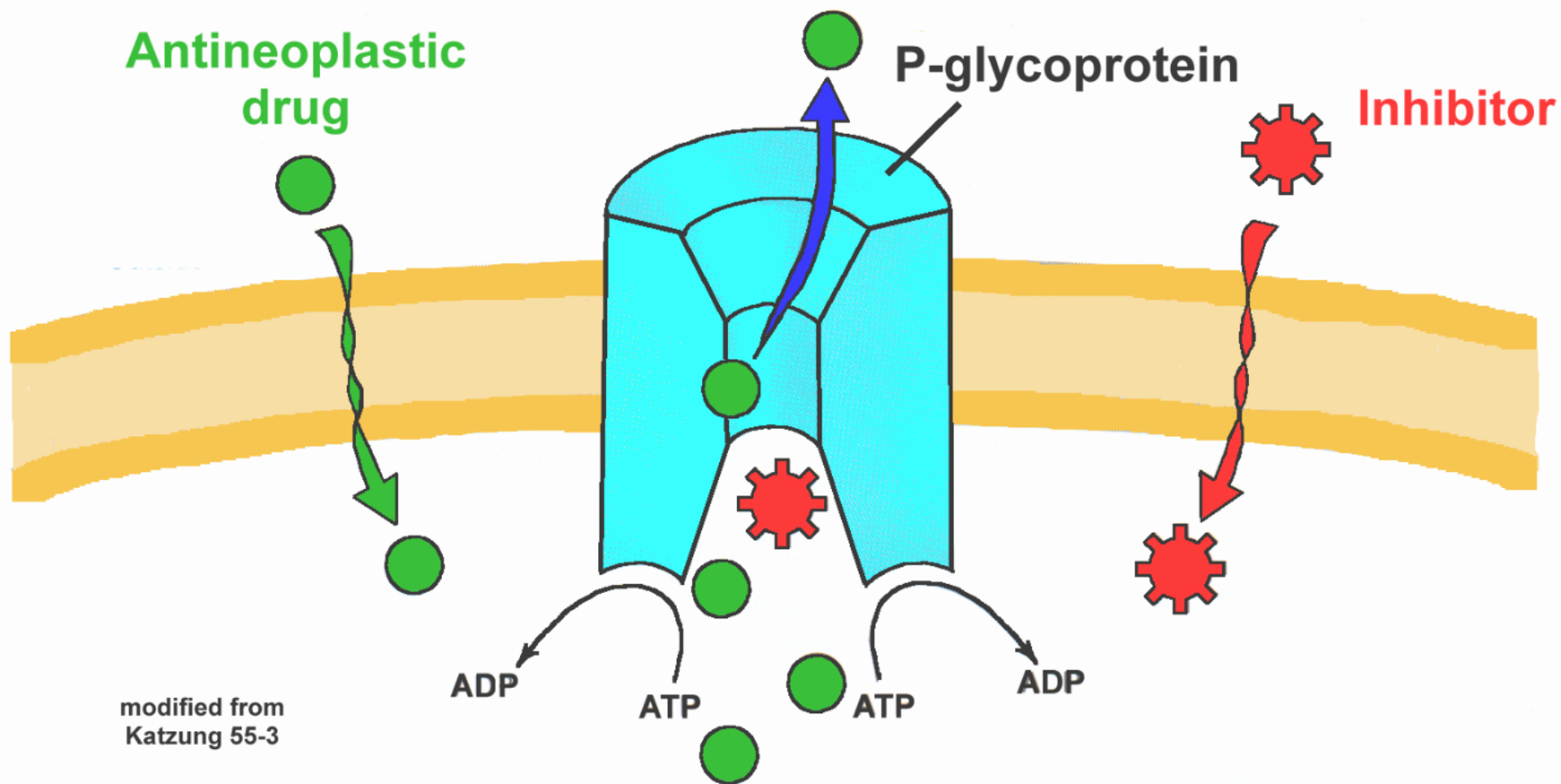
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## Drug and Alcohol Dependence

journal homepage: [www.elsevier.com/locate/drugalcdep](http://www.elsevier.com/locate/drugalcdep)



Short communication

### “I just wanted to tell you that loperamide WILL WORK”: A web-based study of extra-medical use of loperamide

Raminta Daniulaityte<sup>a,\*</sup>, Robert Carlson<sup>a</sup>, Russel Falck<sup>a</sup>, Delroy Cameron<sup>b</sup>, Sujan Perera<sup>b</sup>, Lu Chen<sup>b</sup>, Amit Sheth<sup>b</sup>

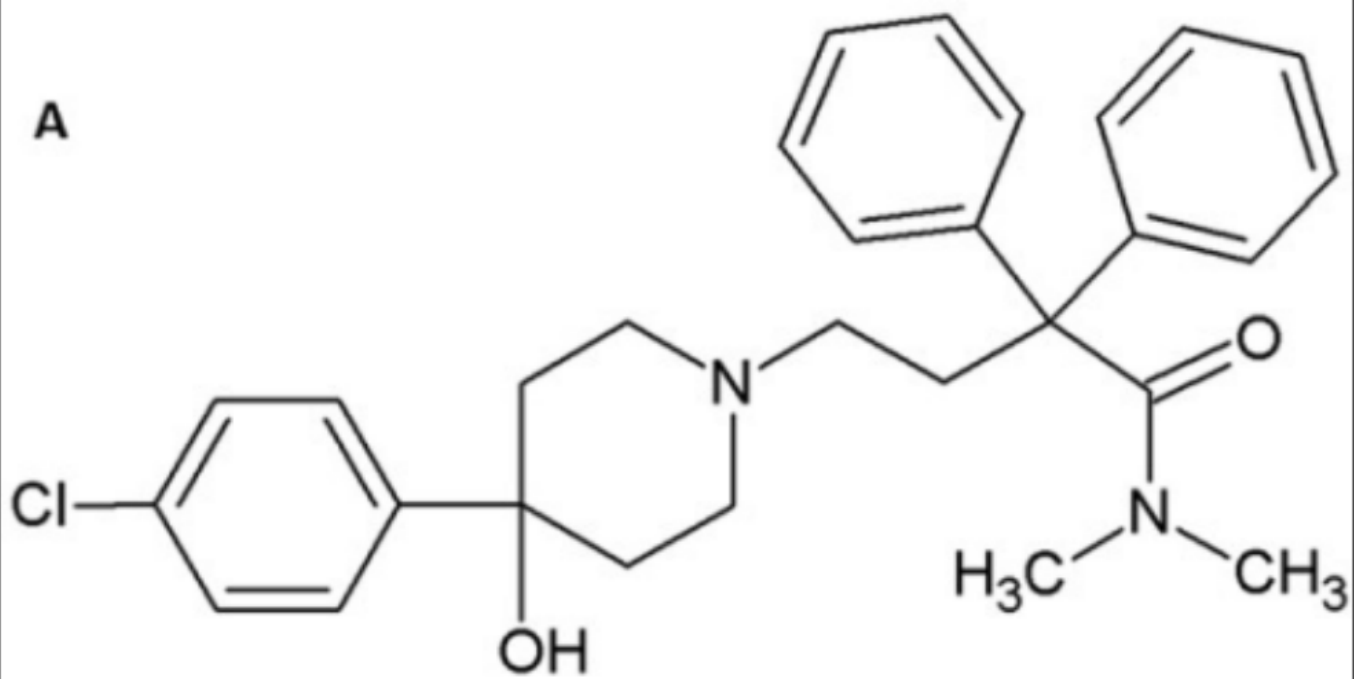
<sup>a</sup> Center for Interventions, Treatment, and Addictions Research (CITAR), Department of Community Health, Boonshoft School of Medicine, Wright State University, United States

<sup>b</sup> Ohio Center of Excellence in Knowledge-Enabled Computing (Kno.e.sis), Wright State University, United States<sup>†</sup>

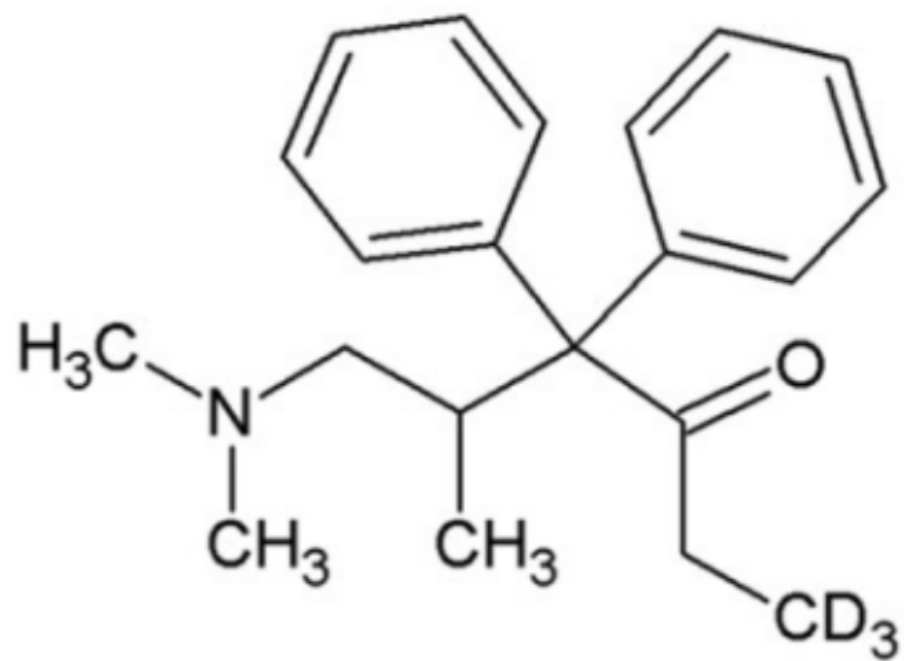
ARTICLE INFO

ABSTRACT



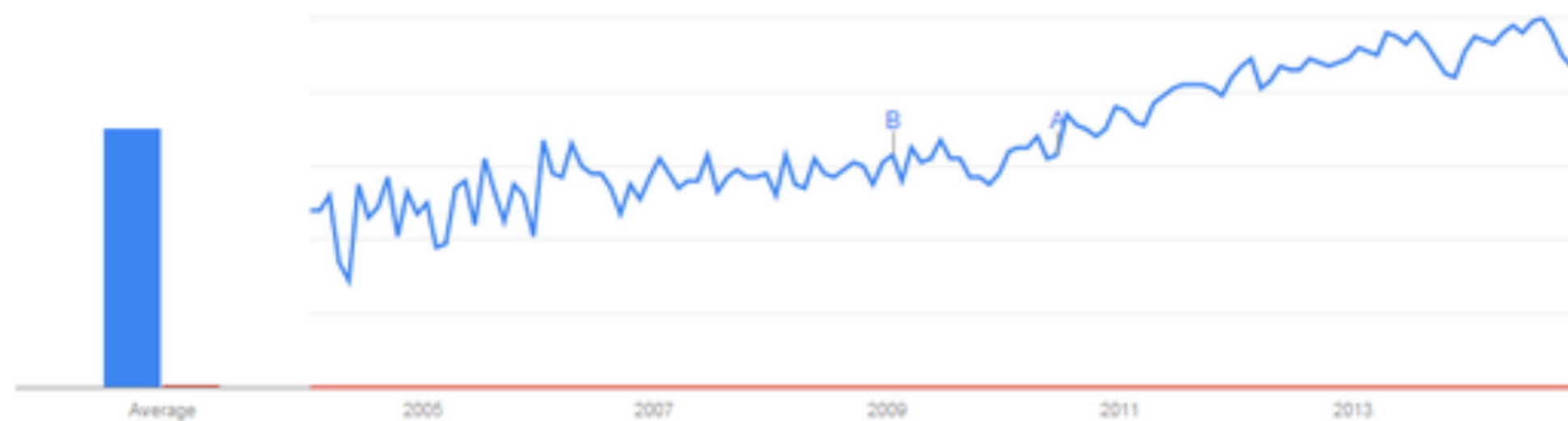


B



## Interest over time

☐ ☐ News headlines ☐ ☐ Forecast



## CASE REPORT

### Ventricular Tachycardia Associated with High-Dose Chronic Loperamide Use

Hannah L. Spinner,<sup>1,\*</sup> Nick W. Lonardo,<sup>1</sup> Roja Mulumalla,<sup>2</sup> and Josef Stehlik<sup>2</sup>

<sup>1</sup>Department of Pharmacy, University of Utah Health Care, Salt Lake City, Utah; <sup>2</sup>Division of Cardiovascular Medicine, University of Utah Health Care, Salt Lake City, Utah

Loperamide is an antidiarrheal medication deemed by the U.S. Food and Drug Administration as safe enough to be sold as an over-the-counter medicine. Unlike other  $\mu$ -opioid receptor agonists, loperamide acts specifically in the myenteric plexus in the gastrointestinal tract, making the potential for abuse low and reports of toxicity extremely rare. We present a case of a patient previously in good health who developed episodes of cardiac pauses, nonsustained ventricular tachycardia, and eventually runs of sustained ventricular tachycardia with hemodynamic instability. She required cardiopulmonary resuscitation, multiple cardioversions, and placement of a pacemaker. Her medical history was remarkable only for type 2 diabetes and chronic postcholecystectomy diarrhea. Meformin was the only prescription medication she was taking at the time of presentation. However, she reported that she had been taking an entire bottle of Equate brand loperamide (144 mg) daily for ~2 years. Loperamide overdoses associated with ventricular arrhythmias have been reported, but this is the first case to describe a serious ventricular arrhythmia associated with long-term use of a high dose of loperamide. Chronic over-treatment with loperamide may induce life-threatening arrhythmias. **Key Words:** loperamide, arrhythmia, ventricular tachycardia. (Pharmacotherapy 2015;35(2):234-238) doi: 10.1002/phar.1540

## Accepted Manuscript

The Long QT Teaser: loperamide abuse

Evbu O. Enakpene, M.D., Irtaz Bin Riaz, M.D., MM, Farshad M. Shirazi, MS, M.D., PhD, Yuval Raz, M.D., Julia H. Indik, MD, PhD

PII: S0002-9343(15)00463-5

DOI: 10.1016/j.amjmed.2015.05.019

Reference: AJM 13016

To appear in: The American Journal of Medicine

Received Date: 14 February 2015



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DOI: 10.1080/15563685.2014.900371

informa  
healthcare

## CRITICAL CARE

### Cardiac conduction disturbance after loperamide abuse

J. M. MARRAFFA,<sup>1</sup> M. G. HOLLAND,<sup>1</sup> R. W. SULLIVAN,<sup>1</sup> B. W. MORGAN,<sup>2</sup> J. A. OAKES,<sup>3</sup> T. J. WIEGAND,<sup>4</sup> and M. J. HODGMAN<sup>1</sup>

<sup>1</sup>Department of Emergency Medicine, Upstate Medical University, Syracuse NY, USA

<sup>2</sup>Department of Emergency Medicine, School of Medicine, Emory University, Atlanta, GA, USA

<sup>3</sup>Department of Emergency Medicine, UBMC and Strong Memorial Hospital, Rochester NY, USA

<sup>4</sup>UBMC and Strong Memorial Hospital, Ruth A. Lawrence Poison and Drug Information Center, Rochester, NY, USA

**Context:** Prescription opioid abuse is a major public health concern and an ongoing epidemic in the United States. Loperamide is a widely available and inexpensive over-the-counter antidiarrheal with peripheral  $\mu$ -opioid receptor activity. Online resources discuss the use of loperamide for the amelioration of withdrawal symptoms or recreational abuse. We describe the clinical course of 5 patients abusing loperamide, 3 of whom had life-threatening cardiac arrhythmias. **Methods:** In this observational case series, patients with cardiac arrhythmias or history of loperamide abuse with cardiac arrhythmias were identified; 5 patients were identified and 4 of the 5 patients were seen directly at the bedside. Clinical profile and outcome of patients is reported. **Results:** We report 5 patients with history of loperamide abuse; 3 of the 5 patients had life-threatening cardiac arrhythmias. One of the patients experienced a second life-threatening arrhythmia after he resumed loperamide abuse. Loperamide levels were obtained in 4 of the 5 patients and were at least one order of magnitude greater than therapeutic concentrations. Discontinuation of loperamide resulted in complete resolution of cardiac conduction disturbances. **Conclusion:** This case series describes several patients with cardiac conduction abnormalities and life-threatening ventricular arrhythmias temporally related to loperamide abuse. With the recent efforts to restrict the diversion of prescription opioids, increasing abuse of loperamide as an opioid substitute may be seen. Toxicologists should be aware of these risks and we urge all clinicians to report such cases to FDA Medwatch<sup>®</sup>.

The Journal of Innovations in Cardiac Rhythm Management, 000 (2015), 1



## LETTER TO THE EDITOR IN CHIEF

### Reply to: "Torsade de Pointes Associated with High-dose Loperamide Ingestion"

We read with great interest the recent article by Marzec et al.<sup>1</sup>, Torsade de Pointes Associated with High-dose Loperamide. Prescription opioid abuse is a major public health concern and an ongoing epidemic in the United States. According to the Centers for Disease Control and Prevention (CDC), unintentional poisoning is the leading cause of accidental death in the US with prescription opioid analgesics being most commonly involved.<sup>2</sup> To combat this epidemic, there have been numerous measures both on state-wide levels and nationally to have tighter control on prescription opioid access and availability. Hydrocodone has recently been re-scheduled to a Schedule II controlled substance. Pharmaceutical companies have changed their formulations of several sustained release products to reduce their abuse potential and many states have implemented electronic prescription drug monitoring programs. These restrictions will likely lead to an increase in the use of illicit opioids such as heroin as well as the use of alternative pharmaceuticals. Loperamide, as Marzec et al.<sup>1</sup> point out, is widely available and inexpensive. At therapeutic doses, loperamide has a lack of CNS effects because of the P-glycoprotein efflux pump.<sup>3</sup> Numerous online resources and blogs describe the abuse potential of loperamide. The combined use of a P-glycoprotein inhibitor such as quinidine or quinine has been suggested, as well as just excessive doses of loperamide to overcome the P-glycoprotein efflux pump.

We recently reported a case series of 5 patients and 7 events of excessive doses of loperamide resulting in cardiac

# CASE REPORT

## Ventricular Tachycardia Associated with High-Dose Chronic Loperamide Use

Hannah L. Spinner,<sup>1,\*</sup> Nick W. Lonardo,<sup>1</sup> Roja Mulamalla,<sup>2</sup> and Josef Stehlik<sup>2</sup>

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We recently reported a case series of 5 patients and 7 events of excessive doses of loperamide resulting in cardiac



CRITICAL CARE

# Cardiac conduction disturbance after loperamide abuse

J. M. MARRAFFA,<sup>1</sup> M. G. HOLLAND,<sup>1</sup> R. W. SULLIVAN,<sup>1</sup> B. W. MORGAN,<sup>2</sup> J. A. OAKES,<sup>3</sup> T. J. WIEGAND,<sup>4</sup>  
and M. J. HODGMAN<sup>1</sup>

<sup>1</sup>Department of Emergency Medicine, Upstate Medical University, Syracuse NY, USA

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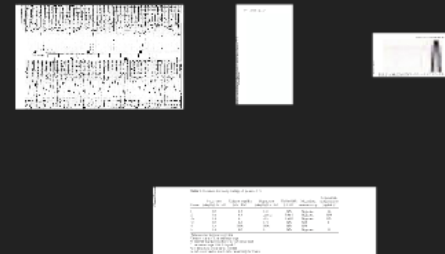
<sup>3</sup>Department of Emergency Medicine, UPMC and Strong Memorial Hospital, Rochester NY, USA

<sup>4</sup>UPMC and Strong Memorial Hospital, Ruth A. Lawrence Poison and Drug Information Center, Rochester, NY, USA

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## Our Experience

- *Multiple Patients with history of loperamide abuse*
- *200-700 tablets per day consumed*
- *None reported use of concurrent p-gp inhibitors*
- *Severe cardiac toxicity*
  - *At least two deaths*

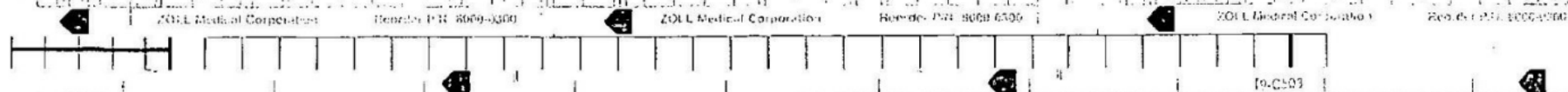
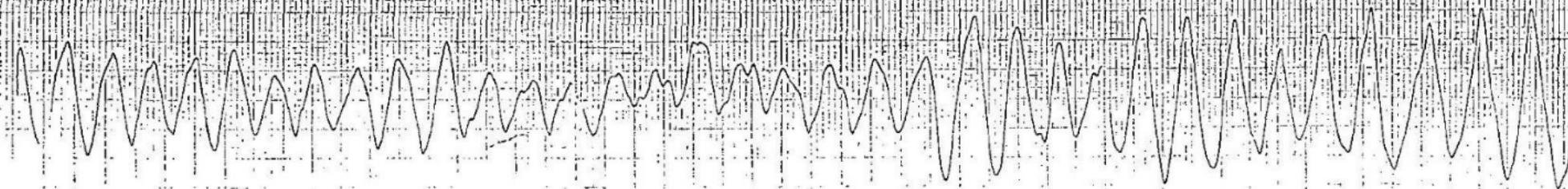


### Next Steps...

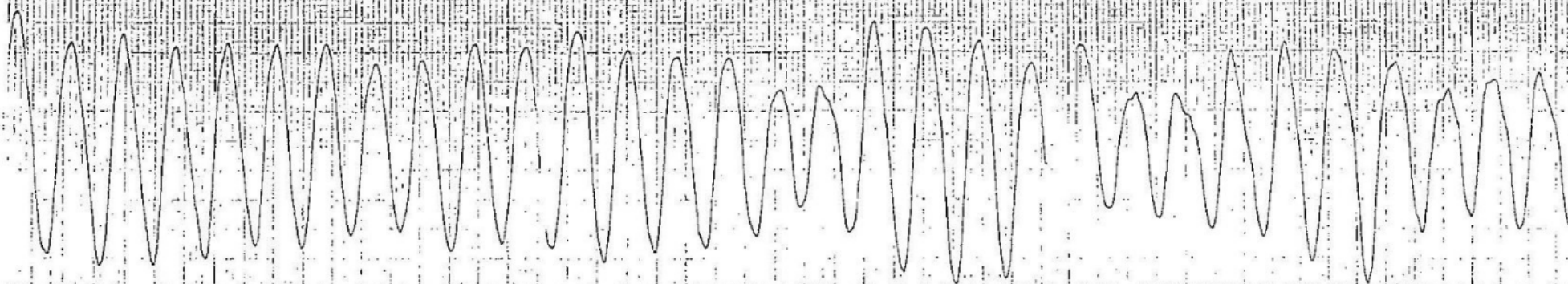
- in-vitro and animal studies need to be done
- These cases need to be reported
- FDA Medwatch

1 13:08:44 21-FEB-12 PADS SIZE 1.0 HR= 15% ANALYZE

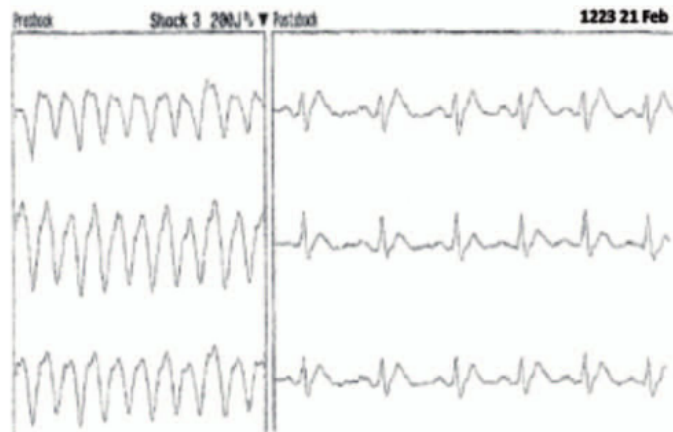
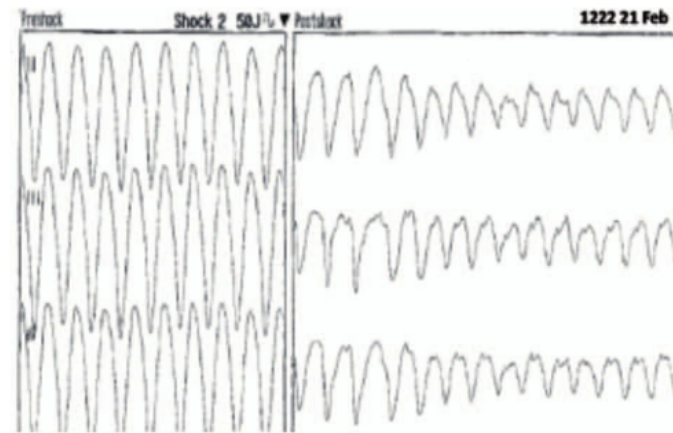
ANALYSIS HALTED



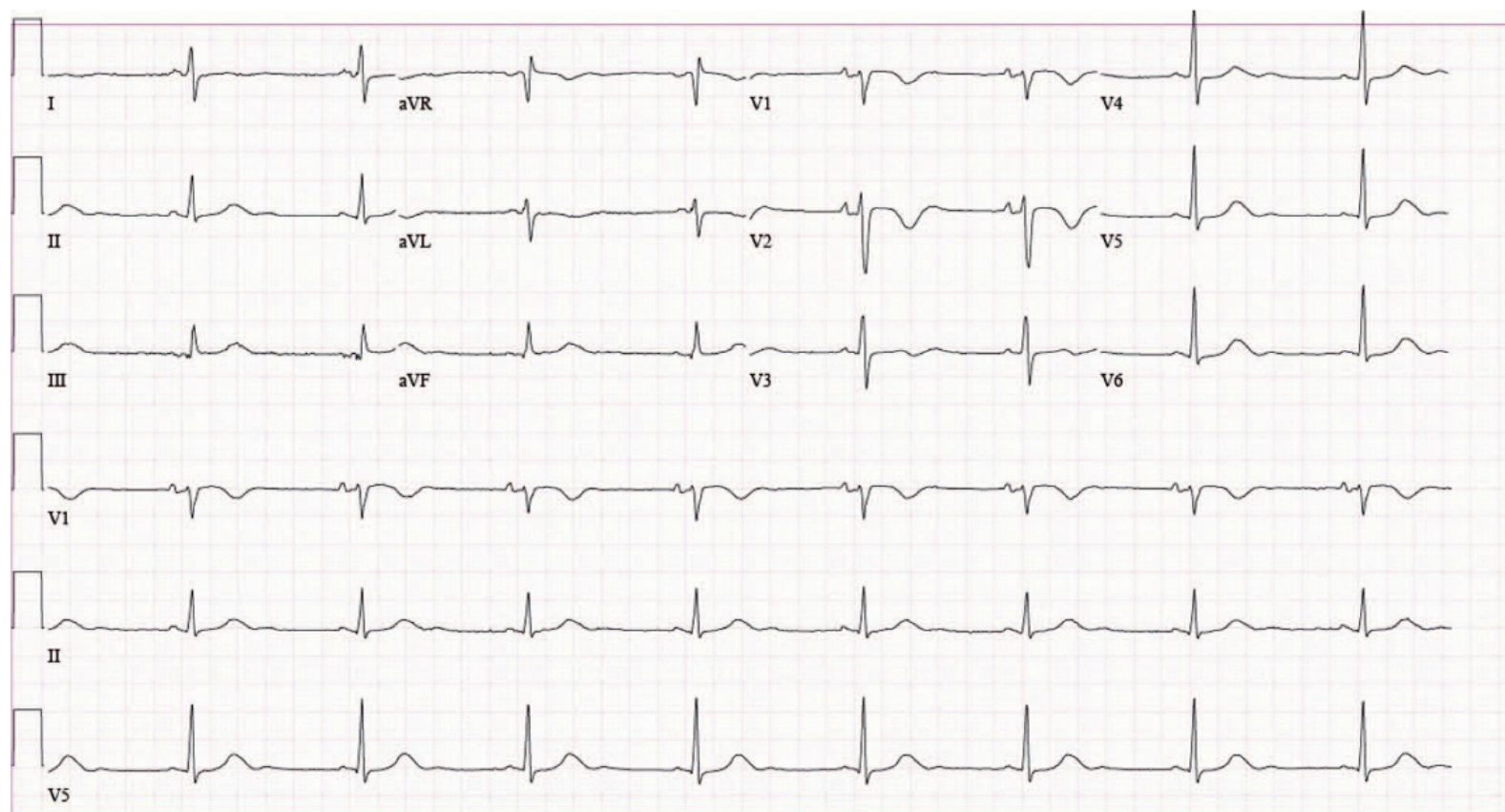
13:09:13 21-FEB-12 PADS SIZE 1.0 HR= 16%



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**Fig. 3.** ECG of Case 2 on hospital day 5 showing sinus rhythm with a narrow QRS and normal QTc interval (colour version of this figure can be found in the online version at [www.informahealthcare.com/ctx](http://www.informahealthcare.com/ctx)).

**Table 1.** Pertinent laboratory findings of patients 1–5.

Patient	Potassium (mEq/L) [3.5–5.0]	Calcium (mg/dL) [8.5–10.8]	Magnesium (mEq/L) [1.5–2.2]	TSH mIU/L [.3–5.0]	Methadone immunoassay	Loperamide concentration (ng/mL)^
1	4.0	9.4	1.8	N/A	Negative	22
2	3.6	9.4	2.6*×	0.963	Negative	N/A
3 a	3.2	8.7	2.5	1.620	Negative	130
3 b	4.0	9.6	1.4	N/A	N/A	97
4	3.5	N/A	N/A	N/A	N/A	77
5	3.2	9.0	1.7	N/A	Negative	33

\*Denotes abnormal laboratory value.

Values in brackets [ ] are reference range.

X: received magnesium sulfate prior to drawing blood.

^: therapeutic range: 0.24–1.2 ng/mL<sup>1</sup>.

N/A: denotes not available/not provided.

3a and 3b are presentations 1 and 2, respectively, for Case 3.



## *Next Steps....*

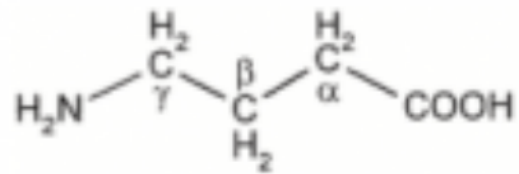
*In-vitro and animal studies need to be done*  
*These cases need to be reported*

- *FDA Medwatch*

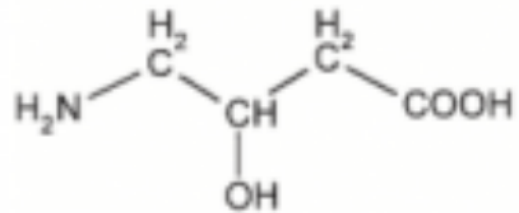
# Case

- 33 year old female
  - Altered Mental Status
  - Withdraws to painful stimuli
  - "Twitchy"
- Vital signs:
  - Heart rate 70 bpm
  - Blood pressure 115/75 mmHg
  - Resp Rate 18/min
  - 100% saturation RA
- Physical Exam:
  - PERL
  - Moist mucus membranes
  - Positive bowel sounds
  - Myoclonic jerking
- Normal sinus rhythm

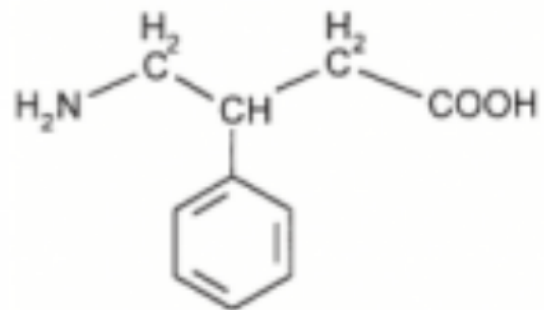




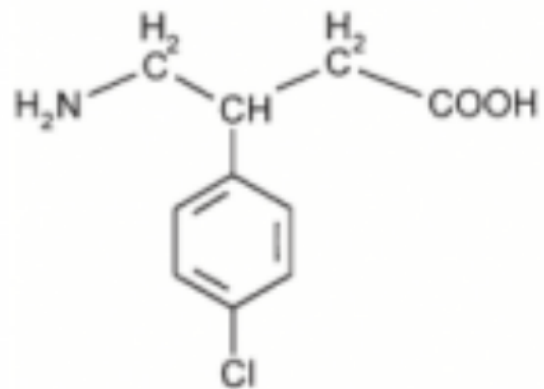
GABA –  $\gamma$ -amino-butyric acid



GABA-OH –  $\beta$ -hydroxy- $\gamma$ -amino-butyric acid



Phenibut (PB) –  $\beta$ -phenyl- $\gamma$ -amino-butyric acid

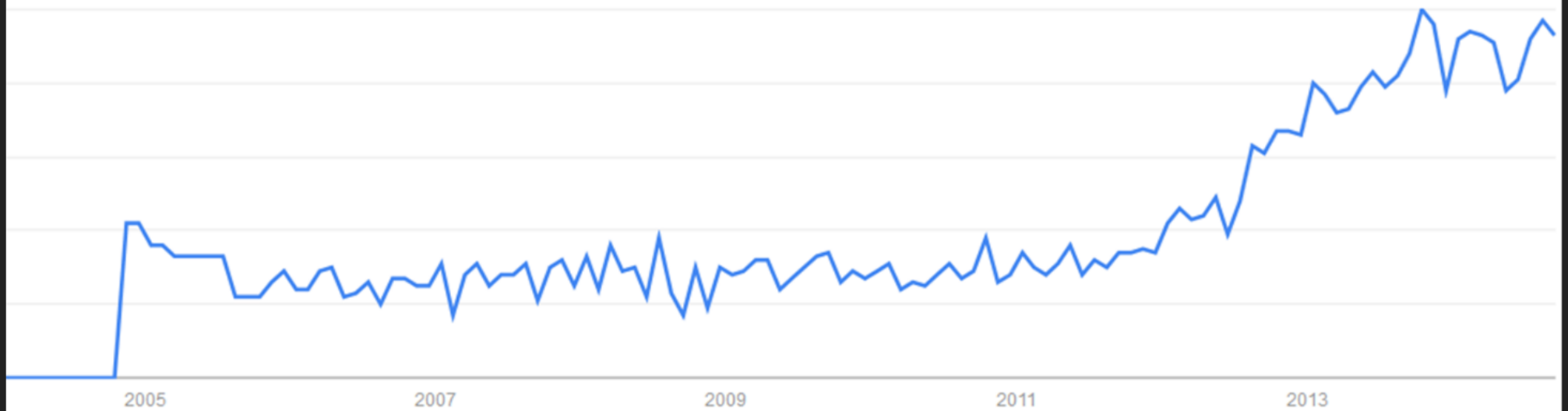


Baclofen (BAC) –  $\beta$ -p-Cl-phenyl- $\gamma$ -amino-butyric acid,  
Cl-PB

Fig. 1

## Interest over time ?

☐ News headlines ? ☐ Forecast ?



BRIEF COMMUNICATION

# Acute behavioural disturbance associated with phenibut purchased via an internet supplier

MICHAEL A. DOWNES,<sup>1,2</sup> INGRID L. BERLING,<sup>1,2</sup> AHMED MOSTAFA,<sup>3,4</sup> JEFFREY GRICE,<sup>4</sup> MICHAEL GEOFFREY K. ISBISTER<sup>1,2</sup>

<sup>1</sup>Department of Clinical Toxicology and Pharmacology, Calvary Mater Newcastle, Waratah, New South Wales, .

<sup>2</sup>School of Medicine and Public Health, University of Newcastle, Newcastle, New South Wales, Australia

<sup>3</sup>Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Helwan University, Egypt

<sup>4</sup>Therapeutics Research Centre, School of Medicine, University of Queensland, Brisbane, Queensland, Australia

<sup>5</sup>School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, Australia

**Context.** Toxicity from recreational substances marketed for other purposes is a well-documented clinical entity phenibut toxicity procured via the internet. **Case Details.** A 20-year-old female presented to the emergency dep phenibut the prior day. The main finding was a decreased level of consciousness, however when roused she became only was required with no specific intervention. The patient made a full recovery over a 24-hour period and a purchased online. Plasma phenibut concentration was 29.7 µg/ml. A 38-year-old male presented to ED with an evening he had used tetrahydrocannabinol or THC, alcohol and phenibut, the latter purchased via the internet. He had a suboptimal response to parenteral sedation. He was subsequently intubated for airway protection in the context of ongoing sedation to optimally manage his behavioural state. Post extubation the next morning he admitted using phenibut. Plasma phenibut concentration was 36.5 µg/ml. **Discussion.** Altered mental status was the predominant manifestation of phenibut toxicity in these cases. Clinicians to be aware of how phenibut toxicity may present as the internet has widened access to such substances.

**Keywords** Phenibut; Toxicity; Poisoning; Internet

University Health Sciences Library | at 08:30 05 October 2015

## 167. Reports of phenibut usage to the Dutch Poisons Information Center (DPIC).

Arjen Koppen, Antoinette van Riel, Chantal Roelen, Irma de Vries, Jan Meinenbelt

Dutch Poisons Information Center, University Medical Center Utrecht, Utrecht Netherlands

**Background:** In the Netherlands the abuse of gamma-hydroxy butyric acid (GHB) has been considerable in the last 10 years. In 2013 the DPIC was consulted in 107 cases of both acute GHB intoxications and severe GHB withdrawal symptoms. GHB addicts use several drugs in an attempt to reduce these withdrawal effects. One of these drugs is phenibut, a p-Cl-derivative of baclofen, with similar psychopharmacological activity as baclofen. Phenibut is a GABA mimetic (mainly GABA-B), stimulant of dopamine receptors, and an antagonist of beta-phenylethylamine. Since 2005 phenibut is mentioned on drug fora found on Google Netherlands, and in 2014 over 20 different internet drug fora contained user information about the drug. Since 2007 a strong increase is observed of websites selling phenibut, usually as a dietary supplement. Little is known about the clinical effects of phenibut overdoses or its potential for abuse and dependency. With this report we discuss the cases the DPIC received on phenibut use.

**Methods:** All cases of phenibut exposure in the DPIC-database were reviewed retrospectively from the first reported case in 2011 until March 2015.

**Results:** Since 2011 the DPIC received 8 reports about phenibut (1 in 2011, 3 in 2013, 3 in 2014 and 1 in 2015). In 2 cases patients developed clear withdrawal symptoms after stopping phenibut

## Rare disease

### CASE REPORT

## Phenibut dependence

Andriy V Samokhvalov,<sup>1,2</sup> C Lindsay Paton-Gay,<sup>1,2</sup> Kam Balchand,<sup>1,2</sup> Jürgen Rehm<sup>1,2,3,4</sup>

<sup>1</sup>Centre for Addiction and Mental Health, Toronto, Ontario, Canada  
<sup>2</sup>Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada  
<sup>3</sup>Bata Lara School of Public Health, Toronto, Ontario, Canada  
<sup>4</sup>Yonge Psychiatric & Rehabilitation Institute, University of Toronto, Toronto, Ontario, Canada

**Correspondence to:** Dr Andriy V Samokhvalov, anamokh@cmh.mcgill.ca

**SUMMARY**  
Phenibut is a γ-aminobutyric acid (GABA) agonist designed and used as an anxiolytic in Russia. In Western countries, phenibut is not a registered medication but is available through online stores as a supplement. We present a case of a patient who used phenibut to self-medicate anxiety, insomnia and cravings for alcohol. While phenibut was helpful initially, the patient developed dependence including tolerance, significant withdrawal symptoms within 3–4 h of last use and failure to fulfil his roles at work and at home. He finally sought medical assistance in our addiction clinic. We have gradually, over the course of 9 weeks, substituted phenibut with baclofen, which has similar pharmacological properties, and then successfully tapered the patient off baclofen. This required approximately 10 mg of baclofen for each gram of phenibut.

was able to abstain from alcohol since then. However, he submitted a variety of substances to cope with ongoing stress, depression, anxiety and insomnia. He used opioids (various preparations of codeine, poppies, kratom) and benzodiazepines (phenazepam and diazepam). These were obtained from friends' prescriptions, purchased over the counter or online. There is a family history of alcohol use disorders on both the maternal and paternal sides. The patient had never received specialised addiction treatment before.

At the time of the assessment, he was abstinent from alcohol and actively using the 'supplements' phenibut (for 10 months) and kratom (for 2 years). He was taking 8 g of phenibut and 18 g of kratom per day. The patient found these two 'supplements' very helpful for coping with withdrawal symptoms from alcohol, benzodiazepines and poppies. He was unable to stop using them. He made several attempts to decrease the use of phenibut, but experienced heightened anxiety, anger and irritability.

### BACKGROUND

## 272. Retrospective review of Phenibut exposures reported to Ohio poison control centers

Sheila Goertemöller, Alysha Behrman, Robert Goetz, HA Spiller

Nationwide Childrens Hospital, Columbus OH USA

Phenibut dose	Co-ingestants	Symptoms	Treatment	Medications/Intake
"No exact dose"	None reported	Agitation, drowsiness, confusion, hallucinations, elevated creatine kinase and muscle stiffness	Lorazepam, haloperidol	Tobacco, cocaine
Unknown	Quetiapine, Unknown drug	Elevated creatine kinase, hypernatremia, agitation, diaphoresis, tachycardia, muscle rigidity, confusion, drowsiness	Lorazepam, Propofol, Diazepam, Naloxone, oxygen, sodium bicarbonate, intravenous fluids	Unknown
9 grams	Alcohol	Nausea, flushing, anxiety, insomnia, agitation	Unkown	None
Unknown	None reported	Agitation, confusion, lethargy, drowsiness	Unkown	Unknown
9.5 grams	Water	Hypertension, tachycardia, vomiting, agitation, confusion, irritability	Lorazepam, intravenous fluids	Lithium Serenquel, Risperidone
Unknown	None reported	Hypertension, agitation, confusion, drowsiness, hange eyes on head CT	Unspecified benzodiazepine	None





# Behavioural disturbance associated with phenibut purchased from an internet supplier

<sup>1,2</sup> INGRID L. BERLING,<sup>1,2</sup> AHMED MOSTAFA,<sup>3,4</sup> JEFFREY GRICE,<sup>4</sup> MICHAEL L. GRICE<sup>1,2</sup>

*Psychiatry and Pharmacology, Calvary Mater Newcastle, Waratah, New South Wales, Australia*  
*Public Health, University of Newcastle, Newcastle, New South Wales, Australia*  
*Physical Chemistry, Faculty of Pharmacy, Helwan University, Egypt*  
*Centre, School of Medicine, University of Queensland, Brisbane, Queensland, Australia*  
*Medical Sciences, University of South Australia, Adelaide, Australia*

Recreational substances marketed for other purposes is a well-documented clinical entity accessed via the internet. *Case Details.* A 20-year-old female presented to the emergency department with a main finding was a decreased level of consciousness, however when roused she became responsive. No specific intervention. The patient made a full recovery over a 24-hour period and a phenibut concentration was 29.7 µg/ml. A 38-year-old male presented to ED with an acute presentation of hydrocannabinol or THC, alcohol and phenibut, the latter purchased via the internet. The behavioural state had a pattern of arenteral sedation. He was subsequently intubated for airway protection in the context of ongoing sedation to a comatose state. Post extubation the next morning he admitted using phenibut. Plasma phenibut concentration was 29.7 µg/ml. Mental status was the predominant manifestation of phenibut toxicity in these cases. Clinicians to be aware of the fact that the internet has widened access to such substances.

Phenibut; Poisoning; Internet

Rare disease

## CASE REPORT

### Phenibut dependence

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Phenibut dose	Co-ingestants	Symptoms	Treatment	Medication history
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Unknown	Quetiapine, Unknown drug	Elevated creatine kinase, hypertension, agitated, diaphoresis, tachycardia, muscle rigidity, confusion, drowsiness	Lorazepam, Precedex, Diazepam, Naloxone, oxygen, sodium bicarbonate, intravenous fluids	Unknown
9 grams	Alcohol	Nausea, bloating, anxious, insomnia, agitated	Unknown	None
Unknown	None reported	Agitated, confusion, lethargy, drowsiness	Unknown	Unknown
9.5 grams	Wine	Hypertension, tachycardia, vomiting, agitated, confusion, miosis	Lorazepam, intravenous fluids	Lithium Seroquel, flomax
Unknown	None reported	Hypertension, agitation, confusion, drowsiness, benign cyst on head CT	Unspecified benzodiazepine	None

## 167. Reports of phenibut usage to the Dutch Poisons Information Center (DPIC).

Arjen Koppen, Antoinette van Riel, Chantal Roelen,  
Irma de Vries, Jan Meulenbelt

*Dutch Poisons Information Center, University Medical Center  
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# Our Experience

## Several Cases since 2014

- All had altered, depressed mental status
- N=1 myoclonic jerking
- N=2 tonic clonic seizure activity
- N=3 prolonged duration of toxicity

1 gram phenibut = 10 mg baclofen

Treatment is largely supportive

ADRAFINIL NOOPEPT PYRACETAM ANIRACETAM PRAMIRACETAM PHENIBUT PHENYLPYRACETAM OXIRACETAM SUNIFIRAM



Want to buy Phenibut at GNC? There are a lot of different brands of this nootropic anti-anxiety supplement. Beta-Phenyl-G-Aminobutyric Acid, better known as phenibut is derived from the neurotransmitter G-Aminobutyric Acid, better known as GABA. Phenibut is considered one of the safest as well as one of the most effective nootropics, known as "smart drugs". It has been scientifically and clinically demonstrated that phenibut can enhance neurological functions. Due to its phenyl ring phenibut can penetrate the blood-brain barrier and bind to the GABA receptor. This stimulates the release of the neurotransmitter GABA in the brain. [Click here to buy Phenibut online.](#)

## BUY PHENIBUT

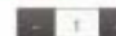
- ✓ Powerful Anxiolytic
- ✓ Reduce Stress & Depression
- ✓ Promote Relaxation
- ✓ Improve Sleep & Mood
- ✓ Enhance Memory
- ✓ Blood Regulation



PHENIBUT  
50 G



\$23.99



Add to cart

English



PHENIBUT  
50 G



Add to cart



ADRAFINIL  
30 CAPSULES



Add to cart



NOOPEPT  
100 G

## Next Steps

- Attempt to confirm exposure with quantitative testing
- Easily purchased in stores/internet
- Urge reporting to the FDA
  - Poses risk as a dietary supplement



# *Case*

29 year old male presents to the ED

- AAOx3
- Diaphoretic
- Nausea/vomiting/diarrhea
- Piloerection

Previous opioid addiction

- Ran out of an 'herbal' product yesterday





## Seizure and Coma Following Kratom (*Mitragynina speciosa* Korth) Exposure

Jamie L. Nelsen · Jeff Lapoint · Michael J. Hodgman · Kenneth M. Aldous

Published online: 22 April 2010  
© American College of Medical Toxicology 2010

**Abstract** Reports of toxicity secondary to Kratom are rare and lack of diagnostic testing in human specimens has prevented confirmatory explanation of observed clinical effects. We present a novel case of serious human toxicity following Kratom use confirmed via quantitative analysis of urine by high performance liquid chromatography coupled to electrospray tandem mass spectrometry. A 64 year-old male was witnessed to have a seizure at home following kratom consumption. Upon arrival to the emergency department (ED), the patient was unresponsive. While in the ED, the patient sustained a second seizure. He was intubated to protect

his airway. The remainder of his hospital course was uneventful. A urine specimen was collected shortly after admission and sent for analysis. The mitragynine concentration in the urine was  $167 \pm 15$  ng/ml. We report a rare case of Kratom toxicity characterized by a seizure and coma confirmed by urinary analysis of mitragynine by high performance liquid chromatography coupled to electrospray tandem mass spectrometry. The proposed mechanism for this reaction is unclear but suggested mechanisms include adenosine binding or stimulation of adrenergic and/or serotonergic receptors similar to tramadol.

**Keywords** Kratom · *Mitragynina speciosa* Korth · Seizure · Coma

This report was presented as a Platform Presentation: NACCT 2009, San Antonio, TX. AACT's SIG on Herbs and Dietary Supplements.

## Self-treatment of opioid withdrawal using kratom (*Mitragynia speciosa korth*)

Edward W. Boyer<sup>1</sup>, Kavita M. Babu<sup>1</sup>, Jessica E. Adkins<sup>2</sup>, Christopher R. McCurdy<sup>2,3</sup> & John H. Halpern<sup>1</sup>

Division of Medical Toxicology/Department of Emergency Medicine, University of Massachusetts Medical School, Worcester, MA, USA<sup>1</sup>; Departments of Medicinal Chemistry<sup>2</sup> and Pharmacology<sup>3</sup>, School of Pharmacy, University of Mississippi, Oxford, MS, USA and Biological Psychiatry Laboratory/Alcohol and Drug Abuse Research Center, McLean Hospital, Harvard Medical School, Belmont, MA, USA<sup>4</sup>

### ABSTRACT

**Background** Kratom (*Mitragynia speciosa korth*) is recognized increasingly as a remedy for opioid withdrawal by individuals who self-treat chronic pain. **Case description** A patient who had abruptly ceased injection hydromorphone abuse self-managed opioid withdrawal and chronic pain using kratom. After co-administering the herb with modafinil he experienced a tonic-clonic seizure, but he reported only modest abstinence once kratom administration stopped. We confirmed the identity of the plant matter he ingested as kratom and identified no contaminants or adulterants. We also conducted high-throughput molecular screening and the binding affinity at mu, delta and kappa receptors of mitragynine. **Conclusion** We report the self-treatment of chronic pain and opioid withdrawal with kratom. The predominant alkaloid of kratom, mitragynine, binds mu- and kappa-opioid receptors, but has additional receptor affinities that might augment its effectiveness at mitigating opioid withdrawal. The natural history of kratom use, including its clinical pharmacology and toxicology, are poorly understood.

**Keywords** Dependence, kratom, molecular screening, opioid, opioid replacement, withdrawal.

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## Short Communication

### PSYCHOACTIVE PROPERTIES OF MITRAGYNINE (KRATOM)

Karl L.R. Jansen, M.D.\*  
Colin J. Prast\*\*

Mitragynine and several related alkaloids are derived from the leaves of *Mitragyna speciosa* (kratom), a tree that is found principally in Thailand and Malaysia. Despite their intriguing, contradictory psychoactive properties, possible medical applications and widespread use in Thailand, very little new research has appeared on these substances for over a decade (Jansen & Prast 1988).

### HISTORY

In 1836, Low noted the use of kratom by Malaysians as

orthoses remained in good health despite heavy use, being mentally and physically "normal." Cling Marcan (1934, 1929), Thuan maintained that kratom did not have a bad reputation like opium, nor did it cause changes in physical condition or character. The effects were once again said to resemble those of cocaine.

In the 1960's, new analytical techniques were applied to these alkaloids (Shellard 1974). Twenty-two alkaloids were isolated from *M. speciosa*, with the alkaloid content of individual trees varying according to location and season. The molecular structures were found to be indoles and oxindoles having a closed or open E ring, with substitution occurring at the C9 position (Beckett et al. 1966). Mitragynine, found only in *M. speciosa* (Shellard 1974), is the dominant alkaloid. With the methoxyl group at position 4 of the indole (see Figure 1), mitragynine appears to be analogous to the 4-substituted indole psychedelics, such as

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DOI 10.1007/s13181-011-0155-5

#### TOXICOLOGY OBSERVATION

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# Our Experience

- Several cases
- Both stimulant and opioid properties
- Used for opioid withdrawal
- Expensive
- Altered Mental Status
- Seizures
  - *Liver dysfunction*

## Next Steps

Quantitative Analytical Testing  
Reporting of cases  
Likely to become more widespread

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## Next Steps

Quantitative Analytical Testing

Reporting of cases

Likely to become more widespread

# Final Thoughts



# Questions?

- [marraffj@upstate.edu](mailto:marraffj@upstate.edu)



# Toxicology Trends: Keeping Us On Our A-game

*Jeanna M. Marraffa, Pharm.D., DABAT, FAACT*



Case:  
- 30 year old male presents  
with syncope  
- PMH: Opioid addiction



[ ... ]