Mystery Case

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Assistant Professor (Internal Medicine /Psychiatry)

Associate Program Director (UH Addiction Medicine Fellowship)

Today…

- I have no disclosure
- I will be discussing off label treatments

It will be an interactive session, so I hope you will participate!

Please hold your questions until the end because I won’t be able to check the chat as I am presenting…!

Young male in his 20s presented to our clinic….

- CC: “I hope you guys can help me because I really need help!”
- PMH: allergy (tearing / nasal discharge), intermittent constipation, and hyperhidrosis
- Meds: Oxybutynin 5mg po qd (compliant but takes in AM, PM or night)

What is oxybutynin most likely for?

- A. Anticholinergic drug for excessive sweating
- B. Anticholinergic drug for excessive urination
- C. Anticholinergic drug for excessive tearing/ nasal discharge
- D. Cholinergic drug for constipation
- E. Cholinergic drug to washout irritant in the eyes and nose

Answer

What is oxybutynin most likely for?

- A. Anticholinergic drug for excessive sweating
- B. Anticholinergic drug for excessive urination
- C. Anticholinergic drug for excessive tearing/ nasal discharge
- D. Cholinergic drug for hard stool
- E. Cholinergic drug to washout irritant in the eyes and nose

Hyperhidrosis:

- Excessive sweating beyond the physiological needs of the patient's body → can impact quality of life.

- Campanati A, Gregoriou S, Kontochristopoulos G, Offidani A. Oxybutynin for the Treatment of Primary Hyperhidrosis: Current State of the Art. *Skin Appendage Disord*. 2015;1(1):6-13. doi:10.1159/000371581
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4857824/

Oxybutynin

- Oxybutynin is an **anticholinergic medication** able to antagonize the muscarinic acetylcholine receptor.
- It is generally used to relieve urinary and bladder difficulties

- Campanati A, Gregoriou S, Kontochristopoulos G, Offidani A. Oxybutynin for the Treatment of Primary Hyperhidrosis: Current State of the Art. *Skin Appendage Disord*. 2015;1(1):6-13. doi:10.1159/000371581

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4857824/

Oxybutynin and hyperhidrosis

- Effect of Oxybutynin was first associated with hyperhidrosis in 1988
- Many studies showed safety and efficacy
- Great alternative for those who can’t undergo i.e. sx

- Campanati A, Gregoriou S, Kontochristopoulos G, Offidani A. Oxybutynin for the Treatment of Primary Hyperhidrosis: Current State of the Art. *Skin Appendage Disord*. 2015;1(1):6-13. doi:10.1159/000371581
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4857824/

Let’s go back to the case…

Young male in his 20s….

- Meds: Oxybutynin 5mg po qd, OTC allergy medications as needed
- FH: denies psych illness in the family

Case

- SH: Quit EtOH 1-1.5 years ago → wants to be healthy and lose weight
- Vapes daily, uses nicotine 3mg/ml liquid and refills 2-3 x a day
  - Size of the chamber for nicotine liquid is unknown…
- Reports vaping q 30 minutes while at work and while driving, does not vape at home because he lives with his parents
- When he stays over at his friends' house or on the trip, he vapes whenever
- Reason for Vaping: "It energizes me…!"

SH (cont):

Drinks coffee (black) first thing in the morning with health supplement → otherwise he can't get going

https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcT6Q7o356tZCLEhZKgw3195_81aLw1_bR3P_Q&usqp=CAU

SH (cont)

- He started to use health supplement 1-2 years ago
- Recommended by a friend for back discomfort → Lot of heavy lifting at work
- Started out with 1 Tbsp → felt good all day
- He takes supplement with his coffee because it is bitter.

Case #1

- Recently, he noted insomnia and restless leg at night.
- S/S occurs whether he was at home, friends' house or Las Vegas
- Other s/s –
  - excessive sweating,
  - feels warm/cold at the same time
  - back discomfort
- He also noted worsening allergy s/s at night

Which of the following maybe causing his s/s ?

- A. Withdrawal from caffeine
- B. Withdrawal from nicotine
- C. Worsening of allergy
- D. Tolerance to Oxybutynin
- E. Withdrawal from health supplement

Answer

Which of the following maybe causing his s/s ?

- A. Withdrawal from caffeine
  - Not associated with insomnia
- B. Withdrawal from nicotine
  - Occurs whether he vapes at night (on the trip) or not (at home)
- C. Worsening of allergy
  - Occurs at night only, occurs wherever
- D. Tolerance to Oxybutynin
  - It is rare but this is a legitimate dx: Only explains excessive sweating, but not the other s/s…. Even excessive sweating, pt sometimes takes oxybutynin at night, making nightly s/s unlikely from tolerance to oxybutynin.
- E. Withdrawal from health supplement

So… what is this health supplement?

Here is another case

Case #2: Young male in his 20s….

- CC: Please help me like you helped my friend (case #1)!”
- PMH: denies
- Meds: denies
- FH: denies psych illness in the family

Case #2: Young male in his 20s….

- SH: stopped smoking 1-1.5 years ago
- Drinks 2x/ month, 12 pack at a time, denies illicit drugs

SH (cont)

- He started to use the same health supplement 10 years ago, mix in fruit juices
- Recommended by his friend for back discomfort
- Started out with taking ½ a pinky nail size scoop per day (1-2 g)
- He bought initially at the local store but he now buys it online

SH (cont)

- 1 year after using, he increased the use to 3x a day (still ½ a pinky nail size scoop) with meals to get similar effect

Case #2

- 5 years ago he stopped → had flu like s/s
  - Cold and sweaty
  - Pain all over
  - Fatigue
  - Nasal discharge
  - Insomnia
  - Anxiety
  - Decrease appetite
- NO tearing/ LBM/ Abdominal pain

Case #2: Young male in his 20s….

- Has been trying to get off the past 2 years → not successful
- If he doesn’t take this health supplement, he can’t go to work
- Now spending $100/month online to get this supplement

So what is this supplement?

Hint:

- ✓ Can be bought at the local store or online
- ✓ Causes tolerance (need increase in dose)
- ✓ Causes s/s when dose is skipped (withdrawal ?)
- ✓ Both patient started for back pain/discomfort relief

What is this supplement?

A. Ibogaine
B. Phenibut
C. Mitragyna speciosa
D. Kartoshka
E. Mạnfrạ̀ng

Answer…

What is this supplement?

A. Ibogaine
B. Phenibut
C. Mitragyna speciosa
D. Kartoshka
E. Mạnf̄rạ̀ng

What is Mitragyna speciosa?

A. Member of the Coffee Tree
B. Tree with beautiful whitish/yellowish flowers
C. Grown in Africa
D. A and B
E. A, B, and C

Answer

What is Mitragyna speciosa?

A. Member of the Coffee Tree
B. Tree with beautiful whitish/yellowish flowers
C. Grown in Africa
D. A and B
E. A, B, and C

Mitragyna Speciosa

AKA Kratom: Member of coffee family

- Native to Southeast Asia
  - Also found in Africa
- For a long time, leaves are consumed for stimulant effect:
  - Chewed / consumed as powder
  - In seamen and manual laborers.
  - Some religious practices which prohibited EtOH
- Currently, in US, people use to self medicate for various reasons including pain and opioid withdrawal

- Warner ML, Kaufman NC, Grundmann O. The pharmacology and toxicology of kratom: from traditional herb to drug of abuse. *Int J Legal Med*. 2016;130(1):127-138.
- https://www.uspharmacist.com/article/the-dea-changes-its-mind-on-kratom

Drug Enforcement Administration
Diversion Control Division
Drug & Chemical Evaluation Section

KRATOM (*Mitragyna speciosa korth*)
(Street Names: Thang, Kakuam, Thom, Ketum, Biak)

November 2019

- Effect occurs within 5-10 minutes after ingestion and lasts 2-5 hours.
- Acute side effects: Nausea, itching, sweating, dry mouth, constipation etc..
- Long term effect: addiction, anorexia, weight loss etc…
- Withdrawal: hostility/aggression/moody, wet nose, pain all over
- Psychosis and hallucination has been observed

- https://www.deadiversion.usdoj.gov/drug_chem_info/kratom.pdf

Kratom Pharmacology

- Effect is DOSE dependent:
  - Lower dose: stimulant like (1-5g of leaves)
    - Alert, euphoria, increase sexual arrousal
  - Higher dose: opioid like (5-15g)
    - Manage pain, diarrhea, opioid withdrawal s/s
  - ABOVE 15g: sedative effects, intoxication,
    - High-dose use: tachycardia, dizziness, hypotension, constipation, tremor, anorexia, seizures, and psychosis.

- https://www.uspharmacist.com/article/the-dea-changes-its-mind-on-kratom
- Corkery JM, Streete P, Claridge H, et al. Characteristics of deaths associated with kratom use. Journal of psychopharmacology (Oxford). 2019;33(9):1102-1123. doi:10.1177/0269881119862530
- https://www.uspharmacist.com/article/the-dea-changes-its-mind-on-kratom

What is one of the identified chemicals in Kratom?

A. Methadone
B. Paynantheine
C. Heroin
D. Magic Mushroom
E. Bathsalt

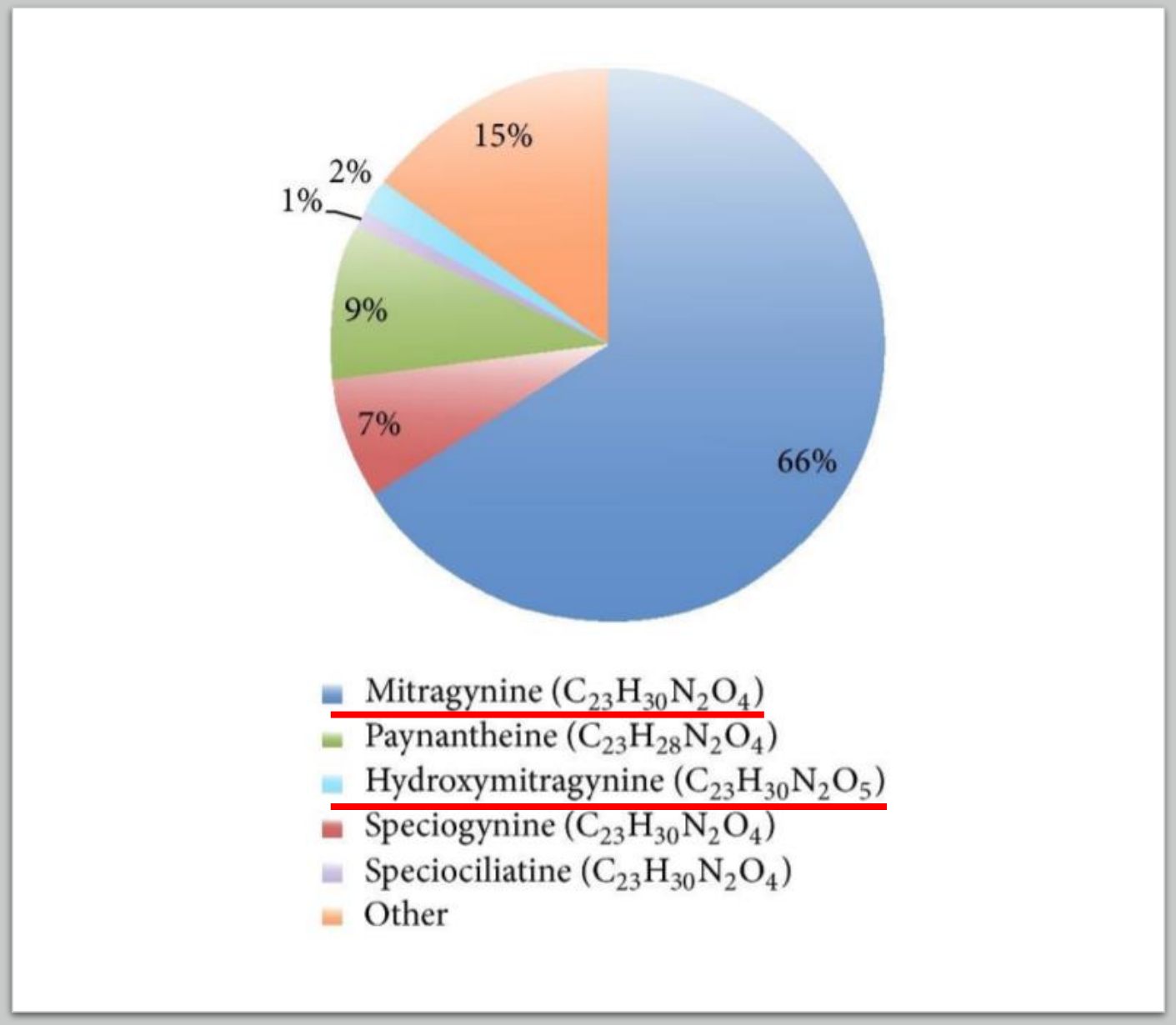
Answer…

What is one of the identified chemicals in Kratom?

A. Methadone
B. Paynantheine
C. Heroin
D. Magic Mushroom
E. Bathsalt

Cinosi E.; Martinotti; et all. Following “the Roots” of Kratom (Mitragyna speciosa): The Evolution of an Enhancer from a Traditional Use to Increase Work and Productivity in Southeast Asia to a Recreational Psychoactive Drug in Western Countries; Biomed Res Int. 2015; 2015: 968786

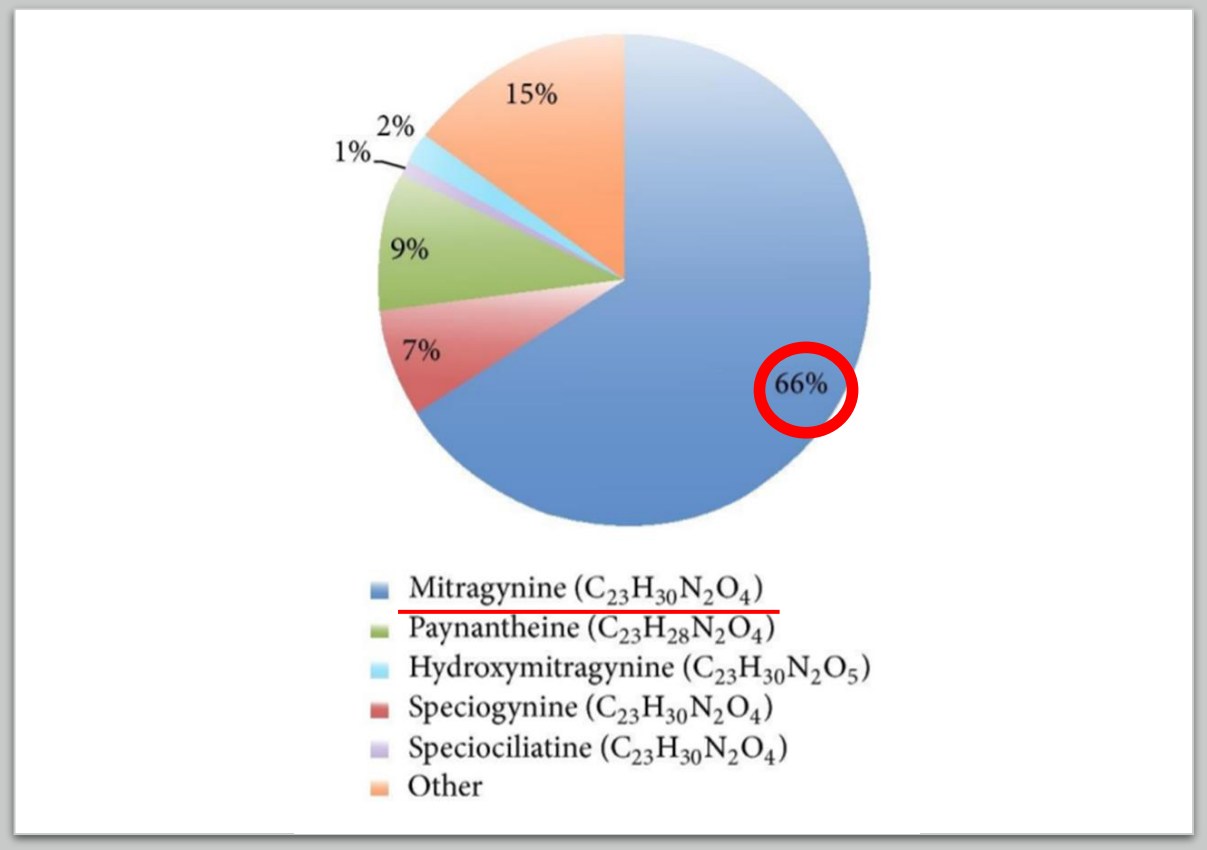
- Kratom contain varying amounts of phytochemicals → very complex
- More than 20 alkaloids in kratom have been identified in the laboratory
- Mitragynine/OH-mitragynine thought to be responsible for the opioid-like effects



https://www.samhsa.gov/sites/default/files/samhsas_15th_annual_prevention_day_afternoon_plenary_recording.pdf

Mitragynine

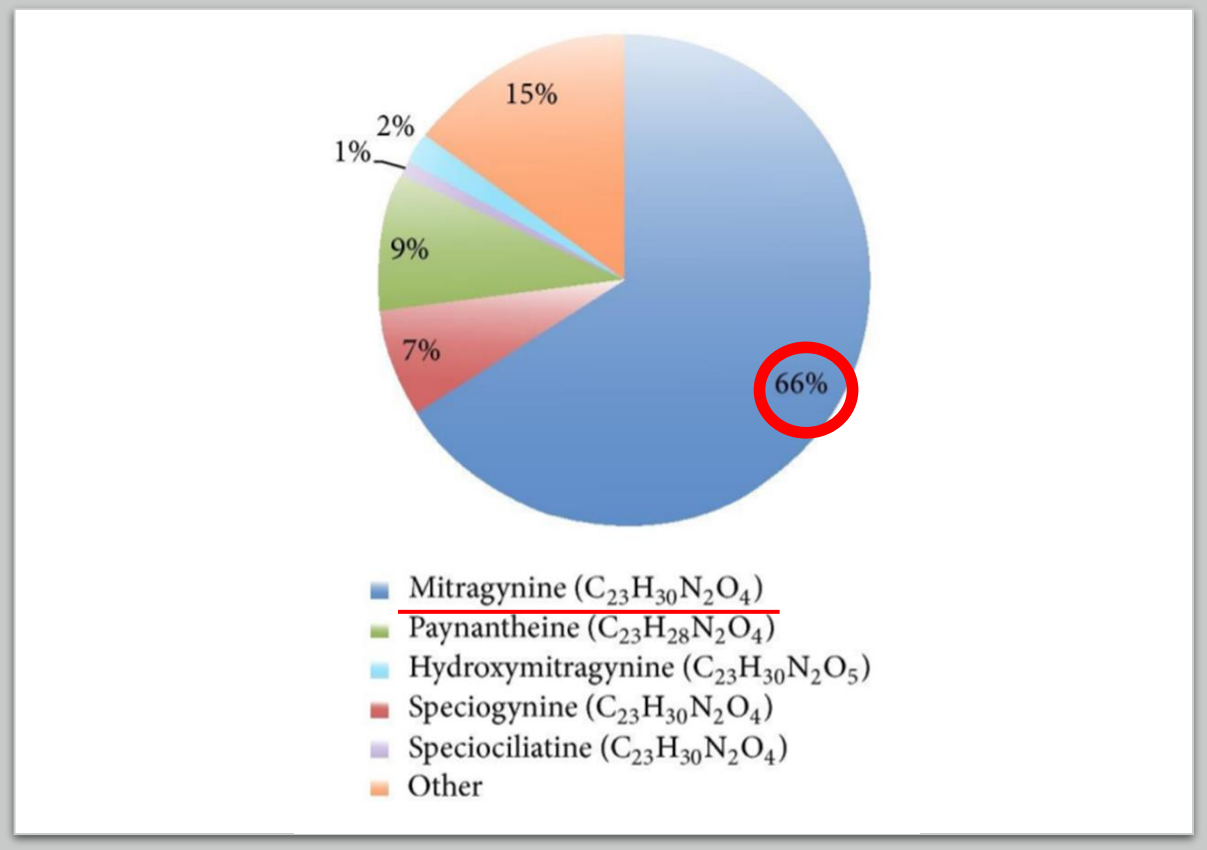
- Major alkaloid in Kratom
- It has stimulatory, and opiate-like effects (partial agonist), acting through noradrenergic (alpha 2A, 2B, 2C), serotonergic, and opioid receptors.



7-hydroxy Mitragynine

- Active metabolite of mitragynine - Oxidation of mitragynine
- 13x higher potency than morphine, 46x higher potency than mitragynine
- WEAKER affinity at adrenergic and serotonin receptors
- Structurally categorized as an opioid

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7053747/pdf/pone.0229646.pdf



ASPET | THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS

Reserch Article | Behavioral Pharmacology

Obeng S. et al., Pharmacological Comparison of Mitragynine and 7-Hydroxymitragynine: In Vitro Affinity and Efficacy for μ-Opioid Receptor and Opioid-Like Behavioral Effects in Rats. J Pharmacol Exp Ther. 2021 Mar;376(3):410-427. doi: 10.1124/jpet.120.000189. Epub 2020 Dec 31. PMID: 33384303; PMCID: PMC7923387.

Pharmacological Comparison of Mitragynine and 7-Hydroxymitragynine: In Vitro Affinity and Efficacy for μ-Opioid Receptor and Opioid-Like Behavioral Effects in Rats

Samuel Obeng, Jenny L. Wilkerson, Francisco León, Morgan E. Reeves, Luis F. Restrepo, Lea R. Gamez-Jimenez, Avi Patel, Anna E. Pennington, Victoria A. Taylor, Nicholas P. Ho, Tobias Braun, John D. Fortner, Morgan L. Crowley, Morgan R. Williamson, Victoria L.C. Pallares, Marco Mottinelli, Carolina Lopera-Londoño, Christopher R. McCurdy, Lance R. McMahon, and Takato Hiranita

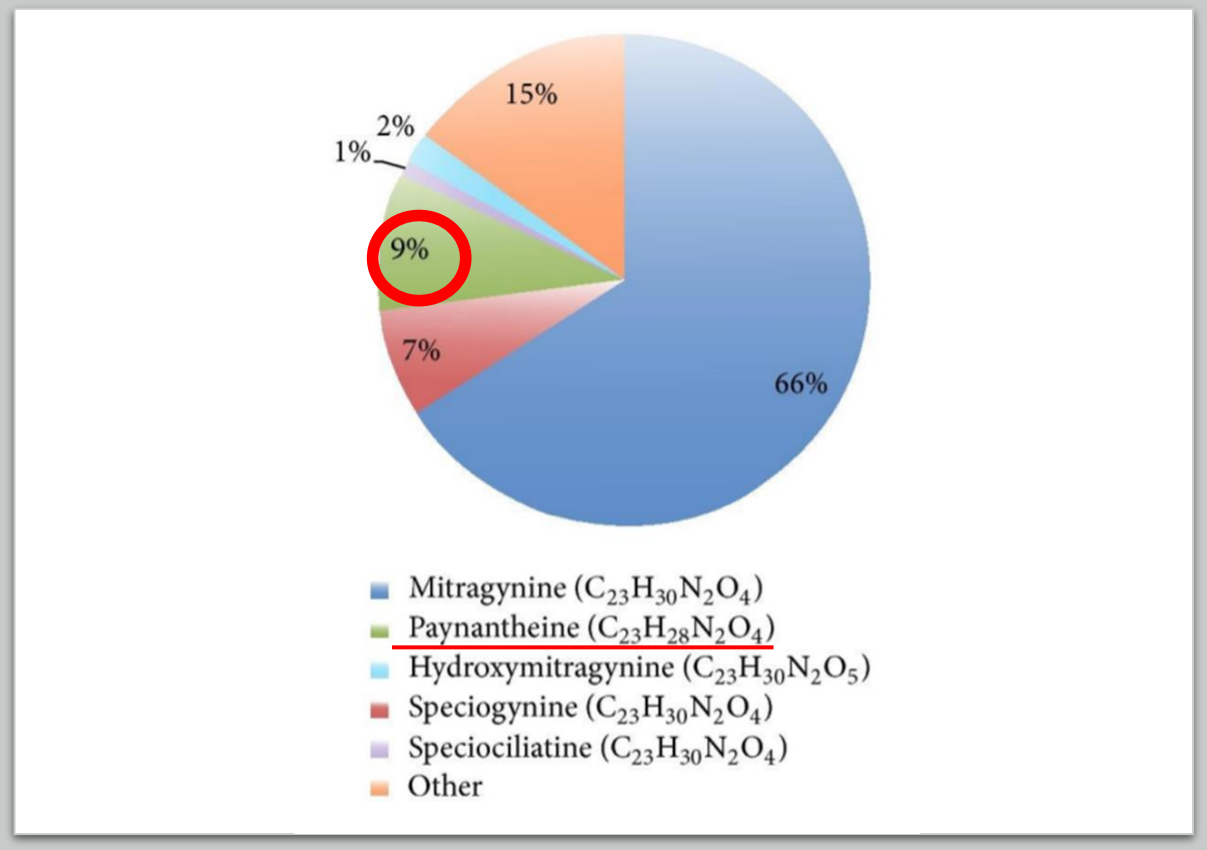
Journal of Pharmacology and Experimental Therapeutics March 2021, 376 (3) 410-427; DOI: https://doi.org/10.1124/jpet.120.000189

- Published in 2021:
- 7-hydroxymitragynine has antinociception effect, mitragynine does not
- Naltrexone antagonized all effect

Paynantheine

- Not well defined in terms of affinity and target receptors (binds to mu – this is known!)
- Paynantheine may have **cardiotoxic** effects
- Paynantheine can be detected in urine after kratom ingestion. Standard UDS does NOT screen for Kratom

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7053747/pdf/pone.0229646.pdf



Introducing The Kratom Single-Dip

Volume 154, Issue Supplement_1
October 2020

Article Contents

< Previous Next >

A Kratom Metabolite Causes False Positive Urine Drug Screening Results for Methadone FREE

Christina Pierre, Catherine Gineste, Lindsay Bazydlo

American Journal of Clinical Pathology, Volume 154, Issue Supplement_1, October 2020, Pages S19–S20, https://doi.org/10.1093/ajcp/aqaa137.035
Published: 28 October 2020

Abstract

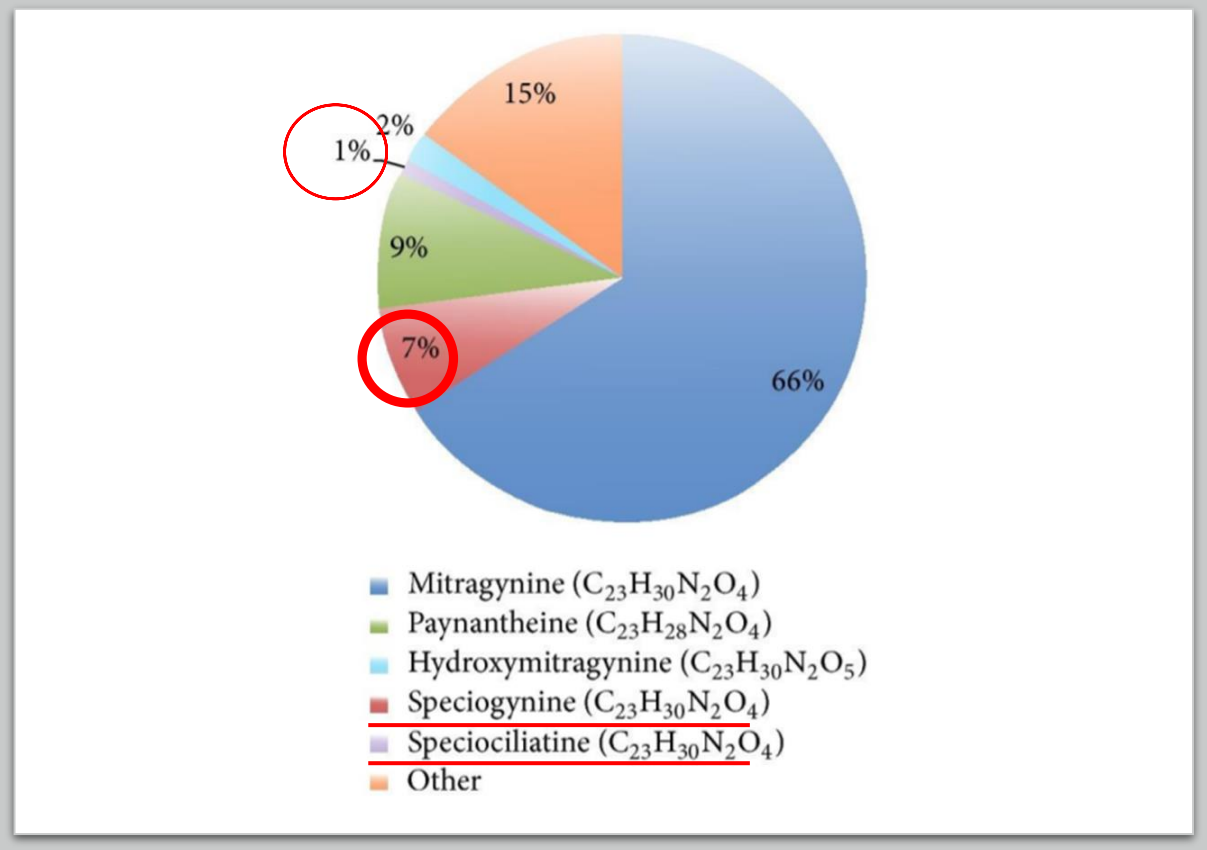
Background

The synthetic opioid methadone is utilized in pain management and opioid addiction therapy. Patients with methadone prescriptions are monitored for compliance using immunoassay-based urine drug screens (UDS) for methadone and its primary metabolite, 2-ethylidene-1,5-dimethyl-3,3-

Speciogynine
Speciociliatine

- Structurally similar to opioids.
- Stereoisomers of Mitragynine
- Like Mitragynine, binds to adrenergic and serotonin receptors

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7053747/pdf/pone.0229646.pdf



Is Kratom Legal?

https://besthotelshome.com/map-of-hawaii-and-flag/

Is Kratom legal?

A. It is legal in US but illegal in Hawaii
B. It is illegal in US but legal in Hawaii
C. It is legal in US and legal in Hawaii
D. It is illegal in US and illegal in Hawaii
E. Don’t answer this…

Answer

https://besthotelshome.com/map-of-hawaii-and-flag/

Is Kratom legal?

A. It is legal in US but illegal in Hawaii
B. It is illegal in US but legal in Hawaii
C. It is legal in US and legal in Hawaii
D. It is illegal in US and illegal in Hawaii
E. Don’t answer this…

https://www.wired.com/story/release-the-kratom-inside-drug-culture/

Available Kratom Products

Kratom products in US…

A. Are sold as gum, like nicotine gum
B. Have different potency and strength
C. Have Red, White, and Blue Kratom
D. A and B
E. B and C

Answer

Kratom products in US…

A. Are sold as gum, like nicotine gum
B. Have different potency and strength
C. Have Red, White, and Blue Kratom (red, white, GREEN and YELLOW)
D. A and B
E. B and C

- Kratom extracts available in the US are mostly powders that can be dissolved in fluid or consumed with food.
- Potency of Kratom is distinguished by strain, time of harvest, and how it was processed

https://i1.wp.com/www.mountkratom.com/wp-content/uploads/2020/08/kratom-colors-1.jpg?w=810&ssl=1

White Vein Kratom

- Harvested at earliest stage of the Kratom trees,
- Dried indoors (no light on them)
- highest mitragynine → increased energy and alertness (mild stimulant effect)
- https://kratomspot.com/kratom-strains/

Red Vein Kratom

Corkery JM, Streete P, Claridge H, et al. Characteristics of deaths associated with kratom use. Journal of psychopharmacology (Oxford). 2019;33(9):1102-1123. doi:10.1177/0269881119862530

- Harvested from mature kratom trees
- Dried using sunlight / UV lamp. Some are fermented
- High 7-hydroxymitragynine content
- Most mellow, classified as mild sedatives → help users to remain calm, pain relief
- https://kratomspot.com/kratom-strains/

https://i0.wp.com/kingdomkratom.com/wp-content/uploads/2019/08/products-Super_Red-100-scaled.jpg?fit=1020%2C680&ssl=1

Green Vein Kratom

- Middle road of white and red
- Harvested in the middle stage of Kratom tree's life cycle
- Dried indoor first in airconditioned room → then moved to outside
- Subtle stimulant effect → for mental clarity and focus task
- https://kratomspot.com/kratom-strains/

Yellow vein Kratom

- White and green or green and red are mixed together
- Basically means blends of other colored strains kratom

- https://kratomspot.com/kratom-strains/

https://www.google.com/url?sa=i&url=https%3A%2F%2Ftheislandnow.com%2Fblog-112%2Ftypes-of-kratom-strains%2F&psig=AOvVaw13eeKrznRR03Ag_kiBoG4w&ust=1631091347216000&source=images&cd=vfe&ved=0CAgQjRxqFwoTCKiJ7YC_7PICFQAAAAAdAAAAABAD

Who uses Kratom?

ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

SHORT REPORT

doi:10.1111/add.15082

Prevalence and description of kratom (*Mitragyna speciosa*) use in the United States: a cross-sectional study

Jonathan Schimmel[1,2], Elise Amioka[1], Karilynn Rockhill[1], Colleen M. Haynes[1], Joshua C. Black[1], Richard C. Dart[1] & Janetta L. Iwanicki[1]

Rocky Mountain Poison and Drug Safety, Denver Health and Hospital Authority, Denver, CO, USA[1] and Department of Emergency Medicine, Division of Medical Toxicology, Mount Sinai Hospital Icahn School of Medicine, New York, NY, USA[2]

- Cross-sectional survey, conducted on line in US, 2020
- 59714 respondents aged 18 yrs or older, weighted to represent the adult US populations. Included DAST 10 (The Drug Abuse Screening Test)

Schimmel J, Amioka E, Rockhill K, Haynes CM, Black JC, Dart RC, Iwanicki JL. Prevalence and description of kratom (Mitragyna speciosa) use in the United States: a cross-sectional study. Addiction. 2021 Jan;116(1):176-181. doi: 10.1111/add.15082. Epub 2020 Apr 28. PMID: 32285981.

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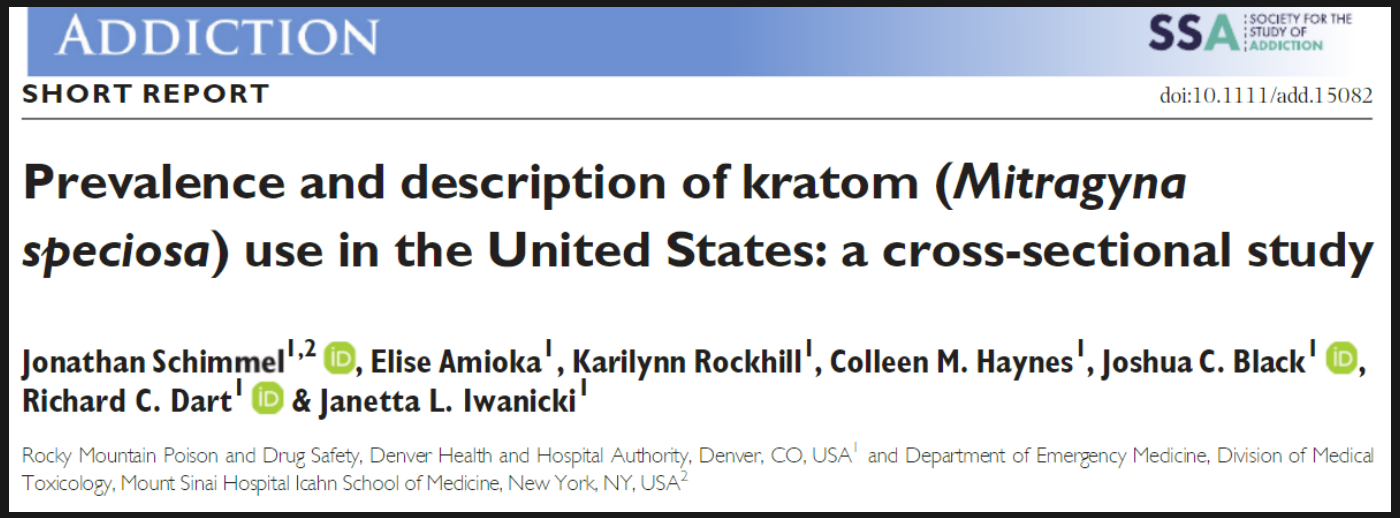

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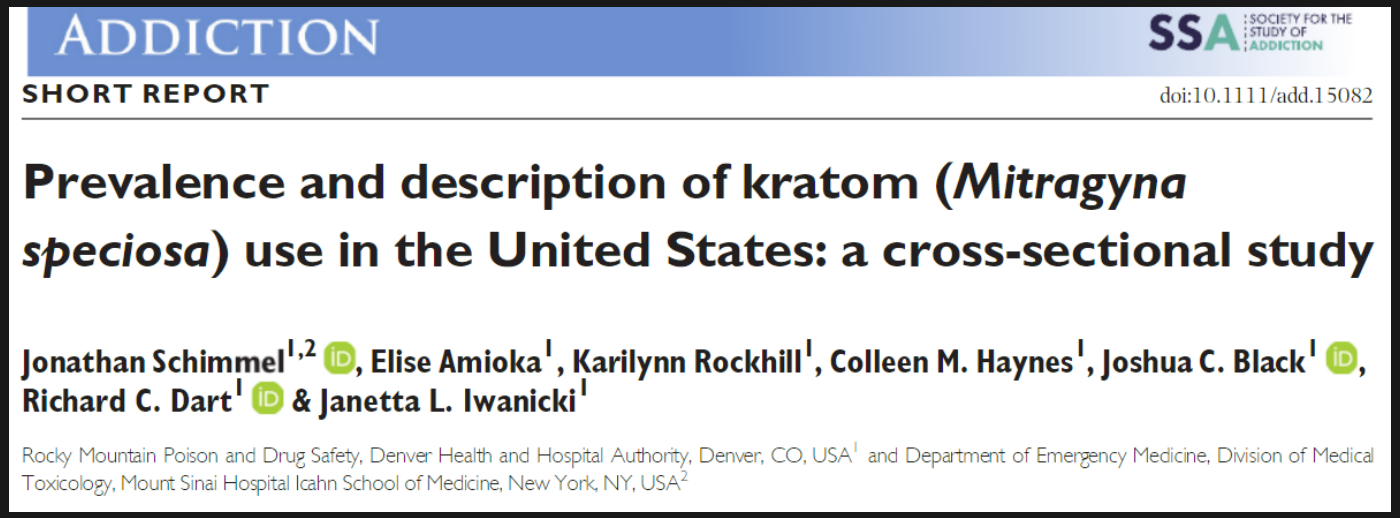
Rocky Mountain Poison and Drug Safety, Denver Health and Hospital Authority, Denver, CO, USA[1] and Department of Emergency Medicine, Division of Medical Toxicology, Mount Sinai Hospital Icahn School of Medicine, New York, NY, USA[2]

Epidemiology:

- Kratom use in US adults was 0.8%
- Life-time prevalence was 1.3%

Schimmel J, Amioka E, Rockhill K, Haynes CM, Black JC, Dart RC, Iwanicki JL. Prevalence and description of kratom (Mitragyna speciosa) use in the United States: a cross-sectional study. Addiction. 2021 Jan;116(1):176-181. doi: 10.1111/add.15082. Epub 2020 Apr 28. PMID: 32285981.



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Rocky Mountain Poison and Drug Safety, Denver Health and Hospital Authority, Denver, CO, USA[1] and Department of Emergency Medicine, Division of Medical Toxicology, Mount Sinai Hospital Icahn School of Medicine, New York, NY, USA[2]

Demographics:

- Kratom users were younger (mean 35y/o)
- Mostly males
- Fewer BS/advanced degree graduates compared to non-users
- Inconclusive: race, income, employment status

Schimmel J, Amioka E, Rockhill K, Haynes CM, Black JC, Dart RC, Iwanicki JL. Prevalence and description of kratom (Mitragyna speciosa) use in the United States: a cross-sectional study. Addiction. 2021 Jan;116(1):176-181. doi: 10.1111/add.15082. Epub 2020 Apr 28. PMID: 32285981.

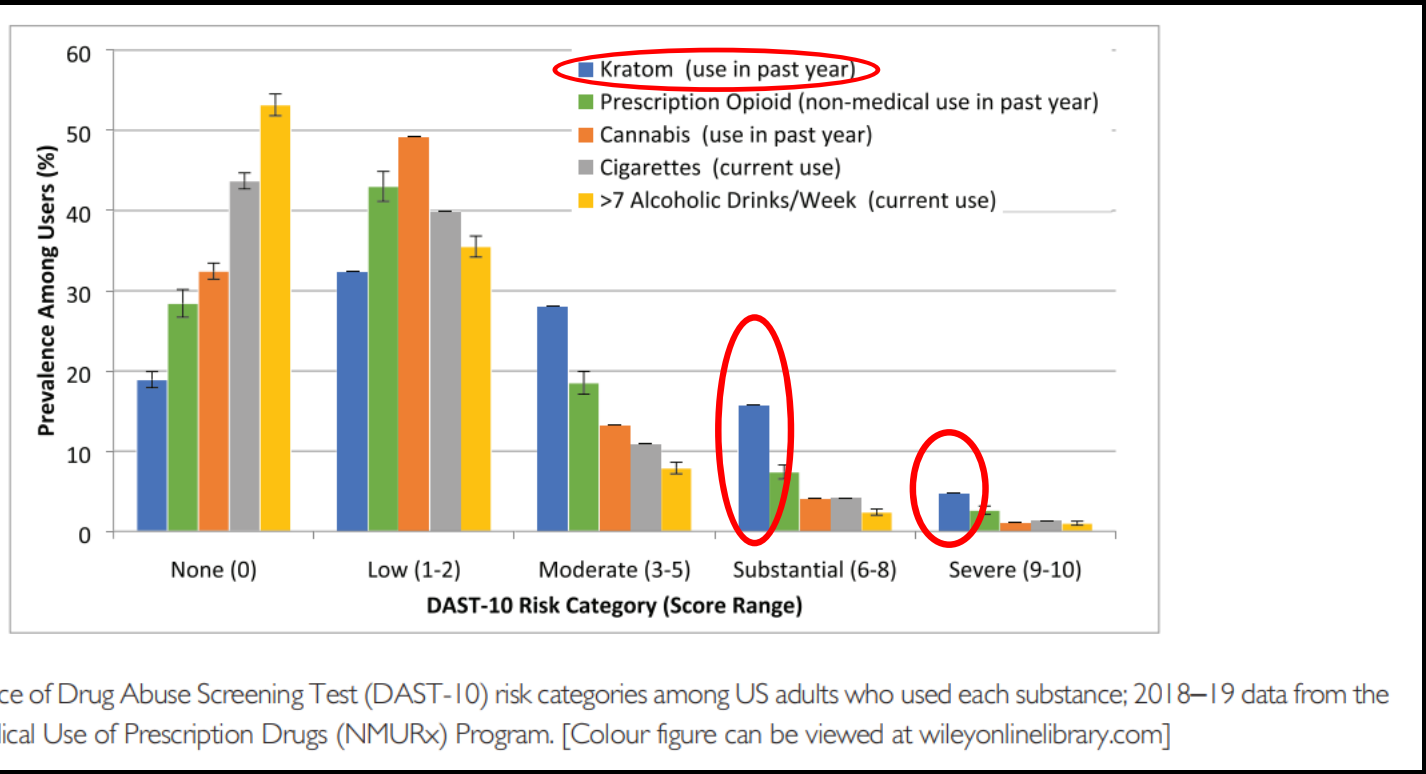
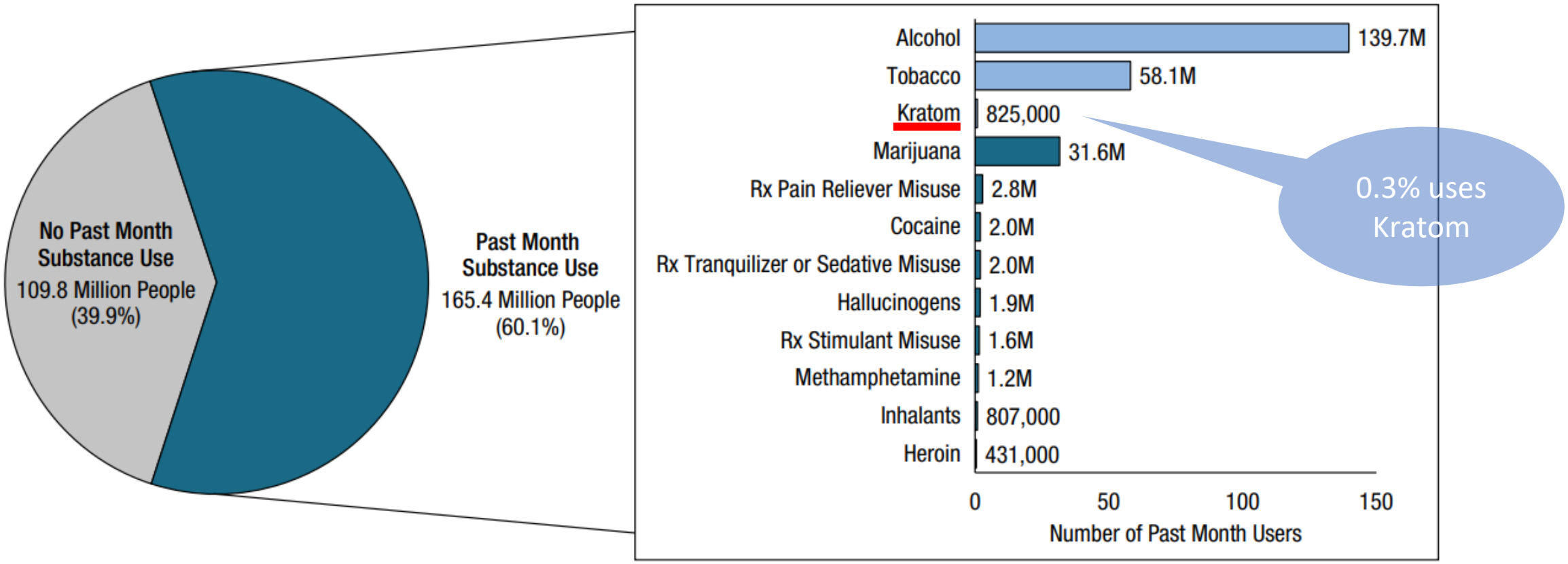


Figure 1 Prevalence of Drug Abuse Screening Test (DAST-10) risk categories among US adults who used each substance; 2018–19 data from the Survey of Non-Medical Use of Prescription Drugs (NMURx) Program. [Colour figure can be viewed at wileyonlinelibrary.com]

- Kratom users tend to have **more serious** substance abuse profiles than non- users or users of cannabis, alcohol or cigarettes
  - Compared with non-kratom users; 21% of kratom users had a DAST-10 of substantial or severe ($P < 0.001$)
  - The DAST-10 examines general features of drug abuse behaviors that are not specific to a single drug, and is therefore interpreted in the context of which drugs a person reports using.

Figure 1. Past Month Substance Use among People Aged 12 or Older: 2019



Rx = prescription.

Note: Substance Use includes any illicit drug, kratom, alcohol, and tobacco use.

Note: The estimated numbers of current users of different substances are not mutually exclusive because people could have used more than one type of substance in the past month.

Kratom History in USA

Kratom History - US

- Kratom was first documented in science journal in 1836. Described how kratom leaves were used as substitute for opium by Malays
- Kratom was introduced in US in late 1990s
- Kratom was regulated as “herbal product” under FDA (until 8/2016)
  - 2011: poison Control Centers received 13 calls about Kratom
  - 2011-2017: Total of 1807 Kratom calls, 2/3 occurred 2016-2017

- https://www.uspharmacist.com/article/the-dea-changes-its-mind-on-kratom
- Todd, D.A., Kellogg, J.J., Wallace, E.D. *et al.* Chemical composition and biological effects of kratom (*Mitragyna speciosa*): In vitro studies with implications for efficacy and drug interactions. *Sci Rep* **10,** 19158 (2020). https://doi.org/10.1038/s41598-020-76119-w
- https://www.vdh.virginia.gov/environmental-epidemiology/2019/02/26/kratom/
- https://www.federalregister.gov/documents/2016/08/31/2016-20803/schedules-of-controlled-substances-temporary-placement-of-mitragynine-and-7-hydroxymitragynine-into

FEDERAL REGISTER

The Daily Journal of the United States Government

PR Proposed Rule

Schedules of Controlled Substances: Temporary Placement of Mitragynine and 7-Hydroxymitragynine Into Schedule I

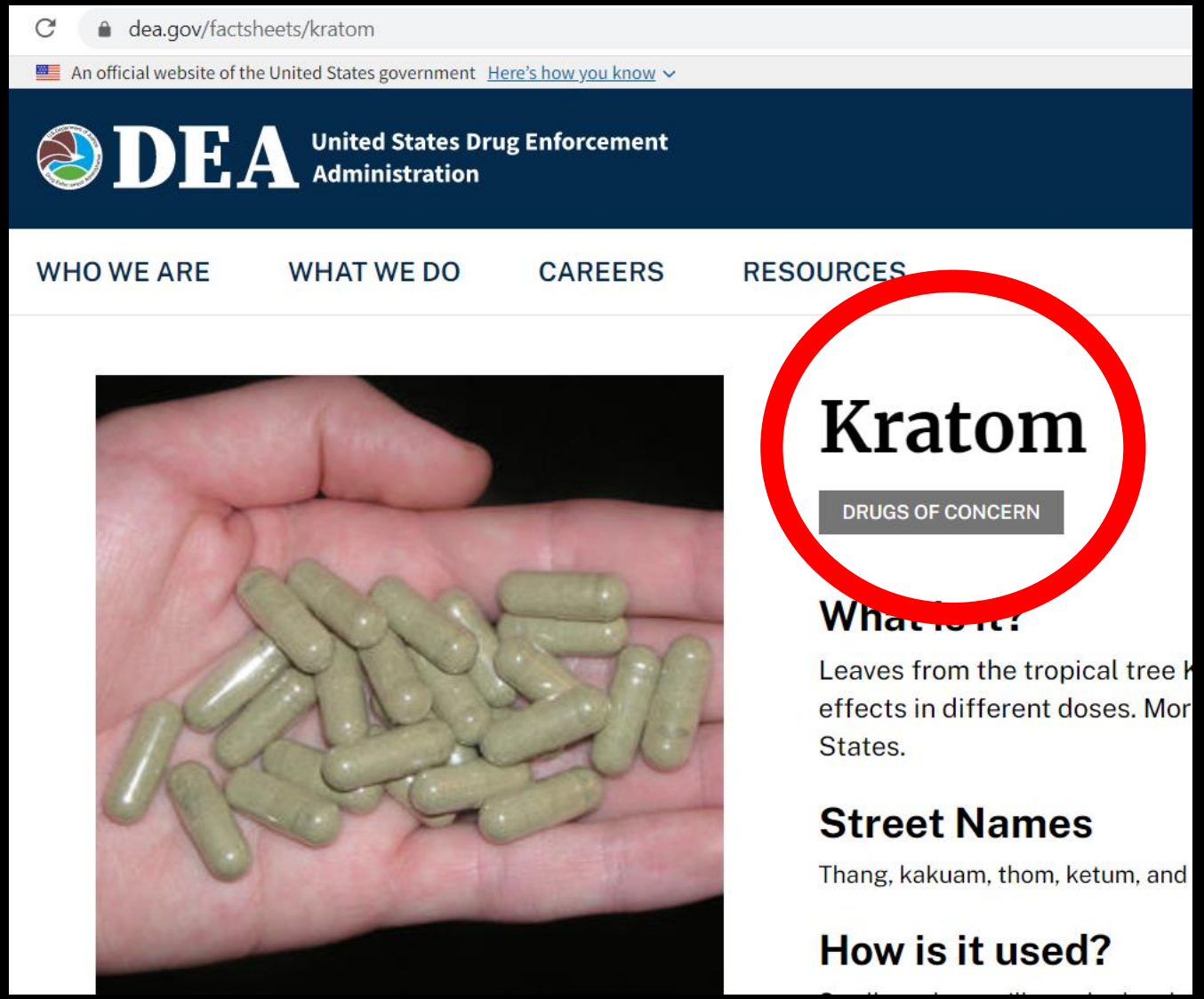
A Proposed Rule by the Drug Enforcement Administration on 08/31/2016

- 8/2016, DEA placed Kratom in schedule I TEMPORARILY
- Schedule I: High potential for abuse, **no currently accepted medical use** in treatment in the United States, and a **lack of accepted safety** for use

https://www.federalregister.gov/documents/2016/08/31/2016-20803/schedules-of-controlled-substances-temporary-placement-of-mitragynine-and-7-hydroxymitragynine-into

2 months later… 10/13/2016

- DEA announced to **withdrawal its intent** to temporarily schedule Kratom
- Now listed as “drugs of Concern”



- https://www.uspharmacist.com/article/the-dea-changes-its-mind-on-kratom

Is Kratom Safe?

- “Kratom is a difficult toxin to manage for several reasons….the **doses are not well defined** because it is a plant product. There are a lot of variables,”

Dr. Rais Vohra

The medical director,

Fresno/Madera Division of the CA Poison Control System.

Kratom Overdosehttps://www.healthline.com/health-news/how-to-spot-a-kratom-overdose#What-is-kratom?-

- “We clearly saw respiratory depression. We saw coma…but…[we saw] things like **seizure, agitation, tachycardia, hypertension**…the person is seizing in front of you, and everybody who knows anything about opiates knows that they don’t seize.”

Rick Spiller

Director, Central OH Poison Center

JOURNAL OF FORENSIC SCIENCES

J Forensic Sci, January 2013, Vol. 58, No. S1
doi: 10.1111/1556-4029.12009
Available online at: onlinelibrary.wiley.com

CASE REPORT

TOXICOLOGY

Michael F. Neerman,[1] Ph.D.; Randall E. Frost,[1] M.D.; and Janine Deking,[1] B.S.

A Drug Fatality Involving Kratom

- First (?) case report, 2013
- A 17-year-old white man who showed no obvious signs of trauma was found unresponsive in bed and was pronounced dead at the scene.
- (+) h/o heroin use with chronic back pain
- Self medicated with Kratom (mitragynine).

Neerman MF, Frost RE, Deking J. A Drug Fatality Involving Kratom. Journal of forensic sciences. 2013;58:S278-S279. doi:10.1111/1556-4029.12009

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CASE REPORT

TOXICOLOGY

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A Drug Fatality Involving Kratom

- A laboratory work-up revealed therapeutic levels of over-the-counter cold medications and benzodiazepines and Kratom (0.6mg/L).
- The Medical Examiner certified the cause of death as “possible Kratom toxicity” and the manner of death was classified as “accident”

FIG. 1—*The bag of Kratom and bottle of liquid Kratom found at the scene.*

Neerman MF, Frost RE, Deking J. A Drug Fatality Involving Kratom. Journal of forensic sciences. 2013;58:S278-S279. doi:10.1111/1556-4029.12009

11alive.com/article/news/health/my-son-is-proof-it-kills-dads-message-after-son-dies-on-kratom/85-492057651

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ttps://www.11alive.com/article/news/health/my-son-is-proof-it-kills-dads-message-after-son-dies-on-kratom/85-492057651

HEALTH

'My son is proof it kills' | Dad's message after son dies on Kratom

"Hopefully with this news being spread around it will be able to save some lives down the road."

- 2016
- OD of Kratom causing **heart attack**.
- Off opioids for 2 years before death but was consuming Kratom to stay under the radar of his probation officer

NEWS > NATIONAL

Herbal supplement Kratom linked to death in Florida

- 7/7, 2017 first ever confirmed death from using Kratom
- County Medical Examiner's autopsy report said "Intoxication by Mitragynine (Kratom)"
- The victim struggled with an addiction to prescription painkillers for more than a decade.
- The victim was found with two empty packets of Kratom.

https://www.wptv.com/news/national/exclusive-hillsborough-confirms-first-ever-death-by-herbal-supplement-kratom-in-the-county

NEWS > NATIONAL

Herbal supplement Kratom linked to death in Florida

- Victim was using Kratom to self treat his OUD
- **1.8mg/L** of Mitragynine was found
- There was NO narcotics found in the victim's system

https://www.wptv.com/news/national/exclusive-hillsborough-confirms-first-ever-death-by-herbal-supplement-kratom-in-the-county

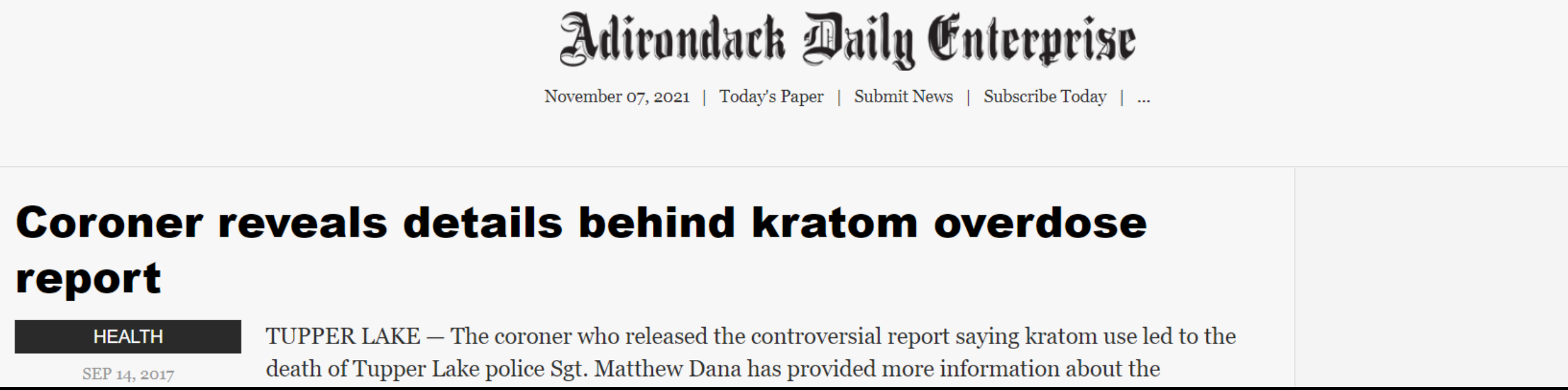
NEWS > NATIONAL

Herbal supplement Kratom linked to death in Florida

- “I don't know how much he took, but it was enough to kill him.”

Mother of the victim

https://www.wptv.com/news/national/exclusive-hillsborough-confirms-first-ever-death-by-herbal-supplement-kratom-in-the-county



A month later…

- Second case, NY
- 3.5mg/L in the system double of FL case

https://www.adirondackdailyenterprise.com/news/local-news/2017/09/coroner-reveals-details-behind-kratom-overdose-report/

Neerman MF, Frost RE, Deking J. A Drug Fatality Involving Kratom. Journal of forensic sciences. 2013;58:S278-S279. doi:10.1111/1556-4029.12009

- No definitive data re: how much mitragynine is lethal
  - Scarcity of published case reports giving blood drug concentrations in Kratom/mitragynine fatalities.

How many deaths from Kratom?

Morbidity and Mortality Weekly Report (*MMWR*)

Notes from the Field: Unintentional Drug Overdose Deaths with Kratom Detected — 27 States, July 2016–December 2017

Weekly / April 12, 2019 / 68(14);326–327

Emily O'Malley Olsen, PhD[1]; Julie O'Donnell, PhD[1]; Christine L. Mattson, PhD[1]; Joshua G. Schier, MD[1]; Nana Wilson, PhD[1] (View author affiliations)

Kratom (*Mitragyna speciosa*), a plant native to Southeast Asia, contains the alkaloid mitragynine, which can produce stimulant effects in low doses and some opioid-like effects at higher doses when consumed (*1*). Use of kratom has recently increased in popularity in the United States, where it is usually marketed as a dietary or herbal supplement (*1*). Some studies suggest kratom has potential for dependence and abuse (*1*,*2*). As of April 2019, kratom was not scheduled as a controlled substance. However, since 2012, the Food and Drug Administration has taken a number of actions related to kratom, and in November 2017 issued a public health advisory*; in addition, the Drug Enforcement Administration has identified kratom as a drug of concern. During 2011–2017, the national poison center reporting database documented 1,807 calls concerning reported exposure to kratom (*3*). To assess the impact of kratom, CDC analyzed data from the State Unintentional Drug Overdose Reporting System (SUDORS).

Kratom detected on postmortem toxicology among OD decedents – based on State unintentional drug overdose reporting system (27 states, 7/2016-12/2017) – Data on 27,338 OD deaths

	(+) Kratom, toxicology, N=152 (%)	Kratom as cause of death, N=91 (%)
Male	116 (76%)	69 (76%)
Female	36 (24%)	22 (24%)
White	119 (92%)	81 (93%)
Non-White	11 (8%)	--
In pain treatment	14 (9%)	11 (12%)
No pain treatment	138 (91%)	80 (88%)
Hx of use (opioid / non-opioid)	123 (81%)	71 (78%)
No Hx of other substance use	29 (19%)	20 (22%)
Data on 27,338 overdose deaths that occurred during July 2016–December 2017 in 27 states, and 152 (0.56%) of these decedents tested positive for kratom on postmortem toxicology (kratom-positive). Probably under-estimated		Co-occurring substances listed as a cause of death: • Opioids (fentanyl/heroin/Rx) • Benzo • Cocaine • Alcohol

Olsen EO, O'Donnell J, Mattson CL, Schier JG, Wilson N. *Notes from the Field:* Unintentional Drug Overdose Deaths with Kratom Detected — 27 States, July 2016–December 2017. MMWR Morb Mortal Wkly Rep 2019;68:326–327. DOI: http://dx.doi.org/10.15585/mmwr.mm6814a2external icon

Original Paper

Characteristics of deaths associated with kratom use

https://www.landlordnews.co.uk/big-ben-and-union-jack-flag-in-england-2/

Journal of Psychopharmacology
2019, Vol. 33(9) 1102–1123

DOI: 10.1177/0269881119862530
journals.sagepub.com/home/jop
SAGE

John M Corkery[1], Peter Streete[2], Hugh Claridge[3], Christine Goodair[3], Duccio Papanti[1], Laura Orsolini[1], Fabrizio Schifano[1], Kanav Sikka[1], Sophie Körber[4] and Amy Hendricks[5]

Corkery JM, Streete P, Claridge H, et al. Characteristics of deaths associated with kratom use. Journal of psychopharmacology (Oxford). 2019;33(9):1102-1123. doi:10.1177/0269881119862530

Abstract

Background: Kratom (*Mitragyna speciosa* Korth) use has increased in Western countries, with a rising number of associated deaths. There is growing debate about the involvement of kratom in these events.

Aims: This study details the characteristics of such fatalities and provides a 'state-of-the-art' review.

Methods: UK cases were identified from mortality registers by searching with the terms 'kratom', 'mitragynine', etc. Databases and online media were searched using these terms and 'death', 'fatal*', 'overdose', 'poisoning', etc. to identify additional cases; details were obtained from relevant officials. Case characteristics were extracted into an Excel spreadsheet, and analysed employing descriptive statistics and thematic analysis.

Results: Typical case characteristics ($n=156$): male (80%), mean age 32.3 years, White (100%), drug abuse history (95%); reasons for use included self-medication, recreation, relaxation, bodybuilding, and avoiding positive drug tests. Mitragynine alone was identified/implicated in 23% of cases. Poly substance use was common (87%), typically controlled/recreational drugs, therapeutic drugs, and alcohol. Death cause(s) included toxic effects of kratom ± other substances; underlying health issues.

Conclusions: These findings add substantially to the knowledge base on kratom-associated deaths; these need systematic, accurate recording. Kratom's safety profile remains only partially understood; toxic and fatal levels require quantification.


1


2


3

Journal of Neonatal-Perinatal Medicine 12 (2019) 109–112
DOI:10.3233/NPM-1863
IOS Press

Case Report

Natural drugs, not so natural effects: Neonatal abstinence syndrome secondary to 'kratom'

L. Davidson[a], M. Rawat[a], S. Stojanovski[b] and P. Chandrasekharan[a,*]
[a]*Division of Neonatology, Department of Pediatrics, University at Buffalo, Oishei Children's Hospital, Buffalo, NY, USA*
[b]*Department of Pharmacy, Oishei Children's Hospital, Buffalo, NY, USA*

Received 24 May 2018
Revised 27 June 2018

Davidson L, Rawat M, Stojanovski S, Chandrasekharan P. Natural drugs, not so natural effects: Neonatal abstinence syndrome secondary to 'kratom'. *J Neonatal Perinatal Med*. 2019;12(1):109-112. doi:10.3233/NPM-1863

- Baby Girl by 29y/o single mother, smoker, second pregnancy, suffering from chronic low back pain, fibromyalgia, anxiety
- Using Kratom 5g-15g/day, UDS was negative
- Finnergan scores on admission was consistently > 10 → warranted pharmacotherapy, s/s consistent with opioid withdrawal
  - Treated with PO morphine 0.1mg/kg/day q4 hours

fda.gov/news-events/public-health-focus/fda-and-kratom

An official website of the United States government Here's how you know

U.S. FOOD & DRUG ADMINISTRATION

Search Menu

Home / News & Events / Public Health Focus / FDA and Kratom

FDA and Kratom

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Public Health Focus

Expanded Access

The U.S. Food and Drug Administration is warning consumers not to use *Mitragyna speciosa*, commonly known as kratom, a plant which grows naturally in Thailand, Malaysia, Indonesia, and Papua New Guinea. FDA is concerned that kratom, which affects the same opioid brain receptors as morphine, appears to have properties that expose users to the risks of addiction, abuse, and dependence.

There are no FDA-approved uses for kratom, and the agency has received concerning reports about the safety of kratom. FDA is actively evaluating all available scientific information on this issue and continues to warn consumers not to use any products labeled as containing the botanical substance kratom or its psychoactive compounds, mitragynine and 7-hydroxymitragynine. FDA encourages more research to better understand kratom's safety profile, including the use of kratom combined with other drugs.

Content current as of:
09/11/2019

- Although it is legal, FDA continues to warn the consumers about using Kratom

Any potential use of Kratom?

YALE JOURNAL OF BIOLOGY AND MEDICINE 93 (2020), pp.283-289.

REVIEW

YALE JOURNAL OF BIOLOGY AND MEDICINE
YJBM
CELEBRATING 90 YEARS 1928–2018

The Potential for Kratom as an Antidepressant and Antipsychotic

Lindsay E. Johnson[a], Lilian Balyan[b], Amy Magdalany[b], Fizza Saeed[b], Robert Salinas[b], Starla Wallace[b], Charles A. Veltri[b], Marc T. Swogger[c], Zach Walsh[d], and Oliver Grundmann[a,b,*]

[a]College of Pharmacy, Department of Medicinal Chemistry, University of Florida, Gainesville, FL; [b]Midwestern University, College of Pharmacy, Department of Pharmaceutical Sciences, Glendale, AZ; [c]Department of Psychiatry, University of Rochester Medical Center, Rochester, NY; [d]Department of Psychology, University of British Columbia, Kelowna, BC, Canada

- Mitragynine has effects on the same receptors as which some antipsychotics bind, such as D2 DA, 5HT and alpha 2 adrenergic receptors – possible indications of kratom to be used as both antipsychotics and antidepressants.

Treatment for Kratom

No standard treatment at this time…

Treatment of Kratom Withdrawal and Dependence With Buprenorphine/Naloxone: A Case Series and Systematic Literature Review

Stephanie T. Weiss, MD, PhD and Heather E. Douglas, MD

- Published in Journal of Addiction Medicine in 2021
- Case series, up to 2020
- Total of 8 patient cases were analyzed
- Recommendation:
- <20g of Kratom/d: initiate therapy 4-8mg
- >40g of Kratom / day: 12-16mg

Weiss, S. T. & Douglas, H. E. (2021). Treatment of Kratom Withdrawal and Dependence With Buprenorphine/Naloxone: A Case Series and Systematic Literature Review. Journal of Addiction Medicine, 15 (2), 167-172. doi: 10.1097/ADM.0000000000000721

How much were our patients taking?

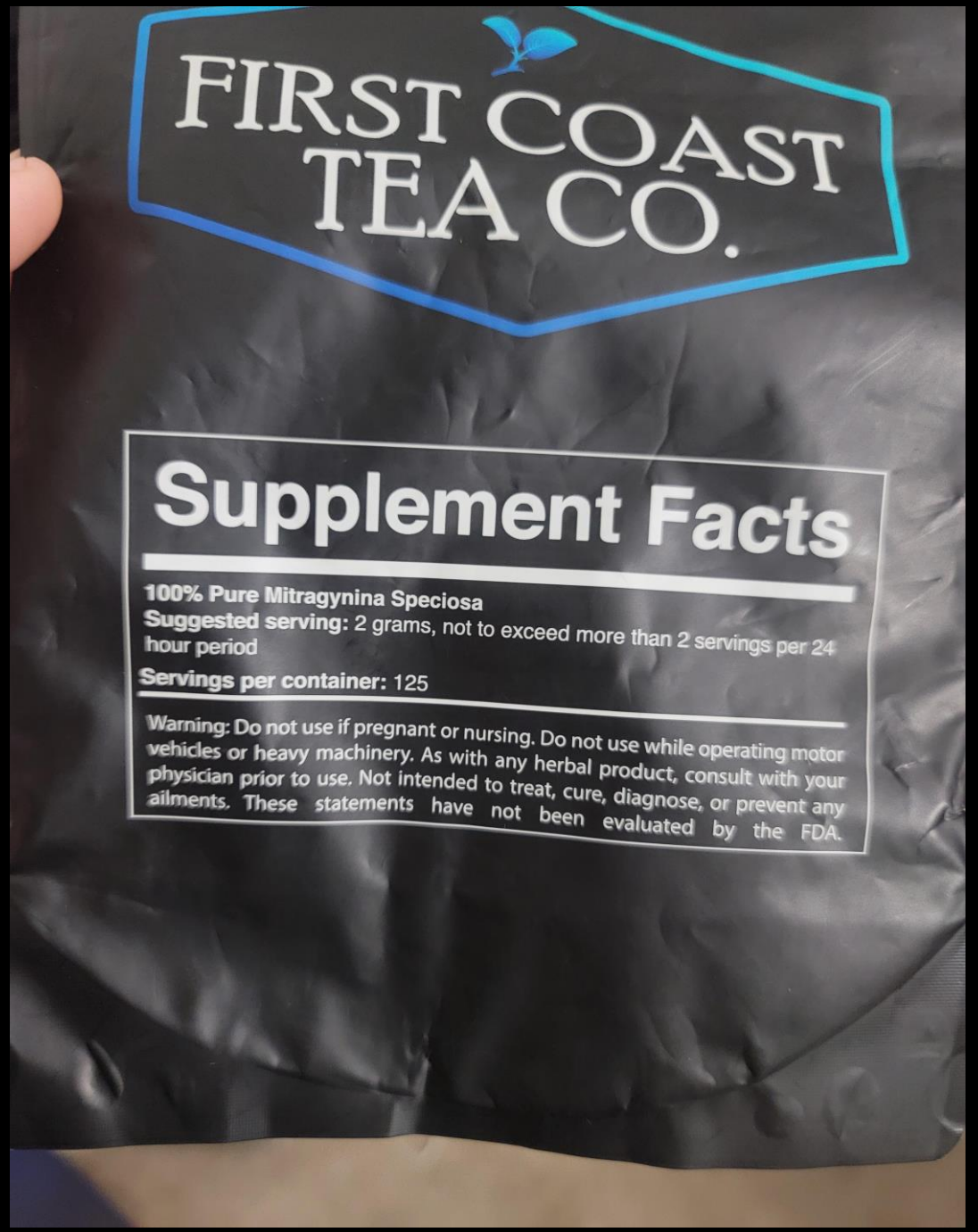
- Patient #1: 1kg of dry Kratom leaves powder lasted 1month ($80/month)
- 1000g/30 = ~33g/day

- Patient #2: 250g of dry Kratom leaves powder lasted 1 week ($100/month)
- 250g/7 = ~35g/day

- Both were taking around the same dose

What kind were they taking?

- Both didn’t know…
- I looked up patient #1 who had the package and said it was the blend of green, white and red of different strains…



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- Total of 8 patient cases were analyzed
- Recommendation:
- <20g of Kratom/d: initiate therapy 4-8mg
- >40g of Kratom / day: 12-16mg

No specific recommendations for 20-40g!!! Our patient use ~ 35g/day: I guess we should start between 8-12g (more toward 12 mg since 35g is closer to 40g) of buprenorphine a day?

Weiss, S. T. & Douglas, H. E. (2021). Treatment of Kratom Withdrawal and Dependence With Buprenorphine/Naloxone: A Case Series and Systematic Literature Review. Journal of Addiction Medicine, 15 (2), 167-172. doi: 10.1097/ADM.0000000000000721

Treatment

- Patient #1 and #2 were given same instruction → take the last dose of Kratom prior to sleeping and go as long as they can before taking ½ or 1 strip of 2mg/0.5mg of buprenorphine-naloxone and call the provider

Treatment: Patient #1

- Patient #1 waited 17 hours → took ½ the strip then another ½ in 1 hour later (total 2mg/0.5mg) → felt withdrawal s/s improved in 20-30 min after taking the second 1mg. Waited another 1 hour and took another 1mg (total 3mg) → 15-20 min later, felt completely well → slept well
- He is now taking just 2mg/ day no withdrawal then. Good appetite, reports more energy exercising etc… no craving toward kratom

Treatment: Patient #2

- Patient #2 waited 12 hours → took ½ the strip of 2mg q 2 hours up to 8mg on the first day → felt completely well
- He is now taking 2mg qid no withdrawal then. Good appetite, reports more energy exercising etc… no craving toward kratom

Why are they taking different doses (suboxone)?

- They are about the same age, same build, same gender,
- They were using about same dose /day. One vapes, other drinks
- Difference: patient #1 – used for 2 years while patient #2 used for 10 years. We are also uncertain about the strain of kratom
- Perhaps the duration of kratom usage and also strain for kratom they were using led to difference in dosage of suboxone

Conclusion - Case

- There are still lots to learn about Kratom and treatment for Kratom “addiction”/ “dependence”
  - Great recommendations, but <10 cases only
  - Kratom is very variable – chemical content, strain, potency etc...
- At least from the 2 cases we presented - Buprenorphine at lower dose may be beneficial so they can come off eventually if they choose to. Both of these patients have no h/o illicit drug use – gives them easier options to taper off in the future.
  - Patient #1 started to taper off from suboxone (just saw him) and doing well
  - Patient #2 is happy with where he is at.

https://nootroholic.com/green-malay-kratom

Take home messages:

- Kratom is sold as herbal supplements – used for various reasons including self-medications for opioid withdrawal
- Providers should be aware of Kratom and potential toxicity/withdrawal effect
- Kratom is NOT picked up by the standard toxicology screen
- Kratom is now recognized as emerging public health threat
- Educate public regarding kratom – both were unaware that it can cause addiction → they thought it was healthy because it is “natural and sold” in the health store.

Thank you! Any Questions?

Please feel free to email me:
Kiyokawa@hawaii.edu