PAINWEEK®

Kratom or Bait'em: History, Pharmacology, PK, and Regulation Revisited

Jeffrey Fudin, PharmD, DAIPM, FCCP, FASHP

Titles & Affiliations

Jeffrey Fudin, PharmD, FCCP, FASHP, FFSMB
Clinical Pharmacy Specialist & PGY2 Pain Residency Director
Stratton VAMC
Albany NY

Adjunct Associate Professor
Albany College of Pharmacy & Health Sciences
Albany NY
Western New England University College of Pharmacy, Springfield MA
Remitigate Therapeutics
Delmar NY

Disclosures

Affiliation	Role/Activities
Abbott Laboratories	Speaking, non-speakers bureau
AcelRx Pharmaceuticals	Acute perioperative pain (speakers bureau, consulting, advisory boards)
BioDelivery Sciences International	Collaborative publications, consulting, advisory boards
Firstox Laboratories	Micro serum testing for substances of abuse (consulting)
GlaxoSmithKline (GSK)	Collaborative non-paid poster presentations)
Medscape/WebMD	Presentations / webinars on medication assisted treatment (MAT) for opioid-use disorder
Pharmacy Times	Webinars, writing/publishing
Practical Pain Management	Co-Editor-At-Large, writing, and editing
Rockpointe, Inc	REMS opioid presentation/lecture (a continuing education company)
Scilex Pharmaceuticals	Collaborative non-paid publications
Salix Pharmaceuticals	Speakers bureau, consultant, advisory boards
Trnity Health, Inc.	Direct patient care, virtual consultations for pain management akin to a virtual private medical practice

Learning Objectives

- Describe the history and background of Kratom
- Match various pharmacologic and pharmacokinetic mechanisms of kratom to currently available prescription medications
- Identify regulatory concerns, quality control issues, and variability among kratom dosage forms
- Categorize clinical utility, epidemiology, and kratom usage among advocates
- Outline ADRs, benefits v. risks, and drug interactions associated with kratom

Pretest Question #1

Which of the following is/are true regarding kratom's mechanism of action?

A. Blocks reuptake of dopamine
B. Has opioid antagonist properties
C. Is an opiate by definition
D. All of the above

Pretest Question #2

According to the FDA and DEA respectively, kratom…

A. is an unsafe natural substance and classified as Schedule I
B. is legal in some states and illegal in others
C. potentially dangerous, but not Scheduled by Federal Regulation
D. c and c above

Pretest Question #3

Kratom is a…

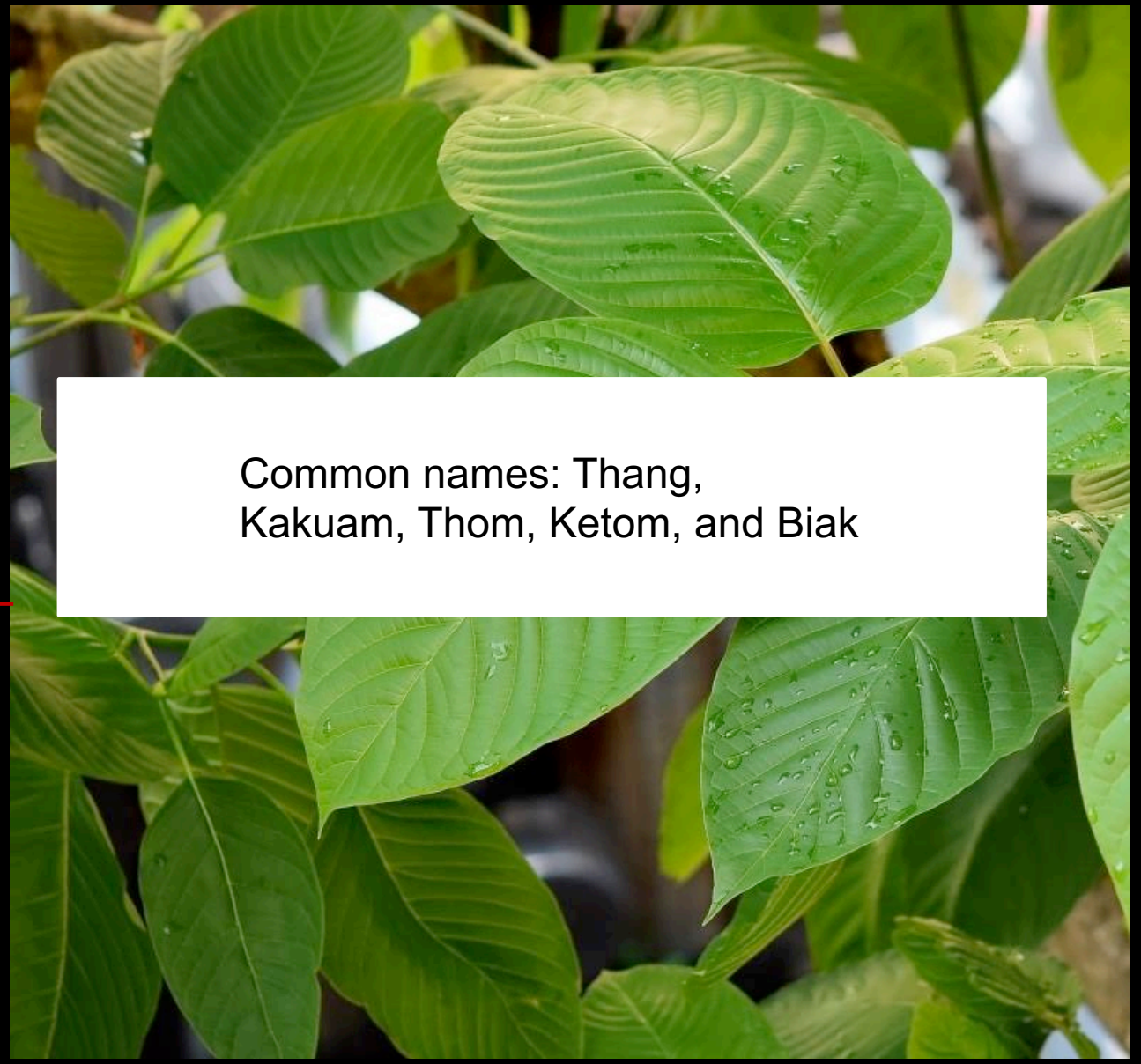
A. CNS psychostimulant
B. CNS sedative hypnotic
C. Antidepressant
D. All of the above

What Inspired this Lecture?

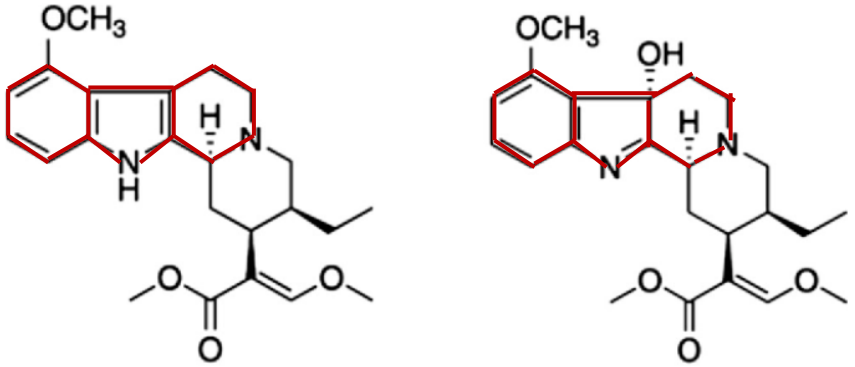
Quotes from Kratom Advocates

- "Kratom is a natural product, so how can it be harmful?"
- "Show me one article that proves kratom can be harmful."
- Dr. Fudin;
  - "…implies kratom is an opioid. It's not. You can simply Google it, and then look up the definition of opioid."
  - "…incorrectly stated that kratom can interact with other drugs and cause agitation, heart attack and stroke.
  - "…either made this up off the top of his head, or someone told him this."
- "If kratom is an opiate, why doesn't it cause a positive urine screen for opiates?"
- "There is no use for using naloxone on a kratom overdose. If you "overdose" you get sick and puke."

Fudin J. Kratom, Save 'em, Bait 'em, or Crate 'em. February 5, 2018. http://paindr.com/kratom-save-em-bait-em-or-crate-em/

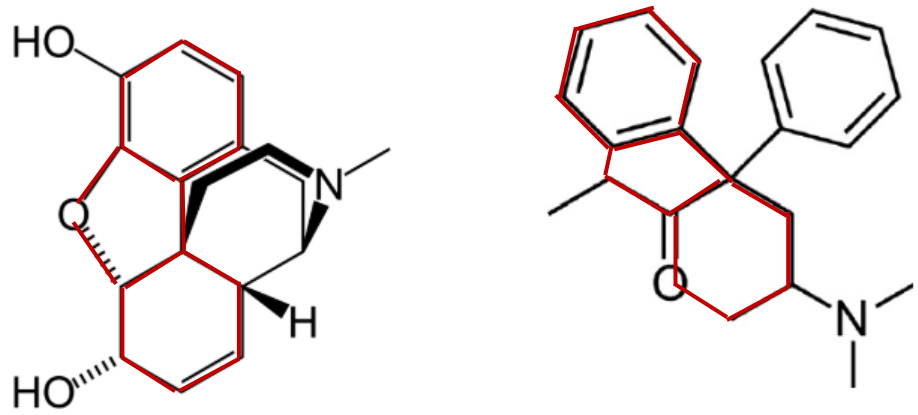


Common names: Thang, Kakuam, Thom, Ketom, and Biak



7-Hydroxymitragynine (kratom)

Mitragynine (kratom)



Morphine

Methadone

Adkins, Jessica, Edward W Boyer, and Christopher R McCurdy. "Mitragyna speciosa, a psychoactive tree from Southeast Asia with opioid activity." Current topics in medicinal chemistry 11, no. 9 (2011): 1165-1175.

Historical Perspective

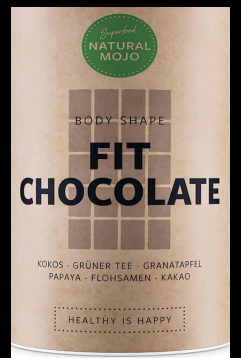
- Source
  - Tropical evergreen shrub or tree related to the cocoa plant
- Location
  - Native to Southeast Asia, Thailand, Malaysia, and Papua New Guinea
- Historical Usage
  - Used by local populations in each of these counties as a stimulant, generally by farm workers to enhance wakefulness and long work days
  - Pain, depressed mood, anxiety
- Southeast Asia Uses
  - Diarrheal, antitussive, diabetes, anthelmintic, heroin addiction
- Outside Asia
  - Chronic pain, opioid withdrawal

Routes of Ingestion

- Raw leaves or dried leaves are chewed or prepared in tea
- Preparation
  - –Citric juice added to enhance flavor and accelerate active ingredient
  - –Bitter Taste
    - Masked with sweeteners (sugar, honey)
- Smoked
  - –Pipe, rolled into cigarettes, vaped
- Chewing
  - –1 to 3 fresh leaves at a time

Kratom Trends

Dried or crushed
Extracts, powders
Available at Head Shops
Capsules, tablets, liquids, and gum/resin
Significant increase in imports (Regulation + CDC)
Millions of doses for recreational are used throughout US
Natural Food supplement, and therefore, claims, purity / quality not regulated



Kratom Pharmacology

- Over 25 chemically similar alkaloids with variable / mixed properties[1]
- Pharmacologically active components
  - 7-hydroxymitragynine
  - Mitragynine
- Opioid (R- enantiomer) agonists[2]
  - Kappa > mu > delta[3]
  - Other mixed mechanisms of action and various pharmcodynamic pathways

1. Suhaimi, Farah W., Nurul HM Yusoff, Rahimah Hassan, Sharif M. Mansor, Visweswaran Navaratnam, Christian P. Müller, and Zurina Hassan. "Neurobiology of Kratom and its main alkaloid mitragynine." Brain research bulletin 126 (2016): 29-40.
2. Takayama, Hiromitsu. "Chemistry and pharmacology of analgesic indole alkaloids from the rubiaceous plant, Mitragyna speciosa." Chemical and Pharmaceutical Bulletin 52, no. 8 (2004): 916-928.
3. Taufik Hidayat, M., Evhy Apryani, B. M. Nabishah, M. A. A. Moklas, F. Sharida, and M. A. Farhan. "Determination of mitragynine bound opioid receptors." Adv Med Dent Sci 3 (2010): 65-70.

Dose Dependent Pharmacological Activity

- Low (1-5g)
  - –Stimulatory due to neuroamines
  - –Antidepressant-like effect associated with MAO, serotonin, noradrenaline and dopamine[1]
- High (>5g)
  - –Sedative and analgesic properties due to opiate receptor activiation[2]
  - –Counteracts opioid withdrawal
    - 7-hydroxymitragynine > mitragynine: mu R agonists[2]
    - Mitragynine: alpha-2 adrenergic Rs agonist[2]

1. Suhaimi, Farah W., Nurul HM Yusoff, Rahimah Hassan, Sharif M. Mansor, Visweswaran Navaratnam, Christian P. Müller, and Zurina Hassan. "Neurobiology of Kratom and its main alkaloid mitragynine." Brain research bulletin 126 (2016): 29-40.
2. Boyer, Edward W., Kavita M. Babu, Jessica E. Adkins, Christopher R. McCurdy, and John H. Halpern. "Self-treatment of opioid withdrawal using kratom (Mitragynia speciosa korth)." Addiction 103, no. 6 (2008): 1048-1050.

Kratom Pharmacokinetics

- Mitragynine half-life[1]
  - 7-24 hours depending on alkaloid
- Dosing occurs every 6-12 hours
- Withdrawal symptoms begin ~12 hours after last use[2]
    - Note, WD may be from serotonin or opioid, or both
- Metabolism
- Phase I, Cytochrome P450 (CYP450), 3A4, 2D6, 2C9[3]
- Drug Interactions
  - Substrate interactions from above
  - Mitragynine inhibits CYP P450 2C9, 2D6, 3A4, 1A2[4]

1. Taufik Hidayat M, Apryani E, Nabishah BM, Moklas MA, Sharida F, Farhan MA. Determination of mitragynine bound opioid receptors. Adv Med Dent Sci. 2010;3(3):65-70.Boyer et al. 2007
2. Stanciu CN, Gnanasegaram SA, Ahmed S, Penders T. Kratom Withdrawal: A Systematic Review with Case Series. Journal of psychoactive drugs. 2019 Jan 5:1-7.
3. Kamble SH, Sharma A, King TI, León F, McCurdy CR, Avery BA. Metabolite profiling and identification of enzymes responsible for the metabolism of mitragynine, the major alkaloid of Mitragyna speciosa (kratom). Xenobiotica. 2018 Dec 24:1-0.
4. Hughes RL. Fatal combination of mitragynine and quetiapine–a case report with discussion of a potential herb-drug interaction. Forensic Science, Medicine and Pathology. 2019 Mar 1;15(1):110-3.

Toxicity and Adverse Effects

- Adverse Effects
  - Weight loss; insomnia; constipation; skin hyperpigmentation; extreme fatigue[1]
- According to CDC and other sources, increased…
  - Kratom-related exposure calls to poison control centers[2,3]
  - Fatal overdoses involving kratom
    - Co-ingestions[2]
    - Adulterated and combination products[3,4]

1. Saingam D, Assanangkornchai S, Geater AF, Balthip Q. Pattern and consequences of krathom (Mitragyna speciosa Korth.) use among male villagers in southern Thailand: a qualitative study. International Journal of Drug Policy. 2013 Jul 1;24(4):351-8.Gershman et al., 2018
2. Kronstrand R, Thelander G, Lindstedt D, Roman M, Kugelberg FC. Fatal intoxications associated with the designer opioid AH-7921. Journal of analytical toxicology. 2014 Oct 1;38(8):599-604.
3. Palasamudram Shekar S, Rojas EE, D'Angelo CC, Gillenwater SR, Martinez Galvis NP. Legally Lethal Kratom: A Herbal Supplement with Overdose Potential. Journal of psychoactive drugs. 2019 Jan 1;51(1):28-30.
4. Tang MH, Chong CY, Ching DC, Mak TW. Clinical testing for ketamine. Ketamine: Use and Abuse. 2015 Mar 16:341.

Treating Kratom Withdrawal

- Opioid Withdrawal[1,2,3]
  - Replacement therapy with buprenorphine, methadone, or other and taper
  - Neonatal Abstinence Syndrome[4]
    - Opioid replacement
- Serotonin Withdrawal
  - Options?

1. Suhaimi FW, Yusoff NH, Hassan R, Mansor SM, Navaratnam V, Müller CP, Hassan Z. Neurobiology of Kratom and its main alkaloid mitragynine. Brain research bulletin. 2016 Sep 1;126:29-40.
2. Kruegel AC, Grundmann O. The medicinal chemistry and neuropharmacology of kratom: A preliminary discussion of a promising medicinal plant and analysis of its potential for abuse. Neuropharmacology. 2018 May 15;134:108-20.
3. Stanciu CN, Gnanasegaram SA, Ahmed S, Penders T. Kratom Withdrawal: A Systematic Review with Case Series. Journal of psychoactive drugs. 2019 Jan 5:1-7.
4. Smid MC, Charles JE, Gordon AJ, Wright TE. Use of Kratom, an opioid-like traditional herb, in pregnancy. Obstetrics & Gynecology. 2018 Oct 1;132(4):926-8.

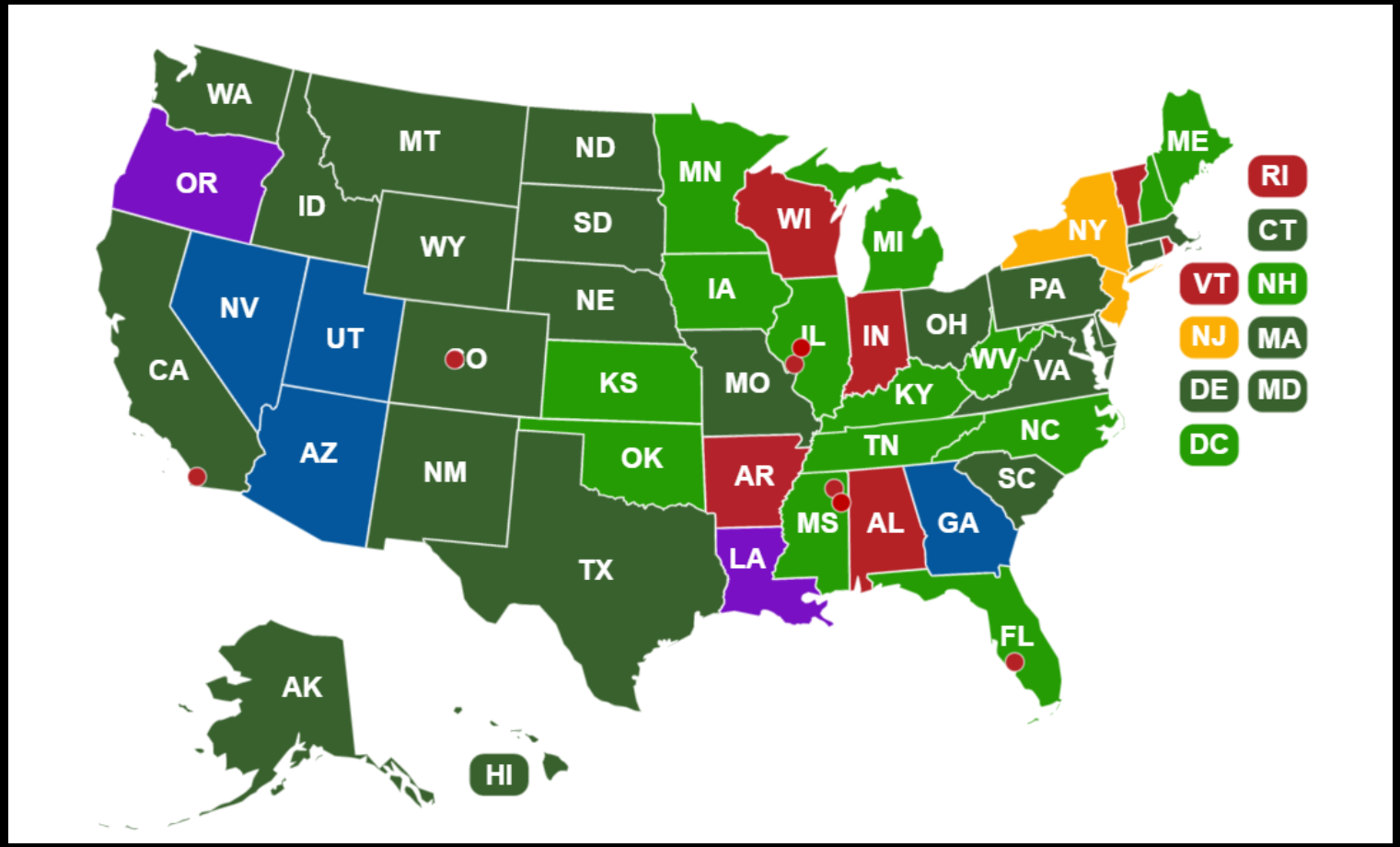
Regulatory Considerations[1-4]

- Up until 2015, Kratom was legal to grow and purchase in all 50 states
- 2011 to 2016, CDC & DEA identified Kratom as a substance of concern
- Illegal in several states as of 2018
  - –Alabama, Arkansas, Indiana, Ohio, Rhode Island, Vermont, Wisconsin
- Illegal in certain counties / cities
  - –Denver CO; San Diego CA; Sarasota FL, Washington DC
- Illegal in Certain Countries
  - –Australia, Denmark, Malaysia, Poland, Sweden, Thailand, and Vietnam

1. Hillebrand J, Olszewski D, Sedefov R. Legal highs on the Internet. Substance use & misuse. 2010 Feb 1;45(3):330-40.
2. Bergen-Cico D, MacClurg K. Kratom (Mitragyna speciosa) use, addiction potential, and legal status. InNeuropathology of Drug Addictions and Substance Misuse 2016 Jan 1 (pp. 903-911). Academic Press.
3. Prozialeck WC, Jivan JK, Andurkar SV. Pharmacology of kratom: an emerging botanical agent with stimulant, analgesic and opioid-like effects. The Journal of the American Osteopathic Association. 2012 Dec 1;112(12):792-9.
4. Griffin OH, Webb ME. The scheduling of kratom and selective use of data. Journal of psychoactive drugs. 2018 Mar 15;50(2):114-20.

Kratom Legality Map

- ✔ Green: Kratom is legal and no restrictions
- ♥ Light Green : Legislation in these states have failed or has been amended
- ✱ Orange: There is pending legislation on Kratom in these states
- ⊘ Red: banned states schedule 1 for Kratom
- ✔ Purple: Study involving Kratom
- ● Red Dot: banned city for Kratom
- ♥ Blue: These states have adopted the Kratom Consumer Protection Act bill



American Kratom Association, Last accessed 7/15/2020, https://speciosa.org/home/kratom-legality-map/

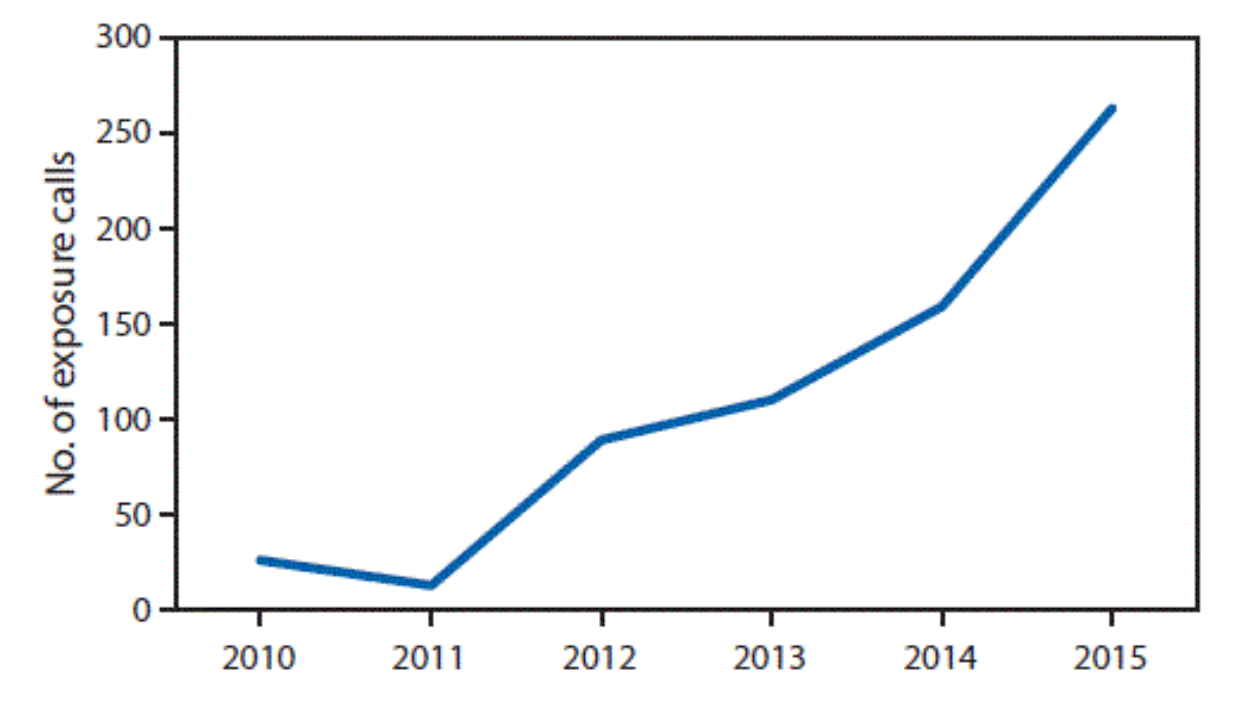
Regulation (continued)

- FDA is watching, but still legal by Federal Regulation
- DEA Notice of Intent, 2016
  - –Implement Schedule I status for mitragynine and 7- hydroxymitragynine
- American Kratom Association (millions)
  - –Non-profit consumer advocacy organization successfully campaigned for withdrawal of planned scheduling
    - Blog, Social media newsfeed experience
- DEA withdrew scheduling request in October 2016

Griffin OH, Webb ME. The scheduling of kratom and selective use of data. Journal of psychoactive drugs. 2018 Mar 15;50(2):114-20.

CDC and Poison Control Center Reports

Number of reported exposure calls to poison centers related to kratom use, by year — National Poison Data System, United States and Puerto Rico, January 2010–December 2015



660 calls about reported exposure to kratom. The number of calls increased tenfold from 26 in 2010 to 263 in 2015

PAINWEEK

Anwar M, Law R, Schier J. Notes from the Field. Kratom (Mitragyna speciosa) Exposures Reported to Poison Centers — United States, 2010–2015. MMWR Morb Mortal Wkly Rep 2016;65:748–749. DOI: http://dx.doi.org/10.15585/mmwr.mm6529a4

Epidemiology of Kratom Use

- US, prevalence widespread but not established
  - CDC Poison Control Center calls (from 2010)
  - American Kratom Association (survey, social media mentions)
- Southeast Asia
  - 55% of regular users of Kratom become dependent
  - Emerging worldwide as substance used in self-management of opioid withdrawal.

Griffin OH, Webb ME. The scheduling of kratom and selective use of data. Journal of psychoactive drugs. 2018 Mar 15;50(2):114-20.

Patterns of Kratom Use and Health Impact

- 10,000 Kratom users surveyed
  - –Who is consuming Kratom and for what purpose?
  - – What perceived beneficial and detrimental effects are reported by users?
  - –What do Kratom users report as a commonly used dose and frequency of consumption?
  - –Does Kratom represent a potential for abuse and withdrawal?
  - –Symptoms/side effects?

Grundman O. Patterns of Kratom Use and Health Impact in the US. Drug and Alcohol Dependence. 2017:176:63-70.

Survey Demographics

- Kratom users are primarily middle aged (31-50, 55.9%)
- Male (56.9%); Married or partnered (54.3%)
  - White non-Hispanic (89.4%)
  - Employed (56.8%)
  - Insured (61.1%)
  - Some college (82.3%)
  - Income > $35,000 (63.2%)

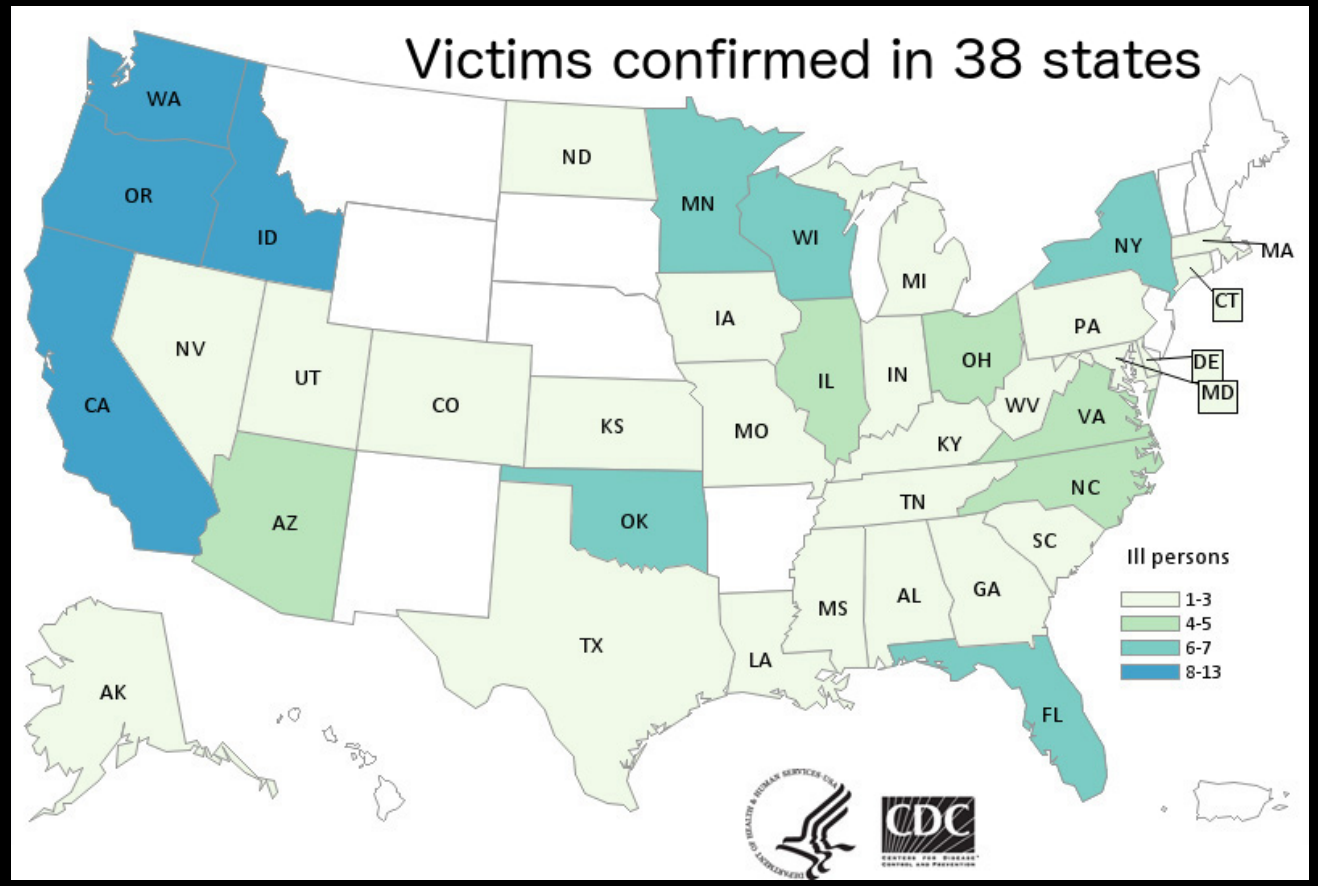
Grundman O. Patterns of Kratom Use and Health Impact in the US. Drug and Alcohol Dependence. 2017:176:63-70.

User Characteristics

- 41% disclosed use to healthcare provider
  - –Self-treatment of chronic pain 68%
  - –Self-treatment of anxiety/depression 65%
  - –Self-treatment related to opioid misuse (including opioid withdrawal)
- 7.7% had previous or current history of illicit drugs use
  - –Including prescribed or illicit RX opioids 26.0%

Grundman O. Patterns of Kratom Use and Health Impact in the US. Drug and Alcohol Dependence. 2017:176:63-70.

Adding Insult to Injury



Poor Quality Control cited for reason…

Kratom products recalled by FDA, April 2018

“Kratom Conspiracy Theory”

Outbreaks > FDA Investigated Multistate Outbreak of Salmonella ...
https://www.fda.gov/food/recallsoutbreaksemergencies/outbreaks/ucm597265.htm
These products have been **linked** to a multistate **outbreak** of **salmonellosis** from ... Mitragyna speciosa, commonly known as **kratom**, is a plant that **grows** ... Thirty-eight **percent** of ill people were hospitalized, and no deaths were reported. ... **Fifty** of these people have been hospitalized and no deaths have been reported.

People also search for

kratom recall list	kratom seized by fda
kratom salmonella fake news	eclipse kratom website
kratom salmonella reddit	salmonella kratom utah

Kratom linked to dozens of illnesses from salmonella, health officials ...
https://www.cbsnews.com/news/kratom-salmonella-fda-cdc-warning/
Feb 20, 2018 - **Kratom grows** naturally in the Southeast Asian countries of Thailand, ... so far, 11 people have been hospitalized with **salmonella** illness **linked** to their ... "Out of 11 people interviewed, eight (73 **percent**) reported consuming **kratom**. Ill people in this **outbreak** report consuming **kratom** in pills, powder or tea.

Salmonella outbreak linked to kratom supplements - New York Post
https://nypost.com/2018/03/19/salmonella-outbreak-linked-to-kratom-supplements/
Mar 19, 2018 - **Salmonella outbreak linked to kratom** supplements. By Mike Wehner, BGR ... with a median age of 39. **Fifty**-five **percent** of ill people are male.

Multistate Outbreak of Salmonella I 4,[5],12:b:- Infections Linked to ...
https://www.cdc.gov/salmonella/kratom-02-18/index.html
May 24, 2018 - Multistate **Outbreak** of **Salmonella** I 4,[5],12:b:- Infections **Linked to Kratom** Products. ... Thirty-eight **percent** of ill people were hospitalized, and no deaths were reported. ... Of 132 people with available information, **50** (38%) were hospitalized. ... As additional strains of **Salmonella** were identified in **kratom** ...
Missing: ~~grows~~ | Must include: grows

Google search term: "salmonella outbreak traced to kratom grows by 50 percent"
https://www.google.com/search?source=hp&ei=T7urXJHoGufc5gKIy6wY&q=salmonella+outbreak+traced+to+kratom+grows+by+50+percent&oq=Salmonella+outbreak+traced+to+kratom+grows+by+50+percent&gs_l=psy-ab.1.0.35i39.1520.1520..3989...0.0..0.1540.1673.0j1j8-1.....0....2j1..gws-wiz.....0.ry3em3vck2g

PAINWEEK

FDA Investigated Multistate Outbreak of Salmonella Infections Linked to Products Reported to Contain Kratom. US Food and Drug Administration. June 29, 2018 Update. https://www.fda.gov/food/recallsoutbreaksemergencies/outbreaks/ucm597265.htm Last Accessed April 8, 2019

Answers to Quotes from Kratom Advocates

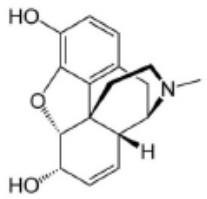
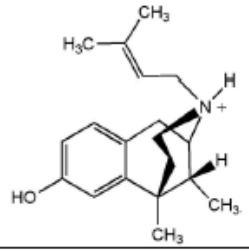
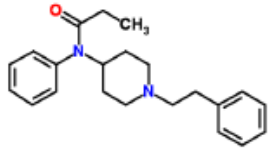
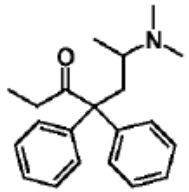
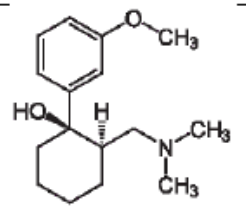
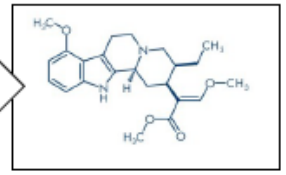
- "Kratom is a natural product, so how can it be harmful?"
  - Vincristine and vinblastine from the periwinkle plant
  - Digitalis from foxglove used to treat supraventricular heart arrhythmias or to strengthen heart rhythm
  - Atropine alkaloids from belladonna (also known as deadly nightshade), the ingredient from berries used by Romeo and Juliet to cause death.
- "Show me one article that proves kratom can be harmful."
  - See 1-7 next slide
- Dr. Fudin;
  - "…implies kratom is an opioid. It's not. You can simply Google it, and then look up the definition of opioid."
    - The original definition of an "opiate" is a drug derived from the poppy plant, or opium, that combines with one or more opiate receptors in the body. Opium is a concentrated form of morphine. Kratom is the only naturally occurring non-poppy derived opiate-type drug, but not an opiate by the strictest definition.
  - "…incorrectly stated that kratom can interact with other drugs and cause agitation, heart attack and stroke.
    - Pharmacology noted on previous slides
- "If kratom is an opiate, why doesn't it cause a positive urine screen for opiates?"
  - More to come…
- "There is no use for using naloxone on a kratom overdose. If you "overdose" you get sick and puke."
  - Two emergencies; 1) noradrenergic overstimulation which can be treated with combined benzodiazepine (alprazolam, diazepam, etc.) to reduce agitation plus beta blockers (propranolol and others) to slow the heart rate and reduce blood pressure; and 2) opioid overdose which can be treated with naloxone to block the opioid receptors.

Fudin J. Kratom, Save 'em, Bait 'em, or Crate 'em. February 5, 2018. http://paindr.com/kratom-save-em-bait-em-or-crate-em/

References from Previous Slide

1. Nelsen JL, Lapoint J, Hodgman MJ, Aldous KM. Seizure and coma following Kratom (Mitragyninaspeciosa Korth) exposure. Journal of medical toxicology. 2010 Dec 1;6(4):424-6.
2. Neerman MF, Frost RE, Deking J. A drug fatality involving Kratom. Journal of forensic sciences.2013 Jan 1;58(s1).
3. Trakulsrichai S, Tongpo A, Sriapha C, Wongvisawakorn S, Rittilert P, Kaojarern S, Wananukul W.Kratom abuse in Ramathibodi Poison Center, Thailand: a five-year experience. Journal ofpsychoactive drugs. 2013 Nov 1;45(5):404-8.
4. Babu KM, McCurdy CR, Boyer EW. Opioid receptors and legal highs: Salvia divinorum andKratom. Clinical Toxicology. 2008 Jan 1;46(2):146-52.
5. Warner ML, Kaufman NC, Grundmann O. The pharmacology and toxicology of kratom: fromtraditional herb to drug of abuse. International journal of legal medicine. 2016 Jan 1;130(1):127-38.
6. Kapp FG, Maurer HH, Auwärter V, Winkelmann M, Hermanns-Clausen M. Intrahepaticcholestasis following abuse of powdered kratom (Mitragyna speciosa). Journal of MedicalToxicology. 2011 Sep 1;7(3):227-31.
7. Galbis-Reig D. A case report of kratom addiction and withdrawal. WMJ. 2016 Feb;115(1):49-52.

“If kratom is an opiate, why doesn’t it cause a positive urine screen for opiates?”

PHENANTHRENES	BENZOMORPHANS	PHENYLPIPERIDINES	DIPHENYLHEPTANES	PHENYLPROPYL AMINES
				
MORPHINE	PENTAZOCINE	FENTANYL	METHADONE	TRAMADOL
Buprenorphine* Butorphanol* Codeine Dextromethorphan* Dihydrocodeine Heroin (diacetyl-morphine) Hydrocodone* Hydromorphone* Levorphanol* Methylnaltrexone** Morphine (Opium, conc) Nalbuphine* Naloxone* Naloxegol* Naltrexone** Oxycodone* Oxymorphone*	Pentazocine	Alfentanil Fentanyl Remifentanil Sufentanil Meperidine Diphenoxylate[a] Loperamide[a] **Illicit Fentanyl** Furanyl fentanyl Acetyl fentanyl Fluoro-fentanyl Carfentanil Others[b]	Methadone Propoxyphene **Mitragynine (Kratom)**	Tapentadol Tramadol 
CROSS-SENSITIVITY RISK				
PROBABLE	POSSIBLE	LOW RISK	LOW RISK	LOW RISK

*Agents lacking the 6-OH group of morphine, possibly decreases cross-tolerability within the phenanthrene group
**6-position is substituted with a ketone group and tolerability is similar to hydroxylation

Jeffrey Fudin, BSPharm, PharmD, DAIPM, FCCP, FASHP, FFSMB

http://paindr.com/resources/quick-references/ (See “Opioid Chemistry”)

a. Previously incorrectly listed as “Benzomorphans”

b. Bettinger JJ, Trotta ND, Fudin J. Wegrzyn EL, Schatman ME. Understanding the differences between pharmaceutical and illicit fentanyl and their analogues could save the opioid crisis. Practical Pain Management. 2018. July/August 18(5):59-67.

Urine Screen

- Kratom is not detected in standard IA urine screens
- Special add-on testing for suspected kratom use, abuse, misuse
  - Unexplained increased heart rate
    - Consider kratom and cathinone add-ons
- Confirmatory testing[1]
  - Gas chromatography/mass spectroscopy (GC-MS)
  - Liquid chromatography with linear ion-trap mass spectroscopy
  - Electrospray tandem mass spectroscopy[3]

1. Benchikh E, McConnell I, Lowry P, Fitzgerald P, inventors; Randox Laboratories Ltd, assignee. Immunoassay for detecting kratom, its constituents and their use. United States patent US 9,952,206. 2018 Apr 24.

Regarding Patient Use of Kratom

Should anyone have access to kratom (save ‘em)?

Will your patient be…

- “Bated”
  - –lured by political and advocacy rhetoric without having all the facts (bait ‘em)?
- Crated
  - –end up a statistic because a drug-drug interaction or drug-disease CI was missed (crate ‘em)?

Post Test Question #1

Which of the following is/are true regarding kratom's mechanism of action?

A. Blocks reuptake of dopamine
B. Has opioid antagonist properties
C. Is an opiate by definition
D. All of the above

Post Test Question #2

According to the FDA and DEA respectively, kratom…

A. is an unsafe natural substance and classified as Schedule I
B. is legal in some states and illegal in others
C. potentially dangerous, but not Scheduled by Federal Regulation
D. c and c above

Post Test Question #3

Kratom is a…

A. CNS psychostimulant
B. CNS sedative hypnotic
C. Antidepressant
D. All of the above

Questions?