

Kratom: Identifying “a drug of concern”

Mitragyna speciosa

Presented by:
Jack Kain, PharmD
Jeff Gudin, MD



Today's discussion

- What is kratom?
- Alkaloids and mitragynine
- A biphasic effect
- Kratom toxicity
- Drug monitoring

What is kratom?

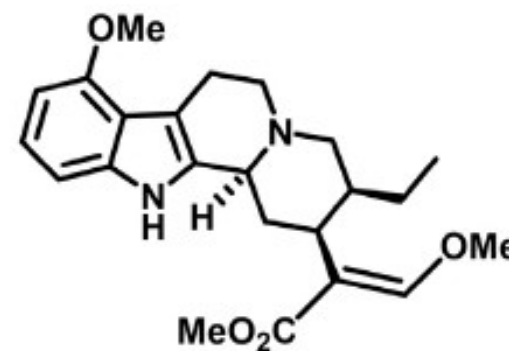
- *Mitragyna Speciosa*
 - 4- to 16-meter-high tropical tree indigenous to Southeast Asia
 - Traditionally, the leaves of the tree have been chewed or made into a tea by local manual laborers to combat fatigue and improve work productivity¹
 - Widely sold as an herbal supplement for boosting mood, energy and relieving pain
- The US Food and Drug Administration is warning consumers not to use *Mitragyna speciosa*, commonly known as kratom, which has properties that expose users to the risks of **addiction, abuse, and dependence**²
- The DEA has kratom listed as a **Drug and Chemical of Concern** as of 2012³
 - DEA attempts to make it Schedule I' substance in 2016 were undermined by significant public backlash⁴

Alkaloids and mitragynine

- Alkaloids are a huge group of naturally occurring organic compounds which contain nitrogen atoms in their structures (eg, opium alkaloids) In 1804, morphine was the first alkaloid ever isolated⁵
- Over 40 alkaloids extracted from kratom which makes pharmacological and toxicological assessment challenging. Alkaloid content can vary between trees.^{6,7} Some common alkaloids in kratom:
 - **Mitragynine**
 - Hydroxymitragynine
 - Paynantheine
 - Speciogynine
 - Speciociliatine
 - **Mitragynine**
 - The most abundant alkaloid in kratom^{6,7}
 - High affinity for the **Mu-opioid receptor**



Mitragyna Speciosa
(kratom) Leaf



Mitragynine

A biphasic effect

Stimulant at low doses, sedative/opioid like effects at high doses

- **Self medicating and/or chasing “euphoria?”**
 - Self-medicate
 - Opioid withdrawal – Kratom is easier to purchase and access than opioids and medication-assisted treatment (eg, buprenorphine)
 - Chase ‘feel good’ effect
 - Mu-receptor agonist – inherent abuse liability
 - Used at music festivals and other recreational settings
 - Do people really know what they are getting? Hard to gauge the effect of a given dose
- An opportunity for “legitimate medical use?”
 - There is currently **no strong scientific evidence** that Kratom is effective or safe for treating withdrawal and cravings caused by opioid and other addictive substances such as alcohol
 - Further research is needed

Kratom toxicity

- Kratom exposures reported to United States (US) Poison Control Centers (PCCs) increased **tenfold** from 2010 to 2015
- Emory researchers presented: Kratom Exposures Reported to US Poison Centers, 2010–2018⁸ and identified:
 - 2483 kratom exposures met criteria
 - Median **age was 30 years**; 70% were **male**
 - 262 (10.6%) exposures resulted in a severe outcome, including 17 deaths, **3 of which were single-agent exposures**
 - The most common clinical effects were **tachycardia, nausea, and drowsiness**
 - The most common co-exposures were **sedative hypnotics, ethanol, and opioids**
- In addition, **heavy metal** and **salmonella contamination** have also been found in kratom products, resulting in numerous illnesses and product recalls

Quest Drug Monitoring

- Do Prescription Drug Monitoring Programs (PDMP) identify kratom use?
 - Drug testing provides objective information on medication compliance, empowering behavioral health clinicians and treatment teams to make more informed decisions that can improve patient care
- Quest Diagnostics uses a **2-step testing approach** with presumptive identification of possible use or non-use of the tested drugs and definitive confirmation to identify specific drugs present
 - **39241** - Potential for low positivity rates (~5%) make presumptive with reflex definitive testing the most economical choice while balancing clinical benefit
 - **39240** - Straight to definitive testing option is available for those who do in-house screening first
- Our accurate results help clinicians and treatment teams facilitate conversations and maintain therapeutic alliances with patients and clients.

39241
Mitragynine, Presumptive
w/ Confirmation

39240
Mitragynine,
Quantitative

Summary: Quest Diagnostics

- The abuse and misuse of prescription drugs remains epidemic in the US
- Quest serves 1 in 3 adult Americans and half the physicians and hospitals in the United States
 - Quest Diagnostics has the world's largest database of clinical lab results; our diagnostic insights help improve healthcare management
- A properly implemented drug testing program is an important step in tackling drug misuse and abuse
- By performing more than 10 million drug tests annually, Quest Diagnostics has the experience to help you implement a successful drug monitoring program—one that helps protect your practice, helps your patients, and helps keep your community safe
 - Rx Tox Line available to help clinicians with test ordering or result interpretation
 - 1.877.40.RXTOX (1.877.407.9869)
 - Visit [QuestDrugTesting.com](https://www.questdiagnostics.com/questdrugtesting) or subscribe through your favorite podcast venue

References

1. Cinosi E., Martinotti G., Siminato P., et al., 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
2. FDA. Published June 25, 2019. Accessed May 17, 2020. <https://www.fda.gov/news-events/press-announcements/fda-issues-warnings-companies-selling-illegal-unapproved-kratom-drug-products-marketed-opioid>
3. DEA. Kratom. Published June 16, 2017. Accessed May 17, 2020. <https://www.dea.gov/factsheets/kratom>
4. DEA, DOJ, 2016b. Withdrawal of Notice of Intent to Temporarily Place Mitragynine and 7-hydroxymitragynine into Schedule I. Federal Register. Document Citation 81 FR 70652. United States Government. Publication date October 13, 2016. Accessed May 14, 2020. <https://www.federalregister.gov/documents/2016/10/13/2016-24659/withdrawal-of-notice-of-intent-to-temporarily-place-mitragynine-and-7-hydroxymitragynine-into>
5. Encyclopedia Britannica. Alkaloid. Published 2017 Accessed May 15, 2020. <https://www.britannica.com/science/alkaloid>
6. H. Takayama, “Chemistry and pharmacology of analgesic indole alkaloids from the rubiaceous plant, *Mitragyna speciosa*,” *Chemical and Pharmaceutical Bulletin*, 2004; 52(8): 916-928.
7. 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. *J Neuropharm.* Published May 15, 2018. Accessed May 17, 2020. <https://doi.org/10.1016/j.neuropharm.2017.08.026>
8. American College of Medical Technology 2019 Annual Scientific Meeting Abstracts---San Francisco, CA. *J. Med. Toxicol.* 2019; 15:53-107. Published March 1, 2019. Accessed May 17, 2020. <https://doi.org/10.1007/s13181-019-00699-x>