



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

KRATOM

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GENERAL DISCLOSURES

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GENERAL DISCLOSURES

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SPEAKER DISCLOSURES

✓ No relevant conflicts of interest

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose:

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KRATOM CASE

- 27 year old man with history of opioid use disorder presents with difficulty stopping kratom
- Two year history of prescription opioid use after an injury – prescribed, then from friends, street
- Went to inpatient treatment, left early
- Used kratom purchased on line to complete detox
- Taking it 4 times daily and gets opioid withdrawal symptoms when tries to taper

KRATOM

- What is it?
- How does it work?
- Is it legal?
- Is it harmful?

KRATOM: WHAT IS IT?

- Kratom is *Mitragyna speciosa*, a plant native to Southeast Asia and Africa
- Leaves can be smoked, brewed, chewed
- Sold as a leaf, tablet, or powder/extract form as a “dietary supplement”
- Easy to obtain over the internet or in health stores
- Also called thang, kakuam, thom, ketom, biak
- Used 1-5 million people in US (1.3% lifetime use)

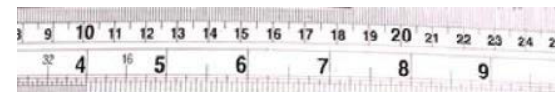
<https://www.drugabuse.gov/publications/drugfacts/kratom>

KRATOM (MITRAGYNA SPECIOSA) IN SOUTHEAST ASIA



Singh D, et al. Hum Psychopharmacol 2017 May;32(3).

KRATOM



KRATOM IN SOUTHEAST ASIA

- Long used by rural populations as remedy (women) or stimulant (men), in social interaction among men, and in religious functions
- Replacement for opium during opium shortages
- Replacement for alcohol in some Muslim groups
- Less stigmatized (hard working, not lazy or violent)
- New uses are as treatment for opioid withdrawal and among youth in urban areas, to induce euphoria
- Legal sanctions have preceded scientific investigation

Singh D, et al. Hum Psychopharmacol 2017 May;32(3).

KRATOM USE IN THE US

- Used primarily for pain, anxiety, PTSD, depression, low energy, opioid dependence/withdrawal
- One study of 2,798 users:
 - 91% for pain
 - 67% for anxiety
 - 65% for depression
 - 41% for opioid withdrawal

Garcia-Romeu A, Cox DJ, Smith KE, Dunn KE, Griffiths RR. Kratom (*Mitragyna speciosa*): User demographics, use patterns, and implications for the opioid epidemic. *Drug Alcohol Depend.* 2020;208:107849.

KRATOM: HOW DOES IT WORK?

- Mitragynine and 7-hydroxymitragynine are the main active alkaloids
- Stimulant effects at lower doses
- At higher doses, opioid effects and side effects
- Lasts 1-6 hours
- Side effects include nausea, itching, sweating, dry mouth, constipation, increased urination, loss of appetite, seizures, psychosis and hallucinations

KRATOM PHARMACOLOGY: ATYPICAL OPIOID

- Lipophilic and easily crosses blood-brain barrier
- Opioid activity:
 - Agonist/partial agonist at mu- and delta-opioid receptors
 - Antagonist at kappa opioid receptor (↓ pain sensitivity)
 - No β -arrestin recruitment (↓ respiratory depression)
- Other receptors:
 - Central serotonin modulation
 - Adrenergic pathways
 - Inhibit prostaglandin production
- Cytochrome P-450 metabolism

KRATOM WITHDRAWAL

- Increasing reports of individuals presenting with symptoms due to abrupt cessation of kratom
- Mimics opioid withdrawal
- Occurs 12-24 hours after cessation of regular use and usually lasts less than four days
- Associated with duration and quantity of use

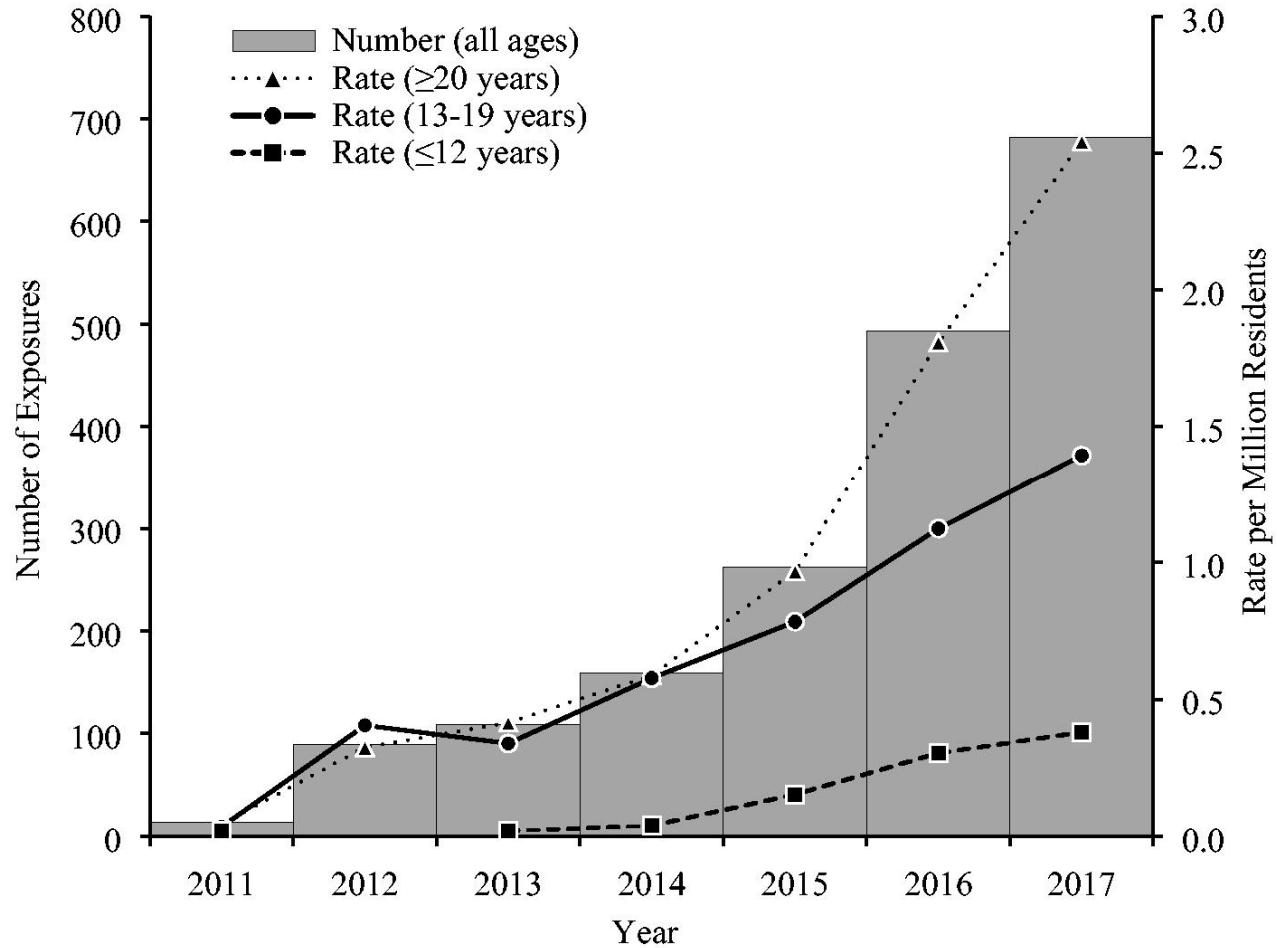
Stanciu CN, Gnanasegaram SA, Ahmed S, Penders T. Kratom Withdrawal: A Systematic Review with Case Series. *J Psychoactive Drugs* 2019; 51:12.

KRATOM: TOXICOLOGY REPORTS

- Scattered reports of altered mental status, agitation, CNS depression, seizures, tachycardia, cholestasis, dependence and withdrawal
- From 2011-17, 1807 exposures reported to poison control centers - 65% reported in 2016-17
- In 2017 FDA identified 44 deaths related to kratom, with most polysubstance related or adulterated
- In 2019 CDC found 152 kratom-related deaths, mostly with fentanyl, heroin, other opioids
- No urine tests available

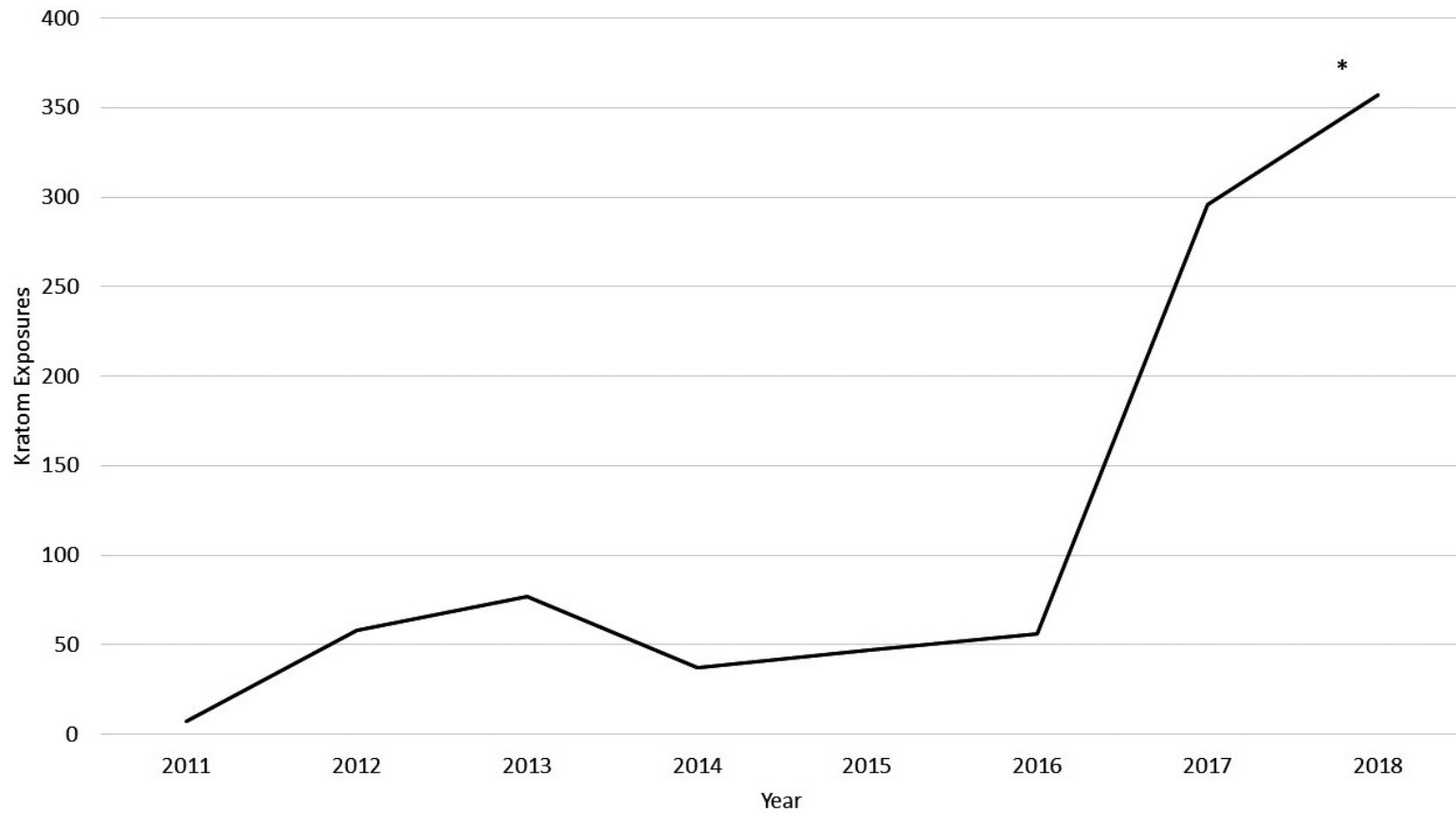
Post et al, 2019. *Clinical Toxicology* Feb 20:1-8.

KRATOM EXPOSURES



Post et al, 2019. *Clinical Toxicology* Feb 20:1-8.

KRATOM USE AND TOXICITIES IN THE US



Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, Volume: 39, Issue: 7, Pages: 775-777, First published: 16 May 2019, DOI: (10.1002/phar.2280)

KRATOM: POTENTIAL BENEFITS

- Users identify benefits for pain, opioid withdrawal
- Safety may be better than current therapies
- While dependence is possible, withdrawal may be less severe
- May have less abuse potential
 - Recent studies do not show rat self-administration
- No high quality studies have been done

Prevete E, Kuypers KPC, Theunissen EL, Corazza O, Bersani G, Ramaekers JG. A systematic review of (pre)clinical studies on the therapeutic potential and safety profile of kratom in humans. *Hum Psychopharmacol*. 2021 Jul 26:e2805.

KRATOM: IS IT LEGAL?

- Kratom is currently legal in the US
- Classified as a Drug of Concern by the DEA
- Several states have classified it as schedule 1
- FDA has not approved Kratom for any medical use

KRATOM: IS IT LEGAL?

- In 2016, HHS recommended that DEA make kratom a Schedule 1 drug
- Public backlash delayed DEA action
 - >20,000 public comments
- FDA actions:
 - 2012-16 Import alerts, seizures
 - 2017-8 Salmonella outbreak: 199 people in 41 states
 - 2018 voluntary recall notice
 - 2018 Warning letter to companies – illegal advertising
- 2017 HHS letter to DEA supporting Schedule 1 status

REGULATION OF KRATOM

- Pros:
 - Evidence of increasing use and harms
 - No known therapeutic indications
 - Unsafe/unregulated distribution
- Cons:
 - Evidence for potential therapeutic value
 - Harm to research efforts
 - Harm to current users
- Larger issues of regulation of drugs

Prozialeck WC, Avery BA, Boyer EW, Grundmann O, Henningfield JE, Kruegel AC, McMahon LR, McCurdy CR, Swogger MT, Veltri CA, Singh D. Kratom policy: The challenge of balancing therapeutic potential with public safety. *Int J Drug Policy*. 2019 Aug;70:70-77.

ALTERNATIVES TO REGULATION

- Regulation of kratom concentration
 - Avoidance of “black market,” adulterants
- Further research
 - Difficult to fund trials of natural products
 - Could study mitragynine, but may miss important effects of other constituents
 - Severe regulation would make research more difficult

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KRATOM CASE

- What is the diagnosis?
- What are the treatment options?
- Is medication treatment for OUD indicated?

KRATOM

- Emerging drug of concern
- Has stimulant and opioid effects
- Increasing reports of toxicity and withdrawal
- Some pre-clinical evidence of benefit
- Regulation may precede science due to risks

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