Kratom Education









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Objectives

- Gain a comprehensive understanding of kratom.
- Evaluate the scientific evidence supporting the safety of kratom.
- Distinguish between high-quality evidence and low-level evidence from single case studies.
- Identify the potential risks associated with synthetic substances.
- Analyze addiction potential and kratom as a harm reduction tool.
- Discuss government relationships with kratom.
- Recognize the significance of regulating kratom.

What is Kratom?

- Kratom tree (Mitragyna Speciosa) is indigenous to Southeast Asia.
- Traditionally used for pain relief and energy by agricultural workers.
- Kratom and coffee are members of the Rubiaceae family of plants.
- Strains: Red, Green, White





Nature's Symphony Orchestra

- Kratom has over 40 alkaloids. The most abundant is mitragynine. 7hydroxymitragynine (7OH) is found in less than 2% of the plant (most often in trace amounts).
- Kratom is most stimulating (similar to coffee) at low doses. Higher doses can cause relaxing and analgesic effects.
- Kratom is a <u>partial</u> opioid agonist, unlike full agonists like oxycodone, fentanyl and heroin.



Who Uses Kratom & Why?

61% Women

Avg Age is 40 yrs old

84% College Educated

91% for Pain Relief

67% Anxiety

64% Depression

41% Opioid Dependence

Of those using it for opioid withdrawal, 87% reported relief from withdrawal symptoms.

35% were free from Opioids for >1 year. (14)

Survey of Adult Kratom Users in the U.S. Provides Insight Into Potential for Harm or Abuse 2,798 kratom users WHO: 84% at least some college 40 years old on average 61% are women 91% pain relief 67% treat anxiety 64% treat depression 41% treat opioid dependence Of those treating opioid dependence: 1.9% serious² 87% reported relief from 9.5% withdrawal withdrawal symptoms 35% were free from opioids <10% met criteria for mild kratom substance use disord or severe kratom substance use disorder JOHNS HOPKINS

1. many people reported multiple reasons for use

2. including symptoms like anxiety, irritability, depression and insomnia

Truth

Kratom should not be consumed in conjunction with other substances like alcohol, opioids and benzodiazepines.

• TRUE – Like with any other herbs or botanical substances, interactions can occur. Check with your doctor before you consume Kratom.

Kratom effects on pregnancy and infant development have not been sufficiently studied at this point in time.

TRUE – Kratom is not recommended for those who are pregnant, becoming pregnant or breastfeeding. Typical

There is science behind Kratom.

TRUE – There are many published studies about Mitragynine (Kratom). It is always important to look at study size, case parameters and be wary of information that suggests bias.

Kratom regulation is possible.

• **TRUE** – Passage of the Kratom Consumer Protection Act works to ensure that Kratom purchased in your state is tested, pure, properly labeled and only sold to adults.

Fiction

Kratom has no long-term FALSE - Kratom has been consumed for centuries in Southeast Asia without evidence of exposure data. adverse effects. **FALSE** – Kratom is consumed orally by powder, capsule or in liquid extract/tincture form. Kratom is smoked or injected. FALSE - Kratom is a partial opioid agonist and does not suppress breathing unlike full opioids Kratom is a full opioid. (oxycodone, fentanyl, heroin). Mitragynine and 7-hydroxymitragynine (7OH) are the most active compounds in kratom. Pure Kratom leaves contain trace amounts of 70H. FALSE – 7-OH products are fully synthetic, and lab created. Kratom can be found in extract 7-OH is Kratom. form (concentrated), but these are produced from the leaf. Kratom causes delusions, FALSE - Reports of such side effects are rare and come from cases where the individuals were hallucinations and previously diagnosed with mental illnesses like schizophrenia and bipolar disorders and/or polypharmacy. confusion.



A Pain & Mental Health Perspective

- Low serving amounts have been reported to alleviate or control chronic pain, improve anxiety symptoms and even aid in depression.
- Higher doses are often used for acute pain or more severe mental health challenges.
- Serving sizes vary between individuals due to varying levels of pain and other symptoms.
- Less is more with Kratom. Consumers should take the lowest dose possible to achieve the desired effects. Breaks are suggested to avoid tolerance.
- Kratom produces effects within 15-20 minutes of consumption and lasts 3-6 hours.
- Consumers select strains to achieve desired effects:

Red – Pain

Green - Pain & Mood

White - Energy

Higher Kratom consumption, especially if consumed due to addiction tendencies, may cause withdrawals to be more pronounced due to Post Acute Withdrawal Syndrome (PAWS).

Kratom vs. Pharmaceuticals

- Dependence <u>does not</u> mean addiction.
- ► OTC medications are often not sufficient to treat severe pain.
- We are in the midst of an opioid epidemic crisis! Opioid prescriptions are being restricted or even denied. Many pain patients, out of desperation, have turned to alternative forms of pain control (Kratom and Cannabis). To restrict access to these alternatives will result in suicides and black-market purchases (which often contain deadly Fentanyl).
- Many patients prefer to treat their symptoms with plant supplements rather than pharmaceuticals.
- Many physicians are not educated about kratom and can stigmatize patients who opt to use alternative medicine.
- Organizations like the Veterans Administration (VA) are unable to legally recommend kratom although many veterans could benefit from the pain and PTSD relief that kratom can provide.





Synthetic Products are NOT Kratom

- ➤ 7 Hydroxymitragynine (7-OH) is a metabolite of mitragynine. It is less than 1% of the natural plant.
- ▶ 7-OH products have a binding affinity 14-22 times greater than morphine.
- Animal studies have demonstrated respiratory depression.
- Extreme addiction concerns.
- Many products have brand names that allude to narcotics.

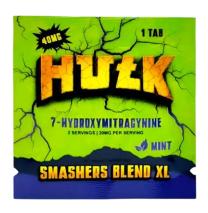


7-OH Synthetics









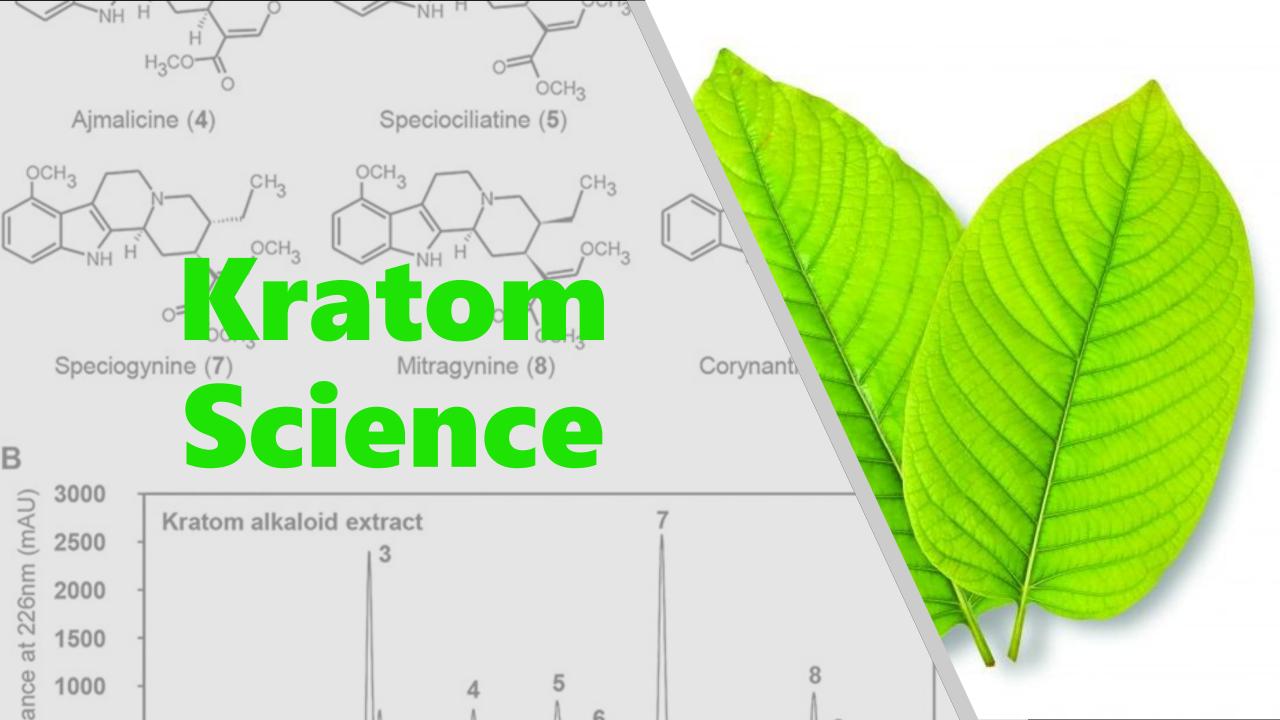




Are you evil or just totally ignorant?
7oh is DANGEROUS.
It should not be available with no regulations.
Take a peek at the quitting7oh subreddit.

I'm a mom of 4 who works in healthcare. In my past life, I was a heroin addict. I've been off the hard stuff for over a decade, but have used plant kratom consistently. The guy at the vape store gave me a sample of Pressd a year ago. It is NOT the same thing as kratom.





EVALUATING RESEARCH IS NOT...

A Google search.

Reading Wikipedia.

Listening to a podcast.

A personal story.

Reading the title of a journal article.

Reading the abstract of an article.

Reading an article summarizing research in a popular magazine or newspaper.

Evaluating research takes time, skill and critical thinking.

Correlation Does Not Imply Causation





Mayo Clinic
vs.
Johns Hopkins
&
University of
Florida



Mayo Clinic has never conducted research on Kratom. The information cited on their website is not supported by any scientific study or any real-world experience.



Johns Hopkins and University of Florida are championing Kratom research. Each boast a team of researchers committed to furthering the science around Kratom. Many of the lead researchers have published several papers helping consumers and the medical community understand this plant supplement.







Correlation Does Not Imply Causation



Many of the claims regarding kratom's effects come from individual case reports or anecdotal accounts.

As a result, these reports are often prone to bias and do not establish causality.

Many cited case reports have confounding variables such as polypharmacy, preexisting health conditions and lifestyle factors (like diet, exercise, and substance use).

Without isolating these variables, it becomes difficult to determine if kratom is the sole cause of the reported outcomes.

Read Terms Carefully.



The terms often used in reports such as:

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"linked to"
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"related to"

"associated with"

"potential effects"

- These terms reflect uncertainty and a lack of direct evidence.
- ► The use of terms that imply causality without supporting evidence can lead to misleading impressions, especially in public health communications or media reports.
- ▶ This can create unnecessary fear or stigma surrounding the use of kratom.

Read Titles Carefully.

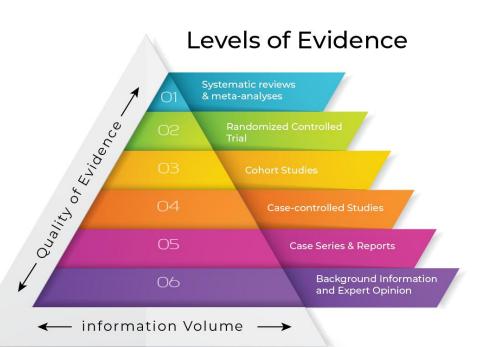
★ Article titles and abstracts can be biased and may not **★** accurately reflect the content or outcomes.

"Seizure and coma following Kratom (Mitragynina speciosa Korth) exposure." Nelsen JL, et.al., (13)

- ► The content of this article states that the patient's drug screen was positive for multiple other substances including Datura, yet the article title and abstract only mentions kratom.
- ▶ The authors acknowledge this in the content of the article by stating...

"It remains a leap to infer there is causality based on an association."

What is the evidence for the effectiveness and safety of kratom?



- Clinical and public policy decisions should be grounded in the highest quality evidence, carefully weighing benefits against potential risks for the broader population.
- Consumers have a right to make informed decisions based on accurate evidence.
- At the same time, a free society upholds individual values and preferences, ensuring that personal autonomy remains respected.

BIASED CLAIMS: Physical Effects of Kratom

Correlation Does Not Imply Causation

- Although this is large comprehensive review it is based on references with low levels of evidence-mostly single case reports with multiple confounding variables.
- Additionally, case reports may overemphasize certain outcomes and overlook mitigating factors like preexisting health conditions and polypharmacy use.
- In all cited case reports complete toxicology reports and testing of the specific Kratom products consumed were never conducted.

Kratom – Pharmacology, Clinical Implications, and Outlook: A Comprehensive Review 2020 (5)

Organ system	Presentation signs and conditions	References
Hepatic	Acute liver failure, hepatitis,	<u>23</u> , <u>108</u> - <u>116</u> , <u>131</u>
	transaminitis, intrahepatic	
	cholestasis, hepatomegaly	
Endocrine	Hypothyroidism, hypogonadism	<u>26</u> , <u>100</u>]
Renal	Acute kidney injury	<u>67</u>
Cardiac	Cardiotoxicity, arrhythmia	<u>98, 99</u>
Pulmonary	Acute lung injury, ARDS	<u>101</u> , <u>102</u>]
Obstetric	Neonatal abstinence syndrome	<u>103</u> - <u>107</u>]
Neurological	Acute brain injury, seizure, coma,	<u>21</u> , <u>81</u> , <u>117</u> , <u>118</u>
	cognitive impairment	

Correlation Does Not Imply Causation

Hepatic (Liver) - Cited Case Studies

Mitragynine metabolizes via the P450 pathway (CYP34A enzyme) through the liver. (6)

9 single patient case reports regarding hepatic effects were cited: Acute liver failure, hepatitis, transaminitis, intrahepatic cholestasis, hepatomegaly were reviewed that were used as references to the article.

Many drugs metabolize via the CYP34A enzyme. Kratom (mitragynine) has potential to interact with those.

Talk to your doctor and pharmacist.

Hepatocyte Mitragynine Phase I CYP3A4 Phase II Conjugate Smooth Endoplasmic Ret 7-Hydroxymitragynine

Correlation Does Not Imply Causation

Hepatic (Liver) - Cited Case Reports

A 58-year-old man was admitted due to jaundice and possible liver damage.

- No toxicology test was completed to test for other substances.
- Prior to this visit he had blood work done which showed liver abnormalities.
- Kratom use was discontinued for a short time and then introduced again "without the reoccurrence of liver test abnormalities."
- No ongoing liver abnormalities, yet this is a study that is cited as evidence of hepatic damage. (7)

Correlation Does Not Imply Causation

Hepatic (Liver) - Cited Case Reports

A 47-year-old male was admitted with urinary symptoms, a fever and fatigue.

- History: obesity, hypertension, prediabetic, high triglycerides, acute liver injury, nonalcoholic fatty liver disease (NAFLD), CMV hepatitis.
- The patient reported taking kratom several times over a 3-week period for his back pain. Test showed elevated liver enzymes.
- This man had a fatty liver and hepatitis, but his extremely short-term
 Kratom use caused this????
- Nine months later he was seen again for fatigue, low appetite and itching.
 He had taken kratom again a few days before being seen (his first
 consumption in nine months). It was determined Kratom had caused
 drug induced liver injury. (8)

Correlation Does Not Imply Causation

Hepatic (Liver) - Cited Case Reports

A 25-year-old man was admitted to the hospital after abdominal discomfort, jaundice and discolored urine. (published in 2011)

- Reported kratom consumption 14-20 grams/day kratom for 2 weeks.
- Severely prolonged elimination half time suggests preexisting liver damage.
- The report claims that Kratom was responsible for his intrahepatic cholestasis.
- Later in the report it states, "It seems plausible and might have been amplified by the preexisting liver damage (steatosis hepatis)." (translated-hepatitis)
- How can a preexisting condition be ignored over the short-term use of a botanical substance that millions use daily with no such results? (9)



Comprehensive Review Liver Toxicity





Nine (9) single case studies cited for evidence of liver toxicity since 2011.



All of the single case studies citing liver toxicity have confounding variables such as cooccurring substances, underlying conditions, and lack of product information.



None were fatal.



Tylenol liver toxicity:
30,000 people are
hospitalized each year for
acetaminophen toxicity.
(420,000 since 2011).



Acetaminophen toxicity is the number one cause of liver transplantation in the United States.



300 people die annually from acetaminophen toxicity.

Comprehensive Review 2024

Other Single Case Studies



All with confounding variables





Seizures:

4 single case reports



Cardiotoxicity:

2 single case reports

1 experiment on cardiac cells

Comprehensive Review 2024

Frontiers in Pharmacology

Kratom safety and toxicology in the public health context: research needs to better inform regulation.

Henningfield, Grundmann, Huestis, and Smith. (12)



Kratom- Partial Opioid Agonist

Does NOT cause respiratory depression

"In rare cases, deaths have been associated with kratom use, as confirmed by a medical examiner or toxicology reports. However, in these cases, kratom was usually used in combination with other drugs, and the contribution of kratom in the deaths is unclear."

FDA 2/2024

Full Agonist Opioids (oxycodone, morphine, fentanyl)

Causes respiratory depression

80,000 Opioid overdose deaths in 2021

Study

Effects of Kratom on Driving

- Conducted March 2024
- ► Study Size was 357 participants
- detailed survey and a 15-day ecological momentary assessment (EMA)
- For the in-person sub-study, 10 adults consumed their typical kratom products and their driving performance on a high-fidelity driving simulator pre- and post-kratom administration was evaluated.





- ► Over 90% of participants surveyed self-reported driving under the influence of kratom.
- Most reported low rates of risky driving behavior and expressed high confidence in their driving ability after taking kratom.
- Consistent with EMA findings: participants reported feeling confident in their driving ability and perceived little impairment within 15-180 min after using kratom.
- In the in-person sub-study, there were no significant changes in simulated driving performance after taking kratom. (15)

FDA Single Ascending Dose Study 2024



Randomized Controlled Trial

- ▶ To determine the tolerability of kratom.
- Subjects in both groups had nausea at 12 grams (24 capsules).
- Baylor College of Medicine is currently conducting a human abuse potential (HAP) study.

Key Kratom Study Findings

Whole leaf kratom <u>does not</u> lead to respiratory depression.

It does not recruit the beta-arrestin pathway like classical opioids

A large John Hopkins survey indicates that <10% report symptoms of mild Kratom Use Disorder.

Kratom has a wide safety range in dosing.

An FDA study demonstrated no adverse effects (other than nausea) for 12 grams (24 capsules) in a 5-minute period of time.

Despite millions of users, there are rare reports of physical harm from kratom alone.





Kratom – A Harm Reduction Perspective

- Any transition away from "one pill kills" is a win!
- Since Kratom is a partial opioid agonist and does not suppress breathing, it becomes a much safer option than opioids or illicit drugs.
- Kratom can be an affordable option when drug rehabilitation stays or ongoing suboxone treatment is not possible.
- Kratom effectively "pushes the pause button" on cravings making it possible for addicts to discontinue using dangerous substances. NOTE: Kratom is not to be taken in conjunction with alcohol.
- Kratom has been shown to reduce alcohol cravings.
- Those suffering from Substance Use Disorder can have physical pain conditions. Kratom can be a viable option to treat their pain and to transition them away from harmful opioids or illicit drugs.

An Addiction & Recovery Story

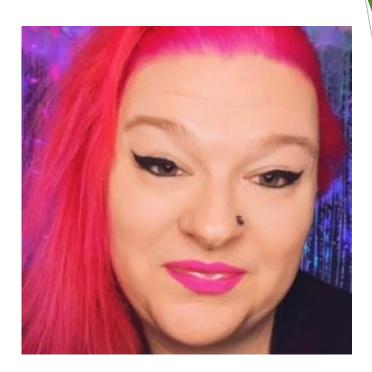
I was addicted to FDA approved pain pills, benzos and muscle relaxers for 11 years. I was fired from pain management in 2019 for being 11 pills short at a mandated pill count. I ended up going to the streets to find pills and started cocaine. In June of 2019 I watched the documentary called "A Leaf of Faith" and my journey with Kratom began the very next day.

Kratom shut that "I need one more pill, or one more escape" noise in my brain. It allowed me to work on the "whys" of my addiction. If Kratom had not been legal and accessible at a local smoke shop, I don't know where I would be today. I shudder at the thought.

I do know that five years later, I am a functioned member of society again. I am a thriving mother, and I am no longer a burden to my kids. I will be forever grateful that I found labtested whole-leaf Kratom powder.

I now pass on my journey, wisdom and science to help those struggling with addiction, chronic pain, anxiety and depression.

Misty Brown, CO





Kratom's Addiction Profile

Determining an accurate addiction profile for Kratom is challenging for the following reasons:

- Varying medical histories.
- Past or current opioid and/or illicit drug use,
- Various reasons for consuming Kratom (pain control, mood, anxiety, recreational).
- Ever growing number of different Kratom formulations and products.
- Presence of unregulated, untested and potentially contaminated Kratom products.
- Increase in 7OH addiction reports wherein these products are being misrepresented as Kratom.



Addiction Recovery Centers

It's good to know...



Suboxone is the main method of treatment for Substance Abuse Disorder. The FDA was warned that this drug has been known to cause severe dental decay. It is not meant to be taken long-term.



The US Suboxone market is estimated to be valued at \$2.29 billion in 2024 and is expected to reach \$3.15 billion by 2031. Factors such as rising opioid abuse & addiction rates, growth in awareness about drug are driving the market.

Withdrawals

"When kratom withdrawal occurs, consumers usually characterize it as <u>mild to</u> <u>moderate</u> and specify symptoms such as kratom craving, low energy, fatigue, irritability, fatigue, anxiety, depressed mood, restless legs, difficulty sleeping gastrointestinal upset, cold and hot flashes, goosebumps, and muscle twitches." (17)

Factors that play into withdrawals: (credit - Reddit thread)

- •Dosage (obviously)
- •Frequency (are you taking it every day, spread out through the day, etc)
- •Purity (are you ordering it from an AKA approved vendor with quality control or buying whatever you find at the smoke shop)
- •Extracts (do you stick to just powder or do you use extracts)
- •Past opiate use (this one is something I'm not as sure about, but I have seen a correlation between people who have abused hard drugs like heroin, fent, pills, etc. for years and having more severe withdrawals)
- •Cessation (do you slowly taper down or cold turkey)

Kratom & Addiction Summary



Like any other substance, food, medication or supplement, Kratom must be respected.

While not classified as a highly addictive substance like opioids or other controlled drugs, Kratom does have the potential to lead to dependence in some individuals (especially those with past drug abuse), especially if misused.

The vast majority of Kratom consumers are not abusing Kratom.

Caution should be taken if consuming Kratom extracts since they contain more concentrated mitragynine content and can more quickly cause tolerance issues.

7-OH products are addictive and must be avoided. These products are NOT Kratom.

Banning or severely restricting access to Kratom products due to some reports of abuse is not the answer. Millions consume alcohol responsibly, yet there are abusers. History has shown that prohibition comes with unintended consequences.



Is Kratom Deadly?

SUBSTANCE	MECHANISM OF DEATH	APPROXIMATE ANNUAL NUMBER OF DEATHS (2023)
Tobacco	Lung cancer, heart disease, or chronic obstructive pulmonary disease (COPD	480,000
Alcohol	Liver failure, respiratory depression, or accidents due to impaired motor skill	95,000
Opioids including Fentanyl	Respiratory failure due to depression of the brain's respiratory centers	81,083
Methamphetamine	Hyperthermia, cardiac arrest, or stroke due to increased heart rate and blood pressure	33,000
Cocaine	Cardiac arrest or stroke due to increased heart rate and blood pressure	24,000
Benzodiazepines	Respiratory depression	11,537
Antidepressants (SSRI, SNRI)	Cardiac arrest, seizures	2,700
Acetaminophen (Tylenol)	Liver damage	500
Antihistamines	Cardiac arrest, seizures	200
	https://www.cdc.gov/nchs/data/databriefs/db521.pdf https://www.medicalnewstoday.com/articles/off-label- drug-use#reasons-for-use	

Deaths attributed to Kratom often lack thorough investigations.

Most cases are missing one or more critical elements, including:



Incomplete toxicology testing for substances other than mitragynine, including novel substances.

A thorough scene investigation to identify the presence of all potentially toxic compounds.

A consideration of all the circumstances of death.

An investigation into the decedent's past drug use history, past medical history of overdoses, rehabilitation stays, law enforcement records etc. to determine potential additional relevant drugs to test.

Preexisting Health Conditions.

Things to Consider in a "Kratom Death"



- 1. Has the full toxicology report been released?
- 2. Was polydrug use involved?
- 3. Were underlying health conditions reviewed?
- 4. Was the product found in the home/car/location of the death. If so, were other substances tested for?
- 5. Was the product found on the scene tested?
- 6. Was the product 7-OH or another synthetic?
- 7. If the family member (in a news story) claims that the decedent was spending hundreds of dollars per day, this is most likely abuse of 7-OH. These tablets can be \$10/each which could add up quickly. Regular kratom is relatively inexpensive.
- 8. Kratom has a built-in ceiling effect. If a consumer consumes too much, the person will vomit. For a person to drink or swallow hundreds of dollars per week worth of kratom, this person would be extremely sick. No so with 7-OH products.
- 9. Often these "deaths" occur in those who are addicts. Surviving family members will often dismiss other drug seeking behaviors and assign blame to kratom claiming that the decedent "thought the product was natural and safe."

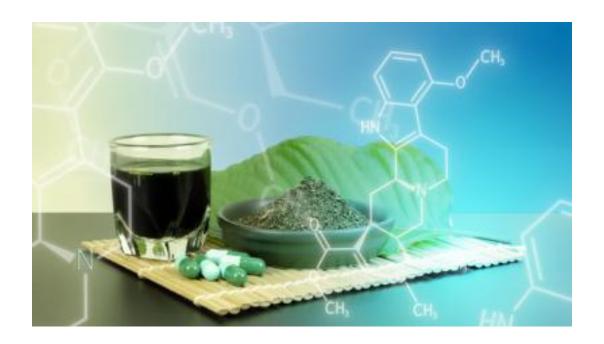




The most compelling statement is from the FDA's own website:

"In rare cases, deaths have been associated with kratom use, as confirmed by a medical examiner or toxicology reports. However, in these cases, kratom was usually used in combination with other drugs, and the contribution of kratom in the deaths is unclear."

https://www.fda.gov/news-events/publichealth-focus/fda-and-kratom



Kratom * Government * Regulations * Safety







FDA & DEA



The FDA has had a long-standing concern regarding Kratom claiming safety concerns, lack of regulation, potential for abuse and lack of scientific evidence.

Timeline & Facts

- 2016 Due to public outcry, the rescheduling is postponed.
- In August, HHS Assistant Secretary for Health Brett Giroir MD formally withdrew the FDA's scheduling recommendation for kratom, citing "disappointingly poor evidence & data and a failure to consider the overall public health." This is the first time in history that the DEA has withdrawn a scheduling request.
- 2024 FDA announces their intent to conduct a Human Abuse Potential (HAP) Study for Kratom.
- FDA conducts Single Ascending Dose (SAD) Study and finds that Kratom is safe so HAP study can occur at a future date.
- FDA refuses to testify in a court case. "They [FDA] have refused to provide us with witnesses or documents to support our position . . . The reason they gave was that they have not yet made a determination regarding whether kratom is dangerous."
- FDA publishes safety notice regarding 7-OH products.

2025 Kratom State Legality & Legislation



Blue – Legal & KCPA passed

Green – Legal states

Yellow – States with some local bans

Red – States with kratom bans in place

Key Elements of the Kratom Consumer Protection Act

Age restricted

Good Manufacturing Practices (GMP)

Proper labeling

Lab testing

Limitations on concentrating or synthesizing

Properly Labeled GMP Kratom Product







KCPA State and Local Legislation

Enact
Educate
Enforce

It's the way forward!

Protect consumers while preserving safe access.

For More Information About Kratom:

www.kratomanswers.org
www.americankratom.org
www.protectkratom.org
www.kratomstoriespodcast.com



Understanding Kratom Use: A Guide for Healthcare Providers

Marc T Swogger ^{1,*}, Kirsten E Smith ², Albert Garcia-Romeu ³, Oliver Grundmann ^{4,5}, Charles A Veltri ⁴, Jack E Henningfield ^{3,6}, Lorna Y Busch ¹

in Pharmacology

<u>Link:</u> <u>Understanding Kratom Use: A Guide for Healthcare</u> Providers - PMC



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