AMERICAN KRATOM ASSOCIATION

KEY KRATOM QUESTIONS AND ANSWERS

Why does the FDA claim kratom is unsafe for consumers?

The FDA has a long-standing bias against any dietary ingredient, botanical supplement, or dietary supplement that is not a chemical formulation subject to regulatory approval as a new drug. In 1994, Congress passed the Dietary Supplement Health and Education Act (DHEA) to reign in the FDA's overregulation of dietary supplements FDA wanted banned on the premise they were highly addictive, being used to self-medicate without physician supervision, or were so poorly formulated these products posed a threat to public health requiring them to be banned.

Today, FDA maintains the same three common objections about kratom, i.e., kratom is unsafe, is highly addictive, and has no approved medical use — and people are using it to self-medicate to withdraw from opioid addictions. Accordingly, FDA has made three specific attempts to have kratom's constituents, mitragynine ("MG") and 7-hydroxymitragynine ("7-HMG"), as Schedule I substances. Based on current science, leading public health officials have reviewed the current evidence and data on kratom and vigorously disagree with the FDA's assessment of kratom's addiction and safety profile. All three of the FDA's recommendations for scheduling have been rejected by the Drug Enforcement Administration; the U.S. Department of Health and Human Services (HHS); and the Expert Committee on Drug Dependence (ECDD) for the U.N. Commission on Narcotic Drugs.

The FDA claims kratom should be classified as a Schedule I substance, so why is kratom not scheduled today at the federal level?

The short answer is because the FDA is wrong on the science, and wrong on the policy. Other federal and international agencies have carefully evaluated the FDA's claims and they find they lack sufficient evidence to support the FDA claims.

- October 13, 2016: The DEA withdrew the Notice of Intent recommending the temporary scheduling of kratom and requested a full 8-Factor Analysis from the FDA.
- August 16, 2018: HHS Assistant Secretary for Health, Brett Giroir, M.D., formally withdrew the FDA scheduling recommendation for kratom that had been submitted to the DEA and called out the FDA for "disappointingly poor evidence & data and a failure to consider the overall public health."
- December 1, 2021: The Expert Committee on Drug Dependence at the World Health Organization and the U.S. Commission of Narcotic Drugs, comprised of 12 international experts on substance safety and addiction, unanimously concluded that there was insufficient evidence to recommend a critical international scheduling review of kratom.

- March 16, 2022: Letter from HHS Secretary Becerra acknowledging "knowledge gaps" on kratom and that "kratom-involved overdose deaths have occurred after use of adulterated kratom products or taking kratom with other substances."
- December 29, 2022: President Biden signs the FY23 Omnibus with kratom report language commending NIDA for funding studies on kratom that "may provide help for some Americans struggling with addictions, given its analgesic and less addictive properties as compared to opioids."

While the FDA has previously maintained the position that kratom poses a danger to the public, the agency refused to participate in a hearing ordered by a federal judge scheduled on February 8, 2024, in the Southern District of California, to provide witnesses and documents to prove the validity of the FDA's claims that kratom is a dangerous substance. This case was initiated by the FDA against an importer who had falsely identified kratom raw materials on the shipping manifest documents which resulted in a guilty plea. In the sentencing phase of the case, the Judge wanted more information from the FDA on their claims on the danger of kratom. In an email from the Assistant U.S. Attorney[1] the following explanation was provided to the Court on why the FDA refused to participate in the Hearing:

> "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**." (emphasis added)

The reason for that change in the FDA's position reportedly is because the FDA had recently completed a Single Ascending Dose ("SAD") study on whether kratom can be safely consumed by humans, and an abstract of the results of that study were reported at the 3rd International Kratom Symposium in Orlando, Florida on February 16, 2024. This study concluded that **"kratom appears to be well tolerated in humans at all dose levels."** (emphasis added)

Commented [LK1]: What should be emphasized here?

In the SAD study, the FDA found that only two human subjects of the 40 participants experienced nausea only after the consumption of 12 grams of kratom, 24 capsules, within five minutes. The response was the same for both the kratom cohort and the placebo cohort demonstrating the nausea was related to consuming a high volume of plant material in a five-minute period. None of the subjects reached the study's "stopping criteria" that would have resulted in termination of the study, but the FDA stopped the study because it concluded that kratom is well tolerated even at extremely high levels. This FDA study demonstrates conclusively that kratom does not meet the criteria for scheduling.

Is it true there is no approved medical use for kratom?

> That claim is true, but it is also true for tens of thousands of foods, dietary ingredients, botanical supplements, and dietary supplements that are available to consumers in the U.S., many of which are regularly used to self-medicate by consumers to maintain their health and well-being. Federal law provides adequate authority for the FDA to prosecute any vendors who make illegal therapeutic claims to induce consumers to buy their products for therapeutic uses. In response, the AKA has submitted more than 70 documented cases of kratom vendors using illegal marketing claims on some therapeutic benefits they claim are associated with kratom consumption. Despite having sufficient legal authority to protect consumers from such illegal

[1] *Case 3:23-cr-00179-TWR Filed 12/06/23 Page ID.1032 Exhibit 6; United States of America, Plaintiff, v. Nine2Five, LLC (1) Sebastian Guthery (2), Defendants*

marketing schemes, the FDA has not initiated a single prosecution against any of those violators.

How many states have enacted the Kratom Consumer Protection Act?

As of today, 14 states have passed similar versions of the KCPA: Utah, Georgia, Arizona, Nevada, Oregon, Colorado, Oklahoma, West Virginia, Virginia, Texas, Florida, Kentucky, Maryland, and South Dakota.

What is the status of the six states that banned kratom at the request of the FDA?

The FDA has vigorously engaged in a disinformation campaign against kratom for more than a decade. Six states did enact bans from 2021 to 2017, all in good faith, and all on the premise the FDA information was accurate: Alabama, Arkansas, Wisconsin, Indiana, Vermont, and Rhode Island. Now those states are starting to push back against the FDA disinformation, and most are actively working to correct the mistakes made in response to the requests by the FDA.

- Vermont followed the FDA's recommendation to schedule kratom in 2016. Pursuant to a petition filed with the Vermont Department of Health to remove mitragynine and 7-hydroxymitragynine from the Regulated Drug Rule, the Department granted the petition submitted by the American Kratom Association ("AKA") on March 1, 2023, and will commence rulemaking shortly to complete that process, stating as follows: "This email it to apprise you that the Department is granting your petition to remove mitragynine and 7-hydroxymitragynine form the Regulated Drug Rule."

- Wisconsin is another state that banned kratom on the recommendation of the FDA, and the Wisconsin Controlled Substances Board ("CSB") received a report from Dr. Chris Cunningham, Associate Professor of Pharmaceutical Sciences at Concordia University Wisconsin, with the following conclusion:

  > "Based on our review of the available literature, we conclude that regulation of M. speciosa in Wisconsin as a schedule-I substance is not justified at this time. We base this conclusion, in part, on the scientific evidence demonstrating that M. speciosa and its chemical constituents have lower potential for overdose and abuse relative to other agents that are not scheduled in this way. We believe that controlling M. speciosa and its chemical constituents under schedule-I harms public health and stifles much-needed research into its therapeutic and toxic properties."

  In response, members of the Wisconsin Legislature asked the CSB for an assessment of whether kratom's constituents meet the statutory requirements for scheduling under the 8-factor analysis. On March 10, 2023, the CSB approved a motion to affirm mitragynine and 7 hydroxymitragynine do not meet the required 8-factors for scheduling under Wisconsin law.

- The Interim Director of the Rhode Island Department of Health, Utpala Bandy, M.D., has acknowledged that kratom does not meet the criteria for scheduling set forth in Rhode Island statutes.

- In Indiana, the House of Representatives took the first step to remove the kratom ban and enact the Kratom Consumer Protection Act in a vote of 54-30 on February 21, 2024. The bill has now under consideration in the Senate.

Is the FDA claim true that kratom is an opioid?

No, kratom is not an opioid by plant genetics, by chemical structure, or by legal definition.

While some naturally occurring substances in kratom act on opioid receptors, kratom is not a prototypical opioid based on its chemical structure, botanical origins, or law – nationally or internationally. Like many natural products it has diverse effects and mechanisms of action that contribute to these effects and the reasons people use kratom.

Properly characterized as “partial agonists” some kratom constituents bind to opioid receptors and relieve pain whereas others do not. Unlike opioids which sedate and can impair mental functioning, kratom is used by many people in place of coffee for its alerting, mental focusing, and occupational performance enhancing effects.

Animal and human studies, as well as neuropharmacology mechanisms of action studies, show that kratom does not carry the substantial opioid-like risks of deadly respiratory depression or powerfully addictive euphoria. A misunderstanding of one of kratom’s self-reported beneficial uses, recognized by researchers and NIDA, providing relief of opioid withdrawal, is sometimes interpreted as evidence that it must be an opioid. In fact, the nonopioid adrenergic blocking drugs developed for treating high blood pressure, clonidine and lofexidine, were prescribed for decades to treat opioid withdrawal. FDA approved lofexidine (Lucemyra) for treating opioid withdrawal in 2018. Mitragynine and other kratom constituents also produce adrenergic effects.

Is the FDA claim true that kratom is dangerously addictive?

No, the FDA is completely wrong on this point. There is a significant difference between addiction and dependency, and there is a similar significant difference between a dangerous addiction and a socially acceptable benign addiction or dependency. Caffeine is the most widely used drug in the world and it has an addiction profile that is characterized by scientists, and the FDA, as having an acceptable addiction profile.

NIDA has conducted two specific animal studies on the addiction liability of kratom, with the following results:

- Abuse liability and therapeutic potential of the Mitragyna speciosa (kratom) alkaloids mitragynine and 7-hydroxymitragynine. "The present findings indicate that MG does not have abuse potential and reduces morphine intake, desired characteristics of candidate pharmacotherapies for opiate addiction and withdrawal, whereas 7-HMG should be considered a kratom constituent with high abuse potential that may also increase the intake of other opiates.” (*See* https://pubmed.ncbi.nlm.nih.gov/29949228/)

- Abuse liability of mitragynine assessed with a self-administration procedure in rats. "These results suggest a limited abuse liability of mitragynine and potential for mitragynine treatment to specifically reduce opioid abuse. With the current prevalence of opioid abuse and misuse, it appears currently that mitragynine is deserving of more extensive exploration for its development or that of an analog as a medical treatment for opioid abuse.” (*See* https://pubmed.ncbi.nlm.nih.gov/30039246/)

The available data suggest relatively low abuse potential as compared to morphine-like opioids, stimulants, and other drugs of abuse that demonstrate robust rewarding effects across all such abuse potential models. Similarly, MG’s potential to produce physical dependence and withdrawal appears relatively low, but not absent, as compared to opioids in animal models. These findings are generally consistent with human reports that MG has a relatively low abuse and withdrawal potential as compared to recreationally used opioids but can reduce opioid self-administration and withdrawal.

Is the FDA claim true that kratom is a deadly drug that people are dying from?

No, this FDA claim about deaths associated with kratom has been reviewed by experts and found to be untrue. It is well understood that kratom's respiratory effects are not like those of morphine-like opioids and peer-reviewed published studies since 2018 support the conclusion that kratom is not simply weaker than opioids with respect to respiratory depression, kratom does not cause respiratory suppression and associated overdose death.

Specifically, mitragynine and other alkaloids in kratom act as partial agonists at opioid receptors, meaning that their maximal effects reach a ceiling beyond which higher doses produce little additional effect. This was demonstrated in several animal species (including cats, dogs, mice, and rats) with mitragynine doses increased to levels far beyond what is or can be consumed by even high intake chronic kratom consumers.

The most recent study employed a sophisticated rodent model developed by FDA to compare a broad range of mitragynine doses to therapeutic and toxic oxycodone doses across blood gases and other parameters. Whereas oxycodone produced the signature dose-related plummeting blood oxygen levels and deaths, mitragynine produced no evidence of respiratory depression at any dose, and no life-threatening effects.

Why does the DEA list kratom as a "Drug of Concern"?

The DEA has appropriately listed kratom as a "Drug of Concern" based on the conflicting reports made by the FDA, particularly with the deliberate adulteration and mislabeling of kratom products by some unscrupulous vendors in the kratom marketplace. Common adulterants include fentanyl, heroin, buprenorphine, and morphine. The DEA simply maintains surveillance of kratom to review reports of adverse events to potentially identify and interdict such adulteration with dangerous substances.

Importantly, kratom has never been listed by the DEA on their National Drug Threat Assessment (NDTA) report. This report assesses the threat posed to the U.S. by the trafficking and abuse of illicit drugs.

Why does the FDA have two import alerts on kratom?

The FDA has used import alerts to create a de-facto ban on kratom since they cannot meet the requirements for scheduling under the Controlled Substances Act (CSA). While clearly an abuse of its regulatory authority, the premise of the import alerts is based entirely on the contrived and wholly inaccurate addiction and safety profile promoted by the FDA itself.

Can you overdose on kratom itself?

The overall risk for kratom overdose appears at least 1,000 times lower for kratom as compared to opioids.

There were no deaths in which either the FDA or CDC confirmed as appropriately categorized as due to kratom consumption. Kratom consumers should not assume that kratom is without risk, but like many common consumer products, responsible use is a key safety factor. The CDC did not list kratom as a cause of any of the more than 108,000 drug overdose deaths in 2021, or in any other year of which we are aware.

In contrast, opioids were concluded by the CDC and NIDA to account for more than 80,000 overdose deaths in 2021. Overdose is possible with many readily available consumer substances, including caffeine, but kratom's most common side-effect, transient stomach upset and nausea, also limits intake and is discomforting but not seriously harmful. In February 2018,

after announcing that kratom carried opioid-like death risk, the FDA noted that only one of 43 deaths occurring in kratom consumers did not involve other respiratory depressing substances. Further investigation found that the final cause was a motor vehicle fatality involving a kratom consumer.

In a review of the 44th death reported by the FDA to have been caused by kratom ingestion, when the autopsy report was obtained the actual cause of death was two gunshot wounds to the chest that occurred during a drug sting operation by law enforcement. The decedent had incidentally consumed a kratom tea on the morning he was shot.

NIDA, FDA, HHS, and ECDD all have concluded that most kratom-associated deaths involved other substances.

What is the profile of the typical kratom consumer.

According to surveys in the US, most consumers report are White adults, aged 35-55, with jobs and health care insurance, who report that their consumption is primarily for health and wellbeing. This includes consumption as an alternative to caffeinated products for alertness and increased focus, for the self-management of pain, and to improve mood.

Many consumers state that kratom worked better for them, had fewer side-effects than the FDA-approved medicines that had been taken, and/or that they preferred natural products. A smaller but especially important fraction of consumers are people who consider kratom as a “life-line” or a path away from opioids. They use kratom to manage opioid withdrawal and reduce or eliminate opioid use.

What forms do kratom products use in the marketplace?

It is well known that kratom has a bitter taste, which accounts for why pure, unadulterated kratom products are not attractive to minors. Kratom is sold in powder form, which is typically brewed into a tea by adding hot water – although some consumers consume the powder orally; in capsule or pill forms that bypass the bitter taste; and in liquids much like a five-hour energy drink. Kratom critics frequently point to kratom products being sold in convenience stores or gas stations as evidence of their harm. To the contrary, the most important protection for consumers is to make certain that every kratom product offered meets the manufacturing criteria for its content; is free from dangerous adulterants; is labeled properly; and is not sold to minors.

Some kratom products are “extracted” to (1) purify to remove any microbial contaminants; and (2) to standardize the alkaloid content of each serving size recommended for use of those products. Like any other consumer product similarly extracted, including coffee, plants and fruits, and essential oils, these extracts must use approved FDA food-grade solvents to complete the extraction process safely.

Many kratom critics claim all liquid kratom products are extracts. That is not true. Extracted kratom products are across all product forms, and the key to their safety is the use of safe extraction solvents and directions on appropriate serving sizes.

What does recent science reveal about kratom?

Since 2018, there have been more than 100 new published research articles on kratom. While there are public references to that research, a recent presentation on new science on kratom

was made at the UN Commission on Narcotic Drugs Conference in Vienna on March 16, 2023.

Here are links to video of presentations made by 4 of the world's leading experts on kratom at that conference:

- Here is the link to the entire presentation (about 50 minutes long): https://youtu.be/oztAWZAaxGo
- Here are individual segments from each presenter – each is about 10 minutes long.
    - Dr. Marilyn Huestis, former NIDA official now with Thomas Jefferson University:

      https://youtu.be/SbQtzs4uphQ
    - Dr. Kirsten Smith, NIDA:

      https://youtu.be/aLS-ZbV5kIk
    - Dr. Jack Henningfield, Pinney Associates and Johns Hopkins University:

      https://youtu.be/oZj9TlFF8eI
    - Dr. Chris McCurdy, University of Florida:

      https://youtu.be/KBRXbRcydoE

Summary:

Kratom is safely used by consumers for a variety of purposes, chief of which is for its energy boost and increased focus effects, typically as a replacement for a cup of coffee. Research indicates kratom can act as a pain reliever for acute and chronic pain and potentially even treat opioid withdrawal. The National Institute on Drug Abuse (NIDA) has currently funded more than $30 million in kratom research studies, including several grants totaling $15 million at the University of Florida. The U.S. Congress issued Report Language in each of the last four annual budgets calling for further research to expand studies on kratom.

Pure kratom products, when used responsibly, are safe. Studies conducted by the NIDA confirm kratom has no significant addiction liability. Any deaths allegedly associated with kratom are due to adulterated kratom, polydrug use, or underlying health conditions. To protect American consumers, suitable public policy kratom solutions require appropriate regulation.

For additional information go to www.kratomanswers.org.