AMERICAN KRATOM ASSOCIATION

POLICY BRIEF

No. 1001 | January 2021

What Is Kratom?

Kratom is a tree that grows naturally in South East Asia (SEA) and is a part of the coffee family. Kratom is typically consumed by chewing on the natural leaves or to brew them in a tea. Kratom has been used safely in SEA for centuries for an energy boost, increased focus, and general well-being. Kratom has also been safely used in the U.S. since the early 1970's.

At higher serving sizes, kratom has been found by many to be an effective pain reliever for acute and chronic pain, and to wean off highly-addictive and potentially deadly opioid medications. In the United States, where it is estimated between 11 - 15 million American consume kratom regularly, and kratom products are typically sold as powders, capsules, or liquid tinctures (like a 5-hour energy drink).

Importantly, SEA authorities have not reported any kratom overdose deaths. The reasons for kratom use in this region largely mirror those in the U.S., including as a mild stimulant by agricultural workers and as an alternative to opioids for pain relief and addiction treatment. Such traditional use is reported to benefit quality of life, and improve social and occupational behavior, with little evidence of serious personal or social harm. Overdose deaths attributed to kratom by the FDA in the U.S have been found to be from polydrug use and adulterated kratom products.

Kratom is currently legal for sale as a food in all but 6 states, but the FDA has repeatedly recommended scheduling the two primary alkaloids in kratom, mitragynine (MG) and 7-hydroxymitragynine (7-HMG).

The DEA has not acted on the FDA's recommendation. If the FDA's assertions on the safety and pharmacological profile were credible, particularly with the claims of deaths and opioid-like effects of kratom, the DEA would have quickly published a Notice of Scheduling to protect

KEY FINDINGS

Kratom is a tree that grows in Southeast Asia that is part of the coffee family and has been safely consumed there for centuries.

Between 11 and 16 million Americans safely consume kratom products as a preference to conventional medicines because of its low rate for adverse events and its relative safety.

Kratom is not an opioid, and the FDA**'s** disinformation campaign incorrectly misleads public policy makers on the pharmacology of kratom.

Kratom is not addictive like classic opioids, and studies funded by NIH and NIDA demonstrate kratom does not have any significant addiction liability.

The DEA has refused to accept the FDA's recommendation to schedule kratom. The DEA is the decision-maker on scheduling per the Controlled Substances Act.

A 2020 Johns Hopkins study of adult kratom users revealed 87% of those using kratom for opioid dependence reported kratom provided relief from withdrawal symptoms, and 35% were free from opioids > 1 year.

the public health. More than four years has elapsed since the FDA scheduling petition was first submitted to the DEA without any scheduling action. The DEA typically acts with 90 days of any scheduling recommendation where evidence proves a public safety or health risk to justify such action.

Is the FDA Correct that Kratom is an Opioid:

Kratom is a tree that is a part of the coffee family. The pharmacological effects of kratom's alkaloids are fundamentally different from morphine and other euphoriant opioids that induce respiratory suppression. The FDA's claims on this issue are based on their efforts to seize regulatory control over kratom to force kratom processors into being required to submit a new drug application (NDA).

MG and 7-HMG are G-protein biased, partial agonists whereas morphine is a non-biased, full agonist at mu opiate receptors. Furthermore, the binding profiles of MG and 7-HMG differ from morphine in terms of their affinities and selectivities for opiate and other receptors. Thus, whereas morphine serves as a robust reinforcer for animals, MG did not serve as a reinforcer in the two animal intravenous self-administration studies that have evaluated it (*Hemby et al., 2018; Yue et al., 2018*).

Like a significant number of dietary ingredients and supplements currently on the market in the United States, no one can say that kratom has never caused or contributed to death, that kratom carries no risks, or that kratom and specific alkaloids cannot under some conditions cause respiratory depression. However, the science does not support the conclusion that it is a morphine-like opioid on this critical aspect of opioid pharmacology and toxicology.

A recent peer-reviewed published article (Henningfield, Grundmann, Babin, Fant, Wang, & Cone[i]) found that opioids have at least a 1,000 times greater risk of overdose deaths than using kratom. The study emphasizes that more research on kratom safety and risks is needed, and regulation of commercial kratom products to ensure that consumers are informed by FDA labeling and that kratom products are not contaminated or adulterated with other substances.

Is Kratom Addictive like Classic Opioids:

Kratom is not addictive because it does not produce the reinforcing euphoric high as opioids do. Withdrawal from kratom dependency generally matches caffeine withdrawal (4-5 days of mild headache, upset stomach, etc.)[ii]. Kratom's alkaloids, like caffeine in coffee, can result in a consumer developing a dependency with regular use. Classic opioid withdrawal mostly involves severe symptoms and typically requires extensive in-patient detox treatment programs that can last months.

Importantly, kratom's alkaloids do not have a significant addiction liability as classic opioids do. Even then, kratom's alkaloids have been classified as "atypical opioids" (*Kruegel, et. al*.[iii]) that do not have the same respiratory suppression effects as classic opioids like morphine. Most of the published literature references to kratom's "opioid-like activity" is derived from findings in cell and animal studies where mitragynine has been found to bind to and activate opioid receptors and produce some analgesic effects (*Adkins, et. al.*[iv], *Boyer et. al.*[v], *Kruegel, et. al.*[vi]), but there is strong evidence indicating that kratom's effects are distinct from those of classic opioids (*Henningfield, et. al.*[vii], *Singh, et. al.*[viii], *Vicknasingam*[ix]).

The U.S. National Institutes of Health (NIH) and NIDA each commissioned an independent animal study, the gold standard in addiction research, to determine the addiction liability of kratom's alkaloids.

- A NIH funded peer-reviewed and published study concluded (1) that **kratom is not dangerously addictive** and does not act in the same way as classic opioids in suppressing the respiratory

system of the consumer, and (2) that the **alkaloids in kratom actually have the effect of reducing the cravings in the animals for morphine** (*Hemby, Addiction Biology, 27 June 2018*[x]) That finding helps explain why so many struggling with opioid use disorder in the United States are attempting to use kratom to reduce their opioid use or wean off opioids entirely, and helps us understand why kratom shows up in toxicology screens of opioid overdose victims who apparently had turned to kratom for its potential benefits in fighting their opioid addictions.

- A second intramural NIDA study confirmed that kratom **is not dangerously addictive** and concluded that more research needed to be done on the value kratom could have as an alternative pain management therapy to opioids (*Yue, Psychopharmacology, July 2018*[xi]).

NIDA has currently funded more than $15 million in kratom research studies, including two grants totaling $6.9 million over the next 5 years at the University of Florida[xii] that will investigate the potential for kratom's alkaloids to treat opioid withdrawal. The University of Florida research team supported in their grant submissions affirming that "studies indicate that mitragynine does not exhibit abuse-related effects and can attenuate opioid intake"[xiii].

Additionally, the U.S. House of Representatives has called on NIH to expand studies on kratom (*House Committee on Appropriations LHHS, 2020*[xiv]), and specifically opposed a ban on kratom that would significantly impede needed new research. The House Report also stated the Committee "is aware of the potential promising results of kratom for acute and chronic pain patients who seek safer alternative to sometimes dangerously addictive and potentially deadly prescription opioids".

A 2020 Johns Hopkins University survey of adult kratom consumers revealed that for those using kratom to treat opioid dependence, 87% reported relief from withdrawal symptoms. An astounding 35% reported they were opioid free > 1 year[xv].

Conclusion:

Pure kratom used responsibly, like thousands of other dietary supplements and over-the-counter drugs, is safe for use. It is estimated that about a third of kratom consumers use it to manage acute and chronic pain as an alternative to dangerous opioids or to reduce or wean off opioids entirely.

Some unscrupulous bad actors in the kratom marketplace have found a lucrative market for dangerously adulterated kratom products spiked with fentanyl, heroin, morphine, and other opioids to deceive consumers by giving the kratom product an "opioid kick" when they think they are purchasing pure kratom. These spiked kratom products should be banned from the marketplace just like any other adulterated or misbranded drug. NIDA conducted its own review of the deaths reported by the FDA to be associated with kratom and concluded that all resulted from polydrug use or adulterated kratom products, and even the FDA now concurs with that assessment[xvi].

Consumers currently are put at unacceptable risk by an unregulated kratom marketplace where it is the "wild west" and no appropriate regulatory scheme is in place to ensure kratom products are pure and unadulterated. The Kratom Consumer Protection Act requires kratom be pure, not adulterated or synthesized to alter the alkaloids in the natural plant, be labeled properly, and be subject to an appropriate age restriction.

[i] Risk of Death associated with kratom use compared to opioids; Henningfield, Grundmann, Babin, Fant, Wang, Cone, Preventative Medicine, Nov. 2019, https://www.ncbi.nlm.nih.gov/pubmed/31647958
[ii] *Kratom use and mental health: A systematic review*; Swogger, and Walsh; Drug and Alcohol Dependence, 2018.
[iii] Kruegel, A. C., Uprety, R., Grinnell, S. G., Langreck, C., Pekarskaya, E. A., Le Rouzic, V., … Sames, D. (2019). 7-Hydroxymitragynine Is an Active Metabolite of Mitragynine and a Key Mediator of Its Analgesic Effects. *ACS central science*, *5*(6), 992–1001. doi:10.1021/acscentsci.9b00141
[iv] Adkins, J. E., Boyer, E. W., & McCurdy, C. R. (2011). Mitragyna speciosa, a psychoactive tree from Southeast Asia with opioid activity. Current Topics in Medicinal Chemistry, 11(9), 1165–1175 doi:BSP/CTMC/E-Pub/-00019-11-3 [pii].
[v] Boyer, E. W., Babu, K. M., Adkins, J. E., McCurdy, C. R., & Halpern, J. H. (2008). Self treatment of opioid withdrawal using kratom (Mitragyna speciosa korth). Addiction, 103(6), 1048–1050 doi:ADD2209 [pii];10.1111/j.1360-0443.2008.02209.x.
[vi] Kruegel, A. C., & Grundmann, O. (2018). The medicinal chemistry and neuropharmacology of kratom: A preliminary discussion of a promising medicinal plant and analysis of its potential for abuse. Neuropharmacology, 134(Pt A), 108–120. https://doi.org/10.1016/j.neuropharm.2017.08.026
[vii] Henningfield, J. E., Fant, R. V., & Wang, D. W. (2018). The abuse potential of kratom according the 8 factors of the controlled substances act: Implications for regulation and research. Psychopharmacology (Berl), 235(2), 573–589. https://doi.org/10.1007/s00213-017-4813-4.
[viii] Singh, D., Muller, C. P., & Vicknasingam, B. K. (2014). Kratom (Mitragyna speciosa) dependence, withdrawal symptoms and craving in regular users. Drug and Alcohol Dependence, 139, 132–137 doi:S0376-8716(14)00793-5 [pii];10.1016/j.drugalcdep. 2014.03.017.
[ix] Vicknasingam, B., Narayanan, S., Beng, G. T., & Mansor, S. M. (2010). The informal use of kratom (mitragyna speciosa) for opioid withdrawal in the northern states of peninsular Malaysia and implications for drug substitution therapy. International Journal on Drug Policy, 21(4), 283–288 doi:S0955-3959(09)00164-9 [pii];10.101 j.drugpo.2009.12.003.
[x] Hemby et al. "Abuse liability and therapeutic potential of the Mitragyna speciosa (kratom) alkaloids mitragynine and 7-hydroxymitragynine," Addiction Biology, 27 June 2018, doi: 10.1111/adb.12639.
[xi] Yue K, Kopajtic, Katz, Abuse liability of mitragynine assessed with a self-administration procedure in rats, Psychopharmacology, 2018, https://www.ncbi.nlm.nih.gov/pubmed/30039246
[xii] https://www.floridatrend.com/article/26834/nida-awards-uf-college-of-pharmacy-additional-34-million-kratom-grant
[xiii] https://addictionresearch.health.ufl.edu/2019/08/30/research-kratom/
[xiv] U.S. House of Representatives, Departments of Labor, Health And Human Services, and Education, and Related Agencies Appropriations Bill, 2020, pages 100 and 102. https://www.congress.gov/116/crpt/hrpt62/CRPT-116hrpt62.pdf.
[xv] 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. doi:10.1016/j.drugalcdep.2020.107849
[xvi] https://www.drugabuse.gov/publications/drugfacts/kratom