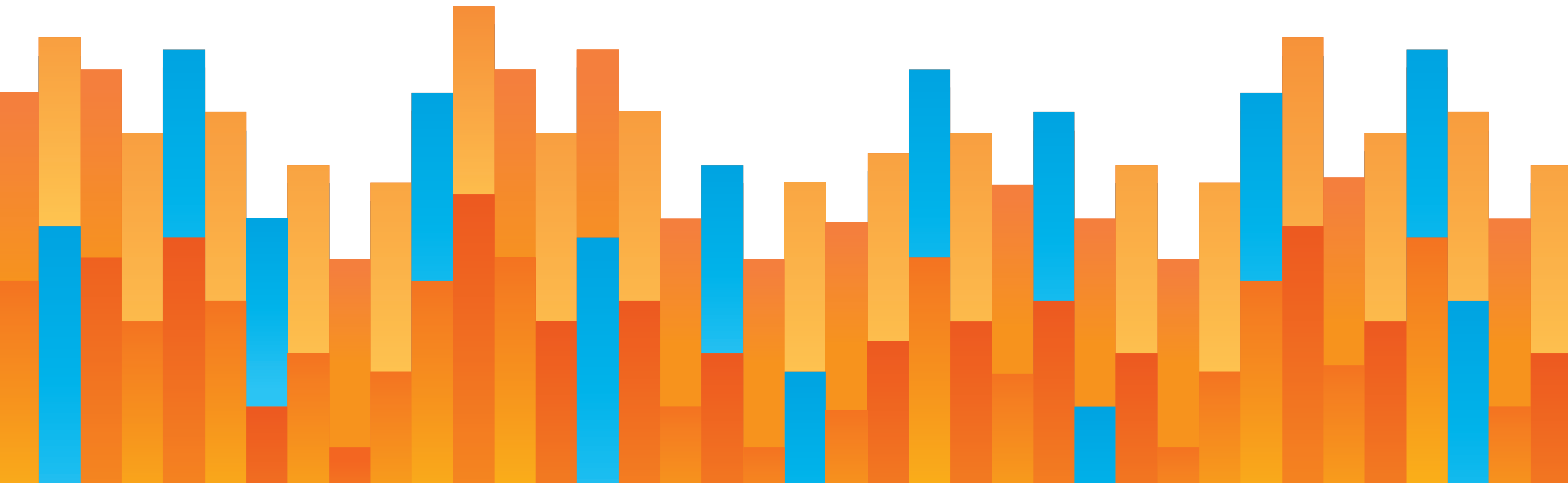
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KRATOM AND ITS ALKALOIDS:
A BALANCED REVIEW OF THE SCIENCE AND STATE REGULATION

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EXECUTIVE SUMMARY

Kratom (Mitragyna speciosa) is a tree native to Southeast Asia, where its leaves have been chewed or brewed into tea for generations to manage pain, combat fatigue, and ease opioid withdrawal. In recent decades, its use has spread to the Europe and the United States, where it has become a subject of intense scientific, regulatory, and public health debate. In the U.S., kratom is mostly sold as loose powder or in capsules made from minimally processed leaves, though a growing market now offers concentrated extracts with stronger effects. This paper offers a balanced, evidence-based review of the scientific literature on kratom and its primary alkaloids—mitragynine and 7-hydroxymitragynine (7-OH)—as well as its various product forms, with a focus on informing state-level policy.

National survey data show that kratom use remains relatively rare, with less than one percent of adults reporting any past-year use, though prevalence rises significantly in certain subgroups, such as those with serious psychological distress or substance use histories. The typical kratom consumer in the U.S. is middle-aged, non-Hispanic white, and male and survey data consistently show that pain management and reducing or replacing opioids are the main reasons for use.

Kratom's pharmacological profile is both unusual and consequential for its therapeutic promise and potential risks. Its major alkaloids act on the same receptors as opioids, but only partially activate them. This mechanism produces kratom's pain-relieving effects while also contributing to a potential for dependence and withdrawal symptoms. Kratom is further distinguished from classic opioids by its significantly lower risk of overdose,

with mitragynine posing no risk of slowed breathing, the primary cause of fatal opioid overdose. This means that products with alkaloid compositions similar to unprocessed leaves (mitragynine dominant) pose essentially no risk of fatal respiratory depression.

> *Kratom's pharmacological profile is both unusual and consequential for its therapeutic promise and potential risks.*

The overdose evidence on 7-OH and concentrated products is more mixed. Animal studies indicate that direct, intravenous 7-OH administration can slow breathing. However, it is unclear how this translates to typical oral use in humans. Based on all available evidence, this risk appears to be minimal compared to classic opioids and is reversible with the same widely available medication used to reverse opioid overdose. Concentrated products may be more effective for severe chronic pain or substance use disorder but may also pose a heightened risk of dependence and withdrawal.

Few consumers of kratom report serious adverse events and few report concerns about kratom use disorder. When kratom use disorder does become clinically significant, studies show it responds well to buprenorphine/naloxone treatment, the same medication used for opioid use disorder. Overdose deaths linked to all types of kratom products also remain exceedingly low, even among those using high doses of concentrated products.

The most comprehensive analysis, reviewing over 27,000 overdose deaths between 2016 and 2017, identified just 152 overdoses "involving" kratom. Just seven of those deaths involved solely kratom. The rest involved the co-use of classic opioids, like fentanyl and other substances with established overdose dangers. For concentrated products, specifically, federal agencies have identified just 85 overdoses cases since 2019, 55 of which were fatal and most of which involved substances in addition to 7-OH. Given its prevalence of use, the near absence of overdose deaths even tangentially related to these products indicates a low risk. Researchers have estimated that the risk of death among those consuming kratom is approximately 1,390 times lower when compared to those using any opioid.

> *The most consistently documented risks related to kratom products stem not from the plant itself but from the unregulated supply chain.*

The most consistently documented risks related to kratom products stem not from the plant itself but from the unregulated supply chain. Testing has repeatedly found kratom products contaminated with heavy metals, salmonella, and residual solvents, and frequently mislabeled with inaccurate alkaloid concentrations, making safe dosing difficult for consumers.

In response to its rising popularity and concerns surrounding its use, states have begun to adopt regulations on kratom products. As of June 2026, eight states ban all kratom and 17 have adopted regulatory frameworks that may include a minimum age of purchase, rules on manufacturing and labeling, and product standards that may include limits on alkaloid concentrations. This study finds that most of these state approaches are improperly calibrated to achieve maximum consumer safety and optimal public health outcomes.

The research reviewed in this paper associates prohibition with higher overdose mortality and adverse events as users shift to unregulated markets and products and associates enforced regulation with reduced contamination risk. Based on this evidence, the paper recommends that states adopt age restrictions, good manufacturing practice (GMP) standards, mandatory product testing, and clear labeling requirements for both leaf kratom and concentrated products, rather than banning kratom outright.

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PART 1

INTRODUCTION

Kratom (Mitragyna speciosa) has been used for centuries in Southeast Asia, where leaves are traditionally chewed, consumed as tea, or dried and prepared as a powder that can be inserted into capsules, tablets, or beverages. Kratom is consumed to manage pain, combat fatigue, and mitigate opioid withdrawal with few reports of adverse events.

In recent decades, its use has spread to the United States and Europe, where it has become a subject of intense scientific, regulatory, and public health debate. In the United States, kratom products are typically sold as loose powder and powder-filled capsules or tablets made from kratom leaves, though there is a growing market for more potent extracts produced by processing raw leaf to create concentrated products.

Advocates point to kratom's potential as a lower-risk alternative to illicit opioids and a tool for self-managing chronic pain. Critics emphasize risks of dependence, adverse effects, and product contamination. Both claims carry some truth but often have been exaggerated in policy debates beyond what is supported by the evidence.

This paper aims to provide a balanced, evidence-based review of the scientific literature on kratom and its primary alkaloids, mitragynine and 7-hydroxymitragynine (7-OH), with a focus on informing state-level policy. We synthesize recent research across five domains: pharmacology, user demographics and motivations, therapeutic potential, risks, and regulation.

This paper aims to provide a balanced, evidence-based review of the scientific literature on kratom and its primary alkaloids, mitragynine and 7-hydroxymitragynine (7-OH), with a focus on informing state-level policy.

The pharmacological profile of kratom is unusual and consequential. Its major alkaloid, mitragynine, acts as a weak partial agonist (a trigger) at the mu-opioid receptor, which activates the receptor and produces pain-relieving effects (analgesia). But kratom also appears to have a ceiling effect that limits the risk of respiratory depression—the primary cause of fatal overdose from derivatives of the opium plant and synthetic alternatives, like morphine, heroin, and fentanyl. At the same time, mitragynine is metabolized in the liver to 7-OH; a more potent metabolite, though mitragynine retains its own pharmacological activity alongside this conversion. Understanding this dual action is essential for evaluating both therapeutic claims and safety concerns.

The current U.S. market for kratom products includes leaf powder in capsule or tablet form, extracts, beverages, and infused foods. Some of these products contain exclusively minimally processed leaf and others contain synthesized versions of mitragynine and 7-OH.[1]

User survey data reveal a diverse population of kratom consumers, most commonly middle-aged, white, and male, but including substantial subgroups who use kratom for chronic pain management or as a substitute for prescription or illicit opioids. Prevalence of regular use in the general adult population remains low (approximately 0.68%) but rises significantly among those with serious psychological distress or substance-use histories. Stated motivations for use are predominantly practical rather than recreational: pain relief, anxiety management, and opioid harm reduction.

[1] James B. Leonard, Kait Brown, and Jonathan M. Colvin, "Kratom Exposure Cases Reported to United States Poison Centers: 2016–July 2025," *The American Journal of Emergency Medicine* 105 (July 2026). 136–40. www.doi.org/10.1016/j.ajem.2026.04.006 (16 June 2026).

> *Preclinical studies show clear analgesic effects, but human trials have been limited and methodologically constrained.*

On therapeutic potential, the evidence is uneven. Preclinical studies show clear analgesic effects, but human trials have been limited and methodologically constrained. By contrast, user survey data consistently report high perceived efficacy for pain and opioid withdrawal, with large numbers of users crediting kratom with enabling sustained abstinence from heroin or prescription opioids. The disconnect between controlled studies and observed outcomes in practice reflects both regulatory barriers to research and the difficulty of translating experimental pain models to real-world clinical populations.

On risks, the picture is more nuanced than is often portrayed. Kratom's primary alkaloid, mitragynine, does not appear to produce life-threatening respiratory depression at any dose tested in animal models and, in fact, has been shown to increase respiration. It's minor alkaloid, 7-hydroxymitragynine (7-OH) has shown some respiratory depressant effects, but few if any overdose deaths have been linked to kratom, mitragynine, or 7-OH use in isolation. Fatalities attributed to kratom almost invariably involve co-ingestion of other drugs, particularly fentanyl, heroin, or benzodiazepines. However, kratom use is associated with mild to moderate adverse effects (nausea, constipation, dizziness), and regular use can produce physical dependence and withdrawal, though these are generally mild and resolve with discontinued use.

A more serious but often overlooked risk stems from the unregulated supply chain. Commercial kratom products have been found to be contaminated with bacteria (salmonella), toxic heavy metals, and residual solvents, and many products have been shown to contain higher concentrations of kratom compounds than reflected on labels, making proper dosing difficult.

Finally, we also examine state-level regulatory responses and discuss approaches that balance consumer safety and public health without stimulating the creation of a potentially more hazardous illicit kratom market. As of September 2026, 12 states have banned kratom outright through statute or emergency rule; 23 have adopted regulations which keep some

kratom products legal while imposing age restrictions, manufacturing standards, and/or testing requirements; and 15 impose no regulations. Evidence suggests that kratom prohibition is associated with increased opioid overdose mortality, as consumers shift to unregulated markets, while well-enforced regulation can mitigate contamination risks without driving users to more dangerous alternatives.

> *… we recommend that states reject prohibition in favor of a regulatory framework…*

Based on this evidence, we recommend that states reject prohibition in favor of a regulatory framework: age restrictions (21+), good manufacturing practice (GMP) standards, mandatory product testing, detailed labeling rules, and an age-gated access model that preserves access for legitimate uses while preventing accidental overexposure.

The goal of this paper is to provide policymakers, public health officials, and researchers with an accurate, evidence-grounded foundation for regulation that serves public health and respects the autonomy of adults managing their own health.

PART 2

WHAT ARE KRATOM AND 7-OH? PHARMACOLOGY AND MECHANISM OF ACTION

Kratom is derived from the leaves of *Mitragyna speciosa*, a tropical tree native to Southeast Asia. For centuries, people in countries like Thailand and Malaysia have chewed raw kratom leaves or brewed them as teas to manage chronic pain, boost energy for intense manual labor, or ease opioid withdrawal.[2]

Kratom's effects are driven by its alkaloids—naturally occurring compounds, like caffeine and nicotine.[3] The primary alkaloid in kratom is mitragynine (about 66% of total alkaloid content).[4] A secondary alkaloid, 7-hydroxymitragynine (7-OH), is present in much smaller

2 Charles Veltri and Oliver Grundmann, "Current Perspectives on the Impact of Kratom Use," *Substance Abuse and Rehabilitation* 10 (1 July 2019). 23–31. www.doi.org/10.2147/SAR.S164261 (16 June 2026).

3 Doug McVay, "Kratom, Mitragynine, and 7-Hydroxymitragynine (7-OH)," Webpage, Drug Policy Facts, Real Reporting Foundation, 5 Feb. 2026. www.drugpolicyfacts.org/chapter/kratom (15 June 2026).

4 Christopher R. McCurdy, Abhisheak Sharma, Kirsten E Smith, et al., "An update on the clinical pharmacology of kratom: uses, abuse potential, and future considerations," *Expert Review of Clinical Pharmacology* 17 (2024). 131–142. www.doi.org/10.1080/17512433.2024.2305798 (4 March 2026).

amounts (less than 2% of total alkaloid content).[5] The body also produces 7-OH as a metabolite when the liver breaks down mitragynine.

Classic opioids—derived from the opium poppy plant, like fentanyl and methadone, are full agonists. They fully activate mu-opioid receptors—brain receptors that produce pain relief when activated—producing up to 100% of the body's possible response. That high activation or "high intrinsic efficacy" is why they relieve pain and withdrawal symptoms so effectively, but also why, at sufficient doses, they can suppress breathing to the point of fatal overdose.

Mitragynine and 7-OH bind to those same mu-opioid receptors, which explains kratom's reported pain-reducing effects. However, studies show that mitragynine acts as a weak partial agonist and 7-OH acts as a partial agonist, rather than either being a full agonist.[6] Researchers have measured mitragynine's maximal efficacy at approximately 34% and 7-OH at 47% in cell-based assays, compared to full agonists.[7]

This partial agonism creates a biological ceiling effect. Even if an individual ingests massive amounts of mitragynine, or if mitragynine and its active metabolite 7-hydroxymitragynine saturated every available mu-opioid receptor in the brain, the partial agonist activity of these compounds would prevent them from exceeding a sub-maximal level of receptor activation. As such, kratom lacks the biological mechanism to readily depress the respiratory system.

> *"… kratom lacks the biological mechanism to readily depress the respiratory system."*

[5] Andrew C Kruegel, Rajendra Uprety, Steven G Grinnell, et al., "7-Hydroxymitragynine Is an Active Metabolite of Mitragynine and a Key Mediator of Its Analgesic Effects," *ACS Central Science* 5(6) (29 May 2019) 992-1001. www.doi.org/10.1021/acscentsci.9b00141 (29 May 2026).

[6] Andrew C. Kruegel et al., "Synthetic and Receptor Signaling Explorations of the Mitragyna Alkaloids: Mitragynine as an Atypical Molecular Framework for Opioid Receptor Modulators," *Journal of the American Chemical Society* 138 (2016). 6754–6764. www.doi.org/10.1021/jacs.6b00360 (15 April 2026).

[7] Andrew C. Kruegel, "7-Hydroxymitragynine Is an Active Metabolite of Mitragynine and a Key Mediator of Its Analgesic Effects."

Mitragynine also behaves uniquely at other opioid receptors. While some full agonists activate kappa and delta receptors in ways that compound their effects, mitragynine instead blocks these receptors (acting as an antagonist). This is particularly important for kappa receptors, which are associated with negative mood effects (stress, dysphoria, depression) when activated. By blocking these receptors, mitragynine may help avoid some of those negative mood effects while still providing therapeutic benefits through mu-opioid activation.[8] Delta receptor activation has been shown to produce antidepressant and anti-anxiety effects, so mitragynine's antagonism at this receptor could theoretically work against the beneficial mood effects of the mu-opioid agonism and kappa receptor antagonism. However, related compounds with a mu agonist/delta antagonist profile, such as mitragynine pseudoindoxyl, have demonstrated potent analgesic effects in animal models without evidence of dysphoria or negative mood effects that would cause aversion.[9]

For raw, botanical kratom preparations, there is a second safety mechanism created by the liver's natural limit on converting mitragynine into the more potent 7-OH.[10] Liver enzymes (CYP3A) convert mitragynine to 7-OH, which binds to opioid receptors at tenfold greater potency than the parent mitragynine.[11] However, the rate of conversion into 7-OH is limited by the available liver enzymes that carry out this reaction. This suggests that the amount of 7-OH generated from a given kratom dose may vary between individuals, reflecting differences in liver enzyme activity. Because 7-OH is the more potent species and is produced only through this rate-limited step, the opioid-like component of kratom's effects depends substantially on the extent of this conversion.[12]

8 Andrew C. Kruegel et al., "Synthetic and Receptor Signaling Explorations of the Mitragyna Alkaloids."

9 András Váradi, Gina F. Marrone, Travis C. Palmer, et al., "Mitragynine/Corynantheidine Pseudoindoxyls As Opioid Analgesics with Mu Agonism and Delta Antagonism, Which Do Not Recruit β-Arrestin-2," *Journal of Medicinal Chemistry* 59 (2016). 8381-8397. www.doi.org/10.1021/acs.jmedchem.6b00748 (25 Sep. 2026).

10 Rob Hill, Andrew C Kruegel, Jonathan A Javitch, et al., "The respiratory depressant effects of mitragynine are limited by its conversion to 7-OH mitragynine," *British Journal of Pharmacology* 179 (July 2022). 3875–3885. www.doi.org/10.1111/bph.15832 (3 March 2026).

11 Andrew C Kruegel, "7-Hydroxymitragynine Is an Active Metabolite of Mitragynine and a Key Mediator of Its Analgesic Effects."

12 Hill, "The Respiratory Depressant Effects of Mitragynine Are Limited by Its Conversion to 7-OH Mitragynine."

This has drawn comparisons to codeine, which similarly requires liver conversion to become pharmacologically active (as morphine). But the analogy has limits. Unlike codeine, which is largely inert until converted into morphine, mitragynine appears to have direct pharmacological activity of its own, though much of it is non-opioid.[13] Its opioid-like effects, by contrast, appear to depend heavily on conversion to 7-OH. For example, in mice mitragynine's opioid-mediated respiratory effects are capped by that rate of conversion.[14] Meanwhile, in rats mitragynine produces little or no opioid antinociception (pain blocking) when CYP3A is inhibited and its conversion to 7-OH is prevented.[15]

Additionally, at low doses mitragynine produces stimulant effects. These effects are mediated through non-opioid pathways like alpha-2 adrenergic receptors (receptors that bind to the hormones epinephrine and norepinephrine, slowing the nervous system), the same target as the blood pressure medicine clonidine, and this does not require liver conversion at all.[16]

A 2022 study published in the *British Journal of Pharmacology* tested this potential ceiling effect directly. In mice, a moderate dose of mitragynine (10mg/kg) slowed breathing as expected. But when the researchers tripled the dose of mitragynine to 30 mg/kg and eventually increased it ninefold to 90 mg/kg, breathing never stopped. The effect plateaued and respiratory suppression did not increase at higher doses, which the study's authors attributed to the limited rate at which the liver converts mitragynine into 7-OH. In contrast, administering 7-OH directly produced a dose-dependent decline in breathing with no ceiling at the doses tested, up to 30 mg/kg.[17]

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13 Samuel Obeng, Morgan L. Crowley, Marco Mottinelli, et al., "The Mitragyna speciosa (Kratom) Alkaloid Mitragynine: Analysis of Adrenergic α2 Receptor Activity in Vitro and in Vivo," *European Journal of Pharmacology* 980 (5 Oct 2024). 176863. www.doi.org/10.1016/j.ejphar.2024.176863 (15 June 2026).

14 Rob Hill, "The Respiratory Depressant Effects of Mitragynine Are Limited by Its Conversion to 7-OH Mitragynine."

15 Shyam H. Kamble, Samuel Obeng, Francisco León, et al., "Pharmacokinetic and Pharmacodynamic Consequences of Cytochrome P450 3A Inhibition on Mitragynine Metabolism in Rats," *Journal of Pharmacology and Experimental Therapeutics* 385 (June 2023). 180–192. www.doi.org/10.1124/jpet.122.001525 (16 June 2026).

16 Samuel Obeng, "The Mitragyna speciosa (Kratom) Alkaloid Mitragynine."

17 Rob Hill, "The respiratory depressant effects of mitragynine are limited by its conversion to 7-OH mitragynine."

> *The body can only convert so much mitragynine to 7-OH per hour. This makes fatal overdoses involving only raw kratom highly unlikely because biological processes cannot turn mitragynine it into its more potent metabolite, 7-OH, fast enough to endanger breathing.*

For raw kratom comprised primarily of mitragynine, this creates a built-in bottleneck. The body can only convert so much mitragynine to 7-OH per hour. This makes fatal overdoses involving only raw kratom highly unlikely because biological processes cannot turn mitragynine it into its more potent metabolite, 7-OH, fast enough to endanger breathing. A 2022 study by Jack E. Henningfield and colleagues reinforced this conclusion by showing that even at massive oral doses of mitragynine in rats, direct arterial blood gas measurements revealed no lethal respiratory depression or significant changes in oxygen and carbon dioxide levels, in stark contrast to the effects of oxycodone.[18]

Recent studies also demonstrate qualitative differences between the two kratom alkaloids. At lower doses (roughly 1 to 5 grams of raw leaf), users report stimulant effects—sharpened focus, physical energy, and heightened sociability—while at higher doses, sedation increases.[19] This is because mitragynine appears to operate on two separate tracks simultaneously with the enzymatic conversion limit contributing to kratom's characteristic biphasic dose-response profile. In a 2025 rodent study, mitragynine administration actually increased respiratory frequency in rats at the doses tested—a stimulant effect unaltered by naloxone (the opioid overdose reversal drug)—while 7-OH caused classic, naloxone-reversible opioid-like respiratory depression.[20] This suggests mitragynine has respiratory effects opposing those of its metabolite. While a portion of mitragynine is available for conversion to 7-OH in the liver, the majority circulates through the bloodstream and

[18] Jack E. Henningfield, Joseph V Rodricks, Aaron M Magnuson, Marilyn A Huestis et al., "Respiratory effects of oral mitragynine and oxycodone in a rodent model," *Psychopharmacology* 239 (29 Oct. 2022). 3793–3804. www.doi.org/10.1007/s00213-022-06244-z (2 July 2026).

[19] Mark Sanderson and Adrianna Rowe, "Kratom," *Canadian Medical Association Journal* 191 (7 Oct. 2019). E1105. https://pmc.ncbi.nlm.nih.gov/articles/PMC6779532 (5 June 2026).

[20] Julio D. Zuarth Gonzalez, Alexandria K. Ragsdale, Sushobhan Mukhopadhyay, et al., "Mitragynine and 7-hydroxymitragynine: Bidirectional Effects on Breathing in Rats," *Journal of Pharmacology and Experimental Therapeutics* 392(11) (Nov. 2025). 103720. www.doi.org/10.1016/j.jpet.2025.103720 (15 April 2026).

engages non-opioid receptor systems. As the dose increases, the liver produces enough 7-OH that stimulant effects lessen and sedation slowly increases.

> *At lower doses (roughly 1 to 5 grams of raw leaf), users report stimulant effects—sharpened focus, physical energy, and heightened sociability—while at higher doses, sedation increases.*

PART 3

USER DEMOGRAPHICS AND MOTIVATIONS FOR USE

Several peer-reviewed studies published between 2022 and 2026 have sought to characterize U.S. kratom consumers, revealing a diverse population with distinct subgroups. While findings consistently show a demographic core of middle-aged, non-Hispanic white, male users, this profile is nuanced by specific subpopulations and motivations for use.

The most robust, nationally representative data, drawn from the National Survey on Drug Use and Health (NSDUH) 2021-2023, shows that past-year kratom use among U.S. adults is relatively low at a prevalence of around 0.68%. Among adults reporting serious psychological distress or major depressive episode, prevalence exceeds 2% while among those with certain types of substance or prescription medication misuse, prevalence exceeds 5%.[21] An analysis of college student data from the 2019-2020 Healthy Minds Study further refines this demographic profile, finding that kratom use was more common among college-aged students who are white, male or transgender/gender nonconforming, and those identifying as non-heterosexual.[22]

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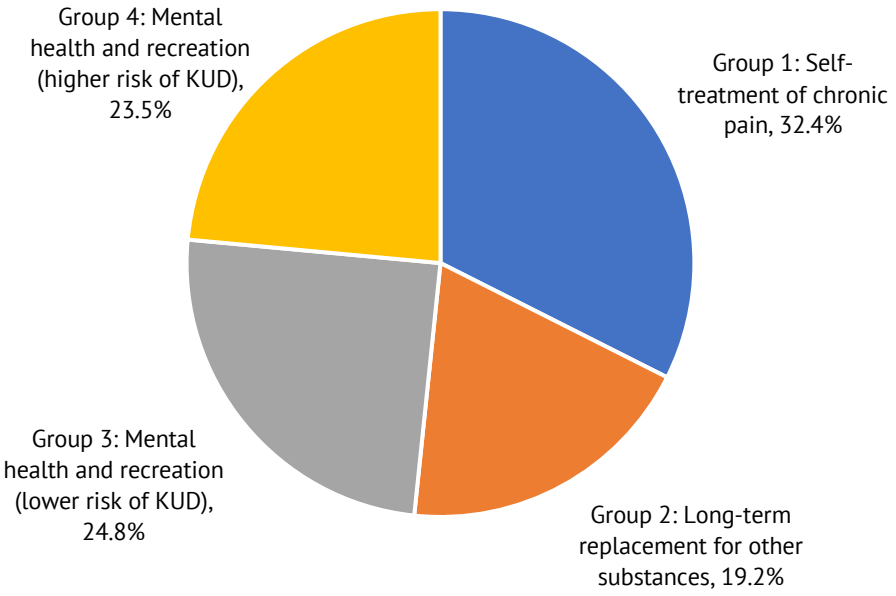
21 Chung Jung Mun, Patricia Timmons, Manuel Cano, "Prevalence and Correlates of Past-Year Kratom Use Among US Adults: Findings From the 2021-2023 National Survey on Drug Use and Health," *Journal of Addiction Medicine* (26 Jan. 2026). www.doi.org/10.1097/ADM.0000000000001637 (2 June 2026).

22 Mike C. Parent, Nathaniel W. Woznicki, Jackie Yang, "Demographic and behavioral factors associated with kratom use among U.S. college students," *Journal of American College Health* 72 (23 Aug 2022). www.doi.org/10.1080/07448481.2022.2112584.

3.1 MOTIVATIONS FOR USE

These demographics align with self-reported motivations for kratom use. For example, a 2025 study by Katherine Hill et al. of 395 regular kratom users categorized participants into four distinct groups based on their primary motivation for kratom use (this sample is the same cohort analyzed by Chung Jun Mun et al., 2025, described below and derived from the parent study by Kirsten E Smith et al., 2024, described below). The largest group (32.4%) was characterized by kratom use for the self-treatment of chronic pain, while the smallest (19.2%) used it primarily as a long-term replacement for other substances, like opioids or alcohol (see Part 5). The remaining two groups (48.3% combined) used kratom both for recreation and the management of anxiety and depression. These two groups, while citing similar motivations for use, were distinguished based on their risks of kratom addiction, also known as "kratom use disorder" (KUD), with 24.8% showing a low probability for KUD and 23.5% showing a high probability for KUD. All four of the groups also cited "performance" motivations, such as boosting energy for work.[23]

FIGURE 1: MOTIVATIONS FOR KRATOM USE AMONG 395 USERS



Source: Katherine Hill, Jeffrey M Rogers, Oliver Grundmann, David H Epstein, Kirsten E Smith, "At least four groups of kratom consumers in the United States: latent-class analysis of motivations for kratom use," *The American Journal of Drug and Alcohol Abuse*, 30(2) (Jan 2025). www.doi.org/10.1080/00952990.2024.2414319 (16 Apr 2026).

[23] Katherine Hill, Jeffrey M Rogers, Oliver Grundmann, David H Epstein, Kirsten E Smith, "At least four groups of kratom consumers in the United States: latent-class analysis of motivations for kratom use," *The American Journal of Drug and Alcohol Abuse* 30(2) (Jan 2025). www.doi.org/10.1080/00952990.2024.2414319 (16 April 2026).

The link to chronic pain and kratom use is particularly strong within the research literature. For example, a 2025 study by Mun et al. on kratom use for self-management of pain found that—despite recruiting their 395 kratom using participants based solely on kratom use—nearly half (49.1%) met the criteria for chronic pain. Nearly 70% of all participants in this study reported difficulties in obtaining adequate pain treatment. This suggests they substituted kratom for prescription opioids they could no longer access. Among those who rated access to treatment as "difficult" or "extremely difficult," over 86% indicated that these challenges directly impacted their decision to try kratom. Ecological momentary assessment (EMA) data—which assesses at-the-moment motivations—confirmed that "relieving pain" was the most frequently endorsed primary motivation for daily kratom use, and recent kratom use was associated with lower current pain levels.[24] In an online survey of 2,798 kratom consumers by Albert Garcia-Romeu et al. (2020), respondents reported using kratom for pain (91.3%), anxiety (67%), and depression (64%). Roughly 41% reported using kratom to reduce or stop opioid use.[25] In their survey of more than 5,000 kratom users, Oliver Grundmann and colleagues (2022) found that 73% of respondents used kratom for the self-treatment of acute or chronic pain.[26]

"In their survey of more than 5,000 kratom users, Oliver Grundmann and colleagues (2022) found that 73% of respondents used kratom for the self-treatment of acute or chronic pain."

Finally, research indicates that use patterns often involve proximal or situation-specific motivations for using kratom in any given instance of use. While most surveys typically ask about overall reasons for initiating kratom use, a 2024 study by Kristen E. Smith and

[24] Chung Jung Mun, Leigh V. Panlilio, Kelly E. Dunn, et al., "Kratom (Mitragyna speciosa) Use for Self-Management of Pain: Insights from Cross-Sectional and Ecological Momentary Assessment Data," *The Journal of Pain* 26 (January 2025). 104726. www.doi.org/10.1016/j.jpain.2024.104726 (30 Sep 2026).

[25] Albert Garcia-Romeu, David J Cox, Kirsten E Smith, Kelly E Dunn, Roland R Griffiths, "Kratom (Mitragyna speciosa): User demographics, use patterns, and implications for the opioid epidemic," *Drug and Alcohol Dependence* 208 (1 Mar 2020). www.doi.org/10.1016/j.drugalcdep.2020.107849 (7 July 2026).

[26] Oliver Grundmann, Charles A. Veltri, Diana Morcos, "Exploring the self-reported motivations of kratom (Mitragyna speciosa Korth.) use: a cross-sectional investigation," *The American Journal of Drug and Alcohol Abuse* 48(4) (7 Apr 2022).433-444. www.doi.org/10.1080/00952990.2022.2041026 (30 Sep 2026).

colleagues used an EMA to capture the real-time motivations of 357 long term kratom users across 13,401 kratom-use events. This approach revealed a key distinction between general motivations for kratom use and motivations for kratom use on a given occasion based on at-the-moment conditions. The study found that these immediate triggers were practical, often involving the desire to boost energy, increase focus, or get through daily tasks. Users reported feeling that kratom's effects were compatible with, or even helpful for, daily responsibilities with few reports of social or functional impairment.[27]

Dependence-related motivations were present, but comparatively uncommon in this group. "Stop kratom craving" was endorsed as a reason for use only in a minority of use events and was a minor motivation relative to pain relief, energy, focus, and mood. Withdrawal-related motivations were similarly infrequent. At random points during the day, participants reported low levels of drug craving overall. Craving for kratom was consistently higher than craving for other drugs, though both were low in absolute terms. The most dependence-like behavioral signals came from the highest frequency use group, which was more likely to use kratom within minutes of waking and reported more symptoms indicating dependence, such as tolerance and withdrawal. Yet, even among that group, withdrawal avoidance was not the dominant reason cited for kratom use on any given occasion.

"Stop kratom craving" was endorsed as a reason for use only in a minority of use events and was a minor motivation relative to pain relief, energy, focus, and mood.

These patterns are important for interpreting the study's finding that around two-thirds of participants met the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for kratom use disorder (KUD). The DSM-5 counts tolerance and withdrawal as diagnostic criteria, with withdrawal simply referring to the body's physiological readjustment after a substance is discontinued, such as how a daily caffeine drinker might experience a headache after skipping their morning cup of coffee. Individuals can meet the

[27] Kristen E. Smith, Leigh V Panlilio, Jeffrey D Feldman, et al., "Ecological Momentary Assessment of Self-Reported Kratom Use, Effects, and Motivations Among US Adults," JAMA Network Open, 7(1) (26 Jan 2024). www.doi.org/10.1001/jamanetworkopen.2023.53401 (30 Sep 2026).

criteria for KUD based on symptoms of physical dependence without experiencing the social or functional impairments typically associated with addiction. In this study, such impairment was rare, with psychosocial harm or hazardous use reported by very few participants.

That said, this study cannot cleanly separate the cited proximal motivations for use from potential kratom withdrawal-related symptoms. Boosting energy or improving focus may reflect uncomplicated motivations, but they may also reflect the need to address emerging but unrecognized symptoms of kratom withdrawal, a limitation the study's authors acknowledge. Still, the data reported in this study indicates kratom dependency, when it does appear, does not significantly interfere with the daily lives of most regular kratom users. Supporting this, the evidence investigating KUD generally indicates that it is usually mild in severity.[28] This is discussed in greater depth in Part 4 of this paper.



… the data reported in this study indicates kratom dependency, when it does appear, does not significantly interfere with the daily lives of most regular kratom users.



3.2 USER PERCEPTIONS OF EFFICACY AND ADVERSE EVENTS

Kratom consumers typically report high levels of perceived effectiveness for several purposes. The 2025 Mun et al. study on pain management found that participants reported substantial pain relief, rating kratom's effectiveness highly for both acute and chronic pain, with over 93% of long-term regular kratom users reporting pain relief. Of those users with chronic pain, nearly 84% expressed no concerns about overuse and 88% reported no side effects from kratom use for pain management. About 7% reported concerns of overuse and 7.6% reported problematic side effects. Interestingly, this study also found that higher levels of pain were not associated with greater kratom use frequency and that those with chronic pain did not use significantly more kratom than those without chronic pain.[29]

[28] Kirsten E Smith, Kelly E Dunn, Jeffrey M Rogers, et al., "Assessment of kratom use disorder and withdrawal among an online convenience sample of US adults," *Journal of Addiction Medicine* 16(6) (Nov-Dec 2022).666-670. www.doi.org/10.1097/adm.0000000000000986 (28 April 2026).

[29] Mun, "Kratom (Mitragyna speciosa) use for self-management of pain."

Despite high perceived efficacy, adverse effects are common though typically minor. In one survey of kratom use among patrons of two Colorado ethnobotanical tea bars by Cianna J. Piercey, et al. (2025), researchers found that most users reported experiencing at least one adverse reaction to kratom in the past, with gastrointestinal symptoms the most frequently reported. These reactions were often linked to specific contexts, such as consuming kratom on an empty stomach, dehydration, or combining kratom with other substance use.[30]

The first large-scale controlled human study on kratom safety, published by Marilyn A. Huestis et al. in 2026, offers critical data. In this randomized trial of 116 healthy volunteers who had not recently used kratom, 67 were given a placebo and 49 received a single dose of dried kratom leaf powder of between 6.65 mg and 53.2 mg mitragynine and followed for 10 days. Those receiving kratom were then given 15 daily doses at the same level and followed for 27 days. No serious adverse events were reported with kratom administration. However, mild side effects generally increased as the dose increased. The most common side effects reported were dizziness, nausea, and a feeling of relaxation. After multiple administrations, the most common side effects were headache, feeling hot, nausea, and elevated alanine aminotransferase (ALT) levels, indicating potential liver inflammation. The indications of potential liver inflammation were generally mild, with no participant meeting the FDA's threshold for drug-induced liver injury, no indication of serious liver injury, and resolved after stopping kratom. Elevated aminotransferase levels were also observed in several of the participants who received the placebo.[31]

> *Of those users with chronic pain, nearly 84% expressed no concerns about overuse and 88% reported no side effects from kratom use for pain management.*

[30] Cianna J Piercey, Joseph Bunch, Joseph Cameron, et al., "Kratom use among ethnobotanical tea bar patrons in Colorado: Subjective drug effects, adverse reactions, and perceived benefits of use," *Drug and Alcohol Dependence Reports* 16 (12 July 2025). 100361. www.doi.org/10.1016/j.dadr.2025.100361 (30 Sep 2026).

[31] Marilyn A Huestis, John Bothmer, Thomas Hudzik, et al., "Safety and Tolerability of Single and Multiple Daily Oral Doses of Dried Kratom Leaf Powder in a Randomized Trial in Healthy Volunteers," *Therapeutic Drug Monitoring* 48(5) (2 Oct 2026). 665-675. www.doi.org/10.1097/ftd.0000000000001427 (30 Sep 2026).

3.3 DURATION, PATTERNS OF USE, AND DOSING

Research indicates that for many users, kratom use is a long-term habitual practice. The 2024 EMA study by Smith et al., for example, found that around 78% of the 357 participants reported using kratom for one year or longer. Additionally, 39% reported two to five years of continuous use, with nearly 20% reporting more than five years of continuous use. Cluster A, which represented the highest-frequency users, was the group most likely to report using kratom as a long-term substitute for opioids, with around 45% self-reporting as "in recovery" from substance use disorder.[32]

In the Colorado tea bar study, which surveyed 102 patrons at two bars where kratom preparations are sold, 98 reported ever using kratom. Of the participants who used kratom, 73.4% reported at least weekly use, 19.4% reported at least daily use, and 7.1% reported more than daily use.[33] Whereas the tea bar surveyed participants with any kratom use history, studies surveying specifically long-term regular kratom users tend to find higher frequencies of use. For example, around 77% of participants in the 2024 EMA study used kratom daily at 2.52 times per day on average.[34]

In a large survey of over 8,000 current kratom users, Oliver Grundmann (2017) found that most respondents consumed kratom in powder form, either mixed into a beverage (48.6%) or as pure powder or pure powder in pill form (32.6%).[35] The most commonly reported doses were between 1 and 5 grams of kratom and the most common frequency of dosing was between 1 and 14 times per week, with adverse effects showing a dose-dependent relationship. Specifically, users experienced significantly lower odds of nausea, constipation, vomiting, and other negative effects at doses up to 5 grams per dose and at frequencies of 21 or fewer doses per week (i.e. up to three doses per day). By contrast, adverse effects were significantly more likely at 8 or more grams per dose or more than 21 doses per week. The most frequently reported adverse effects in this study were gastrointestinal, including nausea (12.8%) and constipation (9.2%), followed by dizziness or drowsiness (4.8%) with all effects appearing to be dose-dependent except for diarrhea.

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32 Kristen, "Ecological Momentary Assessment of Self-Reported Kratom Use, Effects, and Motivations Among US Adults."

33 Cianna J. Piercey, "Kratom Use Among Ethnobotanical Tea Bar Patrons in Colorado."

34 Smith, "Ecological Momentary Assessment of Self-Reported Kratom Use, Effects, and Motivations Among US Adults."

35 Oliver Grundmann, "Patterns of Kratom Use and Health Impact in the US — Results from an Online Survey," *Drug and Alcohol Dependence* 176 (1 July 2017). 63–70. www.doi.org/10.1016/j.drugalcdep.2017.03.007 (7 July 2026).

TABLE 2: DOSING LEVEL AND FREQUENCY AMONG KRATOM USERS

Grams of kratom/dose	N = 7605	**Doses of kratom/week**	N = 7605
<1g	504 (6.8%)	**1 – 7**	2607 (43.3%)
1g – 3g	3094 (40.7%)	**8 – 14**	2162 (28.4%)
3g – 5g	2487 (32.7%)	**15 – 21**	1834 (24.1%)
5g – 8g	1160 (15.3%)	**22 – 28**	554 (7.3%)
>8g	360 (4.7%)	**29 – 36**	295 (3.9%)
		37 – 48	76 (1%)
		>48	77 (1%)

Source: Oliver Grundmann, "Patterns of Kratom Use and Health Impact in the US — Results From an Online Survey," *Drug and Alcohol Dependence* 176 (1 July 2017). 63–70. www.doi.org/10.1016/j.drugalcdep.2017.03.007 (7 July 2026).

These dosing patterns are consistent with the findings presented by Garcia-Romeu et al. (2020), who surveyed 2,798 current kratom users and found that most respondents (49%) reported taking oral doses of kratom of between 1 and 3 grams and 33.4% reported doses of 4 to 6 grams. Most respondents reported taking these doses at least once per day (59%), with daily users averaging approximately three doses per day. Those in the study who reported using kratom to stop or reduce the use of prescription or illicit opioids generally reported taking higher doses of kratom and were more likely to report daily use.[36] While this study did not measure alkaloid concentrations consumed by participants, considering that the natural expression of alkaloids in raw kratom leaves is approximately 1.8% (1.8 mg per gram) for mitragynine and 0.03% (0.03 mg per gram) for 7-OH, this suggests an average consumption of 18-108 mg of mitragynine and 0.3-1.8 mg of 7-OH per dose (though this estimate would only apply to raw or powdered leaf, as opposed to concentrated products).[37]

TABLE 3: DOSING LEVEL AND FREQUENCY AMONG KRATOM USERS AND THOSE USING KRATOM FOR OPIOID REDUCTION

Grams of kratom/dose	Total sample (n= 2,798)	Opioid reduction users (n = 1,144)	**Frequency of kratom dosing**	Total sample (n= 2,798)	Opioid reduction users (n = 1,144)
<1g	242 (8.6%)	60) (5.2%)	**<1/ month**	(109) 3.9%	26 (2.3%)
1g – 3g	1372 (49%)	542 (47.4%)	**2-4/ month**	(152) 5.4%	27 (2.4%)
4g – 6g	935 (33.4%)	424 (37.1%)	**2-3 / week**	(375) 13.4%	99 (8.2%)
≥7g	249 (8.9%)	118 (10.3%)	**4-6/ week**	(508) 18.2%	197 (17.2%)
			Daily	(1654) 59.1%	795 (69.5%)

Source: Albert Garcia-Romeu, David J Cox, Kirsten E Smith, Kelly E Dunn, Roland R Griffiths, "Kratom (Mitragyna speciosa): User demographics, use patterns, and implications for the opioid epidemic," *Drug and Alcohol Dependence* 208 (1 Mar 2020). www.doi.org/10.1016/j.drugalcdep.2020.107849 (7 July 2026).

36 Garcia-Romeu, "Kratom (Mitragyna speciosa)."

37 Andrew C. Kruegel, Oliver Grundmann, "The medicinal chemistry and neuropharmacology of kratom: A preliminary discussion of a promising medicinal plant and analysis of its potential for abuse," *Neuropharmacology* 134(Part A) (15 May 2018). 108-120. www.doi.org/10.1016/j.neuropharm.2017.08.026 (7 July 2026).

A direct-observational study by Kirsten E. Smith et al. (2024) provides further detail on typical dosing among regular users. In this study, 10 participants took their typical morning dose of kratom using their typical products, averaging just over 5 grams per dose. Most reported using kratom daily, typically taking one to five doses per day. This study quantified the alkaloid concentration in the products used by participants, reporting alkaloids as weight relative to participant body mass. On average, participants received a mitragynine dose of 0.77 mg per kilogram of body weight and a 7-OH dose of 0.006 mg per kilogram of body weight. For a person weighing 70 kg (about 150 lbs.), this would translate to 53.9 mg of mitragynine and 0.42 mg of 7-OH per the mean session dose of 5.16 grams—or 10.45 mg mitragynine and 0.08 mg of 7-OH per gram of kratom powder. No adverse events were reported in any participant.[38]

Frequency of use among kratom users also varies with product type. Using the same cohort of 357 kratom consumers from the 2024 EMA study by Smith et al., researchers in a subsequent 2024 study found that of the 220 brands identified by kratom users, the most reported product forms were loose powder (55.8%) and encapsulated powder (26.8%). Extracts were used less frequently, accounting for only 419 "use events" across 9.48% of participants.[39]

While extracts may be used less frequently than other formats, motivations for use may influence the choice to use concentrated products. For example, a 2025 study by Grundmann et al., using a nationally representative sample of 1,049 current kratom users, found a significant correlation between increased frequency of consuming kratom shots or extract powder and pain relief.[40] This suggests that individuals using kratom for pain may be more likely to use concentrated products and may use them more frequently. High-frequency kratom users may be at increased risk for dependency and withdrawal symptoms. A 2024 study by Jeffrey M.

[38] Kirsten E. Smith, Jeffrey M. Rogers, Abhisheak Sharma, et al., "Responses to a 'Typical' Morning Dose of Kratom in People Who Use Kratom Regularly: A Direct-Observation Study," *Journal of Addiction Medicine* 18(2) (March-April 2024). 144-152. www.doi.org/10.1097/ADM.0000000000001259 (7 July 2026).

[39] Kirsten E. Smith, Leigh V. Panlilio, Abhisheak Sharma, "Time course of kratom effects via ecological momentary assessment, by product type, dose amount, and assayed alkaloid content," *Drug and Alcohol Dependence* 264 (1 Nov 2024). www.doi.org/10.1016/j.drugalcdep.2024.112460 (16 Apr 2026).

[40] Oliver Grundmann, MeShell Green, Erin Berthold, Saunjoo L Yoon, Diane Ray, "Prevalence and Use Patterns of Kratom (Mitragyna speciosa Korth.) in a US Nationally Representative Sample," *Journal of Psychoactive Drugs* 48(4) (1 Mar 2025). 1-9. www.doi.org/10.1080/02791072.2025.2474249 (16 Apr 2026).

Rogers and colleagues found that among regular kratom consumers, withdrawal symptoms were more closely associated with dose frequency than dose amount.[41]

> *After multiple administrations, the most common side effects were headache, feeling hot, nausea, and elevated alanine aminotransferase (ALT) levels, indicating potential liver inflammation.*

3.4 CO-USE OF OTHER SUBSTANCES WITH KRATOM

Along with dosing amounts and frequency, another important consideration is how consumers of kratom products may use them in conjunction with other substances and their potential interactions. The research literature broadly indicates that kratom use frequently occurs in the context of other substance use, including over-the-counter drugs, recreational substances, prescription medications, and illicit substances. In the direct-observational study by Smith et al. (2024), the most commonly reported substances used by the 10 participants in the 24 hours before or during kratom use were coffee (90%), multivitamins/supplements (60%), antidepressants (40%), nonsteroidal anti-inflammatory drugs (30%), and cannabis/THC (30%).[42] Similarly, in the EMA study by Smith et al. (2024), the most commonly co-used substances among the 357 participants were coffee/caffeine, cannabis, and nicotine.[43]

Evidence also indicates that many kratom consumers are also users of stimulants, sedatives, and opioids. In a 2021 study using data from the 2019 National Survey on Drug Use and Health, Kevin Y Xu et al. found that those reporting kratom use were significantly more likely to report past-year opioid use (8.9%) compared to those who had never used kratom (0.5%), as well as prescription stimulant use (2.8% versus 0.2%), methamphetamine (4.3% versus 0.3%), cocaine (4% versus 0.3%), tranquilizers or sedatives (3.6% versus 0.2%).

41 Jeffrey M. Rogers, Stephanie T. Weiss, David H. Epstein, et al., "Kratom addiction per DSM-5 SUD criteria, and kratom physical dependence: Insights from dosing amount versus frequency," *Drug and Alcohol Dependence* 206 (1 Jul 2024). www.doi.org/10.1016/j.drugalcdep.2024.111329 (29 July 2026).

42 Smith, “Responses to a ’Typical’ Morning Dose of Kratom in People Who Use Kratom Regularly.”

43 Smith, "Ecological Momentary Assessment of Self-Reported Kratom Use, Effects, and Motivations Among US Adults."

Kratom users in this study were also significantly more likely to report having a substance use disorder (31%) versus those who never used kratom (5.9%).[44]

A few studies have sought to determine if the initiation of kratom use occurs before, during or after other substance use. In their 2022 survey of 5,152 kratom users, Grundmann et al. found that among the respondents who reported a substance use disorder, 94.8% used kratom after discontinuing illicit or other drugs. Only 5.2% of those who reported use of other drugs maintained that other drug use following initiation of kratom use, with 94.8% reportedly stopping concurrent use of other substances with kratom.[45] A subsequent study by Jordan R. Covvey et al. (2026) found that of 161 kratom using adults, 86.2% used it for pain and 27.7% said they used it to address a substance use disorder, with around 52% reporting a past SUD related to opioids. Among those respondents reporting other drug use, kratom was rarely initiated first. For example, of those who reported use of non-prescribed opioids, only 1 (2.6%) reported using kratom prior to the use of non-prescribed opioids.[46]

These results are broadly consistent with data indicating that kratom is often used as a substitute for opioids, to reduce opioid use, or to manage substance use disorders.

These results are broadly consistent with data indicating that kratom is often used as a substitute for opioids, to reduce opioid use, or to manage substance use disorders. The potential risks of combining kratom use with various over-the-counter, prescription, and illicit substances is discussed in detail in Part 5 of this paper.

44 Kevin Y Xu, Carrie M Mintz, Jacob Borodovsky, et al., "Prevalence of Kratom Use and its Co-Occurring Substance Use Disorders in the United States, 2019," Primary Care Companion for CNS Disorders 23(4) (5 Aug 2021). 21br02930. www.doi.org/10.4088/PCC.21br02930 (17 Sep 2026).

45 Grundmann, "Exploring the self-reported motivations of kratom (Mitragyna speciosa Korth.) use."

46 Jordan R. Covvey, Oliver Grundmann, Nina Vadiei, Kirk E. Evoy, "An Initial Survey Assessing the Temporal Relationship of Kratom Initiation With Medical Treatment and Substance Use," *Substance Use* 20 (2 Jul 2026). www.doi.org/10.1177/29768357261465591 (30 Sep 2026).

PART 4

THE PROMISES AND POTENTIAL OF KRATOM: PAIN MANAGEMENT AND HARM REDUCTION

There are many prospective therapeutic benefits of kratom and its main alkaloids, and a significant share of survey participants across large, diverse user populations report using kratom products to attain these benefits. Principally, they include relief from chronic pain, managing mood or mental health conditions, and assistance in managing opioid or other substance use disorder. However, while there is strong evidence that many people are using kratom for these purposes, there remains a significant gap in data regarding the efficacy of kratom for these uses, particularly a lack of controlled clinical trials. Yet, the picture that emerges from the existing research indicates that kratom alkaloids and kratom products have considerable potential as therapeutics, both for addressing undertreated physical and mental health conditions, and as potential harm reduction tools.

4.1

PAIN MANAGEMENT: THE GAP BETWEEN PRECLINICAL AND HUMAN EVIDENCE

The preclinical case for kratom as an analgesic is compelling and appears related to 7-OH, in particular, at least in animal models and in vitro studies.[47] Moreover, 7-OH and mitragynine's profiles as G-protein-biased partial agonists at the mu-opioid receptor has led researchers to hypothesize that kratom alkaloids could deliver analgesia with a lower risk of respiratory depression than classic opioids—a genuinely meaningful distinction given that respiratory failure is the proximate cause of most opioid overdose deaths.[48]

The human evidence is more cautious and more complicated. In a 2024 Phase 1 trial, Elisabeth Prevete and colleagues administered isolated mitragynine to healthy volunteers in doses ranging from 5 to 40 mg under placebo-controlled conditions, measuring cold-pressor pain tolerance at regular intervals. Across all dose levels, mitragynine failed to significantly increase pain tolerance compared to placebo—even as participants reported noticeable subjective effects, including increased arousal and attention at lower doses and mild psychopathological distress at the highest dose tested.[49]

This null analgesic finding should not be read as definitive, as the study's authors are careful to note. Several factors may explain the gap between the preclinical and clinical results. First, plasma mitragynine concentrations in the Prevete study were substantially lower than those observed in natural-use contexts—the authors note that mitragynine concentrations in regular kratom users after a single traditional drink are at least 10 times higher than what their dosing protocol produced. Second, the Prevete study used a synthetic mitragynine isolate, the effects of which may differ from preparations made out of plant material. Third, the Prevete study enrolled primarily kratom-naive volunteers with only two out of 15 reporting any past kratom use. A randomized controlled trial conducted

47 Andrew C. Kruegel, "7-Hydroxymitragynine Is an Active Metabolite of Mitragynine and a Key Mediator of Its Analgesic Effects."; Samuel Obeng, Jenny L. Wilkerson, Francisco Leon, et al., "Pharmacological Comparison of Mitragynine and 7-Hydroxymitragynine: In Vitro Affinity and Efficacy for m-Opioid Receptor and Opioid-Like Behavioral Effects in Rats," *The Journal of Pharmacology and Experimental Therapeutics* 376(3) (Mar 2021). www.doi.org/10.1124/jpet.120.000189 (25 Sep 2026); Samuel Obeng, Francisco Leon, Avi Patel, et al., "Interactive Effects of m-Opioid and Adrenergic-a2 Receptor Agonists in Rats: Pharmacological Investigation of the Primary Kratom Alkaloid Mitragynine and Its Metabolite 7-Hydroxymitragynine," *The Journal of Pharmacology and Experimental Therapeutics* 383(3) (Dec 2022). 182-198. www.doi.org/10.1124/jpet.122.001192 (25 Sep. 2026).

48 Kruegel, "Synthetic and Receptor Signaling Explorations of the Mitragyna Alkaloids."

49 Elisabeth Prevete, Eef L. Theunissen, Kim P. C. Kuypers, et al., "An Exploratory Study of the Safety Profile and Neurocognitive Function After Single Doses of Mitragynine in Humans," *Psychopharmacology* 242 (26 Dec. 2024). 1363–1376. www.doi.org/10.1007/s00213-024-06734-2 (15 June 2026).

by Balasingam Vicknasingam and colleagues (2020) studied the analgesic effects of a kratom leaf decoction in long-term, daily kratom users in Malaysia. This study found significant analgesic effects following kratom ingestion.[50] This suggests that repeated dosing and developed tolerance may be preconditions for the analgesic response. Third, whole-plant kratom contains more than three dozen alkaloids, and the contribution of minor alkaloids to the analgesic effect remains poorly understood.[51] Finally, there is a well-established distinction between experimental pain models—which use acute, induced stimuli in healthy participants—and the chronic, pathological pain that motivates most kratom use in the real world.

> *… there is a well-established distinction between experimental pain models—which use acute, induced stimuli in healthy participants—and the chronic, pathological pain that motivates most kratom use in the real world.*

The preclinical evidence for kratom's effect on pain is strong and mechanistic plausibility is high while the clinical evidence is limited but not negative and may simply be underpowered and methodologically mismatched to the population using kratom for pain. Controlled trials in chronic pain patients, using whole-plant formulations and ecologically realistic dosing, have not yet been conducted.

4.2 KRATOM AS OPIOID REPLACEMENT THERAPY AND HARM REDUCTION

Whatever uncertainty exists around kratom's analgesic effects in controlled settings, the evidence that people are using kratom to manage opioid dependence is robust and consistent across multiple large surveys. The Smith et al. (2024) EMA study of 357 kratom consumers found that 28% and 7.8% of respondents reported using kratom as a long-term

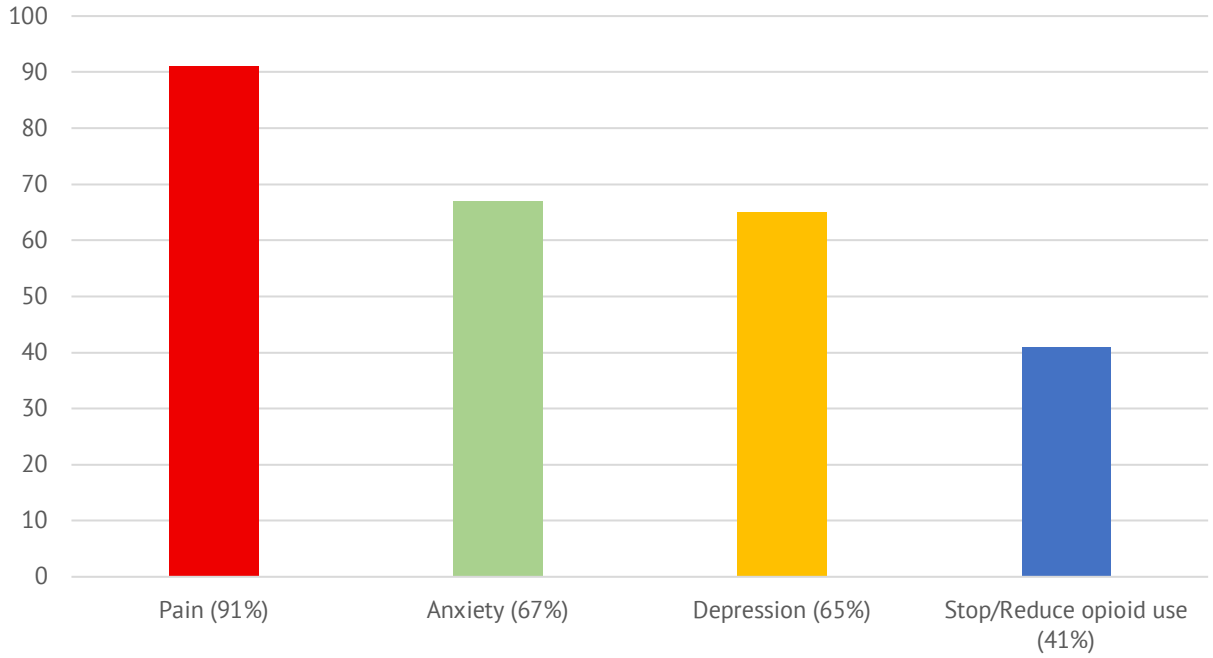
[50] Balasingam Vicknasingam, Weng Tink Chooi b, Azlan Abdul Rahim, "Kratom and Pain Tolerance: A Randomized, Placebo-Controlled, Double-Blind Study," *Yale Journal of Biology and Medicine*, 93(2) (29 June 2020). 229-238. pmc.ncbi.nlm.nih.gov/articles/PMC7309661 (28 April 2026).

[51] D. A. Todd, J.J. Kellogg, E.D. Wallace, et al., "Chemical Composition and Biological Effects of Kratom (Mitragyna speciosa): In Vitro Studies with Implications for Efficacy and Drug Interactions," Scientific Reports 10 (5 Nov. 2020). 19158. www.nature.com/articles/s41598-020-76119-w (16 June 2026).

or short-term substitute for opioids, respectively. Some also reported using kratom as a long-term (15.7%) or short-term (6.7%) replacement for alcohol, 5.3% used it as a long-term replacement for buprenorphine or methadone, and 10.9% reported using kratom to relieve withdrawal symptoms from one or more substances.[52]

Grundmann's 2017 survey of 8,049 U.S. kratom users found that 7.7% and 26% of respondents reported using kratom specifically to address dependence on a prescription or illicit substance, respectively. Of this group, 78.6% reported "reduced or stopped use of opioid painkillers" as a perceived benefit of their kratom use and those at higher kratom doses were more likely to report this benefit.[53] A subsequent and more detailed survey by Albert Garcia-Romeu et al. (2020) of 2,798 kratom users found that 41%—1,144 individuals—reported using kratom expressly to stop or reduce opioid use, citing significant reductions in both withdrawal symptoms and cravings.[54]

FIGURE 4: SELF-REPORTED MOTIVATION FOR KRATOM USE AMONG 2,798 USERS



Source: Albert Garcia-Romeu, David J Cox, Kirsten E Smith, Kelly E Dunn, Roland R Griffiths, "Kratom (Mitragyna speciosa): User demographics, use patterns, and implications for the opioid epidemic," *Drug and Alcohol Dependence* 208 (1 Mar 2020). www.doi.org/10.1016/j.drugalcdep.2020.107849 (7 July 2026).

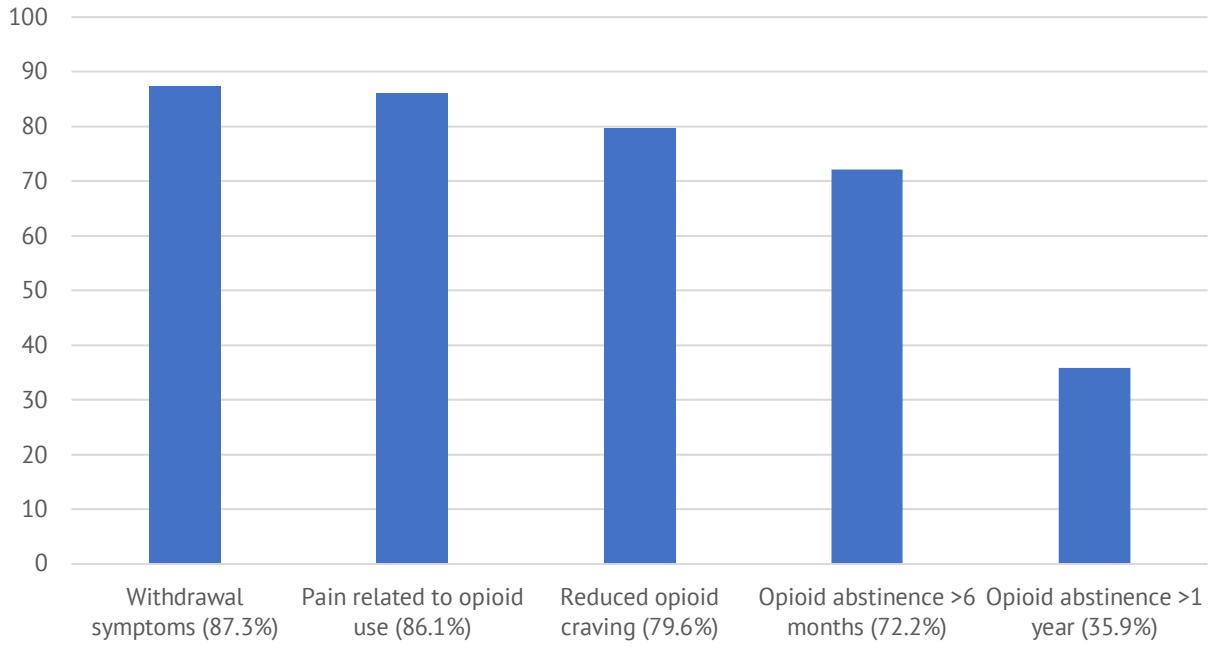
52 Smith, "Ecological Momentary Assessment of Self-Reported Kratom Use, Effects, and Motivations Among US Adults."

53 Grundmann, "Patterns of Kratom use and health impact in the US—Results from an online survey."

54 Garcia-Romeu, "Kratom (Mitragyna speciosa)."

Of the 1,411 participants in Garcia-Romeu et al. (2020) who said they used kratom to address opioid use disorder or opioid withdrawal, 87.3% endorsed kratom as effectively treating their opioid withdrawal symptoms and 86.1% endorsed it as effective for reducing opioid cravings. Additionally, 849 (74.2%) in this group reported achieving opioid abstinence for greater than six months attributable to kratom use with 411 (36%) reporting greater than one year of continuous opioid abstinence.[55]

FIGURE 5: SELF-REPORTED EFFICACY OF KRATOM FOR OPIOID WITHDRAWAL/ ABSTINENCE AMONG 1,411 USERS



Source: Albert Garcia-Romeu, David J Cox, Kirsten E Smith, Kelly E Dunn, Roland R Griffiths, "Kratom (Mitragyna speciosa): User demographics, use patterns, and implications for the opioid epidemic," *Drug and Alcohol Dependence* 208 (1 Mar 2020). www.doi.org/10.1016/j.drugalcdep.2020.107849 (7 July 2026).

On the other hand, regular kratom use has been shown to produce physical dependence. While the literature is unclear about the severity and scope of that risk, it generally indicates that kratom-related withdrawal symptoms are milder in intensity compared to opioid withdrawal.[56]

[55] Ibid.

[56] Jack E Henningfield, Marek C Chawarski, Albert Garcia-Romeu, et al., "Kratom Withdrawal: Discussions and Conclusions of a Scientific Expert Forum," *Drug and Alcohol Dependence Reports* 7 (15 March 2023). www.doi.org/10.1016/j.dadr.2023.100142 (29 April 2026).

In the survey by Garcia-Romeu et al. (2020), 9.5% of respondents reported kratom-related withdrawal symptoms and an additional 17.5% reported possible kratom-related withdrawal. However, only 68 participants—roughly 2.4% of respondents—met DSM-5 criteria for moderate or severe KUD in the past year and this was more likely in the subgroup who reported using kratom for opioid reduction.[57] In Grundmann's 2017 survey, around 20.9% of respondents reported any negative perceived side effects of kratom, most of which were mild gastrointestinal effects. About 42.5% of those who reported any negative effects noted experiencing negative effects in the 24 to 48 hours after discontinuing kratom, indicating potential dependence on kratom.[58] In Grundmann et al.'s 2022 survey of 5,152 people who use kratom, 34.1% reported experiencing any negative effects from kratom use, mostly gastrointestinal, and 20.3% reported negative effects after stopping kratom use for more than 12 hours, indicating potential dependence on kratom.[59]

Among study participants who report KUD, kratom withdrawal symptoms, or other negative effects of kratom use, the overwhelming majority managed these effects without clinical intervention. In Grundmann's 2017 survey, just 51 out of 7,893 respondents (0.7%) reported seeking treatment for physical or mental health issues related to kratom use.[60] In Grundmann et al. (2022), just 48 respondents—less than 1%—reported seeking treatment because of their kratom use.[61] Garcia-Romeu et al. (2020) found similar results, with just 17 (0.6%) of respondents seeking medical treatment for adverse effects from kratom use.[62]

A growing body of case reports also indicates that KUD generally responds well to treatment with buprenorphine/naloxone treatment—the same medication used for opioid use disorder. A case series of 28 patients diagnosed with KUD and treated with buprenorphine/naloxone found that after 12 weeks of treatment, 82% tested negative for mitragynine, indicating abstinence from kratom.[63] These rates of abstinence from kratom

57 Garcia-Romeu, "Kratom (Mitragyna speciosa)."

58 Grundmann, "Patterns of Kratom use and health impact in the US—Results from an online survey."

59 Grundmann, "Exploring the self-reported motivations of kratom (Mitragyna speciosa Korth.) use."

60 Grundmann, "Patterns of Kratom use and health impact in the US—Results from an online survey."

61 Oliver Grundmann, Charles A. Veltri, Diana Morcos, et al., "Exploring the self-reported motivations of kratom (Mitragyna speciosa Korth.) use: a cross-sectional investigation," *The American Journal of Drug and Alcohol Abuse* (2022), 4 Jul 4;48(4):433-444. https://www.tandfonline.com/doi/10.1080/00952990.2022.2041026

62 Garcia-Romeu, "Kratom (Mitragyna speciosa)."

63 Viktoriya R Broyan, Jessica K Brar, Tristen Allgaier Student, Jeffrey T Allgaier, "Long-term buprenorphine treatment for kratom use disorder: A case series," *Substance Abuse* (renamed *Substance Use & Addiction Journal*) 43(1) (1 Feb 2022). 763-766. www.doi.org/10.1080/08897077.2021.2010250 (28 April 2026).

are comparable to those achieved among people receiving the same treatment for opioid use disorder, with research indicating that opioid abstinence rates for those on buprenorphine maintenance therapy for opioid use disorder are between 54% and 82%.[64] While more research is needed, this evidence suggests that kratom may be viable as an alternative or adjunctive therapy for some patients with opioid use disorder, despite the risk of kratom dependence.

While more research is needed, this evidence suggests that kratom may be viable as an alternative or adjunctive therapy for some patients with opioid use disorder, despite the risk of kratom dependence.

[64] Brandon S. Bentzley, Kelly S. Barth, Sudie E. Back, and Sarah W. Book, "Discontinuation of Buprenorphine Maintenance Therapy: Perspectives and Outcomes," *Journal of Substance Abuse Treatment* 52 (May 2015). 48–57. www.doi.org/10.1016/j.jsat.2014.12.011 (11 May 2026).

PART 5

RISKS: POLYDRUG INTERACTIONS

In the discussion about the dangers of kratom, deaths associated with its use often receive disproportionate attention. In 2017 the U.S. Food and Drug Administration (FDA) issued public statements citing 36 deaths associated with kratom-containing products.[65] The Drug Enforcement Administration (DEA) similarly referenced kratom-related fatalities in its 2016 attempt to schedule kratom compounds as controlled substances.[66] But a closer look at the data reveals that most of these deaths involved multiple substances (polydrug use), and standard forensic methods often cannot determine whether kratom—rather than other drugs present—played any causal role. Understanding this distinction is critical for sound policy, as finding a substance in someone's bloodstream at the time of death does not mean that substance caused the death.

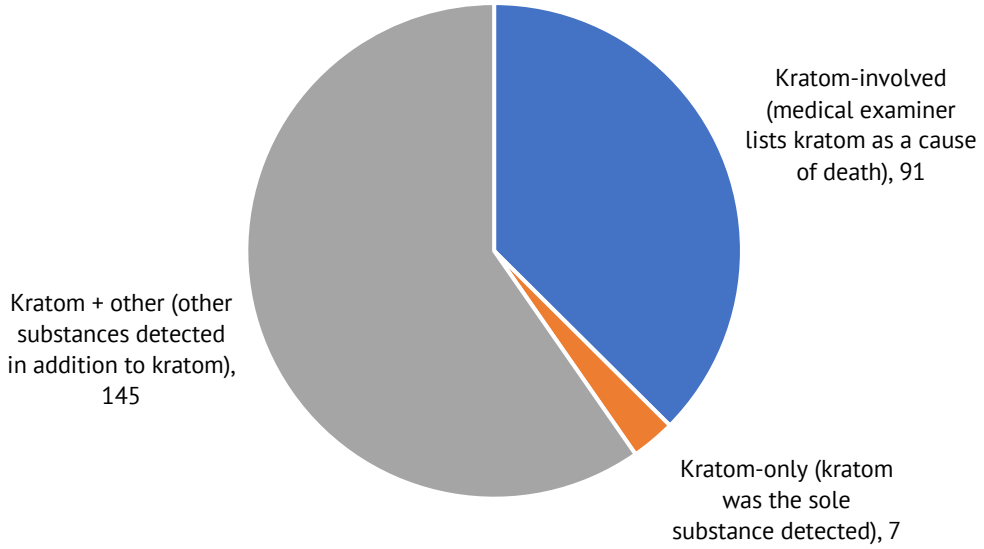
65 Scott Gottlieb, "Statement from FDA Commissioner Scott Gottlieb, M.D. on FDA Advisory About Deadly Risks Associated with Kratom," U.S. Food and Drug Administration, originally published 14 Nov. 2017, archived from the original on 21 Nov. 2017. web.archive.org/web/20171121050854/www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm584970.htm (4 June 2026).

66 Drug Enforcement Administration, "Schedules of Controlled Substances: Temporary Placement of Mitragynine and 7-Hydroxymitragynine Into Schedule I," *Federal Register* 81, no. 169 (31 Aug 2016). 59929–34. www.federalregister.gov/documents/2016/08/31/2016-20803/schedules-of-controlled-substances-temporary-placement-of-mitragynine-and-7-hydroxymitragynine-into (1 June 2026).

The most comprehensive federal analysis (reviewing 27,338 overdose deaths across 27 states) found kratom detected in just 152 of those deaths (0.56% of the total). Medical examiners listed kratom as contributing to the cause of death in 91 of those 152 cases. Of those 91, only seven listed kratom as the sole substance detected. Even then, the authors cautioned that the presence of additional substances cannot be ruled out due to testing limitations.[67]

The Centers for Disease Control and Prevention (CDC) surveillance system distinguishes between kratom-positive deaths (where kratom was detected on toxicology without causal attribution) and kratom-involved deaths (where the medical examiner listed kratom as contributing to death). These are different categories. The 152 kratom-positive deaths include all 91 kratom-involved deaths, but kratom-positive status requires only that kratom was found on toxicology.

FIGURE 6: KRATOM INVOLVEMENT IN 152 OVERDOSE DEATHS WHERE KRATOM WAS DETECTED IN TOXICOLOGY, 2016-2017



Source: Emily O'Malley Olsen, Julie O'Donnell, Christine L. Mattson, Joshua G. Schier, Nana Wilson, "Notes from the Field: Unintentional Drug Overdose Deaths with Kratom Detected — 27 States, July 2016–December 2017," Morbidity and Mortality Weekly Report 68(14) (12 April 2019). 326–327. www.doi.org/10.15585/mmwr.mm6814a2 (12 March 2026).

[67] Emily O'Malley Olsen, Julie O'Donnell, Christine L. Mattson, Joshua G. Schier, Nana Wilson, "Notes from the Field: Unintentional Drug Overdose Deaths with Kratom Detected — 27 States, July 2016–December 2017," Morbidity and Mortality Weekly Report 68(14) (12 April 2019). 326–327. www.doi.org/10.15585/mmwr.mm6814a2 (12 March 2026).

In forensic pharmacology, attributing a death to a specific substance requires that the detected concentration is consistent with lethality through a plausible biological mechanism and that competing causes be reasonably excluded. Peer-reviewed methodology describes this as "extremely difficult" even for drugs with established reference ranges, because post-mortem concentrations shift after death and cannot reliably reflect levels at the time of death.[68] This is even more challenging for novel substances, like kratom, for which no lethal blood concentration and no lethal dose have been established.

7-OH is also unstable in biological samples after death.[69] As such, detecting 7-OH alongside mitragynine in a post-mortem sample cannot reliably distinguish between direct ingestion of a concentrated 7-OH product versus post-mortem conversion from mitragynine. This limitation has important implications for cases being used to justify regulation of 7-OH products specifically.

In their 2025 study, Sarah Smallets et al. reviewed 55 toxicologically confirmed mitragynine-associated adverse events—35 fatal and 20 non-fatal. Of the 35 fatalities, 32 had other drugs in their system—substances like fentanyl, benzodiazepines, and antipsychotics, which all carry well-established lethal mechanisms of their own. Only three of the fatal cases involved mitragynine as the only detected substance. Among the 20 who survived, 13 had mitragynine as the only detected substance. The statistical difference ($p = 0.0002$) indicates that polydrug use was the factor associated with fatal outcomes. The authors conclude that there is insufficient evidence that kratom consumption alone increases the risk of severe acute adverse health effects.[70]

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68 R.E. Ferner, "Post-mortem clinical pharmacology," *British Journal of Clinical Pharmacology*, 66(4) (15 Jul 2008). 430-443. www.doi.org/10.1111/j.1365-2125.2008.03231.x (1 June 2026).

69 Oliver Grundmann, Kirsten E. Smith, Walter C. Prozialeck, Charles A. Veltri, Edward W. Boyer, "Commentary: Presence of Kratom in Opioid Overdose Deaths: Findings From Coroner Postmortem Toxicological Report," *Frontiers in Psychiatry* 15 (23 May 2024). 1411964. www.doi.org/10.3389/fpsyt.2024.1411964 (15 June 2026).

70 Sarah Smallets, Sydney Litvin, Grayson Abele, Sarah Kirsh, and Dennis Paustenbach, "The Acute Adverse Health Effects of Kratom: An Evaluation of Case Reports," *Frontiers in Pharmacology* 16 (29 Aug. 2025). www.doi.org/10.3389/fphar.2025.1620601 (15 June 2026).

Researchers have attempted to project the actual mortality risk of kratom separate from the risks associated with polydrug use or adulterated products. In their 2019 study Jack E. Henningfield et al. concluded that the risk of overdose death was more than 1,000 times greater for opioids than for kratom.[71] That estimate has since been supported by additional work, with Smallets et al. (2025) calculating that the risk of death among those using any opioid is approximately 1,390 times greater than that of kratom users and approximately 15,926 times greater for heroin users specifically.[72]

Researchers have attempted to project the actual mortality risk of kratom separate from the risks associated with polydrug use or adulterated products.

The data on co-occurring substances in kratom-associated deaths adds to the picture. Among the 152 kratom-positive deaths previously reported, fentanyl or fentanyl analogs were the most frequently identified co-occurring substances, listed as a cause of death for 65.1% of these decedents. Heroin was listed for 32.9%, benzodiazepines for 22.4%, prescription opioids for 19.7%, and cocaine for 18.4%. Approximately 80% of decedents had a documented history of substance misuse, and 90% had no evidence of medically supervised pain treatment, suggesting that the opioids found in their system were unlikely to have come from prescription pain treatment.[73]

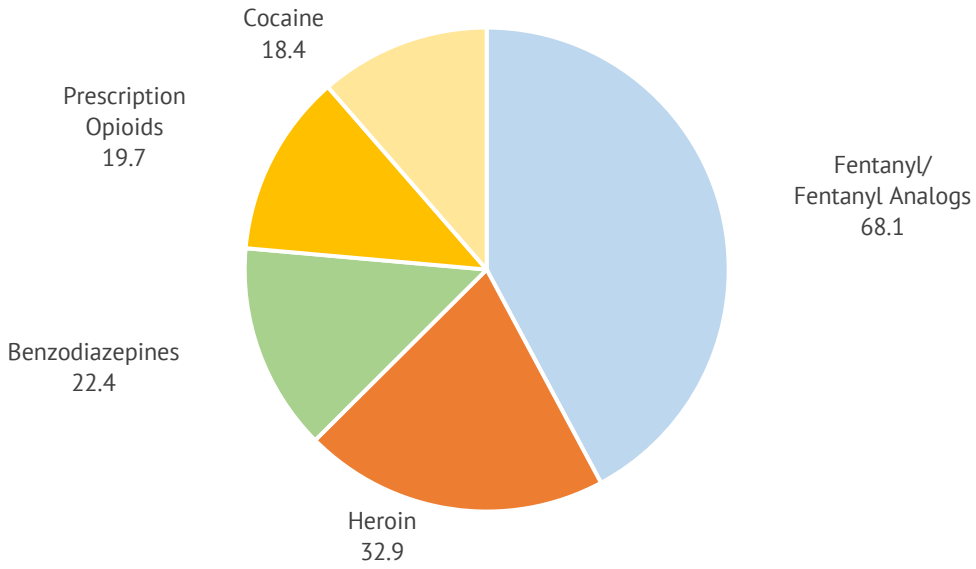
This is not a coincidental pattern. It describes a population managing serious substance use issues without medical oversight—a group that would show high rates of polydrug use regardless of whether kratom was present.

71 Jack E. Henningfield, Oliver Grundmann, Jane K. Babin, et al., "Risk of Death Associated With Kratom Use Compared to Opioids," *Preventive Medicine* 128 (Nov 2019). www.doi.org/10.1016/j.ypmed.2019.105851 (15 June 2026).

72 Smallets, "The Acute Adverse Health Effects of Kratom."

73 Olsen, "Notes From the Field."

FIGURE 7: CO-OCCURRING SUBSTANCES LISTED AS A CAUSE OF DEATH IN 152 KRATOM POSITIVE OVERDOSE DEATHS



Source: Emily O'Malley Olsen, Julie O'Donnell, Christine L. Mattson, Joshua G. Schier, Nana Wilson, "Notes from the Field: Unintentional Drug Overdose Deaths with Kratom Detected — 27 States, July 2016–December 2017," Morbidity and Mortality Weekly Report 68(14) (12 April 2019). 326–327. www.doi.org/10.15585/mmwr.mm6814a2 (12 March 2026).

In a polydrug death involving fentanyl and mitragynine, the pharmacologically conservative hypothesis is that fentanyl was the primary lethal agent. Fentanyl has a well-established mechanism for fatal respiratory depression while mitragynine does not. At the receptor level, a low-efficacy partial agonist (like mitragynine) competing with a higher-efficacy partial agonist (like 7-OH) or a full agonist (like fentanyl) would be expected pharmacologically to limit the overall receptor response rather than add to it. This competitive principle is well established in opioid pharmacology and is why buprenorphine (Suboxone) can precipitate opioid withdrawal by displacing stronger full agonists and reducing their effects. Because mitragynine itself binds with lower efficacy than 7-OH, its presence alongside 7-OH would be expected to reduce receptor response rather than compound it.[74] By the same reasoning, mitragynine's lower efficacy suggests that, when present with a full agonist like fentanyl, mitragynine is more likely to blunt than to amplify overall receptor activation.

[74] Hill, "The respiratory depressant effects of mitragynine are limited by its conversion to 7-OH mitragynine."

There is a separate question about drug interactions relating to kratom's impact on liver metabolism. Two liver enzymes, CYP3A and CYP2D6, metabolize many prescribed and over-the-counter drugs.[75] Mitragynine binds to these enzymes, potentially inhibiting their ability to metabolize other drugs. This means co-ingested drugs may stay in the bloodstream longer and reach higher levels than expected.

The case of Matthew Davenport—who died with kratom in his system and for whom a law banning kratom was named in Tennessee—is an illustrative case study.[76] Davenport's autopsy showed a mitragynine concentration of 810 ng/mL alongside diphenhydramine (Benadryl) at 3,000 ng/mL—far above the therapeutic range of 15-112 ng/mL, within the documented toxic range, and at a concentration associated with fatal outcomes in forensic casework.[77] Diphenhydramine overdose is associated with serious cardiac conduction abnormalities, ventricular dysrhythmias, and central nervous system (CNS) depression.[78] Duloxetine—a serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressant and nerve pain medication—was also found in Davenport's system at levels above its therapeutic ceiling. He had also consumed buspirone—an anti-anxiety medication. The medical examiner listed his cause of death as the combined effect of all four substances without identifying a primary lethal agent. Yet his death was attributed to a kratom-medication interaction, and this framing was used to enact "Matthew Davenport's Law"—a statewide kratom ban.

Another example of this is seen in a published case report of a 36-year-old man who had been consuming approximately 90 grams of kratom daily alongside prescribed venlafaxine (an antidepressant) and quetiapine (an antipsychotic medication). He presented with signs of serotonin toxicity and altered cardiovascular functioning. Clinicians suspected mitragynine-mediated inhibition of CYP enzymes caused both of his prescribed drugs to

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75 Yuqing Zhang, Ziying Wang, Yuchao Wang, et al., "CYP3A4 and CYP3A5: the crucial roles in clinical drug metabolism and the significant implications of genetic polymorphisms," PeerJ 12 (5 Dec 2024). www.doi.org/10.7717/peerj.18636 (16 June 2026).

76 Hamilton County Medical Examiner, "Autopsy Report: Matthew Martin Davenport, Case No. 240318-252," Southeast Tennessee Regional Forensic Center, 15 June 2024. Republished online at www.cato.org/sites/cato.org/files/2026-02/matthew-davenport-autopsy-report.pdf (15 April 2026).

77 Enrica Macorano, Ilaria Tarozzi, and Lorenzo Gitto, "Death Due to Diphenhydramine Toxicity: A 9-Year Review from the Cook County Medical Examiner's Office and a Review of the Literature," *Journal of Forensic Sciences* 71 (7 Mar 2026). 1079–1084. www.doi.org/10.1111/1556-4029.70239 (16 June 2026).

78 George G Kidess, Nathan Roberts, Lauren Harvey, et al., "Assessing Cardiovascular Dysfunction Using Cardiac Strain After Diphenhydramine Overdose," Cureus 18(1) (10 Jan. 2026). www.doi.org/10.7759/cureus.101242 (15 June 2026).

accumulate to toxic levels. Ten days after discontinuing use of venlafaxine and quetiapine, his vitals normalized.[79]

In 2023, a team of researchers sought to quantify kratom's effect on these liver enzymes by giving 12 healthy adults a single low dose of kratom tea and then administering probe drugs to measure enzyme activity. Those probe drugs were midazolam (a sedative metabolized almost exclusively by the CYP3A enzyme) and dextromethorphan (the active ingredient in over-the-counter cough syrup) to test the effect of kratom on the CYP2D6 enzyme. The authors found that kratom caused a slight 40% to 50% increase in midazolam exposure and had no significant effect on dextromethorphan.[80]

The modest interaction at this low dose may seem to contradict severe overdose reports. But the discrepancy is likely related to differences in dose and duration. Habitual kratom users consume significantly more kratom—up to 850 grams daily. At such levels, mitragynine is predicted to act as a time-dependent inhibitor, inactivating enzymes more durably and requiring the liver to synthetize new enzyme proteins—a process that takes days, though the precise inactivation mechanism has not been fully established.[81]

This risk is addressable through consumer-facing labeling that discloses the relevant drug interaction risks and identifies the medication classes most likely to be affected—the same kind of disclosure already standard for grapefruit juice, St. John's wort, and other enzyme-affecting substances. For chronic kratom users, monitoring co-use with other drugs (including over-the-counter medications) may be necessary.

5.1 RISKS: ADVERSE EVENTS AND BAD MANUFACTURING PRACTICES

The evidence indicates that kratom on its own poses little risk of fatal overdose. The pharmacological ceiling effects and metabolic bottlenecks built into the plant's chemistry make death from isolated kratom use extraordinarily rare. However, kratom consumption is

79 Hazel D Brogdon, Mackenzie M McPhee, Mary F Paine, Emily J Cox, Amy G Burns, "A Case of Potential Pharmacokinetic Kratom-drug Interactions Resulting in Toxicity and Subsequent Treatment of Kratom Use Disorder With Buprenorphine/Naloxone," *Journal of Addiction Medicine* 16(5) (Sep-Oct 2022). 606-609. www.doi.org/10.1097/ADM.0000000000000968 (15 June 2026).

80 Rakshit S. Tanna, James T. Nguyen, Deena L. Hadi, et al., "Clinical Assessment of the Drug Interaction Potential of the Psychotropic Natural Product Kratom," *Clinical Pharmacology & Therapeutics* 113(6) (Jun 2023). 1315–1325. www.doi.org/10.1002/cpt.2891 (15 April 2026).

81 Ibid.

not without other risks. Users report a range of non-fatal adverse effects, and testing of commercially available products indicates that many brands suffer from potentially hazardous quality-control issues.

In addition to polydrug interactions, the most salient risks posed by kratom products stem from manufacturer negligence, accidental contamination, mislabeling, and adulteration.

In addition to polydrug interactions, the most salient risks posed by kratom products stem from manufacturer negligence, accidental contamination, mislabeling, and adulteration. Reported adverse events associated with kratom in the United States appear to be different and more severe than the effects experienced by traditional users in Southeast Asia, indicating that a potentially substantial share of the adverse events observed in the U.S. may be attributable to products purchased from businesses engaging in bad manufacturing practices.[82]

Bacterial contamination stemming from unsanitary kratom processing, such as drying leaves on floors where they are exposed to contaminants like animal waste, bacteria, and groundwater, is also a documented problem. In 2018 the FDA and the CDC investigated a multistate salmonella outbreak linked to kratom, identifying 199 cases across 41 states with 54 hospitalizations and no deaths. The investigation could not identify a single source or supplier, which is consistent with multiple contamination points in the supply chain.[83] Independent testing found that six out of eight off-the-shelf kratom samples tested were positive for bacteria and fungi.[84]

82 Walter Prozialeck, Alexandra Fowler, and Joshua Edwards, "Public Health Implications and Possible Sources of Lead (Pb) as a Contaminant of Poorly Regulated Kratom Products in the United States," *Toxics* 10(7) (19 July 2022). 398. www.doi.org/10.3390/toxics10070398 (4 June 2026).

83 Johnson Nsubuga, Joseph Baugher, Elizabeth Dahl, et al., "Multistate Outbreak Investigation of Salmonella Infections Linked to Kratom: A Focus on Traceback, Laboratory, and Regulatory Activities," *Journal of Food Protection* 85(5) (1 May 2022). 747–754. www.doi.org/10.4315/JFP-21-319 (16 June 2026).

84 Walter C. Prozialeck, Joshua R. Edwards, Balbina J. Plotkin, et al, "Evaluation of the Mitragynine Content, Levels of Toxic Metals and the Presence of Microbes in Kratom Samples Purchased in the Western Suburbs of Chicago," *FASEB Journal* 34 (S1) (17 April 2020). www.doi.org/10.1096/fasebj.2020.34.s1.04422 (16 June 2026).

Contamination with potentially toxic levels of heavy metals, including lead, nickel, and chromium, is also a concern.[85] A 2024 analysis of 68 commercially available kratom products found that at a modest daily intake of 3 grams, 7.4% of products exceeded the permissible daily exposure limit for lead and 3.1% exceeded the limit for arsenic. At 25 grams per day—within the range reported by heavier users—70.6% exceeded the lead limit, 20.6% exceeded the nickel limit, and 9.4% exceeded the arsenic limit. Non-extract products (the powders and capsules made from raw kratom that most consumers use) contained the highest concentrations of heavy metals.[86] In a separate analysis of 16 kratom samples, the only brand whose products showed no detectable metals or microbial contamination was from the only vendor that had voluntarily adopted industry-established good manufacturing standards. Though the sample was small, this finding alongside the higher purity of extract products suggests that contamination is largely a manufacturing standards problem rather than an intrinsic property of the plant, which good manufacturing standards can address.[87]

Heavy-metal contamination can come not only from polluted soil but also from low-quality or aged industrial grinders that shed microscopic metal dust into the kratom powder. The types of adverse events in cases of "kratom toxicity" in the U.S.—such as nausea, vomiting, seizures, arrhythmias, and hepatic injury—are also associated with heavy metal exposure. Lead, for example, is known to damage the same organs reportedly affected by kratom.[88] This raises an important possibility that the severe adverse effects attributed to long-term kratom use—such as toxic hepatitis, severe gastrointestinal issues, or cognitive decline—may actually be symptoms of chronic heavy metal poisoning from contaminated products, not direct effects of the plant itself.

In rare cases, kratom products have been laced with non-kratom drugs. In Sweden in 2010, nine deaths were initially blamed on a botanical kratom supplement called "krypton." However, forensic toxicologists later established that the deaths were caused by O-

85 U.S. Food and Drug Administration, "Laboratory Analysis of Kratom Products for Heavy Metals," FDA, News & Events, Public Health Focus, 3 April 2019. www.fda.gov/news-events/public-health-focus/laboratory-analysis-kratom-products-heavy-metals (30 Sep 2026).

86 Kimberly Snow Caroti, Alen Joseph, Amy Sapowadia, C. Michael White, "Elemental Impurities (Heavy Metals) in Kratom Products: An Assessment of Published Individual Product Analyses," *Clinical Toxicology* 62(10) (Oct 2024). 651–660. www.doi.org/10.1080/15563650.2024.2395552 (2 June 2026).

87 Prozialeck, "Evaluation of the Mitragynine Content, Levels of Toxic Metals and the Presence of Microbes in Kratom Samples Purchased in the Western Suburbs of Chicago."

88 Prozialeck, "Public Health Implications and Possible Sources of Lead (Pb) as a Contaminant of Poorly Regulated Kratom Products in the United States."

Desmethyltramadol—a synthetic pharmaceutical opioid metabolite and full agonist—fraudulently added to the product.[89] Yet the DEA cited those nine Swedish deaths in its August 2016 Notice of Intent to temporarily place kratom compounds in Schedule I of the Controlled Substances Act.[90] The FDA similarly cited those nine deaths in its 2018–2019 "kratom-related deaths" tally, which was used in support of restrictive import alerts, though FDA's current kratom webpage now states that "the contribution of kratom in the deaths is unclear."[91]

> *…these issues are directly addressable by strict manufacturing and testing standards, clear labels, warnings against mixing kratom with certain contraindicated medications, and an advisory to consult with a physician prior to use.*

Adverse events stemming from poor manufacturing practices, adulteration, or polydrug use are worthy of concern. However, these issues are directly addressable by strict manufacturing and testing standards, clear labels, warnings against mixing kratom with certain contraindicated medications, and an advisory to consult with a physician prior to use. In Sweden, for example, no regulatory framework required ingredient verification or third-party testing, which would have caught the adulteration prior to products reaching consumers. Prohibition, on the other hand, typically pushes both production and demand into unregulated markets, where consumers have no guarantees about product quality and no assurance that products are accurately labeled. Based on the evidence of kratom's relatively low intrinsic risk, the proliferation of unregulated products would likely result in far more harm than would occur in a properly regulated legal market.

89 Robert Kronstrand, Markus Roman, Gunilla Thelander, Anders Eriksson, "Unintentional Fatal Intoxications with Mitragynine and O-Desmethyltramadol from the Herbal Blend Krypton," *Journal of Analytical Toxicology* 35(4) (May 2011). 242–247. www.doi.org/10.1093/anatox/35.4.242 (2 June 2026).

90 Drug Enforcement Administration, "Schedules of Controlled Substances: Temporary Placement of Mitragynine and 7-Hydroxymitragynine Into Schedule I."

91 U.S. Food and Drug Administration, "FDA and Kratom," FDA, News & Events, Public Health Focus, 2 Dec 2025. www.fda.gov/news-events/public-health-focus/fda-and-kratom (30 Sep 2026).

PART 6

REGULATION OF KRATOM VERSUS PROHIBITION

Due to high-profile cases of “kratom-associated” deaths and popular characterization of kratom as an “opioid” product, numerous states have sought to impose restrictions on the manufacture, sale, or possession of kratom and kratom products. This section reviews existing state-level laws governing kratom and kratom-derived products, drawing on drug policy research to argue that prohibition is both ineffective and counterproductive. This brief contends that regulation offers a more rational, compassionate, and beneficial alternative to prohibition.

While 15 states have yet to enact legislation regulating kratom, the remaining 35 states have adopted varying degrees of oversight, with many actively updating existing laws. As of September 2026, 10 states (Alabama, Arkansas, Connecticut, Indiana, Kansas, Louisiana, Massachusetts, Tennessee, Vermont, and Wisconsin) completely outlaw kratom products, classifying both mitragynine and 7-hydroxymitragynine (7-OH) as controlled substances through statute or agency rulemaking. However, Massachusetts’s classification is based on

a temporary order.[92] The California Department of Public Health has also interpreted state law as outlawing all kratom products.[93]

Some jurisdictions have opted to keep kratom and its primary alkaloid, mitragynine, legal while banning its derivatives. For example, Kentucky, Florida, and the District of Columbia do not control all "kratom," but classify 7-OH as a Schedule I substance. However, only the District of Columbia has done so through statute, with Kentucky and Florida scheduling 7-OH through temporary emergency rulemaking authority. Additionally, the Ohio Board of Pharmacy recently adopted rules classifying 7-OH as a Schedule I controlled substance.[94] Seventeen states have also adopted regulatory structures that impose strict caps on the concentration of 7-OH in kratom products or bar processed kratom, effectively banning all but raw leaf kratom products. Most of these (Arizona, Colorado, Kentucky, Maryland, Nebraska, Oregon, South Dakota, Texas, Utah, West Virginia, and Wyoming) limit 7-OH in kratom products to no more than 2% of alkaloid content, while three (Oklahoma, Mississippi, and Virginia) set this limit at no more than 1% of alkaloid content. Georgia and Rhode Island, meanwhile, limit 7-OH to no more than 0.5mg per gram and no more than 1mg per serving.[95]

6.1 ASSESSING THE HARMS OF KRATOM PROHIBITION

In enacting full or partial kratom bans, lawmakers and regulators typically cite potential dangers associated with kratom use, such as accidental overdose, abuse liability, youth use, and product quality issues like contamination and mislabeling. The underlying assumption is that prohibition will reduce these individual and social harms. However, a careful review of the evidence suggests that this assumption is flawed. Not only is it unlikely that prohibition will achieve the goals of reduced use and reduced harm, but the costs of prohibition—increased enforcement, lost tax revenue, the emergence of illicit markets, and the erosion of public health—are likely to outweigh any potential gains.

92 Legislative Analysis and Public Policy Association, "Kratom: Summary of State Laws," April 2025. www.legislativeanalysis.org/wp-content/uploads/2025/07/Kratom-Summary-of-State-Laws.pdf (2 June 2026). Note that this total has been updated to reflect changes in state law between April 2025 and September 2026.

93 Benson Yee, "Prohibition on the Sale of Kratom and 7-OH Products," letter to licensed tobacco retailers, California Department of Public Health, 9 Jan. 2026. https://www.cdph.ca.gov/Programs/CEH/DFDCS/CDPH%20Document%20Library/FDB/FoodSafetyProgram/KratomLetterTobaccoRetailers.pdf (5 June 2026).

94 Ibid.

95 Legislative Analysis and Public Policy Association, "Kratom: Summary of State Laws."

PUSHING DEMAND TOWARD ILLICIT PROVIDERS

The most cited justification for kratom bans is the alleged risk of overdose, yet data contradict the scale of this threat. Between 2015 and 2025 the FDA recorded 233 kratom-associated deaths, 184 of which (79%) involved polydrug use.[96] That figure pales in comparison to the more than 600,000 opioid-related deaths during the same period (2015-2025).[97] This low fatality rate—which may be overestimate due to the confounding presence of other drugs and adulterants in unregulated products—along with the common use of kratom as a substitute for more harmful substances, like opioids and benzodiazepines, suggests that for a substantial population, kratom may serve as a risk-reduction tool.

A ban would likely drive a portion of this population toward more dangerous substances and supply channels, including the very opioids they had replaced with kratom-based products. When the DEA published its notice of intent to temporarily place mitragynine and 7-hydroxymitragynine into schedule I of the controlled substances act, the agency received more than 20,000 public comments. Many kratom users—both in those comments and in surveys—expressed fear that outlawing kratom would send them back to opioid use.[98]

> *Many kratom users—both in those comments and in surveys—expressed fear that outlawing kratom would send them back to opioid use.*

This concern was reflected in the U.S. Department of Health and Human Services' 2018 kratom scheduling recission letter, which cited "significant risk of immediate adverse public health consequences," by pushing kratom users to switch to opioids, potentially increasing

96 Eleanor Blair Towers, Ynhi T. Thomas, Christopher P. Holstege, and Rita Farah, "Increases in Kratom-Related Reports to Poison Centers — National Poison Data System, United States, 2015–2025," Morbidity and Mortality Weekly Report 75(11) (26 March 2026). 139–145. www.doi.org/10.15585/mmwr.mm7511a1 (16 June 2026).

97 Lori Ann Post, Daniel Ciccarone, George Jay Unick, et al., "Decline in US Drug Overdose Deaths by Region, Substance, and Demographics," JAMA Network Open 8(6) (2 June 2025). www.doi.org/10.1001/jamanetworkopen.2025.14997. (16 June 2026).

98 Jack E. Henningfield, Daniel W. Wang, and Marilyn A. Huestis, "Kratom Abuse Potential 2021: An Updated Eight Factor Analysis," *Frontiers in Pharmacology* 12 (28 Jan. 2022). www.doi.org/10.3389/fphar.2021.775073 (2 June 2026).

overdose deaths and disease transmission from intravenous drug use, discouraging patients from discussing their kratom use with physicians, and stifling research.[99]

A doctoral dissertation examining the association between state-level kratom bans and opioid overdose mortality has provided preliminary empirical support of this concern. Lyndsey Blair (2022) found that state-level kratom bans in Indiana, Vermont, Wisconsin, Arkansas, and Alabama were associated with an increase in overdose mortality, though these findings have not yet been published in a peer-reviewed journal.[100] This pattern aligns with broader conclusions from drug policy research, finding that bans on the sale or possession of substances tend to push consumers toward unregulated markets where more dangerous products may prevail, often increasing rather than decreasing harm.

YOUTH USE

Youth exposure to kratom is another commonly cited justification for kratom-control laws. But evidence thus far indicates an exceedingly low prevalence of youth use. Data from the 2022 National Survey on Drug Use and Health (NSDUH) found that just 0.1% of adolescents aged 12 to 17 reported any past-year kratom use.[101] A 2026 systematic review of kratom use among adolescents and college students, covering studies from Malaysia, Thailand, and the United States, similarly concluded that while kratom use among youth warrants attention, available data do not indicate a widespread youth epidemic. Notably, however, the review also noted that national surveys such as the NSDUH may underestimate prevalence due to the exclusion of certain populations and the reliance on self-reported data in regions with strict drug laws.[102] These limitations suggest that while current

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99 Brett P. Giroir, "2018 Letter from the Assistant Secretary of Health to the Administrator of the Drug Enforcement Administration to Rescind Previous Support to Permanently Place Mitragynine and 7-Hydroxymitragynine in Schedule I of the Controlled Substances Act," U.S. Department of Health and Human Services, 16 Aug. 2018. images.go02.informamarkets.com/Web/Informa02/%7b548e6d56-2ea4-4da4-9404-0348b56e9a88%7d_dhillon-8.16.2018-response-letter-from-ash-radm-giroir.pdf (2 June 2026).

100 Lyndsey Blair, "Investigating the Relationships Between Socioeconomic Status, Kratom Legislation, and the COVID-19 Pandemic on Opioid Overdose Mortality in the United States" (PhD diss., University of Louisville, Aug. 2022). https://ir.library.louisville.edu/etd/3829 (2 June 2026).

101 Substance Abuse and Mental Health Services Administration, "Key Substance Use and Mental Health Indicators in the United States: Results from the 2022 National Survey on Drug Use and Health," HHS Publication No. PEP23-07-01-006, NSDUH Series H-58 (Rockville, MD: Center for Behavioral Health Statistics and Quality, 2023). www.samhsa.gov/data/report/2022-nsduh-annual-national-report (2 June 2026).

102 Neshalatha Govarthnapany, Ladislav Dékány, Roman Gabrhelík, and Darshan Singh, "Kratom Use in Adolescents and College Students: A Systematic Review of Prevalence, Patterns, and Risk Factors Across Community and Rehabilitation Settings," *The American Journal of Drug and Alcohol Abuse* 52(1) (27 Jan 2026). 5–17. www.doi.org/10.1080/00952990.2025.2609965 (16 June 2026).

evidence does not justify prohibition, improved surveillance is needed to accurately track youth use patterns.

> *… while current evidence does not justify prohibition, improved surveillance is needed to accurately track youth use patterns.*

Prohibition is a blunt and often ineffective tool for protecting youth from substance-related harm. While it may deter some youth, it may perversely increase youth access to kratom products and the risks posed by those products. Prohibition, while eliminating legal pathways for youth access, would also hand control of the market to illicit operators who do not typically comply with laws, including those age-restricting purchases. The proliferation of illicit purveyors, attracted by the increased prices and potential profits triggered by prohibition, may increase the points at which youth can access kratom without presenting identification. Moreover, the "forbidden fruit effect" or "psychological reactance"—a motivation to restore a perceive loss of freedom—may make prohibited substances more appealing to adolescents, driving experimentation with kratom rather than deterring it.[103]

Criminalizing substances also typically makes them more potent and more dangerous for those who continue to use them. As Jeffrey Miron et al. observed in their 2019 study on opioids, diverted or illicit opioids are more dangerous than legally provided versions, because there is little, if any, quality control in underground markets and consumers cannot seek legal recourse or damages when products are contaminated or misrepresented.[104] Drugs in illicit markets also tend to become increasingly potent as heightened enforcement incentivizes suppliers to develop products that are smaller, easier to smuggle, and can be

[103] Petter Grahl Johnstad, "Does Drug Criminalization Increase Harmful Drug Use? A Scoping Review of Underlying Mechanisms," *Drug Science, Policy and Law* 11 (17 June 2025). www.doi.org/10.1177/20503245251348260 (2 June 2026).

[104] Jeffrey Miron, Greg Sollenberger, and Laura Nicolae, "Overdosing on Regulation: How Government Caused the Opioid Epidemic," Cato Institute, Policy Analysis No. 864, 14 Feb. 2019. www.cato.org/policy-analysis/overdosing-regulation-how-government-caused-opioid-epidemic (4 June 2026).

subdivided into more sellable units in order to balance the increased risk of being caught with greater profitability.[105] This logic applies directly to kratom.

As documented throughout this paper, the existing evidence indicates that much of the health risk associated with kratom products stems not from the plant or its primary alkaloids but from an unregulated market with poor quality controls, no labeling or testing requirements, and no or lax restrictions on minimum purchasing age. Outlawing legal kratom sales will only exacerbate these risks for both youth and adults as production moves into illicit channels, as has been observed with other banned substances.

6.2 ALTERNATIVE APPROACHES TO KRATOM PROHIBITION

Several states have also enacted regulatory structures for kratom products, with many adopting versions of the "Kratom Consumer Protection Act" (KCPA), a model bill developed by the American Kratom Association, which represents the interests of traditional leaf-based kratom businesses.[106] Thus far, 18 states have enacted regulations modeled on the KCPA, often with variations: Arizona, Colorado, Florida, Georgia, Kentucky, Maryland, Mississippi, Nebraska, Nevada, Oklahoma, Oregon, Rhode Island, South Carolina, South Dakota, Texas, Utah, Virginia, and West Virginia.

While each state's KCPA varies, these typically include statutory definitions for kratom and its products, age restrictions, prohibitions against adulterated products, standards for manufacturing, testing, labeling, and retailing, as well as other provisions aimed at creating an orderly market that stems youth access while permitting the sale of the plant and products derived from it to adults.[107] However, KCPA laws tend to severely limit or outright prohibit products with 7-OH concentrations higher than what naturally occurs in kratom leaves.

There is no scientific basis to limit 7-OH concentration to what is available in unprocessed kratom leaves. Moreover, there is evidence that public health may benefit by creating a

[105] Leo Beletsky and Corey S. Davis, "Today's Fentanyl Crisis: Prohibition's Iron Law, Revisited," *International Journal of Drug Policy* 46 (Aug. 2017). 156–59. www.doi.org/10.1016/j.drugpo.2017.05.050 (4 June 2026).

[106] Josh Long, "Kratom Groups Are Divided over California Bill to Regulate Botanical," *SupplySide Supplement Journal*, 15 Aug. 2024. www.supplysidesj.com/herbs-botanicals/kratom-groups-are-divided-over-california-bill-to-regulate-botanical (4 June 2026).

[107] The Ohio State University, Mortiz College of Law, Drug Enforcement and Policy Center, "Regulating Kratom in Ohio and Beyond," 27 Oct 2025, https://moritzlaw.osu.edu/research/regulating-kratom-ohio-and-beyond (28 April 2026).

regulated market where certain populations of kratom users may access higher potency products. Despite such a flaw, these state-level regulations demonstrate that most of the policy goals motivating kratom-prohibiting legislation could be better achieved, with fewer negative consequences, through a measured regulatory approach.

> *There is no scientific basis to limit 7-OH concentration to what is available in unprocessed kratom leaves.*

PART 7

RECOMMENDATIONS FOR STATE REGULATION OF KRATOM

The evidence compiled in this study concludes that the prohibition of kratom products is counterproductive, while at the same time demonstrating that an absence of regulation creates notable public health risks. State-level regulatory frameworks offer a middle ground that can keep kratom products legal for adults while establishing enforceable standards for product safety, labeling, and retail access. This section outlines specific policy recommendations grounded in the available data and aligned with successful elements of existing state kratom laws and analogous product regulations.

The primary harms posed by kratom products stem from polydrug interactions and poor manufacturing practices. For each of these documented risks, corresponding regulatory solutions already exist in standard supplement and food-safety regulation. Accordingly, we recommend that states adopt regulatory frameworks that can directly address known risks and keep products away from minors without unnecessarily depriving or criminalizing adult kratom consumers. State policymakers should seek a regulatory balance that allows consumer access to regulated products without raising costs or barriers to a degree that consumers are incentivized to shift to competing illicit products—an outcome that would be counterproductive for both public health and regulatory oversight.

These authors have helpfully distilled the recommendations described below into model legislation designed to provide a comprehensive regulatory framework for states that balances consumer protection with adult access and enforceability. We call this model the Kratom Product Regulation and Accountability Act. Lawmakers concerned with the possible adverse consequences of poor manufacturing standards or polydrug use involving kratom or its derivatives should consider this model approach to regulation.

AGE RESTRICTIONS

Adolescent kratom use, while relatively low in prevalence, remains a concern. As previously noted, survey data from 2022 indicate that approximately 0.1% of adolescents aged 12-17 report past-year kratom use.[108] However, while youth consumption is uncommon, the lack of scientific evidence on the developmental impact of adolescent kratom use, along with the risks of dependence, warrants reasonable controls to prevent unauthorized youth access.

To limit youth access while preserving adult access, states should establish a minimum purchase age of 21 for all kratom products. This aligns with many kratom regulatory models adopted by states and is consistent with tobacco and alcohol regulations.

That said, in order to discourage youth use of more dangerous substances, such as opioids, or illicit products (opioids or kratom), we recommend states adopt pathways that allow minors access to kratom products for therapeutic purposes with permission from a parent, legal guardian, or medical practitioner, similar to laws that allow qualifying minors to access medical cannabis in states like Connecticut, Illinois, and Pennsylvania.[109]

SYNTHETIC AND SEMI-SYNTHETIC ALKALOIDS

Products containing semi-synthetic 7-OH (derived from kratom mitragynine via chemical conversion) should be treated the same as naturally occurring 7-OH under state law, with

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[108] Govarthnapany, "Kratom Use in Adolescents and College Students."

[109] Conn. Gen. Stat. § 21a-408d(a) (2025), "Palliative use of marijuana," www.cga.ct.gov/2025/pub/chap_420f.htm (20 Oct 2026); 410 Ill. Comp. Stat. § 130/60(b), "Compassionate Use of Medical Cannabis Program Act," www.ilga.gov/Legislation/ILCS/Articles?ActID=3503&ChapterID=35 (20 Oct 2026); 28 Pa. Code § 1191a.32, "Medical marijuana patient authorization letters," www.pacodeandbulletin.gov/Display/pacode?file=/secure/pacode/data/028/chapter1191a/s1191a.32.html (20 Oct 2026).

the only differentiations based on potency, because the risks associated with high-concentration products derive from potency, not the method of synthesis.

A distinction may therefore be warranted, not between "natural" and "synthetic" sources, but between chemically identical molecules and novel synthetic analogs. Novel synthetic analogs of 7-OH that do not occur naturally in kratom present different risks compared to naturally occurring alkaloids. These unstudied compounds lack historical use data and safety data and lack the botanical matrix that may moderate absorption and effects. States may wish to grant the regulatory agency governing kratom the authority to prohibit the inclusion of such novel synthetic analogs that may pose risks to consumers, unless and until they undergo independent safety review.

That said, we recommend against scheduling these alkaloids as controlled substances or applying criminal penalties for possession for several reasons. First, under a regulatory system where consumers have access to adequately potent, regulated products, demand for synthetic analogs would likely be minimal. Second, some of these compounds may prove to have pharmaceutical value upon further research; scheduling would make such research far more difficult, expensive, and less likely to occur. Third, while states may pursue criminal penalties against manufacturers who knowingly incorporate unauthorized synthetic analogs, penalizing consumers who may unwittingly possess such products would be counterproductive to public health. Consumer-level enforcement exacerbates systemic harms—including health disparities and increased risk of drug use, incarceration, and overdose—without meaningfully advancing regulatory goals.[110]

PRODUCT REGISTRATION AND MANUFACTURER ACCOUNTABILITY

To ensure effective market oversight and product traceability, states should require that all finished kratom products sold within the state be registered with the designated regulatory agency, such as the state Department of Health. Registration should include submission of product labeling, ingredient information, and a certificate of analysis demonstrating compliance with contaminant and alkaloid limits. Registration should be product-specific, differentiated by ingredients rather than by weight, volume, or size to minimize unnecessary burdens on manufacturers.

[110] Alice Zhang, Joseph A. Balles, Jennifer E. Nyland, et al., "The Relationship Between Police Contacts for Drug Use-Related Crime and Future Arrests, Incarceration, and Overdoses: A Retrospective Observational Study Highlighting the Need to Break the Vicious Cycle," *Harm Reduction Journal* 19 (27 June 2022). www.doi.org/10.1186/s12954-022-00652-2 (16 June 2026).

States should also consider requiring manufacturers to maintain product liability insurance (e.g. an occurrence limit of $3 million or more). This will ensure consumers have recourse in the event of harm and incentivizes manufacturers to maintain high safety standards.

7.1 STANDARDS FOR GOOD MANUFACTURING PRACTICES

As discussed throughout this paper, many health concerns related to kratom products arise from unsanitary or improper manufacturing processes that introduce contaminants into finished products or fail to fully remove solvents or pesticides. Kratom leaves may absorb heavy metals from environmental sources, and products may be contaminated with heavy metals via manufacturing equipment.[111] Solvents used to create concentrated products or extracts may also pose a risk to consumers if not properly removed. Additionally, mold, microbes, and residual pesticides may pose risks to consumer safety.

> *"The need for rigorous manufacturing standards is underscored by empirical research documenting contamination in commercially available kratom products..."*

The need for rigorous manufacturing standards is underscored by empirical research documenting contamination in commercially available kratom products, including microbes, bacteria, fungi, and significant levels of toxic metals.[112]

While the FDA currently regulates manufacturing of food and most pharmaceuticals by prescribing the processes, equipment, batching, and tracking parameters producers must follow (known as current "Good Manufacturing Practices" or GMP), such standards do not yet exist for federally legal kratom products. In the absence of federal GMPs, several states

[111] Atikarn Janthongkaw, Tanaporn Khamphaya, Supabhorn Yimthiang, Phisit Pouyfung, "A Preliminary Assessment of Heavy Metal (Pb, Cd, and As) Contamination in the Leaves and Cultivation Area of Mitragyna speciosa (Korth.) Originating from Thailand," *Asia-Pacific Journal of Science and Technology* 29(4) (27 June 2024). www.doi.org/10.14456/apst.2024.56 (16 June 2026).

[112] Prozialeck, "Evaluation of the Mitragynine Content, Levels of Toxic Metals and the Presence of Microbes in Kratom Products Purchased in the Western Suburbs of Chicago."

have enacted their own manufacturing and testing standards to ensure kratom products are processed in sanitary conditions, using safe equipment and solvents, and that finished products adhere to contaminant thresholds. However, the robustness of these standards vary by state.

For instance, Oregon requires all kratom processors conduct third-party testing on each batch, following similar testing standards for adulterants imposed on cannabis and hemp processors. These requirements cover microbiological analyses (e.g., E. coli, salmonella), pesticide residue screening, residual solvent testing, heavy metals, and mycotoxins.[113] Similarly, West Virginia has established strong contaminant thresholds for kratom products, including a zero tolerance for pathogenic E. coli, listeria, salmonella, and other pathogens.[114]

Beyond contaminant testing, some states require GMP certification as a condition for market access. Nebraska, which adopted a regulatory framework for kratom products in May 2025 under Legislative Bill 230, mandates that kratom manufacturers maintain a valid third-party certificate of good manufacturing practices along with a current FDA food facility registration.[115] This is a forward-thinking approach, though, as discussed below, Nebraska's standards stop short of requiring comprehensive batch testing for contaminants.

Recommended Manufacturing Standards:

- **Facility and FDA standards:** Manufacturers must be properly registered with the FDA and comply with federal Current Good Manufacturing Practice (cGMP) regulations for supplements (21 CFR Part 210), including requirements for clean, well-maintained buildings with proper ventilation, plumbing, and lighting; sanitized equipment; and workspaces arranged to prevent cross-contamination. Additionally, states may wish to require annual inspections and a state-issued food establishment permit (or equivalent) for any business distributing kratom products.
- **Batch testing:** Each batch of finished kratom product must be tested by an independent, ISO-IEC 17025-accredited laboratory prior to distribution, with no

[113] Anresco Laboratories, "Kratom Oregon Requirements," anresco.com/services/kratom-oregon-requirements (16 June 2026).

[114] West Virginia Department of Agriculture, "List of Contaminants for Hemp and Kratom," https://agriculture.wv.gov/wp-content/uploads/List-of-Contaminents-for-Hemp-and-Kratom.pdf (2 June 2026).

[115] Neb. Leg. Bill 230, 109th Leg., 1st Sess. 2025. nebraskalegislature.gov/FloorDocs/109/PDF/Intro/LB230.pdf (20 Oct 2026).

direct or indirect financial or economic interest between the processor and the laboratory or accrediting body. A certificate of analysis (COA) for each batch must be retained by the manufacturer for a minimum of one year following the product's expiration date and be made available to regulators upon request. The COA must demonstrate compliance with limits for:

- Alkaloid and alkaloid metabolites;
- Residual solvents;
- Heavy metals (including cadmium, arsenic, mercury, and lead);
- Microbes;
- Pesticides; and
- Any other substances limited by department rule.

Contaminant thresholds: Finished products must not exceed contaminant limits as established by department rule, with reference to U.S. Pharmacopeia (USP) standards, which are regularly updated and reflect current scientific consensus. At a minimum, contaminant limits should address heavy metals (USP Chapter 2232), residual solvents (USP Chapter 467), microbial contaminants including zero tolerance for salmonella, E. coli, and listeria (USP Chapter 2021), and pesticide residues (USP Chapter 561, incorporating EPA tolerances under 40 CFR part 180). States may adopt explicit numeric thresholds that implement these USP standards, as Rhode Island has done, but referencing the USP chapters directly is sufficient and avoids creating duplicative or potentially conflicting state-specific limits.

Recordkeeping protocols: Manufacturers, importers, distributors, and retailers must maintain records sufficient to ensure product traceability and post-market safety monitoring. This includes: (1) transaction records (invoices or equivalent records for all kratom-related sales, purchases, and transfers) for at least three years; (2) batch traceability records linking each batch of finished product to its COA and manufacturing date, sufficient to support a product recall if necessary; and (3) adverse event and consumer complaint records maintained by manufacturers for at least three years. States may impose additional requirements, such as employee training documentation, but these are not necessary for basic consumer protection and may create unnecessary burdens, particularly for small manufacturers.

FACILITY STANDARDS

In Florida, kratom is classified as a food product and manufacturers are required to comply with federal cGMP regulations for dietary supplements via 21 CFR Part 111.[116] This means facilities must use clean, well-maintained buildings with proper ventilation, plumbing, and lighting, must keep equipment sanitized, and arrange workspaces to prevent cross-contamination between different ingredients or products. Florida also requires any business distributing kratom products to obtain a state food establishment permit and receive annual inspections.[117] The permit process includes an initial onsite inspection to verify equipment and processes, with annual renewals and continued compliance expected.[118] This combination of federal cGMP compliance with state-level inspections is a model worth replicating.

Nebraska, like Florida, requires that kratom products be manufactured in facilities meeting federal cGMP regulations for dietary supplements (21 CFR Part 111). Additionally, state law requires processors to register with the FDA as food facilities.[119]

BATCH TESTING

Few states impose proactive batch testing requirements for kratom products. Oklahoma, for example, does not require vendors to test every batch before sale. Instead, the law stipulates that, upon request by the State Department of Health, vendors must produce test results from a U.S.-based independent testing laboratory to confirm the accuracy of product label information.[120]

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116 Fla. Department of Agriculture & Consumer Services, Kratom Products, Fla. Admin. Code r. 5K-4.030(3)(c) (2024), https://flrules.org/gateway/RuleNo.asp?id= 5K-4.030 (20 Oct 2026). 21 C.F.R. pt. 111 (2026) www.ecfr.gov/current/title-21/chapter-I/subchapter-B/part-111 (2 June 2026).

117 Fla. Admin. Code r. 5K-4.030(3)(c); Fla. Dep't of Agric. & Consumer Servs., "Wholesale/Manufactured Food Program," Florida Department of Agriculture and Consumer Services, accessed October 20, 2026, https://www.fdacs.gov/Business-Services/Food/Food-Establishments/Wholesale-Manufactured-Food-Program (20 Oct 2026).

118 Fla. Admin. Code r. 5K-4.020(2)(c), (4)(b) (2025), https://flrules.org/gateway/RuleNo.asp?id=5K-4.020. (20 Oct 2026).

119 Neb. Rev. Stat. § 71-3807(2)(b)(vi)–(vii) (2025), https://nebraskalegislature.gov/laws/statutes.php?statute=71-3807 (20 Oct 2026).

120 63 Okla. Stat. § 1-1432.4(D) (2025), https://www.oklegislature.gov/OK_Statutes/CompleteTitles/os63.pdf (20 Oct 2026).

Nebraska takes a different approach. Under the Nebraska Kratom Consumer Protection Act, processors must submit a certificate of analysis (COA) from an ISO/IEC 17025-accredited laboratory as part of the product registration process before a product can be sold in the state. However, Nebraska law requires only that the COA disclose the product's alkaloid content and certify that the product's 7-OH level is less than two percent of the alkaloid composition in compliance with state law.[121] Absent from the statutory requirements are any mandates to test for heavy metals, microbial contaminants, residual solvents, or pesticides.

Though bills in several states would institute more robust batch testing requirements, including for contaminants, none have yet been adopted as of May 2026.

Not all kratom products present equal risk, and batch testing requirements should reflect that spectrum. Minimally processed kratom leaf powder or tea—without chemical extraction, concentration, or alkaloid enrichment—differs fundamentally from extracts and concentrates. Evidence from product testing indicates that non-extract products (powders, capsules, tablets) generally contain higher concentrations of heavy metals than extract products, likely because extracts remove much of the raw plant material that absorbs contaminants from the soil. Conversely, extracts may require stricter oversight for residual solvents due to chemicals used in processing, while unprocessed leaf products may justify lighter solvent testing. While unprocessed leaf may still be exposed to contaminants through unsanitary manufacturing or handling processes, strong GMP requirements are generally sufficient to address such concerns.

Consequently, a more targeted regulatory approach is appropriate. For minimally processed leaf kratom products, states may forgo mandatory pre-distribution batch testing in favor of post-market random spot testing of finished products available at retail, coupled with strong facility sanitation and contaminant threshold requirements. This approach addresses the most pressing public health concerns (contamination and label accuracy) while avoiding the substantial compliance burden that batch testing would impose on small, traditional kratom vendors. By contrast, any product that has undergone chemical concentration, extraction, or alkaloid enrichment should be subject to full batch testing requirements, as these manufacturing processes introduce additional risks related to residual solvents, unpredictable potency, and higher per-serving alkaloid loads. This risk-

[121] Neb. Rev. Stat. § 71-3807(2)(b)(v) (2025), https://nebraskalegislature.gov/laws/statutes.php?statute=71-3807 (20 Oct 2026)..

proportionate framework protects consumers where risk is highest without imposing unnecessary costs where evidence of elevated risk is minimal.

> *… any product that has undergone chemical concentration, extraction, or alkaloid enrichment should be subject to full batch testing requirements…*

CONTAMINANT THRESHOLDS

Following Rhode Island's repeal of a total ban on kratom, the state adopted one of the most detailed and comprehensive contaminant thresholds of any state. The law explicitly sets heavy metal limits in parts per million: arsenic less than 2 ppm, cadmium less than 0.82 ppm, lead less than 1.2 ppm, and mercury less than 0.4 ppm. It also limits residual solvents in kratom extracts to levels allowed in U.S. Pharmacopeia Chapter 467.[122] These specific numeric thresholds provide clear, enforceable standards that manufacturers can test against.

Similarly, South Carolina prohibits kratom products containing levels of residual solvents higher than the standards set forth in Chapter 467 of the U.S. Pharmacopeia. However, while the law prohibits products that contain any "poisonous or otherwise harmful non-kratom ingredient," it does not set numerical thresholds for other potential contaminants, such as microbes or heavy metals.[123]

Arizona's approach is likely insufficient yet common to other states that regulate kratom products. The state prohibits contaminated products generally, but lacks a federal reference or state-determined numeric standards of thresholds for heavy metals, residual solvents, or other contaminants.[124]

[122] R.I. Gen. Laws § 21-28.12-3(a)(6), (2026), webserver.rilegislature.gov/Statutes/TITLE21/21-28.12/21-28.12-3.htm (20 Oct 2026).

[123] S.C. Code Ann. §§ 44-53-2010 to 44-53-2040 (2025), www.scstatehouse.gov/code/t44c053.php (20 Oct 2026).

[124] Ariz. Rev. Stat. Ann. § 36-795.02(2025), www.azleg.gov/arsDetail/?title=36 (20 Oct 2026).

RECORD-KEEPING PROTOCOLS

Rhode Island has extensive requirements for record-keeping that are largely commendable. The law requires all manufacturers, importers, distributors, and retailers to maintain invoices or equivalent records for any transaction (sale, purchase, transfer, consignment, receipt) for three years, including the other party's name, address, and the quantity/type of kratom.[125] This transaction record requirement provides for traceability for product recalls and should be emulated.

However, Rhode Island law does not require the maintenance of records related to the manufacture of kratom products, adverse events, or consumer complaints, which may hamper adequate post-market safety monitoring.

Oklahoma's record-keeping rules, by contrast, are significantly less detailed. Vendors must provide test results from an independent, U.S.-based testing laboratory upon request by the State Department of Health, but the law does not specify retention periods, required formats, or submission obligations. No other recordkeeping mandates exist regarding transaction invoices, employee training, manufacturing records, adverse events, or consumer complaints.[126] While this minimalist approach avoids unnecessary burdens on businesses, it may also leave regulators unaware of emerging safety issues and provides no mechanism for recalls.

7.2 PRODUCT TESTING AND LABELING

Consumer safety requires mandatory testing of finished kratom products by accredited laboratories. Testing panels should include:

Alkaloid potency: Testing should measure mitragynine percentage, 7-OH percentage, and total alkaloid content. Laboratory testing of kratom products in the U.S. has found high variability in alkaloid concentrations and potency in kratom products, often differing substantially from label claims.[127]

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125 R.I. Gen. Laws § 44-20.3-4, (2026), https://webserver.rilegislature.gov/Statutes/TITLE44/44-20.3/44-20.3-4.htm (20 Oct 2026).

126 63 Okla. Stat. §1-1432.4(D) (2025), https://www.oklegislature.gov/OK_Statutes/CompleteTitles/os63.pdf (20 Oct 2026).

127 Paula N. Brown, Michael Chan, Xiaohui Zhang, Thomas Brendler, "Elevated 7-Hydroxymitragynine Levels Found in Products Misbranded as Kratom," Journal of Analytical Chemistry and Microbiology 109(1) (9 Oct. 2025). 124–130. www.doi.org/10.1093/jaoacint/qsaf094 (16 June 2026).

The inability to correctly dose kratom due to mislabeling may explain, at least in part, the rise of kratom-associated side effects and increased calls to poison control centers.

Heavy metals: Testing for heavy metals should require compliance with standards dictated by agency rule or based on limits set forth by the U.S. Pharmacopeia (USP) Chapter 2232 to "Elemental Contaminants in Dietary Supplements" (testing for lead, arsenic, cadmium, mercury, and nickel). FDA laboratory testing of 30 kratom products in the U.S. found many with high concentrations of lead and nickel at levels not considered safe for human consumption.[128] As noted, reports of toxicities associated with kratom use have only appeared in the literature recently, as kratom usage spread to Europe and the United States, with adverse effects in the West differing in quality and severity compared to reported effects among traditional users in Southeast Asia. In the U.S., adverse effects often involve the same organs damaged by lead exposure, indicating that some cases of toxicity are not related to kratom, per se, but to contamination by heavy metals from poor manufacturing practices.[129]

Microbial contaminants: Microbial limits should be tested against standards set by legislation, agency rule, or refer to limits set forth in USP Chapter 2021, with testing for salmonella, E. coli, total aerobic count, and yeast/mold. A multistate outbreak investigation in 2018 linked kratom to 199 salmonella infections across 41 states, with 55% of FDA-tested samples positive for the bacteria.[130] The extent of genetic diversity among isolates suggested widespread contamination at growing, harvesting, or packaging stages rather than a single source.

Residual solvents: Residual solvents used in processing kratom may pose serious risks to consumers if not properly removed. Thresholds of known harmful solvents should be limited by legislation, agency rule, or refer to thresholds permitted under the United States Pharmacopeia (USP) Chapter 467.[131]

Pesticide residues: Pesticide residues should be tested and limited to tolerances established by the regulating agency or may refer to limits set forth in USP Chapter 561,

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128 U.S. Food and Drug Administration, "Laboratory Analysis of Kratom Products for Heavy Metals."

129 Prozialeck, "Public Health Implications and Possible Sources of Lead (Pb) as a Contaminant of Poorly Regulated Kratom Products in the United States."

130 Nsubuga, "Multistate Outbreak Investigation of Salmonella Infections Linked to Kratom."

131 U.S. Pharmacopeial Convention, "(467) Residual Solvents," *USP 30*, 1 July 2007. www.uspnf.com/sites/default/files/usp_pdf/EN/USPNF/generalChapter467Current.pdf (4 June 2026).

"Articles of Botanical Origin," which incorporates EPA tolerances for pesticide chemical residues in food (40 CFR part 180) for non-listed pesticides.[132]

Labeling requirements should include the following information for consumers:

- Serving size and alkaloid content: mitragynine percentage, 7-OH percentage, and total alkaloid content in milligrams per serving;
- Number of servings per package;
- Milligrams of 7-hydroxymitragynine and mitragynine per serving;
- Recommended maximum of servings that can be safely consumed in a 24-hour period;
- Warning prohibiting use by minors;
- Pregnancy and breast-feeding warning;
- Warning against combining kratom consumption with all known contraindicated medications or substances (e.g. opioids, alcohol, benzodiazepines, sleep aids, muscle relaxants, selective serotonin reuptake inhibitors, antihistamines that cause drowsiness, and other sedatives), as well as a blanket warning that "This product may interact in unknown and potentially harmful ways with other substances. Please consult your doctor before consuming this item;"
- Warning that statements have not been evaluated by the U.S. Food and Drug Administration and the product is not intended to diagnose, treat, cure, or prevent any disease;
- The expiration date; and
- The name and place of the business of the registrant.

Packaging requirements: State legislation should also set certain limits on packaging, including:

- A definition and prohibition of packaging or labeling deemed to be "attractive to children"; a requirement that containers be food-safe;
- Compliance with the U.S. Poison Prevention Packaging Act of 1970 (15 U.S.C. Section 1471 et seq.); and

[132] Code of Federal Regulations, Title 40, Part 180, "Tolerances and Exemptions for Pesticide Chemical Residues in Food," www.ecfr.gov/current/title-40/chapter-I/subchapter-E/part-180 (2 June 2026).

- A mandate that packages contain a graduated measuring device for liquid or bulk powdered products.

7.3 ALKALOID CONCENTRATION/POTENCY LIMITS

Laboratory testing of commercial products has revealed alarming variability in kratom product potency, sometimes exceeding labeled concentrations of mitragynine by 150%.[133] While strict testing and labeling standards address the majority of potential harms associated with high-potency products and give consumers the information and warnings necessary for informed choices, states may wish to erect some guardrails around access to the most potent products.

This, however, should be approached with extreme caution to avoid depriving consumers who need higher potency products or driving them toward illicit markets.

Animal studies indicate that higher doses of mitragynine are necessary to attenuate the effects of morphine withdrawal in rats.[134] Observational studies lend support to the idea that higher dosing may be necessary to achieve sufficient effects in humans for opioid use disorder or withdrawal. For example, Albert Garcia-Romeu and colleagues observed that kratom consumers citing opioid reduction as a motivation for use tend to consume higher-potency products and more doses per day compared to other kratom users.[135] This group was also more likely to show signs of past-year kratom-related SUD, likely related in part to their higher and more frequent dosing. Certain patients or conditions may therefore require higher dosing for adequate therapeutic results, but they may also face higher risks of dependence and side effects.

To ensure access to adequate care and discourage illicit opioid use, statutory potency limits should be carefully calibrated to ensure that those individuals who may benefit from highly concentrated products maintain access with the fewest barriers possible while making sure the general public is not unwittingly exposed to such products.

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133 Bharathi Avula, Syed Kashif Ali, Kiran K. Tatapudi, et al., "Quantitative Analysis of 7-Hydroxymitragynine in Commercial Kratom Products and Its Stability Under Chemical and Physiological Conditions," *Phytochemistry* 247 (July 2026). www.doi.org/10.1016/j.phytochem.2026.114871 (16 June 2026).

134 Norsyifa Harun, Illa Syafiqah Johari, Sharif Mahsufi Mansor, and Mohammed Shoaib, "Assessing Physiological Dependence and Withdrawal Potential of Mitragynine Using Schedule-Controlled Behaviour in Rats," *Psychopharmacology* 237(3) (12 Dec 2019). 885–97. www.doi.org/10.1007/s00213-019-05418-6 (16 June 2026).

135 Garcia-Romeu, "Kratom (Mitragyna speciosa)."

EXISTING STATE POTENCY LIMITS

Many existing state regulatory frameworks establish a 2% 7-OH cap for general-sale products, including Arizona, Colorado, Georgia, Rhode Island, South Carolina, South Dakota, and Utah, while Oklahoma imposes a one percent limit on 7-OH. Georgia and Rhode Island, additionally, sets a limit of no more than 0.5 mg of 7-OH per gram and no more than 1 mg 7-OH per serving. Rhode Island additionally caps mitragynine at 150 mg per serving.[136]

These limits, while predicated on protecting public health, typically reflect only the natural alkaloid concentrations found in kratom leaves. However, this distinction is largely arbitrary relative to public health. Restricting potency to what naturally occurs in kratom leaves is neither scientifically supported nor ideal for achieving the optimal regulatory balance. Limiting potency to this low level would likely leave many kratom consumers underserved and could thwart regulatory goals by pushing consumers toward potentially more dangerous illicit substitutes.

> *Many of the conditions that motivate kratom use—chronic pain, opioid use disorder, anxiety with co-occurring substance use—may require higher dosing than is feasible through leaf kratom alone.*

Many of the conditions that motivate kratom use—chronic pain, opioid use disorder, anxiety with co-occurring substance use—may require higher dosing than is feasible through leaf kratom alone. Research has shown that 7-OH dosing in animals up to 1mg/kg of weight (approximately 45 mg per 100 pounds) was well-tolerated with no observed adverse events.[137] As such, we recommend states avoid imposing a single potency cap, above which products are deemed illegal and instead imposing restrictions as milligrams per serving, e.g. 100 milligrams of total kratom alkaloids per serving. Setting these thresholds on a per-

[136] Legislative Analysis and Public Policy Association, "Kratom: Summary of State Laws."

[137] Elizabeth A. Maxwell, Tamara I. King, Shyam H. Kamble, et al., "Oral Pharmacokinetics in Beagle Dogs of the Mitragynine Metabolite, 7-Hydroxymitragynine," *European Journal of Drug Metabolism and Pharmacokinetics* 46(3) (May 2021). 459–463. www.doi.org/10.1007/s13318-021-00684-2 (16 June 2026).

serving milligram basis rather than alkaloid concentration is more easily enforced and understood by consumers.

States should refrain from imposing percentage-based potency caps that effectively ban products with higher alkaloid concentrations while permitting the same absolute alkaloid content through larger servings of less concentrated products. Such distinctions are arbitrary relative to public health and may inadvertently encourage harmful alternative behaviors, such as turning to illicit products. Furthermore, limiting products to alkaloid concentrations equivalent to those found in natural leaves may force consumers to ingest higher quantities of low-concentrated products or plant material to achieve desired effects, potentially exposing them to higher levels of heavy metals, contaminants or other harmful constituents.

7.4 RETAIL ACCESS AND DISPENSING CONTROLS

The retail function is the portion of the production chain over which states can exert the most direct and enforceable control, particularly when products are manufactured outside the state or imported from overseas. Unlike manufacturing, which often falls under federal jurisdiction or occurs beyond state lines, retail sales happen within state borders and are subject to routine local inspection. Therefore, retail regulation is an appropriate and effective focal point for state-level kratom policy.

> *The long history of traditional use and the absence of unique safety signals from leaf kratom itself (as opposed to contaminated or adulterated products) support continued general retail access.*

We recommend that kratom product sales be limited to age-gated establishments (21+), with secure, locked storage of inventory. However, states may wish to adopt a dual or tiered approach where minimally processed kratom products with no additives or added alkaloids remain available for sale in general retail establishments already authorized to sell age-restricted products, including convenience stores, gas stations, and pharmacies, subject to age-gating, product testing, and labeling requirements. The long history of traditional use

and the absence of unique safety signals from leaf kratom itself (as opposed to contaminated or adulterated products) support continued general retail access.

We further recommend that states consider steps to discourage kratom products from being served in a form that combines or mixes finished kratom products with other substances known to have a potentially harmful compounding effect on the central nervous system, including alcohol, caffeine, kava, cannabinoids, and nicotine. Such limits, adjustable as scientific evidence emerges, may reduce the risk of polydrug interactions.

ONLINE AND DELIVERY SALES

Direct-to-consumer online sales should be authorized for pharmacy-operated mail-order or medical delivery services, as well as for all other delivery services authorized by agency rule to dispense kratom products, provided they follow the same age-verification standards as in-person dispensing.

INTERSTATE COMMERCE AND IMPORTATION

Kratom remains legal at the federal level and therefore will involve interstate commerce. As such, states should institute a clear pathway through which compliant out-of-state products may verify compliance with state law and standards and lawfully enter that state's market.

For example, West Virginia allows individuals outside of the state to distribute or sell kratom products across state lines into West Virginia if they obtain a West Virginia business registration certificate. They must also comply with all permitting, labeling, and age-verification requirements.[138]

Rhode Island similarly allows out-of-state kratom products to enter its market, but any out-of-state manufacturer or distributor must first obtain a license from the Rhode Island Department of Health's Center for Food Protection, submitting product labels and vendor lists as part of the application. Out-of-state manufacturers may sell only to licensed in-state distributors, while out-of-state distributors may sell only to licensed in-state distributors or retailers. All products must comply with the state's strict safety, labeling, and alkaloid

[138] W. Va. Code § 19-12F-4(c), code.wvlegislature.gov/19-12F-4 (20 Oct 2026).

limits, and the Department of Health may order independent third-party testing at the licensee's expense. Direct delivery of kratom to consumers is prohibited.[139]

States should require that wholesalers, distributors, or retailers importing kratom products manufactured outside the state ensure that the out-of-state manufacturer or processor has:

- Registered with the department on a form prescribed by that department;
- Paid an annual registration fee per product;
- Provided documentation demonstrating that the out-of-state manufacturer holds a valid permit or license to produce kratom products, if such state regulates kratom products; and
- Provided documentation demonstrating that the home-state regulations governing kratom product manufacturing or processing are compliant with the state's manufacturing standards

For manufacturers or processors from states without kratom product regulations, compliance with the rules of the receiving state could instead be demonstrated by submitting to the department a certification of analysis for each batch and requiring importers to attest, under penalty of perjury, that products were manufactured, tested, and packaged in full compliance with state law.

[139] R.I. Gen. Laws §§ 21-28.12-5(b), 21-28.12-6(a), (f) (2026), https://webserver.rilegislature.gov/Statutes/TITLE21/21-28.12/21-28.12-5.htm, https://webserver.rilegislature.gov/Statutes/TITLE21/21-28.12/21-28.12-6.htm; R.I. Gen. Laws § 11-9-13.23 (2026), https://webserver.rilegislature.gov//Statutes/TITLE11/11-9/11-9-13.23.htm (20 Oct 2026).

PART 8

CONCLUSION

The evidence reviewed in this paper supports several clear conclusions, while also identifying significant gaps requiring further research.

First, complete prohibition of kratom is counterproductive. State-level bans have been associated with increased overdose mortality, consistent with the broader drug policy literature showing that drug criminalization shifts consumers to unregulated, more dangerous markets. When the DEA proposed scheduling kratom in 2016, it received more than 20,000 public comments—overwhelmingly from users who reported using kratom to manage chronic pain or opioid dependence—and the Department of Health and Human Services rescinded the proposal, citing the risk of pushing users toward potentially lethal opioids.[140] The World Health Organization's Expert Committee on Drug Dependence reached a similar conclusion in 2021, recommending surveillance but not international scheduling.[141] Prohibition does not eliminate demand; it merely displaces it.

Second, the absence of regulation creates clear risks. The 2018 multistate salmonella outbreak linked to kratom and the detection of toxic heavy metals in commercial products stem from a market with no enforceable manufacturing, testing, or labeling standards.

140 Henningfield, "Kratom Abuse Potential 2021: An Updated Eight Factor Analysis."

141 World Health Organization, WHO Expert Committee on Drug Dependence: Forty-Fourth Report, WHO Technical Report Series, No. 1038 (Geneva: World Health Organization, 2022). iris.who.int/server/api/core/bitstreams/d14c8922-00d4-46cb-8504-439d6d3fa182/content (16 June 2026).

These are not inherent risks of the plant or its main alkaloids—traditional use in Southeast Asia is not associated with such toxicities—but rather risks of an unregulated supply chain.

Third, the therapeutic potential of kratom, particularly as a harm reduction tool, deserves serious consideration. Large surveys consistently find that a substantial portion of users—up to 41% in some samples—report using kratom specifically to reduce or stop opioid use. Large majorities say it is effective for this purpose, and many report months or years of continuous opioid abstinence they attribute to kratom. In the context of an ongoing overdose crisis that has claimed hundreds of thousands of lives over the last decade, a substance that enables sustained abstinence from fentanyl and heroin, even if it produces its own mild dependence, is a harm reduction tool, not a public health threat.

Fourth, the risks of kratom, while real, appear manageable through regulation rather than prohibition. Mild adverse effects (nausea, constipation, dizziness) are common but typically transient. Physical dependence occurs with regular use, but withdrawal symptoms are generally milder than opioid withdrawal, and few participants in surveys meet DSM-5 criteria for moderate or severe kratom use disorder (KUD). More serious adverse events are rare and predominantly occur in cases of polydrug use or contaminated product consumption. Polydrug use is always inherently risky because drugs may interact in unforeseen ways.

Fifth, an evidence-based regulatory framework is feasible. We have outlined a balanced approach that sets a minimum purchase age of 21, requires GMP-certified manufacturing, third-party testing for contaminants or potentially harmful constituents, imposes labeling requirements including alkaloid content per serving and safety warnings, and establishes a tiered access system where all products are restricted to age-gating at the point of sale and higher-potency products are available only through age-gated establishments. We also recommend that manufacturers be prohibited from using packaging or labeling that may be attractive to children and that labels include warnings to indicate known contra-indications of use.

Much remains unknown about the pharmacology of kratom. Controlled trials of kratom for chronic pain and opioid use disorder would help clarify its effectiveness while longitudinal studies of KUD prevalence and progression would better inform the relative risks. The pharmacokinetics of 7-OH, such as the rate of conversion from mitragynine to 7-OH after ingestion among different populations and product types requires further study. And the

optimal regulatory parameters—including specific potency thresholds and the efficacy of registered access models—should be refined as evidence accumulates.

> *Controlled trials of kratom for chronic pain and opioid use disorder would help clarify its effectiveness while longitudinal studies of KUD prevalence and progression would better inform the relative risks.*

The central policy takeaway is that kratom is neither a harmless botanical nor a dangerous narcotic requiring criminalization. It is a complex plant with risks and benefits used by millions of Americans primarily for practical health management. Its major alkaloid, mitragynine, and its derivatives appear to produce a variety of effects in the body. The appropriate policy response is not prohibition nor continued inaction but rather a thoughtful, evidence-based regulatory approach that can directly address risks while preserving access for those who rely on kratom products as a lower-risk alternative to illicit opioids or a tool for managing chronic pain.

ABOUT THE AUTHORS

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