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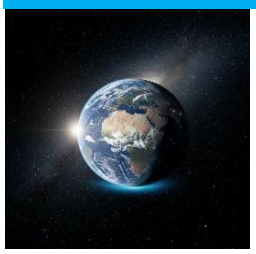

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Clinical presentation and treatment in kratom withdrawal: a narrative review of case studies

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Abstract
Background. Kratom (*Mitragyna speciosa*) use is increasing internationally and case reports describe a range of withdrawal syndromes. Clinical guidance for recognizing and managing kratom withdrawal is limited. This narrative review of case reports synthesizes clinical features, management strategies, and outcomes among published patient cases.
Aim. To characterize the clinical features, management strategies, and outcomes reported in published cases of kratom withdrawal. Additionally, identify common patterns in presentation and treatment that may inform preliminary clinical guidance for recognition and management.
Methods. Article databases were searched for case studies related to kratom withdrawal. After screening titles/abstracts and full texts, 12 reports describing 16 individual patients were included. Data was extracted and findings were narratively synthesized across demographics/use characteristics, clinical presentation, pharmacological management, and outcomes.
Results. Reported reasons for kratom use included self-treatment of opioid use disorder, pain, and psychiatric symptoms. Presentation varied from mild autonomic and gastrointestinal symptoms to severe, atypical syndromes. Opioid-like features of mild severity relative to usual opioid use predominated. Pharmacological management most commonly involved buprenorphine/naloxone. Clonidine and benzodiazepines were common adjuncts.
Conclusions. Case-level evidence and existing literature indicates that kratom withdrawal most often presents as an opioid-like syndrome and that buprenorphine, with symptom-driven, conservative induction, was the most consistently effective treatment in reported cases. Interpretation is limited by small numbers, heterogeneous and incomplete reporting (dose/formulation/duration). Prospective, standardized reporting of exposure and outcomes and kratom-specific validation of withdrawal assessment tools are needed to inform evidence-based management.
Key words: Mitragyna; Substance Withdrawal Syndrome; Opioid-Related Disorders; Herbal Medicine; Buprenorphine

1. Introduction

Kratom is a plant-derived substance obtained from the leaves of *Mitragyna speciosa*, an arboreal tree species belonging to the family *Rubiaceae*. The species grows in tropical climatic zones, where it predominantly inhabits humid environments such as swamps and marshes. Its natural distribution includes regions of Southeast Asia and parts of Oceania, specifically Philippines, Papua New Guinea, Thailand, and Malaysia [1]. For centuries, kratom was utilized by indigenous populations within its native range as part of traditional practices. In recent years, however, its use has expanded beyond these regions and gained popularity in Western countries [2,3].

Kratom has demonstrated analgesic and antinociceptive effects. Moreover, certain preclinical studies have suggested potential antidepressant, anxiolytic, stress-mitigating, and antipsychotic effects [4]. The active constituents of kratom are indole alkaloids classified as atypical opioids. This classification reflects their pharmacological profile, which differs from that of classical opioids derived from plants of the family *Papaveraceae*, such as morphine [5]. Among the alkaloids identified in the leaves, the most abundant is mitragynine, which may account for up to approximately 66% of the total alkaloid content [6,7]. The most pharmacologically potent constituent is its oxidized metabolite, 7-hydroxymitragynine, which exhibits approximately threefold greater affinity for opioid receptors compared with morphine [8]. Studies conducted in murine models have demonstrated that the analgesic effects are primarily attributable to the activity of mitragynine and 7-hydroxymitragynine. Both compounds bind to human μ-opioid and κ-opioid receptors and function as partial agonists at the μ-opioid receptor, while acting as weak antagonists at κ-opioid and δ-opioid receptors [3,7]. Additionally 7-hydroxymitragynine has been shown to have greater μ-opioid receptor affinity than mitragynine [9]. Moreover, the efficacy of mitragynine in neuropathic pain is hypothesized to be associated with its activity at α-adrenoceptors [7,10], as well as with indirect modulation of cannabinoid receptor signaling and activation of TRPV1 [11]. The complex pharmacodynamic profile of kratom is further supported by the fact that mitragynine activates GABAB receptors and acts as a weak antagonist at AMPA and NMDA receptors. In addition, it has been reported to interact with serotonergic and dopaminergic receptor systems, contributing to its multifaceted mechanism of action within the central nervous system [12]. Other pharmacologically active constituents include speciociliatine, and corynanthidine [6].

In medical contexts, kratom has been primarily used in the management of opioid use disorder, particularly to alleviate withdrawal symptoms [1,8]. It has gained popularity among individuals who self-medicate for chronic pain and has also emerged as a less expensive alternative to opioid substitution therapies for those experiencing opioid withdrawal or dependence. More recently, however, it has increasingly been used as a recreational substance. Its opioid-like effects and stimulant properties have raised concerns regarding its addictive potential and capacity to induce dependence. Consequently, its legal status has been restricted in certain countries, including Malaysia, Thailand [2,8] and Australia [1].

Traditional routes of administration of kratom involve the ingestion of fresh leaves or the preparation of a water infusion from the leaves. In Western countries, the most commonly used forms consist of powdered or crushed dried leaves, frequently administered in capsules or tablets, or prepared as an herbal tea. These products typically contain up to approximately 2% mitragynine. Highly concentrated formulations are also commercially available, including soft gels, gummies, semisolid resins, and liquid extracts, with reported mitragynine concentrations ranging from approximately 7% to as high as 40% [7].

Current estimates indicate that the number of kratom users in the United States ranges from approximately 2 million to as many as 10 million, suggesting that national surveillance systems may underestimate true prevalence [13]. Despite its growing popularity and use for perceived benefits, kratom poses significant health risks. Adverse effects associated with kratom consumption include nausea, vomiting, tachycardia, hypertension [1,12], dizziness, constipation, and heart palpitations [13]. Reported toxic effects can involve multiple organ systems, including hepatotoxicity, cardiotoxicity, acute brain injury, seizures, renal injury, and lung injury [2,8], and they typically occur following ingestion of doses exceeding 8 grams [8]. It is difficult to determine whether kratom use alone can result in fatal outcomes. Reports indicate that in 2018, the FDA documented 44 deaths "involving the use of kratom," while in 2019, the CDC reported 91 overdose deaths associated with kratom. In 2021, the NPDS recorded 67 cases linked to kratom use with major medical outcomes, including four deaths. Kratom-associated fatalities however almost always involve the presence of toxic concentrations of other substances, and a definitive lethal dose for kratom or its individual constituents has not been established [13].

Kratom has addictive potential, and its withdrawal manifests with physiological and psychological symptoms similar to those observed with opioids, though generally of lesser severity. Currently, there are no official clinical guidelines for the management of kratom withdrawal [1,7]. Severe cases of kratom withdrawal are being reported with increasing frequency [1], highlighting the importance of physicians being able to accurately recognize and manage these symptoms. This narrative review of case studies compiles information on reported instances of kratom withdrawal, detailing the clinical course, management strategies employed, and observed outcomes.

2. Methods

PubMed and Scopus databases were searched on February 17, 2026, with the terms: "kratom withdrawal" OR "mitragynine withdrawal" and publishing date no older than 5 years. This yielded 23 and 24 results respectively. Duplicates were removed, leaving 27 articles. Abstracts were screened to identify case reports relevant to the topic of this review, resulting in 15 potentially eligible articles. Following full-text review, three articles were excluded as they were not relevant to the study topic, and one article was excluded due to unavailability of the full text. An additional case was identified through manual searching of references. A total of 10 case reviews and two case series three patients each, totaling 16 patient cases were included in this narrative review.

For each patient, the following data items were attempted to be extracted and tabulated: demographics, past medical history, circumstances under which the patient contacted medical professionals, symptoms (both in relation to kratom withdrawal and not), kratom formulation and dosage, as well as origin of its use, course of treatment, outcome.

Findings were narratively synthesized across four domains: patient demographics and kratom use characteristics, clinical presentation, pharmacological management, and outcomes.

3. Results

3.1. Characteristics of the patients

The 16 patients included in this review ranged in age from 29 to 72 years, with a median age of 54 years. The majority of patients were male (12 out of 16). Past medical histories of the

patients most commonly included a prior diagnosis of some form of substance use disorder. Patients presented a variety of symptoms which are provided in Table 1.

Table 1. Characteristics and reported withdrawal symptoms of patients described in included case

Case study	Age	Sex	Past medical history	Symptoms (Somatic)	Symptoms (Neuropsychiatric)
Abidali et al.	56	Male	Depression, CUD	-	Aggression, mania
Alghalith et al.	72	Male	Benign prostate hyperplasia, hyperlipidemia, hypertension	Diaphoresis, diarrhea, muscular spasms, yawning	Anxiety
Bleifuss et al.	45	Male	Depression, OCD, AUD	Muscle spasms	Anxiety, hallucinations, insomnia
Giancola et al.	57	Male	SUD, OUD, ischemic cardiomyopathy	Arthralgia *	Irritability, malaise *
Goodwin et al.	29	Male	OUD, AUD, SUD	Bradycardia, hypoxia, muscle spasms	Confusion, lethargy
Hong et al.	65	Male	OUD	Arthralgia, myalgia	Restlessness
Lei et al. P1	62	Male	OUD, CUD	Body aches, chills, diaphoresis, muscular spasms	Decreased energy, restlessness
Lei et al. P2	54	Male	OUD, AUD	Headache, myalgia, nausea, stomach cramps	-
Lei et al. P3	59	Female	SUD	Myalgia, nausea, paresthesia	-
Settle and Yang	38	Female	Depression, OUD	Abdominal pain, diarrhea, muscle spasms	Anxiety, depression, irritability, poor sleep, restlessness
Sivakumar et al.	54	Female	Depression, OUD, AUD, type 2 diabetes	Nausea, vomiting	-
Teixeira et al.	30s	Male	OCD	-	Anxiety, irritability
Weiss and Douglas P1	36	Male	Depression, OCD, AUD	-	Anxiety
Weiss and Douglas P2	37	Male	Depression, OUD	N/A	N/A
Weiss and Douglas P3	42	Female	Depression	N/A	N/A
Jarka and Gregoire	56	Male	Dyslipidemia, hypertension, obesity, obstructive sleep apnea	Diaphoresis, tachycardia	Aggression, agitation, hallucinations, restlessness

* Symptoms reported by the patient as typical but not observed during the reported hospitalization.
CUD – cannabis use disorder, OCD – obsessive compulsive disorder, AUD – alcohol use disorder, SUD – substance use disorder, OUD – opioid use disorder

In analyzed cases kratom was consumed in a variety of formulations and dosages including raw powder, extract liquids, “shots” and tonics. One patient used a 7-hydroxymitragynine extract specifically [14]. One case involved a kava-kratom combination product ("Feel Free") [15]. In only three cases, actual alkaloid dosage could have been extracted. In Lei et al. Patient 2 it was 1 g of mitragynine per day. In Sivakumar et al. it was 30 mg of 7-hydroxymitragynine. In Bleifuss et al. the dose was inferred by the authors of this review, based on product information [16], to be around 0.3 – 0.4 g based on product information.

Duration of regular kratom use prior to presentation was scarcely and inconsistently reported across all cases. The longest reported usage was stated to be over 10 years [17]. Kratom discontinuation prior to presentation has been reported in some cases [15,17–19] with the timing varying: from four weeks before presentation to continued use at the time of presentation.

The reasons patients reported for initiating and maintaining kratom use fell into three broad categories: self-management of opioid use disorder or opioid withdrawal [14,20–23], pain relief [17,19,21,24], self-treatment of psychiatric symptoms [23,25]. Those categories sometimes overlapped within individual patients, and they weren’t always easy to discern, e.g. substituting tramadol for kratom [21] or losing access to primary OUD maintenance drug [22]. There was one case of precipitated withdrawal caused by another clinician prescribing naltrexone for weight loss [24].

3.2. Clinical presentation

The clinical presentation of kratom withdrawal across the reviewed cases demonstrated considerable heterogeneity, ranging from mild autonomic symptoms to life-threatening cardio-vascular instability leading to cardiac arrest and subsequent intensive care [26]. Despite this variability, a predominant pattern of opioid-like withdrawal features emerged across the majority of patients.

Cases included here can be divided into major categories: with patients presenting to Emergency Department or tertiary care hospital [14,15,17–20,22,24,26] or substance abuse clinics [21,23,25]. Three patients were hospitalized for reasons unrelated to kratom; coughing related to a lung mass (later diagnosed as a stage IV adenocarcinoma) [19], cardiac decompensation in heart failure [20] and deep vein thrombosis [17]. In these cases withdrawal was identified incidentally during the course of hospital stay and subsequent cessation of kratom intake.

Only six cases employed COWS (Clinical Opioid Withdrawal Scale) to assess the severity of kratom withdrawal symptoms. Five of these reported scores fell within ranges interpreted as mild withdrawal [17,19,21,22,25]. One case provided only a qualitative interpretation of "high" withdrawal severity [14], a non-standard descriptor that does not align with established COWS categories ("mild", "moderate", "moderately severe", "severe" [27]), limiting interpretability.

The outliers from expected opioid-like withdrawal symptoms were: a patient who underwent a manic episode [18], the case of cardio-vascular instability leading to cardiac arrest [26] and precipitated withdrawal [24].

3.3. Treatment and outcomes

The majority of patients (10 out of 16) [15,17,19,21–23] received buprenorphine-naloxone as the primary pharmacological intervention for kratom withdrawal and additional two received just buprenorphine [14,25]. Alternative treatment included olanzapine and aripiprazole in case of mania [18], gabapentin in case of earlier buprenorphine-naloxone intolerance [20] and phenobarbital in case of a mixed-drug withdrawal [15]. One patient (first diagnosed with alcohol withdrawal) received diphenhydramine, benzodiazepines and olanzapine with minimal effect before he eventually was given α2-agonist - dexmedetomidine as primary intervention [24]. Common adjunctive treatments included clonidine (in 5 patients [14,15,17,23]) and benzodiazepines (in 3 patients [15,17,24]). Two cases [24,26] required escalation to intensive care, and of those one requiring mechanical ventilation and cardiopulmonary resuscitation [26]. One patient experienced buprenorphine side effects and was treated with lactulose and macrogol [25].

Where buprenorphine-naloxone was initiated de novo, the induction unit dose was consistently 2/0.5 mg, administered at frequencies ranging from once to four times daily, yielding total induction doses of 2/0.5 to 8/2 mg daily [15,17,19,21,22]. Doses were subsequently titrated upward based on symptom control, with final maintenance doses ranging from 6/1.5 mg [22] to 24/6 mg daily [21]. Buprenorphine monotherapy followed a similar induction pattern, with maintenance doses of 2 mg and 16 mg reported in the two relevant cases [14,25].

Outcomes were generally favorable. In all Emergency Department cases the treatment was effective and patients were quickly discharged once acute withdrawal symptoms were controlled [14,15,17,18,22,24]. Planned hospitalization outcomes both ended with full symptom control, with discharge timeframes dependent on patients' primary condition [19,20].

Outcomes in Substance Abuse Clinics were different, with symptom control achieved in longer timeframes. Treatment courses in these cases were complicated with relapses [25] or intermittent opioid use [21].

4. Discussion

4.1. Kratom withdrawal as an opioid-like syndrome

Kratom withdrawal presented most commonly with an opioid-like constellation, consistent with opioid receptor antagonism or cessation of agonist activity: gastrointestinal distress, myalgias/arthralgias, autonomic hyperactivity (tremor, diaphoresis), and prominent neuropsychiatric features such as anxiety, restlessness, and insomnia [28]. Clinical features were heterogeneous: from mild to life-threatening.

Kratom should be included in the differential diagnosis for patients presenting with opioid-like withdrawal features without a confirmed opioid exposure, particularly in regions where kratom use is prevalent. A detailed substance use history, explicitly asking about kratom or herbal supplements, is recommended, as routine urine immunoassay screens do not detect mitragynine or its metabolites and will generally fail to detect kratom use unless a targeted LC-MS/MS or a validated immunoassay is performed [29–31].

The pattern of kratom withdrawal is consistent with mitragynine's established activity at μ-opioid receptors, and with the substantially higher affinity of its primary metabolite, 7-hydroxymitragynine [9]. Cessation of chronic μ-opioid agonism predictably produces the adrenergic rebound, smooth muscle hyperactivity, and dysphoria that characterize the classical opioid withdrawal syndrome [28]. The Clinical Opiate Withdrawal Score scores reported mild severity relative to classical opioid withdrawal; however, the scale has not been validated for kratom limiting direct comparison. Despite that, when kratom withdrawal is confirmed or suspected, severity assessment using the COWS represents the most pragmatic currently available tool for guiding treatment decisions. Its limitations in this context should be acknowledged, and neither clinical judgment nor potential pharmacological treatment should be subordinated to numeric scores alone [27].

4.2. Predictors of severity and clinical course

Although the limited and heterogeneous case base precludes formal predictor analysis, patterns emerged when demographic variables, use characteristics, and comorbidities were considered together.

Clinical setting was the most consistent correlate of presentation severity. Patients presenting to emergency departments or inpatient hospital settings tended to have more acute and severe withdrawal syndromes. Those managed in substance use disorder clinics generally exhibited milder, more gradual withdrawal courses, which could reflect planned discontinuation, lower baseline severity, earlier acute intervention (being referred to such a clinic by another clinician) and the self-selection of patients willing to engage in structured treatment.

No clear relationship between the reason for initiating kratom use, past medical history, and the clinical phenotype was identified, likely due to the heterogeneous clinical presentations and frequently complex medical histories described in the reports. However, patients who reported using kratom as a means to treat a pre-existing psychiatric condition or for recreational purposes seemed to have more pronounced neuropsychiatric symptoms.

Kratom's dose and formulation relationship to withdrawal severity across the reviewed cases could not have been analyzed, largely because reporting was inconsistent and units were non-

comparable. This severely limits any inference about dose-severity relationships and underscores the need for standardized pharmacokinetic characterization of commercial kratom products in future research. Notably, only a single publication combining a case series with a systematic review, was identified, that meaningfully linked kratom exposure to subsequent treatment requirements. In that analysis, the authors reported a strong correlation between the amount of kratom used at presentation for opioid use disorder treatment and the buprenorphine/naloxone dose required for initiation of opioid agonist therapy [23]. This finding suggests that dose-response relationships may be detectable when kratom exposure is measured in a sufficiently systematic manner.

4.3. Generalization of treatment courses

Despite variability in clinical context, a coherent treatment algorithm is identifiable across the reported cases. Buprenorphine, with or without naloxone, was the primary pharmacological intervention in 12 of 16 cases, consistent with its established capacity of alleviating opioid withdrawal [32] while carrying a ceiling effect on respiratory depression [33].

Buprenorphine-naloxone represents the most well-supported pharmacological intervention based on current case and literature evidence. Induction should begin conservatively at 2 – 4 mg, with careful monitoring and verification of withdrawal onset prior to the first dose to avoid potential precipitation [34]. Subsequent doses should be titrated upward on a symptom-driven basis, with no fixed maintenance target [35]. Such strategies are consistent across literature with discrepancy as to day one dosage limit being in range of 8 – 16 mg [36].

Clonidine was the most common adjunctive agent (in 5 out of 16 patients), consistent with its established role in attenuating adrenergic hyperactivity in the noradrenergic neurons in the locus coeruleus during opioid withdrawal [37]. α_2-agonists seem to be reasonable adjunctive agents for patients with prominent autonomic features such as diaphoresis, tremulousness, and tachycardia [37,38] which are typical symptoms during withdrawal.

Benzodiazepines were used adjunctively in three cases, involving patients with hallucinations and anxiety. In the case describing simultaneous kava and kratom withdrawal, given kava's GABAergic mechanism [39], phenobarbital was the primary agent, however with clonidine and benzodiazepines as adjuncts and the patient was eventually discharged on buprenorphine-naloxone.

Gabapentin successfully managed withdrawal in one patient unable to tolerate buprenorphine-naloxone due to his reported, earlier intolerance. While this observation is notable, it should be interpreted cautiously in light of studies showing inconsistent efficacy of gabapentin for opioid withdrawal, as well as documented safety and misuse concerns. [37,40]. Taken together, this suggests that gabapentin may represent a context-specific option when first-line therapies are contraindicated, rather than a broadly applicable intervention.

The single case of mania required antipsychotic treatment (olanzapine progressing to aripiprazole) rather than opioid-modulating agents, as the clinical presentation was dominated by manic rather than classical withdrawal features. This case illustrates that the conceptual framework of "kratom withdrawal as an opioid-like syndrome" does not apply universally, and that clinicians should remain alert to atypical presentations that may require a distinct treatment approach.

Unusual presentations with confirmed kratom exposure should prompt further evaluation, more thorough history-taking, focusing on extra substance and herbal supplement use and may require different pharmacological treatment rather than, or in addition to, opioid-modulating agents.

Patients managed in acute care settings should be referred to structured SUD services upon discharge, as the short-term symptom control achieved in emergency and inpatient settings does

not address the longer-term dimensions of kratom use disorder. Relapse prevention strategies, including naltrexone, represent a logical next step following buprenorphine stabilization.

4.4. Limitations

Several limitations of this review warrant consideration. First and foremost, the evidence base is restricted to 16 patients drawn from 12 case reports and series, which precludes any statistical generalization and limits conclusions to descriptive observations. Secondly, data quality and completeness varied markedly across reports: kratom dosage, formulation, duration of use, and time since last use were inconsistently documented, and COWS scores were employed in only a minority of cases. The heterogeneity of kratom products represented complicated cross-case comparison, as alkaloid composition and bioavailability differ substantially between formulations. Additionally, publication bias is a substantial concern inherent to case report literature: severe, atypical, or treatment-resistant presentations are disproportionately likely to be reported, potentially skewing the apparent clinical picture toward more serious manifestations of kratom withdrawal. The patient cohort was demographically narrow, being predominantly male, which may not reflect the broader population of kratom users. Finally, follow-up was uniformly short across all included reports, with no long-term outcome data available, rendering any conclusions about relapse, maintenance pharmacotherapy, or sustained recovery speculative.

5. Conclusions

Based on the synthesized evidence from the reviewed cases, the following practice considerations can be offered. These are necessarily preliminary and descriptive given the case-level evidence base.

Kratom withdrawal presents predominantly as an opioid-like syndrome. The withdrawal course is generally of mild to moderate severity relative to classical opioid withdrawal, though severe and atypical presentations have been documented and should not be discounted. Complexity is heightened by the heterogeneity of commercially available kratom products, frequent polydrug use, and the high prevalence of co-occurring psychiatric and substance use disorders among affected individuals.

Buprenorphine, with or without naloxone, represents the most consistently employed and effective pharmacological intervention, with a conservative induction approach and symptom-driven titration appearing appropriate across varied clinical contexts. Adjunctive use of α_2-agonists and benzodiazepines reflects the multifactorial nature of withdrawal in some patients, with α_2-agonists potentially providing symptomatic benefit and enhancing the effectiveness of primary therapy.

Clinicians should maintain a low threshold for including kratom in the differential diagnosis of unexplained opioid-like withdrawal, given the current limitations of routine toxicological screening combined with kratom's rising popularity. Crucially, acute symptom management should be followed by referral to structured substance use disorder services, as stabilization in emergency or inpatient settings addresses only the immediate withdrawal episode and not the longer-term dimensions of kratom use disorder.

More systematic reporting, standardized product characterization and validated withdrawal assessment tools specific to kratom are needed to establish evidence-based treatment guidelines and improve outcomes for this growing patient population.

Disclosure

Supplementary Materials
Not applicable.
Author Contributions
Conceptualization: Wojciech Baran, Patrycja Bartkiewicz, Ewelina Lachowska, Tomasz Jędrasek, Adrian Korman, Wafa Al-Batool;
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References

1. Kerrigan S, Basiliere S. Kratom: A systematic review of toxicological issues. WIREs Forensic Science. 2022;4:e1420. https://doi.org/10.1002/wfs2.1420

2. Eastlack SC, Cornett EM, Kaye AD. Kratom—Pharmacology, Clinical Implications, and Outlook: A Comprehensive Review. Pain Ther. 2020;9:55–69. https://doi.org/10.1007/s40122-020-00151-x

3. Todd DA, Kellogg JJ, Wallace ED, Khin M, Flores-Bocanegra L, Tanna RS, et al. Chemical composition and biological effects of kratom (Mitragyna speciosa): In vitro studies with implications for efficacy and drug interactions. Sci Rep. Nature Publishing Group; 2020;10:19158. https://doi.org/10.1038/s41598-020-76119-w

4. Prevete E, Kuypers KPC, Theunissen EL, Esposito G, Ramaekers JG, Pasquini M, et al. Clinical Implications of Kratom (Mitragyna speciosa) Use: a Literature Review. CURRENT ADDICTION REPORTS. 2023;10:317–34. https://doi.org/10.1007/s40429-023-00478-3

5. Garcia-Romeu A, Cox DJ, Smith KE, Dunn KE, Griffiths RR. Kratom (*Mitragyna speciosa*): User demographics, use patterns, and implications for the opioid epidemic. Drug and Alcohol Dependence. 2020;208:107849. https://doi.org/10.1016/j.drugalcdep.2020.107849

6. Annuar NAK, Azlan UK, Mediani A, Tong X, Han R, Al-Olayan E, et al. An insight review on the neuropharmacological effects, mechanisms of action, pharmacokinetics and toxicity of mitragynine. Biomedicine & Pharmacotherapy. 2024;171:116134. https://doi.org/10.1016/j.biopha.2024.116134

7. Grundmann O, Hendrickson RG, Greenberg MI. Kratom: History, pharmacology, current user trends, adverse health effects and potential benefits. Disease-a-Month. 2023;69:101442. https://doi.org/10.1016/j.disamonth.2022.101442

8. Sokup B, Pippin MM. Kratom. StatPearls [Internet] [Internet]. StatPearls Publishing; 2023 [cited 2026 Feb 23]. https://www.ncbi.nlm.nih.gov/sites/books/NBK585120/. Accessed 23 Feb 2026

9. Ganasan J, Karunakaran T, Marimuthu Y, Rusmadi N, Firouz N, Jenis J, et al. Chemistry and toxicity of 7-hydroxymitragynine (7-OHMG): an updated review on the oxidized derivative of mitragynine. Phytochemistry Reviews. 2024;24:4051–64. https://doi.org/10.1007/s11101-024-10029-x

10. Foss JD, Nayak SU, Tallarida CS, Farkas DJ, Ward SJ, Rawls SM. Mitragynine, bioactive alkaloid of kratom, reduces chemotherapy-induced neuropathic pain in rats through α-

adrenoceptor mechanism. Drug and Alcohol Dependence. 2020;209:107946. https://doi.org/10.1016/j.drugalcdep.2020.107946

11. Farkas DJ, Inan S, Heydari LN, Johnson CT, Zhao P, Bradshaw HB, et al. Cannabinoid mechanisms contribute to the therapeutic efficacy of the kratom alkaloid mitragynine against neuropathic, but not inflammatory pain. Life Sciences. 2023;328:121878. https://doi.org/10.1016/j.lfs.2023.121878

12. Hossain R, Sultana A, Nuinoon M, Noonong K, Tangpong J, Hossain KH, et al. A Critical Review of the Neuropharmacological Effects of Kratom: An Insight from the Functional Array of Identified Natural Compounds. Molecules. Multidisciplinary Digital Publishing Institute; 2023;28:7372. https://doi.org/10.3390/molecules28217372

13. Henningfield JE, Grundmann O, Huestis MA, Smith KE. Kratom safety and toxicology in the public health context: research needs to better inform regulation. Front Pharmacol [Internet]. Frontiers; 2024 [cited 2026 Feb 23];15. https://doi.org/10.3389/fphar.2024.1403140

14. Sivakumar D, Pascual J, Kennedy M, Clark KT, Mason JM, Walfield AL, et al. The successful use of buprenorphine to manage kratom withdrawal secondary to self-treatment of opioid withdrawal. Clin Toxicol (Phila). England; 2025;63:1018–9. https://doi.org/10.1080/15563650.2025.2552436

15. Bleifuss W, Boley S, Bardwell J, Goebel C, Wilkinson J. Severe kava withdrawal managed with phenobarbital. Am J Emerg Med. United States; 2025;96:298.e5-298.e7. https://doi.org/10.1016/j.ajem.2025.06.016

16. Kava Shots for Focus [Internet]. Botanic Tonics. [cited 2026 Feb 17]. https://botanictonics.com/products/feel-free-classic-tonic. Accessed 17 Feb 2026

17. Alghalith A, Nguyen H, Tennant R. The Complexities of Kratom: Insights on an Increasingly Frequent Clinical Encounter. Cureus. United States; 2024;16:e59650. https://doi.org/10.7759/cureus.59650

18. Abidali M, St Victor G, Mashaly S, Dahal P. Red kratom and red corvette: A case of mania induced by kratom withdrawal. Int J Psychiatry Med. United States; 2025;60:221–5. https://doi.org/10.1177/00912174241281980

19. Hong S, Zimmerman PE, Rao V, Markwalter DW. Buprenorphine-Naloxone in the Setting of Kratom Withdrawal, Opioid Use Disorder, and Stage IV Lung Adenocarcinoma. J Palliat Med. United States; 2023;26:734–6. https://doi.org/10.1089/jpm.2022.0491

20. Giancola NB, Caplan JP, McKnight CA. “A Kratom Konundrum”: Management of Kratom Withdrawal With Gabapentin in a Patient With a Left Ventricular Assist Device. J Acad Consult Liaison Psychiatry. Netherlands; 2021;62:368–9. https://doi.org/10.1016/j.psym.2020.10.004

21. Lei J, Butz A, Valentino N. Management of kratom dependence with buprenorphine/naloxone in a veteran population. Subst Abuse. Routledge; 2021;42:497–502. https://doi.org/10.1080/08897077.2021.1878086
22. Settle AG, Yang C. A Case of Severe Kratom Addiction Contributing to a Suicide Attempt. Cureus. United States; 2022;14:e29698. https://doi.org/10.7759/cureus.29698
23. Weiss ST, Douglas HE. Treatment of Kratom Withdrawal and Dependence With Buprenorphine/Naloxone: A Case Series and Systematic Literature Review. J Addict Med. Netherlands; 2021;15:167–72. https://doi.org/10.1097/ADM.0000000000000721
24. Jarka C, Gregoire K. Precipitated withdrawal with kratom use following naltrexone administration. Mental Health Clinician. American Association of Psychiatric Pharmacists; 2023;13:155–8. https://doi.org/10.9740/mhc.2023.06.155
25. Teixeira F, Ajewole O, Picior M, Roberts E. Treatment of obsessive compulsive disorder and Kratom dependence with buprenorphine and supportive care. BMJ Case Rep. England; 2025;18:e265834. https://doi.org/10.1136/bcr-2025-265834
26. Goodwin BJ, Chaudhri M, Jain A, Alahdadi T, Vohra A, Patel S, et al. Kratom Withdrawal: A Case Report and Review of Epidemiology, Incidence, and Prevalence. Prim Care Companion CNS Disord. United States; 2025;27:25cr04043. https://doi.org/10.4088/PCC.25cr04043
27. Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). Journal of Psychoactive Drugs. Taylor & Francis; 2003;35:253–9. https://doi.org/10.1080/02791072.2003.10400007
28. Pergolizzi Jr JV, Raffa RB, Rosenblatt MH. Opioid withdrawal symptoms, a consequence of chronic opioid use and opioid use disorder: Current understanding and approaches to management. Journal of Clinical Pharmacy and Therapeutics. 2020;45:892–903. https://doi.org/10.1111/jcpt.13114
29. Jasim RK, Singh D, Gam L-H. Development and validation of ELISA for screening of Kratom (Mitragyna speciosa) habitual users using urinary AZ122 biomarker. Biotechnology and Applied Biochemistry. 2023;70:707–15. https://doi.org/10.1002/bab.2392
30. Mustafa RR, Sukor R, Mohd Nor SM, Saari N, Mohsin AZ. Development of Methyl Ester Antibody-Based Competitive Indirect ELISA for Quantitative Detection of Mitragynine in Human Urine. ACS Omega. American Chemical Society; 2023;8:47412–26. https://doi.org/10.1021/acsomega.3c02734
31. Le D, Goggin MM, Janis GC. Analysis of Mitragynine and Metabolites in Human Urine for Detecting the Use of the Psychoactive Plant Kratom. J Anal Toxicol. 2012;36:616–25. https://doi.org/10.1093/jat/bks073

32. Gowing L, Ali R, White JM, Mbewe D. Buprenorphine for managing opioid withdrawal. Cochrane Database of Systematic Reviews [Internet]. John Wiley & Sons, Ltd; 2017 [cited 2026 Feb 23]; https://doi.org/10.1002/14651858.CD002025.pub5

33. Walsh SL, Preston KL, Stitzer ML, Cone EJ, Bigelow GE. Clinical pharmacology of buprenorphine: Ceiling effects at high doses. Clinical Pharmacology & Therapeutics. 1994;55:569–80. https://doi.org/10.1038/clpt.1994.71

34. Chapter 3D: Buprenorphine. Medications for Opioid Use Disorder: For Healthcare and Addiction Professionals, Policymakers, Patients, and Families: Updated 2021 [Internet] [Internet]. Substance Abuse and Mental Health Services Administration (US); 2018 [cited 2026 Mar 5]. https://www.ncbi.nlm.nih.gov/books/NBK574909/. Accessed 5 Mar 2026

35. Prescribing guidelines. Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence [Internet]. World Health Organization; 2009 [cited 2026 Mar 5]. https://www.ncbi.nlm.nih.gov/books/NBK143167/. Accessed 5 Mar 2026

36. Greenwald MK, Herring AA, Perrone J, Nelson LS, Azar P. A Neuropharmacological Model to Explain Buprenorphine Induction Challenges. Annals of Emergency Medicine. 2022;80:509–24. https://doi.org/10.1016/j.annemergmed.2022.05.032

37. Srivastava AB, Mariani JJ, Levin FR. New directions in the treatment of opioid withdrawal. The Lancet. 2020;395:1938–48. https://doi.org/10.1016/S0140-6736(20)30852-7

38. Kuszmaul AK, Palmer EC, Frederick EK. Lofexidine versus clonidine for mitigation of opioid withdrawal symptoms: A systematic review. Journal of the American Pharmacists Association. 2020;60:145–52. https://doi.org/10.1016/j.japh.2019.10.004

39. Sarris J, LaPorte E, Schweitzer I. Kava: A Comprehensive Review of Efficacy, Safety, and Psychopharmacology. Aust N Z J Psychiatry. SAGE Publications Ltd; 2011;45:27–35. https://doi.org/10.3109/00048674.2010.522554

40. Martin JC, Gainer D. Psychiatric Uses of Gabapentin. Innov Clin Neurosci. 2022;19:55–60.