Review Article

Understanding the Effects and Clinical Potential of Kratom *(Mitragyna speciosa)*: A Narrative Review

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Abstract

OBJECTIVES: The rising use of kratom across Southeast Asia has driven interest in its potential applications while also raising questions about its safety.

Materials and Methods: A comprehensive review spanning the past two decades was conducted, encompassing peer-reviewed articles and data issued by Southeast Asian health agencies.

RESULTS: Kratom's stimulant- and opioid-like properties have been associated with both potentially beneficial and adverse effects, including applications in managing alcohol and opioid use disorders, pain, depression, and anxiety, as well as risks involving dependence and withdrawal. Although preliminary animal studies and limited human case reports suggest a possible therapeutic role, the absence of well-controlled, standardized trials prevents definitive conclusions regarding its efficacy and safety.

Conclusion: Historically, kratom has been utilized in medical treatments and substance use disorder management. Present evidence points to a similar clinical potential; however, without clear regulations and robust clinical research, kratom carries significant health risks and warrants further rigorous study.

Keywords: kratom, kratom effects, clinical potential, substance use disorders, Safety

Kratom, a tropical evergreen tree, is indigenous to Southeast Asia, found primarily in Thailand, Indonesia, Malaysia, Myanmar, and Papua New Guinea. Its scientific name is *Mitragyna speciosa*. For centuries, it has been used in traditional medicine.[1] Mitragynine (MG) is the primary active alkaloid in kratom. In the brain, it interacts with opioid receptors to produce a variety of effects, such as euphoria, sedation, and pain reduction. Furthermore, Kratom's alkaloids, which include 7-hydroxymitragynine (7-HMG), contribute to its overall effects. Kratom is available in a variety of formulations, including capsules, resin, tinctures, and powder, and is sold in headshops and online.[2] Recent evidence indicates that kratom products are gaining popularity in darknet markets as well.[3] Kratom is utilized recreationally as a plant-based substance by certain individuals. In modest dosages of up to 5 g of plant material, its effects are characterized as psychostimulant, while at higher doses of approximately 5 to 15 g, they are related to opioids.[4] Nevertheless, its indigenous application in Southeast Asia has been linked to the nonmedical self-treatment of a variety of conditions, including hypertension, stomach ailments, diarrhea, infections, and diabetes, as well as substance use disorder (SUD) symptoms, including the withdrawal of opioids and other drugs, pain, and an increase in energy, which have been documented in the West.[5-7]

Preclinical Data

From a pharmacological perspective, MG is recognized as the principal lipophilic alkaloid in kratom. Its psychoactive metabolite, 7-HMG, has received considerable attention in preclinical models due to its analgesic

properties, although investigations of other alkaloids—such as speciociliatine—remain limited.[2] Early findings indicate that MG's polypharmacological profile involves activity at mu-opioid receptors (MOR), seemingly without engagement of β-arrestin-2 in the signaling cascade.[8] This receptor profile may explain kratom's analgesic potential and suggests a distinct mechanism compared to conventional opioids.

Notably, animal studies indicate that oral administration of MG in high doses (20–400 mg/kg) does not provoke the respiratory depression observed with oxycodone.[8] Nevertheless, the overall safety profile of MG is still inadequately defined, prompting the Food and Drug Administration (FDA) to express concern about the misuse potential of unregulated kratom products containing MG and 7-HMG.[9] The FDA further underscores that no medical applications have been officially approved for these herbal supplements. Against this backdrop, the present review evaluates both preclinical and clinical findings on kratom, aiming to clarify its risk-benefit profile, explore its mechanisms of action, and guide future therapeutic research. Comparable apprehensions have arisen in Europe, where kratom is prohibited in several nations, including Sweden, Poland, Romania, and Denmark, among others. Specifically, our objectives include: (a) assessing clinical and anecdotal evidence regarding kratom's therapeutic efficacy, (b) identifying clinical and health-related concerns, and (c) examining the extent of available data on kratom's effects in populations new to its use.

Methods

This narrative review was conducted to identify, synthesize, and critically appraising existing literature on the effects and clinical potential of kratom (Mitragyna speciosa). A literature search was performed in the PubMed, Scopus, Web of Science, and Google Scholar databases for articles published from January 2003 to December 2023. The following search terms included "Kratom," "*Mitragyna speciosa*," "Mitragynine," "7-hydroxymitragynine," "Opioid receptors," "Pain management," "Substance use disorder," "Safety," and related keywords. In addition to the database searches, the reference list of relevant articles was manually screened to identify any additional pertinent studies.

Peer-reviewed original research, reviews, case reports, and official health reports focusing on kratom's pharmacology, therapeutic potential, or risks were included. Editorials, commentaries, and non-English publications were excluded. Titles and abstracts were screened, and full-text reviews were conducted when necessary.

To provide a thorough overview of this subject, we performed a literature analysis spanning the previous two decades, including peer-reviewed articles and data disseminated by health organizations throughout Southeast Asia.

Results

Clinical Evidence Indicating the Therapeutic Value of Kratom

Preclinical Evidence

Preliminary preclinical evidence corroborates anecdotal claims that kratom may be effective in alleviating pain and addressing mental health issues.[10] In vitro and/or in vivo investigations have demonstrated that kratom and its alkaloids provide analgesic and antinociceptive effects, as indicated by the prolonged latency of antinociceptive responses in hot plate or tail-flick assays, as well as in models of inflammatory pain generated by acetic acid.[11,12] The anti-allodynic efficacy in neuropathic pain has also been documented.[13,14] Furthermore, certain preclinical models have indicated kratom's antidepressant, anxiolytic, stress-reducing, and antipsychotic properties. Kratom and its alkaloids have been found to possess gastroprotective, anti-inflammatory, antibacterial, antioxidant, antimutagenic, and anticancer properties. A recent preclinical investigation shown that MG and speciociliatine functioned as chemo-sensitizers for cisplatin and suppressed cell growth in nasopharyngeal carcinoma, a malignant disease.[15] A recent study indicates that MG inhibits the enzyme acetylcholinesterase (AChE), which is implicated in Alzheimer's disease.[16] It may also demonstrate a lipolytic impact and antidiabetic action by blocking certain biological enzymes (α-glucosidase, pancreatic lipase) when used in conjunction with the type 2 diabetes medication acarbose (α-glucosidase inhibitor). Preclinical evidence indicates its potential in addressing (i) alcohol use disorder, alcohol withdrawal, and alcohol-seeking behavior, exhibiting a substantial therapeutic window[17,18]; (ii) dependence and withdrawal from opioids[12] without inducing anxiogenic symptoms[19] while concurrently enhancing cognitive performance[20]; and (iii) craving and addiction related to methamphetamine.[21]

Clinical Studies Evidence

The discourse regarding the clinical ramifications of kratom consumption has been augmented by findings from observational studies conducted in traditional settings (Malaysia or Thailand) involving long-term daily kratom users who consume several glasses of kratom juice daily (ranging from 2 to 6 mg/day).[3,10,22] The estimated daily intake of MG in these instances varies from 76 to 434 mg[22,23], with no information known on other alkaloids. Certain research has indicated a correlation between prolonged kratom consumption and health complications. This encompasses kratom's influence on visual episodic memory and modification of cholesterol levels [24,25], initial stages of renal impairment[26,27], and cravings accompanied by physical and psychological withdrawal symptoms.28 These effects last for approximately three days but are milder than those observed in the West or those associated with traditional opioids.[28,29]

At this point, there is no evidence of kratom-induced psychosis, abnormalities in social functioning, or long-term

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cognitive or biochemical/endocrinological damage.[30-32] Moreover, initial clinical data indicate kratom's therapeutic potential as (i) an analgesic, evidenced by a randomized controlled trial (RCT) involving kratom users that demonstrated increased pain tolerance following kratom consumption without notable adverse health effects[33], and (ii) a harm reduction strategy, with reports of kratom mitigating regular use of drugs (heroin, methamphetamine, amphetamine), alleviating opioid side effects, and reducing HIV risk behaviors among illicit and opioid users.[34,35] Evidence indicates that kratom may have a beneficial lipid profile and could offer protection against metabolic syndrome, coronary heart disease, or cerebrovascular illness.[31,36] Even so, this evidence contradicts the modest elevation in serum lipids associated with increased kratom usage as reported by Leong Bin Abdullah et al.[37] Ultimately, two investigations assessed the pharmacokinetic characteristics of MG in humans, indicating that it adheres to a two-compartment model with a terminal half-life of one day.[38,39]

Health Hazards Related to Kratom Use

The reported negative clinical consequences of kratom should also be considered when evaluating its clinical implications. The safety profile of kratom has been the subject of numerous case reports and case series, particularly when it is consumed outside of controlled environments. The risks of kratom dependence or addiction with withdrawal symptoms, cases of neonates with abstinence syndrome born from mothers with or without kratom withdrawal, and neurological and psychiatric manifestations are among the issues that have been raised.[40,41] Recent research has documented instances of mental and psychological distress, particularly when kratom is combined with nonmedical analgesics and methamphetamine.[42] Endocrinological damages, dermatological manifestations, electrolytic and kidney alterations, hepatic and gastrointestinal injuries, and respiratory and cardiological health hazards are additional negative consequences that require further investigation.[42-44] The data regarding the effects of kratom on cardiological functioning remains inconsistent. A transient increase in pulse rate and blood pressure was observed in kratom users, underscoring the necessity of further research into the cardiological effects of kratom use. There have been reports of conditions of multiorgan dysfunction, undifferentiated shock, serotonin syndrome, and autonomic nervous system dysfunction.[45,47]

Discussion

Kratom has garnered increasing scientific and public attention for its potential in pain management, substance withdrawal support, and other therapeutic applications. Preclinical studies point to the analgesic, anxiolytic, and anti-inflammatory properties of kratom's primary alkaloids—particularly mitragynine (MG) and 7-hydroxymitragynine (7-HMG)—which align with traditional usage in Southeast Asia for managing pain and improving work stamina. Observational and case reports from these regions also suggest kratom may reduce opioid cravings and withdrawal symptoms.

Despite these encouraging findings, the existing clinical data are limited in scope and often derived from studies with small sample sizes, cross-sectional designs, or non-standardized kratom preparations. Reported benefits, such as reduced opioid dependence and improved pain tolerance, coexist with risks that include dependence, withdrawal, metabolic alterations, and adverse interactions when kratom is combined with other substances. Variations in kratom alkaloid content, product adulteration, and unregulated marketing practices—particularly in Western countries—further complicate the assessment of both efficacy and safety.

Additionally, cultural and regulatory contexts greatly influence perceptions and usage of kratom. In Southeast Asia, where kratom holds a longstanding place in traditional medicine, new legal frameworks are emerging to regulate its cultivation and consumption. In contrast, Western health authorities often emphasize product quality concerns and potential misuse, leading to differing legal statuses and enforcement strategies. These regulatory inconsistencies underscore the need for standardized quality control and clear guidelines to mitigate possible health risks.

Overall, while preliminary evidence supports kratom's utility in managing pain and substance use disorders, more robust clinical research is necessary to define safe dosing parameters, clarify long-term effects, and determine its efficacy relative to established treatments. Such data will be crucial for healthcare providers, policymakers, and patients when considering kratom as a therapeutic agent.

Conclusion

Kratom has shown promise in both preclinical and observational studies for pain management and substance use disorder support. However, the lack of high-quality, controlled clinical trials and standardized manufacturing processes poses challenges to ensuring consistent therapeutic outcomes and consumer safety. Addressing these gaps through well-designed research can establish evidence-based guidelines for kratom's use, paving the way for its responsible integration into clinical practice while minimizing potential risks.

This article reviews the most current evidence about the clinical implications of kratom usage, as research on the subject is continually advancing. Although there is an increasing volume of anecdotal self-reported evidence indicating the therapeutic efficacy of kratom for managing acute and chronic pain, as well as psychiatric disorders, including substance use disorder, in nonmedical contexts, numerous studies document instances of acute intoxication or the onset of dependence associated with prolonged heavy use in these environments. Notably, the majority of safety apprehensions originate from Western (non-native) nations, where kratom consumption often coincides with the use of other narcotics. Kratom products are marketed online and elsewhere using alluring tactics that often provide incorrect or insufficient information regarding ingredients, dose, kind, and alkaloids,

among other factors. These factors complicate the assessment of the dose–response relationship and/or the causal association with kratom exposure. Conversely, the majority of studies conducted in native countries, primarily of a cross-sectional design, yield promising data regarding the potential therapeutic efficacy of kratom, further corroborated by preliminary preclinical evidence. Notwithstanding these inconsistencies, it is essential to ascertain the dosage of MG and other alkaloids deemed safe and therapeutically beneficial in medicinal applications. This understanding could aid in kratom's risk evaluation and provide further information to physicians and regulatory bodies considering kratom as a treatment for pain, mental health issues, and other chronic or benign health disorders. Ultimately, controlled and longitudinal studies conducted under meticulous clinical supervision, involving healthy and naïve subjects and/or participants who utilize other substances or medications outside conventional parameters, will enhance kratom research and elucidate the fundamental clinical, pharmacological, and toxicological mechanisms essential for guiding future therapeutic applications of kratom.

Disclosure statement

The authors affirm that there are no recognized conflicts of interest related to this publication. The writers used AI-assisted technologies (ChatGPT-4o) to verify grammar and enhance readability throughout the development of this work.

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