

Current Management Approaches and Future Directions for Kratom Use Disorder: A Comprehensive Review

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ABSTRACT

This comprehensive literature review examines the current state of knowledge regarding the management of kratom use disorder (KUD). Kratom, a tropical plant containing psychoactive alkaloids, has seen rising popularity and concerns about dependence and public health impacts. The review covers the pharmacology of kratom, diagnostic criteria and assessment of KUD, and various treatment approaches. Psychosocial interventions like cognitive-behavioral therapy, motivational interviewing, contingency management, and peer support groups are discussed. Pharmacological treatments explored include opioid agonist therapy, alpha-2 agonists, antidepressants, and emerging potential therapies. Integrative and alternative approaches like acupuncture, mindfulness, and supplements are also examined. Challenges highlighted include limited research, societal stigma, and barriers to treatment access. Future directions emphasize developing novel pharmacotherapies, improving treatment availability through specialized programs and telehealth, longitudinal studies on comorbidities and harm reduction, and evidence-based policies balancing public health and therapeutic considerations. The review underscores the need for a multidisciplinary approach combining psychosocial, pharmacological, and alternative modalities supported by robust research to effectively address the growing public health challenge of KUD.

Keywords: Kratom Use Disorder (KUD); pharmacological treatments; psychosocial interventions; public health impacts; multidisciplinary approach.

INTRODUCTION

Kratom (*Mitragyna speciosa*) is a tropical tree from the coffee family, native to Thailand, Malaysia, Indonesia, and Papua New Guinea (1). The leaves of the kratom plant contain several alkaloids, with mitragynine and 7-hydroxymitragynine being the primary psychoactive compounds (2). Kratom has been used traditionally for its stimulant and pain-relieving properties, as well as for treating opioid withdrawal symptoms (3). While kratom has been used for centuries in Southeast Asia, its use has become increasingly popular in Western countries, particularly in the United States (4) and the rise in kratom use has led to concerns about its potential for abuse and dependence, as well as its impact on public health (5).

Kratom use disorder (KUD) is characterized by a problematic pattern of kratom use leading to clinically significant impairment or distress, as defined by the Diagnostic and Statistical Manual of

Mental Disorders (DSM-5) for substance use disorders (6). Individuals with KUD may experience cravings, difficulty controlling their kratom use, continued use despite adverse consequences, and the development of tolerance and withdrawal symptoms (3).

The significance of kratom use disorder stems from its potential for adverse health consequences and the growing public health concerns surrounding its use (7). While kratom has been touted as a potential alternative to opioids for pain management and as a treatment for opioid withdrawal, its long-term safety and efficacy remain uncertain (8). Furthermore, kratom has been associated with various adverse effects, including nausea, vomiting, constipation, respiratory depression, seizures, and psychosis (9,10). Cases of kratom-related overdoses and deaths have also been reported, highlighting the potential risks associated with its use (11,12).

The prevalence of kratom use and KUD has been challenging to estimate due to the lack of comprehensive epidemiological studies (13). However, available data suggest an increasing trend in kratom use, particularly among individuals with substance use disorders seeking an alternative to opioids or as a means of self-medication (5,9). A survey conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA) in 2019 found that approximately 1.3 million individuals aged 12 and older had used kratom in the past year (14). Additionally, data from the National Poison Data System (NPDS) revealed a tenfold increase in kratom-related exposure cases between 2010 and 2015 (9).

Given the increasing prevalence of kratom use and the potential risks associated with KUD, there is a pressing need to understand the current state of knowledge regarding its management and treatment. This literature review aims to provide a comprehensive overview of the current approaches to managing kratom use disorder, encompassing both psychosocial and pharmacological interventions, as well as integrative and alternative approaches.

PHARMACOLOGY AND EFFECTS OF KRATOM

A. Active Compounds and Mechanisms of Action

The pharmacological effects of kratom are primarily attributed to its alkaloid constituents, with mitragynine being the most abundant and well-studied compound (1). Mitragynine is a mu-opioid receptor agonist, meaning it binds to and activates the same receptors as opioid drugs like morphine (15). However, mitragynine exhibits a unique profile, with additional actions on other receptors, including kappa-opioid receptors, serotonergic receptors, and adrenergic receptors (16). This multifaceted mechanism of action contributes to kratom's diverse effects and potential therapeutic applications. Another alkaloid present in kratom, 7-hydroxymitragynine, is a more potent mu-opioid receptor agonist than mitragynine and is thought to contribute significantly to kratom's analgesic and sedative effects (17). Other alkaloids, such as speciogynine and paynantheine, may also play a role in kratom's pharmacological profile, although their mechanisms are less well-understood (18).

The binding of mitragynine and other alkaloids to opioid receptors in the brain and spinal cord is responsible for kratom's analgesic (pain-relieving) and euphoric effects (19,20). However, unlike classical opioids, mitragynine exhibits a unique pattern of receptor activation, which may explain its lower potential for respiratory depression and constipation (21). In addition to its opioid receptor activity, kratom has been shown to interact with other neurotransmitter systems, including the serotonergic, dopaminergic, and noradrenergic systems (16). These interactions are thought to contribute to kratom's stimulant and mood-altering effects, as well as its potential for modulating addiction and withdrawal symptoms (3).

B. Effects on the Body and Mind

The effects of kratom on the body and mind can vary depending on the dose, the individual's metabolism, and other factors (2). At low doses, kratom is reported to produce stimulant-like effects, such as increased energy, euphoria, and sociability (22). These effects are likely due to kratom's ability to stimulate the release of neurotransmitters like dopamine and norepinephrine (23). At higher doses, kratom tends to produce more sedative and analgesic effects, similar to those of opioid drugs (9). People who use Kratom report experiencing pain relief, relaxation, and a sense of well-being (22). These effects are primarily mediated by the activation of mu-opioid receptors in the brain and spinal cord (15). However, kratom's effects can also include adverse reactions, such as nausea, vomiting, constipation, respiratory depression, and seizures (9,10). These adverse effects may be more common at higher doses or with prolonged use, and they may be related to kratom's interactions with various neurotransmitter systems (11).

In terms of its effects on the mind, kratom has been reported to produce both stimulant-like and sedative-like effects, depending on the dose (22). At low doses, users may experience increased alertness, improved mood, and increased sociability. At higher doses, users may experience sedation, euphoria, and altered perception of reality (2). Kratom has also been associated with psychological effects, such as anxiety, psychosis, and hallucinations, particularly with long-term or high-dose use (10,22). These effects may be related to kratom's interactions with serotonergic and dopaminergic systems in the brain (16).

C. Potential for Abuse and Dependence

Despite its traditional use and potential therapeutic applications, there is growing concern about the potential for abuse and dependence associated with kratom use (5). Kratom's ability to activate opioid receptors and produce euphoric effects has raised concerns about its addictive potential (9). Several case reports and studies have documented the development of kratom dependence and withdrawal symptoms upon cessation of use (22). Withdrawal symptoms reported include muscle aches, irritability, anxiety, insomnia, and cravings, similar to those observed with opioid withdrawal (9). The development of tolerance to kratom's effects has also been reported, with people who use Kratom requiring higher doses to achieve the desired effects over time (4). This tolerance development may contribute to the escalation of kratom use and the potential for abuse and dependence (5). Moreover, the use of kratom has been associated with the development of opioid use disorder and the potential for cross-sensitization to other opioid drugs (10). This raises concerns about the potential for kratom to serve as a gateway to the use of more potent and illicit opioids. While the exact prevalence of kratom abuse and dependence is not well-established, data from poison control centers and emergency department visits suggest an increasing trend in kratom-related adverse events and complications (9,11).

It is also important to note that the potential for abuse and dependence may vary depending on the individual's genetic and environmental factors, as well as the patterns of kratom use (22). However, the growing concerns about kratom's addictive potential have led to increasing scrutiny and regulatory actions in various countries, including potential classification as a controlled substance (9,24).

DIAGNOSIS AND ASSESSMENT OF KRATOM USE DISORDER

A. Criteria for Kratom Use Disorder

As kratom use has gained popularity in recent years, particularly in Western countries, there has been an increasing recognition of the potential for KUD. However, the diagnosis and assessment of KUD present unique challenges due to the limited research and lack of standardized diagnostic criteria (22). Currently, there are no specific diagnostic criteria for KUD in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) or the International Classification of Diseases (ICD-11). Instead, the diagnosis of KUD is typically based on the criteria for substance use disorders outlined in these diagnostic manuals (6,25).

The DSM-5 defines a substance use disorder as a problematic pattern of substance use leading to clinically significant impairment or distress, as manifested by the presence of at least two of the following criteria within a 12-month period (6):

- 1) The substance is taken in larger amounts or over a longer period than was intended.
- 2) There is a persistent desire or unsuccessful efforts to cut down or control substance use.
- 3) A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
- 4) Craving, or a strong desire or urge to use the substance.
- 5) Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home.
- 6) Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.
- 7) Important social, occupational, or recreational activities are given up or reduced because of substance use.
- 8) Recurrent substance use in situations in which it is physically hazardous.
- 9) Continued substance use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
- 10) Tolerance, as defined by either a need for markedly increased amounts of the substance to achieve intoxication or desired effect or a markedly diminished effect with continued use of the same amount.
- 11) Withdrawal, as manifested by either the characteristic withdrawal syndrome for the substance or the substance is taken to relieve or avoid withdrawal symptoms.

These criteria can be applied to kratom use, with individuals meeting the diagnostic threshold for KUD if they exhibit two or more of these symptoms within a 12-month period (5,22). It is important to note that the severity of KUD can range from mild to severe, based on the number of criteria met. Additionally, specific withdrawal symptoms associated with kratom cessation, such as muscle aches, irritability, anxiety, insomnia, and cravings, may be observed in individuals with KUD (9).

B. Screening and Assessment Tools

While there are no specific screening or assessment tools designed specifically for KUD, several general substance use disorder screening instruments have been used to identify potential kratom use problems (4,22). One commonly used screening tool is the Drug Abuse Screening Test (DAST), which consists of 28 questions aimed at identifying problematic substance use patterns (26). The DAST has been used in various settings, including primary care and mental health clinics, to screen for potential substance use disorders, including those related to kratom (22).

Another widely used screening instrument is the Alcohol Use Disorders Identification Test (AUDIT), which was originally developed by the World Health Organization (WHO) to identify problematic alcohol use (27). Although designed for alcohol use, the AUDIT has been adapted and used to screen for other substance use disorders, including kratom use disorder (4).

In addition to these general screening tools, clinicians may use structured clinical interviews, such as the Substance Use Disorder module of the Structured Clinical Interview for DSM-5 Disorders (SCID-5), to assess the presence and severity of KUD (28). These interviews involve a series of questions designed to evaluate the diagnostic criteria for substance use disorders and can be adapted to focus specifically on kratom use.

Furthermore, self-report questionnaires and surveys have been used in research settings to assess patterns of kratom use, motivations for use, and potential problematic behaviors associated with KUD (4,22). However, these instruments are typically not standardized or validated for clinical use and may have limitations in terms of reliability and generalizability.

C. Comorbidities and Associated Conditions

Kratom use disorder has been associated with various comorbid conditions and co-occurring disorders, which can complicate the diagnosis and management of KUD (5,22). One of the most commonly reported comorbidities is the presence of other substance use disorders, particularly opioid use disorder (OUD). Many individuals with KUD report using kratom as an alternative to opioids or as a means of self-medicating for opioid withdrawal symptoms (3,9). This co-occurrence of OUD and KUD can present challenges in terms of treatment and recovery, as individuals may need to address both disorders simultaneously.

Mental health disorders, such as depression, anxiety, and post-traumatic stress disorder (PTSD), have also been reported in individuals with KUD (22). These conditions may contribute to the development of substance use disorders, including KUD, or may be exacerbated by kratom use and withdrawal symptoms. Additionally, chronic pain conditions and physical health problems have been associated with KUD, as some individuals use kratom for its purported analgesic properties (4,22). However, the long-term safety and efficacy of kratom for pain management remain uncertain, and its use may potentially exacerbate or complicate existing health conditions. Other comorbidities that have been reported in individuals with KUD include psychotic disorders, traumatic brain injury, and attention-deficit/hyperactivity disorder (ADHD) (5,22). These conditions may interact with kratom use and contribute to the development of problematic patterns of use or adverse effects.

MANAGEMENT OF KRATOM USE DISORDER

Psychosocial Interventions in the Treatment of Kratom Use Disorder

While research on the effective treatment of KUD is still limited, several psychosocial interventions have been explored and adapted from their application in other substance use disorders. These interventions aim to address the cognitive, behavioral, and social factors contributing to problematic kratom use, with the goal of promoting behavior change, enhancing motivation for recovery, and preventing relapse.

A. Cognitive-Behavioral Therapy (CBT)

Cognitive-behavioral therapy (CBT) is a widely used and evidence-based psychotherapeutic approach for treating substance use disorders, including those involving kratom (8,22). CBT is based on the premise that maladaptive thoughts and behaviors contribute to the development and maintenance of substance use problems, and it focuses on modifying these cognitive and behavioral patterns.

In the context of KUD, CBT can be adapted to address the specific cognitions, emotions, and behaviors associated with kratom use. The therapy typically involves identifying and challenging dysfunctional thoughts and beliefs related to kratom use, developing coping strategies for managing cravings and triggers, and promoting behavioral changes to support abstinence or harm reduction goals (29). CBT for KUD may involve techniques such as cognitive restructuring, where individuals learn to identify and modify irrational or distorted thoughts about kratom use, and behavioral strategies like stimulus control and urge-surfing to manage cravings and high-risk situations. Additionally, CBT may incorporate relapse prevention strategies, such as identifying potential triggers and developing coping mechanisms to prevent or manage lapses (29).

Research on the effectiveness of CBT for KUD is limited, but several studies have reported positive outcomes, including reductions in kratom use and improvements in overall functioning (8,22).

Furthermore, CBT has demonstrated efficacy in treating other substance use disorders, suggesting its potential utility for KUD as well (29).

B. Motivational Interviewing

Motivational interviewing (MI) is a patient-centered, directive counseling approach that aims to enhance an individual's motivation for change and resolve ambivalence about behavior modification (30). MI has been widely used in the treatment of substance use disorders and has shown promise in addressing kratom use problems (8). The core principles of MI include expressing empathy, developing discrepancy between current behavior and personal goals, rolling with resistance rather than confronting it directly, and supporting self-efficacy (30). In the context of KUD, MI can be used to explore an individual's ambivalence about kratom use, elicit change talk, and strengthen their intrinsic motivation for achieving abstinence or reducing harm (29). MI techniques, such as open-ended questioning, affirmations, reflective listening, and summarizing, can be used to facilitate a collaborative and non-confrontational therapeutic relationship (30). This approach can be particularly effective for individuals who are ambivalent or resistant to change, as it avoids confrontation and instead encourages self-exploration and autonomous decision-making (8).

While research on the efficacy of MI for KUD is limited, several studies have reported promising results in reducing kratom use and increasing treatment engagement (8,22). Additionally, MI has been shown to be effective in enhancing treatment outcomes for various substance use disorders, suggesting its potential utility as an adjunctive or standalone intervention for KUD (29).

C. Contingency Management

Contingency management (CM) is a behavioral intervention that involves providing tangible rewards or incentives contingent upon achieving specific treatment goals, such as abstinence or treatment attendance (31,32). CM has been extensively studied and proven effective in treating various substance use disorders, including opioid and stimulant use disorders (31–33).

In the context of KUD, CM can be used to reinforce and incentivize desired behaviors, such as abstinence from kratom use, engagement in treatment, or participation in recovery-related activities (22). The rewards or incentives used in CM can vary, including vouchers, employment, prizes, or cash-based reinforcement systems (31,32).

The effectiveness of CM in treating KUD has not been extensively studied, but its success in treating other substance use disorders suggests its potential utility (8,22,32). Additionally, CM may be particularly useful in addressing the challenges of kratom withdrawal and cravings, as the immediate rewards can reinforce abstinence and provide motivation during the early stages of treatment (29).

D. Peer Support and Self-Help Groups

Peer support and self-help groups, such as mutual aid groups like Kratom Anonymous or Narcotics Anonymous (NA), can play a crucial role in the treatment and recovery process for individuals with KUD (8,22). These groups provide a supportive and non-judgmental environment where individuals can share their experiences, learn from others, and receive encouragement and accountability.

Peer support groups offer several potential benefits for individuals with KUD, including:

1. Emotional support and a sense of community: Connecting with others who have experienced similar struggles can help reduce feelings of isolation and provide a supportive social network (34).
2. Role modeling and inspiration: Observing and interacting with individuals who have achieved long-term recovery can serve as a source of inspiration and motivation (8).
3. Practical advice and coping strategies: Members can share effective coping strategies, relapse prevention techniques, and practical advice for navigating the challenges of recovery (22).
4. Accountability and structure: Regular meeting attendance and participation can provide a sense of accountability and structure, which can be beneficial in maintaining recovery efforts (34).

While peer support groups are not a substitute for professional treatment, they can serve as a valuable adjunct to other psychosocial interventions and provide ongoing support throughout the recovery process (8).

Pharmacological Interventions in the Treatment of Kratom Use Disorder

While psychosocial interventions are crucial in the management of KUD, pharmacological treatments can play a complementary role in addressing the physiological aspects of dependence, withdrawal, and cravings. However, research on effective pharmacotherapies for KUD is still limited, and most of the evidence is derived from case reports, small clinical studies, or extrapolated from treatments for other substance use disorders.

A. Opioid Agonist Therapy (e.g., Buprenorphine, Methadone)

Due to kratom's partial agonist activity at the mu-opioid receptor, opioid agonist therapies, such as buprenorphine and methadone, have been explored as potential treatments for KUD (9,22). These medications are commonly used in the treatment of opioid use disorders and can assist in managing withdrawal symptoms and cravings.

Buprenorphine, a partial opioid agonist, has been reported to be effective in attenuating kratom withdrawal symptoms and reducing cravings in several case reports and small studies (22,35).

Buprenorphine's high affinity for the mu-opioid receptor may help to displace kratom alkaloids and mitigate withdrawal effects, while its partial agonist properties provide a reduced risk of respiratory depression compared to full agonists (9).

Methadone on the other hand, a full opioid agonist, has also been used in the treatment of KUD, particularly in cases where buprenorphine was ineffective or poorly tolerated (9,22). However, due to the potential for respiratory depression and other adverse effects associated with full opioid agonists, methadone is not commonly used.

While opioid agonist therapies may be effective in managing kratom withdrawal and cravings, they also carry the risk of perpetuating opioid dependence and potential misuse (9). Therefore, their use should be carefully considered, and appropriate monitoring and support should be provided to minimize the risk of adverse outcomes.

B. Alpha-2 Adrenergic Agonists (e.g., Clonidine)

Alpha-2 adrenergic agonists, such as clonidine, have been explored as potential adjunctive treatments for KUD, primarily for their ability to alleviate withdrawal symptoms (9,22). These medications are commonly used in the management of opioid withdrawal and can help mitigate symptoms such as anxiety, muscle cramps, and autonomic hyperactivity.

Clonidine, in particular, has been reported to be effective in reducing the severity of kratom withdrawal symptoms in several case reports (9,35). Its mechanism of action involves reducing the release of norepinephrine, which can help to counteract the increased noradrenergic activity associated with kratom withdrawal (9).

While clonidine and other alpha-2 adrenergic agonists may be useful in managing kratom withdrawal, they are typically not sufficient as a monotherapy and should be used in combination with other interventions, such as psychosocial therapies and, in some cases, opioid agonist therapy (22).

C. Antidepressants and Mood Stabilizers

Antidepressants and mood stabilizers have been explored as potential adjunctive treatments for KUD, primarily due to their ability to modulate neurotransmitter systems involved in mood regulation, anxiety, and addictive behaviors (8,22).

Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine and sertraline, have been used to manage symptoms of depression and anxiety associated with kratom withdrawal and cravings (9,35). Additionally, some evidence suggests that SSRIs may help to reduce the rewarding effects of kratom and other opioids, potentially decreasing the risk of relapse (22).

Mood stabilizers, such as valproic acid and lithium, have also been explored for their potential utility in KUD (8). These medications may help to modulate the dopaminergic and glutamatergic systems involved in addictive behaviors and cravings, potentially reducing the reinforcing effects of kratom and promoting abstinence (22).

While antidepressants and mood stabilizers may be useful adjunctive treatments for KUD, particularly in individuals with comorbid mood or anxiety disorders, their efficacy as a monotherapy for KUD has not been well-established. Additionally, their use should be carefully monitored for potential adverse effects and interactions with other medications or substances (9).

D. Other Potential Pharmacotherapies

Researchers have explored various other pharmacological agents as potential treatments for KUD, although the evidence is generally limited to case reports or preclinical studies (8,22).

Naltrexone, an opioid receptor antagonist, has been proposed as a potential treatment for KUD due to its ability to block the rewarding effects of opioids and reduce cravings (9). However, the effectiveness of naltrexone in KUD has not been extensively studied, and there are concerns about potential precipitated withdrawal symptoms in individuals with physical dependence on kratom.

Gabapentin and pregabalin, anticonvulsant medications with potential anxiolytic and analgesic properties, have also been explored for their potential utility in managing kratom withdrawal symptoms and cravings (8,22). These medications may modulate the activity of various neurotransmitter systems involved in addiction and withdrawal, but their efficacy in KUD remains to be determined.

Other potential pharmacotherapies that have been mentioned in the literature include N-acetylcysteine (NAC), a glutamatergic modulator, and cannabidiol (CBD), a non-psychoactive compound derived from cannabis (8,22). However, these treatments have not been extensively studied in the context of KUD, and their potential benefits and risks remain largely speculative.

It is important to note that most of these potential pharmacotherapies have not been extensively studied in controlled clinical trials for KUD, and their efficacy, safety, and optimal dosing regimens remain unclear. Additionally, many of these medications may have significant adverse effects or interactions with other substances.

Overall, while pharmacological interventions may play a role in the management of KUD, particularly in addressing withdrawal symptoms and cravings, their use should be considered within the context of a comprehensive treatment plan that incorporates psychosocial interventions and ongoing monitoring and support.

Integrative and Alternative Approaches in the Treatment of Kratom Use Disorder

While conventional psychosocial and pharmacological interventions remain the primary focus in the treatment of KUD, there is growing interest in exploring integrative and alternative approaches as complementary or adjunctive therapies. These approaches often aim to address the holistic well-being of individuals, targeting various physical, emotional, and spiritual aspects of addiction and recovery.

A. Acupuncture and Traditional Chinese Medicine

Acupuncture, a core component of traditional Chinese medicine (TCM), has been investigated as a potential adjunctive treatment for substance use disorders, including KUD (22). This ancient healing practice involves the insertion of thin needles into specific points on the body, with the aim of restoring the balance of vital energy (known as qi) and promoting natural healing processes.

Specific acupuncture points, such as those located on the ear (auricular acupuncture), have been associated with potential benefits in reducing cravings and improving mood and sleep quality (22). While research on the efficacy of acupuncture for KUD is limited, several studies have reported promising results in reducing kratom use and withdrawal symptoms when used in combination with other interventions (8). Additionally, acupuncture has been shown to be effective in treating other substance use disorders, such as opioid and alcohol use disorders, suggesting its potential utility for KUD (36,37). Other TCM modalities, such as herbal medicine and Qigong (a form of meditative movement), have also been explored as potential adjunctive treatments for KUD (22). However, the evidence for their efficacy remains limited, and further research is needed to understand their potential benefits, risks, and mechanisms of action.

B. Mindfulness-Based Interventions

Mindfulness-based interventions, such as mindfulness-based stress reduction (MBSR) and mindfulness-based relapse prevention (MBRP), have gained increasing attention as complementary approaches in the treatment of substance use disorders, including KUD (8,29). Mindfulness practices involve cultivating present-moment awareness, non-judgmental acceptance, and self-compassion through techniques such as meditation, body scans, and mindful movements (38,39). These practices aim to increase awareness of thoughts, emotions, and cravings, allowing individuals to respond to them in a more adaptive and less reactive manner.

In the context of KUD, mindfulness-based interventions may help individuals develop greater self-regulation, emotional regulation, and coping strategies to manage cravings and reduce the risk of relapse (8,29). Additionally, mindfulness practices have been associated with reductions in stress, anxiety, and depression, which are common comorbidities in individuals with substance use disorders (40).

While research on the effectiveness of mindfulness-based interventions for KUD is limited, several studies have reported promising results in reducing substance use and improving overall well-being when used as an adjunctive treatment for other substance use disorders (29,40). Furthermore, mindfulness-based approaches have been found to enhance the effectiveness of other evidence-based treatments, such as CBT and CM (29).

C. Nutritional and Herbal Supplements

The use of nutritional and herbal supplements has also been explored as a potential complementary approach in the treatment of KUD, although the evidence remains limited and largely anecdotal (8,22). Some individuals have reported using supplements such as N-acetylcysteine (NAC), a precursor to the antioxidant glutathione, to help alleviate kratom withdrawal symptoms and cravings (8). NAC is believed to modulate glutamatergic neurotransmission, which may play a role in addiction and withdrawal processes (22). However, the efficacy and safety of NAC for KUD have not been extensively studied in controlled clinical trials.

Other supplements that have been mentioned in the context of KUD include vitamins and minerals, such as vitamin C, zinc, and magnesium, which are thought to support overall health and potentially aid in the recovery process (8). However, the evidence for their specific benefits in KUD is largely anecdotal and requires further investigation. In addition to nutritional supplements, some individuals have explored the use of herbal remedies, such as St. John's wort, for their potential mood-enhancing and anxiolytic effects (22). However, the safety and efficacy of these herbal remedies for KUD, as well as their potential interactions with other substances or medications, remain largely unknown.

It is important to note that the use of nutritional and herbal supplements in the treatment of KUD should be approached with caution, as many of these products are not regulated by government agencies and may have the potential for adverse effects or interactions with other medications or substances (8). While integrative and alternative approaches hold promise as complementary treatments for KUD, it is crucial to recognize that they should not be considered as a monotherapy treatments or replacements for evidence-based psychosocial and pharmacological interventions (22,29). Instead, these approaches may be most effective when integrated into a comprehensive treatment plan that addresses the multifaceted nature of addiction and promotes overall well-being.

Challenges and Barriers to Treatment of Kratom Use Disorder

Despite the growing recognition of KUD as a significant public health concern, numerous challenges and barriers exist that hinder the effective treatment and management of this condition. These barriers encompass a range of factors, including limited research and evidence-based guidelines, societal stigma and misconceptions, and issues

related to the accessibility and availability of appropriate treatment options.

A. Limited Research and Evidence-Based Guidelines

One of the primary challenges in addressing KUD is the lack of extensive research and evidence-based guidelines for its treatment and management (8,22). Unlike other substance use disorders, such as opioid or alcohol use disorders, which have been extensively studied and have established treatment protocols, the research on KUD is relatively nascent. The limited understanding of the pharmacological mechanisms, clinical manifestations, and long-term effects of kratom use poses significant challenges for healthcare professionals in developing effective treatment strategies (9,22). Many of the current treatment approaches for KUD are extrapolated from interventions for other substance use disorders or are based on anecdotal reports and case studies, which may not adequately address the unique aspects of KUD. Also, the lack of standardized diagnostic criteria and assessment tools specifically designed for KUD can make it challenging to accurately identify and assess the severity of the condition (5,22). This can lead to inconsistencies in diagnosis and treatment approaches, potentially compromising the effectiveness of interventions and patient outcomes.

B. Stigma and Misconceptions

Stigma and misconceptions surrounding kratom use and KUD present significant barriers to seeking and receiving appropriate treatment (8,22). Despite its growing popularity, kratom remains a relatively unknown substance to many healthcare professionals and the general public, which can contribute to misunderstandings and stigmatization. The perception of kratom as a "legal high" or a "natural" substance can lead to the misconception that it is inherently safe or less harmful than other substances (9,22). This can result in individuals minimizing the potential risks and consequences of problematic kratom use, potentially delaying or avoiding seeking treatment.

Additionally, the stigma associated with substance use disorders in general can create barriers for individuals seeking treatment for KUD (8). Negative societal attitudes, discrimination, and concerns about confidentiality may deter individuals from disclosing their kratom use or seeking professional help, exacerbating the challenges of addressing this condition.

C. Accessibility and Availability of Treatment Options

Even when individuals recognize the need for treatment, they may face significant barriers in accessing appropriate and effective treatment options for KUD (8,22). Several factors contribute to the limited accessibility and availability of treatment services for KUD.

Firstly, the lack of specialized treatment programs or facilities specifically designed to address KUD can make it challenging for individuals to find appropriate

care (22). Many existing substance abuse treatment programs may not have the necessary expertise or resources to effectively treat KUD, which may require tailored interventions and specialized knowledge.

Secondly, geographic and socioeconomic barriers can further limit access to treatment for KUD (8). Individuals living in rural or underserved areas may have limited access to treatment facilities or qualified healthcare providers, while those with financial constraints or lack of adequate insurance coverage may struggle to afford the costs associated with treatment.

Moreover, the legal status of kratom and its varying regulations across different jurisdictions can create additional barriers to accessing treatment (9,22). In areas where kratom is classified as a controlled substance or illegal, individuals may be hesitant to seek treatment due to fears of legal consequences or stigma, further exacerbating the challenges of addressing KUD.

FUTURE DIRECTIONS AND RECOMMENDATIONS

As the understanding of KUD continues to evolve, several areas present opportunities for future directions and recommendations to enhance the treatment and management of this condition.

A. Emerging Research and Potential Treatments

One of the most promising avenues for future research lies in the exploration of novel pharmacotherapies specifically targeting the unique pharmacological mechanisms of kratom and its active alkaloids. While existing treatments, such as opioid agonist therapies and antidepressants, have shown some promise, they may not fully address the complex interactions of kratom with various neurotransmitter systems (8,22).

Emerging research is investigating the potential of developing selective kratom alkaloid receptor modulators or antagonists, which could potentially mitigate the rewarding effects of kratom and alleviate withdrawal symptoms without the risk of perpetuating opioid dependence (18). Additionally, research into the potential repurposing of existing medications with affinity for kratom's target receptors may yield new treatment options (9).

In addition, the integration of pharmacogenomic approaches, which consider an individual's genetic makeup in tailoring treatment strategies, could lead to more personalized and effective interventions for KUD (22). By understanding the genetic factors that influence an individual's response to kratom and various pharmacotherapies, clinicians may be better equipped to develop targeted treatment plans.

B. Strategies for Improving Treatment Access and Outcomes

Addressing the barriers to accessing appropriate treatment for KUD is crucial for improving outcomes and supporting individuals in their recovery journey.

Strategies to improve treatment access and outcomes may include:

1. Developing specialized treatment programs and facilities: Establishing dedicated treatment programs and facilities specialized in treatment of KUD can ensure that individuals receive tailored interventions and care from healthcare professionals with specialized knowledge and expertise (8,22).
2. Expanding training and education for healthcare professionals: Providing comprehensive training and education for healthcare professionals, including physicians, therapists, and counselors, can enhance their ability to recognize, diagnose, and effectively treat KUD (9,22).
3. Improving access to telehealth and remote treatment options: Leveraging telehealth and remote treatment options can help overcome geographic barriers and increase access to care, particularly for individuals living in rural or underserved areas (8).
4. Addressing socioeconomic barriers: Implementing strategies to reduce financial barriers, such as providing affordable treatment options, sliding-scale fees, or improving insurance coverage for KUD treatment, can help ensure that individuals from all socioeconomic backgrounds can access necessary care (22).
5. Promoting public awareness and education: Conducting public awareness campaigns and educational initiatives can help combat stigma, dispel misconceptions, and encourage individuals struggling with KUD to seek appropriate treatment (8,9).

C. Areas for Further Investigation

While significant progress has been made in understanding KUD, several areas warrant further investigation to advance the field and improve treatment outcomes:

1. Longitudinal studies: Conducting long-term, longitudinal studies can provide valuable insights into the natural course of KUD, the long-term effects of kratom use, and the durability of treatment outcomes (22).
2. Comorbidity and polydrug use: Exploring the complex interplay between KUD and co-occurring mental health disorders, as well as the impact of polydrug use, can inform the development of integrated and comprehensive treatment approaches (5).
3. Harm reduction strategies: Investigating harm reduction strategies, such as safe consumption practices, supervised consumption sites, and education on safer use, can potentially mitigate the risks associated with kratom use and provide alternative approaches for individuals not ready for abstinence-based treatment (8).

4. Cultural and social factors: Examining the cultural and social factors that influence kratom use patterns, perceptions, and treatment-seeking behaviors can inform the development of culturally-sensitive and tailored interventions (22).

5. Policy and regulatory considerations: Conducting research on the impact of varying legal and regulatory frameworks surrounding kratom can inform evidence-based policies and guidelines to balance public health concerns with individual freedoms and access to potential therapeutic applications (8,9).

By prioritizing these areas for further investigation, researchers, healthcare professionals, and policymakers can contribute to a more comprehensive understanding of KUD and develop effective strategies to address this growing public health challenge.

CONCLUSION

This comprehensive review highlights the complexities and challenges associated with the management of KUD. The management of KUD involves a multifaceted approach. Psychosocial interventions such as cognitive-behavioral therapy (CBT), motivational interviewing (MI), and contingency management (CM) have shown promise in treating KUD by addressing the behavioral and cognitive aspects of addiction. Additionally, peer support and self-help groups play a crucial role in providing ongoing support and promoting recovery. Pharmacological interventions, although still under-researched, offer potential complementary treatments. Opioid agonist therapies like buprenorphine and methadone, alpha-2 adrenergic agonists such as clonidine, and antidepressants and mood stabilizers have been explored for their efficacy in managing withdrawal symptoms and cravings. Integrative and alternative approaches, including acupuncture, mindfulness-based interventions, and nutritional supplements, have also been considered as adjunctive treatments. However, their effectiveness requires further validation through rigorous research.

The review equally highlights several implications for clinical practice and policy. Firstly, there is a pressing need for the development of standardized diagnostic criteria and assessment tools specific to KUD. This would facilitate accurate diagnosis and tailored treatment plans. Clinicians should be aware of the potential for kratom dependence and withdrawal symptoms and incorporate evidence-based psychosocial and pharmacological interventions into treatment plans. Training and education for healthcare professionals on KUD and its management are crucial to improve patient outcomes. Policy-wise, there is a need for balanced regulation that considers both the therapeutic potential and the risks associated with kratom use. Public awareness campaigns can help dispel misconceptions and reduce the stigma associated with KUD, encouraging individuals to seek treatment.

In addition, improving access to treatment through telehealth services, reducing financial barriers, and developing specialized treatment programs can enhance treatment engagement and success. Overall, a multidisciplinary approach integrating psychosocial, pharmacological, and alternative treatments, supported by robust research and informed policies, is essential to address the public health challenge posed by kratom use disorder.

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