



Review

Kratom use and mental health: A systematic review

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ABSTRACT

Background: Kratom (*Mitragyna speciosa*) is a psychoactive plant native to Southeastern Asia that is receiving increased international attention as a potential therapeutic agent. While much of the limited scientific research on kratom is focused on its analgesic potential, kratom use also has important risks and benefits in the domain of mental health.

Methods: We conducted a comprehensive systematic review of all studies on kratom use and mental health published between January 1960 and July 2017.

Results: Findings indicate kratom's potential as a harm reduction tool, most notably as a substitute for opioids among people who are addicted. Kratom also enhances mood and relieves anxiety among many users. For many, kratom's negative mental health effects – primarily withdrawal symptoms – appear to be mild relative to those of opioids. For some users, however, withdrawal is highly uncomfortable and maintaining abstinence becomes difficult.

Conclusion: Results inform clinicians working in the mental health and substance use fields, policy-makers, and researchers about the mental health effects of this plant.

1. Introduction

Kratom (*Mitragyna speciosa*; also known as kratom or ketum) is a psychoactive plant in the Rubiaceae, or coffee, family that has been used medicinally for centuries in Southeastern Asia (Cinosi et al., 2015; Pendell, 2010). In Thailand and Malaysia, individuals use kratom across diverse contexts; as an opium substitute and to relieve symptoms of opioid withdrawal, medicinally to relieve pain, diarrhea, and cough, and by manual laborers to enhance stamina and energy (Tanguay, 2011; Prozialeck et al., 2012). People chew raw leaves of the kratom plant, boil them and serve as a tea, or smoke or vaporize them. Recent years have witnessed the expansion of kratom use beyond Asia; kratom leaves, powders, gums, capsules, and extracts are widely accessed via the internet and retail outlets across North America and Europe (Prozialeck et al., 2012; Singh et al., 2016), leading to novel concerns regarding the potential for adverse consequences of use (Boyer et al., 2008; Ward et al., 2011). In the absence of robust scientific data, some warnings about kratom from government and press sources exhibit features of drug hysteria (Hart, 2013), threatening researchers' ability to study the plant and the public's ability to evaluate pros and cons of kratom use, making this a critical time for collecting and evaluating evidence for the risks and benefits of this substance. Some of the most important potential risks and benefits of kratom are in the mental

health realm. For this reason, we conducted a systematic review of all identified studies on kratom use and mental health.

As with many psychoactive substances before it, several factors have led to baseless and potentially unwarranted fears about kratom in North America; these include the marketing of kratom as a “legal high” (Cinosi et al., 2015), the confusion between kratom and other novel psychoactive substances (e.g., synthetic cannabis, bath salts), and sensationalized media coverage of putative harms (e.g., “Kratom: The supplement that will kill Godzilla”; Bloom, 2016). In the medical literature, the number of published case studies that have highlighted adverse events coincident with kratom use including liver toxicity and death (Kapp et al., 2011; McIntyre et al., 2015; Neerman et al., 2012; Nelsen et al., 2010; Sheleg and Collins, 2011) is disproportionately high relative to the number of rigorous investigations. Case studies present a relatively low level of evidence due to overrepresentation of extreme events, unknown validity and generalizability, and other potential biases (Merriam, 2009). These limitations render a causal linkage between kratom and serious adverse events impossible. Nonetheless, results of these studies have contributed to the issuance of dire public warnings. For example, the U.S. Centers for Disease Control and Prevention (CDC) and Drug Enforcement Administration (DEA) have explicitly warned that kratom may cause psychosis or death (Anwar et al., 2016; DEA, 2016) and the DEA has recommended criminalizing kratom

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possession and distribution despite robust public opposition to “cruel and irresponsible” governmental policy (Swogger, 2016) and the clear failure of such measures to do public good (Mallea, 2014).¹

Kratom is understudied and, as such, the risks and benefits of kratom use have not been characterized in detail. Whereas caution in light of this lack of research is warranted, recent public discourse and policy approaches related to kratom exhibit characteristics associated with a *drug hysteria* (see Hart, 2013), including the promulgation of sensationalistic and biased information and the pursuit of regulatory approaches that appear overmatched to apparent risks. Indeed, dangers of drug hysterias include the tendency toward the adoption of blunt and reactive strategies that risk inhibiting scientific study and thus deprive the public of useful medicine. Drug hysteria also creates harmful stigma around users and increases the risk of ineffective and harsh policies that lead to unnecessary incarceration. The need for evidence-based policy to manage the growing adoption of kratom in North America and Europe makes this a critical time for evaluating risks and benefits. Moreover, the potential salutary role of kratom use in the context of opioid use, coupled with increasing demand for effective options for reducing harms associated with problematic opioid use, make the investigation of kratom a critical research priority. Understanding the influence of kratom use on mental health and well-being is important for evaluating the therapeutic potential of kratom in the context of harmful opioid use and other psychopathology, as psychological factors are key determinants of the acceptability kratom-based medicines.

Increased scientific attention is beginning to organize and clarify the state of knowledge about kratom. Thorough reviews describe the longstanding uses of kratom in Southeastern Asia and detail modes of consumption, side effects (including withdrawal), and kratom’s legal and social status in different parts of the world (Aziz, 2014; Hassan et al., 2013; Singh et al., 2016). They indicate kratom’s potential to help with a variety of problems, perhaps most notably pain (Ahmad and Aziz, 2012; Grundman, 2017). Importantly, kratom use also impacts several domains of mental health. The nascent scientific literature on kratom’s beneficial impact on mood and as a substitute for opioids deserves careful attention, as do the potential mental health risks of kratom use. To this end, the present work is the first to systematically review the literature on kratom and mental health. In this review, we aim to inform clinicians practicing in mental health or substance use treatment settings who may encounter kratom use in the course of their clinical work, policy-makers interested in understanding the potential public health impact of kratom use, and researchers who will base their scientific investigations on this preliminary knowledge.

2. Methods

2.1. Search strategy

We conducted a search for literature that addresses kratom use and mental health. In order to ensure coverage of all relevant studies and guided by recent, high-quality mental health review papers (e.g., Walker et al., 2015; Walsh et al., 2017), we chose search terms that comprise the broad emotional, psychological, and social domains of mental health (Ryff and Keyes, 1995). Electronic databases (Psycinfo, Medline) were used to identify all published studies using human samples between January 1960 and February 2017 on *Mitragyna speciosa* OR *kratom* and anxiety, posttraumatic stress, social, dependence, abuse, harmful substance use, tobacco, cocaine, alcohol, opiates, opioids, heroin, amphetamine, depression, bipolar, mania, mood, psychosis, schizophrenia, neuropsychology, cognitive, IQ, intelligence, violence, aggression, therapeutic, substitution, suicide, self-harm.

¹ The DEA has withdrawn its notice of intent to schedule kratom following a public backlash and pending further gathering of information on the substance and consequences of its use.

2.2. Inclusion/Exclusion criteria

Identified studies were inspected for redundancy and retained for further review if they contained original data on kratom use and mental health. We established two *a priori* exclusion criteria to ensure that we reviewed only studies of adequate quality that would contribute meaningfully. First, we excluded case studies due to limitations on both internal and external validity, a tendency to over-represent extreme events, and an unacceptable potential for researcher effects (Merriam, 2009). Additionally, we excluded studies that did not supply adequate information for a review of study methods.

3. Results

Our search yielded 49 results. After eliminating redundant results, theoretical and review papers without novel empirical data ($n = 19$), case studies ($n = 9$), and papers determined to contain no data relevant to mental health ($n = 6$), we examined 15 studies. We then eliminated studies ($n = 2$) whose methods were inadequately reported for us to evaluate their limitations. Thirteen studies were retained for full review. The combined sample for these studies is 28,745, of which 25,189 were drawn from two large surveys. All studies were cross-sectional or retrospective in design, with 9 of 13 reporting results of surveys from Thailand and Malaysia, two reporting on calls to US poison control centers, one study based on submissions to a US-based website that provides user reports of a variety of psychoactive substances, and an anonymous online survey made available through the American Kratom Association Web page (Table 1). Based on the content of these articles, we organize the review around the categories of harm reduction, mood, and adverse effects.

3.1. Harm reduction

Substitution is a form of harm reduction involving the use of a substitute compound in order to replace or decrease the use of another substance that is deemed undesirable (Lucas et al., 2016). The consequences of substitution can be observed at the individual and public health levels. Long-acting opioids like methadone or buprenorphine are prescribed as substitutes for potentially more dangerous compounds (e.g., oxycodone, heroin) and there is evidence that cannabis can be successfully substituted for alcohol, opioids, and cocaine (Bachhuber et al., 2014; Lucas and Walsh, 2017; Lucas et al., 2016; Socias et al., 2017). Consistent with older descriptions of kratom use in Asia, recent research indicates that kratom is being used as a harm-reducing, substitute substance.

One study that signals the substitution potential of kratom was conducted in Northern Malaysia and used convenience sampling to identify 136 kratom users (99% male) in areas of where heavy kratom use was reported (Vicknasingam et al., 2010). Of these people, seventy-seven percent had lower secondary education or less and the mean age (38.7; SD = 10.9) was older than other reviewed samples. Many individuals (46%) were using other substances concomitantly with kratom and most (76%) had a prior drug use history. Results indicated that a 90% were using kratom as a substitute for opioids; 84% indicated that kratom helped with their opioid withdrawal symptoms. Another Malaysian survey (Singh et al., 2015) used snowball sampling to engage 293 adult males who had used kratom for a minimum of six months prior to the interview. This sample consisted largely (87%) of manual laborers who were younger (mean age = 28) and more educated (66% upper secondary education) than the Vicknasingam et al. (2010) sample. Fifty-two percent reported kratom use for three years or more. Fifteen percent indicated that they had used kratom in an effort to reduce or eliminate addictions to illicit substances (e.g., opioids, cannabis) and/or to ameliorate opioid withdrawal symptoms (Singh et al., 2015).

Across the world, nearly half of 8049 respondents (56.9% male and

Table 1
Study characteristics – kratom use and mental health.

Publication	Sample	Location	Design	Summary
Ahmad and Aziz (2012)	n = 562; > 99% male; most daily users; 94% upper secondary education or above	Northern Malaysia	cross-sectional	kratom used for stamina, recreation, performance; most users reported inability to abstain
Anwar et al. (2016)	660 poison control calls over 5 years; predominantly male (72% where gender was reported)	United States	retrospective	some callers reported acute irritability/agitation
Grundman (2017)	8049 survey respondents; 57% male; 82% some college; 66% > 1 year kratom use	United States	cross-sectional	users reported improved mood and relaxation; successful substitution for opioids; 9% reported withdrawal symptoms following non-use
Kittirapanpaiboon et al. (2014)	17,140 survey respondents; 50% male 537 were illicit substance users (59% kratom)	Thailand	cross-sectional	regular kratom use without comorbid alcohol or mental disorder did not increase suicide risk over that of non-substance users
Forrester (2013)	14 poison control calls over 1.5 years; 79% male	Texas	retrospective	agitation, confusion, hallucinations reported; comorbid substances limit conclusions
Saingam et al. (2012)	34 male “continuous” users; 3–50 years of use	Rural Thailand	qualitative	acute consequences include enhanced energy, “happiness”; dependence seen for long-term use
Saingam et al. (2014)	1118 males, 526 with kratom use histories; 67% regular users (3 times per week for minimum 3 months)	Rural Thailand	cross-sectional	more than half of regular users developed withdrawal, including muscle spasms, pain, insomnia, hot flashes, decreased appetite
Saingam et al. (2016)	Same sample as Saingam et al. (2014); 526 males; 67% regular users	Rural Thailand	cross-sectional	4 dimensions of withdrawal symptoms: craving/fatigue, musculoskeletal and insomnia, mood; autonomic nervous system/physical sickness
Singh et al. (2014)	293 males; most laborers, all > 6 months use; mean use frequency = 3.5 times per day	Northern Malaysia	cross-sectional	significant cravings and withdrawal following non-use
Singh et al. (2015)	Same sample as (Singh et al., 2014); 293 males; most laborers, all > 6 months use; mean use = 3.5 times per day	Northern Malaysia	cross-sectional	chronic and heavy kratom use does not significantly impair social functioning
Swogger et al. (2015)	161 users of a Western drug information website; 89% males among those who reported gender	Various; mostly Western	qualitative	pros: successful substitution for opiates, mood elevation, social enhancement; Cons: 10% reported withdrawal symptoms following non-use
Trakulsrichai et al. (2013)	52 kratom exposure cases at poison center; 85% male; 67% kratom only substance of use	Thailand	cross-sectional	good prognosis for kratom exposure; modest withdrawal symptoms
Vicknasingam et al. (2010)	136 active substance users, 99% male; mean age = 39; > 75% had < 9 years of education	Northern Malaysia	cross-sectional	90% used kratom as substitute for opioids; 84% report success in relieving opioid withdrawal; other benefits were increased energy and sexual desire

43.1% female) to a U.S.-based, online kratom survey indicated that kratom enabled them to reduce or discontinue the use of opioids (Grundman, 2017). In this sample, 51% were between 31 and 50 years old, greater than 80% had some college or more education, and 56.6% had used kratom for greater than one year. Kratom use for harm reduction purposes (i.e., reducing withdrawal from opioids or other unwanted drugs) was more likely in participants between the ages of 21–30 years (OR: 1.89, CI: 1.02–3.51), those with self-insurance (OR: 1.57, CI: 1.18–2.10), Medicaid (OR: 2.11, CI: 1.49–3.00), Medicare (OR: 2.41, CI: 1.53–3.79), or no insurance (OR: 1.97, CI: 1.51–2.59). A minimum dose of 5 g was perceived as effective for decreasing the use of opioids. Those less likely to use kratom for substitution were females (OR: 0.63, CI: 0.51–0.78), married participants (OR: 0.69, CI: 0.54–0.87), and retired individuals (OR: 0.26, CI: 0.07–0.93) and those unable to work (OR: 0.29, CI: 0.16–0.51).

In a study of 161, self-selected respondents (approximately 89% male) to a US-based internet forum, over 10% reported using kratom to successfully decrease or abstain from a substance that was unwanted or considered to be causing harm (Swogger et al., 2015). Whereas opioids – both heroin and pharmaceuticals – were the most frequent substances to be replaced, kratom was also used to replace antidepressants, including selective serotonin reuptake inhibitors (SSRIs).

3.2. Mood

Kratom has been reported to have an energizing effect at lower doses (Saingam et al., 2012) and a calming effect at higher doses (Singh et al., 2016). In the Malaysian sample of 293 male kratom users, described above, 29% reported using kratom to enhance energy or fight fatigue and 6% to improve mood or ease boredom (Singh et al., 2014). In another Malaysian sample, approximately 28% of primarily male kratom users indicated that they felt increased energy and alertness and approximately 26% indicated euphoria, relaxation, or contentment as a result of kratom ingestion (Ahmad and Aziz, 2012). Similarly, 30% of the 161 individuals who reported their experiences to a US-based drug information website indicated that kratom produced an enhanced sense of well-being and nearly 9% reported an increase in energy (Swogger et al., 2015). Relaxation and reduced anxiety also appeared in the narratives of 24% of the sample in a US-based qualitative study (Swogger et al., 2015). However, none of these studies clearly delineated the nature of kratom's apparent anxiolytic effect and thus did not speak to the extent to which kratom decreases anxiety without unwanted sedation. Generally, sedation has been reported by very low percentages of participants; 0.6% (Ahmad and Aziz, 2012), 3.1% (Swogger et al., 2015), and, combined with dizziness, 4.8% (Grundman, 2017). Drowsiness and sedation were reported by 19.4% of 660 people who called U.S. poison control centers from 2010 to 2015 (Anwar et al., 2016). The higher level of sedation in the poison control study may be due to the self-selected sample or the fact that over 40% had used other substances concurrently with kratom. It is interesting to note that approximately 9% of Swogger et al.'s sample indicated enhanced sociability and/or empathy following kratom ingestion, suggesting that kratom may exert anxiolytic effects without accompanying apathy and impaired social motivation.

Sixty-six percent of respondents to a large Western survey indicated they use kratom to relieve negative moods or mental states, including anxiety, depression, and posttraumatic stress (Grundman, 2017). Kratom use for this purpose was significantly related to female gender (OR: 1.3, CI: 1.16–1.46), being a homemaker (OR: 1.34, CI: 1.05–1.71) or student (OR: 1.86, CI: 1.34–2.59), and on either Medicaid (OR: 1.36, CI: 1.08–1.73), Medicare (OR: 1.35, CI: 1.05–1.74), or having no insurance (OR: 1.31, CI: 1.10–1.57). Being age 41 or older, being married, having a Bachelor's degree, and earning \$75,000 or more were negatively associated with mood-related use. In this study, Kratom was perceived by 79.4% of users to increase energy. Moreover, 75.6% of users indicated relief from depressed mood and 74.3% reported

decreased anxiety. Benefits for energy were reported at low doses (≤ 1 g) and benefits for depression and anxiety were dose-dependent up to 5 g, with higher doses correlating with greater perceived benefits (Grundman, 2017). Kratom's positive potential in the areas of mood and anxiety notwithstanding, kratom withdrawal can lead to the opposite effects, including depressed mood, hostility, and heightened anxiety (Ahmad and Aziz, 2012; Singh et al., 2014). A significant portion (23.8%) of callers to U.S. poison centers during a 5-year period reported agitation or irritability after ingesting kratom, though other substances may have contributed to these experiences (Anwar et al., 2016).

3.3. Adverse effects

Several studies described kratom-related adverse effects (Ahmad and Aziz, 2012; Anwar et al., 2016; Forrester, 2013; Grundman, 2017; Saingam et al., 2016; Singh et al., 2014; Singh et al., 2015; Swogger et al., 2015; Trakulsrichai et al., 2013). Evidence related to negative psychosocial effects converges to indicate that regular use can result in tolerance, withdrawal symptoms upon cessation of use, and difficulty in abstaining from kratom (Ahmad and Aziz, 2012; Grundman, 2017; Singh et al., 2014; Swogger et al., 2015). Interestingly, a comprehensive survey of 530 predominantly male, regular kratom users in Malaysia (94% daily, with a mean history of 4.6 [SD = 3.8] years of use) reported lower user education level was protective for uncontrolled use (Ahmad and Aziz, 2012). Another study of 293 male, frequent kratom users in Malaysia found that 73% experienced withdrawal symptoms for approximately one to three days after discontinuing use (Singh et al., 2014). The U.S.-based studies reported lower rates of withdrawal symptoms: nearly 9% and 10%, respectively (Grundman, 2017; Swogger et al., 2015).

While the incidence of withdrawal appears to vary according to the sample, the evidence converges across studies to characterize the nature of withdrawal symptoms. Results of a factor analysis of symptoms of kratom withdrawal conducted among 526 kratom-using males in Thailand (67% of whom reported kratom use ≥ 3 three times per week), describe the withdrawal syndrome across four symptom dimensions: 1) craving and fatigue, 2) musculoskeletal system and insomnia, 3) mood symptoms, and 4) autonomic nervous system/physical sickness (Saingam et al., 2016). These categories of kratom withdrawal symptoms are consistent with evidence from ethnically and culturally diverse samples indicating that prominent withdrawal symptoms include fatigue and cravings, tremor, cramping, muscle aches and insomnia, anxiety and tension, depressed mood, and nausea, hot flashes, sweating, diarrhea, vomiting, and watering eyes and nose (Grundman, 2017; Singh et al., 2014; Swogger et al., 2015; Trakulsrichai et al., 2013).

Kratom withdrawal symptoms resemble the opioid withdrawal syndrome (Miranda and Taca, 2017). Extant data suggest that kratom's withdrawal syndrome is uncomfortable, but generally milder and of shorter duration than is characteristic of opioid withdrawal (Singh et al., 2015; Swogger et al., 2015). Symptoms of withdrawal are not insignificant, however; among the 9% of respondents to a U.S.-based survey who had experienced kratom withdrawal within 12–48 h of non-use, most rated the severity of symptoms at either '2' (40.4%), '3' (36.1%), or '4' (11.5%) on a 5-point Likert scale, with '1' as most severe (Grundman, 2017). Preliminary survey data among Western respondents indicates that withdrawal and other negative effects were more highly reported by people who were partnered but not married (OR: 1.37, CI: 1.12–1.68), had Medicare (OR: 1.69, CI: 1.31–0.218), Medicaid (OR: 1.6, CI: 1.27–2.00), or no insurance (OR: 1.64, CI: 1.37–1.95), and earned between \$35,000 to \$49,999 (OR: 1.38, CI: 1.11–1.73). By contrast, being self-employed (OR: 0.77, CI: 0.65–0.92), a student (OR: 0.72, 0.53–0.99), or having a Bachelor's (OR: 0.46, CI: 0.30–0.72) or advanced degree (OR: 0.41, CI: 0.25–0.66) was associated with lower odds for consuming Kratom for a prescription drug

dependency (Grundman, 2017).

Apart from kratom dependence, available studies give no indication that kratom causes psychopathology. In Grundmann's large survey, only about 3% of respondents indicated they had sought mental health treatment "because of kratom consumption." Approximately 4% of interviewees in a Malaysian study that directly asked about hallucinations during kratom use endorsed them (Ahmad and Aziz, 2012). One study (Forrester, 2013) reported psychotic-like symptoms among a small number of callers to a U.S. poison center (i.e., hallucinations following the ingestion of kratom), though the extent to which these reported hallucinations are directly attributable to kratom rather than concurrent use of other substances, existing psychopathology, or drug naiveté is unclear.

We searched for scientific information on kratom use and self-and-other directed aggression. Although few studies directly assessed aggression, reports of this outcome were notably absent from studies that indirectly enabled such reporting (e.g., Anwar et al., 2016; Saingam et al., 2012; Swogger et al., 2015; Trakulsrichai et al., 2013). No studies indicated increased self-or-other directed aggression following acute ingestion. Approximately 1% of Malaysian interviewees indicated that they had engaged in aggression or experienced hostility while in kratom withdrawal (Ahmad and Aziz, 2012). Consistent with above results, findings of a large epidemiological study (n = 17,140; Thai National Mental Health Survey; Kittiranapaiboon et al., 2014) provide indirect support for the proposition that kratom use does not increase risk for self-directed aggression. Specifically, an aggregated group of users of illicit substances (n = 537), of whom nearly 60% used regularly used kratom, did not differ from a non-substance-using group with regard to suicide risk on the Mini International Neuropsychiatric Interview, Suicidality Module (Kittiranapaiboon and Khamwongpin, 2005). This study has several limitations; most notably that analyses combine kratom users with other drug users (e.g., 24% were methamphetamine users) and do not provide an analysis of risk associated with any particular substance except alcohol. However, while the study found that drug users who also used alcohol or had mental health problems were at higher risk for suicide than individuals without mental illness or alcohol problems, preliminary findings indicate no increased suicide risk related to kratom in healthy individuals.

4. Discussion

We conducted a comprehensive systematic review of the scientific literature on kratom use and mental health. Perhaps our most robust finding is that the study of kratom's effects on humans, and mental health in particular, is in its infancy. This was revealed by a lack of rigorous, well-controlled, prospective studies; the kind that will eventually lead to a sophisticated and nuanced clinical understanding of the benefits and harms of kratom use. Females were excluded or underrepresented in most of the studies. Moreover, the integration of a scant literature is complicated by the diversity of samples and methodologies; for example, frequent users of kratom in Southeast Asia, where use is embedded in complex cultural traditions, differ in myriad ways from potentially drug naïve individuals who call into a U.S. poison centers.² Despite these challenges and limitations, we were able to draw some conclusions about kratom use and mental health from converging evidence across 13 studies.

With regard to adverse effects, kratom use carries risk for physiological dependence, though this risk has not been adequately quantified. Additional research is necessary to estimate the incidence of kratom dependence in various populations, which varies widely in the

extant literature. There is good evidence that kratom dependence is typically less severe than opioid dependence, with which kratom shares some mechanisms of action (Hassan et al., 2013). Moreover, unlike opioids, kratom use does not appear to result in significant respiratory depression (Kruegel et al., 2016) and is thus far less likely to cause fatal overdose. The perception that kratom is a milder and less dangerous opioid-like psychoactive substance is supported by the uptake of kratom use as an opiate substitute (Vicknasingam et al., 2010) and is consistent with data on the unimpaired social functioning of regular kratom users (Singh et al., 2015). For future research on the effects of heavy kratom use, a scale designed to measure kratom dependence has shown good preliminary reliability and validity (the Kratom Dependence Scale; Saingam et al., 2014).

Findings indicate that kratom has potential as a harm reduction tool in the context of problematic opioid use. Substitution therapy has demonstrated substantial effectiveness as a harm reduction strategy for problematic opioid use, as evidenced by the widespread proliferation and success of methadone maintenance therapy and the emergence of buprenorphine treatment to decrease or eliminate the use of potentially more harmful opioids (Li et al., 2016). However, extant approaches do not meet the needs of all those who struggle with opioid addiction, making the development of additional options an important target (Stitzer et al., 2017). As an example of the utility of substitution agents at the public health level, opioid deaths have decreased following an increase in legal medical cannabis availability in select U.S. states (Bachhuber et al., 2014). As a catastrophic North American opioid epidemic continues, a natural experiment into the harm reducing potential of kratom as a substitute for opioids is well underway. Across the U.S., daily visits to the American Kratom Association webpage average greater than 9000, including an average of 2262 unique visitors (Grundman, 2017). Proposed restriction of legal access to kratom can be reasonably expected to have unintended negative public health consequences by removing a harm reduction tool.

Regarding kratom's effect on mood and anxiety, kratom appears to be more akin to a stimulant than an antidepressant medication, based on the relatively rapid onset and limited duration of action. There is good evidence that, in the short-term, low doses of kratom can boost energy and enhance mood, whereas higher doses may have anxiolytic effects (Ahmad and Aziz, 2012; Saingam et al., 2012; Singh et al., 2014; Swogger et al., 2015). There is also preliminary evidence that kratom has empathogenic effects and can lead to enhanced sociability (Swogger et al., 2015). If these findings are replicated, kratom might be studied as a potential anxiolytic that does not lead to emotional blunting or feelings of disconnection associated with widely used anxiolytics (Ashton, 1986; Price et al., 2009). Clinicians who work with people who are already using kratom to manage anxiety might encourage adding evidence-based psychosocial treatment strategies (e.g., gradual exposure to feared stimuli, mindfulness meditation) in order to enhance self-efficacy and increase experiential acceptance and functionality in a lasting way (Hofman and Smits, 2008; Kishita et al., 2016). Only anecdotal reports are available that address the long-term, moderate use of kratom use to enhance mood (see Henningfield, 2016; Erowid, 2017), and clinical trials are necessary to more carefully evaluate kratom's impact on mood and anxiety over the course of weeks or months. Clinicians should be aware of the potential for dependence in heavy users. Withdrawal symptoms may include depression, irritability, and anxiety.

Discrepant findings in existing data appear to be closely tied to cultural and demographic moderators of kratom use patterns and consequences. In the West, females are more likely than males to use kratom for emotional help (Grundman, 2017), probably due to their higher incidence of mood disorders relative to males (Seney and Sibille, 2014). By contrast, males have a higher incidence of substance use disorders (SAMHSA, 2014), potentially increasing the likelihood of kratom use for substitution. Data from North America indicates that higher education is associated with less incidence of withdrawal

² The dangers of comparison are highlighted by the fact that Texas Poison Center study (Forrester, 2013) included at least two individuals who inhaled kratom. This is a method of consumption that is largely recognized as unpleasant and/or dangerous in informed samples and highlights the importance of education.

(Grundman, 2017). By contrast, Malaysian individuals with higher education had more difficulty abstaining from kratom than less educated people. Ahmad and Aziz (2012) speculate that, because individuals with lower education are more likely to be laborers who regularly use low doses of kratom for energy, they may be less likely to become dependent than individuals with more education who use high doses for recreation. The incidence of kratom withdrawal varies widely in existing studies (9%–73%), indicating the importance of rigorous and sophisticated research that elucidates moderators of kratom use patterns and outcomes.

In general, this comprehensive review of a preliminary, scant, and diverse literature yields no indication that kratom use carries significant mental health risks beyond the possible development of kratom dependence, which is generally mild compared to that of opioids. A low proportion of Malaysian participants in one study endorsed hallucinations following acute use, although it is unclear whether these were true hallucinations or a nonspecific labeling of kratom's visual effects. These have been reported as pleasant among individuals experimenting with kratom in the U.S. (Swogger et al., 2015). Most studies did not examine psychosis directly. It is notable, given CDC and DEA warnings in the U.S., that psychotic symptoms were not described in most studies that enabled their reporting (Anwar et al., 2016; Saingam et al., 2012; Swogger et al., 2015; Trakulsrichai et al., 2013). The lack of evidence for psychosis or other psychopathology combines with the very low percentage of people in North America who report seeking mental health care as a result of kratom use (Grundman, 2017) to indicate minimal to no short-term risk of psychosis due to kratom. Similarly, we found no evidence for kratom-induced risk for self-or-other directed aggression. In one investigation, approximately 1% of Malaysian interviewees endorsed aggression during kratom withdrawal (Ahmad and Aziz, 2012). As with all reviewed studies, the design does not enable causal inferences and no aggressive behavior was found among participants of the other studies that enabled its reporting (Anwar et al., 2016; Saingam et al., 2012; Swogger et al., 2015; Trakulsrichai et al., 2013). Importantly, our review was limited to mental health consequences and other sources should be reviewed for data on other health correlates of kratom use.

In conclusion, kratom use appears to have several important mental health benefits that warrant further study. Kratom dependence is a risk for some people, though the dependence syndrome appears to be mild in its psychosocial and physiological effects relative to that of opioids. More and better research, including well-controlled, prospective studies is necessary to further elucidate kratom's potential for good and harm and the moderators of its effects. Studies that address kratom's mental health effects in women and across understudied cultures and ethnicities are particularly needed. Moreover, there are no good data on kratom use in the severely mentally ill or on interactions between kratom and other substances. The extent to which the adverse effects of kratom are accepted by the public and policy makers in the North America (akin to caffeine, for example) will depend largely on the results of further research and the further development of sociocultural norms around this relative newcomer to the pharmacopeia of North America and Europe.

Conflict of interest

No conflicts declared

Contributors

Dr. Swogger conducted the research for and wrote initial drafts. Dr. Walsh provided additional text and substantive input that contextualized findings within the broader literature. All authors approved of the submission.

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