



Kratom as a substitute for opioids: Results from an online survey

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ARTICLE INFO

Keywords:

Kratom
Opioids
Pain
Survey

ABSTRACT

Background: Kratom is a South Eastern Asian tree whose leaves are used to make tea-like brews or swallowed in powdered form for various health and well-being reasons including to relieve pain and opioid withdrawal. It is important to learn more about the potential public health impact of kratom in the context of the opioid epidemic. **Methods:** An anonymous online survey of kratom users (2867 current users and 157 former users) was conducted in September 2017 through the American Kratom Association and associated social media sites.

Results: Kratom was used primarily to relieve pain (endorsed by 48% of respondents), for anxiety, PTSD, or depression (22%), to increase energy or focus (10%) and to help cut down on opioid use and/or relieve withdrawal (10%). Over 90% of respondents who used it in place of opioids indicated that it was helpful to relieve pain, reduce opioid use, and relieve withdrawal. The reported incidence of bad adverse reactions was 13%, and reactions were overwhelmingly mild and self-managed.

Conclusions: Respondents reported using kratom for conditions which often require use of opioids, including pain and reduction of opioid use. The high self-reported efficacy and low incidence of adverse reactions associated with kratom use suggest that it may provide a potential alternative to opioids for some persons even though it has not been evaluated in multi-center clinical trials or approved for any therapeutic purpose. Further study of kratom, including systematic characterization of its safety and efficacy for various conditions is warranted.

1. Introduction

Kratom (*Mitragyna speciosa*) is a tree in the coffee family native to Southeast Asia, where its leaves have been used medicinally for centuries. It is sold in the United States (U.S.) in a variety of formulations (e.g., chopped or whole leaves, extracts, liquids, powders) and is commonly orally consumed by making tea-like extractions with leaf powder, swallowing powder with food or liquids, or swallowing leaf powder-filled capsules. Kratom is used worldwide for a variety of health-related reasons including pain relief, decreased fatigue, increased energy and focus, alleviation of depression and anxiety, and as a substitute for alcohol, opioids, and/or other drugs to manage withdrawal and sustain abstinence (Assanangkornchai et al., 2007; Grundmann, 2017; Singh et al., 2014; Swogger et al., 2015; Vicknasingam et al., 2010). The effects of kratom are reported to be dose-dependent, with smaller doses producing mild stimulant-like effects and larger doses producing opioid-like effects. Importantly, there

is little evidence of respiratory depression associated with kratom use, which is consistent with the characterization of its main active alkaloid, mitragynine, as well as the minor alkaloid 7-hydroxymitragynine as partial agonists and mechanism of action as G protein-biased agonists of the mu-opioid receptor (Kruegel et al., 2016; Varadi et al., 2016).

Many of the reported reasons for use of kratom (pain relief, opioid substitution, etc.) are supported by basic and preclinical research. The chemistry of kratom is complex; it is comprised of several dozen alkaloids that vary in concentration by species, growing condition, and other factors (Brown et al., 2017; Gogineni et al., 2014; Hassan et al., 2013; Tanguay, 2011), with mitragynine often accounting for approximately 60% of the total alkaloid content (Adkins et al., 2011). Mitragynine has long been thought to be primarily responsible for the pharmacological effects of kratom consumption because it is present in leaves at pharmacologically active levels, whereas other alkaloids are either of little pharmacological activity and/or at very low concentrations and often not present in consumed kratom products (Brown et al.,

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<https://doi.org/10.1016/j.drugalcdep.2019.05.005>

Received 4 March 2019; Received in revised form 1 May 2019; Accepted 2 May 2019

Available online 29 June 2019

0376-8716/ © 2019 Published by Elsevier B.V.

2017; Kruegel et al., 2016; Kruegel and Grundmann, 2018; Takayama et al., 2002). Mitragynine behaves as a partial mu-opioid receptor agonist and competitive antagonist at kappa- and delta-opioid receptors, and it binds to a variety of non-opioid receptors, which might also contribute to the diverse constellation of kratom effects (Kruegel et al., 2016; Kruegel and Grundmann, 2018; Matsumoto et al., 2004; Prozialeck et al., 2012).

Two preclinical intravenous drug self-administration studies reported that mitragynine was more similar to saline than heroin or morphine in reinforcing efficacy; furthermore, mitragynine administration reduced subsequent self-administration of these opioids. In the Yue et al. study (Yue et al., 2018), the self-administration of mitragynine and heroin was compared in rats that were trained to self-administer methamphetamine. Both methamphetamine and heroin sustained robust lever-pressing and self-administration rates as compared to saline. In contrast, mitragynine self-administration was similar to saline—indicating low reinforcing effects and limited abuse potential. Subsequently, in sessions in which the animals were allowed to self-administer either heroin or methamphetamine, mitragynine pretreatment produced dose-related decreases in heroin but not methamphetamine self-administration. In a study by Hemby et al., rats that learned to self-administer morphine did not readily self-administer either mitragynine or saline (Hemby et al., 2018). However, mitragynine pretreatment reduced subsequent morphine self-administration (Hemby et al., 2018). The authors of both studies suggested that mitragynine merited further research as a possible low abuse potential pharmacotherapy for opioid use disorder (OUD).

Any compound that produces opioid-like effects and binds to the mu-opioid receptor warrants careful scrutiny, particularly now as the U.S. is in the midst of an opioid epidemic (Centers for Disease Control and Prevention, 2018). Concerns about abuse potential, safety, and adverse reactions due to kratom use have been raised, both in the scientific literature (Anwar et al., 2016; Warner et al., 2016) and by the U.S. Drug Enforcement Administration (DEA) and Food and Drug Administration (FDA) (Gottlieb, 2017, 2018; Grundmann et al., 2018; Henningfield et al., 2018a, c; US Drug Enforcement Administration, 2016a,b). In fact, the FDA has recommended that mitragynine and 7-hydroxymitragynine be placed in Schedule I of the Controlled Substances Act (CSA) along with heroin and LSD (Food and Drug Administration, 2017; Henningfield et al., 2018a; Swelitz, 2018; US Drug Enforcement Administration, 2016a). Kratom is currently regulated as a dietary supplement, and the FDA has taken action both on contaminated kratom products (Food and Drug Administration, 2018c) and kratom products making unauthorized claims (e.g., addiction treatment (Food and Drug Administration, 2018a)). However, the FDA has not issued guidance or regulatory standards for allowable product contents, alkaloid concentrations, packaging, labeling, or marketing of kratom products as is routinely done for dietary ingredients.

There are potential public health consequences of banning a substance many people use for a variety of reasons, including as a substitute for opioids (Henningfield et al., 2018a; Swelitz, 2018). Surveys of more than 20,000 kratom users, (Anson, 2018; Grundmann, 2017; Smith and Lawson, 2017) and comments submitted to the DEA (US Drug Enforcement Administration, 2016b) suggest that such a ban may cause increased opioid consumption among persons currently using kratom to abstain from opioids, as well as an emergence of a black market for obtaining kratom. These survey findings and public comments suggest kratom use is not uncommon. Although reasons for use vary, the most common reasons are self-treatment of pain, emotional, and mental health conditions. Few persons report using kratom to get high, and effects are dose-dependent with larger doses (> 5 g) or more frequent dosing (> 22 times per week) producing more negative effects. Kratom is also frequently reported to be used as a substitute for prescription and illicit opioids, either to manage pain or withdrawal symptoms.

The current survey, conducted in September 2017, builds on prior

surveys by focusing more on the interrelationship of kratom and opioid use. The key objectives of this survey were to provide a more complete description of how and why individuals may use kratom in place of opioids, specific reasons for use, perceptions of the efficacy of kratom as an opioid substitute, the safety/tolerability of kratom, and anticipated reactions if legal access to kratom were restricted.

2. Methods

2.1. Participants and procedures

An online survey was conducted by Research Now in September 2017 with 3024 kratom users aged 18 years and older residing in the U.S., including 2867 current and 157 former kratom users. Respondents were recruited via announcements on the homepage of the American Kratom Association (<http://www.amerikan kratom.org/>) and its social media outlets (e.g., American Kratom Association Facebook page, website forums, Reddit, and membership email distribution).

Individuals who responded to an online announcement (by clicking on the link to complete the survey) were screened for eligibility. Eligible respondents had to be age 18 or older and report ever using kratom. Exclusion criteria included residing outside the U.S. and employment with the FDA, the DEA, or a kratom vendor or manufacturer at the time of the survey. Respondents were not compensated for completing the survey. Internet protocol (IP) addresses were not stored to ensure respondent anonymity but were used to prevent multiple responses from the same device to prevent completion of the survey multiple times by the same individual. The survey and protocol were approved by Western IRB.

2.2. Survey items

Respondents were asked demographic questions (e.g., age, race, education, etc.) and about their use of kratom (duration of use, number of times used, and forms of kratom used). Current kratom use was self-defined by respondents' answer to the question, "Are you currently using kratom?". Frequency of kratom use was assessed by asking "How many times have you used kratom in lifetime/last 12 months/last 30 days/last week?". Response options were 0 times/1–2 times/3–5 times/6–9 times/10–19 times/20–39 times/40 or more times.

Reasons for kratom use were assessed with two questions. The first asked, "For what reasons are you using/did you use kratom? Select all that apply." Response options were: to relieve pain/to relieve withdrawal symptoms/anxiety or depression/PTSD/insomnia/to control blood sugar/to increase focus or energy/to cut down or quit using prescription pain medicine/to cut down or quit using illicit or illegal drugs/to cut down or quit using over-the-counter pain medicine/to cut down or quit using alcohol/to cut down or quit using tobacco/recreational use (for the feeling you get)/curiosity/or other reason (please specify). The second question asked "What is the main reason you are using/used kratom?", and response options were the same as above. All respondents were asked, "How helpful has kratom been for [main condition for which kratom was used]?". Those reporting only past kratom use were asked "Why did you stop using kratom?".

All respondents were asked "Have you ever had a bad reaction from using kratom?" and to select all the bad reactions they had experienced from the list: stomach problems (nausea, diarrhea, vomiting, upset stomach)/constipation/heart palpitations/shortness of breath/dizziness/drowsiness/fainting/irritability or irritation/high blood pressure/headaches/body aches/fever/hallucinations/weight gain or weight loss/hair loss/rash/other (please specify). If respondents indicated they had experienced a bad reaction, they were asked "Did you get medical help because of the bad reaction you had from using kratom?" and if yes "What was the outcome of the medical help you received?".

Respondents were also asked "Have you ever used any opioid pain medicine such as hydrocodone (Lortab, Lorcet, Vicodin), oxycodone

(OxyContin, Percocet, Percodan), or another opioid?”. If they responded yes, additional questions were asked about reasons for using the opioid pain medicine and how many times they had used an opioid pain medicine in their lifetime, the past 12 months, past 30 days, and past week.

Respondents reporting current kratom use were asked, “What would you do if you were no longer able to buy kratom legally? Select all that apply.” Response options were: try to get it where it is legally available/start using something else/stop using kratom and not replace it with anything else/try to get it even if were illegal/I am already unable to buy it legally/other (please specify). If respondents indicated they would use something else, the question, “Which of these would you likely start using if you were no longer able to buy kratom legally? Select all that apply.” was asked. Response options were: prescription drugs/over-the-counter drugs/dietary supplement(s) or herbal remedy/illicit or illegal drug(s)/alcohol/ cigarettes or other tobacco products/I don’t know/other (please specify).

2.3. Data analysis

The data were analyzed using SAS version 9.4 for Windows. Only responses from completed surveys were included in the analysis. Demographic characteristics were tabulated for the full sample (N = 3024), as well as among current kratom users (N = 2867), former kratom users (N = 157), and opioid pain medication users (N = 2803), who were comprised of both current and former kratom users. Descriptive results – including number and proportion – were reported for survey items among the full sample, current kratom users, former kratom users, and various subgroups specific to certain items. Where relevant, statistical comparisons used chi-square tests, and were deemed significant if the p-value < 0.05.

3. Results

3.1. Sample demographics

A total of 3024 respondents completed the survey. Respondents were an average of 42.3 years old (SD 12.6), slightly more than half (53.6%) were male, and the majority (93.4%) were Caucasian and non-Hispanic (96.4%). All demographic data are listed in Table 1.

3.2. Description of kratom use: frequency and formulations

Of the 2867 respondents who reported “current kratom use” (i.e., current kratom use was self-defined and not restricted to a specific timeframe), 72% reported using kratom for more than 1 year. The number of kratom uses in the past month varied from fewer than 10 times (n = 341; 11.9%), 10 to 39 times (n = 1354; 47.2%), to 40 or more times (n = 1172; 40.9%). Slightly more than half currently using kratom (n = 1540; 53.7%) reported using it fewer than 10 times in the past week. 1167 (40.7%) used kratom 10 to 39 times, and 160 (5.6%) used kratom 40 or more times in the past week.

157 respondents reported past kratom use only, and over half (n = 97; 61.8%) reported kratom use for 6 months or less. 44 (28.0%) reported kratom use for more than 1 year. Lifetime number of times using kratom varied from fewer than 10 times (n = 41; 26.1%), 10–39 times (n = 47; 29.9%), to 40 or more times (n = 69; 44.0%).

Among all respondents, the kratom formulations most commonly used were powders (n = 2681), capsules (n = 864), teas (n = 444), leaf materials (n = 358), and extract or enhanced materials (n = 235). Kratom was most commonly obtained from online vendors (n = 2540; 84.0%) and retail stores (n = 322; 10.7%). The remaining respondents reported obtaining kratom from direct importation (n = 54; 1.8%), friends or relatives (n = 54; 1.8%), or from other sources (n = 54; 1.8%).

3.3. Description of opioid use

Nearly all (n = 2803; 92.7%) respondents reported having ever used an opioid medication. Respondents currently using kratom reported significantly less opioid use in the past week [$\chi^2(1) = 33.02$, $p < 0.0001$ and the past month [$\chi^2(1) = 18.93$, $p < 0.0001$] than respondents endorsing only past kratom use. This was also the case among the subset of respondents whose main reason for using kratom was either for pain relief or to help them cut down or quit use of prescription opioids and/or heroin (see Fig. 1).

3.4. Reasons for kratom use

When asked to select *all the reasons* for kratom use, similar reasons were given by respondents who endorsed current and past kratom use. See Table 2 for numbers of respondents endorsing each reason. Those who used kratom in the past (but not currently) were significantly more likely to report using kratom to relieve withdrawal symptoms [$\chi^2(1) = 19.18$, $p < 0.0001$] or out of curiosity [$\chi^2(1) = 35.72$, $p < 0.0001$] than those reporting current kratom use.

When asked their *primary reason* for kratom use, three of the five most commonly reported reasons are associated with opioids: pain relief (n = 1451; 48.0%), to cut down or quit use of prescription opioids or heroin (n = 209; 6.9%), and to relieve withdrawal symptoms (n = 83; 2.7%). The other two most common reasons for kratom use were to relieve anxiety (including PTSD) or depression (n = 651; 21.5%) and to increase focus or energy (n = 300, 9.9%).

3.4.1. Relief of pain

The most frequently reported pain-related conditions for which kratom was used included: spine or back pain (n = 596), fibromyalgia (n = 165), injury-related (n = 138), and osteoarthritis (n = 95). Less commonly reported pain conditions were rheumatoid arthritis (n = 55), migraine and headaches (n = 44), joint pain (n = 77), multiple sclerosis (n = 11), cancer (n = 9), autoimmune diseases (n = 32), inflammatory bowel disease (n = 16), and pain following surgery (n = 32).

Respondents currently using kratom primarily for pain relief reported that kratom was “very” (90.7%) or “somewhat” (9.0%) helpful in relieving their pain condition. Respondents who used kratom in the past for pain relief reported that kratom was “very” (60.3%) or “somewhat” (30.2%) helpful in relieving their pain condition. Nearly all respondents (97.6%) who used kratom primarily for pain reported that they had tried something else before kratom to relieve their pain (commonly cited therapies were prescription and OTC medications, physical therapy, chiropractic adjustments).

3.4.2. Cut down or quit opioid use

Kratom was used to cut down or quit use of prescription opioids by 173 respondents. The most common prescription opioids respondents reported using kratom to reduce their use of were hydrocodone (n = 115) and oxycodone (n = 98). While most respondents were trying to reduce or stop use of short-acting, full opioid agonists, 21 reported that they were using kratom to cut down or quit use of buprenorphine (n = 14) and methadone (n = 7). An additional 35 respondents reported using kratom to cut down or quit their use of heroin.

Respondents currently using kratom primarily to cut down or quit their use of prescription opioids or heroin reported that kratom was “very” (98.4%) or “somewhat” (1.6%) helpful. Likewise, respondents who used kratom in the past to cut down or quit their use of prescription opioids or heroin reported that kratom was “very” (81.3%) or “somewhat” (12.5%) helpful. Only one respondent (who reported only past kratom use) indicated that kratom was “not very helpful” for quitting prescription opioids or heroin.

Table 1
Sample Demographics.

	Number; % of respondents			
	All respondents (N = 3,024)	Those reporting...		
		Current kratom use (N = 2,867)	Past kratom use only (N = 157)	Opioid pain medicine use ^a (N = 2,803)
Ever used any opioid pain medicine				
Yes	2,803; 92.7%	2,665; 93.0%	142; 90.4%	—
No	205; 6.8%	188; 6.6%	13; 8.3%	—
Don't know	16; 0.5%	14; 0.5%	2; 1.3%	
Gender				
Male	1,620; 53.6%	1,528; 53.3%	92; 58.6%	1,488; 53.1%
Female	1,404; 46.4%	1,339; 46.7%	65; 41.4%	1,315; 46.9%
Age, Mean (SD)	42.3 (12.6)	42.3 (12.5)	42.1 (13.7)	42.5 (12.4)
18-24	183; 6.1%	171; 6.0%	12; 7.6%	147; 5.2%
25-30	383; 12.7%	355; 12.4%	28; 17.8%	343; 12.2%
31-40	957; 31.6%	921; 32.1%	36; 22.9%	911; 32.5%
41-50	677; 22.4%	643; 22.4%	34; 21.7%	633; 22.6%
51-60	526; 17.4%	498; 17.4%	28; 17.8%	495; 17.7%
61 and older	298; 9.9%	279; 9.7%	19; 12.1%	274; 9.8%
Race				
Caucasian or White	2,824; 93.4%	2,680; 93.5%	144; 91.7%	2,625; 93.6%
African American or Black	30; 1.0%	27; 0.9%	3; 1.9%	25; 0.9%
Asian or Pacific Islander	22; 0.7%	20; 0.7%	2; 1.3%	17; 0.6%
American Indian or Alaskan	31; 1.0%	31; 1.1%	0; 0.0%	31; 1.1%
Native				
Other	117; 3.9%	109; 3.8%	8; 5.1%	105; 3.7%
Hispanic or Latino				
Yes	108; 3.6%	104; 3.6%	4; 2.6%	99; 3.5%
No	2,916; 96.4%	2,763; 96.4%	153; 97.4%	2,704; 96.5%
Education				
High school or less	519; 17.2%	497; 17.3%	22; 14.0%	486; 17.3%
Some college	962; 31.8%	912; 31.8%	50; 31.8%	899; 32.1%
Associate degree	487; 16.1%	463; 16.1%	24; 15.3%	462; 16.5%
Bachelor degree	741; 24.5%	701; 24.5%	40; 25.5%	675; 24.1%
Masters or doctoral degree	315; 10.4%	294; 10.3%	21; 13.4%	281; 10.0%
Marital status				
Never married	780; 25.8%	732; 25.5%	48; 30.6%	683; 24.4%
Married or living as married	1,661; 54.9%	1,587; 55.4%	74; 47.1%	1,571; 56.0%
Divorced	445; 14.7%	417; 14.5%	28; 17.8%	419; 14.9%
Separated	69; 2.3%	66; 2.3%	3; 1.9%	65; 2.3%
Widowed	69; 2.3%	65; 2.3%	4; 2.6%	65; 2.3%
Annual household income				
< \$10,000	164; 5.4%	153; 5.3%	11; 7.0%	148; 5.3%
\$10,000 to \$19,999	227; 7.5%	218; 7.6%	9; 5.7%	205; 7.3%
\$20,000 to \$29,999	303; 10.0%	290; 10.1%	13; 8.3%	280; 10.0%
\$30,000 to \$39,999	332; 11.0%	311; 10.9%	21; 13.4%	311; 11.1%
\$40,000 to \$49,999	373; 12.3%	351; 12.2%	22; 14.0%	352; 12.6%
\$50,000 to \$74,999	624; 20.6%	50; 20.6%	34; 21.7%	5874 20.8%
\$75,000 to \$99,999	389; 12.9%	372; 13.0%	17; 10.8%	353; 12.6%
\$100,000 or more	612; 20.2%	582; 20.3%	30; 19.1%	570; 20.3%
Employment status				
Work full-time	1,623; 53.7%	1,541; 53.7%	82; 52.2%	1,489; 53.1%
Work part-time	333; 11.0%	320; 11.2%	13; 8.3%	301; 10.7%
Unemployed or seeking work	120; 4.0%	106; 3.7%	14; 8.9%	112; 4.0%
Retired	181; 6.0%	172; 6.0%	9; 5.7%	163; 5.8%
Full-time student	94; 3.1%	87; 3.0%	7; 4.5%	82; 2.9%
Homemaker or caregiver	232; 7.7%	224; 7.8%	8; 5.1%	222; 7.9%
Disabled	366; 12.1%	344; 12.0%	22; 14.0%	361; 12.9%
Other	75; 2.5%	73; 2.5%	2; 1.3%	73; 2.6%
Military service				
Yes, active duty now	6; 0.2%	6; 0.2%	0; 0.0%	6; 0.2%
Yes, in last 12 months, but not now	1; < 0.1%	1; < 0.1%	0; 0.0%	1; < 0.1%
Yes, but not in last 12 months	227; 7.5%	215; 7.5%	12; 7.6%	216; 7.7%
No, training for Reserves or National Guard only	26; 0.9%	25; 0.9%	1; 0.6%	23; 0.8%
No/Never	2,764; 91.4%	2,620; 91.4%	144; 91.7%	2,557; 91.2%
Cigarette smoker				
Every day	279; 9.2%	264; 9.2%	15; 9.6%	262; 9.3%
Some days	651; 21.5%	624; 21.8%	27; 17.2%	629; 22.4%

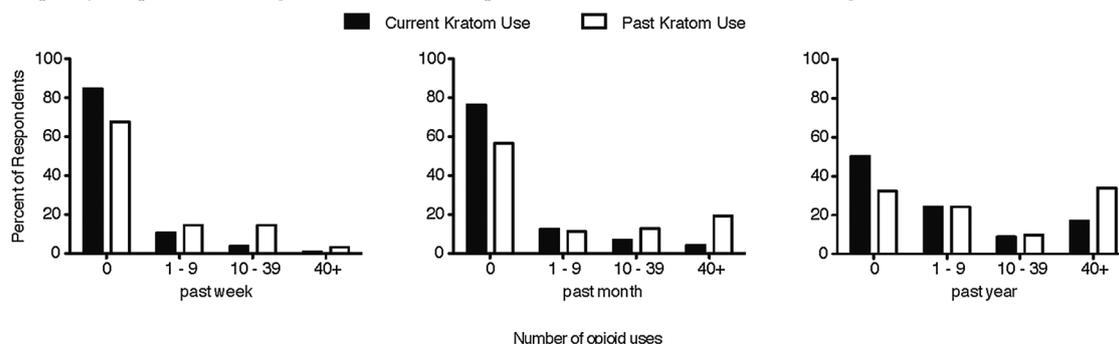
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Table 1 (continued)

	Number; % of respondents			
	All respondents (N = 3,024)	Those reporting...		
		Current kratom use (N = 2,867)	Past kratom use only (N = 157)	Opioid pain medicine use* (N = 2,803)
Not at all	2,094; 69.3%	1,979; 69.0%	115; 73.2%	1,912; 68.2%
Census region				
Northeast	481; 15.9%	462; 16.1%	19; 12.1%	448; 16.0%
Midwest	593; 19.6%	577; 20.1%	16; 10.2%	550; 19.6%
South	1,182; 39.1%	1,105; 38.5%	77; 49.0%	1,094; 39.0%
West	768; 25.4%	723; 25.2%	45; 28.7%	711; 25.4%

* Opioid pain medicine use defined as “yes” response to the question, “Have you ever used any opioid pain medicine such as hydrocodone (Lortab, Lorcet, Vicodin), oxycodone (OxyContin, Percocet, Percodan), or another opioid?”.

Frequency of opioid use among those who endorsed "pain relief" as their main reason for using kratom



Frequency of opioid use among those who endorsed "to cut down or quit prescription opioids or heroin" as their main reason for using kratom

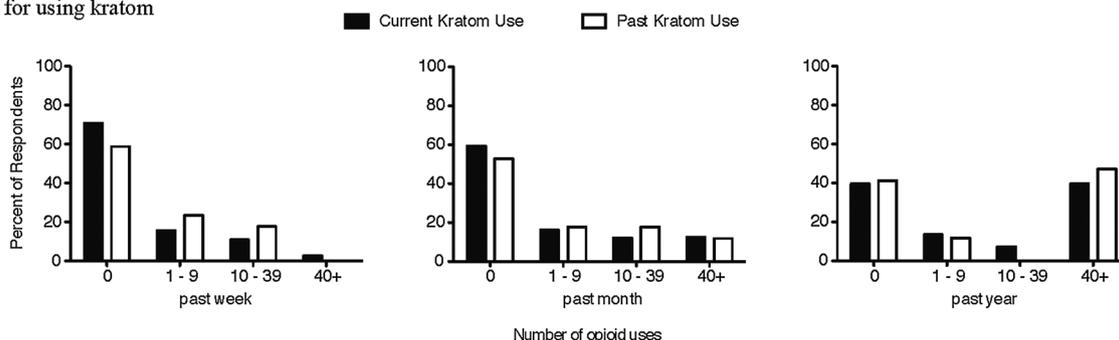


Fig. 1. Frequency of opioid use among respondents reporting their main reason for using kratom as pain relief (top row; n = 1386 with respondents reporting current kratom use and n = 62 with respondents reporting only past kratom use) and to cut down or quit prescription opioids or heroin (bottom row; n = 192 with respondents reporting current kratom use and n = 17 with respondents reporting only past kratom use).

3.4.3. Relief of withdrawal symptoms

Respondents currently using kratom primarily to relieve withdrawal symptoms (n = 62) reported that kratom was “very” (95.2%) or “somewhat” (4.8%) helpful. Those who used kratom in the past to relieve withdrawal symptoms (n = 19) reported that kratom was “very” (73.7%) or “somewhat” (5.8%) helpful. Two (10.5%) respondents who no longer used kratom rated its efficacy as less than “somewhat” helpful. The survey was not structured to assess which specific substance (e.g., opioids or alcohol or other) the respondents were experiencing withdrawal from.

3.5. Kratom safety and tolerability

More than half of all respondents (n = 1939; 64.1%) had never spoken to a healthcare provider about their kratom use. 392 (13.0%) respondents reported having ever experienced a “bad reaction” while

using kratom. Bad reactions were more frequently reported by respondents who used kratom in the past (n = 31; 19.8%) than currently (n = 361; 12.6%), [$\chi^2(1) = 6.75, p = 0.0094$]. See Table 3 for reported bad reactions.

Of all respondents who had ever used kratom, eight (0.3%) sought medical attention for a bad reaction: five were told to stop taking kratom, three were told to take another medication, and one was admitted to the hospital. Of the respondents who had stopped using kratom (n = 157), 12 (7.6%) said they stopped using kratom because of a bad reaction, and 13 (8.3%) stopped using kratom because they did not like the way it made them feel. More common reasons given for stopping kratom use were not safety-related and included that it was not needed anymore (n = 49; 31.2%), it was too expensive (n = 25; 15.9%), and it was no longer available (n = 20; 12.7%).

Table 2
Reasons for kratom use.

	Number; % of respondents			
	All reasons ^a for use among those endorsing...		Main reason for use among those endorsing...	
	Current kratom use (N = 2,867)	Past kratom use (N = 157)	Current kratom use (N = 2,867)	Past kratom use (N = 157)
To relieve pain	2,344; 81.8%	109; 69.4%	1,388; 48.4%	63; 40.1%
Anxiety or depression	1,903; 66.4%	82; 52.2%	579; 20.2%	23; 14.6%
To increase focus or energy	1,569; 54.7%	55; 35.0%	292; 10.2%	8; 5.1%
Cut down or quit using prescription pain medication	1,054; 36.8%	49; 31.2%	160; 5.6%	14; 8.9%
Insomnia	808; 28.2%	29; 18.5%	28; 1.0%	3; 1.9%
To cut down or quit using OTC pain medicine	792; 27.6%	20; 12.7%	16; 0.6%	1; 0.6%
To cut down or quit using alcohol	517; 18.0%	18; 11.5%	64; 2.2%	0; 0.0%
Recreational use (e.g., to get high)	475; 16.6%	33; 21.0%	70; 2.4%	11; 7.0%
To relieve withdrawal symptoms	416; 14.5%	43; 27.4% ^b	62; 2.2%	21; 13.4%
PTSD	442; 15.4%	13; 8.3%	48; 1.7%	1; 0.6%
To cut down or quit using illicit or illegal drugs	346; 12.1%	15; 9.5%	55; 1.9%	3; 1.9%
To cut down or quit using tobacco	154; 5.4%	4; 2.6%	2; 0.1%	0; 0.0%
Control blood sugar	129; 4.5%	1; 0.6%	6; 0.2%	0; 0.0%
Curiosity	80; 2.8%	18; 11.5% ^b	3; 0.1%	6; 3.8%
Other	179; 6.2%	3; 1.9%	94; 3.3%	3; 1.9%

^a Percentages sum to over 100 because respondents were able to select multiple options.

^b Indicates a significant difference between those reporting current and past kratom use, χ^2 , $p < .0001$.

Table 3
Reported bad reactions to kratom.

	Number; % of respondents		
	All respondents (N = 3024)	Those reporting...	
		Current kratom use (N = 2867)	Past kratom use only (N = 157)
Those reporting at least 1 bad reaction	392; 13.0%	361; 12.6%	31; 19.7%
Stomach problems (nausea, diarrhea, vomiting, upset stomach)	301; 76.8%	282; 78.1%	19; 61.3%
Constipation	143; 36.5%	134; 37.1%	9; 29.0%
Heart palpitations	34; 8.7%	30; 8.3%	4; 12.9%
Shortness of breath	17; 4.3%	14; 3.9%	3; 9.7%
Dizziness	142; 36.2%	133; 36.8%	9; 29.0%
Drowsiness	69; 17.6%	67; 18.6%	2; 6.5%
Fainting	7; 1.8%	6; 1.7%	1; 3.2%
Irritability or irritation	77; 19.6%	74; 20.5%	3; 9.7%
High blood pressure	11; 2.8%	10; 2.8%	1; 3.2%
Headaches	76; 19.4%	70; 19.4%	6; 19.4%
Body aches	13; 3.3%	11; 3.0%	2; 6.5%
Fever	11; 2.8%	8; 2.2%	3; 9.7%
Hallucinations	3; 0.8%	2; 0.6%	1; 3.2%
Weight gain or weight loss	18; 4.6%	16; 4.4%	2; 6.5%
Hair loss	9; 2.3%	9; 2.5%	0; 0.0%
Rash	8; 2.0%	4; 1.1%	4; 12.9%
Other	55; 14.0%	50; 13.9%	5; 16.1%

3.6. What respondents would do if kratom were no longer legally available

If no longer able to get kratom legally, respondents currently using kratom stated they were most likely to get it where it was legally available ($n = 1043$; 36.4%), try to get it illegally ($n = 764$; 26.7%), or replace it with something else ($n = 687$; 24.0%). Among those respondents who would replace kratom with something else, many reported that they would turn to prescription ($n = 463$; 67.4%) and/or illegal ($n = 220$; 32.0%) drugs. Only 5.1% ($n = 145$) said they would stop using kratom and not replace it with anything else if it were no longer legally available.

4. Conclusions

The findings from this survey indicate that many individuals are taking kratom for conditions that often involve the prescribing of or self-medication with opioids (i.e., pain, withdrawal relief). Survey respondents overwhelmingly reported that kratom was helpful for these conditions and that bad effects from kratom, including those leading them to seek medical care, were uncommon.

Opioids are frequently prescribed for both acute and chronic pain, and while some people benefit from opioid therapy, there are others who may be better treated with alternatives to opioids (Dowell et al., 2016; US Department of Health and Human Services, 2018). Given the scope and severity of the opioid epidemic, in which an estimated six million people may currently meet diagnostic criteria for an OUD (Charumilind et al., 2018) and opioid-related deaths are approaching 50,000 annually (Centers for Disease Control and Prevention, 2018), there is significant impetus to encourage patients with pain to try non-opioid treatments (even those without fully validated efficacy [e.g., acupuncture]) in hopes of reducing or eliminating their use of opioids (Dowell et al., 2016). Results of this survey and others (Grundmann, 2017) suggest that kratom may be a useful alternative to opioids for some persons with pain, and this would be consistent with what is known about kratom pharmacology (Kruegel et al., 2016; Raffa et al., 2018; Takayama et al., 2002).

Similarly, for persons with OUDs attempting to reduce or eliminate their opioid use, kratom may serve as a useful aid in managing opioid withdrawal symptoms. FDA-approved, medication-assisted treatments for OUD (i.e., buprenorphine, methadone, and naltrexone) are highly efficacious, but there are significant barriers preventing its utilization. Some of these barriers include high cost, lack of coverage by insurance, stigma, and lack of access to nearby providers (particularly in rural areas) (Knudsen et al., 2011). For some respondents to this survey, kratom was used to reduce or eliminate their use of prescription opioids and/or heroin and to relieve their withdrawal symptoms, suggesting that kratom may be able to help some fraction of the large number people with OUD who are not receiving adequate treatment. While this survey did not specifically assess whether respondents were using kratom as a direct substitute for opioids, the finding that respondents using kratom currently were less likely to have used opioid medications in the past week and month than persons who reported past kratom use only (though lifetime use of opioids was similar across both groups) was

compelling and suggestive that substitution of kratom for opioids may be occurring.

The survey did not address whether respondents experienced any physical dependence or craving as a result of kratom use, but it appears likely that chronic kratom use is associated with physical dependence and withdrawal, albeit both are reportedly milder and more readily self-managed compared to opioid dependence and withdrawal (Singh et al., 2014, 2016; 2018). Furthermore, kratom use and dependence reportedly do not interfere with social, family, and occupational functioning (Singh et al., 2014, 2016; Swogger and Walsh, 2018; Vicknasingam et al., 2010) to the extent that conventional opioids do. The foregoing observations along with the apparent lower abuse potential of kratom and its primary active alkaloid, mitragynine, (Harun et al., 2015; Hemby et al., 2018) suggest that kratom, mitragynine, and/or mitragynine analogs should be evaluated as potential medications for treating pain and OUD (Grundmann et al., 2018; Hemby et al., 2018; Henningfield et al., 2018b; Varadi et al., 2016; Yue et al., 2018).

This survey provided insights related to kratom safety and tolerability. In contrast to the well-documented and serious risks associated with opioids (Baldini et al., 2012; Benyamin et al., 2008), respondents reported kratom effects as relatively minor, with few requiring medical attention. The rates and severity of “bad reactions” were generally similar to those reported previously (Grundmann, 2017), occurring in approximately 13% of respondents. Although severity and relatedness of the bad reactions to kratom were not assessed, only 0.8% of respondents stopped using kratom because of a bad reaction or because they didn’t like the way it made them feel. These survey findings are consistent with the known pharmacology and toxicology of kratom and its alkaloids and with observational evidence from Southeast Asia where kratom use is widespread (Assanangkornchai et al., 2007; Singh et al., 2017).

Available evidence suggests that serious adverse effects associated with kratom use are rare, and there are no well-documented cases of overdose deaths solely attributable to kratom (Babin, 2018). The absence of documented deaths caused by kratom alone does not mean that kratom has not contributed to or caused a death or that its use is without risk; however, contrary to the FDA reports and statements (Gottlieb, 2017, 2018), there is not yet reliable evidence that kratom poses the same level of risk as opioids such as morphine (Henningfield et al., 2018b).

The findings of this study support other studies (Grundmann, 2017; Swogger and Walsh, 2018) and expert analyses (Henningfield et al., 2018a, b; c) and suggest that it may be in the interest of public health to ensure continued access to kratom while FDA works to implement appropriate regulatory standards, oversight, and communications to minimize unintended consequences. Moreover, results from the present survey indicate that a ban on licit kratom (via its placement in Schedule I, which is being considered by FDA (Food and Drug Administration, 2017; US Drug Enforcement Administration, 2016a)) may pose public health risks, including renewed/increased use of opioids by persons who had successfully eliminated or cut down their use. A ban on licit kratom could also lead to the emergence of an illicit market for kratom. Whereas an FDA-regulated market could reassure consumers that lawful kratom products are what they claim to be and are not adulterated with fentanyl, excessive levels of alkaloids, and/or other substances, kratom obtained on an illicit market would have no such safeguards. Schedule I placement of kratom would also impose significant barriers to future research on kratom, including important pharmacological and toxicological testing and potential development of novel medicines based on kratom constituents and analogs.

Kratom cannot be endorsed as an evidence-based safe and effective treatment for pain, OUD, or any other medical condition as it has not yet been evaluated in appropriate clinical trials or approved for therapeutic use by the FDA or, to our knowledge, any national drug regulatory agency. However, results from this and other surveys, which indicate that kratom is successfully used by many people to manage

their pain, OUD, and to substitute for opioids, strongly suggest that further scientific investigation of kratom is warranted. While the survey did measure self-reported use of kratom products, it could not assess purity or potency of the various kratom products used. There are well-documented cases of contaminated kratom products causing serious adverse effects (Food and Drug Administration, 2018b; Scott et al., 2014). The concentrations of active alkaloids in each product may also significantly contribute to efficacy (or lack thereof). This survey, as well as others, relied on convenience samples of those who use or have used kratom, and thus may have included individuals who were more likely to find kratom useful and tolerable than the general population. This limitation underscores the need for expanded surveillance and epidemiologic efforts to better understand patterns and reasons for use, as well as risks and benefits of kratom use. Such research could also help guide regulatory efforts and provide better information on the nature and extent of potential consequences of banning or restricting kratom.

A nationally representative assessment is needed to assess the prevalence of kratom use, including geographic and demographic differences in prevalence, as well as to estimate perceived effectiveness of kratom for managing pain, OUD, withdrawal, and supporting opioid abstinence and the nature and severity of side effects. In addition, it would be important to understand whether the perceived effectiveness of kratom varies by the level of opioid use (e.g., daily intake) and/or by type of opioid used (drug or route), or type or severity of pain. Inclusion of psychometric scales to assess OUD and pain severity would allow for better description of kratom and its efficacy for these conditions. Further information is needed on whether perceived effectiveness of kratom for managing various conditions varies by type of kratom product used, route of use, or frequency/amount of use. It would also be informative for future surveys to query the frequency of use of other substances (alcohol; illicit, prescription, and over-the-counter drugs) along with kratom and if co-use patterns predict specific safety of efficacy outcomes.

Role of the funding source

The American Kratom Association provided financial support for the conduct and analysis of the survey on which this manuscript is based. The American Kratom Association had no role in the study design, data collection or analysis, interpretation of the results, writing of the report, or decision to submit the article for publication.

Contributors

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us. Individual author contributions are: Marion A. Coe, PhD: analysis and interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content; Janine L. Pillitteri, PhD: conception and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content; Mark A. Sembower, MS: statistical analysis; Karen K. Gerlach, MPH, PhD: conception and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content; Jack E. Henningfield, PhD: conception and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content.

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