

HHS Public Access

Author manuscript

Drug Alcohol Depend. Author manuscript; available in PMC 2022 September 01.

Published in final edited form as:

Drug Alcohol Depend. 2021 September 01; 226: 108879. doi:10.1016/j.drugalcdep.2021.108879.

Therapeutic benefit with caveats?: Analyzing social media data to understand the complexities of kratom use

Kirsten E. Smith^{1,*}, Jeffrey M. Rogers¹, Destiny Schriefer¹, Oliver Grundmann²

¹National Institute on Drug Abuse Intramural Research Program, 251 Bayview Blvd. Baltimore, Maryland 21224, USA

²College of Pharmacy, Department of Medicinal Chemistry, University of Florida, FL, 32610, U S A

Abstract

Background: *Mitragyna speciosa*, referred to as "kratom", is increasingly used in the United States for self-treating pain, psychiatric, and substance use disorder symptoms. It is used by some to attenuate opioid withdrawal and as a longer-term drug substitute. Most self-report data have come from online surveys, small in-person surveys, and case reports. These may not be representative of the broader kratom-using population.

Purpose: Analyze user-generated social media posts to determine if independent, descriptive accounts are generally consistent with prior U.S. kratom survey findings and gain a more nuanced understanding of kratom use patterns.

Methods: Reddit posts mentioning kratom from 42 subreddits between June 2019-July 2020 were coded by two independent raters.

Findings: Relevant posts (number of comments, upvotes, and downvotes) from 1,274 posts comprised the final sample (n=280). Of the 1,521 codes applied, 1,273 (83.69%) were concordant. Desirable kratom effects were described among a majority, but so too were adverse effects. Reports of kratom as acute self-treatment for opioid withdrawal were more prominent compared to longer-term opioid substitution. Quantitative analysis found higher kratom doses associated (p<.001) with greater odds of reported kratom addiction (OR=3.56) or withdrawal (OR=5.88), with slightly lower odds of desirable effects (OR=0.53, p=.014). Despite perceived therapeutic

Conflict of Interest

The authors have no conflicts of interest to disclose.

Corresponding author: National Institute on Drug Abuse, Intramural Research Program, Translational Addiction Medicine Branch, 251 Bayview Blvd. Suite 200, Room 01B340, Baltimore, Maryland, 21224, USA, kirsten.smith@nih.gov. Contributors

All authors developed the manuscript concept based off of a parent study designed by OG. JR and DR coded data and conducted data analysis, with the analysis plan developed by all authors, including KS and OG. KS drafted most of the initial manuscript; JR managed data and drafted the Methods section. All authors provided critical feedback, additions, and edits. All authors approved this version of the manuscript for submission.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

benefits, kratom was characterized by some in terms of addiction that, in some cases, appeared dose-dependent. Polydrug use was also prominently discussed.

Conclusions: Results validated many prior survey findings while illustrating complexities of kratom use that are not being fully captured and require continued investigation.

Keywords

kratom; opioids; harm-reduction; polydrug use; kratom withdrawal

1.0 Introduction

Mitragyna speciosa (referred to as kratom) is a plant indigenous to Southeast Asia (SEA). Its leaves produce approximately 40 pharmacologically active alkaloids, several of which are responsible for kratom's analgesic, stimulatory, and anxiolytic effects (Kruegel & Grundmann, 2018; Kruegel et al., 2019; Todd et al., 2020). Its two most studied constituents, mitragynine (MG) and 7-hydroxymitragynine (7-HMG), act as partial agonists at mu opioid receptors (Obeng et al., 2020; Todd, et al., 2020). These actions are atypical, seemingly "biased", in that they show selectivity for the G-protein signaling pathway, rather than the β-arrestin pathway, indicating that kratom, may produce therapeutic analgesia, but with potentially fewer adverse effects than traditional opioids (Basiliere & Kerrigan, 2020; Behnood-Rod et al., 2020; Henningfield, Fant, & Wang, 2018; Henningfield et al., 2019; Singh, et al., 2018; Singh, et al., 2019; Todd, et al., 2020; Vicknasingam et al., 2020). Kratom's pharmacology also indicates additional non-opioid mechanisms of action (Hiranita et al., 2019).

Kratom has been used in SEA for over a century (Brown et al., 2017; Jansen & Prast, 1988; Singh, et al., 2016; Suwanlert, 1975). Self-reported reasons for use in SEA include medicinal, recreational, and mood and energy improving properties (Singh et al., 2019; Singh et al., 2017; Veltri & Grundmann, 2019). Kratom has also been used in SEA to self-treat opium, heroin, amphetamine, and alcohol misuse (Singh et al., 2020; Singh et al., 2021; Vicknasingam, et al., 2010). In the U.S., kratom has been reported as being used to self-treat chronic pain, psychiatric (e.g., mood, anxiety, attention deficit, post-traumatic stress disorder), fatigue, and substance use disorder (SUDs) symptoms and to mitigate opioid withdrawal (Bath et al., 2020; Boyer et al., 2008; Coe, et al., 2019; Garcia-Romeu, et al., 2020; Grundmann, 2017; Smith & Lawson, 2017). A substantial subpopulation of U.S. adults report using kratom to attenuate opioid withdrawal, as a substitute for prescription or illicit opioids, and possibly (though not verified) to address alcohol or stimulant misuse (Assanangkornchai, et al., 2007; Coe, et al., 2019; Garcia-Romeu, et al., 2020; Saref, et al., 2019; Singh, et al., 2015; Singh et al., 2021; Smid, et al., 2018; Smith & Lawson, 2017; Swogger, et al., 2015; Swogger & Walsh, 2018; Tanguay, 2011; Vicknasingam, et al., 2010). Kratom is typically consumed either as a tea or beverage or as plant matter ground into powder that is prepared as capsules or consumed in tablespoons (Eastlack, et al., 2020; Garcia-Romeu, et al., 2020; Leong Bin Abdullah et al., 2020; Saingam et al., 2013; Singh et al., 2013, 2018, 2019).

Prevalence of U.S. kratom use is estimated at 5-15 million, although there is no scientific consensus. The 2019 National Survey on Drug Use and Health (NSDUH) estimated that 0.3% (825,000) of people aged 12 or older had used kratom within the past month, however, this may be an underestimate due to the fact that homeless and incarcerated persons were not sampled (both populations have high rates of chronic pain and SUDs, making them potentially more likely to have used kratom) and NSDUH kratom survey item wording, which excluded some kratom product types (Substance Abuse and Mental Health Services Administration, 2020). Data collected between 2018-2019 as part of the cross-sectional Survey of Non-Medical Use of Prescription Drugs estimated lifetime kratom use prevalence among a self-selected sample (59,714) of U.S. adults at 1.3% (2,031,803) and past-year use at 0.8%, extrapolating from 490 respondents who endorsed lifetime use (Schimmel et al., 2021). These two-year old data may not reflect present rates of use. Indeed, these estimates are partially offset by indirect indicators of more widespread use, including kratom industry growth, increased kratom advocacy, and upticks in kratom-related calls to poison control centers or polydrug exposures associated with kratom (Cinosi et al., 2015; Olsen et al., 2019; Post et al., 2019). Among smaller samples of substance-using adults, lifetime kratom use rates ranged from approximately 13-20% (Smith & Lawson, 2017; Smith et al., forthcoming).

Because some using kratom have a history of opioid-use disorder (OUD) and are using for withdrawal-mitigation or opioid substitution, (among other reasons), it is important to better understand such "self-treatment" (Assanangkornchai et al., 2007; Coe et al., 2019; Garcia-Romeu et al., 2020; Saref et al., 2019; Singh et al., 2015; Smid et al., 2018; Swogger et al., 2015; Swogger & Walsh, 2018; Tanguay, 2011; Vicknasingam et al., 2010). No U.S.-based controlled clinical studies investigating kratom's safety, tolerability, or effects in humans exist. Preclinical research continues to demonstrate kratom's effects and potential to substitute for full opioid agonists (Hassan et al., 2013; Hemby et al., 2019; Ismail et al., 2017; Kamble et al., 2021; Maxwell et al., 2020; Obeng, et al., 2020; Yue, Kopajtic, & Katz, 2018). This complements self-report among users. However, direct comparisons between preclinical work and self-report are complicated, as people use kratom orally in several forms (Garcia-Romeu, et al., 2020; Grundmann, 2017; Singh et al., 2016, 2018a, 2019).

Another complication is that most U.S. self-report data have been obtained from large surveys which typically include regular/current users self-selecting into kratom-specific studies. These samples represent a large portion of the kratom-using population, but are not fully representative, or may be biased towards people with highly favorable attitudes about kratom. People who may have only used kratom once, or used but subsequently quit, may not be captured. Likewise, people potentially *mi*susing kratom may not be participating. Thus, in the U.S. context, we have an increasingly clear, but still limited, picture of kratom use, making it important to examine all available data sources. Despite ubiquity of social media, only one study (Swogger et al., 2015), has examined kratom experiences using social media (Erowid) text. Since then, kratom use and online discussion of kratom have proliferated, making publicly available text a relevant, timely source for feasible collection of descriptive data.

1.1. Aims

The aim of this study was to evaluate posts made on the popular social media platform, Reddit. This was done to determine if these independent descriptive accounts were consistent with common kratom survey questions and prior findings, which are presently the best, but still limited, source of self-reported kratom use data in the U.S, and to add more nuanced self-report data to the kratom literature than exists among current and (possibly) former, users. By identifying and coding text across widely-viewed, user-generated Reddit posts, a more comprehensive understanding of kratom use can be advanced to help inform future work. This text analysis was not intended as an in-depth qualitative study. Rather, it aimed to tap a highly relevant but underutilized data source to provide additional insight into kratom use among adults on social media and add more detailed self-report information that may help develop or refine new survey or qualitative interview questions. We and our collaborators are actively working to advance our understanding of kratom by using these and other methods. Formative findings reported here constitute one of our multiple starting points.

2.0. Methods

2.1. Data collection

We collected post data from Reddit, a self-organizing social aggregation website where registered members create and engage with topic-based communities and subcommunities (i.e., subreddits). Text and other content is posted such that members can promote content they find helpful or interesting. Reddit data have been examined in other studies pertaining to a wide range of topics (Brett et al., 2019; Bunting et al., 2019; Chanderasekharan et al., 2018; Sowles et al., 2018; Vosburg et al., 2021). We used the R package {RedditExtractoR}, which utilizes Reddit's application programming interface (API) to extract post text, comment text, and metadata utilizing search terms within subreddit communities, or for all subreddits. We selected Reddit data for analyses not only because it provides rich, unfiltered data, but also partially because other platforms with long-form posts (e.g., Facebook) impose data collection barriers (e.g., restricted API access; privacy restrictions). Reddit data are accessible, contextualized, and can provide insights into substance use experiences. Reddit does not require researchers to register an account, purchase access to API tokens, nor obtain consent from individuals, as Reddit data are primarily anonymous and publicly available. Indeed, Reddit provides not only a source of available text data to examine, but a unique level of protection to persons posting, in that Reddit usernames are seldom connected with personally identifiable information (PII) and typically only when the person posting shares it, making reverse-identification difficult or impossible in most circumstances, unlike other social media data (e.g. Twitter, Facebook) (Ayers et al., 2018; Kilgo et al., 2018).

Because Reddit has not recently released platform source code, we were unable to leverage traditional scientific database search strategies when collecting post data. Reddit's search function is designed to display relevant content and may rely on built correlations between related words, displaying posts and subreddit communities based on correlation strength, post recency, proportion of upvotes, number of upvotes, number of comments, and other metadata. Utilizing common misspellings of "kratom" yielded fewer but identical post

content than using only "kratom". Page limits appeared to throttle number of obtainable posts when searching the entire Reddit front page. Accordingly, we conducted a preliminary search to determine which subreddits contained a high frequency of posts mentioning kratom. After identifying the top 30 kratom-relevant subreddits, we conducted individual searches and collected all posts explicitly mentioning "kratom" made between June 2019-July 2020. We selected this time frame as it coincided with data collection for a separate survey study. From this search we found 5 kratom-specific subreddits and 13 subreddits dedicated to substance use broadly. Next, we conducted a general Reddit-wide search for posts containing "kratom" to include posts that may have been omitted when searching individual subreddits. This resulted in a sample of 1,274 unique posts across 42 subreddits. Next, we truncated posts to 280 by sampling the most relevant 20 unique posts from each month within our specified timeframe. Relevance was determined by examining the Reddit community interaction with the post based on three specific criteria: number of comments, upvotes, and downvotes. Per NIH IRB policy for public data without associated PII, this study was exempt from the IRB review.

2.2. Generation of codebook and text analysis

Ten codes were generated *a priori* from what we expected to encounter based on prior findings. We did this, in part, by reverse engineering questions from other surveys we (O.G., K.S.) and others have developed into a guide for analyzing Reddit text. Two additional *a priori* codes were generated based on prior direct clinical contact with kratom-using adults and analysis of social media data pertaining to kratom use during Covid-19 (Grundmann et al., submitted) and of Reddit text pertaining to tianeptine, which was often co-used with kratom (Smith et al., 2021). Accordingly, we were confident that our 12 *a priori* codes could be applied to Reddit data and serve as a foundation for initial coding.

Upon first inspection of the sample of 280 posts, group consensus resulted in finalization of the codebook with 12 primary a priori codes with 9 additional subcodes (presented in Table 1). This initial pass reaffirmed the presence of what we anticipated finding based on prior work and helped us develop subcodes. This codebook was subsequently used for coding by two independent raters (J.R. and D.S.). Only the unique initial posts that we identified were coded (not post comments). Had our initial pass through the post sample found posts pertaining to novel or unexpected kratom-related topics that were reoccurring within the text, those would have been incorporated into the codebook as additional codes/subcodes, supplementing our initial 12 a priori codes and 9 subcodes. Raters could apply codes to any text segment in order to calculate proportion of rater agreement. Thus, no text that raters believed corresponded to a code was left uncoded; only posts deemed unassociated with any code were left uncoded. Multiple, different codes could be contained in the same post (requiring application of more than one code within a post). Thus posts, and text within a single post, could have more than one code. Although the codebook was developed in advance and refined via conference, the coding process was still open to et vade coding and documentation of unexpected or inconsistent findings that did not fall into a code/subcode. Raters were instructed to highlight any novel or unexpected text identified during coding to discuss further. Raters independently coded posts using MAXQDA 2020 (VERBI Software, Berlin).

As total percent agreement was substantial (see Results) and no discordance for any code applied was less than a majority, we did not conference and subsequently *re-code* text to achieve a higher agreement rate. This is partially for transparency's sake and because we were not seeking to preform iterative coding and sampling for theory-building. Additionally, the percent agreement, whether low or high, shows the complexity of how people wrote posts and described kratom-related experiences. In other words, if two independent raters did not have 100% agreement, or potentially low agreement in one area, that could itself be an important finding ¹.

2.3. Quantitative analyses

A subset of posts (n=62) identified as containing reported daily doses were examined in relation to other codes treated as outcome variables. These codes included "professed kratom addiction" and "desirable kratom effects" which we suspected would be dosedependent. For instance, perceived kratom addiction may potentially be associated with higher daily doses, whereas perceived desirable effects from kratom, similar to other substances, may be best achieved by low or moderate doses. The dose-effect relationships were assessed using binomial logistic regression with dose coded as gm/day and log-transformed to refine distributional properties and interpretation. These analyses were conducted using R.

3.0. Results

Table 1 displays codes, interrater agreement rate(s) (IRR), versus disagreements, and agreement percent. A total of 1,521 unique codes were applied. Of these, 1,273 were concordant and 248 were discordant, with an IRR of 83.69% (range=57.15%--95.24%). Corrected kappa for IRR was 0.83, indicating substantial agreement, uring coding, interesting points of discussion related to kratom which emerged, but which were not reflected in the codebook, were documented for group consideration. However, these occurred at such low rates so as not to constitute a reoccurring kratom-related topic that would warrant adding it as an additional code, though we have quantified them here for potential future exploration (e.g., strategies for avoiding kratom bitterness when consuming crushed leaf or powder, n=9/280; meta commentary on the style Reddit posters tend to discuss kratom, n=14/280, negative experiences discussing kratom use with healthcare provider, n=5/280; discussion of thoughts or events unrelated to kratom, n=12/280; thus, 0 codes were applied to 40 posts). Codes applied to a given post out of the total of 280 ranged from 0-12. Unique Reddit usernames were associated with 273 of the 280 posts.

Ultimately, posts made during this one-year period contribute to a complex narrative of kratom. Partially reflecting this complexity is that the two most prominent codes applied corresponded to professed kratom addiction (n=183/280) and desirable kratom effects (n=169/280). Findings largely fell across *desirable*, therapeutic kratom effects and *unwanted* effects that, for some, involved discontinuation of use. Details of dosing and contemporaneous use were also prominent across posts.

¹All raw text data are available upon request.

3.1. Perceived desirable and therapeutic kratom effects

Kratom was discussed as being used to self-treat pain symptoms (n=58/280) or psychiatric conditions (n=58/280). Specific mentions for the latter included self-treatment for depressive (n=32/280) and anxiety (n=35/280) symptoms. A prominent reported benefit from kratom pertained to self-treating SUD or drug dependence (n=133/280); captured in greater depth in in Table 2, column 1 (presented as direct quotes). This included frequent mentions of kratom use to mitigate opioid (n=103/280) or other drug withdrawal (n=17/280; e.g., alcohol). Kratom's continued use as longer-term opioid substitute was mentioned less often (n=38/280) than shorter-term attenuation of withdrawal, though was described in striking detail (Table 2, column 2). Overall, desirable effects were wide-ranging, and included mood enhancement, increased energy, cognitive alertness, analgesia, and relaxation. These appear in Table 3. Number of codes pertaining to kratom's regulatory status (n=30/280) were fewer than expected given that many Reddit users reside in the U.S., where kratom's regulatory and legal status is provisional and varied.

3.2. Unwanted effects, polydrug use, and kratom use discontinuation

Despite perceived benefits of kratom use for many, people also described unwanted or adverse effects (n=79/280), such as GI upset, fatigue, memory lapses, irritability, and restlessness (see Table 3). As noted above, a prominent finding included reported kratom addiction (n=183/280). This phenomenon was evidenced both directly and indirectly as shown by quotes in Table 2, column 3. In particular, specific descriptions of kratom withdrawal (n=86/280) and kratom tolerance (n=41/280) were found. Descriptions portrayed tolerance typically developing slowly, with some exceptions. Withdrawal descriptions were wide-ranging, although effects were typically described as mild-moderate. For a minority, kratom withdrawal was described as severe (see Table 2, column 3).

Other drug use, including polydrug use, was commonly reported (n=155/280). These included concomitant use of kratom with another substance or use which was contemporaneous based on described context. Drugs from distinct classes frequently co-used with or mentioned in relation to kratom appear in Table 4. These included stimulants (n=103/280), opioids (n=91/280), benzodiazepines (55/280), cannabinoids (42/280), hallucinogens/psychedelics (61/280), and "nootropics" (n=28/280). Specific drug names appear in Table S1, and in raw text form, in Table S2 (see supplementary materials). Unwanted kratom effects were partially reflected by posts describing a desire to quit using kratom (n=43/280) or active and/or successful quit attempts (n=53/280).

3.3. Kratom dosing

Dosing ranges were frequently mentioned (n=137/280). However, specific doses that occurred within a 24-hour period could only be established for 62/280 posts. These ranged from 1.0 to 100.0 grams (mean=17.9, SD=21.6; transformed mean=2.26, SD=1.13). Higher doses were associated with greater odds of professed kratom addiction OR=3.56 [1.84,6.87], p<.001), greater odds of kratom withdrawal OR=5.88 [2.42,14.29], p<.001) and slightly lower odds of desirable kratom effects OR=0.53 [0.32,0.88], p=.014). See supplementary material for full model fit measures and coefficients. Doses were also discussed in-text as escalating (n=42/280) or being titrated over time (n=22/280).

4.0 Discussion

This study examined Reddit posts made between June 2019-July 2020 in order to determine if independent descriptive accounts were generally consistent with prior survey findings. As discussed more below, these Reddit data both converge and diverge from previously reported survey findings. Overall, the most relevant kratom posts from the subreddits sampled were consonant with prior survey findings and items, partially supporting the use of such items. This is evidenced by the fact that no a priori code was unapplied. It is also evidenced via the direct quotes provided in Table 2 which provide rich personal perspectives related to many prior survey work (e.g., kratom used to mitigate opioid withdrawal). Data examined here suggest experiences with kratom vary widely. For instance, people during different stages of use conceptualized and discussed kratom in more or less positive regard with respect to effects. This is indicated by conflicting accounts of optimal doses and attitudes towards kratom on top subreddits. Many prospective kratom users expressed positive and hopeful sentiments about kratom, while current and former users expressed conflicting opinions about kratom's short- or long-term therapeutic potential when balanced against adverse effects and addictive properties.

4.1. Similarities between Reddit posts and U.S. survey data

Our findings overlap with some findings from large online surveys and smaller focused surveys of kratom-using adults in the U.S. with respect to motivations for use and desirable effects (Garcia Romeu et al., 2020; Grundmann; Coe et al., 2019). These include selftreatment for pain, psychiatric, or SUD symptoms. It is noteworthy that these are found across large U.S. surveys and convenience samples in SEA (Bath et al., 2020; Boyer et al., 2008; Coe, et al., 2019; Garcia-Romeu, et al., 2020; Grundmann, 2017; Singh et al., 2019; Singh et al., 2017; Smith & Lawson, 2017; Veltri & Grundmann, 2019), but also here, meaning that Reddit posts made independently and without the possibility of certain (but not all possible) biases help validate prior work. Thus, preliminary evidence about kratom use motivations is converging to indicate that use initiation and continued use occurs for primarily pragmatic forms of self-treatment or drug substitution, rather than primarily hedonic or recreational reasons (Grundmann, 2017; Prevete et al., 2021; Smith & Lawson, 2017). Here and elsewhere, using kratom for "euphoria" or expressing preference for kratom compared to other drugs to achieve a recreational "high" is not absent, but does not appear to be a primary driving factor or widespread when looking at the preponderance of findings (Coe et al., 2019; Prevete et al., 2021; Smith & Lawson, 2017; Singh et al., 2021; Swogger et al., 2015).

4.2. Attenuating opioid withdrawal symptoms or self-treating SUD as primary motive for use

Among the most relevant kratom subreddits, none described motivations for high-risk misuse (e.g., intravenous use). Although it is likely that some people had primary motivations for use other than self-treatment, these could not be easily discerned. Still, one of the greatest distinctions between these findings and those from U.S. surveys is the degree of self-reported polydrug use that included kratom and at least one other licit or illicit substance, which warrants further study.

Perhaps the greatest point of divergence of these findings from those of U.S surveys is that a majority of people posting on kratom subreddits attributed primary reasons for use as a self-treatment of opioid withdrawal or illicit drug substitution more frequently than other motivations. Although many kratom-using adults express multiple motivations for use, survey findings largely indicate greater self-treatment for physical health conditions, pain, psychiatric symptoms, mood improvement, or *licit* opioid supplementation or substitution (Bath et al. 2020; Grundmann et al., 2017). In this sample, these were represented, but at lower rates, appearing similar to findings from Smith & Lawson (2017) which surveyed treatment-enrolled adults with illicit polydrug use history. Here, many people reported using kratom for both licit *and* illicit opioid withdrawal and self-treatment, rather than primarily medically prescribed opioids. These specific findings, somewhat contrasting those of large online surveys, could be due to our examining unsolicited self-report data about kratom from a population that included prospective, active, and remitted users which may be more difficult to reach, and which have been less explored than active, regular users who may be using for ongoing health conditions and more likely to self-select into kratom survey studies.

Kratom was consistently conceptualized as an opioid and sometimes associated with adverse effects similar to those derived from traditional opioids (e.g., GI upset, fatigue, memory impairment), albeit with less perceived or actual acute risk (e.g., likelihood of overdose). Kratom was also characterized as having the capacity to substitute for prescription opioids and heroin, which converges with preclinical work and self-report (Ahmad & Aziz, 2012; Hassan et al., 2013; Hemby et al., 2019; Ismail et al., 2017; Kamble et al., 2021; Maxwell et al., 2020; Obeng, et al., 2020; Singh et al., 2015, 2018a, 2018c; Vicknasingam et al., 2020; Wilson et al., 2021; Yue, Kopajtic, & Katz, 2018). For some, there were clearly enduring therapeutic benefits from "self-treating" with kratom that people believed achieved their desired result, including abstinence.

4.3. Adverse effects, tolerance, withdrawal, and perceived addiction

From the limited dosing data analyzed, positive effects appeared to be mediated by dose, with more beneficial effects at low to moderate doses. Still, in the context of dosing, many reported developing kratom tolerance and increasing their dose, or dosing frequency, to achieve desired effects previously felt at lower doses. Although adverse effects and withdrawal symptoms characteristic of those derived from traditional opioids have not been reported with the same incidence with respect to kratom in U.S. survey findings (Garcia-Romeu et al., 2020; Grundmann, 2017)-- but have been found among some SEA samples of regular, long-term users-- our findings are differentiated in that we identified specific, kratom-related adverse effects. Many were similar to those expected from traditional opioids (e.g., nausea, vomiting, fatigue), though these primarily ranged from mild to moderate. Specific adverse effects included tolerance, moderate withdrawal, and professed addiction. These are in keeping with limited findings from SEA and U.S. case reports but diverge from U.S. survey findings (Singh et al., 2014; Stanciu et al., 2019; Weiss & Douglas, 2021). DSM-5 use disorder for kratom could not be assessed using Reddit data, but that a majority of posts described aspects of SUD or descriptions of feeling "addicted" to kratom is a departure from one prior U.S. finding which indicated that most regular kratom-using adults sampled did not experience symptoms characteristic of addiction, when using a

modified DSM-5 SUD checklist (Garcia-Romeau et al., 2020). It is important to note that while tolerance and withdrawal are two DSM-5 diagnostic criteria for SUD, they are not necessarily indicative of SUD---meaning that tolerance and withdrawal descriptions cannot be presumed an indicator of misuse. Still, some believed they were addicted and articulated impairments in psychosocial functioning related to use. It is important to not diminish or delegitimize such perceptions, even if conceptualizations of "addiction" among people on Reddit may not correspond to clinical nosology. That some felt that they had a problematic relationship with kratom characteristic of addiction are sentiments that have not been widely documented. Our findings from top kratom subreddits, though limited, suggest that current U.S. kratom literature may be underestimating some adverse effects, specifically potential for developing kratom use disorder. That kratom dependence and withdrawal have been documented in case reports (Stanciu et al., 2019; Weiss & Douglas, 2021), but not on large-scale surveys, means further exploration is warranted, particularly among younger people and people with histories of polydrug use or SUDs.

4.4. Limitations

This study has several limitations. First, data were collected solely from Reddit. By examining Reddit posts, we were able to capture nuanced accounts of kratom from a more diverse group of current, former, and prospective kratom-using adults than previous work permitted. Still, Reddit is a platform that people self-select to engage with, presenting one bias. Indeed, these posts may not be representative of most people's experiences with kratom, or of the broader kratom-using U.S. population, (which may be considered a strength as well as a limitation) and might differ from accounts of kratom from another online source (e.g., chronic pain forum). Posts also did not contain demographic information or location; although it appears that most posts were written by Americans. It is also likely that most people posting were likely younger or male (Bunting et al., 2021; Pew Research Center, 2019; Vosburg et al., 2021). Additionally, posts were examined for only a one-year period. Because kratom products and use continue to evolve, social media data should be examined regularly. In future work, exploring Reddit posts with less community interaction, which failed to meet our criteria for relevance, may be another point for exploration. That people used kratom contemporaneous to or concomitantly with other substances makes scrutinizing reported effects (good or bad) challenging, if not impossible. Information on reported daily dosage could be only gleaned from a limited number of posts, meaning that dose-effect relationships should be interpreted with caution pending further study of doseresponse effects. Quantitative analyses only examined a small number of posts, lowering the overall confidence with which those estimates could be made. Those exploratory findings should be considered a preliminary starting point for larger, more precise investigations.

4.5. Conclusion: It's complicated....

The detailed accounts of people posting on Reddit about kratom analyzed here, while different in some respects from U.S. survey findings, echo a similar takeaway: kratom is a complex and diverse plant and its use among U.S. adults is equally complex and diverse. As kratom pharmacology continues to be explored via preclinical investigations (Hassan et al., 2013; Hemby et al., 2019; Ismail et al., 2017; Kamble et al., 2021; Maxwell et al., 2020; Obeng, et al., 2020; Wilson et al., 2021; Yue, Kopajtic, & Katz, 2018), human studies reliant

on self-report must continue and must become increasingly methodologically refined (e.g., including purposeful sampling and designs beyond cross-sectional). Our findings partially validate large online surveys insofar as survey questions could be used to code kratom Reddit data with high agreement. Our *a priori* codes based largely on prior surveys were found along with related subcodes (e.g., self-treatment for anxiety). The heterogeneity of the broader kratom-using population was refined here.

Ultimately, kratom subreddit posts contained complicated narratives that do not make for simple characterizations. For some, kratom was lifesaving and for others it was ruinous, or yet another substance to which they had become beholden. Like other findings, the (provisional) takeaway is that it is premature to laud kratom as a cure-all and equally premature to demonize it as a dangerous substance with risk that outweighs benefit. At base, this stems from insufficient information, but also from the fact that "kratom" in the U.S. constitutes many different products with variability in alkaloid content, composition, and purity (Fowble & Musah, 2019; Griffin et al., 2016). Findings reinforce the current scientific consensus, which is that kratom is a highly varied psychoactive substance being used in different doses and for different reasons among a diverse group of people that we are only beginning to understand. Areas for focused work include those related to dose, opioid substitution efficacy, dependence, withdrawal, and addiction. In-depth qualitative work, ecological momentary assessment, and longitudinal studies can also help inform the controlled human laboratory studies critically needed to move this area of research forward.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The study team would like to acknowledge the people who posted on Reddit and whose data we analyzed for this study, without them and their voices such work would not be possible.

Role of Funding Source

Support for KS, JR, and DS was provided by NIH NIDA Intramural Research Program

References

- Ahmad K, Aziz Z, 2012. Mitragyna speciosa use in the northern states of Malaysia: A cross-sectional study. J. Ethnopharmacol141, 446–450. 10.1016/j.jep.2012.03.009 [PubMed: 22440259]
- Assanangkornchai S, Muekthong A, Sam-angsri N, Pattanasattayawong U, 2007. The Use of *Mitragynine speciosa* ("Krathom"), an Addictive Plant, in Thailand. Subst. Use Misuse42, 2145–2157. 10.1080/10826080701205869 [PubMed: 18097996]
- Ayers JW, Caputi TL, Nebeker C, Dredze M, 2018. Don't quote me: reverse identification of research participants in social media studies. Npj Digit. Med1, 1–2. 10.1038/s41746-018-0036-2 [PubMed: 31304287]
- Basiliere S, Kerrigan S, 2020. CYP450-Mediated Metabolism of Mitragynine and Investigation of Metabolites in Human Urine. J. Anal Tox44, 301–313. 10.1093/jat/bkz108
- Bath R, Bucholz T, Buros AF, Singh D, Smith KE, Veltri CA, Grundmann O, 2020. Self-reported Health Diagnoses and Demographic Correlates With Kratom Use: Results From an Online Survey. J. Addict. Med14, 244–252. 10.1097/ADM.0000000000000570 [PubMed: 31567595]

Behnood-Rod A, Chellian R, Wilson R, Hiranita T, Sharma A, Leon F, McCurdy CR, McMahon LR, Bruijnzeel AW, 2020. Evaluation of the rewarding effects of mitragynine and 7-hydroxymitragynine in an intracranial self-stimulation procedure in male and female rats. Drug Alcohol Depend. 215, 108235. 10.1016/j.drugalcdep.2020.108235 [PubMed: 32889450]

- Boyer EW, Babu KM, Adkins JE, McCurdy CR, Halpern JH, 2008. Self-treatment of opioid withdrawal using kratom (*Mitragynia speciosa korth*). Addiction. 103, 1048–1050. 10.1111/j.1360-0443.2008.02209.x [PubMed: 18482427]
- Brown PN, Lund JA, Murch SJ, 2017. A botanical, phytochemical and ethnomedicinal review of the genus Mitragyna korth: Implications for products sold as kratom. J. Ethnopharmacol202, 302–325. 10.1016/j.jep.2017.03.020 [PubMed: 28330725]
- Brett EI, Stevens EM, Wagener TL, Leavens EL, Morgan TL, Cotton WD, & Hébert ET 2019. A content analysis of JUUL discussions on social media: Using Reddit to understand patterns and perceptions of JUUL use. Drug Alcohol Depend. 194, 358–362. 10.1016/j.drugalcdep.2018.10.014. [PubMed: 30472576]
- Bunting AM, Frank D, Arshonsky J, Bragg MA, Friedman SR, Krawczyk N, 2021. Socially-supportive norms and mutual aid of people who use opioids: An analysis of Reddit during the initial COVID-19 pandemic. Drug Alcohol Depend. 222, 108672. 10.1016/j.drugalcdep.2021.108672 [PubMed: 33757708]
- Chandrasekharan E, Samory M, Jhaver S, Charvat H, Bruckman A, Lampe C, ... & Gilbert E 2018. The Internet's hidden rules: An empirical study of Reddit norm violations at micro, meso, and macro scales. Proceedings of the ACM on Human-Computer Interaction, 2(CSCW), 1–25. 10.1145/3274301
- Cinosi E, Martinotti G, Simonato P, Singh D, Demetrovics Z, Roman-Urrestarazu A, Bersani FS, Vicknasingam B, Piazzon G, Li J-H, Yu W-J, Kapitány-Fövény M, Farkas J, Di Giannantonio M, Corazza O, 2015. Following "the Roots" of Kratom (*Mitragyna speciosa*): The Evolution of an Enhancer from a Traditional Use to Increase Work and Productivity in Southeast Asia to a Recreational Psychoactive Drug in Western Countries. BioMed Res. Int2015, 1–11. 10.1155/2015/968786
- Coe MA, Pillitteri JL, Sembower MA, Gerlach KK, Henningfield JE, 2019. Kratom as a substitute for opioids: Results from an online survey. Drug Alcohol Depend. 202, 24–32. 10.1016/j.drugalcdep.2019.05.005 [PubMed: 31284119]
- Eastlack SC, Cornett EM, Kaye AD, 2020. Kratom—Pharmacology, Clinical Implications, and Outlook: A Comprehensive Review. Pain Ther. 9, 55–69. 10.1007/s40122-020-00151-x [PubMed: 31994019]
- Fowble KL, Musah RA, 2019. A validated method for the quantification of mitragynine in sixteen commercially available Kratom (Mitragyna speciosa) products. Forens. Sci. Int299, 195–202. 10.1016/j.forsciint.2019.04.009
- Garcia-Romeu A, Cox DJ, Smith KE, Dunn KE, Griffiths RR, 2020. Kratom (Mitragyna speciosa): User demographics, use patterns, and implications for the opioid epidemic. Drug Alcohol Depend. 208, 107849. 10.1016/j.drugalcdep.2020.107849 [PubMed: 32029298]
- Griffin OH, Daniels JA, Gardner EA, 2016. Do You Get What You Paid For? An Examination of Products Advertised as Kratom. J. Psychoactive Drugs48, 330–335. 10.1080/02791072.2016.1229876 [PubMed: 27669103]
- Grundmann O, 2017. Patterns of Kratom use and health impact in the US—Results from an online survey. Drug Alcohol Depend. 176, 63–70. 10.1016/j.drugalcdep.2017.03.007 [PubMed: 28521200]
- Hassan Z, Muzaimi M, Navaratnam V, Yusoff NHM, Suhaimi FW, Vadivelu R, Vicknasingam BK, Amato D, von Hörsten S, Ismail NIW, Jayabalan N, Hazim AI, Mansor SM, Müller CP, 2013. From Kratom to mitragynine and its derivatives: Physiological and behavioural effects related to use, abuse, and addiction. Neurosci. Biobehav. Rev37, 138–151. 10.1016/j.neubiorev.2012.11.012 [PubMed: 23206666]
- Hemby SE, McIntosh S, Leon F, Cutler SJ, McCurdy CR, 2019. Abuse liability and therapeutic potential of the *Mitragyna speciosa* (kratom) alkaloids mitragynine and 7-hydroxymitragynine: kratom abuse liability. Addict. Biol24, 874–885. 10.1111/adb.12639 [PubMed: 29949228]

Henningfield JE, Fant RV, Wang DW, 2018. The abuse potential of kratom according the 8 factors of the controlled substances act: implications for regulation and research. Psychopharmacol. 235, 573–589. 10.1007/s00213-017-4813-4

- Henningfield JE, Grundmann O, Babin JK, Fant RV, Wang DW, Cone EJ, 2019. Risk of death associated with kratom use compared to opioids. Prev. Med128, 105851. 10.1016/ j.ypmed.2019.105851 [PubMed: 31647958]
- Hiranita T, Leon F, Felix JS, Restrepo LF, Reeves ME, Pennington AE, Obeng S, Avery BA, McCurdy CR, McMahon LR, Wilkerson JL, 2019. The effects of mitragynine and morphine on schedule-controlled responding and antinociception in rats. Psychopharmacol. 236, 2725–2734. 10.1007/s00213-019-05247-7
- Ismail NIW, Jayabalan N, Mansor SM, Müller CP, Muzaimi M, 2017. Chronic mitragynine (kratom) enhances punishment resistance in natural reward seeking and impairs place learning in mice: Mitragynine and cognition. Addict. Biol22, 967–976. 10.1111/adb.12385 [PubMed: 26990882]
- Jansen KLR, Prast CJ, 1988. Ethnopharmacology of kratom and the Mitragyna alkaloids. Journal of Ethnopharmacology23, 115–119. 10.1016/0378-8741(88)90121-3 [PubMed: 3419199]
- Kamble SH, Berthold EC, King TI, Raju Kanumuri SR, Popa R, Herting JR, León F, Sharma A, McMahon LR, Avery BA, McCurdy CR, 2021. Pharmacokinetics of Eleven Kratom Alkaloids Following an Oral Dose of Either Traditional or Commercial Kratom Products in Rats. J. Nat. Prodacs.jnatprod.0c01163. 10.1021/acs.jnatprod.0c01163
- Kilgo DK, Ng YMM, Riedl MJ, & Lacasa-Mas I (2018). Reddit's Veil of Anonymity: Predictors of engagement and participation in media environments with hostile reputations. Social Media + Society, 4(4), 205630511881021. 10.1177/2056305118810216
- Kruegel AC, Grundmann O, 2018. The medicinal chemistry and neuropharmacology of kratom: A preliminary discussion of a promising medicinal plant and analysis of its potential for abuse. Neuropharmacol. 134, 108–120. 10.1016/j.neuropharm.2017.08.026
- Kruegel AC, Uprety R, Grinnell SG, Langreck C, Pekarskaya EA, Le Rouzic V, Ansonoff
 M, Gassaway MM, Pintar JE, Pasternak GW, Javitch JA, Majumdar S, Sames D, 2019. 7Hydroxymitragynine Is an Active Metabolite of Mitragynine and a Key Mediator of Its Analgesic
 Effects. ACS Cent. Sci5, 992–1001. 10.1021/acscentsci.9b00141 [PubMed: 31263758]
- Leong Bin Abdullah MFI, Tan KL, Mohd Isa S, Yusoff NS, Chear NJY, Singh D, 2020. Lipid profile of regular kratom (Mitragyna speciosa Korth.) users in the community setting. PLoS ONE. 15, e0234639. 10.1371/journal.pone.0234639 [PubMed: 32525924]
- Maxwell EA, King TI, Kamble SH, Raju KSR, Berthold EC, León F, Avery BA, McMahon LR, McCurdy CR, Sharma A, 2020. Pharmacokinetics and Safety of Mitragynine in Beagle Dogs. Planta. Med86, 1278–1285. 10.1055/a-1212-5475 [PubMed: 32693425]
- Mudge EM, Brown PN, 2017. Determination of Mitragynine in *Mitragyna speciosa* Raw Materials and Finished Products by Liquid Chromatography with UV Detection: Single-Laboratory Validation. J Aoac. Int100, 18–24. 10.5740/jaoacint.16-0220 [PubMed: 27725074]
- Obeng S, Wilkerson JL, León F, Reeves ME, Restrepo LF, Gamez-Jimenez LR, Patel A, Pennington AE, Taylor VA, Ho NP, Braun T, Fortner JD, Crowley ML, Williamson MR, Pallares VLC, Mottinelli M, Lopera-Londoño C, McCurdy CR, McMahon LR, Hiranita T, 2021. Pharmacological Comparison of Mitragynine and 7-Hydroxymitragynine: In Vitro Affinity and Efficacy for μ-Opioid Receptor and Opioid-Like Behavioral Effects in Rats. J Pharmacol. Exp. Ther376, 410–427. 10.1124/jpet.120.000189 [PubMed: 33384303]
- Olsen EO, O'Donnell J, Mattson CL, Schier JG, Wilson N, 2019. *Notes from the Field:* Unintentional Drug Overdose Deaths with Kratom Detected 27 States, July 2016–December 2017. MMWR Morb. Mortal. Wkly. Rep68, 326–327. 10.15585/mmwr.mm6814a2 [PubMed: 30973850]
- Pew Research Center, 2019. Who uses YouTube, WhatsApp and Reddit. Pew Research Center: Internet, Science & Tech. URL https://www.pewresearch.org/internet/chart/who-uses-youtube-whatsapp-and-reddit/ (accessed 5.6.21).
- Post S, Spiller HA, Chounthirath T, Smith GA, 2019. Kratom exposures reported to United States poison control centers: 2011–2017. Clin. Toxicol57, 847–854. 10.1080/15563650.2019.1569236
- Prevete E, Hupli A, Marrinan S, Singh D, Udine BD, Bersani G, Kuypers KPC, Ramaekers JG, Corazza O, 2021. Exploring the use of Kratom (Mitragyna speciosa) via the YouTube Data

Tool: A Novel Netnographic Analysis. Emerging Trends in Drugs, Addictions, and Health100007. 10.1016/j.etdah.2021.100007

- Saingam D, Assanangkornchai S, Geater AF, Balthip Q, 2013. Pattern and consequences of krathom (Mitragyna speciosa Korth.) use among male villagers in southern Thailand: A qualitative study. Int. J. Drug Policy24, 351–358. 10.1016/j.drugpo.2012.09.004 [PubMed: 23083922]
- Saref A, Suraya S, Singh D, Grundmann O, Narayanan S, Swogger MT, Prozialeck WC, Boyer E, Chear NJY, Balasingam V, 2019. Self-reported prevalence and severity of opioid and kratom (Mitragyna speciosa korth.) side effects. J. Ethnopharmacol238, 111876. 10.1016/ j.jep.2019.111876 [PubMed: 31014959]
- Schimmel J, Amioka E, Rockhill K, Haynes CM, Black JC, Dart RC, Iwanicki JL, 2021. Prevalence and description of kratom (*Mitragyna speciosa*) use in the United States: A cross-sectional study. Addiction. 116, 176–181. 10.1111/add.15082 [PubMed: 32285981]
- Singh D, Müller CP, Murugaiyah V, Hamid SBS, Vicknasingam BK, Avery B, Chear NJY, Mansor SM, 2018a. Evaluating the hematological and clinical-chemistry parameters of kratom (Mitragyna speciosa) users in Malaysia. J. Ethnopharmacol214, 197–206. 10.1016/ j.jep.2017.12.017 [PubMed: 29248450]
- Singh D, Müller CP, Vicknasingam BK, Mansor SM, 2015. Social Functioning of Kratom (*Mitragyna speciosa*) Users in Malaysia. J. Psychoactive Drugs47, 125–131. 10.1080/02791072.2015.1012610 [PubMed: 25950592]
- Singh D, Murugaiyah V, Hamid SBS, Kasinather V, Chan MSA, Ho ETW, Grundmann O, Chear NJY, Mansor SM, 2018b. Assessment of gonadotropins and testosterone hormone levels in regular Mitragyna speciosa (Korth.) users. J. Ethnopharmacol221, 30–36. 10.1016/j.jep.2018.04.005 [PubMed: 29626673]
- Singh D, Narayanan S, Müller CP, Swogger MT, Rahim AA, Leong Bin Abdullah MFI, Vicknasingam BK, 2018c. Severity of Kratom (*Mitragyna speciosa* Korth.) Psychological Withdrawal Symptoms. J. Psychoactive Drugs50, 445–450. 10.1080/02791072.2018.1511879 [PubMed: 30152738]
- Singh D, Narayanan S, Müller CP, Swogger MT, Chear NJY, Dzulkapli EB, Yusoff NSM, Ramachandram DS, León F, McCurdy CR, Vicknasingam B, 2019. Motives for using Kratom (Mitragyna speciosa Korth.) among regular users in Malaysia. J. Ethnopharmacol233, 34–40. 10.1016/j.jep.2018.12.038 [PubMed: 30594604]
- Singh D, Narayanan S, Vicknasingam B, 2016. Traditional and non-traditional uses of Mitragynine (Kratom): A survey of the literature. Brain Res. Bull126, 41–46. 10.1016/ j.brainresbull.2016.05.004 [PubMed: 27178014]
- Singh D, Narayanan S, Vicknasingam B, Corazza O, Santacroce R, Roman-Urrestarazu A, 2017. Changing trends in the use of kratom (*Mitragyna speciosa*) in Southeast Asia. Hum. Psychopharmacol. Clin. Exp32, e2582. 10.1002/hup.2582
- Singh D, Narayanan S, Vicknasingam B, Prozialeck WC, Smith KE, Corazza O, ... & Grundmann O 2021. The Use of Kratom (Mitragyna speciosa Korth.) Among People Who Co-use Heroin and Methamphetamine in Malaysia. J. Addict. Med 10.1097/adm.000000000000876
- Singh D, Yeou Chear NJ, Narayanan S, Leon F, Sharma A, McCurdy CR, Avery BA, Balasingam V, 2020. Patterns and reasons for kratom (Mitragyna speciosa) use among current and former opioid poly-drug users. J. Ethnopharmacol249, 112462. 10.1016/j.jep.2019.112462 [PubMed: 31816368]
- Smid MC, Charles JE, Gordon AJ, Wright TE, 2018. Use of Kratom, an Opioid-like Traditional Herb, in Pregnancy. Obst. Gynecol132, 926–928. 10.1097/AOG.0000000000002871 [PubMed: 30204686]
- Smith KE, Lawson T, 2017. Prevalence and motivations for kratom use in a sample of substance users enrolled in a residential treatment program. Drug Alcohol Depend. 180, 340–348. 10.1016/j.drugalcdep.2017.08.034 [PubMed: 28950240]
- Smith KE, Rogers JM, Strickland JC, & Epstein DH 2021. When an obscurity becomes trend: social-media descriptions of tianeptine use and associated atypical drug use. Am. J. Drug Ale. Abuse, 1–12. 10.1080/00952990.2021.1904408

Smith KE, Rogers JM, Dunn KE, Garcia-Romeu A, Grundmann O, Swogger MT, Epstein DHForthcoming. Social, psychological, and substance use characteristics of adults who use kratom in the United States: Preliminary findings from an online crowdsourced study.

- Sowles SJ, McLeary M, Optican A, Cahn E, Krauss MJ, Fitzsimmons-Craft EE, Wilfley DE, Cavazos-Rehg PA, 2018. A content analysis of an online pro-eating disorder community on Reddit. Body Image24, 137–144. 10.1016/j.bodyim.2018.01.001 [PubMed: 29414146]
- Stanciu CN, Gnanasegaram SA, Ahmed S, Penders T, 2019. Kratom Withdrawal: A Systematic Review with Case Series. J. Psychoactive Drugs51, 12–18. 10.1080/02791072.2018.1562133 [PubMed: 30614408]
- Suwanlert S, 1975. A Study of Kratom Eaters in Thailand. Bulletin on Narcotics27, 21–27. [PubMed: 1041694]
- Swogger MT, Hart E, Erowid F, Erowid E, Trabold N, Yee K, Parkhurst KA, Priddy BM, Walsh Z, 2015. Experiences of Kratom Users: A Qualitative Analysis. J. Psychoactive Drugs47, 360–367. 10.1080/02791072.2015.1096434 [PubMed: 26595229]
- Swogger MT, Walsh Z, 2018. Kratom use and mental health: A systematic review. Drug Alcohol Depend. 183, 134–140. 10.1016/j.drugalcdep.2017.10.012 [PubMed: 29248691]
- Tanguay P, 2021. Kratom in Thailand. Kratom in Thailand. URLhttp://speciosa.org/wp-content/uploads/2016/03/Transitional-Institutes-Analysis-Legislative-Reform-of-Drug-Policies-Addresses-Kratom-Law-Reform-in-Thailand.pdf
- Todd DA, Kellogg JJ, Wallace ED, Khin M, Flores-Bocanegra L, Tanna RS, McIntosh S, Raja HA, Graf TN, Hemby SE, Paine MF, Oberlies NH, Cech NB, 2020. Chemical composition and biological effects of kratom (Mitragyna speciosa): In vitro studies with implications for efficacy and drug interactions. Sci. Rep10, 19158. 10.1038/s41598-020-76119-w [PubMed: 33154449]
- Veltri C, Grundmann O, 2019. Current perspectives on the impact of Kratom use. SAR Volume10, 23–31. 10.2147/SAR.S164261
- Vicknasingam B, Chooi WT, Rahim AA, Ramachandram D, Singh D, Ramanathan S, Yusof NSM, Zainal H, Murugaiyah V, Gueorguieva R, Mansor SM, Chawarski MC, 2020. Kratom and Pain Tolerance: A Randomized, Placebo-Controlled, Double-Blind Study. Yale J. Biol. Med93, 229– 238. [PubMed: 32607084]
- Vicknasingam B, Narayanan S, Beng GT, Mansor SM, 2010. The informal use of ketum (Mitragyna speciosa) for opioid withdrawal in the northern states of peninsular Malaysia and implications for drug substitution therapy. Int. J. Drug Policy21, 283–288. 10.1016/j.drugpo.2009.12.003 [PubMed: 20092998]
- Vosburg SK, Robbins RS, Antshel KM, Faraone SV, Green JL, 2021. Characterizing Pathways of Non-oral Prescription Stimulant Non-medical Use Among Adults Recruited From Reddit. Front. Psychiatry11. 10.3389/fpsyt.2020.631792
- Weiss ST, Douglas HE, 2021. Treatment of Kratom Withdrawal and Dependence With Buprenorphine/Naloxone: A Case Series and Systematic Literature Review. J. Addict. Med15, 167–172. 10.1097/ADM.000000000000721 [PubMed: 32858563]
- Wilson LL, Chakraborty S, Eans SO, Cirino TJ, Stacy HM, Simons CA, Uprety R, Majumdar S, McLaughlin JP, 2021. Kratom Alkaloids, Natural and Semi-Synthetic, Show Less Physical Dependence and Ameliorate Opioid Withdrawal. Cell. Mo.l Neurobiol10.1007/s10571-020-01034-7
- Yue K, Kopajtic TA, Katz JL, 2018. Abuse liability of mitragynine assessed with a self-administration procedure in rats. Psychopharmacol. 235, 2823–2829. 10.1007/s00213-018-4974-9
- Zhang M, Sharma A, León F, Avery B, Kjelgren R, McCurdy CR, Pearson BJ, 2020. Effects of Nutrient Fertility on Growth and Alkaloidal Content in Mitragyna speciosa (Kratom). Front. Plant Sci11, 597696. 10.3389/fpls.2020.597696 [PubMed: 33408731]

Highlights

 Kratom was often used to self-treat opioid withdrawal or as an opioid substitute.

- Polydrug use that included kratom and at least one other substance was common.
- Kratom was perceived as lifesaving, but also potentially addictive.
- Kratom dependence and withdrawal symptoms were described in detail.
- Most used kratom for pragmatic health reasons, rather than to achieve euphoria.

Author Manuscript

Table 1.

All codes applied to the sample kratom subreddit posts (N=280) made between June 2019 to July 2020, interrater agreements (versus disagreements), agreement percent, and the total number of codes applied.

Code	Concordant	Discordant	Total Codes Applied	% Agreement
Desirable kratom effects	137	32	169	81.07
Kratom dosing	120	17	137	87.59
Escalating dose over time	40	2	42	95.24
Titrating dose over time	14	∞	22	63.64
SUD or dependence on non-kratom substance	104	29	133	78.20
Self-treatment for opioid drug withdrawal	85	18	103	82.52
Self-treatment for other drug withdrawal	11	9	17	64.71
Kratom as long-term opioid substitute	34	4	38	89.47
Self-treatment for chronic pain symptoms	53	5	58	91.38
Reports psychiatric symptoms or history	40	18	58	26.89
Self-treatment for depression	24	8	32	75.00
Self-treatment for anxiety	29	9	35	82.86
Self-treatment for other psychiatric symptoms	4	3	7	57.14
Polydrug use with kratom	130	25	155	83.87
Professed kratom addiction	160	23	183	87.43
Kratom Withdrawal	69	17	98	80.23
Kratom Tolerance	39	2	41	95.12
Adverse kratom effects	75	4	62	94.94
Desire to quit kratom	36	7	43	83.72
Quitting kratom	41	12	53	77.36
Kratom regulation discussion	28	2	30	93.33
Total	1,273	248	1,521	83.69

Author Manuscript

Author Manuscript

Table 2.

A sample of quotes from top kratom subreddit posts made between June 2019 to July 2020 detailing kratom self-treatment, kratom opioid substitution, and kratom addiction, tolerance, and withdrawal. $^{\pm}$

Smith et al.

Kratom addiction, tolerance, and withdrawal Long-term use as opioid substitute Kratom self-treatment for SUD, drug dependence, or drug withdrawal

100%. There were no withdrawals, and even a little relaxation "I had a comparable experience switching to kratom. I went *cold turkey * off 100 mg of METHADONE, and it worked

"I'll admit, kratom absolutely helped me decrease my daily amount from around 600mg to around 300mg, but I still have a long way to go.

"After realizing that 100mg of hydro at once wasn't even doing the trick anymore, I "quit" using it with the help of kratom, the "fantastic and not at all harmful" plant. Two years of excessive kratom use later, I was forced to quit by way of a six-month backpacking trip to South America.

makes me feel ĂLMOST entirely normal. I still feel slightly out could just be me, but the withdrawal seems so much worse now. of it, but have been experiencing no chills, shits, global apathy, or body pain. Though I'm still taking quite a bit at once." "I've been taking it since the first day of withdrawal, and it "in the last three to four months I've begun IV use and it Kratom is barely helping at this point"

"I took kratom for several weeks and that really sustained me, likely couldn't have quit [hydrocodone] without it."

Self-treating alcohol abuse with kratom

I went into a drinking spiral that went on for 2 years, but I gave withdrawals, and it really really helped. A lot. I haven't had the it up about 9 months ago. My friend told me to try kratom for urge to drink since then.

Still, I nearly killed myself on several occasions when I was still drinking. Kratom has helped me stay sober, and I'm never going back to that life.

have a medical weed card so there's constant access and when decision to not drink alone anymore - like most of my drinking alone, I know I can't be sober for very long. Kratom has mostly for the last twelve years. I considered getting totally sober, but Twas arrested again after blacking out, so I finally made the relieved my withdrawals, so that's good.'

'So now I've totally stopped using traditional opiates and happiness! I use kratom once a day and sometimes take Essentially, compared with my relationship to alcohol marriage, really all of my relationships, fitness, general "I dosed 1.5g twice on my first day, and I thought, "no long as availability persists). It easily changed my life. miracle. My life has become infinitely better - my job, days off to get better effects. It saved my life." "I let my doctor know that I've been using kratom for opioids (I still take kratom, and plan to use kratom so way". I didn't have restless legs, and my anxiety was around two years for medicinal purposes and it does and compared with others' drug habits, kratom is a wonders to help me avoid using other opioids.

night panic attacks thinking of the opioid feelings. I'm so thankful I don't have to contend with the constant urge to lessened. It felt subtle, but oh my god, it was working!! been a miracle to me. I even passed up a connection for I'm on my fourth day of kratom, and it is working. It's have the temptation to search for pills whenever I visit "I am so grateful for Kratom and thankful that I don't someone's home. I'm so thankful I no longer get late pills. I could never do this without kratom. get back into what I left behind."

family, I found kratom. Kratom relieved nearly all of the was home free after the first 3-4 days I was home free." Some time passed and after some help from friends and life again. Heroin held its grip on me, and I was stuck. "I felt so fucking hopeless about ever living a normal withdrawals and I got clean without feeling too sick. and how much it helps

"In retrospect, I was addicted within six months, but I wouldn't even consider the possibility until about 2 years ago, and it's only been during the most recent weeks that I have admitted that this is an

so I can't speak for people that use more, but physical withdrawals are "I now average around 3g - 4g per day and have for around two years typically minor (like a cold) and last three to four days. I'm sure if you're using 50g per day, they'll be much worse.

"Coming down off kratom feels similar to that of a mild anti-depressant "I've been off kratom for a year, but remembering the days when I was actively addicted scares me. I had little to no control over my impulses, emotional control, stuttering, poor comprehension, memory problems, "The dependency is so fucking real both mentally and physically" and mild opiate... also reminiscent of Tramadol.

withdrawal hits really quick. I start to feel extremely uncomfortable and morning I wake up in agonizing withdrawal. I had a full blown panic attack the last time I attempted quitting, causing my mental health to anxious after going more than two hours without kratom, and every "I take up to 20 grams/day now, but I re-up every couple hours and and a short attention span. spiral out of control."

to dose at 2am then 6am. The restless legs and the agitation are the most are at their worst, I use about 16g per day (which is good for me). The withdrawals kick in at night are the most troublesome, and I'm having "This week I have cut down to 2.5g doses, and when the withdrawals severe - right along with the hot sweats and cravings to use more and make all the pain go away.

> "Without kratom I would certainly be a drunken wreck today. I really wish more people were aware of kratom

my skin - on my arms but all over, lack of appetite, and the blacking out that happens from being dizzy when I stand up. I used to get that feeling as a runner, before I started using kratom but forgot how extreme it is. I absolute complete hell. The worst part is the painful tingly feeling on "Emotionally, it feels good to have told them, but physically, this is can't even focus on the show I planned on watching.

nausea. Much harder to portray is the anxiety, restless legs, and sense of "It's difficult to explain to people that haven't experienced withdrawals of any kind. People understand having lethargy, aches, a runny nose, or uneasiness, which is far and away the worst - especially when trying to sleep at night. It's brutal when the seconds feel like hours. I struggle to "I attempted a taper, but it didn't work, and now I'm having severe explain how it actually feels even worse than what it sounds."

'My problem began when I no longer got the same feelings and effects withdrawals, anxiety, diarrhea, hot/cold sweats and the infamous legendary restless legs syndrome."

that I had originally. I started using more and was shocked to see that

before long, I was taking approximately 12g, four times a day."

Topon recommendation the quotes that appear in this table do not appear verbatim. Some were taken from longer post excerpts. All have been slightly modified to help safeguard the privacy of the people who posted on Reddit and whose data were examined as part of this investigation (e.g., making reverse searching the posts more challenging). We have done this while attempting to retain substance and richness as close to the original post as possible, which is of scientific and clinical interest. **Author Manuscript**

Author Manuscript

Author Manuscript

Table 3.

Desirable effects, adverse effects, and withdrawal symptoms associated with kratom use that appeared at least once among the sample of kratom subreddit posts (N=280) made between June 2019 to July 2020.

Desirable effects	Z	%	Adverse effects	Z	%	Withdrawal symptoms	Z	%
Increased energy	7	16%	Nausea	4	12%	Muscle aches	7	29%
Mood enhancement	∞	18%	Vomiting	9	18%	Muscle spasms	7	8%
Relaxation and sedation (anxiolytic)	6	20%	Poor taste	6	27%	Insomnia	5	21%
Decreased feelings of depression	4	%6	Increased apathy	∞	24%	Anxiety	10	42%
Decreased feelings of anxiety	2	11%	Irritability	5	15%	Depression	7	29%
Improved cognitive function (e.g., focus)	4	%6	Feelings of anxiety	4	12%	Runny nose	4	17%
Boosted productivity	33	7%	Feelings of depression	33	%6	Perspiration	33	13%
Pain relief/analgesia	2	11%	Fatigue	2	%9	Hot flashes	4	17%
Sleep aid	3	7%	Lethargy	4	12%	Chills	4	17%
Euphoria	∞	18%	Itchy skin	2	%9	Irritability	9	25%
Improved Sexual performance	2	2%	Lapses in memory	2	%9	Hostility	3	13%
			Insomnia	2	%9	Aggression	2	8%
			Restlessness	33	%6	Fatigue	33	13%
			Increased heart rate	33	%6	Lethargy	4	17%
			Decreased libido	9	18%	Pins and needles (paresthesia)	2	8%
			Increased urine retention	1	3%	Loss of appetite	S	21%
			Increased urination	_	3%	Sense of uneasiness	6	38%
			Constipation	-	3%	Dizziness	-	4%
			Decreased motivation	S	15%	Nausea or vomiting	S	17%
			Decreased impulse control	2	%9	Vomiting	_	4%
			Liver injury	2	%9	Diarrhea	7	8%
			Headache	2	%9	Restlessness	3	13%
						Restless leg syndrome	5	21%
						Craving	3	13%
						Suicidal Ideation	2	8%

Author Manuscript

Table 4.

Frequencies for drug classes appearing in a sample of kratom subreddit posts (N=280) made between June 2019 to July 2020 related to kratom use and/or kratom polydrug use.

Stimulant	103
Opioid	91
Benzodiazepine	55
Cannabinoids	42
Hallucinogen	31
Psychedelic	30
Nootropic/Supplement	28
CNS Depressant	16
Designer Drug / Benzodiazepine	111
Designer Drug / Stimulant	12
Antidepressant	6
Antitussive	7
General Anesthetic	7
Inhalant	9
Sedative	9
Antidepressant / Opioid	S
GABA analog	S
Sedative / Antihypertensive	4
Antipsychotic	3
Muscle Relaxant	2
Nonbenzodiazepine	2
Anti-diahrreal	1
Beta Blocker	1
Nasal Decongestant	1

Page 21