

Journal of Psychoactive Drugs



ISSN: 0279-1072 (Print) 2159-9777 (Online) Journal homepage: http://www.tandfonline.com/loi/ujpd20

Experiences of Kratom Users: A Qualitative Analysis

Marc T. Swogger Ph.D., Elaine Hart M.S., Fire Erowid B.A., Earth Erowid B.A., Nicole Trabold Ph.D., Kaila Yee B.A., Kimberly A. Parkhurst B.A., Brittany M. Priddy B.S. & Zach Walsh Ph.D.

To cite this article: Marc T. Swogger Ph.D., Elaine Hart M.S., Fire Erowid B.A., Earth Erowid B.A., Nicole Trabold Ph.D., Kaila Yee B.A., Kimberly A. Parkhurst B.A., Brittany M. Priddy B.S. & Zach Walsh Ph.D. (2015): Experiences of Kratom Users: A Qualitative Analysis, Journal of Psychoactive Drugs, DOI: 10.1080/02791072.2015.1096434

To link to this article: http://dx.doi.org/10.1080/02791072.2015.1096434

	Published online: 23 Nov 2015.
	Submit your article to this journal $oldsymbol{\mathcal{Z}}$
Q ^L	View related articles ☑
CrossMark	View Crossmark data ☑

Full Terms & Conditions of access and use can be found at http://www.tandfonline.com/action/journalInformation?journalCode=ujpd20

ISSN: 0279-1072 print / 2159-9777 online DOI: 10.1080/02791072.2015.1096434



Experiences of Kratom Users: A Qualitative Analysis

Marc T. Swogger, Ph.D.^a; Elaine Hart, M.S.^b; Fire Erowid, B.A.^c; Earth Erowid, B.A.^c; Nicole Trabold, Ph.D.^d; Kaila Yee, B.A.^b; Kimberly A. Parkhurst, B.A.^b; Brittany M. Priddy, B.S.^b and Zach Walsh, Ph.D.^e

Abstract — Kratom (*Mitragyna speciosa*) is a psychoactive plant that has been used since at least 1836 in folk medicine in Southeast Asian countries. More recently, kratom has become widely available in the West and is used for both recreational and medicinal purposes. There has, however, been little scientific research into the short- and long-term effects of kratom in humans, and much of the information available is anecdotal. To supplement the increasing scientific understanding of kratom's pharmacology and research into its effects in animals, we report the results of a qualitative analysis of first-hand descriptions of human kratom use that were submitted to, and published by, a psychoactive substance information website (Erowid.org). Themes that emerged from these experience reports indicate that kratom may be useful for analgesia, mood elevation, anxiety reduction, and may aid opioid withdrawal management. Negative response themes also emerged, indicating potential problems and unfavorable "side" effects, especially stomach upset and vomiting. Based on our analyses, we present preliminary hypotheses for future examination in controlled, quantitative studies of kratom.

1

Keywords — analgesia, kratom, Mitragyna speciosa, social anxiety, substance use

Kratom (*Mitragyna speciosa*) is a psychoactive plant that has long been used in Southeast Asian countries, with reports of its use dating to at least as early as 1836. In folk medicine, kratom has been used for its reported analgesic and euphoric effects, as well as for intestinal infections, diarrhea, and cough (Lu, Tran, Nelson, and Aldous 2009; McWhirter and Morris 2010). Malay and Thai natives have used kratom to aid with the ability to work long days in the heat (Tanguay 2011). Kratom has also been used in

Asia as an opium substitute (Burkill 1935), a practice that continues today due to the plant's reported utility as an aid for opioid withdrawal (Prozialeck, Jivan, and Andurkar 2012). Kratom, which is consumed orally or smoked, is now widely available on the Internet and in street shops across the United States and Europe (Prozialeck, Jivan, and Andurkar 2012). In Thailand and surrounding areas, people have begun to use a "kratom cocktail"—a mixture of boiled kratom leaves, coke, antitussis syrup, coffee or codeine, served with ice (Chittrakarn, Penjamras, and Keawpradub 2012).

The expanding international profile of kratom has resulted in increased research attention, and animal studies have begun to reveal details of kratom's effects and their potential mechanisms. Kratom has a high affinity for μ -opioid receptors (Yamamoto et al. 1999) and lower affinity for κ - and δ -opioid receptors (Hassan et al. 2013). It has been shown to prolong the latency of nociceptive responses (e.g., spinal reflex) to noxious stimuli in

^aAssistant Professor, Department of Psychiatry, University of Rochester Medical Center, Rochester, NY.

^bResearch Associate, University of Rochester Medical Center, Rochester, NY.

^cErowid Center, Grass Valley, CA.

^dResearch Associate, University of Rochester School of Nursing, Rochester, NY.

^eAssociate Professor, University of British Columbia, Kelowna, BC, Canada

Please address correspondence to Marc T. Swogger, Ph.D., Department of Psychiatry, 300 Crittenden Boulevard, Box PSYCH, Rochester, NY 14642; email: marc_swogger@urmc.rochester.edu

mice and rats (Reanmongkol, Itharat, and Bouking 2007; Botpiboon et al. 2007), providing evidence for its potential for pain reduction. Kratom's effects can be blocked by pre-administration of an opioid antagonist, which suggests an opioid-receptor mediated effect (Sabetghadam, Ramanathan, and Mansor 2010). Additionally, some studies have found that kratom's anti-nociceptive effects are comparable to widely used opiate analyssics (e.g., Watanabe et al. 1997). There is evidence to suggest that nociceptive responses to kratom differ from morphine and codeine, however, and that kratom may interact with opioid receptor subtypes involving serotonin pathways (Hassan et al. 2013; Macko, Weisbach, and Douglas 1972; Watanabe et al. 1997). Recent animal research has also indicated that kratom has anti-inflammatory actions, antimicrobial activity, and can lead to suppression of food and water intake (Azizi et al. 2010; Shaik et al. 2009; Parthasarathy et al. 2009), making kratom an attractive area of basic research for a wide variety of human conditions.

Most empirical studies designed to elucidate kratom's properties have involved animal research, with minimal scientific research into the short- and long-term effects of kratom in humans. Much of the data on kratom use in humans is informal and anecdotal. As of early 2015, there are 10 published medical case reports on PubMed, with seven involving severe adverse reactions. These selfand case reports document seizures and seizure-like movements, fever, aspiration pneumonia, jaundice, and pruritis following acute or short-term (e.g., two weeks) kratom consumption (Boyer et al. 2008; Hassan et al. 2013; Kapp et al. 2011; Nelsen et al. 2010; Roche et al. 2008). Case reports involving long-term use of kratom note tolerance, withdrawal symptoms, anorexia, hyperpigmentation, psychosis, constipation, insomnia, and poor concentration (McWhirter and Morris 2010). One case of severe hypothyroidism was reported in a 44-year-old patient in coincidence with "addiction" to kratom, leading the authors to speculate that high doses of the substance may suppress thyroid function (Sheleg and Collins 2011). Deaths associated with, but not attributable to, kratom use have also been reported (Hassan et al. 2013; McIntyre et al. 2015). While these reports suggest the potential for harmful kratom use, they suffer from the limitations generally associated with retrospective case reports. That is, results are of an unknown generalizability to the wider population of kratom users, and researcher bias may have an influence on the data reported. Moreover, causation cannot be established. Several of the case reports, including all of those involving deaths, note co-administration of kratom with other substances or consumption among individuals with alcohol dependence or a history of heroin abuse (Backstrom et al. 2010; Boyer et al. 2008; Kronstrand et al. 2011; McWhirter and Morris 2010; Neerman, Frost, and Deking 2013), raising the question of whether adverse events were due to kratom ingestion, ingestion of other substances

including adulterants, the effect of combining psychoactive substances, or pre-existing medical conditions.

There are few studies of kratom use in humans and therefore the consequences of kratom consumption are not well understood in the scientific literature (Hassan et al. 2013). An early study of regular kratom users in Thailand reported beneficial effects including an increased tolerance for work and increased calm (Suwanlert 1975). In the same study, the possible negative effects were reported to be darkened skin, dry mouth, constipation, and withdrawal symptoms that included hostility, aggression, aching in muscles and bones, and jerky movements of the limbs (Suwanlert 1975). A more recent survey of Malaysian kratom users found reports of increased capability to do hard work, increased energy, and increased libido (Vicknasingam et al. 2010). The same survey found that long-term consumption was associated with reports of weight loss, constipation, dehydration, and excessive thirst. However, as noted by Hassan et al. (2013) in their comprehensive review of research on the effects of kratom in humans, these studies need to be cautiously interpreted because well-controlled experiments have not been conducted and it is unclear whether the effects described are attributable to kratom versus other substances, conditions, or a narrow range of extreme use behaviors.

Available evidence suggests that kratom has potential for addiction (Hassan et al. 2013). Studies in mice indicate that some of the kratom metabolites and derivatives are rewarding and result in tolerance, as assessed by a significant reduction in analgesia (Matsumoto et al. 2005, 2008). Signs of physical withdrawal were noted in mice after injection with the opioid inhibitor naloxone. After repeatedly administering mitragynine in mice, Yusoff et al. (2014) found signs of severe somatic withdrawal within 12 hours of discontinuing the drug. Moreover, increased anxiety became evident after 24 hours. Chronic administration led to impaired passive avoidance learning and memory deficits.

In humans, one case report on withdrawal in a man with a history of harmful alcohol use and anxiety described a craving for kratom along with anxiety, sweating, restlessness, and tremor (McWhirter and Morris 2010). A recent study examined 293 regular kratom users in Malaysia. Results indicated that the development of symptoms of dependence occurred at high rates and that these symptoms worsened with longer periods of use (Singh, Muller, and Vicknasingam 2014).

The limited information on the risks and benefits of kratom in humans contrasts with sensationalistic, and often inaccurate, reports in the popular media regarding the dangers of kratom use. The United States Drug Enforcement Agency Fact Sheet (Drug Enforcement Administration 2015) indicates that kratom is a drug of abuse and that cases of psychosis have resulted from using kratom, a claim that is not consistent with our interpretation of the

existing literature. It is likely that similar rhetoric has contributed to the banning of kratom possession in many countries. In contrast to governmental and media-driven sources of information, online forums provide a place for the exchange of information among individuals concerned with the support and safety of themselves and others who take drugs (Soussan and Kjellgren 2014). Indeed, methods for harm reduction are shared in drug-related discussion forums (Barratt, Allen, Lenton 2014), which may also aid in the rapid dissemination of reports of adverse drug events.

Further research is required to assess the harms and benefits of kratom and to guide the development of policy and legal responses to this psychoactive substance. For this reason, we analyzed the reported effects of kratom in humans using qualitative data provided by kratom users. Specifically, we conducted a study of reports of kratom users submitted to the popular psychoactive substance education website Erowid.org. Doing so enabled us to compile reported beneficial and adverse experiences associated with kratom use in a sample of self-selected kratom users.

METHOD

Participants

Participants were 161 individuals who voluntarily submitted "Experience Reports" to Erowid.org regarding their experiences with kratom. Not all participants submitted information regarding gender. Of those who did (n = 122), 109 (89.3%) were male and 13 (10.7%) were female.

Procedure

We conducted a qualitative study involving publicly available documents on Erowid.org. The web site aims to publish all valid reports that it receives. Minor editing is done to remove information that might be incriminating, and to correct spelling and punctuation. Reports that (1) contain no information about substance effects, or (2) are so poorly written as to be incomprehensible, are deleted during Erowid.org's review process prior to publication (Erowid and Erowid 2006).

A total of 198 reports on Erowid.org—representing all reports on kratom published on the site between September 2001 and July 2012—were downloaded. Two authors (MTS and EH) conducted a preliminary review of the reports in order by date of experience. For individuals who submitted multiple reports, we kept the first report for analysis and eliminated subsequent reports in order to reduce the possibility of undue influence by one participant. Thirty-seven reports were excluded, leaving 161 for analysis.

We used conventional content analysis (Hsieh and Shannon 2005) to analyze the data. Two investigators (MTS and EH) participated in initial data coding and analysis. Reports were read to achieve initial understanding of

the material, followed by a line-by-line analysis to derive codes and themes that reflect concepts. For example, "I feel pretty energetic and things are ok" was coded *stimulation* and "the pain I had been experiencing . . . disappeared" was coded *analgesia*. After all transcripts were coded, the two investigators met to discuss any discrepancies in codes, cluster codes into themes, and discuss potential relationships among themes that constituted categories (Hsieh and Shannon 2005). Four broad categories of themes were developed.

Finally, we examined the inter-rater reliability of the theme coding process. A researcher new to the dataset (KP) was given the generated list of available theme codes and qualitatively processed 30 experience report texts by placing codes on previously identified excerpts, while blind to the previously chosen theme codes. The inter-rater agreement for final theme codes on the 30 report texts was 89.7%, supporting the validity and reproducibility of our coding methodology.

RESULTS

From the reports, 15 experiential themes (themes related to the individual's experiences directly after consuming, and while under the influence, of kratom) emerged and are presented in Table 1. For ease of presentation, themes are arranged according to whether (1) a participant described an experience as positive, negative, or other (cannot establish valence); or (2) an experience could

TABLE 1 Experiential themes along with number and percentage of authors whose reports expressed the coded themes				
Themes	n	%		
Positive				
euphoria/sense of well-being	49	30.4		
relaxation	48	23.6		
enhanced sociability/empathy	15	9.3		
increase in energy	14	8.7		
analgesia	14	8.7		
sensory enhancement	12	7.5		
warmth/tingling	9	5.6		
Negative				
nausea/stomachache	26	16.1		
alternating chills/sweats	15	9.3		
dizziness/unsteadiness	11	6.8		
vomiting	9	5.6		
itching	5	3.1		
Other				
numbness in mouth/throat	10	3.8		
visual alterations	10	3.8		
sedation	5	3.1		

TABLE 2 General themes with the number and percentage of authors whose reports expressed these themes				
Themes	n	%		
Successfully used kratom as replacement for unwanted substance (i.e., substitution)	17	10.6		
Withdrawal symptoms after period of non-use	16	9.9		
Symptoms of tolerance	8	5.0		
Hangover after use	7	4.3		

reasonably be seen to be positive, negative, or other to the exclusion of other categories. Additionally, four general themes—those that go beyond the experience of being under the influence of kratom—are presented in Table 2. We present each theme by category and, for many, we include quotes from the experience report as examples of quotes grouped into the theme.

Positive Experiences

The most prominent theme (30.4%) was a sense of well-being that extended in degree to euphoria, especially at higher doses. Numerous individuals described this effect as similar to that of opiates.

"Intense happiness and pleasant thoughts" (exp: 36932)

"Kratom seems to create a pleasant, mellow and happy effect, like laying in a field of poppies." (exp: 40593)

Approximately 24% of reporters experienced relaxation.

"... very relaxed and confident about things." (exp: 28819)

"... body relaxation and mental calm with no loss of clarity." (exp: 18482)

Other positive experience themes, while consistent in description and reported at adequate rates to be considered themes, were reported by far fewer individuals (5.6–9.3%). Approximately 9% of individuals reported increases in energy, especially at lower doses.

"Starting to feel more energized and slightly hyperactive." (exp: 58314)

"Strong desire to work." (exp: 45625)

Some participants reported combinations of relaxation and increased activity.

"I felt very relaxed in my body but felt the need to be active . . . in my mind." (exp: 65923)

Numerous individuals (9.3%) reported increased sociability and/or empathy.

"Still feeling incredible, strong desire to communicate with loves ones. Very empathetic." (exp: 60574).

Nearly 9% of reports included the experience of analgesia.

"For back pain . . . it worked better than any reasonable dose of a pharmaceutical opiate/opioid I've used." (exp: 38490)

"The pain I had been experiencing from a torn shoulder muscle disappeared and my mind became exceedingly clear." (exp: 29753)

Nearly 8% of reports noted sensory enhancement across one or more senses that was perceived as pleasant.

"... the urban sprawl takes on a special beauty and hidden meaning" (exp: 63899)

"I can feel a very mild sense of psychedelia" (exp: 40793)

"Music felt softer, almost cotton-like." (exp: 79456)

Negative Experiences

A number of individuals had experiences that either they reported as negative or can reasonably be inferred to have been negative. The most highly reported negative effect was stomach upset, including nausea, stomachache, and cramping, reported by 16.1% of the sample.

"I feel some nausea set in. It is mild, but definitely unsettling." (exp: 57960)

A total of 9.3% experienced alternating chills and sweats. Fewer people (6.8%) reported an unpleasant dizziness/unsteadiness.

"Felt a bit wobbly and dizzy." (exp: 33179)

"Attempts to walk uncomfortable due to nausea and dizziness." (exp: 46142)

A substantial number of individuals reported vomiting (5.6%), sometimes multiple times over the course of hours.

"... the nausea was just too much and I sprinted to the bathroom, projectile vomiting ... 90 minutes into the experience." (exp: 40466)

A few people (3.1%) reported itching, often relating it to experiences they had had with opiates.

"Some itching, the classic opiate itch." (exp: 40793)

Neutral Experiences

Several people reported experiences that could not easily be classified as positive or negative, but were worth noting due to their frequency. For example, 3.8% of the sample indicated numbness of the mouth and throat just after ingesting the kratom. This occurred primarily with ingestion methods other than capsules. Another 3.8% of users reported visual alterations, including visual flanging, decreased ability to focus, and "fuzzy vision." Finally, 3.1% of individuals noted sedation—generally mild.

General Themes

In addition to reports regarding experiences in the approximately eight-hour (acute) period following kratom ingestion, four additional themes appeared; substitution, withdrawal, tolerance, and hangover. Substitution effects

refer to how variation in the use of one substance affects the use of another. Prominent examples of substitution include the prescription use of methadone as a substitute to injection heroin use, and the use of cannabis as a substitute for alcohol (Mikuriya 2004) and opiates (Lucas 2012; Ramesh et al. 2011). A number (10.6%) of individuals reported successfully using kratom as a substitute to help abstain from the use of other substances perceived as addictive and/or causing harm. These substances were primarily opioids, such as oxycodone and heroin, but also included benzodiazepines and antidepressants. In addition to substitution, 9.9% of the sample reported withdrawal symptoms after using kratom, generally perceived as milder than, but similar to, those caused by withdrawal from opiates. Five percent of the sample reported tolerance to kratom, and a willingness to take higher doses in order to achieve the same effect. Finally, 4.3% of experience reports referenced hangover-like symptoms such as headache and nausea on the day after ingestion of kratom.

Adverse Experiences

While serious adverse experiences following kratom consumption were infrequently reported, we note that two individuals described liver problems, potentially in association with kratom. One female described having been hospitalized with jaundice and itching following acute kratom consumption (exp: 88678) and one male indicated a diagnosis of hepatitis after approximately two weeks of kratom consumption. Three years later, Erowid.org contacted the female author, who said she never tried kratom again and had "no ongoing problems associated with that bout of hepatitis." The latter recovered, though reportedly with elevated liver enzymes six weeks after the initial illness.

DISCUSSION

Online drug use forums offer opportunities for the rapid exchange of information and the monitoring of risks associated with use of particular substances. We analyzed and thematically coded kratom experience reports sent to Erowid.org.in order to gather information on humans' experiences with kratom. In reviewing our findings, it is notable that the theme codes our analysis generated corroborate traditional reports of kratom use from Southeast Asia. Kratom users reported relaxation, a sense of well-being, and pain relief, along with typical opiate side-effects, including stomach upset, vomiting, itching, and mild sedation. A subset of users reported both tolerance to, and symptoms of withdrawal from, kratom, though many indicated that, in their experience, these symptoms were milder than those that follow heavy opiate use. A subset of participants also reported using kratom to ease symptoms of opiate withdrawal and many indicated that they had success in discontinuing opiates.

However, consistent with basic research findings that suggest that opiates and kratom have differences in their biological action (Hassan et al. 2013), participants reported a number of experiences that are not typical of opiate use and that suggest that some individuals are engaged in the non-addictive use of kratom as an instrument to aid in the achievement of their goals (see Muller and Schumann 2011 for a discussion of drug instrumentalization). First, nonopiate-typical themes included a stimulant effect, whereby users felt capable-even motivated-to be active and do work. This effect seemed to be present primarily at lower doses of kratom and, for some participants, somewhat paradoxically coincided with relaxation. Such reports raise the possibility that kratom may represent a substance that provides pain relief for some individuals, with less sedation and less temporary cognitive impairment than similarly analgesic levels of opiates. However, further research is necessary to determine safety and administration guidelines for the use of kratom or its active chemicals in a clinical capacity. Second, users reported enhanced sociability and empathy with others for a number of hours after ingesting kratom. Based on this theme, we hypothesize that kratom might be used successfully by individuals to decrease symptoms of social anxiety. Third, it has been noted that kratom may help to manage opioid withdrawal (Ward et al. 2011), and the themes extracted from our data support the use of kratom for easing opiate, and other drug, withdrawals. We hypothesize that kratom could be an effective alternative to opiate drugs currently used as substitutes (e.g., buprenorphine, methadone), noting that kratom is already used for this purpose in Asia and findings are emerging that indicate that regular kratom users do not experience major impairments in their social functioning, even if they are dependent on kratom for prolonged stretches of time (Singh et al. 2015). These findings suggest that kratom may have therapeutic potential as a substitute for opiates and may also be an effective adjunct to treatments for problematic opiate use. These potential uses are particularly interesting given the tragic and growing cost of harmful opioid use. Indeed, recent findings regarding the use of cannabis in place of opioids demonstrate the potential public health benefits of opioid substitution (Bachhuber et al. 2014).

Regarding the safety of consumption, themes were not indicative of acute, serious kratom toxicity. Nor did users report the loss of inhibitions that led to aggressive or otherwise antisocial behavior. Nonetheless, in addition to two reports of liver problems following kratom ingestion, themes included stomach upset, chills and sweats, dizziness, and vomiting, suggesting that considerable caution is warranted in the consumption of kratom. Moreover, reports of visual alterations and sedation suggest that kratom should never be taken while operating vehicles or in other situations where alertness and coordination are required for safety. Given the preliminary nature of data on kratom

and a lack of controlled human studies, chronic ingestion is of unknown safety. Case reports of seizures and coma (Nelson et al. 2010) and other serious adverse reactions (e.g., Sheleg and Collins 2011) are reason for caution. Pending further research, no individual can be assured that acute consumption of this substance will not do harm.

Finally, for some individuals, kratom may have the potential to produce withdrawal and tolerance. Withdrawal symptoms and developing tolerance to the substance were generally, though not uniformly, reported to be mild relative to opiates. The fact that nearly 10% of the sample reported withdrawal symptoms after a period of heavy use followed by at least one day of non-use underscores the importance of education regarding the potential risks of kratom use. Moreover, it suggests that individuals who have had substance use problems in the past should carefully weigh the potential pros and cons of using kratom in a manner that balances the potential of kratom to serve as a less harmful substitute with the recognition that cessation of prolonged and frequent kratom use may involve distinct challenges.

This research has several limitations. First, sampling bias could reduce generalizability. Participants were selfselected based on submitting their own experiential reports to a website, and may not be representative of experiences in a broader group of kratom users. Second, we cannot infer that kratom caused all of the experiences reported-positive or negative—given the lack of controls. Indeed, analyzed reports may be biased by a number of factors, including expectations and placebo effects. Moreover, there is evidence that, apart from providing a place for the exchange of knowledge associated with harm reduction, online forums may also contain discourse that is biased toward dangerous drug use and against harm reduction (Barratt, Allen, and Lenton 2014). Such discourse may promote the downplaying of negative features of drug experiences (Soussan and Kjellgren 2014). To the extent that our sample was biased in this way, our conclusions may not apply as strongly to individuals who are less interested in pleasure or alternate states of consciousness and more interested in the alleviation of pain without "side effects." Third, our sample may be distinctive in that they may be of higher socioeconomic status as indicated by Internet access, may have greater interest in substance use information, or may have had a more impactful kratom experience than that of kratom users as a whole.

In sum, our findings suggest that the subjective effects of kratom are generally mild and pleasant, with some important negative physical side-effects, including what appears to be a mild (i.e., relative to opiates) dependence syndrome. Our findings also corroborate prior reports of the therapeutic potential of kratom as an opiate substitute. However, given the limitations of existing research, discussion of the harms and benefits of kratom are tentative and further research is required to more comprehensively estimate the therapeutic potential and abuse potential of kratom. In particular, given growing anecdotal and preclinical evidence, it appears that clinical trials are warranted to investigate the efficacy of kratom for pain relief, as part of an opioid addiction management program, or as a direct treatment for opiate addiction. It is our hope that such research will not be impeded by premature, overly restrictive policies regulating kratom, or by bias against this understudied traditional plant-based medicine.

ACKNOWLEDGMENTS

We thank individuals who reported their experiences with kratom. Those who provided pseudonyms and were quoted in this article include Seifuru Exp: 36932, Steve in Colorado Exp: 40593, Sirk Exp: 28819, Reville Exp: 18482, Jamie Exp: 58314, Anonymous Exp: 45625, Pillowz Exp: 65923, Younger Cole Exp: 60574, Sepulfreak Exp: 38490, Nitram Exp: 29753, Natural Healing Exp: 79133, Seaborg Exp: 63899, Chretien S. Exp: 40793, P Exp: 79456, Kratom Exp: 57960, Sugeshotcha Exp: 33179, Agean Moss Exp: 46142.

REFERENCES

- Azizi, J., S. Ismail, M. N. Mordi, S. Ramanathan, M. I. M. Said, and S. M. Mansor. 2010. In vitro and in vivo effects of three different Mitragyna speciosa korth leaf extracts on phase II drug metabolizing enzymes glutathione transferases (GSTS). *Molecules* 15:432–41. doi:10.3390/molecules 15010432.
- Bachhuber, M. A., B. Saloner, C. O. Cunningham, and C. L. Barry. 2014. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999–2010. JAMA Internal Medicine 174:1668–73. doi:10.1001/jamainternmed.2014.4005.
- Backstrom, B. G., G. Classon, P. Lowenhielm, and G. Thelander. 2010. Krypton–ny, dodlig Internetdrog. Sedan oktober 2009 har nio unga personer dott i Sverige. [Krypton–new, deadly Internet drug. Since October 2009 nine young persons have died in Sweden]. Lakartidningen 107:3196–97.
- Barratt, M. J., M. Allen, and S. Lenton. 2014. "PMA sounds fun": Negotiating drug discourses online. Substance Use & Misuse 49:987–98. doi:10.3109/10826084.2013.852584.
- Botpiboon, O., S. Prutipanlai, B. Janchawee, and S. Thainchaiwattana. 2007. Effects of caffeine and codeine on antinociceptive activity of alkaloid extract from leaves of kratom (Mitragyna speciosa korth). Paper presented at the 35th Congress on Science and Technology of Thailand, The Tide Resort (Bangsaen Beach), Chonburi, Thailand, October 15-17, 2009.
- Boyer, E. W., K. M. Babu, J. E. Adkins, C. R. McCurdy, and J. H. Halpern. 2008. Self-treatment of opioid withdrawal using kratom (Mitragynia speciosa korth). Addiction 103:1048–50. doi:10.1111/j.1360-0443.2008.02209.x.
- Burkill, I. H. (Ed.). 1935. A dictionary of the economic products of the Malay Peninsula, Vol. II, London: Crown Agents for the Colonies.

Chittrakam, S., P. Penjamras, and N. Keawpradub. 2012. Quantitative analysis of mitragynine, codeine, caffeine, chlorpheniramine and phenylephrine in a kratom (mitragyna speciosa korth) cocktail using high-performance liquid chromatography. Forensic Science International 217:81–86. doi:10.1016/j.forsciint.2011.10.027.

- Drug Enforcement Administration, U.S. Department of Justice. 2013. Kratom (Mitragyna speciosa korth). Retrieved 10/18/15. http://www.deadiversion.usdoj.gov/drug_chem_info/kratom.pdf
- Erowid, E., and F. Erowid The value of experience. Erowid Extracts. June 2006 (10):14–19. https://erowid.org/experiences/exp_info3.shtml.
- Hassan, Z., M. Muzaimi, V. Navaratnam, N. H. Yusoff, F. W. Suhaimi, R. Vadivelu, B. K. Vicknasingam, et al. 2013. From kratom to mitragynine and its derivatives: Physiological and behavioural effects related to use, abuse, and addiction. *Neuroscience & Biobehavioral Reviews* 37:138–51. doi:10.1016/j.neubiorev.2012.11.012.
- Hsieh, H. F., and S. E. Shannon. 2005. Three approaches to qualitative content analysis. *Qualitative Health Research* 15:1277–88. doi:10.1177/1049732305276687.
- Kapp, F. G., H. H. Maurer, V. Auwarter, M. Winkelmann, and M. Hermanns-Clausen. 2011. Intrahepatic cholestasis following abuse of powdered kratom (Mitragyna speciosa). *Journal of Medical Toxicology* 7:227–31. doi:10.1007/s13181-011-0155-5.
- Kronstrand, R., M. Roman, G. Thelander, and A. Eriksson. 2011. Unintentional fatal intoxications with mitragynine and O-desmethyltramadol from the herbal blend krypton. *Journal of Analytical Toxicology* 35:242–47. doi:10.1093/anatox/35.4.242.
- Lu, S., B. N. Tran, J. L. Nelsen, and K. M. Aldous. 2009. Quantitative analysis of mitragynine in human urine by high performance liquid chromatography-tandem mass spectrometry. *Journal of Chromatography B, Analytical Technologies in the Biomedical and Life Sciences* 877:2499–505. doi:10.1016/j.jchromb.2009.06.024.
- Lucas, P. 2012. Cannabis as an adjunct to or substitute for opiates in the treatment of chronic pain. *Journal of Psychoactive Drugs* 44:125– 33. doi:10.1080/02791072.2012.684624.
- Macko, E., J. A. Weisbach, and B. Douglas. 1972. Some observations on the pharmacology of mitragynine. Archives Internationales de Pharmacodynamie et de Therapie 198:145–61.
- Matsumoto, K., L. T. Yamamoto, K. Watanabe, S. Yano, J. Shan, P. K. T. Pang, D. Ponglux, H. Takayama, and S. Horie. 2005. Inhibitory effect of mitragynine, an analgesic from Thai herbal medicine, on neurogenic contraction of the vas deferens. *Life Sciences* 78:187–94.
- Matsumoto, K., H. Takayama, M. Narita, A. Nakamura, M. Suzuki, T. Suzuki, T. Marayama, et al. 2008. MGM-9 [(E)-methyl 2-(3-ethyl-7a,12a-(epoxyethanoxy)-9-fluoro-1,2,3,4,6,7,12,12b-octahydro-8-methoxy indolo[2,3-a]quinolizin-2-yl)-3-methoxyacrylate], a derivative of the indole alkaloid mitragynine: A novel dual-acting mu- and kappa-opioid agonist with potent antinociceptive and weak rewarding effects in mice. Neuropharmacology 55:154–65. doi:10.1016/j.neuropharm.2008.05.003.
- McIntyre, I. M., A. Trochta, S. Stolberg, and S. C. Campman. 2015. Mitragynine "kratom"-related fatality: A case report with post-mortem concentrations. *Journal of Analytical Toxicology* 39:152–55. doi:10.1093/jat/bku137.
- McWhirter, L., and S. Morris. 2010. A case report of inpatient detoxification after kratom (*Mitragyna speciosa*) dependence. *European Addiction Research* 16:229–31. doi:10.1159/000320288.
- Mikuriya T. 2004. Cannabis as a substitute for alcohol: A harm reduction approach. *J Cannabis Therapeutics* 4:79–93.
- Müller, C. P., and G. Schumann. 2011. Drugs as instruments: A new framework for non-addictive psychoactive drug use. *Behavioral and Brain Sciences* 34:293–310. doi:10.1017/S0140525X11000057.
- Neerman, M. F., R. E. Frost, and J. Deking. 2013. A drug fatality involving kratom. *Journal of Forensic Sciences* 58 (Suppl 1):SS278–9. doi:10.1111/1556-4029.12009.

Nelsen, J. L., J. Lapoint, M. J. Hodgman, and K. M. Aldous. 2010. Seizure and coma following kratom (Mitragynina speciosa korth) exposure. *Journal of Medical Toxicology* 6:424–26. doi:10.1007/s13181-010-0079-5.

- Parthasarathy, S., J. Bin Azizi, S. Ramanathan, S. Ismail, S. Sasidharan, M. I. Said, and S. M. Mansor. 2009. Evaluation of antioxidant and antibacterial activities of aqueous, methanolic and alkaloid extracts from Mitragyna speciosa (Rubiaceae family) leaves. *Molecules* 14:3964–74. doi:10.3390/molecules14103964.
- Prozialeck, W. C., J. K. Jivan, and S. V. Andurkar. 2012. Pharmacology of kratom: An emerging botanical agent with stimulant, analgesic and opioid-like effects. *The Journal of the American Osteopathic Association* 112 (12):792–99.
- Ramesh, D., G. R. Ross, J. E. Schlosburg, R. A. Owens, A. Abdullah, S. G. Kinsey, J. Z. Long, D. K. Nomura, L. J. Sim-Selley, B. F. Cravatt, H. I. Akbarali, and A. H. Lichtman. 2011. Blockade of endocannabinoid hydrolytic enzymes attenuates precipitated opioid withdrawal symptoms in mice. *J Pharmacololgy & Experimental Therapeutics* 339:173–85. doi:10.1124/jpet.111.181370
- Reanmongkol, W., A. Itharat, and P. Bouking. 2007. Evaluation of the anti-inflammatory, antinociceptive and antipyretic activities of the extracts from Smilax corbularia Kunth rhizomes in mice and rats (in vivo). The Songklanakarin Journal of Science and Technology 29:59–67.
- Roche, K. M., K. Hart, B. Sangalli, J. Lefberg, and M. Bayer. 2008. Kratom: A case of a legal high. Clinical Toxicology 46 (7):598.
- Sabetghadam, A., S. Ramanathan, and S. M. Mansor. 2010. The evaluation of antinociceptive activity of alkaloid, methanolic, and aqueous extracts of Malaysian Mitragyna speciosa korth leaves in rats. *Pharmacognosy Research* 2:181–85. doi:10.4103/0974-8490. 65514.
- Shaik Mossadeq, W. M., K. Syamimi, M. P. Azyyati, Z. A. Zakaria, A. K. Arifah, M. A. Rajion, M. L. Jabit, M. Taufik Hidayat, and M. R. Sulaiman. 2009. Anti-inflammatory effect of Mitragyna speciosa crude methanol extract on the guinea pig ileum. *Planta Medica* 75:PH19. doi:10.1055/s-0029-1234736.
- Sheleg, S. V., and G. B. Collins. 2011. A coincidence of addiction to "kratom" and severe primary hypothyroidism. *Journal of Addiction Medicine* 5:300–01. doi:10.1097/ADM.0b013e318221fbfa.
- Singh, D., C. P. Müller, and B. K. Vicknasingam. 2014. Kratom (Mitragyna speciosa) dependence, withdrawal symptoms and craving in regular users. *Drug and Alcohol Dependence* 139:132–37.doi: 10.1016/j.drugalcdep.2014.03.017.
- Singh, D., C. P. Muller, B. K. Vicknasingam, and S. M. Mansor. 2015. Social functioning of kratom users in Malaysia. *Journal of Psychoactive Drugs* 47:125–31. doi:10.1080/02791072.2015. 1012610.
- Soussan, C., and A. Kjellgren. 2014. Harm reduction and knowledge exchange: A qualitative analysis of drug-related Internet discussion forums. *Harm Reduction Journal* 11:25–29. doi:10.1186/1477-7517-11-25.
- Suwanlert, S. 1975. A study of kratom eaters in Thailand. Bulletin on Narcotics 27:21–27.
- Tanguay, P. 2011. Kratom in Thailand: Decriminalisation and community control? Legislative Reform of Drug Policies 13:1–16.
- Vicknasingam, B., S. Narayanan, G. T. Beng, and S. M. Mansor. 2010. The informal use of ketum (Mitragyna speciosa) for opioid with-drawal in the northern states of peninsular Malaysia and implications for drug substitution therapy. *International Journal of Drug Policy* 21:283–88. doi:10.1016/j.drugpo.2009.12.003.
- Ward, J., C. Rosenbaum, C. Hernon, C. R. McCurdy, and E. W. Boyer. 2011. Herbal medicines for the management of opioid addiction: Safe and effective alternatives to conventional pharmacotherapy? CNS Drugs 25 (December):999–1007. doi:10.2165/11596830-0000000000-00000.

- Watanabe, K., S. Yano, S. Horie, and L. T. Yamamoto. 1997. Inhibitory effect of mitragynine, an alkaloid with analgesic effect from Thai medicinal plant Mitragyna speciosa, on electrically stimulated contraction of isolated guinea-pig ileum through the opioid receptor. *Life Sciences* 60:933–42. doi:10.1016/S0024-3205(97)00023-4.
- Yamamoto, L. T., S. Horie, H. Takayama, N. Aimi, S. Sakai, S. Yano, J. Shan, P. K. Pang, D. Ponglux, and K. Watanabe. 1999. Opioid receptor agonistic characteristics of mitragynine
- pseudoindoxyl in comparison with mitragynine derived from Thai medicinal plant Mitragyna speciosa. *General Pharmacology* 33::73–81. doi:10.1016/S0306-3623(98)00265-1.
- Yusoff, N. H., F. W. Suhaimi, R. K. Vadivelu, Z. Hassan, A. Rümler, A. Rotter, D. Amato, H. C. Dringenberg, S. M. Mansor, V. Navaratnam, and C. P. Müller. 2014. Abuse potential and adverse cognitive effects of mitragynine (kratom). *Addiction Biology*. Article first published online: 28 SEP 2014 DOI:10.1111/adb.12185