



The prevalence of psychotic symptoms in kratom (*Mitragyna speciosa* Korth.) Users in Malaysia

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ABSTRACT

Background: Kratom is a traditional medicinal herb widely used in Malaysia and Thailand. Despite its widespread use and statements by regulatory agencies on the potential for kratom-associated psychosis, there is little data regarding the prevalence of psychotic symptoms among kratom users. This study investigated the prevalence of psychosis among kratom users, described psychotic symptomatology and severity, while examining associations between kratom use characteristics and the occurrence of psychotic symptoms.

Methods: This cross-sectional clinical survey recruited 150 regular kratom users. The Mini International Neuropsychiatric Interview (MINI) and Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-V) diagnostic criteria were used to evaluate psychotic symptomatology among kratom users, and the Brief Psychiatric Rating Scale (BPRS) was used to assess the severity of psychiatric symptoms. Chi-square tests with Yate's correction were performed to determine the association between kratom use characteristics and the occurrence of psychotic symptoms among kratom users in this study.

Results: Six out of 150 kratom users (4%) presented with any psychotic symptoms. The psychotic symptoms reported were positive symptoms and thought alienation, with a mean BPRS score of 33 (i.e., mild severity). Variables related to kratom use (such as intake of kratom with diphenhydramine, duration of kratom use, and quantity and frequency of daily kratom use) were not associated with the occurrence of psychotic symptoms among kratom users.

Conclusion: Although psychotic symptoms could occur among regular kratom users, they were rare and not significantly associated with kratom use characteristics. We found no evidence of elevated psychosis among regular users.

1. Introduction

Kratom, or *Mitragyna speciosa* Korth (*M. speciosa*), is a traditional medicinal herb indigenous to Malaysia and Thailand and widely used in these two neighbouring Southeast Asian countries. It is also known as *Ketum* or *biak-biak* in Malaysia, and as Kratom, *Kakuam*, *Ithang*, or *Thom* in Thailand (Ingsathit et al., 2009; Adkins et al., 2011; Hassan et al., 2013). The exact prevalence of kratom use in Malaysia is still unclear. However, reportedly due to addictive potential, kratom use was only permitted until 2003 when it was placed under the Poison Act; selling of the leaves of *M. speciosa* became an offence punishable by penalty and/or jail sentence (Vicknasingam et al., 2010). Despite its potential for harmful use, recent studies indicate that kratom may be a candidate

for replacement therapy in the treatment of opioid dependence, as it suppresses opioid withdrawal symptoms and may treat chronic pain (Vicknasingam et al., 2010; Prozialeck, 2016; Swogger and Walsh, 2018). Nevertheless, the biosafety characteristics of kratom must be thoroughly investigated before it can be considered for further development in modern medicine.

One common psychiatric complication associated with illicit drug use is substance-induced psychosis. Psychostimulants in particular, such as methamphetamine, can induce acute psychosis during intoxication which may continue for a period after use (Glasner-Edwards and Mooney, 2014). Similarly, kratom produces a psychostimulant effect at lower dose (Prozialeck et al., 2012; Ismail et al., 2019) and hence its relationship to psychosis requires investigation. To date, there are

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few studies which assess the presence of psychotic symptoms among kratom users and it is unknown whether the constituents in kratom leaves are psychotogenic. Mitragynine, the most abundant psychoactive alkaloid in kratom leaves, is known to be lipophilic and is passively transported across the intestinal wall and blood brain barrier (Ya et al., 2019). To date, however, there is no literature which reports that mitragynine is psychotogenic in animals or humans. While Swogger and Walsh (2018) found no evidence for psychosis in their comprehensive review of kratom and mental health, US regulatory agencies have warned about a potential link (Swogger and Walsh, 2018) and further research is necessary.

This cross-sectional study was conducted (1) to investigate the prevalence of psychotic symptoms among regular kratom users in Malaysia, (2) to describe any psychotic symptomatology as reported by users, (3) to assess the severity of psychotic symptoms, and (4) to determine the association between characteristics of kratom use (e.g., such as the concurrent use of other drugs, duration of kratom use, quantity and frequency of daily kratom use) and the occurrence of psychotic symptoms in kratom users.

2. Methods

2.1. Study design and participants

This cross-sectional survey ran for a duration of one year following approval from the Human Ethics Committee of Universiti Sains Malaysia (code: USM/JEPeM/16050174). The participants were recruited through snow ball sampling involving three hot spot locations for kratom users in Penang, a northern state of Peninsular Malaysia. Prior to the study, informants, who were kratom users themselves, were first recruited from the targeted locations to help researchers in identifying study participants. Kratom users who were identified and wished to receive information were provided a detailed description of the study by the research team. They were then screened based on inclusion criteria as follows: (1) regular (i.e., daily) kratom use for at least one year, (2) age 18 years and above, and (3) able to read and write in Malay. Exclusion criteria were: (1) pre-existing psychiatric illness, (2) pre-existing medical and surgical illnesses which could induce psychosis and delirium (such as Parkinson's disease, cerebrovascular accidents, cancer, multiple sclerosis, syphilis, toxoplasmosis, meningitis, encephalitis, epilepsy, traumatic brain injury, and electrolyte imbalance), and (3) illicit drug use other than kratom within the past year. Those who fulfilled all inclusion and no exclusion criteria were offered a chance to participate in the study. The kratom users who provided verbal and written informed consent were recruited. Then, their urine samples were tested for illicit drug use using rapid urine-test-kits acquired from Reszon Diagnostic International, Malaysia. The participants were interviewed by a psychiatrist and a research officer from the research team in the community hall at each of the targeted locations. After data collection was completed, those who were diagnosed with psychotic symptoms were referred to the nearest psychiatric out-patient clinic for further treatment.

2.2. Measuring tools

Primary data were collected by administering semi-structured, socio-demographic and substance use history questionnaires to the participants. Variables in the questionnaires included age, gender, ethnicity, occupation, monthly income, marital status, accommodation status, age of first kratom use, current drug use, past history of illicit drug use, duration, as well as quantity and frequency of kratom use. Data were also gathered by interviewing the participants using the MINI and DSM-V diagnostic criteria to assess the occurrence of psychotic symptoms. Participants with any psychotic symptoms were also administered with the Malay version of the Brief Psychiatric Rating Scale (BPRS) in order to assess the severity of their psychotic symptoms.

2.2.1. Mini international neuropsychiatric interview (MINI)

The MINI is a brief structured interview for the major Axis I psychiatric disorders in DSM-IV and ICD-10 which is used to explore 17 disorders. As compared to the SCID-P for DSM-III-R and the CIDI, the MINI can be administered in a shorter period of time (Sheehan et al., 1998). The MINI has good inter-rater and test-retest reliability (Lecrubier et al., 1997). The Malay version of the MINI was validated by Mukhtar et al. (2012). The inter-rater reliability was found to be satisfactory (0.67 to 0.85), and the concordance between the Malay version of the MINI and expert diagnoses was good, with kappa values greater than 0.88 (Mukhtar et al., 2012). In this study, the MINI was used to exclude the kratom users with pre-existing psychiatric illnesses and also to identify the occurrence of psychotic symptoms among the participants.

2.2.2. Brief psychiatric rating scale (BPRS)

The BPRS is an 18-item questionnaire which is administered by trained clinicians to assess the severity of psychiatric symptoms. It can be subdivided into five clusters of symptoms, which are anxiety-depression, anergia, activity, hostility-suspicion, and thought disorder; the latter three clusters are associated with psychotic disorders (Burger et al., 2000). Each item is scored on a Likert scale of seven points (from '1'- not present, to '7'- extremely severe) and the total score of the BPRS is the sum of scores of all items. Hence, the possible total score varies from 24 to 168, in which a higher score indicates more severe psychopathology. A total score of 0 to 30 denotes no notable illness, a score of 31 to 40 indicates minimal illness, a score of 41 to 53 denotes moderate illness, and a score more than 53 indicates severe illness (Leucht et al., 2005). The scale has good validity and reliability (Hedlund and Vieweg, 1980). The Malay version of the BPRS has good preliminary psychometric properties (Yee et al., 2017).

2.3. Data analysis

All data was analysed with Statistical Package for Social Sciences (SPSS) version 24. Descriptive statistics were reported for socio-demographic characteristics, substance history, psychotic symptomatology and the mean BPRS score. Categorical variables were described with frequency and percentage and continuous variables with mean and standard deviation. Pearson's Chi-square test with Yate's correction was performed in order to identify any association between substance history (such as duration of kratom use, concurrent use of cough syrup, quantity of daily kratom use, and frequency of daily kratom use) and the occurrence of psychotic symptoms. Statistical significance for the analysis was set at p -value less than .05.

3. Results

3.1. Socio-demographic characteristics and substance use history

The socio-demographic and substance use characteristics of the participants are summarised in Table 1. The mean age of the participants was 34.42 years (\pm 11.28). All the participants were males, and most of them were Malays (n = 149, 99.3%). More than half of the participants were either single or divorced (n = 84, 56%). Most of them were working (n = 138, 92%) and living with family (n = 132, 88%) at the time the study was conducted.

The mean age of first kratom use among the participants was 25.77 years (\pm 10.70). Approximately half use kratom only (n = 73, 48.7%), while another half of them use kratom mixed with cough syrup (diphenhydramine) (n = 77, 51.3%). Two thirds of the participants had never used illicit drugs other than kratom (n = 100, 66.7%). The others had a history of other illicit drug use, but reportedly stopped using at least one year prior to the study (n = 50, 33.3%). More than half of the participants were chronic users who have used kratom for more than six years (n = 89, 59.3%). The majority of the participants consumed not

Table 1
Socio-demographic characteristics and substance use history of participants.

Number of participants (n)	Percentage (%)	
Gender:		
Males	150	100
Age	34.42 years [#]	11.28 [*]
Ethnicity:		
Malay	149	99.3
Others	1	0.7
Marital status:		
Married	66	44
Single/widow/divorcee	84	56
Education level:		
Primary	14	9.3
Secondary	120	80
Tertiary	16	10.7
Employment status:		
Employed	138	92
Unemployed	12	8
Living condition:		
Live with family	132	88
Live alone or with friends	18	12
First age of kratom use	25.77 years [#]	10.70 [*]
Current drug use:		
Kratom only	73	48.7
Kratom with cough syrup	77	51.3
Past history of other drug use:		
Yes (stop > 1 year)	50	33.3
No	100	66.7
Duration of kratom use:		
< 6 years	61	40.7
≥ 6 years	89	59.3
Quantity of daily kratom use:		
≤ 4 glasses	103	68.7
> 4 glasses	47	31.3
Frequency of daily kratom use:		
≤ 3 times	67	44.7
> 3 times	83	55.3

= mean.

* = standard deviation.

more than four glasses of kratom daily ($n = 103, 68.7\%$); more than half consumed kratom more than three times per day ($n = 83, 55.3\%$).

3.2. Psychotic symptomatology

The psychotic symptoms observed in the participants are summarised in Table 2. Only six of 150 kratom users (4%) were positive for any psychotic symptoms. Two out of the six users with psychotic symptoms had no history of other illicit drug or alcohol use. The other

Table 2
Psychotic symptomatology presented in kratom users.

Number of participants (n)	Percentage (%)	
Presence of psychotic symptoms:		
Yes	6	4
No	144	96
Psychotic symptomatology:		
Auditory hallucination	1	0.7
Visual hallucination	1	0.7
Tactile hallucination	1	0.7
Olfactory hallucination	4	2.7
Persecutory delusion	2	1.3
Delusion of reference	2	1.3
Delusion of control	1	0.7
Grandiose delusion	1	0.7
Thought broadcasting	2	1.3
Thought withdrawal	1	0.7
Total BPRS score	33 [*]	± 10.5 [#]

* = mean BPRS score.

= standard deviation.

four psychotic users with psychotic symptoms had a history of illicit drug use, such as heroin, cannabis, methamphetamine, nimetazepam (Erimin 5) and methadone, but had stopped using for at least three years. The symptoms observed in the kratom users with psychotic symptoms include the following: 1) olfactory hallucinations, i.e., smells of perfume or faulty odour ($n = 4, 2.7\%$); 2) persecutory delusions, i.e., false beliefs that someone is spying on them or people want to beat them up ($n = 2, 1.3\%$); 3) delusions of reference, i.e., false beliefs that strangers are talking bad about them ($n = 2, 1.3\%$); 4) thought broadcasting, i.e., the false belief that people can read their thoughts ($n = 2, 1.3\%$); 5) auditory hallucinations, i.e., heard strange noises outside which were not heard by others while at home ($n = 1, 0.7\%$); 6) visual hallucinations, i.e., visions of clear dark human shape shadows not seen by others ($n = 1, 0.7\%$); 7) tactile hallucinations, i.e., being touched at the back when nobody was around ($n = 1, 0.7\%$); 8) delusions of control, i.e., the false belief that thoughts and movements are being controlled by an external agent ($n = 1, 0.7\%$); 9) grandiose delusions, i.e., the false belief that he is a dignitary and is extremely important ($n = 1, 0.7\%$); and 10) thought withdrawal, i.e., the false belief that thoughts were being withdrawn by someone outside ($n = 1, 0.7\%$). The total mean BPRS score among people with psychotic symptoms was 33 (± 10.5), indicating psychotic symptoms of mild severity.

3.3. Association between kratom use characteristics and the occurrence of psychotic symptoms in kratom users

The findings of Chi-square tests examine associations between kratom use characteristics (i.e., duration of kratom use, concurrent use of cough syrup, quantity of daily kratom use, frequency of daily kratom use) and the occurrence of psychotic symptoms in kratom users are summarised in Table 3. None of these characteristics were significantly associated with the occurrence of psychotic symptoms in kratom users.

4. Discussion

This study aimed to describe the prevalence, severity, and correlates of psychotic symptoms among regular kratom users in Malaysia. Regarding psychotic symptomatology, only six participants (4%) displayed any psychotic symptoms. Although it cannot be ruled out that kratom contributed to these symptoms, their prevalence in a sample of regular kratom users is well within the range expected based on other studies of psychosis in samples worldwide (Nuevo et al., 2012; Rognli et al., 2017). Thus, current findings are inconsistent with kratom as a psychotogenic agent. In comparison, studies have reported a prevalence of methamphetamine-induced psychosis of 36.5% in a meta-analysis of

Table 3

The association between kratom use characteristics (such as duration of kratom use, current drug use - kratom only vs. kratom with cough syrup, quantity of daily kratom use, frequency of daily kratom use) and the occurrence of psychotic symptoms in kratom users.

	Psychotic users (n)	Non-psychotic users (n)	p-value
Current drug use:			
Kratom only	2	72	0.701
Kratom with cough syrup	4	72	
Duration of kratom use:			
< 6 years	2	59	0.814
≥ 6 years	4	85	
Quantity of daily kratom use:			
≤ 4 glasses	2	101	0.146
> 4 glasses	4	43	
Frequency of daily kratom use:			
≤ 3 times	0	67	0.068
> 3 times	6	77	

seventeen studies (Wearne and Cornish, 2018). We note that the prevalence of psychotic symptoms as observed in our study (4%) was higher than the prevalence of schizophrenia (0.5%) as reported by Teoh et al. (2017) in a Malaysian sample of 26,392 mentally ill patients. However, schizophrenia is a disorder comprised of numerous positive and negative symptoms of psychosis, as well as functional impairments, and is thus occurs less frequently than individual psychotic symptoms.

The psychotic symptoms reported in this study were positive symptoms (such as hallucinations and delusions) and also thought alienation (such as thought broadcasting and thought withdrawal). Furthermore, no negative symptoms were observed in this study. These findings are similar to what was reported by Suwanlert (1975) in which five Thai kratom users reported positive psychotic symptoms like hallucinations and delusions (Suwanlert, 1975). However, unlike Suwanlert (1975) we find no reason to conclude, based on our findings, that kratom use and psychosis are related. Notably, some of the psychotic symptoms among the study participants are similar to positive symptoms exhibited by users with methamphetamine-induced psychosis, characterised by auditory and visual hallucinations, persecutory delusions, and delusions of reference. However, individuals with methamphetamine-induced psychosis also exhibit negative symptoms (Wearne and Cornish, 2018). The severity of psychotic symptoms in the six kratom users who exhibited any was of mild (total mean BPRS score = 33 ± 10.5).

Finally, our study demonstrated that no significant differences in psychotic symptomatology based on duration of kratom use, quantity of daily kratom use, frequency of daily kratom use and the co-ingestion of cough syrup with kratom. This fails to corroborate the hypothesis that prolonged and heavy kratom use increases the risk for psychotic symptoms. This is in contrast to studies of methamphetamine users, reporting that the frequency of methamphetamine use and heavy methamphetamine use could increase the risk of developing methamphetamine-induced psychosis (Sulaiman et al., 2014; Arunogiri et al., 2018).

The current study needs to be considered in the light of limitations. First, the study was conducted in a single state in Peninsular Malaysia and therefore, the study findings may not be generalised to represent the kratom user populations in Malaysia. Hence, it is recommended for future studies to be conducted in all states in Peninsular Malaysia at the locations where kratom users are prevalent. Second, four out of six kratom users who reported psychotic symptoms in this study had a history of using other illicit drugs. Hence, it is possible that the psychotic symptoms reported may be due to other drug use. Indeed, the combination of cross-sectional methodology and routine levels of measurement error limit the specificity of conclusions that can be drawn regarding regular kratom use and prevalence of psychosis.

Despite these limitations, this study may be the first observational study of kratom users which clearly describes the nature and prevalence of psychotic symptomatology and in regular kratom users in Malaysia. This data is important given kratom's expanding public health significance worldwide. Since kratom has now become a potential public health issue due to its widespread use around the world, our study findings provide information regarding the prevalence of psychotic symptoms reported by kratom users. Although psychotic symptoms are uncommon in kratom users and we have established no link between kratom and psychosis, psychotic symptoms may occur in this population, making screening important.

5. Conclusion

This cross-sectional study estimated the prevalence of psychotic symptoms in regular kratom users in Malaysia. The prevalence does not appear to be out of the range expected among normal samples and does not support the presence of widespread kratom-induced psychosis. Psychotic symptoms, which may have arisen due to kratom use or other processes, were positive symptoms; no negative symptoms were

reported. The severity of psychotic symptoms was found to be at the mild level and heavy and prolonged kratom use was not significantly associated with the occurrence of psychotic symptoms in regular kratom users. This study has clearly described the limited psychotic symptomatology exhibited by kratom users in a Malaysian sample, providing useful information and guidance for clinicians. Further research with more rigorous methodology is necessary to replicate study findings.

Declaration of Competing Interest

Mohammad Farris Iman Leong Bin Abdullah, Darshan Singh, Marc T. Swogger, Azlan Abdul Rahim, and Balasingam Vicknasingam who authored the manuscript entitled "The Prevalence of Psychotic Symptoms in Kratom (*Mitragyna speciosa* Korth.) Users in Malaysia" declared that we do not have any conflict of interest in conducting this study.

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