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Original article

Beyond mitragynine: Composition survey and stability assessment of kratom teas ordered via food delivery platforms in Bangkok, Thailand

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Abstract

Background: Kratom is a tree native to Southeast Asia. Kratom leaves have long been used medicinally and recreationally because of their stimulative and opioid-like effects attributed to high endogenous levels of mitragynine and related alkaloids. Kratom is widely consumed as tea and is now publicly sold, including on food delivery platforms, after its recent decriminalization even if the sale of kratom products by other acts is still considered illegal.

Objectives: To assess the formulas of kratom teas sold on Thai food delivery platforms, their consistency ,and the stability of the refrigerated teas.

Methods: Kratom alkaloids, mitragynine and 7-hydroxymitragynine, and additive contents of kratom teas purchased from three online food delivery applications at three different times were analyzed by chromatographic analyses. The stability of both alkaloids was evaluated in teas stored at 4°C for 4 weeks.

Results: In addition to kratom alkaloids, kratom teas contained other drugs and narcotics, particularly antihistamines, ketamine, and stimulants. The contents tended to be inconsistent both in and between lots, even from the same vendor. The mitragynine/7-hydroxymitragynine ratio was lower in tea samples than in raw kratom leaves and may have seasonal variations. Both alkaloids were stable in kratom teas despite fermentation.

Conclusion: Kratom teas contain other compounds in addition to alkaloids. The formulas were inconsistent even in products purchased from the same seller. The alkaloids in kratom teas were stable at 4°C for 4 weeks. Analyses of kratom teas from the same vendor, but not the products consumed by the patient or the deceased, may not provide sufficient data to the attending physician or pathologist. Thus, law enforcement agencies and online food delivery platforms must strictly control the sale of kratom products that contain other drugs and narcotics.

Keyword: Drug of abuse, kratom, kratom tea, mitragyna speciose, mitragynine.

Kratom (*Mitragyna speciosa*) is a tropical tree native to Southeast Asia, particularly in Thailand, Malaysia, and Indonesia. In this region, kratom leaves and leaf-derived products are used widely as a treatment for minor illnesses, such as cough, diarrhea, and pain; an aid in drug withdrawal, and a stimulant to enhance physical stamina. Teas made from kratom leaves are also consumed during social events. In southern Thailand, the consumption of kratom products in these ways is perceived in the same way as tea and coffee drinking. [1-4] Since the 2000s, kratom teas (KT) have also been brewed with various drugs and narcotics in a preparation known as 4 × 100. Contrary to traditional KT users, 4 × 100 consumers are considered drug abusers by law enforcement officials and communities. [1, 2] Furthermore, kratom consumption is increasing in Asian and Western countries. [5-7]

Kratom leaves contain various bioactive alkaloids, of which the two most important for physiological effects are mitragynine (MG), which is the most abundant, and 7 - hydroxymitragynine (7HM), which

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is less abundant but more potent. Both are believed to act through opioid receptors. At low to moderate doses (1 - 5 g of raw leaves), these agents have stimulative effects, whereas at moderate to high doses (5 - 15 g of raw leaves), they produce opioid-like sedative and euphoric effects. At very high doses (>15 g), intoxication symptoms, such as constipation, dizziness, hepatotoxicity, acute respiratory distress syndrome, seizure, and coma, may occur. [5 - 8] Kratom-related morbidities and mortalities (KRMMs) usually involve multiple other drugs and narcotics.[5 - 7, 9, 10]

The legal status of kratom varies among jurisdictions. [2, 5, 10] In Thailand, kratom was decriminalized in 2019 [10], and the Kratom Plant Act B.E. 2565 was passed in 2022. The bill allows the private use of kratom products not added with other drugs or narcotics. Although the sale of kratom derived products such as KTs by other acts is still prohibited by other acts, since the decriminalization, kratom products, including trees, leaves, and KTs, have become publicly available, including from online platforms. Despite recent increases in KRMMs, the law against these kratom products is not strictly enforced. [7]

Previous studies on Thai and Malay KTs [11 - 13] have included relatively small samples [11, 12] or used hospital-made [13] rather than commonly consumed products. Furthermore, online platforms have become increasingly important as a distribution channel for kratom products. [5, 6, 14 - 18] In addition, little information on KTs from this channel which has been more prevalent since decriminalization, has been available.

This study aimed to analyze the contents of KTs obtained from various online vendors, including the concentrations of active alkaloids and added drug profiles (DPs), which are other drugs or narcotics that can be found in KTs. Furthermore, the stability of the alkaloids during storage and the consistency of the products were also assessed.

Materials and methods

The study protocol was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University; (IRB no.199/65).

Specimen collection

Apart from direct contact through social media, food delivery applications were the only sources of online shopping platforms that sell kratom products. KTs were purchased through three popular Thai food delivery platforms: Grab, Robinhood, and LINE Man in three lots: in June (L1), September (L2), and October (L3) 2023. Products in L2 and L3 were purchased from the same sellers as L1 if still on the market.

If the seller had more than one KT formula, two formulas were selected and one sample of each formula was purchased. This pair was marked as a "different" (D) pair. If only one formula was available, two bottles were purchased and marked as "same" (*S*). The details of the sellers and products were recorded for subsequent purchases. Samples were stored at 4°C until analysis, which was 1 - 2 days after purchase.

Chemicals and materials

MG powder and methanolic 7HM (0.1 mg/mL) standards were acquired from Cerilliant (Round Rock, TX, USA), liquid chromatography (LC) grade methanol and acetonitrile (Lichrosolv®) from Merck (Darmstadt, Germany), and formic acid (LC-mass spectrometry (MS) grade) from Fisher Chemical (Hampton, NH, USA). Deionized (DI) water was produced by a Barnstead MicroPure Water Purification system (Thermo Scientific, Waltham, MA, USA). 10 M ammonium formate solution and MColorpHast™ universal indicator were purchased from Sigma-Aldrich (Buchs, Switzerland) and nylon syringe filters (width 13 mm; pore size 0.2 μm) from Onepuresci (Shanghai, China).

Method validation

Validated laboratory methods were used for ethanol content measurement and qualitative analyses of DPs. The method for MG and 7HM was developed and validated according to the relevant guidelines. [19, 20] Briefly, the linearity of the calibration range was fit to purpose ($r^2 > 0.99$) for both MG and 7HM for the selected calibration range. The selectivity test did not reveal any interference from other compounds expected to be present in the sample. The intraday and interday accuracy and precision of undiluted and diluted (5×, 10×, and 20×) quality controls were tested by performing five replicates per day for five consecutive days, and all results were within ± 20.0% of the expected values. The limit of detection and the lower limit of detection were set as the lowest calibration level for each compound. The freeze–thaw stability and stability of the processed sample were also determined and were within the stated stability criteria.

Preparation of the calibrators and quality controls

A MG working stock solution was prepared by diluting MG powder in methanol to 1 mg/mL. The MG stock solution and 7HM standards were further diluted in methanol to produce calibrators of 2.5, 5, 25, 50, and 100 mg/L MG and 0.5, 1, 5, 10, and 20 mg/L 7HM. Low, medium, and high concentration quality control standards (4, 30, and 75 mg/L MG; 2, 8, and 15 mg/L 7HM) were also prepared using the same method. For dilutional integrity verification, 200 mg/L of MG and 50 mg/L 7HM quality controls were prepared.

Sample preparation

For the analysis of alkaloids, 1 mL of the KT was pipetted into a 1.5-mL microcentrifuge tube and then centrifuged at 4°C, 12,000 rpm for 10 min. The supernatant was collected and then filtered through a nylon filter. Sets of 1×, 5×, 10×, and 20× dilutions were then prepared with DI water to the volume of 200µL. The aliquots were then transferred into glass vials.

Samples for ethanol content measurements were prepared in the same way as MG and 7HM. After filtration, 200 µL of the aliquot and 200 µL of the internal standard, 100 mg% t-butanol, were pipetted into a glass vial.

For the analysis of other drugs and narcotics, 200 µL of the KT was first mixed with 400 µL of methanol and vortexed for 30 s. The mixture was then centrifuged at 12,000 rpm for 10 min at 4°C. The supernatant was collected and filtered through a nylon membrane, and 200 µL of the sample was pipetted into a glass vial for subsequent analysis.

Chromatographic analysis

Chromatographic hardware and apparatus were acquired from Shimadzu, (Kyoto, Japan). A high-performance liquid chromatography (HPLC) system used for MG and 7HM measurements consisted of a Nexera X2 LC-30AD pump, Nexera X2 SIL-30AC autosampler, DGU-20A5R degasser, CTO-20AC column oven, and SPD-20A prominence UV/VIS detector, which was set at 220 nm. LabSolutions version 5.97 was used as chromatographic software. A SP-C18 Shim-pack Velox column (1.8 µm, 2.1 × 100 mm) was used for separation. The autosampler and oven temperatures were set at 5°C and 35°C, respectively. Mobile phase A was 10 mM ammonium formate in DI water with 0.1% formic acid and mobile phase B was 10 mM ammonium formate in methanol with 0.1% formic acid. The mobile phase B gradient was programmed as follows: 0.0 - 1.5 min 20.0%; 1.5 - 2.3 min, 20.0% - 45.0%; 2.3 - 10.0 min, 45.0%; 10.0 - 10.5 min, 45.0% - 95.0%; 10.5 - 13.5 min, 95%; 13.5 - 14.0, 95.0% - 20.0%; 14.0 - 17.0 min, 20.0%. The injection volume was 5 µL and the flow rate was set at 0.3 mL/min. The retention times of MG and 7HM were 5.4 and 7.6 min, respectively. The concentrations of MG and 7HM were determined based on the values of the lowest dilutional factor that was within the calibration range.

The ethanol content was analyzed using a flame ionization detector GC-2010 gas chromatography coupled with an HS-20 headspace using SH-Rtx-Bac Plus1 (film thickness of 1.80 µm, 0.32 mm × 30.0 m) and SH-Rtx-Bac Plus2 (film thickness of 0.60 µm, 0.32 mm × 30.0 m). The calibration range of ethanol was 10 - 400 mg%. The retention times of ethanol and t-butanol were 3.7 and 5.4 min, respectively.

DP analysis was performed by LC-MS/MS using the same HPLC system and parameters used for alkaloid analyses (with the same column, mobile phases, and flow rate) coupled to an LCMS-8060 triple quadrupole mass spectrometer. The gradient of mobile phase B was programmed as follows: 0.0 - 2.0 min, 5.0% - 15.0%; 2.0 - 10.0 min, 15.0% - 50.0%; 10.0 - 12.0 min, 50.0% - 95.0%; 12.0 - 20.0 min, 95%; 20.0 - 21.0 min, 95.0% - 5.0%; 21.0 - 26.0 min, 5.0%. The mass spectrometer was set in the positive electrospray ionization mode with multiple reaction monitoring. Deuterated standards were used as positive controls. The lower limit of detection of the analytes was 0.1 - 5.0 mg/mL.

Data collection

The general appearances of the KTs, pH, DPs, and concentrations of MG, 7HM, and ethanol were recorded. The concentration of MG and 7HM and the MG/7HM ratio of each sample were also calculated.

Intralot consistency

MG and 7HM concentrations were measured separately for the KT sample pairs (bottles 1 and 2) obtained from the same vendor in the same lot. To allow possible variabilities that may occur in the samples and analytical process [19 - 21], pairs were deemed to have consistent alkaloid contents if the MG_1/MG_2 and $7HM_1/7HM_2$ ratios were within 0.8 - 1.2. The DPs were also compared between these pairs of samples.

Interlot consistency

The interlot consistency of the same formula from the same vendor was also assessed by comparing the concentrations of MG and 7HM of the samples from the two consecutive lots. In total, 10 vendors analyzed in L1 were available in L2 and 9 remained in L3, resulting in 20 products (58 samples) for the analysis of interlot consistency. The product was considered to have consistent alkaloids between lots if the ratios of L1/L2 or L2/L3 values for both MG and 7HM were within 0.8 - 1.2 times in the same comparison. The DPs of the samples were also compared.

Stability testing

The stabilities of MG and 7HM were evaluated by analyzing 20 samples from L2. Each fresh KT sample was divided into four equal volumes and stored in enclosed plastic tubes at 4°C. One tube was immediately analyzed for formula consistency as previously described (week 0) and for alkaloids and ethanol concentrations, whereas the other three tubes were stored for 1 (week 1), 2 (week 2), and 4 (week 4) weeks before analysis. The MG concentration, 7HM concentration, the MG/7HM ratio, pH, and general appearance were recorded at each time point. To assess fermentation, ethanol was also remeasured at week 4.

Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics version 29 (IBM corp., NY, USA). All data were first tested for normality using the Shapiro - Wilk test, and the results were presented as median (minimum–maximum). Medians were compared by the Freidman test and Wilcoxon signed-rank test as indicated. A $P < 0.05$ after the Bonferroni adjustment was considered statistically significant.

Results

Search terms and product names

The search in the three delivery platforms using the Thai term for "kratom" yielded very few results; thus, other search terms were used by browsing social media pages discussing kratom, including (translated from Thai to English) "herbal drink", "palm drink", "ready-to-drink beverage", "red-capped", "silver-capped", "herbal green tea", "tea", "power of leaves", "strawberry juice", and "cherry juice." Product names corresponded to these search terms. Alternatively, no KTs were found using the term "cough syrup", which is a major ingredient in 4 × 100. [1, 2, 11]

Table 1. Number of products obtained from each delivery platform.

Platform	L1		L2		L3	
	S	D	S	D	S	D
Grab	2 (4)	4 (8)	2 (4)	3 (6)	2 (4)	3 (6)
Robinhood	3 (6)	4 (8)	2 (4)	3 (6)	2 (4)	2 (4)
Lineman	1 (2)	6 (12)	-	-	-	-
Total	**20 (40)**		**10 (20)**		**9 (18)**	

Numbers indicate pairs (samples).

Table 2. Alkaloid and ethanol contents of KT samples (median and range).

	All samples	L1	L2	L3
MG (mg/L)	116.7 (14.1 - 427.9)	134.4 (40.5 - 427.9)	99.3 (54.7 - 297.2)	96.0 (14.1 - 153.0)
7HM (mg/L)	43.6 (7.2 - 198.5)	47.3 (10.7 - 198.5)	32.5 (22.8 - 94.6)	35.5 (7.2 - 56.2)
MG/7HM Ratio	2.8 (0.9 - 6.2)	3.1 (1.2 - 4.3)	2.8 (1.9 - 4.6)	2.1 (0.9 - 6.2)
Ethanol (mg%)	11.9 (ND - 316.5)	17.9 (ND - 316.5)	11.2 (ND - 14.5)	10.9 (ND - 36.5)
pH	5 (5 - 7)	5 (5 - 7)	5 (5 - 5)	5 (5 - 6)

ND, not detected

Purchased samples

A summary of the vendors on each delivery platform and the number of sample pairs classified as S (two samples of the same formula obtained from a single vendor) or D (two different formulas obtained from the same vendor) is presented in **Table 1**. After purchasing L1, LINEMAN banned all KTs from the platform. Therefore, only Grab and Robinhood were available for L2 and L3.

Physical characteristics of KTs

All teas were cloudy and greenish-brown and had low (watery) viscosity with a bitter taste, and all were sold in 1 to 1.5 L water bottles.

Analyses of KTs

The median concentrations of each measured alkaloid the MG/7HM ratio, DPs, and associated distributions are summarized for all 78 samples in **Table 2** and **Figure 1.**

Only 5 of the 78 samples did not contain other drugs or narcotics, of which three were L1, L2, and L3 of the same formula from the same vendor. Chlorpheniramine (CPM; n = 45), diphenhydramine (DPM; n = 38), ketamine (KET; n = 32), and caffeine (n = 31) were the most frequently detected compounds **(Figure 2).** The detailed DPs of each KT sample are presented in **Tables 3 and 4.**

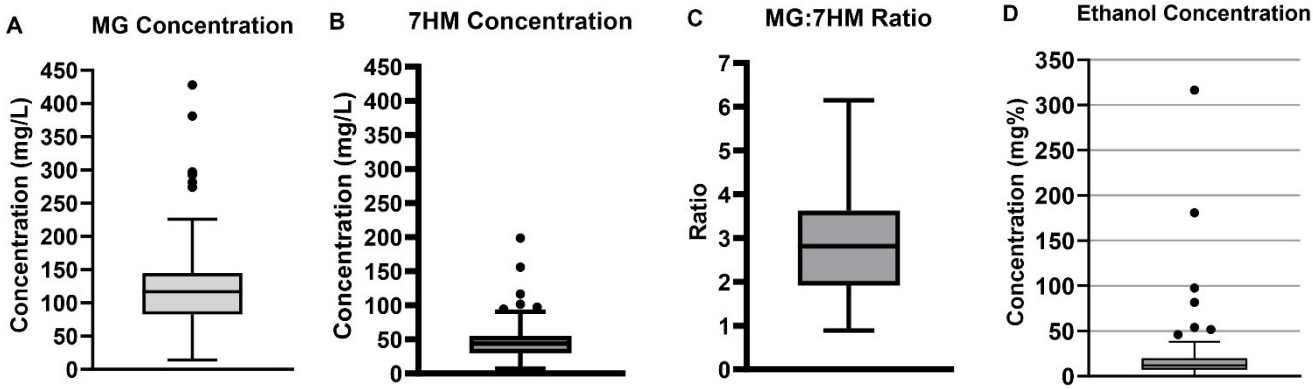

Figure 1. Distributions of MG concentration **(A)** 7HM concentration **(B)** MG:7HM ratio **(C)** and ethanol **(D)** for all samples.

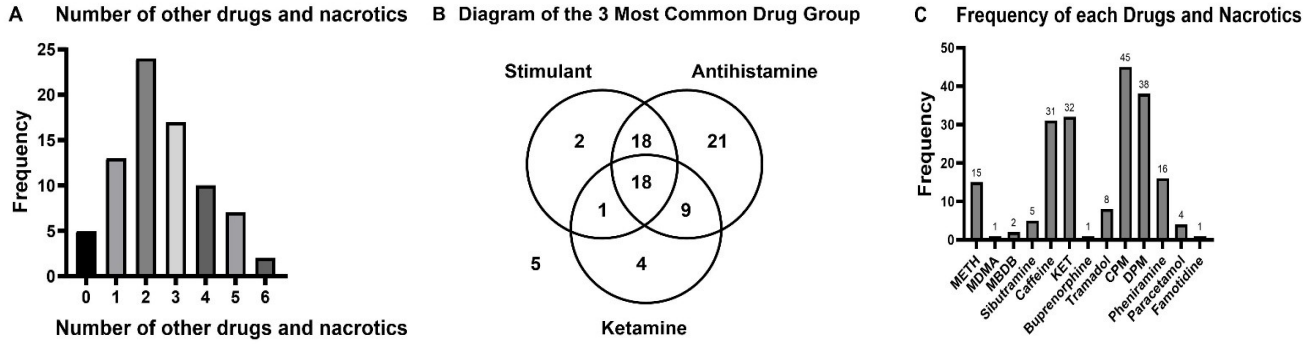

Figure 2. Frequency histogram showing the numbers of drugs and narcotics found in KTs **(A)** the relationship between the three most common drug groups **(B)** and the frequency of each drug and narcotics found in the samples **(C).**

Table 3. Drug profiles of kratom teas available only in L1.

Shop	A		B		C		D		E		G		I		K		L		Q	
Formula	D		D		D		D		D		D		S		D		D		S	
Sample	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
METH									●		●	●								
MDMA																				
MBDB																				
Sibutramine														●						
Caffeine	●	●	●	●							●	●			●	●			●	●
KET	●	●			●	●		●	●	●	●	●	●	●						
BPN																				
Tramadol							●	●												
CPM	●	●	●	●	●	●	●	●		●	●	●	●	●	●	●				
DPM	●	●	●	●			●	●			●	●			●		●	●	●	●
Pheniramine													●	●						
Acetaminophen																				
Famotidine				●																

D, Different; S, Same; METH, Methamphetamine; MDMA, 3, 4 -methylenedioxymethamphetamine; MBDB, N-methyl - 1, 3 - benzodioxolylbutanamine; KET, Ketamine; BPN, Buprenorphine; CPM, chlorpheniramine; DPM, diphenhydramine.

The frequently found drugs and narcotics were classified into three main types: stimulants [methamphetamine (METH), 3, 4 - methylenedioxy-methamphetamine (MDMA), N-methyl-1-(1, 3 - benzodioxol-5-yl)-2-butanamine(MBDB), sibutramine and caffeine], antihistamines [CPM, DPM, and pheniramine], and hallucinative KET. Most samples contained more than one drug type, particulary stimulants plus antihistamines. Indeed, antihistamines were found in most samples (n = 66) and 33 samples contained at least two antihistamines. Caffeine was the most common stimulant (n = 31), and 12 samples contained other stimulants in addition to caffeine.

Intralot consistency

Of the 14 S pairs, 9 were consistent for MG and 7HM. Similarly, 13 of 25 D pairs were consistent. Further, only 10 of the 14 S and 9 of the 25 D pairs had the same DPs. Of the four vendors that provided *S* KTs, only two produced samples with the same intralot DPs in all three lots. Nearly all pairs with different DPs (except the pair with no other drugs found in one of the samples) contained the same common additives plus one or two additional additives in one of the samples.

Overall, only 7 S pairs and 6 D pairs had consistency on both alkaloids and DPs, despite 3 of 7 S pairs coming from the same vendor from each purchase.

Interlot consistency

The interlot consistency was also low, as only 5 of 20 products from 5 sellers of L1 and L2 met the consistency criteria for alkaloids. Furthermore, only 4 of 18 products from 3 sellers met the criteria when comparing L2 with L3. Across all three lots, only 1 of 18 products met the consistency criteria for alkaloid contents. Furthermore, none of the sellers provided tea with the same DPs throughout L1 - L3 except for one seller who provided a formula without any added drugs.

Significant differences in the MG/7HM ratio were found between L1 and L2 ($P = 0.047$) and between L1 and L3 ($P = 0.029$), but not between L2 and L3.

Table 4. Drug profiles of kratom teas that were also available in L2 and L3.

Shop	F						H						J						M						N						O						R						S						T						P			
Formula	S						D						D						D						S						D						S						D						S			S			D			
Sample	1			2			1			2			1			2			1			2			1			2			1			2			1			2			1			2			1			2			1		2	
Lot	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	1	2
METH	●		●	●		●																																●			●										●			●	●	●	●	●
MDMA				●																																																						
MBDB	●			●																																																						
Sibutramine											●			●			●			●																																						
Caffeine	●		●	●							●						●		●	●	●	●	●	●									●	●															●	●		●	●	●	●		●	●
KET	●	●	●	●	●	●													●	●	●	●	●	●	●	●	●	●	●	●																			●			●					●	
BNP																																																										●
Tramadol											●			●			●			●																							●			●												
CPM			●			●				●	●	●			●	●		●	●		●	●		●			●			●	●		●	●		●	●		●	●		●	●		●	●		●			●			●	●		●	
DPM	●	●	●	●	●	●					●	●		●	●	●	●	●														●	●		●	●											●		●	●	●	●	●	●			●	
Pheniramine										●							●		●	●		●	●								●			●			●	●		●	●					●	●											
Acetaminophen										●	●	●		●																																												
Famotidine																																																										

D, Different; S, Same; METH, Methamphetamine; MDMA, 3, 4 - methylenedioxymethamphetamine; MBDB, N-methyl - 1, 3 - benzodioxolylbutanamine; KET, Ketamine; BPN, Buprenorphine; CPM, chlorpheniramine; DPM, diphenhydramine.

Table 5. Chemical stability of tested KT samples.

	Week 0	Week 1	Week 2	Week 4
MG (mg/L)	99.3 (54.7 - 297.2)	103.9 (57.4 - 294.8)	100.1 (61.2 - 291.8)	93.9 (9.6 - 282.4)
7HM (mg/L)	32.5 (22.8 - 94.6)	35.0 (21.9 - 99.6)	32.9 (22.9 - 95.1)	32.2 (1.2 - 98.3)
MG/7HM Ratio	2.8 (1.9 - 4.6)	2.8 (2.0 - 4.3)	2.8 (2.0 - 4.2)	2.7 (1.9 - 72.5)
pH	5.0 (5.0 - 5.0)	5.0 (4.0 - 5.0)	5.0 (4.0 - 5.0)	5.0 (4.0 - 6.0)
Ethanol(mg%)	11.2 (ND - 14.5)	-	-	16.2 (7.1 - 53.7)

ND, not detected

Stability testing

The stability results of 20 L2 samples are summarized in **Table 5**. Compared with those at week 0, no significant differences in MG concentration, 7HM concentration, MG/7HM ratio, and pH were found at weeks 1, 2, and 4 except for 7HM at week 1 with significantly high concentration ($P = 0.006$). However, the median change was only 4.3% (- 9.2% to 14.0%). In contrast, the median ethanol content of KTs stored at 4°C was significantly elevated at week 4. The remaining KTs stored at room temperature showed significant fermentation after 1 week. Bottles also became bloated, and contents emitted an alcoholic smell with increased viscosity. Six samples were randomly sent for bacterial and fungal culture; however, no pathological microorganisms were detected.

Discussion

In this study, the general characteristics and MG concentrations of the KT samples were similar to those previously reported in Thailand and Malaysia. [2, 11, 12] However, previous studies [15 - 17] did not report 7HM concentrations. In kratom leaves, the MG content is approximately 33 times higher than that of 7HM [5, 6, 21 - 23]; however, the median ratio in KTs was just 2.8 (0.9 - 6.4). Although producers may increased the 7HM concentration because of its greater potency [24], this is unlikely in Thailand because the final product would be too expensive. Rather, the relatively higher 7HM content likely results from the greater extractability in water during brewing because it is relatively more hydrophilic than MG. [12] Previous reports on KRMMs primarily focused on MG [5, 9, 10]; however, a low MG/7HM ratio and higher potency of 7HM [5 - 7, 22, 23] may be a critical determinant of the risk particularly in Southeast Asia, where KTs are one of the most common kratom products. Thus, pharmacokinetic studies are also required to determine whether this higher relative 7HM concentration results in proportionately higher blood 7HM concentrations and causes KRMMs.

The copositivity of other drugs and narcotics is also associated with KRMMs in Thailand and Western countries. [5, 7, 9, 10] This study provides evidence that at least some of the drugs associated with KRMMs are contained in the KTs rather than consumed with KTs in other forms. A retrospective study conducted in Thailand from 2015 to 2019 reported that METH and benzodiazepines were the most common psychoactive substances associated with KRMMs, whereas KET has never been reported. [9] In addition, marijuana is used frequently with KTs in Thailand. [7] However, in the present study, KET was the most common psychoactive substance in the products, whereas no cannabinoids were detected. In accordance with studies reporting a high frequency of stimulant and antihistamine ingestion by Thai kratom abusers [9, 11, 14], these agents were also common in the samples obtained from online vendors. Alternatively, the DPs of these Thai samples differed from those analyzed in several other countries, where opioids, stimulants, anxiolytics, antidepressants, antipsychotics, marijuana, and benzodiazepines, except KET have been associated with KRMMs. [5, 7, 10]

KET was also not mentioned among online Thai kratom communities in 2015 -2016 [14], thus, the addition of KET may reflect the overall local and global increases in KET abuse, as evidenced by the frequent detection of KET in seized materials. [25] This shift in DPs may reflect a general shift in consumer demands for the hallucinative effects of KET over the stimulative or opioid-like effects of kratom. [2, 3, 23] These changes again highlight the need for closer surveillance to facilitate both narcotic control and provide up-to-date information for therapeutic purposes.

In this study, MG concentrations differed substantially between vendors [12, 16, 17] and even between different lots from the same vendor. Although intralot inconsistencies were observed, most pairs tested in the same lot (whether S or D) had alkaloid ratios within 0.8 - 1.2. This finding suggests that vendors usually brew KTs before the addition of other drugs to tailor KTs into different formulas. However, when considering the total compositions, nearly no consistency was observed between the products, indicating that clinicians and forensic pathologists may not predict the causative substance in KRMMs, even with knowledge of the product ingested.

Many factors may contribute to the variations in alkaloid contents between samples and lots, including the tea preparation method, plant location, and maturity [12], and seasonal changes in phytochemistry. For instance, the difference in the MG/7HM ratio between L1 and L2 or L3 KTs may result from the use of plants harvested at the beginning (June) compared with that at the end of the rainy season (September and October). In addition, changes in the demand by online KT communities (e.g., for hallucinative effects rather than opioid-like effects) and differences in the availability of other additives may contribute to the variations in DPs. [14]

MG and 7HM were heat- and acid-labile [21, 26, 27] but stable for up to 30 days in solvents and biological samples under refrigeration. [12, 28 - 31] In addition, Trakulsrichai S, *et al*. [13] found that hospital-prepared samples without other additives, specifically sugars or syrups usually found in commercial products, were stable at 4°C for up to 14 days. In the present study, MG and 7HM were relatively stable in street KTs, of which the pH remained close to that of the simulated intestinal fluid [26, 27], because most measures did not change significantly over weeks under refrigeration, which is a reasonable storage period and condition for normal users. Although the 7HM concentration changed significantly from baseline at 1 week after refrigeration, the change was within the acceptable uncertainty of the analytical method. [19, 20]

Significant fermentation was detected by week 4, even under refrigeration, probably due to the sugar or syrup added. [1 - 3, 5, 7, 8, 11, 23] Although the increase in ethanol was significant, reaching approximately four times the baseline value in one sample, the change would not contribute to the psychoactive properties of the product because the ethanol content was still below 1.0% v/v. In addition, if kept unrefrigerated, KTs are probably unconsumable after 1 week, as indicated by the appearance of the unrefrigerated KTs.

After decriminalization, KTs has been publicly available for purchase across Thailand. Although the private use of KTs is not illegal, the consumption of KTs with other drugs or narcotics and the sale of consumable kratom products remain illegal. With lax enforcement of the law, KT sales may currently be exploited as an alternative means of selling. Thus, products to reduce the sale of those containing other drugs and narcotics, law enforcement agencies and online food delivery and shopping platforms should exercise greater control over the sale of kratom. Some platforms may already realize this problem as some products obtained in L1 were unavailable for subsequent purchase on the same platform. In addition, search terms such as “kratom” and “cough syrup” retrieved few products. This may be a strategy of the sellers to evade being banned by the platforms.

The limitations of this study include the small sample size, particularly for L2 and L3, because products are banned by the delivery platform. In addition, not all formulas available from each seller were purchased. Moreover, source information about tea preparations (such as the source and type of kratom leaves, additives, and preparation methods) was not recorded because asking the sellers could lead to sale refusal.

Conclusion

In this study, the concentrations of endogenous alkaloids (MG and 7HM) and exogenous drugs were assessed in Thai KTs sold through online food delivery platforms. The results demonstrate that the MG/7HM ratio is lower in KTs than in raw kratom leaves and appears to vary by harvesting season. More importantly, high inconsistency was observed among samples, even from the same vendor and lot. KET was the most prevalent among the added drugs, which also included various stimulants and antihistamines. The frequent addition of KET may reflect the general global increase in KET abuse. These analyses also suggest that these additives rather than the concurrent use of narcotics in other forms with KTs may result in multidrug intoxication. Therefore, studies such as this are needed to inform healthcare personnel, including clinicians, forensic pathologists, and law

enforcement officials about the current potential for various KRMMs. In addition, MG and 7HM in KTs were stable when stored at 4°C for 4 weeks.

Although kratom is decriminalized in Thailand, nearly all the products purchased here are illegal because of the addition of other drugs and narcotics, which indicates that its decriminalization is exploited by drug dealers. Stricter control of kratom products by both law enforcement agencies and online food delivery platforms must be implemented.

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Conflicts of interest statement

All authors have completed and submitted the International Committee of Medical Journal Editors Uniform Disclosure Form for Potential Conflicts of Interest. None of the authors disclose any conflict of interest.

Data sharing statement

This present review is based on the references cited. All data generated or analyzed in this study is included in this published article and the citations herein. Further details, opinions, and interpretation are available from the corresponding author on reasonable request.

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