



การศึกษารูปแบบของการเสพยาฝิ่นกระท่อมและพฤติกรรมการตายของผู้เสียชีวิตชาวไทยจาก
สถาบันนิติเวชวิทยา

The Study of Patterns of Kratom Abuses and Manner of Death in Thai Cadavers
from Institute of Forensic Medicine (IFM) in Thailand

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กลุ่มงานพิษวิทยา สถาบันนิติเวชวิทยา โรงพยาบาลตำรวจ

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บทคัดย่อ

ฝิ่นกระท่อม (*Mitragyna speciosa* Korth) เป็นพืชเสพติดที่มีถิ่นกำเนิดในประเทศไทย การเสพยาฝิ่นกระท่อมยังคงเป็นการกระทำที่ละเมิดกฎหมาย พบว่ามีการลักลอบเสพยาฝิ่นกระท่อมโดยวิธีการเคี้ยวใบสด ต้มดื่มแบบน้ำชาหรือสูบควัน ในกลุ่มผู้ใช้แรงงาน เพื่อทำให้อดทนและมีแรงทำงานได้มากขึ้น ปัจจุบันพบว่าการเสพยาฝิ่นในลักษณะที่ทำเป็นเครื่องดื่มน้ำต้มใบกระท่อมผสมยาแผนปัจจุบันหรือยาเสพติดที่รู้จักในชื่อ “สี่คูณร้อย” เพิ่มสูงขึ้นและมีความหลากหลายของส่วนผสมมากขึ้น ดังนั้นงานวิจัยนี้ จึงทำการศึกษาแบบย้อนหลังเป็นเวลา 3 ปี ถึงรูปแบบการเสพยา และพฤติกรรมการเสียชีวิต โดยเก็บข้อมูลผลการตรวจศพและผลตรวจทางพิษวิทยาในผู้เสียชีวิตคนไทยที่ส่งมาตรวจที่สถาบันนิติเวชวิทยา โรงพยาบาลตำรวจจากการศึกษาพบว่าร้อยละ 0.94 (90 ราย) มีการเสพยาฝิ่นกระท่อม โดยพบรูปแบบการเสพยาที่แตกต่างกันถึง 34 รูปแบบ มีเพียง 1 รูปแบบที่เสพยาเพื่อเพิ่มประสิทธิภาพในการทำงาน (ร้อยละ 24.4) ส่วนอีก 33 รูปแบบ เป็นการเสพยาเพื่อความบันเทิง นอกจากนี้พบว่า มีการใช้ยาเสพติด (เช่น เมทแอมเฟตามีนและกัญชา) และ/หรือ ยาแผนปัจจุบัน (เช่น ไดเฟนไฮดรามีน, ไฮดรอกซีซีน, เซทิริซีน, ไดอะซีแพม, โคเดอีน, และเด็กโพรเมทอร์ฟาน เป็นต้น) ผสมลงในเครื่องดื่มน้ำต้มใบกระท่อมหรือเสพยาพร้อมกันด้วย จากความแตกต่างในเรื่องสูตรการเสพยา “สี่คูณร้อย” ดังกล่าว การออกกฎหมายเกี่ยวกับการอนุญาตให้การเสพยาฝิ่นกระท่อมได้โดยไม่ผิดกฎหมายนั้น จึงควรมีการพิจารณาให้รอบคอบและรัดกุม รวมถึงผู้ที่เกี่ยวข้องทางด้านสาธารณสุขควรมีการบริหารจัดการกับแนวโน้มการนำฝิ่นกระท่อมมาใช้ในทางที่ผิดที่เปลี่ยนแปลงไปอย่างเหมาะสมด้วย

คำสำคัญ: ฝิ่นกระท่อม, ไมตราเจนนิน, ยาเสพติด, ผู้เสียชีวิตคนไทย, การใช้ยาในทางที่ผิด

Abstract

Kratom (*Mitragyna speciosa* Korth) is a highly addictive plant indigenous to Thailand. Kratom is still categorized as a Penal Drug under Category-5 of the Narcotics Act 2522 (1979), thus its usage is still illegal. Kratom, on the other hand, has been smuggled



and utilized by laborers or farmers to boost output by chewing fresh, smoking, or making an extract. Recently, a popular new recreational Kratom cocktail known as '4x100' has gained popularity and comes in a variety of formulations. As a result, a retrospective study of the patterns of Kratom misuse and manner of death in Thai cadavers was conducted. Data from Thai cadavers' autopsies and toxicology reports were collected and examined during a three-year period at IFM. The discovery of Kratom usage in 0.94% of Thai cadavers (90 cases). The study discovered 34 different addictive patterns, with just one pattern (24.4%) being used as a typical doping agent to enhance work efficiency, and the rest 33 patterns (75.6%) suggesting that they were used as recreational drugs. This group finding narcotic (i.e. Methamphetamine, Cannabis and Ketamine) and/or medicine (i.e. Diphenhydramine, Chlorpheniramine, Promethazine, Hydroxyzine, Cetirizine, Clonazepam, Diazepam, Midazolam, Alprazolam, Methadone, Codeine and Dextromethorphan) mixed in Kratom cocktail or consume together. As a result of the many Kratom abuse patterns, the legislation controlling "Kratom consumption" must be meticulously and firmly created, and those involved in public health-therapy must appropriately address the changing trend of Kratom abuse.

Keywords: Kratom, Mitragynine, narcotic, Thai cadavers, drug abuse

Introduction

Kratom (*Mitragyna speciosa* Korth) is a native plant habitat in tropical regions of South-East Asia, particularly in Thailand and Malaysia. The leaves of Kratom contain active alkaloid substance, known as 'Mitragynine', which has addictive qualities. In Thailand, Kratom is categorised as a Penal Drug in Category-5 under the Narcotics Act 2522 (1979), with a punishment for consumption of no more than a month in prison or a fine of no more than 2,000 Baht. Although the most recent law declares areas of Kratom to be addictive, such legislation has not yet to be legally enacted and the use of Kratom thus remains illegal in Thailand. However, Kratom has been smuggled used by laborers or farmers to enhance productivity by chewing fresh, smoking it, or making it into an extract.

Objectives

The objective of this study is to study of the patterns of Kratom abuses and manner of death in Thai cadavers.

Literature review

Recently, new recreational Kratom beverages called '4x100' (pronounced: sii koon roi) that origin in Thailand become popular. 4x100 is a homemade Kratom cocktail that is



popular in adolescents as a recreational drug beverage similar to alcohol. These cocktails include boiling Kratom extract, sweet-soft drink, cough or antihistamine syrup and psychotropic substances such as Benzodiazepine- anxiolytic or narcotic drugs. Consumption of 4x100 Kratom cocktail might result in fatal effects owing to multidrug overdose (Tungtanuwat & Lawanprasert, 2010, pp. 43-47).

According to a report from the United Nations Office on Drugs and Crime (UNODC), internet surveys conducted by the EMCDDA in 2008 and 2011 revealed that Kratom is one of the most widely offered New Psychotropic Substance (NPS) and respondents to the UNODC questionnaire on NPS identified Kratom as one of the top three plant-based meats, along with Khat and *Salvia divinorum* (Laboratory and Scientific Section, United Nations Office on Drugs and Crime, 2013).

In summary, Kratom is used for two purposes: 1) used for enhancing work efficiency, and 2) used as recreational drugs. Institute of Forensic Medicine (IFM) of Royal Thai Police Headquarter is in charge of the medical examinations in a quarter of the area of Bangkok. Cadavers with unknown causes and manners of death, as well as unnatural death cases, were sent here for autopsies. Therefore, the autopsy report contains significant medical information and information concerning Kratom use is undoubtedly included in this autopsy report.

Because Thailand is a habitat for Kratom plants and is the origin of the various forms of Kratom uses, the authors have attempted to examine the patterns of Kratom uses in Thai cadavers sent to IFM for autopsy. The findings of this study can be used to assess the severity of Kratom problem and plan in the future.

Materials and methods

This was a retrospective study. Autopsy records were collected from the Pathology division of IFM, and toxicological reports were acquired from the Toxicology division of IFM from January 2016 to December 2018. Of the 9,549 cases, 90 cases (0.94%) were detected positive results with Mitragynine, which has been confirmed by Automated Liquid Chromatography / Mass Spectrometry (Toxyper™ 2.0) and they were collected for study. The study was approved by the Ethics Committee on Human Experimentation of Police General Hospital. Concerning data analysis, SPSS version 17 was used for statistical analysis.

Result

The study on the patterns of Kratom uses indicated that there are 34 different patterns, which can be divided into 4 groups as follows.



Group 1: The groups of Kratom users. In this group, the urine analysis of these groups detected only Mitragynine alkaloids from the Kratom plant, but any other drugs, narcotic or psychotropic substances were not detected. This group comprises 22 cases.

Group 2: The groups of Kratom and narcotic drug users. The urine analysis detected Mitragynine alkaloids and various narcotic drugs. But any other drugs or psychotropic substances mixed like the formula 4x100 were not detected. Narcotic drugs in this group have various drug use methods, such as Methamphetamine (ice) or cannabis, which Thai people like to consume by smoke. Thai people, on the other hand, like to consume ketamine via a snort method. This group consists of 20 cases and 4 patterns were discovered. The most prevalent tendency in this group is the use of Kratom in conjunction with methamphetamine (60%, 12 cases), followed by the use of Kratom in conjunction with Cannabis (25%, 5 cases) as seen in Table1.

Table 1 Urine analysis of Group 2 Kratom (non 4x100 formula) and narcotic drug users

Patt ers	Kratom alkaloids	Narcotic drugs	N	Percentage
1	Mitragynine	Metamphetamine (Meth)	12	60.0
2	Mitragynine	THC-COOH (11-nor-9-Carboxy-THC from Cannabis)	5	25.0
3	Mitragynine	Ketamine	1	5.0
4	Mitragynine	Metamphetamine + THC-COOH	2	10.0
Total			20	100.0

Group3: Groups of Kratom cocktail 4x100 formula users. This group mixes Kratom juice with medicine or psychoactive drugs. Users combine sleep or drowsiness-inducing medications with a 4x100 Kratom mixture. The urine analysis of these groups detected antihistamine drugs or Cough medicine such as Chlorpheniramine (CPM), Promethazine, Hydroxyzine, Cetirizine and Diphenhydramine. Some formulas contain Benzodiazepines-anxiolytic drugs such as Clonazepam, Diazepam, Midazolam and Alprazolam. Opiates/opioids, such as Methadone, Codeine, Dextromethorphan, were detected in a small number of cases. The drugs mentioned above are usually found in the form of pills and syrup, which is easy to mix with Kratom juice before drinking.

In this group, there were 21 cases and 11 patterns. The pattern of using 4x100 Kratom juice with benzodiazepines anxiolytic drugs is the most common form in this group (33.3%, 7 cases), followed by those using Kratom juice with Benzodiazepines and Diphenhydramine (23.8%, 5 cases) as seen in Table2.



Table 2 Urine analysis of Group 3: 4x100 Kratom cocktail users

Patterns	Kratom alkaloids	Narcotic drugs	Medication or psychotropic substances	N	Percentage
1	Mitragynine	-	Benzodiazepines (BDZ)	7	33.3
2	Mitragynine	-	BDZ + Diphenhydramine	5	23.8
3	Mitragynine	-	BDZ + Tramadol + Hydroxyzine + Chlorpheniramine	1	4.8
4	Mitragynine	-	BDZ + Tramadol	1	4.8
5	Mitragynine	-	BDZ + Opiates	1	4.8
6	Mitragynine	-	BDZ + Methadone + Promethazine	1	4.8
7	Mitragynine	-	Diphenhydramine	1	4.8
8	Mitragynine	-	Opiates	1	4.8
9	Mitragynine	-	Chlorpheniramine	1	4.8
10	Mitragynine	-	Tramadol + Hydroxyzine	1	4.8
11	Mitragynine	-	Tramadol + Diphenhydramine	1	4.8
Total				21	100.0

Group 4: Kratom juice cocktail (4x100 formula) and narcotic drug users. In this group, four of narcotics were detected, i.e., Methamphetamine, Ecstasy (MDMA), Cannabis (THC-COOH) and Ketamine. There were 27 cases and 18 patterns indicated in this group as illustrated in Table3.

Table 3 Urine analysis of Group 4: Kratom juice cocktail (4x100) with narcotic users

Patterns	Kratom alkaloids	Narcotic drugs	Medication or psychotropic substances	N	Percentage
1	Mitragynine	Meth	Diphenhydramine	3	11.1
2	Mitragynine	Ketamine	BDZ + Diphenhydramine	3	11.1
3	Mitragynine	Meth	BDZ	2	7.4
4	Mitragynine	Meth	BDZ + Hydroxyzine	2	7.4
5	Mitragynine	Meth + THC-COOH	Tramadol	2	7.4



Patterns	Kratom alkaloids	Narcotic drugs	Medication or psychotropic substances	N	Percentage
6	Mitragynine	THC-COOH	BDZ	2	7.4
7	Mitragynine	THC-COOH	BDZ + Diphenhydramine	2	7.4
8	Mitragynine	Meth	BDZ + Diphenhydramine + Opiates	1	3.7
9	Mitragynine	Meth + THC-COOH + Ketamine	Tramadol	1	3.7
10	Mitragynine	Meth + THC-COOH + Ketamine	Tramadol + Diphenhydramine	1	3.7
11	Mitragynine	MDMA + Ketamine	Diphenhydramine	1	3.7
12	Mitragynine	THC-COOH	Tramadol	1	3.7
13	Mitragynine	THC-COOH	Hydroxyzine	1	3.7
14	Mitragynine	THC-COOH	Tramadol + Hydroxyzine	1	3.7
15	Mitragynine	THC-COOH	Opiates + Diphenhydramine	1	3.7
16	Mitragynine	THC-COOH + Ketamine	Tramadol + Hydroxyzine	1	3.7
17	Mitragynine	Ketamine	BDZ + Tramadol + Opiates + Hydroxyzine	1	3.7
18	Mitragynine	Ketamine	Tramadol + Diphenhydramine + Hydroxyzine	1	3.7
Total				27	100.0

Next, information about ages, genders and manner of death of 90 samples were illustrated in Table 4.



Table 4 Distribution of age, sex, and manner of death by groups of 4 patterns of Kratom users

	Age (years)			Gender		Manner of death				
	Mean	S.D.	Range	male	female	Undetermined	Accident	Homicide	Suicide	Total
Group1: Kratom users	48.9	14.3	17-74	22	0	13 (59.1%)	5 (22.7%)	1 (4.5%)	3 (13.6%)	22 (100.0%)
Group2: Kratom with narcotic users	33.2	11.9	15-52	20	0	7 (35.0%)	8 (40.0%)	4 (20.0%)	1 (5.0%)	20 (100.0%)
Group3: Kratom juice cocktail users (4x100)	23.9	7.0	15-41	19	2	6 (28.6%)	10 (47.6%)	4 (19.0%)	1 (4.8%)	21 (100.0%)
Group4: Kratom juice cocktail (4x100) with narcotic users	26.8	10.0	16-59	26	1	5 (18.5%)	14 (51.9%)	5 (18.5%)	3 (11.1%)	27 (100.0%)
Total	33.0	14.6	15-74	87	3	31 (34.4%)	37 (41.1%)	14 (15.6%)	8 (8.9%)	90 (100.0%)

Discussion

When analyzing the age problem, Table 4 above revealed that group 1 had the greatest average age of 48.9 ± 14.3 years (ranging from 17 - 74 years), whereas groups 3, 4, 2 had the lowest average age and a smaller age range, respectively. Probably since group 1 mainly took Kratom to enhance their work efficacy, and they primarily died from unknown causes (59.1 percent, 13 instances), an examination of the autopsy report reveals that 2 cases died from infection and 11 cases died from respiratory and cardiovascular failure. On the other hand, the groups 2, 3, 4 used Kratom as recreational drugs and tended to be young and live life to the fullest, thus they were more likely to die in accidents.



Group 3 is a young age (23.9 ± 7.0 years) group of 4x100 users that began the addiction process and did not have enough money to earn high-cost narcotic drugs.

In this study, in total of 18 cases of undetermined manner of death of the groups 2, 3, 4 (with the average age of 32.33 ± 12.9 years), it revealed that 16 cases died from respiratory and cardiovascular failure with drugs and narcotics detected. That may be presumed to be the result of multi-drugs effect which is in accordance with the study of Tungtanuwat and Lawanprasert (2010, pp. 43-47)

Concerning the genders, of the total of 90 samples, only 3 females with the ages ranging from 17-24 years old died from the accidents. The possible explanation of such a small number of women is that Thai young women are concerned that use of Kratom that it may cause dull skins. In addition, 2 female cases were classified into the group 3 (one with a positive Mitragynine + Benzodiazepines + Tramadol in urine and the other one with positive Mitragynine + Diphenhydramine, as seen in Table 2 in the patterns 4 and 7). Moreover, another 1 female case was classified into the group 4, with positive Mitragynine + THC-COOH + Opiates + Diphenhydramine in urine, as seen in Table 3 in the pattern 7, indicating that this female group preferred to consume 4x100 kratom juice cocktails.

The findings of this study revealed that Kratom users consumed some other narcotics with it, such as Methamphetamine (N=27, 30.0%) > Cannabis (N= 20, 22.2%) > Ketamine (N=10, 11.1%), respectively.

Because Thailand has a significant pandemic of methamphetamines abuses, and methamphetamine users frequently utilize additional drugs. As a result, Methamphetamine is a popular narcotic used among kratom abusers. Methamphetamine abuse alone was associated with a 4-fold increase in risk for cerebral-cardiovascular defects (Tungtanuwat & Choenkhwanma, 2009, pp. 147-151) while use of methamphetamine in combination with other drugs or narcotic increases the chance of death.

From Table 1, Group 2, in Pattern 2, Kratom, and Cannabis are typically use in different methods, however they have been discovered to be utilized together, with user mixing dried Kratom leaves with Cannabis to smoke in order to cut Cannabis costs. As a result, the consuming method is unclear in Pattern 2.

Ketamine is a dissociative anesthetic and a recreational substance of abuse, though death from acute direct toxicity is uncommon (Bokor & Anderson, 2014, pp. 582-586). In all of the 10 cases of Ketamine users, the majority of 9 cases were classified in Group 4, indicating that 4x100 users preferred to take Ketamine together. According to the data analysis, 7 out of 10 cases died in road accidents, which may be due to Ketamine impairing driving capacity and cognitive function (Zhuo et al., 2010).



The most often used medications and psychotropic substances in the in 4x100 mixed formula are Benzodiazepine (N=28, 31.1%) > Diphenhydramine (N= 19, 21.1%) > Tramadol (N=13, 14.4), respectively.

For Benzodiazepine – anxiolytic drugs, Alprazolam is most widely used. Alprazolam, or known as “Mano” or “Zolam” in Thailand, is a short acting sedative drugs with a flatter dose-response curve than other sedative-hypnotics and exhibit a low incidence of toxicity in humans (Tungtananuwat & Lawanprasert, 2010, pp. 43-47). In agreement with the studies of Shah et al. (2012) and Michaud et al. (1990), who reported the fatal case of alprazolam and tramadol overdose, Wolf et al. (2005) also found that alprazolam alone was seldom a cause of death, but death was invariably attributable to combination drug toxicity.

Tramadol and its active metabolite, O-desmethyltramadol, are frequently discovered in urine of 4x100 Kratom cocktail users (groups 3 and 4), who prefer to combine it together to make a potent cocktail. Because Mitragynine, Tramadol and its metabolite are mu-receptor agonists, using them together increases the unintentional overdose and death (Kronstrand et al., 2011). Tramadol can produce CNS side effects such as headache, nausea, vertigo, drowsiness, and somnolence at therapeutic doses. In case of poisoning, seizures and other serious consequences may develop. Tramadol's ability to cause seizures may be exacerbated when used with any drug that might lower the seizure threshold, such as methamphetamine, methadone, or Amitriptyline. Decker et al. (2008) reported one case of fatal intoxication caused by tramadol alone, and Goeringer et al. (1997) documented mortality instances caused by tramadol combined with other drugs. Although Tramadol is currently upgrading to controlled drug by Medicine Act B.E. 2510, it is still being trafficked on the black market.

Nowadays, Diphenhydramine pills or syrup are no longer available in the marketplace, yet urine positive because of 4x100 users use Dimenhydrinate antihistamine instead, which metabolites to Diphenhydramine in the end. Diphenhydramine is inexpensive (1 Baht per pill), and its pharmacologic effect can enhance dopaminergic neurotransmission in the mesolimbic pathway, which is considered to be responsible for rewarding properties (Thomas et al., 2009), therefore Diphenhydramine formula were popular.

From Table 2, Group 3, Pattern 6, approximately five years ago, combined 4x100 with Alprazolam and Promethazine cough syrup was a very popular combination called “Ya-Pro,” but today Promethazine is regulated, therefore this formula is declining in popularity.

From a criminal point of view, Groups 2, 3 and 4 that used Kratom as recreational drugs, indicated dead from Homicide at a similar rate, and seemingly greater than Group



1, as seen in Table 4. Also, those who died from being shot could confirm that this pattern of Kratom abuses can also raise crime risk.

Conclusion

During the three-year data collecting period, 0.94 percent of Thai cadavers (90 instances) showed Kratom usage, which appears to be a high amount, although the actual numbers may be higher. The study discovered 34 distinct addiction patterns, with just one pattern (24.4 percent, group 1) using Kratom as a typical doping agent to enhance work efficiency, and the remaining 33 patterns (75.6%, Groups 2, 3 and 4) using Kratom as a recreational drug. This data pattern is more prevalent than was previously observed in Thailand in 2013. Trakulsrichai et al. (2013) Furthermore, this study found that recreational Kratom users are at a higher risk of murder and accidental death than a group of Kratom users.

Suggestion

As a result of the many Kratom abuse patterns, the legislation controlling "Kratom consumption" must be meticulously and firmly created, and those involved in public health-therapy must appropriately address the changing trend of Kratom abuse.

The penalty rate is relatively low because to the high expense of analyzing mitragynine in biological materials. As a result, there is no broad research. All historical studies It is frequently the subject of the funeral examination. As a result, if further research were conducted on the suspects, the mean concentration levels discovered in Thai individuals would be known. This enables the parameters for establishing the Mitragynine cut-off value in Thai individuals to be determined. However, future studies should take into consideration the restrictions on biological sample collection, standard chemicals, and research expenditures, which are equally costly.

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