Pravalence of Mitragynine in Forensic Autopsy Cases at the Forensic Investigation Center Chulalongkorn University from 2022 to 2023

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Abstract:

Background: Mitragynine is an active compound found in Kratom, a substance experiencing growing usage both in Thailand and globally. While Kratom is commonly perceived as safe with minimal adverse effects, instances of fatalities associated with its use and misuse have been documented.

Objective: Investigating the prevalence of mitragynine in forensic autopsy cases from 2022 to 2023. Analyzing demographic data, causes of death, and proposed lethal level.

Materials and Method: A retrospective study was conducted on the forensic toxicological analysis of 213 forensic autopsy cases from 2022 to 2023 at the Forensic Investigation Center of Chulalongkorn University.

Results: The prevalence of positive mitragynine findings rose significantly from 3.14% in 2021 to 13.39% in the years 2022-2023. The male-to-female ratio was approximately 9:1. The common causes of death were attributed to traffic accidents, undetermined and cardiovascular diseases. Mitragynine concentrations varied widely, ranging from 0.10 to 1,423.23 ng/mL, with a mean concentration of 109.85 ng/mL. However, a definitive proposed lethal level could not be determined based on the data analyzed.

Conclusion: The increasing use of kratom, coupled with the rising number of deaths associated with its consumption, necessitate a comprehensive reassessment of its safety profile. A thorough study on its safe usage, including potential positive effects and adverse reactions, is imperative. Additionally, regulatory measures governing kratom distribution and consumption require re-evaluation to ensure public safety and mitigate the risks associated with its use and misuse.

Keywords: Mitragynine, Kratom, Prevalence, Forensic autopsy

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Introduction

Kratom *(Mitragyna speciosa)* is a tropical plant indigenous to Southeast Asia. In Thailand, tradition use of kratom is prevalence in the southern region, as an herb for increasing energy, reducing fatigue, relieving pain, antidiarrhea and recreational purposes to enhance euphoric, sociability and sexual desire.[1] Kratom was classified and controlled as a schedule 5 substance under Thailand's Narcotic Act of 1979. However, kratom was removed from the list of prohibited narcotic substance in 2021.[2] This alteration in classification has contributed to the increasing popularity of kratom. Since kratom is perceived to be safe and illegal in many countries, it has been popular in recent years globally and classified as a new psychoactive substance (NPS).[3]

Mitragynine is an active component of kratom leaves. It acts as opioid receptors agonist, alpha2-adrenoreceptor agonist and 5-HT_{2A} receptor antagonist. The use of kratom has been linked to various adverse reactions, including agitation, tachycardia, nausea, drowsiness, lethargy, hypertension, confusion, seizures, and in rare instances, renal failure and cardiac arrest.[1,4]

Several case reports linking mitragynine-related death have indicated polysubstance uses. Cotinine, diphenhydramine, ethanol, mirtazapine, naloxone, o-desmethyltramadol, propylhexedrine, quetiapine, temazepam were among the substances identified in polydrug cases, with mitragynine concentrations ranging from 10 to 4,800 ng/mL.[5,6] Our investigation into the presence of mitragynine in forensic autopsy cases aims to elucidate related demographics, causes of death, and potentially establish a lethal level of mitragynine. The study site is situated in Bangkok, the capital city of Thailand.

Materials and method

This retrospective study was conducted using forensic toxicological analysis of 213 forensic autopsy cases obtained from the Forensic Investigation Center at Chulalongkorn University during the years 2022 and 2023. The study focused on examining demographic information, causes of death, and the presence of co-exposure substances in the analyzed cases.

The forensic toxicological analysis of drugs and narcotics in blood was conducted using a validated LC/MS-MS method by the Forensic Toxicology Laboratory within the Department of Forensic Medicine at Chulalongkorn university.

Statistical analysis

Mean, median and range were analyzed by Microsoft Excel 2021.

Results

Among the 1,591 forensic autopsy cases examined, mitragynine was detected in 213 cases, comprising 13.39% of the total sample. The majority of these cases were Thai nationality, accounting for 193 cases (90.61%), followed by individuals from other Asian countries, totaling 15 cases (7.04%), with the remaining 5 cases (2.35%) attributed to individuals of other nationalities. Of the cases with positive mitragynine findings, 197 were male and 16 were female, resulting in an estimated male-to-female ratio of 9:1. The demographic data are summarized in Table 1.

The predominant co-exposure substances detected alongside mitragynine included caffeine, antihistamines, ethanol, methamphetamines, and benzodiazepines. Notably, instances of sole mitragynine use were not observed within the examined cases. Additionally, other substances identified in this study encompassed

sildenafil, metformin, amlodipine, quetiapine, gabapentin, zolpidem, LSD, and cocaine, as detailed in Table 2. During the study period, new psychoactive substances (NPS) such as estazolam, fentanyl, JWH-073, and methcathinone were also identified.

The related causes of death observed in the analyzed cases predominantly included traffic accidents, undetermined circumstances, and cardiovascular diseases, as depicted in Table 3.

The concentrations of mitragynine detected in the bodies of the individuals examined ranged from 0.10 to 1,423.23 ng/mL (mean 109.85 ng/mL), as shown in Table 4.

Table 1 Demographic data of forensic autopsy cases with the presence of mitragynine

Year	Demographic data					
	Gender		Age (years)		Nationality	
	Male	Female	range	mean	Thai	Others
2022	88 (91.7 %)	8 (8.3 %)	3 mo. -66 y	32.83	87 (90.6 %)	9 (9.4 %)
2023	109 (93.2 %)	8 (6.8 %)	15 – 74	33.76	106 (90.6 %)	11 (9.4 %)

Table 2 Substances found in the forensic toxicological analysis along with mitragynine

Drugs and narcotics	2022	2023
Caffeine	49	86
Antihistamine	40	50
Ethanol	36	26
Methamphetamine	21	16
Benzodiazepine	12	13
Morphine	7	8
Tramadol	7	14
Ketamine	10	6
THC	0	3
Others	26	37

Table 3 Causes of deaths attributed to mitragynine

Cause of death	2022	2023
Traffic accident	27 (28.1 %)	35 (29.9 %)
Cardiovascular disease	16 (16.7 %)	23 (19.7 %)
Undetermined	19 (19.8 %)	32 (27.4 %)
Asphyxia	9 (9.4%)	10 (8.5 %)
Fall	5 (5.2 %)	5 (4.2 %)
Gun shot	3 (3.1 %)	3 (2.6 %)
Drowning	4 (4.2 %)	0
Others	13 (13.5 %)	9 (7.7 %)
Total	96	117

Table 4 Mitragynine concentration in forensic autopsy cases

Year	Gender	Mitragynine level (ng/mL)	
		range	mean
2022	male	0.19 – 1,198.73	134.49
	female	0.35 - 675	111.26
2023	male	0.10 – 1,423.23	118.58
	female	0.29 – 487.56	75.07

Discussion

The true prevalence of kratom use and misuse remains uncertain. However, based on the findings of this study between 2022 and 2023, kratom was detected in up to 13.39% of the forensic autopsy cases, compared to 16 cases out of 510 (3.14%) in the year 2021.[2] Traffic accidents, cardiovascular diseases, and undetermined causes were identified as the major causes of death, with mitragynine potentially exerting direct or indirect effects contributing to these outcomes. In some cases of asphyxia and gunshot fatalities, mitragynine was identified as a coincidental finding.

A study conducted at Ramathibodi Hospital, another forensic center in Bangkok, spanning from 2015 to 2019, revealed the presence of mitragynine in approximately 1% (24 from 2,160) of the autopsy cases, predominantly affecting 96% of males.[7] The most common cause of death identified in the study was traffic accidents, with concurrent poly-drug usage being notably prevalent.

A case report detailing a single mitragynine-associated death revealed a blood mitragynine level of 950 ng/mL.[8]

It is critical to state the lethal concentration of mitragynine because of the potential effects of co-intoxicants, variation in individual metabolism, and methamphetamine and opioid tolerance. Postmortem change of mitragynine has not been clearly studied. Data on redistribution, stability, and other factors essential for

interpreting cases are currently unavailable. The synergistic toxicity of mitragynine in conjunction with other drugs targeting opioid and adrenergic receptors in the central nervous and cardiovascular systems may contribute to severe adverse effects and potential lethality.

Notably, our study revealed instances where individuals with mitragynine levels exceeding 1,000 ng/mL were still alive, while a death case report documented a single use with a level of 950 ng/mL. Conversely, some cases in our study exhibited mitragynine levels below 100 ng/mL but were complicated by co-intoxication and underlying diseases. Due to the diverse factors influencing the effects of mitragynine, a definitive proposed lethal concentration of mitragynine could not be established based on the available data. However, based on case reports highlighting the adverse effects of kratom ingestion on traffic safety and its association with fatalities, we propose that a blood concentration of mitragynine exceeding 25 ng/mL should be established as the cutoff point for driving impairment. Furthermore, levels surpassing 1,000 ng/mL may be indicative of sole mitragynine intoxication leading to death.[9]

Given these complexities and the absence of established toxic and lethal levels, it is the responsibility of forensic pathologists and toxicologists to meticulously gather and analyze all pertinent data to accurately interpret the effects of mitragynine found in each case.

In other Southeast Asian countries, kratom remains illegal and is regulated in Laos, Malaysia, Myanmar, Singapore, and Vietnam. In contrast, it is legal in Cambodia, the Philippines, and Indonesia.[10]

Analyzing the benefits and adverse effects of kratom reveals that some of its medicinal uses do not offer advantages over standard and traditional treatments. Most users consume kratom for recreational purposes or in conjunction with other narcotics. Although this study was conducted in the capital city, it may reflect trends in other major cities, suggesting an increasing use of kratom. Therefore, we recommend that kratom be regulated under narcotics legislation, as it has been in the past.

Conclusion

The number of deaths were attributed or possibly associated with kratom use or misuse. Traffic accident, undetermined and cardiovascular diseases were noted with mitragynine findings. Polysubstance use could be traced back to the original kratom product. The growing use and misuse of kratom, particularly following its removal from the Narcotic Act in Thailand, pose significant concerns. Therefore, there is a pressing need to reassess both the safety protocols surrounding its use and the regulatory framework governing its distribution and consumption.

Conflict of interest

The authors declare they have no conflicts of interest with the content of this article.

References

1. Warner ML, Kaufman NC, Grundmann O. The pharmacology and toxicology of kratom: from traditional herb to drug of abuse. Int J Legal Med. 2016;130 (1):127-38.
2. Towithelertkul C, Tansrisawad N. Epidemiology of blood kratom and cannabis detection from postmortem autopsy at the Forensic Medicine Department of Chulalongkorn University before and after the change of narcotic laws in Thailand. J Crim and Forensic Sci. 2023; 9 (1): 37-52.
3. Davidson C, Cao D, King T, et al. A comparative analysis of kratom exposure cases in Thailand and the

United States from 2010-2017. Am J Drug Alcohol Abuse. 2021; 47 (1): 74-83.
4. Coonan E, Tatum W. Kratom: The safe legal high?. Epilepsy Behav. 2021; 117: 107882. doi:10.1016/j.yebeh.2021.107882
5. Striley CW, Hoeflich CC, Viegas AT, et al. Health effects associated with Kratom (Mitragyna speciosa) and polysubstance use : a narrative review. Subst Abuse. 2022;16:1178221822 1095873. doi:10.1177/1178221822 1095873
6. Behonick GS, Vu C, Czarnecki L, El-Ters M, Shanks KG. Two single-drug fatal intoxications by mitragynine. J Anal Toxicol. 2022; 46 (5): e110-e114. doi:10.1093/jat/bkac016
7. Jittasopa W, Srisont S. The causes of death and pathological findings of Kratom users: a 5-year retrospective analysis. Am J Forensic Med Pathol. 2021; 42 (4): 335-40.
8. Schmitt J, Bingham K, Knight LD. Kratom-associated fatalities in Northern Nevada-What mitragynine level is fatal?. Am J Forensic Med Pathol. 2021; 42 (4): 341-9.
9. Papsun D, Schroeder II W, Brower J, Logan B. Forensic implications of Kratom: Kratom toxicity, correlation with mitragynine concentrations, and polypharmacy. Curr Addict Rep. 2023; 10 : 272–81.
10. The Transnational Institute. Kratom in Myanmar and Southeast Asia: time for legal regulation? [Internet]. 2021 [cited October 11,2024].Available from: https://www.tni.org/en/article/kratom-in-myanmar-and-southeast-asia-time-for-legal-regulation.