

TREND OF KETUM USE IN KELANTAN

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Name and

KETUM PLANT: INTRO

Ketum (*Mitragyna speaciosa*) is the tree indigenous to South East Asia which can grow up to 30 metres

Synonims: biak-biak (Malaysia) and kratom (Thailand)

The leaf veins: red, green and white

About 40 alkaloids: Mitragynine (MG), 7-HydroxyMG, speciociliatine, and corynantheidine.

Traditionally, Consumed by and recreational/herbal drink like tea or smoked (rarely)used for energy booster and treat variety of diseases.





PREPARATION OF KETUM JUICE

The fresh ketum leaves are boiled with water in a pot.

Then, the preparation is left to brew at low heat (max: 4 hr).

It is stirred frequently (prevent the leaves get stuck on the surface and burn-will emit an unpleasant burnt taste).

When it has been brewed properly, it emits a strong odour.

The brewed ketum juice is left to cool before being packed into small plastic bags and sold for consumption.

The packets are also chilled with ice to enable it to last for about 3 days.





INTRO:PHARMACOLOGY

Generally, small dose effect acted as stimulant (like cocaine). While large dose shows analgesic properties and produces sedative effect like opiate (Tavakoli et al., 2017).

Consumed traditionally for energy booster, pain killer and treat variety of diseases.

Such as intestinal diseases, muscle pain, coughing and diarrhea (Malaysia, Thailand)

A few Studies suggest: as antipyrectic, euphoric, antidepression





INTRO:TOXICOLOGY

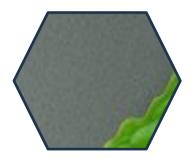
Low to moderate dosages (1–5 g): Assist labourer to combat fatigue (light stimulant effect.

<u>Moderate to high dosages (5-15 g):</u> use for controlling pain, diarrhea, and opioid withdrawal symptoms (opioid-like effects)

High doses (.15g): Has stimulant effects, Some individuals may experience anxiety, irritability, and enhanced aggression due to stimulant effects,

Long-term, high-dose consumption relate to hyperpigmentation of the cheeks, tremor and anorexia (weight loss)

(Vicknasingam B e. al, 2010)





PROBLEM STATEMENT

The number of ketum drink seized by law enforcement in Malaysia increased significantly (UNODC,2020)

From 89,060.1 Litres (2017) to 101,516.7 liters (2019) (UNODC,2020).

Similar trend is seen in Kelantan (Table 1) shows number of weight and volume Ketum related samples received by JKM Kelantan



Year	Weight of sample (Tonnes)	Volume of Sample (L)		
2018	8.1	3203		
2019	15.6	3365		
2020	16.9	7100		
	number of weight and volume K nples received by JKM Kelantan	etum related		

PROBLEM STATEMENT

Worryingly, trends is changing, most ketum dependent more likely drink ketum cocktail (as recreational drink) to get more euphoria effect and caused less risk compare to other illegal drugs (Darshan et al., 2017).

Ketum cocktail drink:

Combination brewed ketum leaves (kratom juice), soft drink, cough syrup or other substances (Yaba, BZO) are added based on consumer preferences (Singh et al, 2017).

May lead to polydrug used among both young & older user as they tend to add other substances (Berita Harian, 2017, Likhitsathina et al., 2018)



AIM & OBJECTIVE

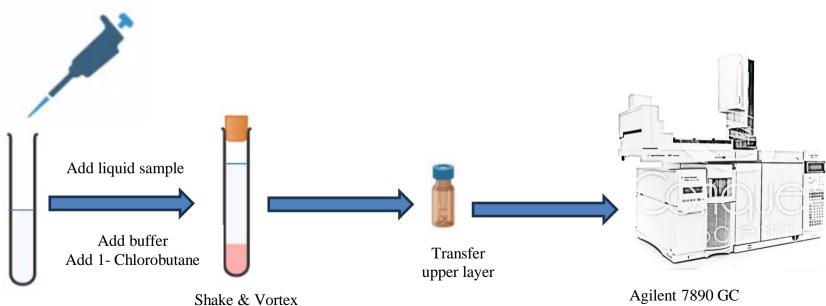
To study a method of analysis for detection mitragynine and other analytes of interest (this study- Meth, DPH, DIA, MG) in ketum drinks seizure in Kelantan.

SIGNIFANT OF STUDY

It is important to detect other controlled substance (this study- Meth, DPH, DIA, MG) in ketum cocktail drink because it would indicate misuse of ketum cocktail drink among people in community.



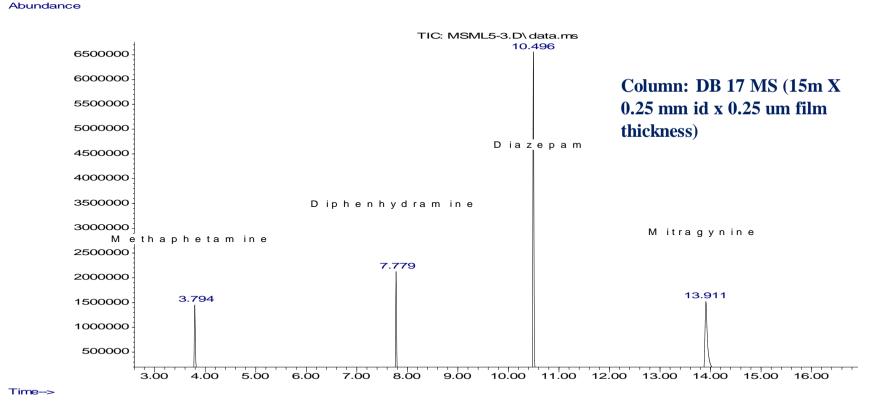
ANALYSIS



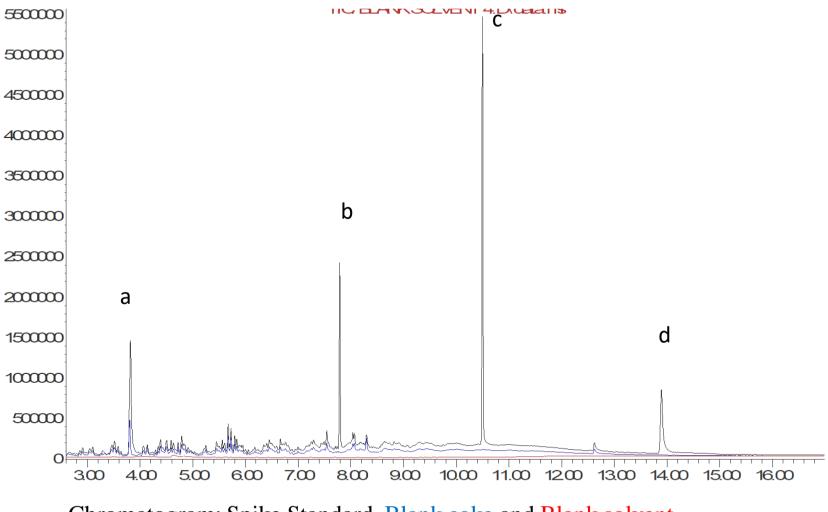
equipped with 5975C MSD

RESULT & DISCUSSION

RT: methamphetamine (3.7 mins) diphenhydramine (7.7 mins), diazepam (10.4 mins) and for MG (13.9 mins) (PBM>80).

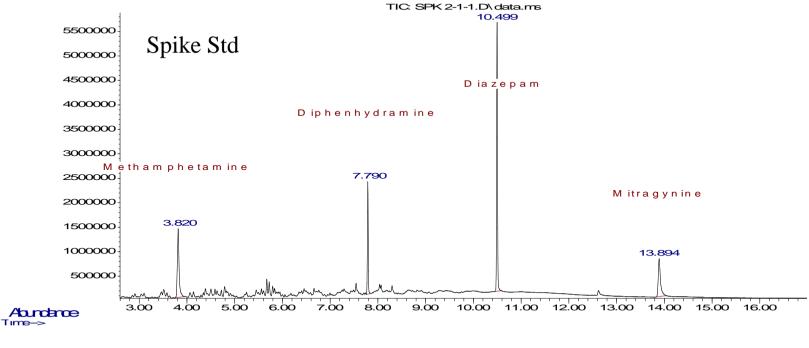


RESULT & DISCUSSION

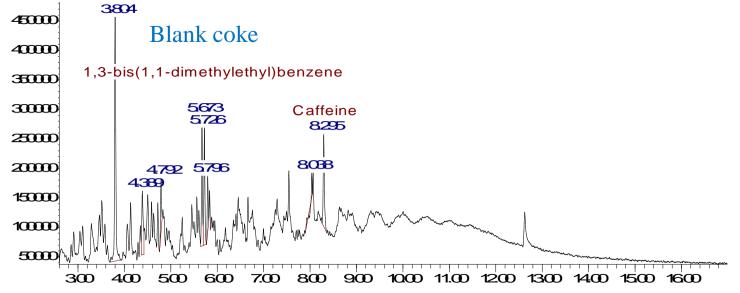


Chromatogram: Spike Standard, Blank coke and Blank solvent

RESULT & DISCUSSION



TIC BLANKCOKE 1. D. detans

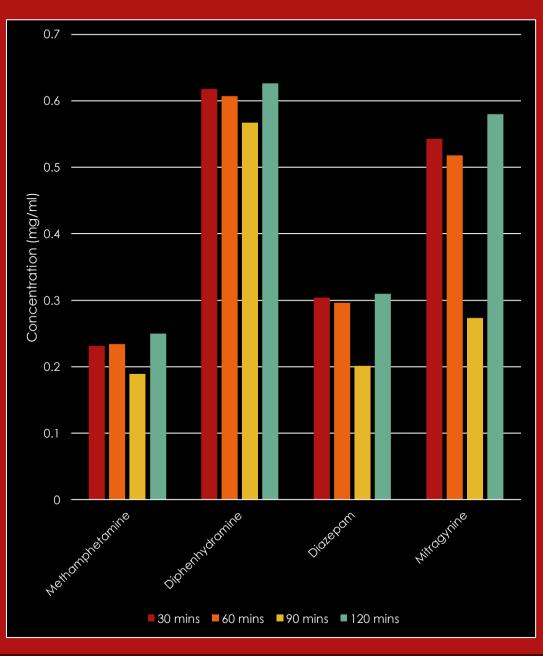


Tine

Abundance

OPTIMIZATION OF SAMPLE PRE-TREATMENT

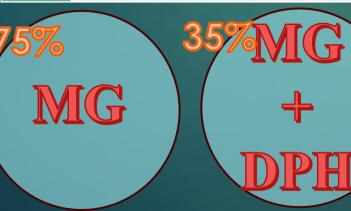
Analysis of variance shows there is no significant difference between roller mixer time (from 30 minutes to 120 minutes) and drug recovery from the sample. Therefore it was decided that samples was rollmixed for 30 mins during extraction process.



RESULT OF EXTRACTION OF REAL CASE SAMPLE

► Table: The result obtained from 20 real case samples.

Sample	Meth	DPH	DIA	MG	Sample	Meth	DPH	DIA	MG
ID					ID				
SPL 1	ND	Detected	ND	Detected	SPL 11	ND	ND	ND	ND
SPL2	ND	Detected	ND	Detected	SPL 12	ND	ND	ND	Detected
SPL3	ND	ND	ND	ND	SPL 13	ND	ND	ND	Detected
SPL4	ND	ND	ND	ND	SPL 14	ND	ND	ND	Detected
SPL5	ND	Detected	ND	Detected	SPL 15	ND	ND	ND	ND
SPL6	ND	Detected	ND	Detected	SPL 16	ND	ND	ND	Detected
SPL7	ND	Detected	ND	Detected	SPL 17	ND	ND	ND	Detected
SPL8	ND	Detected	ND	Detected	SPL 18	ND	ND	ND	Detected
SPL 9	ND	ND	ND	ND	SPL 19	ND	ND	ND	Detected
SPL 10	ND	Detected	ND	Detected	SPL 20	ND	ND	ND	Detected





CONCLUSION & FUTURE WORK

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Applicable for identification of drugs of interest



Polydrug user : ketum drink mix with illegal drugs or consume ketum drink along with illegal drugs



A more proper study : To distinguish the unknown coeluted peak with methamphetamine

Use of internal standard for quantification

Different type of sample matrix

References

- 1. Singh D, Narayanan S, Vicknasingam B, Corazza O, Santacroce R, Roman-Urrestarazu A. Changing trends in the use of kratom (Mitragyna speciosa) in Southeast Asia. *Hum Psychopharmacol.* 2017;32(3). doi:10.1002/hup.2582
- Siti Rohana Idris . 2017. Cámpuran air ketum, ubat batúk, pil kuda makin popular AADK. BH, New Straits Times Press (M) Bhd. Available on: https://www.bharian.com.my/berita/kes/2017/ 10/332283/campuran-air-ketum-ubat-batuk-pil-kudamakin-popular-aadk [September 30, 2017]
- 3. BERNAMA. 2020. Kelantan Dept of Chemistry to become ketum analysis centre by 2022. Malay Mail. [ONLINE] Available on : <u>https://www.malaymail.com/news/malaysia/2020/08/23/kelantan-dept-of-chemistry-to-become-ketum-</u> analysis-centre-by-2022/1896382 [23 August 2020]
- 4. Cinosi E, Martinotti G, Simonato P, et al. Following "the roots" of Kratom (Mitragyna speciosa): the evolution of an enhancer from a traditional use to increase work and productivity in Southeast Asia to a recreational psychoactive drug in western countries. *Biomed Res Int.* 2015;2015:968786. doi:10.1155/2015/968786
- 5. Chan KB, Pakiam C, Rahim, RA. Psychoactive plant abuse: the identification of mitragynine in ketum and in ketum preparations. B. Narcotics, 2005;LVII: 249–256.
- 6. United Nations Office of Drugs and Crime. Guidance for validation of analytical methodology and calibration of equipment used for testing of illicit drugs in seized materials and biological specimens. Vienna: United Nations; 2009.
- 7. Chan KW, Harun H. (2017). Identification of illicit drugs in vapes by GC-MS. Australian Journal of Forensic Sciences, 49(6), 650 659.
- 8. Chan KW, Haru H (2019). Method Validation for The Identification Of Nicotine In Vapes by GC-MS. -Kimia Science Communication Magazine No. 42 Issue 2/2019, 1-5.
- 9. Iain M. McIntyre, Amber Trochta, Susan Stolberg and Steven C. Campman. Mitragynine 'Kratom' related fatality: a case report with postmortem concentrations. <u>J Anal Toxicol</u>. 2015 Mar; 39(2):152-5.
- 10. Singh D, Narayanan S, Vicknasingam B, Corazza O, Santacroce R, Roman-Urrestarazu A. Changing trends in the use of kratom (Mitragyna speciosa) in Southeast Asia. *Hum Psychopharmacol.* 2017;32(3). doi:10.1002/hup.2582
- 11. Mudge & Brown: Determination of Mitragynine in Mitragyna speciosa Raw Materials and Finished Products by Liquid Chromatography with UV Detection: Single-Laboratory Validation .Journal of AOAC International Vol. 100, no. 1, 2017 1. DOI: 10.5740/jaoacint.16-022
- 12. Christine R. Caseya, Thomas Conleya, Andrea Heisea, Terri Thomasa, Patrick R. Ayresa: Quantitative and Qualitative Analysis of Mitragynine in Kratom (Mitragyna Speciosa) by GC-MS, LC-MS/MS and UPLC-PDA. Journal of Regulatory Science 02 (2015) 1–14

- 9. L. Cornara & B. Borghesi & C. Canali & M. Andrenacci & M. Basso & S. Federici & M. Labra : Smart drugs: green shuttle or real drug?. Int J Legal Med (2013) 127:1109–1123 DOI 10.1007/s00414-013-0893-9
- 10. Mei Wang, Emily J. Carrell, Zulfiqar Ali, Bharathi Avula, Cristina Avonto, Jon F. Parcher, Ikhlas A. Khan: Comparison of three chromatographic techniques for the detection of mitragynine and other indole and oxindole alkaloids in *Mitragyna speciosa* (kratom) plants. *J. Sep. Sci.* 2014, *37*, 1411–1418 1411 DOI 10.1002/jssc.201301389
- 11. Sathaporn Prutipanlai, Ornchuma Botpiboon, Benjamas Janchawee, Sittipoom Theanchaiwattana: Solid phase extraction method for determination of mitragynine in urine and its application to mitragynine excretion study in rats receiving caffeine. Tropical Journal of Pharmaceutical Research July 2017; 16 (7): 1675-1682 http://dx.doi.org/ 10.4314/tjpr.v16i7.28
- 16. Atty. Severino P. Uy, Jr, Shaila S. Seville, Jasmyne L. M. Jaranilla, Yvette K. S. Desamito, Reynalyn P. Barbacena, Ronald J. A. Narceda : Determination of Psychoactive Mitragynine Drug in Suspected Kratom Species Collected from Various Geographical Areas in the Philippines: A Pilot Study on Existing Local Plant-based New Psychoactive Substance (NPS). Arab Journal of Forensic Sciences & Forensic Medicine 2019; Volume 1 Issue (10), 1358-1366
- 17. Somsmorn Chittrakarn, Pimpimol Penjamras b, Niwat Keawpradub
- 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 (2012) 81–86. https://doi.org/10.1016/j.forsciint.2011.10.027
- Beate Hammond. New and emerging psychoactive substances –The global perspective https://www.unodc.org/documents/southeastasiaandpacific /2012/07/smartworkshop/06_New_and_emerging_psychoactive_substances_The_global_perspective.pdf. UNODC (2012).
- 20. Nei Jin Lee, Surash Ramanathan, Sharif Mahsufi Mansor, Keng Yoon Yeonga, Soo Choon Tana. Method validation in quantitative analysis of phase I and phase II metabolites of mitragynine in human urine using liquid chromatography-tandem mass spectrometry. Analytical Biochemistry Volume 543, 15 February 2018, Pages 146-161
- 21. Parthasarathy, S.; Ramanathan, S.; Murugaiyah, V. A simple HPLC-DAD method for the detection and quantification of psychotropic mitragynine in Mitragyna speciosa (ketum) and its products for the application in forensic investigation. Forensic Sci. Int. 2013, 226, 183–187.
- 22. Kristen L. Fowble, Rabi A. Musah. A validated method for the quantification of mitragynine in sixteen commercially available Kratom (Mitragyna speciosa) products. Forensic Science International 299 (2019) 195–202