Pharmacokinetics of Eleven Kratom Alkaloids Following an Oral Dose of Either Traditional or Commercial Kratom Products in Rats

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- **Preparation of lyophilized kratom tea (LKT)**

The dried leaves material of Mitragyna speciosa (kratom) were purchased from "Pure Land Ethnobotanicals" and authenticated by Dr. Rita Moraes from the National Center for Natural Products Research, School of Pharmacy, University of Mississippi. The dried leaf powder samples (200 g) were placed in a 2.8 L conical flask, previously filled with boiling water at 100 °C and boiled for approximately 20 minutes. The mixture was then cooled and filtered using fine tea mesh. The volume of the tea was reduced to one third using a rotavapor, followed by being completely dried on a lyophilizer (Labconco® 2.5 L free zone) overnight to produce 22 g of LKT.

Table S1: The recovery and matrix effect of each kratom alkaloids in rat plasma

Analyte	Recovery				Matrix effect			
	LLQC	LQC	MQC	HQC	LLQC	LQC	MQC	HQC
MTG	109.1 ± 4.0	104.5 ± 4.9	97.8 ± 5.6	98.5 ± 6.8	96.6 ± 3.4	95.1 ± 6.7	91.7 ± 5.4	89.2 ± 5.9
7-HMG	91.6 ± 7.3	92.2 ± 9.3	97 ± 5.3	97.7 ± 7.9	91.7 ± 9	91.3 ± 9.4	88.6 ± 5.2	85.9 ± 5.8
COR	102 ± 8.6	96.9 ± 3.2	96.3 ± 5.3	96.7 ± 7.1	90.9 ± 9.5	91.4 ± 5.7	89.6 ± 4.8	87.6 ± 5.8
SPG	94.3 ± 10.3	95.3 ± 3.4	96.8 ± 4.7	97.7 ± 7.1	89.8 ± 7.8	92.1 ± 6.8	90.7 ± 5.2	88.4 ± 6.3
SPC	94.5 ± 2.4	94.7 ± 5.1	96.7 ± 6.1	97.6 ± 6.8	111.6 ±12.4	101.9 ± 4	90.5 ± 5.7	88.4 ± 5.7
PAY	103.4 ± 6.4	98.6 ± 2.7	97 ± 5.8	96.8 ± 7.8	91.2 ± 4.2	92.8 ± 6.2	90.1 ± 5.5	88.1 ± 6.1
COX	97.8 ± 8.9	104 ± 6.6	96.9 ± 5.7	97.2 ± 8.2	93.2 ± 16.5	90.5 ± 8.6	88.7 ± 6.6	86.3 ± 6.6
COX-B	96.3 ± 5.1	97 ± 5.3	97.2 ± 7.1	96.8 ± 6	79.9 ± 5.1	89.1 ± 10.9	84.8 ± 5.8	82.9 ± 6.1
AJM	100.5 ± 7.9	93.4 ± 3.8	95.5 ± 7	95.4 ± 7.2	88.4 ± 9.8	92.4 ± 4.7	86.1 ± 6.3	83.8 ± 6.4
MTP	95 ± 7.9	94.9 ± 4.6	97.4 ± 6.5	97.3 ± 8.3	95.8 ± 10.6	98.7 ± 9.1	97.1 ± 5.7	93.4 ± 6.9
i-SPF	99.8 ± 9.1	93.1 ± 10.1	95.9 ± 5.6	95.8 ± 7.2	87.8 ± 10.1	91.7 ± 6.5	90.6 ± 6.1	87.4 ± 6.4

The values represent mean ± S.D. (n = 6). The recovery was calculated as % ratio of the analyte peak area in pre-spiked to post-spiked rat plasma samples. The matrix effect was calculated as the % ratio of the analyte peak area of the post-spiked plasma sample to the aqueous QC standard samples.

Table S2. Individual and relative alkaloid content in OPMS liquid and lyophilized kratom tea (LKT)

Kratom products	Individual alkaloids										
	MTG	7-HMG	COR	SPG	SPC	PAY	COX	COX-B	MTP	AJM	i-SPF
OPMS liquid (mg/ml)	11.81	BLQ	BLQ	1.51	2.76	2.17	BLQ	0.67	BLQ	BLQ	0.84
Relative alkaloid content in OPMS liquid normalized to mitragynine	1.00	NA	NA	0.13	0.23	0.18	NA	0.06	NA	NA	0.07
LKT (% w/w)	1.57	BLQ	0.04	0.22	0.56	0.30	BLQ	0.04	BLQ	BLQ	BLQ
Relative alkaloid content in LKT normalized to mitragynine	1.00	NA	0.03	0.14	0.36	0.19	NA	0.03	NA	NA	NA

BLQ: below the lower limit of quantification (0.03 mg/ml for OPMS liquid and 0.02% w/w for LKT), NA: Not applicable

Table S3: Source parameters for kratom alkaloids and internal standard

Sr. No.	Alkaloids	Ion transition (*m/z*)	Cone voltage (V)	Collision energy (V)
1	Mitragynine	399.2 > 174.2	60	32
2	7-Hydroxymitragynine	415.2 > 190.1	42	30
3	Corynantheidine	369.2 > 144.1	46	32
4	Speciogynine	399.2 > 174.2	60	32
5	Speciociliatine	399.2 > 174.2	60	32
6	Paynantheine	397.2 > 174.2	58	30
7	Corynoxine	385.2 > 132.1	26	44
8	Corynoxine-B	385.2 > 132.1	26	44
9	Mitraphylline	369.3 > 160.1	2	30
10	Ajmalicine	352.9 > 144.0	68	28
11	Isospeciofoline	401.1 > 257.1	2	30
12	Verapamil (IS)	455.3 > 150.1	28	42