MISSISSIPPI STATE DEPARTMENT OF HEALTH

This is an official

MS Health Alert Network (HAN) - Advisory

MESSAGE ID: MSHAN-202507-00604-ADV (Health Advisory)

RECIPIENTS: **All Physicians, Hospitals, ERs, ICPs, NPs, PAs, and Healthcare Providers – Statewide**

Tuesday, July 1, 2025

SUBJECT: **Risks with Kratom and Semi-Synthetic Alkaloid Products**

Mitragyna speciosa, commonly referred to as kratom, is a tropical tree in the coffee family native to Southeast Asia. It is a chemically complex natural product containing over 40 alkaloids, each with varying pharmacological properties and effects. As a result, it has been commonly used to self-treat many conditions, such as pain, withdrawal, anxiety and depression [1]. The primary alkaloid, mitragynine, acts as a partial agonist at μ-opioid, alpha adrenergic, and serotonergic receptors. Its effects are dose-dependent with stimulation (e.g. anxiety, agitation) at low doses and opioid-like effects (e.g. sedation, euphoria, analgesia) at high doses [1]. Emerging synthetic derivatives, including 7-hydroxymitragynine and mitragynine pseudoindoxyl, show markedly enhanced agonism at the μ-opioid receptor when compared to mitragynine [2]. 7-hydroxymitragynine is predicted to be 30-40x more potent than mitragynine and 5-10x more potent than morphine [3, 4]. Kratom and its constituents are federally unregulated and readily accessible from various retail environments. They are available in many concentrations and forms: leaves (plant-based products), powders, tablets, chewable tablets, films, capsules, gummies, and/or concentrated liquid extracts [6]. Given the aforementioned adverse effects, toxicity in users can be complex and unpredictable [1].

The Mississippi Poison Control Center (MPCC) has received 21 kratom exposure related calls since the start of 2025. However, during the week span of 6/19/2025-6/26/2025, the MPCC observed a concerning trend involving kratom and 7-hydroxymitragynine products after receiving three reports of significant clinical effects in young adults, all of whom experienced respiratory and cardiac arrest following exposure. Notably, all incidents were associated with consuming above the product's recommended dosage or through repeated use over a short timeframe. Two of these cases involved ingestions of 7-hydroxymitragynine products. Although both of these individuals were successfully revived with naloxone administration, one remains in critical condition.

The 2023 National Poison Data System Report, which identifies kratom as an emerging public health threat, cites nausea, vomiting, confusion, tachycardia, agitation, and hypertension as common clinical manifestations associated with kratom exposure [6]. Severe toxicities reported include: cardiotoxicity, such as ventricular fibrillation and sudden cardiac death, seizures, respiratory depression, rhabdomyolysis, and hepatic injury [7, 8, 9, 10, 11]. As of present, there are no well-defined toxic doses. Lastly, case reports suggest naloxone may counteract kratom's opioid-like effects during overdose, while *in vivo* studies indicate this benefit is specific to 7-hydroxymitragynine [12,13].

Currently, there are no standard laboratory procedures for detecting kratom or its alkaloids in a clinical setting. While some toxicology and forensic laboratories have incorporated kratom and select alkaloids into their screening and confirmatory testing, these procedures remain neither time-efficient nor cost-effective.

As you may know, Mississippi House Bill 1077 will go into effect on July 1, 2025, restricting the sale of kratom products to individuals under 21 and banning potent, synthetic formulations, such as 7-hydroxymitragynine. While we are optimistic this regulation will help curb exposures, we urge healthcare providers to remain vigilant. The MPCC is readily available to assist providers with all kratom exposures. Additionally, we have board certified medical toxicologist available free for consultation.

Recommendations for healthcare providers:

1. Emerging synthetic derivatives, including 7-hydroxymitragynine and mitragynine pseudoindoxyl, are potent μ-opioid receptor agonists. Therefore, opioid antagonists (naloxone, etc.) should be considered, in addition to, other supportive care. Furthermore, consider kratom and especially its synthetic alkaloid metabolites for cases of cardiovascular/respiratory arrest and unknown drug overdose.
2. Report ALL kratom exposures, especially those with significant clinical effects such as cardiovascular/respiratory arrest, to the MPCC via **1-800-222-1222.**
3. If product is implicated in significant clinical effects, obtain and provide complete product information (e.g. product name, manufacturer, ingredients and respective concentrations, dose, formulation, etc.) to the MPCC.
4. If able, coordinate with toxicology or forensic laboratories for product and specimen testing if products are associated with significant clinical effects.

References:

1. McCurdy C. R., et al. An update on the clinical pharmacology of kratom: uses, abuse potential, and future considerations. Expert Rev Clin Pharmacol. 2024;17(2):131-142. doi:10.1080/17512433.2024.2305798.
2. Smith, K. E., et al. The rise of novel, semi-synthetic 7-hydroxymitragyine products. Addiction. 2025;120(2):387-388. doi:10.1111/add.16728.
3. Matsumoto, K. et al. Antinociceptive effect of 7-hydroxymitragynine in mice: Discovery of an orally active opioid analgesic from the thai medicinal herb *mitragyna speciosa*. Life Sci. 2024; 74:2143–2155. doi:10.1016/j.lfs.2003.09.054.
4. Takayama, H. et al. Studies on the synthesis and opioid agonistic activities of mitragynine-related indole alkaloids: Discovery of opioid agonists structurally different from other opioid ligands. J. Med. Chem. 2022;45:1949–1956. doi:10.1021/jm010576e.
5. Hill K., et al. De facto opioids: characterization of novel 7-hydroxymitragynine and mitragynine pseudoindoxyl product marketing. Drug Alcohol Depend. 2025;272:112701. doi:10.1016/j.drugalcdep.2025.112701.
6. Gummin DD, Mowry JB, Beuhler MC, et al. Annual Report of the National Poison Data System® (NPDS) from America's Poison Centers®: 41st Annual Report. Clin Toxicol (Phila). 2024;62(12):793–1027. doi:10.1080/ 15563650.2024.2412423.
7. Sangani V., et al. Unusual presentation of kratom overdose with rhabdomyolysis, transient hearing loss, and heart failure. J Investig Med High Impact Case Rep. 2021. 9:23247096211005069. doi:10.1177/23247096211005069.
8. Schimmel J., Dart R.C. Kratom (mitragyna speciosa) liver injury: a comprehensive review. Drugs. 2020; 80(3):263-283. doi:10.1007/s40265-019-01242-6.

9. Dasgupta A., Ye Z. Severe jaundice with life-threatening liver failure after kratom use: reversed by plasma exchange. Transfus Apher Sci. 2024;63(3):103898. doi:10.1016/j.transci.2024.103898.
10. Sheikh M., et al. Report of ventricular fibrillation in a 44-year-old man using kratom. BMJ Case Rep. 2021;14(3):e237837. doi:10.1136/bcr-2020-237837.
11. Miller A.H.F., et al. Kratom cardiotoxicity: reversible brugada pattern and qtc prolongation. JACC: Case Rep. 2025;20(5):103109. doi:10.1016/j.jaccas.2024.103109.
12. Peran D., et al. Mitragyna speciosa (kratom) poisoning: findings from ten cases. Toxicon. 2023;225:107054. doi:10.1016/j.toxicon.2023.107054.
13. Gonzalez J.D.Z., et al. Mitragynine and 7-hydroxymitragynine: bidirectional effects on breathing in rats. bioRxiv. 2025;05(16):654392. doi:10.1101/2025.05.16.654392.

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Alerting Message Specification Settings

Originating Agency:	Mississippi State Department of Health
Alerting Program:	**MS Health Alert Network (MS HAN)**
Message Identifier:	MSHAN-202507-00604-**UPD**
Program (HAN) Type:	**Health Alert Advisory**
Status (Type):	Actual ()
Message Type:	Update
Reference:	MSHAN-00604
Severity:	Unknown
Acknowledgement:	No
Sensitive:	Not Sensitive
Message Expiration:	Undetermined
Urgency:	Undetermined
Delivery Time:	600 minutes

Definition of Alerting Vocabulary and Message Specification Settings

Originating Agency: A unique identifier for the agency originating the alert.

Alerting Program: The program sending the alert or engaging in alerts and communications using PHIN Communication and Alerting (PCA) as a vehicle for their delivery.

Message Identifier: A unique alert identifier that is generated upon alert activation (MSHAN-yyymmdd-hhmm-TTT **(ALT=Health Alert, ADV=Health Advisory, UPD=Health Update, MSG/INFO=Message/Info Service**).

Program (HAN) Type: Categories of Health Alert Messages**.**

Health Alert: Conveys the highest level of importance; warrants immediate action or attention.

Health Advisory: Provides important information for a specific incident or situation; may not require immediate action.

Health Update: Provides updated information regarding an incident or situation; unlikely to require immediate action.

Health Info Service: Provides Message / Notification of general public health information; unlikely to require immediate action.

Status (Type):

- Actual: Communication or alert refers to a live event
- Exercise: Designated recipients must respond to the communication or alert
- Test: Communication or alert is related to a technical, system test and should be disregarded

Message Type:

- Alert: Indicates an original Alert
- Update: Indicates prior alert has been Updated and/or superseded
- Cancel: Indicates prior alert has been cancelled

Reference: For a communication or alert with a Message Type of "Update" or "Cancel", this attribute contains the unique Message Identifier of the original communication or alert being updated or cancelled. "n/a" = Not Applicable.

Severity:

Extreme: Extraordinary threat to life or property
Severe: Significant threat to life or property
Moderate: Possible threat to life or property
Minor: Minimal threat to life or property
Unknown: Unknown threat to life or property

Acknowledgement: Indicates whether an acknowledgement on the part of the recipient is required to confirm that the alert was received, and the timeframe in which a response is required (Yes or No).

Sensitive:

Sensitive: Indicates the alert contains sensitive content
Not Sensitive: Indicates non-sensitive content

Message Expiration: Undetermined.

Urgency: Undetermined. Responsive action should be taken immediately.

Delivery Time: Indicates the timeframe for delivery of the alert (15, 60, 1440, 4320 minutes (.25, 1, 24, 72 hours)).