ACMT | American College of Medical Toxicology

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ACMT Position Statement: Public Health Concerns Associated with 7-Hydroxymitragynine and Other Kratom Compounds

The position of the American College of Medical Toxicology (ACMT) is as follows:

Seven-hydroxymitragynine (7-OH) and other compounds from kratom have been shown in animal studies to function as opioids. Clinical experience indicates that 7-OH is associated with opioid-like effects, including intoxication, respiratory depression, dependence, and withdrawal. Although 7-OH occurs naturally only in trace amounts in the kratom leaf, commercially available products containing concentrated 7-OH have been linked to overdose and death. Cases of 7-OH withdrawal and dependence have been successfully treated using medications for opioid use disorder such as buprenorphine or methadone. At present, there are no proven therapeutic benefits for 7-OH and other kratom-associated compounds. Additional clinical research is needed to better define their pharmacology, safety profile, and potential therapeutic applications. Use of 7-OH should occur in the context of clinical research conducted with appropriate institutional, regulatory, and ethical oversight. ACMT supports measures to prevent the unrestricted, nonprescription sale of opioid agonists.

Kratom and Associated Compounds

Kratom (*Mitragyna speciosa*) is a tree in the coffee family native to Southeast Asia. Kratom leaves and extracts are traditionally consumed for their mild stimulant properties and other medicinal purposes. Dependence on the natural kratom product in Thailand was reported over fifty years ago [1]. In the United States, some people use kratom for stimulant or euphoric effects or to manage pain, depression, anxiety, or opioid use disorder.

Mitragynine, the primary active alkaloid (nitrogen-containing organic compound) in kratom, is a relatively weak mu-opioid receptor agonist, producing analgesia, sedation, and respiratory depression [2]. Seven-hydroxymitragynine (7-OH), a minor alkaloid present at low concentrations in *M. speciosa*, as well as a metabolite of mitragynine, appears to be substantially more potent. Other notable mitragynine-derived compounds include the semisynthetic analogs dihydro-7-hydroxymitragynine (MGM-15) and 9-fluoro-dihydro-7-hydroxymitragynine (MGM-16) as well as mitragynine derivative mitragynine pseudoindoxyl (MP).

Commercial Availability and Use

Beginning in the late 2010s, concentrated products containing 7-OH as the primary active ingredient became commercially available in U.S. retail and online markets, representing a departure from traditional kratom leaf preparations. These products have been sold in gas

stations, convenience stores, and smoke shops, leading to the colloquial moniker “gas station heroin.” Many of these products are labeled as “kratom” and marketed as treatments for conditions such as pain and anxiety [3]. Analyses of some commercial kratom products found constituent profiles inconsistent with natural leaf material, suggesting adulteration or spiking with 7-OH [4].

Independent testing of products labeled to contain 7-OH shows concentrations significantly higher than those found in natural kratom and higher than the labeled 7-OH content [5]. The landscape is continually evolving: online retailers have also sold other kratom derivatives including MP, MGM-15, and MGM-16 [6,7].

Pharmacologic Effects of Kratom-Associated Compounds Such as 7-OH

A preclinical in vivo experimental study evaluating the respiratory pharmacology of intravenous mitragynine and 7-OH in rats found that 7-OH produced opioid-like respiratory depression, significantly reducing breathing frequency, tidal volume, and minute ventilation. These respiratory depressant effects were fully reversed by naloxone, consistent with opioid receptor-mediated respiratory depression [8]. In another preclinical study evaluating the in vitro mu-opioid receptor pharmacology and in vivo opioid-like behavioral effects of mitragynine and 7-OH in rodents, intraperitoneally-administered 7-OH was more potent than mitragynine in producing analgesia and substituting for morphine in drug-discrimination behavioral assays [9]. In mice, repeated subcutaneous administration of 7-OH produced tolerance to its antinociceptive effects and elicited opioid-like withdrawal signs, including naloxone-precipitated withdrawal [10]. In a rodent pharmacokinetic study, only 2.7% of ingested(gavaged) 7-OH was orally bioavailable [11]. This finding raises questions about the applicability of animal models that rely on parenteral 7-OH administration. Nevertheless, even limited oral bioavailability could produce clinically relevant exposure at high doses or with sublingual or buccal absorption. Although data on the human effects of MP, MGM-15, and MGM-16 are more limited, animal studies suggest mu-opioid effects [12][13].

Significant gaps remain in our understanding of the pharmacokinetics and safety profiles of 7-OH, mitragynine pseudoindoxyl (MP), MGM-15, and MGM-16, particularly with respect to non-opioid off-target effects. Although opioid-related adverse effects are generally predictable and dose-dependent, systematic study is needed to identify unexpected adverse effects, which historically have often become apparent in standardized preclinical testing followed by monitored clinical research.

Standardized preclinical testing followed by carefully monitored dose-escalation and controlled clinical trials identifies potential off-target and organ-specific toxicities, characterizes exposure–response relationships, and guides dosing and monitoring, thereby reducing—but not eliminating—the risk of uncommon or delayed adverse effects.

Regulatory Status

Kratom remains unscheduled at the federal level, though at the time of writing there are a patchwork of state laws regulating the sale of kratom or banning it entirely (Legislative Analysis and Public Policy Association 2026) [14]. In 2025, the United States Food and Drug Administration (FDA) recommended placing 7-OH under the Controlled Substances Act [15]. The FDA stated that 7-OH is not lawful in dietary supplements and could not be added to conventional foods. The agency also directed warning letters at companies marketing consumer products containing 7-OH; these actions did not target natural leaf kratom [15].

On July 6, 2026, the U.S. Drug Enforcement Administration (DEA) published two Notices of Intent (NOI), which are formal notices of planned regulatory action [16] [17]. One NOI placed products with 7-OH above specified concentration thresholds into Schedule I of the Controlled Substances Act. Schedule I is the legal designation for drugs that have high abuse potential, no currently accepted medical use, and lack of accepted safety for use under medical supervision. For context, most approved opioids (e.g., fentanyl and morphine) are Schedule II and buprenorphine is Schedule III. The proposed action targets concentrated and processed 7-OH products while excluding traditional kratom products containing ≤0.05% 7-OH by dry weight [16]. The other DEA NOI placed MP, MGM-15, and MGM-16 into Schedule I of the Controlled Substances Act [17]. These temporary scheduling orders are expected to take effect after a required 30-day notice period and remain in effect for two years, while permanent scheduling is considered.

Exposure Reports

Recent reports describe 7-OH dependence and withdrawal [18–21], overdose [21–23], and death [24]. These reports have appeared in public health alerts, medical literature, and poison center reports [18–25]. Kratom exposures reported to U.S. poison centers have increased dramatically in recent years [26]. (Poison center reporting is voluntary and rarely analytically confirmed). America's Poison Centers reported a sharp increase in exposures associated with kratom and 7-OH [27]. Exposures are projected to increase nearly 68% in 2026 compared with 2025. About 1 in 4 patients who were reported to be exposed to kratom or 7-OH alone were hospitalized.

Clinical Considerations

Opioids can produce life-threatening respiratory depression. To the extent that 7-OH and related compounds are mu-opioid agonists, their clinical and toxic effects would be expected to resemble those of opioids. Management of opioid intoxication includes support of ventilation. Naloxone, a mu-opioid receptor antagonist, has been effective at reversing 7-OH-associated respiratory depression based on animal studies and human case reports [8,21]. Clinicians caring for patients with substance use should ask specifically about use of kratom, 7-OH products, and other opioids or sedative use. Individuals using 7-OH have developed dependence, tolerance, and withdrawal typical of other opioids [18]. Buprenorphine has been

used successfully to treat kratom and 7-OH withdrawal [18–20,28]. Currently, 7-OH has no established medical use in humans. Preclinical and clinical safety studies that would identify adverse effects are lacking. The toxic dose of 7-OH remains unknown, and no safe dose can be recommended.

To the extent that 7-OH is an opioid, the combination of the alkaloid with other sedatives such as alcohol, benzodiazepines, or other opioids would be expected to increase respiratory depression and overdose risk [29,30].

Recommendations

Public

Avoid use of 7-OH products outside of monitored clinical research.

Do not use 7-OH products with alcohol, benzodiazepines, or other sedating drugs.

Obtain naloxone and learn how to administer it in case of overdose. Do not use 7-OH by yourself.

Consult with a provider with expertise in substance use disorders for help stopping 7-OH use.

Regulation

We support measures to prevent the unrestricted, nonprescription sale of opioid agonists.

Clinical Management

Respiratory depression should be treated with immediate airway and ventilatory support, including administration of naloxone to restore ventilation.

Obtain a thorough patient history including type of product used (e.g., kratom vs 7-OH, capsules vs tablets), dose, and duration of use.

Manage substance use disorders related to 7-OH and other kratom-derived compounds with evidence-based therapies employed for opioid use disorders, including buprenorphine and longitudinal care.

Research

We lack complete information on the pharmacokinetics and safety profiles of 7-OH, mitragynine pseudoindoxyl (MP), MGM-15, and MGM-16. Although opioid-related adverse effects are generally predictable and dose-dependent, systematic study is needed to identify unexpected

adverse effects, which historically have often become apparent in standardized preclinical testing followed by monitored clinical research. Additional studies are needed to characterize these potential toxicities and establish their clinical relevance.

7-OH has no proven therapeutic benefits. Further research is needed to identify potential therapeutic benefits for treatment of pain, anxiety, opioid use disorder, and other conditions.

Use of these drugs should occur in the context of clinical research conducted with appropriate institutional, regulatory, and ethical oversight.

Reporting

Report cases of toxicity from 7-OH and related compounds to a regional poison center and the FDA MedWatch program for surveillance purposes.

Disclaimer

While individual practices may differ, this is the position of the American College of Medical Toxicology at the time of writing, after a review of the issue and pertinent literature.

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