

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

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



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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.

To view the remainder of the position statement and see recommendations, check out the full press release on our website:

<https://www.acmt.net/news/acmt-position-statement-public-health-concerns-associated-with-7-hydroxymitragynine-and-other-kratom-compounds/>

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