# The Truth About 7-OH as a Partial Opioid Agonist

**CLAIM BY "BIG KRATOM":** Industry groups such as the AKA and the GKC continue to claim that 7-OH is a full mu opioid agonist.

**TRUTH:** As supported by peer-reviewed science as well as their advisory board members and the World Health Organization, **7-OH is a partial opioid agonist.**

## Proof 1

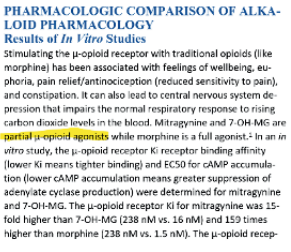
## Peer-Reviewed Primary Research

- **"7-hydroxymitragynine exhibits higher affinity and partial agonist activity at the mu-opioid receptor."**
  - Obeng et al. (2021)
- **"Mitragynine and 7-hydroxymitragynine function as partial agonists of the human μ-opioid receptor."**
  - Todd et al. (2020)
- ***"These results show that mitragynine and the oxidized analogue 7-hydroxymitragynine, are partial agonists of the human mu-opioid receptor and competitive antagonists at the kappa- and delta-opioid receptors"***
  - Kruegel et al. (2016)
- ***"7-OH and mitragynine analogs display partial agonism with reduced tolerance and side effect profiles"***
  - Varadi et al. (2016)

## Proof 2

## Industry Leading Education

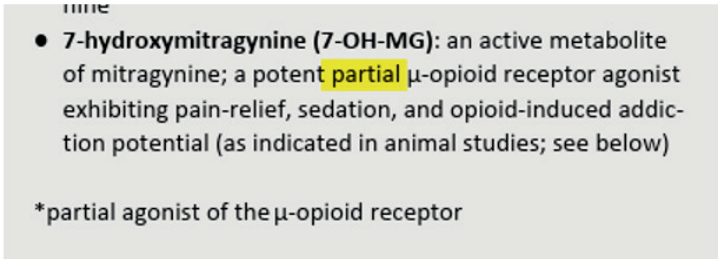
**Pharmacist and Global Kratom Coalition (GKC) advisor Dr. Michael White notes in the only CE course on 7-OH in the US at UCONN that 7-OH is a partial mu opioid agonist. *Link to course***



PHARMACOLOGIC COMPARISON OF ALKALOID PHARMACOLOGY

Results of *In Vitro* Studies

Stimulating the μ-opioid receptor with traditional opioids (like morphine) has been associated with feelings of wellbeing, euphoria, pain relief/antinociception (reduced sensitivity to pain), and constipation. It can also lead to central nervous system depression that impairs the normal respiratory response to rising carbon dioxide levels in the blood. Mitragynine and 7-OH-MG are partial μ-opioid agonists while morphine is a full agonist.[2] In an *in vitro* study, the μ-opioid receptor Ki receptor binding affinity (lower Ki means tighter binding) and EC50 for cAMP accumulation (lower cAMP accumulation means greater suppression of adenylate cyclase production) were determined for mitragynine and 7-OH-MG. The μ-opioid receptor Ki for mitragynine was 15-fold higher than 7-OH-MG (238 nM vs. 16 nM) and 159 times higher than morphine (238 nM vs. 1.5 nM). The μ-opioid recep-



- **7-hydroxymitragynine (7-OH-MG):** an active metabolite of mitragynine; a potent partial μ-opioid receptor agonist exhibiting pain-relief, sedation, and opioid-induced addiction potential (as indicated in animal studies; see below)

*partial agonist of the μ-opioid receptor

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**Proof 3**

## World Health Organization

**The WHO states:**

**"Mitragynine, 7-hydroxymitragynine, and mitragynine pseudoindoxyl are partial agonists at the human mu-opioid receptor"**
**in their** *Expert Committee on Drug Dependence Forty-fourth Meeting Pre-Review Report on Kratom (Mitragyna speciosa), mitragynine, and 7-hydroxymitragynine*

**Proof 4**

## AKA Position Paper

**In the AKA *position paper* used in testimony to the state of Maryland, they state:**

> The pharmacological effects of MG and 7-HMG are fundamentally different from morphine and other euphoriant opioids that induce respiratory suppression. MG and 7-HMG are G-protein biased, partial agonists whereas morphine is a non-biased, full agonist at mu opiate receptors. Furthermore, the binding profiles of MG and 7-HMG differ from morphine in terms of their affinities and selectivities for opiate and other receptors. Thus, whereas morphine serves as a robust reinforcer for animals, MG did not serve as a reinforcer in the two animal intravenous self-administration studies that have evaluated it (*Hemby et al., 2018; Yue et al., 2018*).

# There are two things clear:

1. **The science shows that 7-OH is a partial mu opioid agonist.**
2. **Kratom industry groups created a disinformation campaign claiming 7-OH is a full opioid agonist so that the public would think it works the same as fentanyl, and heroin and rally for a ban.**

**THIS MUST STOP AND REAL SCIENCE MUST PREVAIL.**

**STARTING WITH THE FACT THAT 7-OH IS NOT A FULL OPIOID AGONIST.**

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