Review > Neuropharmacology. 2018 May 15;134(Pt A):108-120.
doi: 10.1016/j.neuropharm.2017.08.026. Epub 2017 Aug 19.

The medicinal chemistry and neuropharmacology of kratom: A preliminary discussion of a promising medicinal plant and analysis of its potential for abuse

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PMID: 28830758 DOI: 10.1016/j.neuropharm.2017.08.026

Abstract

The leaves of Mitragyna speciosa (commonly known as kratom), a tree endogenous to parts of Southeast Asia, have been used traditionally for their stimulant, mood-elevating, and analgesic effects and have recently attracted significant attention due to increased use in Western cultures as an alternative medicine. The plant's active alkaloid constituents, mitragynine and 7-hydroxymitragynine, have been shown to modulate opioid receptors, acting as partial agonists at mu-opioid receptors and competitive antagonists at kappa- and delta-opioid receptors. Furthermore, both alkaloids are G protein-biased agonists of the mu-opioid receptor and therefore, may induce less respiratory depression than classical opioid agonists. The Mitragyna alkaloids also appear to exert diverse activities at other brain receptors (including adrenergic, serotonergic, and dopaminergic receptors), which may explain the complex pharmacological profile of raw kratom extracts, although characterization of effects at these other targets remains extremely limited. Through allometric scaling, doses of pure mitragynine and 7-hydroxymitragynine used in animal studies can be related to single doses of raw kratom plant commonly consumed by humans, permitting preliminary interpretation of expected behavioral and physiological effects in man based on this preclinical data and comparison to both anecdotal human experience and multiple epidemiological surveys. Kratom exposure alone has not been causally associated with human fatalities to date. However, further research is needed to clarify the complex mechanism of action of the Mitragyna alkaloids and unlock their full therapeutic potential. This article is part of the Special Issue entitled 'Designer Drugs and Legal Highs.'

Keywords: 7-hydroxymitragynine; Analgesia; Kratom; Mitragynine; Opioid receptor.

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