

## 99. Increasing incidence of kratom- associated serious adverse effects in medical toxicology patients

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**Background:** “Kratom” refers to preparations derived from the Southeast Asian tree *Mitragyna speciosa*, which contains dozens of psychoactive alkaloids. Kratom has been reported to have both opioid-like and stimulant effects. While most kratom use is not associated with serious adverse effects, cases of kratom-associated toxicity and death have been anecdotally reported to poison centers and in published case reports. To date, there has been no prospective systematic data collection on serious adverse effects associated with kratom use.

**Methods:** This is a prospective, descriptive registry subanalysis that included all single-agent or multiple-agent kratom-related cases seen by attending medical toxicologists and reported to the Toxicology Investigators Consortium (ToxIC) Core Registry from 1 January 2013 through 31 December 2023. Clinical and patient information was recorded using uniform a priori data collection fields entered into a secure REDCap database. These included patient demographic characteristics, reason for kratom exposure, clinical presentation, and case outcome. No hypothesis testing was undertaken, but the increase in entered kratom cases from 2013 to 2023 was analyzed using linear regression. Because all ToxIC Core Registry cases required a medical toxicology consultation or admission to a medical toxicology service, all were classified as serious exposures.

**Results:** Eighty-nine cases met our inclusion criteria, of which 75 were from the United States and 14 were from Thailand. There has been a significant time-trend of increasing kratom cases entered into the ToxIC Core Registry yearly since 2013 (b 1/4 1.16, SE 1/40.26,  $p < 0.01$ ). Most patients were non-Hispanic White, adults (!18), and males. Most cases involved other substances in addition to kratom. Tachycardia was the most common vital sign abnormality, occurring in 15.7% of patients. However, the most common adverse effects were neurological, occurring in 85.4% of the cases. These were primarily agitation (31.5%), central nervous system depression (27.0%), delirium/toxic psychosis (19.1%), hallucinations (14.6%), and seizures (12.4%). Other significant findings included 24.7% of patients with cardiovascular effects and 16.9% of patients with respiratory depression. Notably, only 5.6% of the kratom cases entered in the ToxIC Core Registry presented with an opioid toxidrome. Patient outcomes were mostly good, with 88 patients surviving and one death.

**Conclusion:** Reports of serious adverse effects associated with kratom use in patients cared for by a medical toxicologist increased over the eleven-year period of this study. This trend likely parallels the overall increase in kratom use by the general population over this same time period, as well as increasing patient and clinician awareness of kratom and the possible toxicities associated with its use. Consistent with the known psychoactive effects of kratom alkaloids and previously reported clinical observations, the most common serious adverse effects were neurological, and tachycardia was the most commonly reported cardiovascular effect. However, despite the strong mu opioid receptor agonism of the kratom alkaloid metabolite 7-hydroxymitragynine, an opioid toxidrome was uncommon in this patient population.