
The FDA Kratom Death Data: Exaggerated Claims, Discredited Research, and Distorted Data Fail to Meet the Evidentiary Standard for Placing Kratom as a Schedule I Controlled Substance

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ABSTRACT

The U.S. Food and Drug Administration (“FDA”) claims it has submitted a recommendation to the Drug Enforcement Administration (“DEA”) for the placement of the alkaloids in kratom into Schedule I of the Controlled Substances Act (“CSA”). A key factor the FDA must prove for scheduling is that kratom poses a public health risk to the American people. The data released by the FDA to support its health risk claim is that there are 44 deaths “associated” with kratom use.

FDA points to 9 deaths in Sweden between 2009 and 2010 to support its claim of deaths associated with kratom use, but an independent scientific review of those cases concluded that the deaths were the result of spiking powdered kratom leaves with a lethal concentration of the mu opioid receptor agonist *O*-desmethyltramadolⁱ. Each of the remaining deaths attributed to kratom by the FDA have equally suspect association with kratom. Nearly all of the decedents were using multiple substances, and most included illicit or prescription drugs that carry well-known risks of fatalities. Notable cases include a decedent who had hanged himself after struggling with depression and prescription drug abuse; a “death by homicide” resulting from a gunshot wound to the chest; and a man who had fallen out of a window, broken his arm and refused medical treatment before dying. Many of the case reports were not the reported as the result of FDA investigation, but were previously disclosed in the scientific literature; and as many as one third were deaths that did not occur in the U.S..

The FDA claims it has released a total of 36 case reports (only 26 appear to have any data), and claims it plans to release the additional 8 case reports in the near future. None of the released case reports provides a cohesive or reasonable scientific basis to conclude any of the deaths was caused by kratom, nor does the information released conclusively support any conclusion that kratom was associated to the cited death other than coincidentally. Only one case report released by the FDA suggests that the only substance detected in the decedent’s blood was kratom, but that report provides no substantive detail other than the decedent’s age and ethnicity to support that suggestion.

Introduction:

The DEA made its initial recommendation to place the alkaloids of kratom into Schedule I of the CSA on August 31, 2016 under the emergency scheduling authority of the CSAⁱⁱ. The Notice of Scheduling cited nine deaths in Sweden “from the use of the kratom product ‘Krypton’”; five additional deaths related to kratom exposure reported in scientific literature; and sixteen other deaths related to kratom exposure; for a total of 30 deaths attributed to kratom. The DEA withdrew this scheduling proposal on October 13, 2016 after receiving thousands of public comments challenging the proposal. DEA had

previously requested a full 8-Factor Analysis (“8-FA”) from the FDAⁱⁱⁱ. FDA has taken over a year to scour available sources in an effort to substantiate DEA’s intention to ban kratom.

On November 14, 2017 the FDA issued a public health advisory on the use of kratom^{iv} and stated the FDA “is aware of reports of 36 deaths associated with the use of kratom-containing products.”

On February 6, 2018 the FDA released an adverse events and scientific analysis of kratom’s alleged opioid properties^v, and released the reports of the 36 deaths referenced in the November 14, 2017 statement. In addition, the FDA increased its claim to 44 reported deaths associated with the use of kratom.

Analysis of Claimed Deaths:

<i>Death #</i>	<i>FDA Incident #</i>	<i>Reported Cause of Death</i>	<i>Substances Involved</i>	<i>Circumstances</i>
1	12639316	Death by Homicide	Report redacted	Report completely redacted. Death is recorded in other FDA records as death by homicide due to a gunshot wound to the chest. It is assumed from the FDA listing that the decedent must have used kratom.
2	12639332	Heroin, alcohol, and benzodiazepines intoxication, manner of death is accident	Heroin, alcohol, benzodiazepines, THC, Citalopram, Morphine, Chlordiazepoxide, Demoxepam, Alprazolam, Mitragynine	On the evening of the death, decedent drank alcohol, smoked heroin, and took Xanax and Narco. The decedent had a history of heroin and alcohol abuse; the family requested no autopsy. The Medical Examiner did a toxicology test.
3	12639556	Ligature hanging; suicide	Alcohol, Benzodiazepines, Zolpidem, 7-Aminoclonazepam, Nordiazepam, Zolpidem, Mitragynine, Quetiapine	Decedent was found hanged by the neck with a nylon rope tied to a tree. The decedent suffered from Bipolar disorder, depression, anxiety, insomnia, and had suicidal ideations. Prior to the death, the decedent had started cutting himself.
4	13421666	Aspiration of chime	Fluoxetine, Etizolam, Lorazepam, Mitragynine, Olanzapine, Pipamperone, Pregabalin, Quetiapine, Triazolam, Fluoxetine	Decedent had fallen from a window but refused medical treatment despite reported intense pain resulting from the fall. A hematoma and humerus fracture of the left arm were confirmed in the autopsy. The benzodiazepine in the femoral blood was in a concentration range that was likely to result in toxic effects. Decedent’s father reported his son was using an herbal substance known as kratom.
5	8121551	Accidental drug intoxication/overdose	Pregabalin, Amphetamine, Olanzapine, Diazepam, Fluoxetine, Nordiazepam, Norfluoxetine, Phenazon, O-desmethyltramadol, Mitragynine	Decedent had a history of drug abuse, there was evidence of the use of the herbal preparation Krypton.
6	8121559	Accidental drug intoxication/overdose	Venlafaxene, Zopiclone, O-desmethyltramadol,	Decedent had a history of drug abuse, there was evidence of the use of the

7	8121566	Accidental drug intoxication/overdose	Mitragynine Alimemazine, DMA, O-DMV, Mitragynine	herbal preparation Krypton. Decedent had a history of drug abuse, there was evidence of the use of the herbal preparation Krypton.
8	8124388	Accidental drug intoxication/overdose	Amphetamine, THC, Alprazolam, O-desmethyltramadol, Mitragynine	Decedent had a history of drug abuse, there was evidence of the use of the herbal preparation Krypton.
9	8124494	Accidental drug intoxication/overdose	Alprazolam, O-desmethyltramadol, Mitragynine	Decedent had a history of drug abuse, there was evidence of the use of the herbal preparation Krypton.
10	8132531	Accidental drug intoxication/overdose	Alprazolam, Citalopram, THC, O-desmethyltramadol, Mitragynine	Decedent had a history of drug abuse, there was evidence of the use of the herbal preparation Krypton.
11	12639302	Acute Mitragynine intoxication	Alcohol, Amphetamines, Mitragynine, Carbamazepine	Decedent had a history of drug abuse, and had a history of seizures with a recent hospitalization.
12	13934406	Suicide. Toxicity due to various agents	Bupropion, 3-Methoxyphencyclidine, Delorazepam, Ethanol, Mitragynine, Paroxetine	Patient was found unresponsive with fatal multi drug-intoxication.
13	12665817	Drug abuse	Loperamide HCL, Tramadol, Mitragynine	Decedent collapsed while playing basketball, could not be resuscitated.
14	12665823	Drug abuse	Loperamide HCl, Mitragynine	Decedent was researching natural ways to get high. Loperamide is known to allow users an opioid-like high if used in excess of recommended dose.
15	12665824	Drug abuse	Loperamide HCl, Mitragynine	Decedent was researching natural ways to get high. Loperamide is known to allow users an opioid-like high if used in excess of recommended dose.
16	12639421	Acute Mitragynine, Fentanyl, Alprazolam, and Clonazepam Intoxication	Benzodiazepines, Fentanyl, Cannabinoids, Mitragynine, Alprazolam, 7-Aminoclonazepam	Decedent had a history of alcohol, prescription medication, and illicit drug abuse.
17	12639579	Mixed Mitragynine, Methadone, and Alprazolam Intoxication	Benzodiazepines, Cannabinoids, Methadone, Mitragynine	Decedent had a history of drug abuse, and packaged syringes and a used syringe; half a Xanax tablet, a small unlabeled bottle with an unknown pink liquid; "Royal Kratom" capsules; "Maeng Da" kratom capsules; were found at the scene;
18	12639594	Pulmonary thromboemboli due to deep vein thrombosis. Obesity, dilated cardiomyopathy and chronic polysubstance abuse are listed as contributing factors	Opiates, Benzodiazepines, Cannabinoids, Oxycodone, Fluoxetine, Norfluxoetine, Trazodone, Alprazolam, Nordiazepan, Gabapentin, Mitragynine	Decedent is a 298-pound man who had a history of drug abuse, Tourette's Syndrome, high blood pressure, rheumatoid arthritis, chronic back and shoulder pain, prescription medication abuse and alcohol abuse
19	14037602	Accidental drug intoxication/overdose	No specific report provided	Decedent had a history of drug abuse, there was evidence of the use of the herbal preparation Krypton.

20	8083892	Accidental drug intoxication/overdose	Mirtazapine, Buprenorphine, O-desmethyltramadol, Mitragynine, Alimemazine, Venlafaxine, Diazepam	Decedent had a history of drug abuse, there was evidence of the use of the herbal preparation Krypton. Several other psychotropic drugs were detected and “could have contributed to death.”
21	12569892	Accidental poisoning due to kratom and possibly in combination with other substances detected	Zopiclone, Citalopram, Lamotrigine, Mitragynine	Decedent had a history of substance abuse and well as psychiatric disease. Because of his drug habit, he had been subject to drug testing at work. In order to avoid testing positive, the decedent reportedly bought kratom on the internet.
22	10712257	Severe hypoxic encephalopathy complicating apparent mitragynine toxicity	Lamotrigine, Mitragynine, Paroxetine	The patient experienced generalized tonic-clonic seizure, tachycardia, cardio-respiratory arrest, anoxic brain damage, brain stem hemorrhage, pulmonary embolism, pulmonary infarct, hypoxic encephalopathy and subsequently died.
23	10708286	Cause of death rested “largely on the interpretation of the role mitragynine played in the case”	Clonazepam, Dextromethorphan, Temazepam, Diphenhydramine, Mitragynine	A well-established history of opioid abuse, and kratom use. The active compound of kratom was identified in the decedent's blood.
24	10698706	Mixed drug intoxication - primarily mitragynine	Alcohol, Omeprazole, Venlafaxine, Mirtazapine, Diphenhyramine, Mitragynine, Morphine	The decedent was a 24-year-old man whose medical history was significant for alcohol abuse and depression. He had been drinking alcohol since age 15, had several suicide attempts with pills and had been hospitalized for an accidental overdose.
25	7900650	Propylhexedrine toxicity	Propylhexedrine, Mitragynine, Acetaminophen, Morphine, Promethazine	The decedent, a 20-year-old Caucasian male, was found dead, under his bunk, in his living quarters. His roommate stated that it was not out of the ordinary for the decedent to sleep under his bunk. An investigation of the scene indicated no evidence of foul play. Thirty-nine separate nutritional supplements, herbal supplements, and prescription and nonprescription medications were found at the scene. Analysis of the decedent's computer and internet usage history indicated he had researched herbal supplements, particularly kratom, which he reportedly used to treat insomnia. Further investigation revealed the decedent had researched a procedure to concentrate propylhexedrine from over the-counter inhalers.
26-44	No Data Provided by FDA	No Data Provided by FDA	No Data Provided by FDA	No Data Provided by FDA

Conclusion:

None of the case reports released to date support the evidentiary standard required by the CSA to prove there is a risk to the public health that relies primarily on the “numerous deaths associated with kratom.” A policy decision of this import should be based on valid statistical analysis developed from empirical evidence, and its interpretation should be in accordance with scientific method. The FDA’s attempt to use a flimsy theory to justify the scheduling of kratom fails to meet any reasonable or credible scientific standard to prove a public health risk from the use of kratom. Numerous scientific studies (including the published reports FDA relies upon) directly contradict the FDA claims of deaths being caused by kratom, and the adoption of a less-rigorous and poorly defined standard of deaths being “associated with kratom” substitutes very weak opinion for medical or scientific conclusion on the cause of any death.

FDA Commissioner Gottlieb implicitly acknowledged the fatal defect in the validity of the conclusions drawn by the FDA in support of the 8-FA they have submitted to the DEA when he stated on February 6, 2018 as follows:

“Overall, many of the cases received could not be fully assessed because of limited information provided;
...”

In addition, the FDA uses invalid and circuitous reasoning to justify its concern about kratom, stating that the FDA is “not alone in our evaluation and our public health concerns” because other “states and cities have banned kratom from entering their jurisdictions.” The basis for existing bans on kratom in any state or city likely resulted from the misinformation about kratom disseminated by the FDA itself, including characterization of kratom as a “synthetic” drug lumped together with truly dangerous synthetic substances such as bath salts and synthetic cannabinoids that are banned under federal law.

Of significant note is the fact that FDA has never sought to ban or schedule a substance because it has been mixed or blended with a toxic dose of another substance or substances. The suggestion that there are “risks” associated with combining kratom with “certain drugs” is unsupported by the data released by the FDA, which shows only that the cause of death in each of the released reports is associated with the toxicity of an illegal street drug, the use of a prescription drug in combination with other prescription drugs that are specifically contraindicated, or the use of one or more potentially fatal prescription drugs above the recommended dosage. No reliable scientific data currently exists to show that unadulterated kratom leaf itself is toxic, or that its use in combination with other substances that are ingested or inhaled can be attributed in any way to the kratom plant itself.

ⁱ Robert Kronstrand, Markus Roman, Gunilla Thelander, and Anders Eriksson, Unintentional Fatal Intoxications with Mitragynine and *O*-Desmethyltramadol from the Herbal Blend Krypton, *Journal of Analytical Toxicology*, Vol. 35, May 2011.

ⁱⁱ 21 USC 801 *et seq.* The CSA provides for “temporary scheduling to avoid imminent hazards to public safety,” commonly referred to as the “emergency” scheduling process.

ⁱⁱⁱ Department of Justice, Drug Enforcement Administration, 21 CFR Part 1308, Withdrawal of Notice of Intent to Temporarily Place Mytragynine and 7-Hydroxymitragynine Into Schedule I, *Federal Register*, Vol. 81, No. 198, Thursday, October 13, 2016/Proposed Rules.

^{iv} <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm584970.htm>

^v <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm595622.htm>