

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Gershman K, Timm K, Lampi L, et al. Deaths in Colorado attributed to kratom. *N Engl J Med* 2019;380:97-8. DOI: 10.1056/NEJMc1811055

Appendix Table of Contents

| Content | Page |
|---|-------------|
| 1. Clinical history and drug testing in 15 kratom related deaths in Colorado from 1999-2017 | 2 |

We further investigated the four apparent mitragynine-only deaths by reviewing police investigation records and performing comprehensive toxicology screening using high-performance liquid chromatography with tandem mass spectrometry in the three cases in which residual blood was available.

Table A1. Kratom-related deaths (n=15) from Colorado death registry, 1999-2017. Drug testing performed by national reference toxicology laboratory for county coroners and medical examiners, and in selected cases (n=3) by the University of California San Francisco, Clinical Toxicology and Environmental Biomonitoring Laboratory.

| Death year | Mitragynine @ autopsy testing | Opioid-1 @ autopsy testing | Opioid-2 @ autopsy testing | ETOH @ autopsy testing | Other drugs identified @autopsy testing or comprehensive testing | Past medical history | Comments |
|------------|-------------------------------|-------------------------------------|-----------------------------|------------------------|--|---|--|
| 2013 | positive | | | | | | Apparent seizure leading to cardiorespiratory arrest after ingesting kratom |
| 2015 | positive | Butyryl-fentanyl = 19 ng/mL | Oxycodone (free) = 48 ng/mL | | Etizolam = pos, Diphenhydramine = 68 ng/mL, THC = 1.7 ng/mL | depression with prior suicide attempt & drug use | Found unresponsive in bedroom; illicit, OTC & prescription drugs on scene |
| 2016 | positive | U-47700 mass spec signature present | | | | heroin use & overdose; alcohol use | Found unresponsive in bed; syringes, spoons & plastic bags containing powders (with names of kratom varieties) & vials labeled U-47700 (synthetic opioid) found on scene |
| 2016 | positive | oxycodone (free) = 890 ng/mL | | | fluoxetine = 320 ng/mL, pseudo-ephedrine = 990 ng/mL | alcohol & prescription drug abuse; depression & anxiety | Found unresponsive in bed; meds recovered from scene included morphine, benzotropine, hydroxypam, trazodone, Fetzima, lidoderm, lithium, gabapentin |

| | | | | | | | |
|------|---|------------------------------|-----------------------------|----------|--|--|--|
| 2016 | positive, 16 ng/ml identified by research reference lab | | | 18 mg/dL | Etizolam= 1.3 ng/ml, 5-MeO-AMT = 56.19 ng/ml | opioid & benzodiazepine abuse; recent evaluation for new-onset seizures associated with benzodiazepine withdrawal, and admitted etizolam use | Found in state of decomposition in his apartment. Pathologist stated that ethanol detected likely represents product of microbial activity and/or product of postmortem decomposition process. Green powdered substance, syringes, plastic baggies (one with label "etizolam"), bottle of polyethylene glycol, and empty pill capsules found on scene. Several medications including bupropion, clonidine, diazepam, gabapentin, hydroxyzine, naltrexone present on scene. |
| 2016 | positive | morphine (free) = 220 ng/mL | codeine (free) = 17 ng/mL | | | Schizophrenia, anxiety, suicide attempt; heroin, methamphetamine, alcohol & marijuana use | Found unresponsive at home; drug paraphernalia found on scene. |
| 2016 | 140 ng/mL | oxycodone (urine) = positive | tramadol (urine) = probable | | topiramate = present (<2ug/mL), diphenhydramine <50 ng/mL, Zolpidem (urine) = elevated | chronic pain with prescription opioid abuse | Found unresponsive at work in prone position with head hanging into plastic container; autopsy: pressure injuries of neck consistent with mechanical compression; Pathologist: death due to "probable mechanical asphyxia" accompanied by mixed drug intoxication. |

| | | | | | | | |
|------|-------------|------------------------------|--|--|---|---|--|
| 2016 | 2100 ng/mL | | | | citalopram = 263 ng/ml | major depressive disorder, anxiety, and drug use | Found unresponsive at home. |
| 2016 | 1400 ng/ mL | furanyl-fentanyl = 140 ng/mL | | | | | Found unresponsive at home; containers of marijuana products, plastic bag containing white fine crystalline powder, and bag inscribed "Thai" with green-tan powder found on scene. |
| 2017 | 1000 ng/ mL | | | | temazepam = 20 ng/mL, clonazepam = 3.5 ng/mL, olanzapine = 27 ng/mL, sertraline = 400 ng/mL | recovering alcoholic; had prescriptions for multiple meds | Found unresponsive at home; tox testing also detected THC @ 8.4 ng/mL and hydroxyzine @ 110 ng/mL; autopsy revealed mildly enlarged heart which coroner stated, "may be listed as a significant contributing factor." |
| 2017 | 170 ng/mL | | | | DMMA =157 ng/ml | parents reported likely recent depression | Found unresponsive at home; per police report was taking "a number of health supplements" (some obtained over internet); packing slip for tianeptine sodium, bottles of various supplements, clear bottle of various pills, and foil packets of Selgin found on scene. |
| 2017 | 2700 ng/mL | | | | etizolam = 110 ng/mL, nordiazepam = 53 ng/mL, mirtazapine 31 ng/mL | suicide ideation & attempts; drug & alcohol abuse | Found unresponsive at home; kratom and multiple prescription meds (diazepam, buspirone, mirtazapine, gabapentin, propranolol) found on scene. |

| | | | | | | | |
|------|------------|-----------------------|-----------------------------|-----------|----------------------------|--|--|
| 2017 | 4800 ng/mL | | | | 2, 4, 5 TMA= 2.83 ng/ml | seizures following inhalant abuse and alcohol withdrawal | Found unresponsive at home; aerosol cans were present; huffing from aerosol can followed by "convulsion" observed approximately 3 weeks prior to death; autopsy revealed hepatomegaly ("normal lobular pattern") and chronic interstitial nephritis. |
| 2017 | 250 ng/mL | oxycodone = 300 ng/mL | | 252 mg/dL | | | |
| 2017 | 747 ng/mL | oxycodone = 274 ng/mL | fentanyl (urine) = positive | 175 mg/dL | cocaine (urine) = positive | | Found unresponsive in parked car; reportedly using prescription meds and alcohol with possible cocaine the prior evening. Autopsy revealed liver periportal to septal fibrosis with mild chronic inflammation of portal tracts. |