



Kratom Science Brief Columbus Ohio Public Hearing
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I would like to provide some background on the current state of kratom science, its place in public health, and the opioid epidemic in particular. I'd also like to review how our current knowledge can help determine the most appropriate way to regulate kratom in order to minimize risks to kratom consumers, while contributing to their health and wellbeing, as well as to the public health.

During the 1980s and 1990s I headed the Clinical Pharmacology laboratory of the National Institute on Drug Abuse (NIDA) and led research across a wide range of substances including opioids, cannabis, cocaine and other stimulants, and a myriad of other drugs. I also worked NIDA, FDA and DEA on drug scheduling issues. I have published nearly 450 papers on these topics and contribute to numerous federal and international reports.

I consult on pharmaceutical development and have contributed to the research and/or approval of for most treatments approved for drug, alcohol and nicotine addiction since the 1980s and have advised NIDA, CDC, FDA, the World Health Organization, and other organizations since then. I advise the American Kratom Association on kratom science. That began as a pro bono effort when DEA proposed placing kratom in Schedule I in 2016. My efforts were focused on setting the record straight because my colleagues and I at PinneyAssociates (a team with extensive opioid and other drug experience) believed that DEA and FDA were wrong on the science and policy, and worse, that banning kratom would result in the quick establishment of a deadly kratom black market. We were frankly surprised, but thankful that then DEA Administrator Chuck Rosenberg withdrew the proposal. I discussed this with senior DEA staff who said that the comments from the public and scientists along with other information indicated that many people were using kratom to abstain from opioids and they did not want to risk sending them back to opioids. Surprisingly, a year later FDA again requested DEA to Schedule Kratom. Thankfully, and unusually, DEA has not acted on FDA's request.

First, please allow me to provide a few basic kratom facts:

- Kratom is in the coffee family, not the opium poppy family – it is not an opioid by nature.
- It produces caffeine like stimulation and many users report using kratom as a morning pick-me-up and to help maintain alertness, focus and productivity in the workplace – these are not typical uses of opioids.
- Kratom, like coffee contains many alkaloids, most of which have little pharmacological or toxicological activity. Its primary alkaloid, common to most kratom products is mitragynine. Mitragynine is not an opioid by nature, chemical structure, or overall profile of effects.
- Mitragynine mimics some of caffeine's alerting effects and also mimics some opioid effects like reducing pain and diarrhea, **BUT** with little of the signature powerful brain rewarding addictive effects and lethal respiratory depressing effects of heroin-like opioids.
- Kratom does provide some of the pain relieving and constipating effects of opioids and can help relieve opioid withdrawal but it is not approved for this or any therapeutic use by FDA.
- It is possible to develop some dependence on kratom and this is reported by some heavy kratom users, however, such people surveyed in the US and in studies in South East Asia report that it is

generally far milder than opioid dependence and that unlike opioids, kratom helps them function in the workplace and home. In this sense it is more analogous to caffeine than to opioids.

- NIDA is supporting research on mitragynine analogs as potential future medicines for pain, addiction and other disorders. But potential medicines are likely a decade or more away.
- There are an estimated 10-16 million kratom users in the US. Surveys indicate that the population of kratom users is dominated by adults aged 30-50 with lower rates of use among younger and older persons. Their demographics indicate that most have at least some college education, are married or in monogamous relationships, and have health care.
- These respondents report that they use kratom for health and well-being and that for them, kratom is either more effective, better tolerated with respect to side-effects, and/or more affordable than available pharmaceuticals. For many people, kratom is a path away from opioids, whether for managing pain or addiction.
- The surveys indicate a compelling argument for regulation rather than a ban because kratom consumers are rightly terrified that a ban that would leave them only with black market products or a return to opioid use and risk of overdose. Mortality data show that the overdose risk of opioids is at least one thousand times greater than for kratom.
- **The opioid crisis has hit Ohio hard:** 2nd in per capita opioid overdose and all opioids combined for a total of approximately 4,293 in 2017 (CDC and NIDA reports).
- **Kratom is an informal asset in addressing the opioid epidemic and it is helping people who find formal treatment ineffective, inaccessible or unacceptable.** I estimate that Ohio's population of approximately 11.7 million likely includes approximately 300,000 adult kratom users of which surveys suggest that 20-30% or 60-90 thousand, are at reduced risk of opioid overdose due to their use of kratom in place of opioids. These are estimates based on import and sales data and four national internet surveys as we do not have valid state or nationally projectable data.
- Two misconceptions that are often reported in the general media.
 - **Headline: "CDC reported 91 kratom over dose deaths"** In actual fact, CDC stated that this is what medical examiners stated and then CDC pointed out that most of the deaths for which there were data involved other drug use, and the few that did not find other drug use might have missed other drugs because they did not properly test for them. The CDC made no conclusion about how many deaths (if any) in which kratom was reported by medical examiners could actually be attributed primarily if at all to kratom. From CDC report: "Kratom was determined to be a cause of death (i.e., kratom-involved) by a medical examiner or coroner for 91 (59.9%) of the 152 kratom-positive decedents, including seven for whom kratom was the only substance to test positive on postmortem toxicology, although the presence of additional substances cannot be ruled out (4). In approximately 80% of kratom-positive and kratom-involved deaths in this analysis, the decedents had a history of substance misuse, and approximately 90% had no evidence that they were currently receiving medically supervised treatment for pain. Postmortem toxicology testing detected multiple substances for almost all decedents." (see CDC. O'Malley Olsen et al, 2019, report at: <https://www.cdc.gov/mmwr/volumes/68/wr/mm6814a2.htm>). This does not mean kratom has not contributed to any drug overdose deaths but the media reports misrepresent the CDC article and there is no question that the risk of kratom is far lower than carried by opioids and other drugs that it is substituted for by many people.
 - **Headline: "Kratom-related liver injuries on the rise in the US"** Some articles based on Navarro et al abstract, 2019 titled: "Increasing episodes of hepatotoxicity in the drug induced liver injury network associated with kratom, a botanical product with opioid-like activity" state that kratom carries liver disease risk as though this was an established fact. In actual fact, we

do not know if pure kratom leaf material or any of its mitragynines carry risk of liver disease but we can't rule it out either. Two of the problems with reports, such as that by Navarro et al. are that first, because of restrictions on kratom access in some states, and the lack of regulation to ensure pure kratom in most other states, some kratom is contaminated or adulterated by substances that might contribute to liver disease and other health risks. Secondly, and in my opinion, most importantly, is that many kratom users, especially heavier users, use kratom because of pain and other conditions that led to their likely heavy use and sometime decades long use (as reported in comments to DEA and public testimony) of acetaminophen and other drugs that are known to carry serious risks of liver disease. Sorting out the actual risk, if any, of kratom and is so what should be mentioned in the labeling of regulated kratom will take actual evidence as we have with acetaminophen and which can then be appropriately communicated to consumers.

I believe Ohio's residents would be best served by efforts to ensure adult use but with a regulatory framework to discourage inappropriate use including use by young people and to address kratom's main health risks which are related to impure and adulterated products.

Efforts like a minimum age of purchase of 21 should contribute to discouraging use by young people but would have little impact on people who use kratom for health and well being because the vast majority of kratom consumers are at older than 21.

Conversely a ban on kratom, would predictably result in the emergence of a black market. This is predicted by surveys that have asked adult kratom users what they would do if kratom was banned. Many said they would find other sources because they prefer it to convention medicines either because for them it works better or has fewer side-effects of concern. This include adults with chronic pain who are desperate to get off opioids as well as people with chronic pain for whom opioids were beneficial but can not longer get opioid prescriptions. For people with opioid use disorder, kratom reaches many people who find conventional treatments ineffective, inaccessible, or unacceptable. They are rightly terrified of a kratom ban and deadly black market.

I can provide scientific articles including recent peer-review publications as sources of these facts. I will be pleased to do whatever I can to provide science and regulatory perspective to help you find a path to protect kratom consumers in Ohio address the opioid epidemic and minimize unintended consequences of kratom availability.

Thank you for the opportunity to provide this information.