

A pharmacologist explains the controversy and addictive potential of the herbal substance kratom

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Credit: Anh Nguyen from Pexels

<u>The herbal substance kratom</u>, derived from the leaves of a <u>Southeast Asian tree</u>, is used by <u>nearly 2 million people</u> in the United States



annually. It can be easily purchased at gas stations and convenience stores, smoke shops and online, and is marketed as an "herbal supplement."

Proponents claim that <u>kratom</u> has many of the pain-relieving benefits of traditional opioids and that it can potentially be used as a treatment for opioid dependence.

The primary concern about kratom is that it can mimic how synthetic opioids work in the body, potentially causing overdoses, severe withdrawal symptoms and other serious health issues. As a result, the Food and Drug Administration recommends against its use.

The Conversation asked C. Michael White, a pharmacist at the University of Connecticut who has been <u>studying the science behind</u> <u>kratom</u> for many years, to explain its potential benefits and why consumers should use caution with this product.

How does kratom work in the body?

Kratom doesn't contain just one active ingredient; rather, it is made up of many substances that induce effects in the body. This is very common for <u>natural products</u>, since the cells of the plant make a variety of chemicals for different purposes.

When the body is experiencing pain, it releases hormones called endorphins that <u>stimulate opioid receptors</u> to mildly reduce the transmission of local pain sensations to the brain. This same process also causes the release of the neurotransmitter dopamine, <u>inducing a feeling of pleasure</u> to neutralize the pain.

Traditional opioids, like morphine and fentanyl, stimulate these same receptors to such a degree that they more potently numb pain, induce a



<u>euphoric feeling</u> that can lead to addiction, and suppress the drive to breathe, which can result in death.

One of the key constituents of kratom is an <u>organic compound called</u> <u>mitragynine</u>. It interacts with the same opioid receptors as morphine and fentanyl, but does not recruit the beta-arrestin-2 (the reason for breathing suppression). As a result, kratom can provide <u>pain relief</u> with a lower risk <u>of slowed or stopped breathing</u> compared to traditional opioids.

Kratom also contains a small amount of <u>7-hydroxymitragynine</u>, which is thought to more potently stimulate <u>opioid receptors</u>, leading to a greater risk of opioidlike adverse events.

One of the risks associated with kratom use is that products can <u>differ</u> <u>dramatically in the doses</u> of 7-hydroxymitragynine. In other words, one kratom product could be more dangerous than another. When kratom is used in high doses, it <u>can lead to seizures</u> and other issues. Since kratom products are not FDA-regulated, there is no uniformity to the products.

What is kratom's legal status in the US?

Kratom's current legal status is complicated. Kratom is not a prescription or over-the-counter drug, and while it is derived from a plant, it does not meet the FDA's definition of a <u>dietary supplement</u>, food or food additive

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Natural products marketed in the U.S. <u>before Oct. 15, 1994</u>, were grandfathered in under the FDA's list of dietary supplements. But since kratom came on the market later, the FDA would have to find, based on a history of use or other evidence, that when used under the conditions recommended or suggested in the labeling, the natural product can <u>reasonably be expected to be safe</u>—like the FDA does for all new



dietary supplement ingredients.

In 2016, in response to increasing calls to <u>poison control centers</u>, the Drug Enforcement Administration sought to ban kratom by <u>making it a Schedule I drug</u>. This means the agency felt it had no currently accepted medical use and a high potential for abuse. But backlash from the public and <u>support from congressional members</u> made the agency postpone a final decision. So kratom is currently listed as <u>a "drug of concern."</u>

Seven states and some counties have <u>banned the sale of kratom</u>. But in 2023, the <u>U.S. House</u> and <u>Senate proposed legislation</u> to prevent the FDA from regulating kratom more stringently than they do a dietary supplement or a food additive, in order to keep the product accessible to consumers.

Is kratom an effective pain reliever?

A 2024 literature review concluded that <u>there are no clinical trials</u> evaluating the effects of kratom on <u>chronic pain management</u>.

Research on acute pain tolerance in people is limited to a 2020 study that found participants who took a dose of kratom could endure immersion of their arms in an ice bath for significantly longer than those who did not take a dose of kratom. However, this study was conducted on chronic kratom users, and their pain tolerance before they took their dose for that study was much lower compared to that of non-kratom users in other studies. This suggests that chronic kratom use is lowering people's background pain tolerance.

This is similar to another study showing that when people tried to stop taking kratom after chronic use, they experienced significant <u>pain</u> throughout their body. This increased sensitivity and reactivity to pain, called <u>hyperalgesia</u>, also occurs with traditional opioids and is one of the



reasons why people who use them chronically find it so difficult to get off them.

Taken together, these studies suggest caution before starting kratom as a treatment for chronic pain, especially if safer methods such as acetaminophen, icing and heating, and physical therapy can suffice.

Does kratom effectively treat opioid use disorder?

Some people also claim that kratom could be a natural treatment for withdrawal and other effects of <u>opioid use disorder</u>, the clinical term for <u>opioid dependence</u>.

A few methodologically weak studies reported that <u>participants were</u> <u>able to reduce or stop</u> their use of traditional opioids and that kratom reduced the severity of <u>opioid withdrawal symptoms</u>. These include diarrhea, runny nose and eyes, shaking, fast heartbeat and anxiety.

However, there are no <u>clinical trials</u> comparing kratom to methadone, buprenorphine or naltrexone, the FDA-approved <u>treatment options for opioid use disorder</u>. So if patients have access to traditional FDA-approved therapies, these are the safest and best place to start.

If traditional options are not effective or patients cannot access them due to financial or logistical barriers, kratom may be a <u>potential alternative to illegal opioid products</u>, but it is certainly not risk free. Speaking with a health care professional is critical before making treatment decisions.

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