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File: ■ Kratom (*Mitragyna speciosa*, Rubiaceae)

■ **Traditional Uses**

■ **Emerging Uses**

HC 111645-570

Date: June 15, 2017

RE: Review of Traditional and Non-traditional Uses of Kratom

Singh D, Narayanan S, Vicknasingam B. Traditional and non-traditional uses of mitragynine (kratom): a survey of the literature. *Brain Res Bull.* September 2016;126(Pt 1):41-46.

Kratom is the name most widely used to describe the leaves of *Mitragyna speciosa* (Rubiaceae), a tree which is indigenous to South East (SE) Asia. Traditionally, kratom has been used in SE Asia as a mild stimulant to alleviate fatigue and as a treatment for pain, fever, and wounds. The dose-dependent narcotic-like properties of the leaves have been attributed chiefly to the constituent alkaloids mitragynine and 7-hydroxymitragynine, which are stimulating at lower doses and sedating at higher ones. This herb was initially adopted into Western culture as a dietary supplement with analgesic properties; however, the uses of kratom in both SE Asia and Western countries are evolving.

These authors conducted a review of the literature describing the traditional and non-traditional uses of kratom. PubMed, ScienceDirect, and Scopus were searched using the keywords "kratom" and "*Mitragyna speciosa*." A total of 40 articles referencing human use of kratom were identified—17 describing kratom use in SE Asia and 23 referencing kratom use in the West (Germany, Norway, Sweden, United Kingdom [UK], and United States [US]). It is noted that while kratom is distributed throughout SE Asia, including the Philippines, Borneo, Myanmar, and New Guinea, the publications discussing kratom use were limited to Thailand and Malaysia. The design of the 40 articles were categorized as follows: ten internet-based surveys, eight reviews, 17 case reports, two in-depth interviews, one reference text, two short communications, and one experimental design study. The results were summarized under the following headings: modes of supply, modes of consumption, uses, side effects, addiction, withdrawal effects, legal status, and social status.

In Thailand and Malaysia, the identity of the supplier and the quality of their products are known to the buyer. In the West, the largest volume of kratom is sold anonymously over the internet.

In SE Asia, kratom leaves are chewed, smoked, or decocted to provide a "juice." Due to the bitter taste of the juice, many users prefer to combine it with sweet beverages such as sodas. Modes of consumption in the West must be inferred from the types of kratom

merchandise offered for sale, which include powdered leaves, tablets, capsules, gums, pills, smoking preparations, and a variety of combination products.

The use of kratom is common in rural areas of SE Asia. Its medicinal applications include the treatment of fever, diarrhea, pain, and wounds. In addition, it is socially acceptable for male workers to use kratom to enhance physical endurance and relieve stress, whereas female users may be subject to social stigma. The common usage of kratom in Malaysia to reduce illicit substance dependence and ease withdrawal was reported in 2010. Affordable and readily available, researchers found that it allows addicts to self-manage withdrawal and avoid the public shame associated with official treatment programs. The underground use of kratom by young adults in a cocktail with cough syrup or codeine is another emerging trend.

In Western countries, kratom was introduced as an herbal remedy for chronic pain and subsequently also became known as a self-administered treatment for substance withdrawal. More recently, it has been promoted as a euphoric "legal high," and concentrated extracts and mitragynine products are marketed in several forms, including combinations with other substances. [Note: The "Krypton" product associated with nine fatalities in Sweden contained kratom, caffeine, and the synthetic opioid O-desmethyltramadol.]

The primary adverse effects (AEs) associated with regular kratom use in SE Asian populations are reported to be weight loss, dehydration, constipation, hand shaking, headaches, and hyperpigmentation, and in the longer term, lethargy and fatigue. Among Western users, AEs can only be extrapolated from case reports; kratom use has been linked to seizures, hypothyroidism, and liver injury. The authors note that while reports of toxicity and fatalities continue to emerge from the West, none have been reported in SE Asia. Also, many of the fatalities were associated with dependency/abuse of other substances. There are several hypotheses which may explain these findings—higher tolerance to kratom in SE Asia due to its long history of use or AEs are less likely to be reported; the concentrated extracts and mitragynine products consumed in the West are much more toxic compared to the relatively unprocessed leaf products used in SE Asia; and the possibility that Western users may be buying adulterated, contaminated, or misidentified products.

Studies in SE Asia suggest that regular use of kratom leads to dependence. However, unlike opioid addicts, most kratom users remain healthy and a 2014 Malaysian study found no impairment of social functioning. Although studies in the West are lacking, there have been case reports of kratom addiction, and the burgeoning internet sales of kratom suggest that addiction may also be an emerging concern in the West.

Data from SE Asian studies indicates that sudden withdrawal of kratom can cause unpleasant physical and psychological symptoms. Reported physical symptoms include lethargy, irritability, yawning, runny nose, muscle pain, cramps, joint pain, and diarrhea. Psychological symptoms include restlessness, tension, aggression, sadness, nervousness, delusion, hallucination, and intense cravings; anxiety, depression, moodiness, annoyance, and sleeplessness also have been reported. A Malaysian survey found that users who consumed ≥ 3 glasses/day of kratom juice had greater odds of dependence and withdrawal symptoms. However, it is reported that while kratom withdrawal symptoms are distracting, they are not as painful as opioid withdrawal and the symptoms usually disappear after one to three days. In the West, documentation of kratom withdrawal symptoms are limited to a few case reports, some of which involved other substances.

Kratom is banned in Australia, Bhutan, Malaysia, Myanmar (Burma), and Thailand. However, it is reported that it is still readily available in Malaysia and Thailand. Kratom remains unregulated in the UK and many European countries, although it is controlled in Denmark, Finland, Lithuania, Poland, Romania, and Sweden. In the US, kratom is the subject of an import ban but is not regulated. [Note: In October of 2016, the US Drug Enforcement Administration announced a six-week public consultation on kratom.] It is noted that kratom drug test kits are not available and treatment protocols for kratom dependence have not been developed.

Kratom users in SE Asia may face some family rebuke for their "wasteful" habit but are not considered drug users; they are generally seen as hard-working people who use kratom to work longer hours and earn more money. Surveys indicate that the majority are older adults with regular employment and stable family environments. In traditional Thai culture, kratom was served to guests and was used in ritual worship of ancestors and gods.

In summary, kratom has a long history of safe use in SE Asia with no serious AEs or fatalities associated with its consumption. The authors conclude that "the value of kratom in pain management and opioid withdrawal deserves careful scientific study and evaluation to determine its efficacy, composition, drug interactions and safe dosage limits." They comment that it would be unfortunate if the sporadic case reports of severe AEs or fatalities in the West are used to support the implementation of regulations banning kratom; "any blanket illegalization of kratom poses the danger of casting out the baby with the bathwater." The evidence from SE Asia suggests that kratom has considerable potential as an inexpensive treatment for people who are dependent on more highly addictive substances. Noting that raw kratom leaves lack AEs and have a wide variety of effects depending on the strain and source, the authors suggest future research would be more productive if it was focused on whole kratom leaves rather than isolated constituents like mitragynine. The authors call for international collaboration to conduct the many social and medical research studies that are needed to establish the therapeutic role of kratom.

—*Mariann Garner-Wizard*

Referenced article can be accessed at
<http://www.sciencedirect.com/science/article/pii/S0361923016301010>.

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