File: ■ Kratom (Mitragyna speciosa, Rubiaceae)
■ Mitragyna Species (Rubiaceae)
■ Ethnomedicinal Review

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RE: Review of Kratom and Other Mitragyna Species Reveals Complex Chemistry, Widespread Ethnomedicinal Uses, and Little Evidence of Harm


In light of growing interest in kratom (Mitragyna speciosa, Rubiaceae) leaf in the United States and Europe, and the likelihood of deliberate or accidental substitution of other species for this herb, the authors examine its taxonomy, traditional uses, and phytochemistry using searches of electronic databases and non-digitized texts.

Mitragyna is classified in the subfamily Cinchonoideae, tribe Naucleeae, and subtribe Mitragyninae. It includes ten species, which are native to Africa and southern and southeastern Asia to southern China, with one species extending to New Guinea. Several Mitragyna spp. are used as traditional medications in these areas. Taxonomic rearrangements in Naucleeae have spawned multiple synonyms for most species. Mitragyna spp. are deciduous, semi-deciduous, or evergreen trees found in tropical forests, swamps, or deserts and savannahs subject to periodic rainfall or flooding. Mitragyna spp. are distinguished primarily by reproductive characters, and vegetative morphology varies considerably within species, making identification of sterile material difficult and allowing widespread substitution. Microscopic characters of the leaf anatomy may be useful, though studies are limited. Other Asian species are most likely to be substituted for kratom, though leaves of species from related genera, including Uncaria (Rubiaceae), also may be substituted. In one case, discovery of an unknown species being sold as kratom led not to its withdrawal from the market but re-branding as a kratom alternative. In Sweden, several deaths occurred after use of a kratom blend including other narcotic substances.

Mitragyna species contain many secondary metabolites, including flavonoids, polyphenols, triterpenoids, triterpenoid saponins, monoterpenes, and secoiridoids. The chemistry of the genus has been studied since the early 1900s, with 79 alkaloids identified in Mitragyna material. Bark and stem bark contain terpenoids not found in leaves from the same plants. The indole alkaloids mitragynine and 7-hydroxymitragynine are the most prevalent and best-studied Mitragyna spp. compounds, thought largely responsible for kratom's effects. Of natural compounds in Mitragyna spp., 57, including...
37 alkaloids, are unique to kratom leaf. In kratom, the reported proportion of mitragynine in leaf tissue ranges from 12% to 66% of total alkaloids; 7-hydroxymitragynine, thought to be significantly more bioactive, is less than 2% of alkaloid content. Alkaloid content varies with ecotype and maturity at harvest; commercial products labeled as kratom show considerable variation in alkaloid content.

The pharmacology and toxicology of *Mitragyna* spp. have been extensively studied. The analgesic and psychoactive effects of kratom are primarily associated with 7-hydroxymitragynine and mitragynine, μ-opioid receptor agonists that in rodent studies appear to reduce pain of thermal and mechanical origin. 7-Hydroxymitragynine is a 13-fold greater opioid receptor agonist than morphine (from opium poppy [*Papaver somniferum*, Papaveraceae]), and 46-fold greater than mitragynine. In vivo, methanolic extracts of kratom may have more potent antinociceptive properties than comparable doses of purified alkaloids, possibly because of synergistic and/or potentiating effects of other compounds. An in vitro study suggests an anti-inflammatory action of mitragynine. Several other *Mitragyna* alkaloids exert opioid receptor agonist activity. Vasodilatory, antiarrhythmic, and antihypertensive bioactivities have been seen in vitro. In vivo, muscle-relaxative, antiarrheal, antidepressive, and anti diabetic effects are reported. Toxicity of kratom and its alkaloids is not well understood and lethal dosages are not established. The history of regular kratom consumption in Southeast Asia over hundreds of years suggests it is relatively safe in traditional use. However, in vitro and in vivo studies using very high doses report potential negative effects that should be further investigated.

Ethnomedically, bark, branches or twigs, leaves, fruit, flowers, and roots of *Mitragyna* spp. may be used together, alone, or with other herbs. Reported uses for different plant parts are not evenly distributed among species. Bark, leaves, and roots are most widely used overall; in two species, only bark use is reported, possibly for cultural reasons, whereas in one species, only the leaf of kratom is used. Uses include treating fever, malaria (a reported use for five different species), and African sleeping sickness; as an antidote for poison (possibly through an emetic effect); for skin problems; for gastrointestinal complaints and parasites; for weight loss, poor nutrition, or lack of energy; as a liver and kidney aid for jaundice and diabetes; to treat neurological and psychosomatic problems; for pain, inflammation, rheumatism, and swelling; to ease menstrual and childbirth pain and assist in reproduction; for cough, asthma, and other respiratory conditions; and to treat sexually transmitted diseases and urinary problems. Interestingly, many uses for species besides kratom involve baths or poultices made from leaves. Other preparations include cold infusions from powdered leaves and a syrupy filtrate of boiled leaves that is smoked or ingested. Leaves are also chewed, similar to coca (*Erythroxylum* spp., Erythroxylaceae) leaves, as a mild stimulant. Modern uses of kratom, especially in Thailand, mirror uses touted for Western sales, e.g., pain relief and opioid withdrawal. Despite concerns by the US Drug Enforcement Administration about kratom addiction, traditional use of kratom parallels use of coffee (*Coffea arabica*, Rubiaceae) in terms of habituation more than opiates.

—Mariann Garner-Wizard

The American Botanical Council has chosen not to reprint the original article.