

KAVA

(Other Names: Ava, Intoxicating Pepper, Kawa Kawa, Kew, Sakau, Tonga, Yangona)

Introduction:

Kava, also known as *Piper methysticum* (intoxicating pepper), is a perennial shrub native to the South Pacific Islands, including Hawaii. Kava is harvested for its rootstock, which contains the pharmacologically active compounds kavalactones. The term kava also refers to the non-fermented, psychoactive beverage prepared from the rootstock. For many centuries, Pacific Island societies have consumed kava beverages for social, ceremonial, and medical purposes. Traditionally, kava beverages are prepared by chewing or pounding the rootstock to produce a cloudy, milky pulp that is then soaked in water before the liquid is filtered to drink.

Kava is increasingly used for recreational purposes. Kava's reinforcing effects include mild euphoria, muscle relaxation, sedation, and analgesia.

Licit Uses:

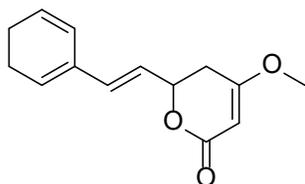
In the United States, kava is sold as a dietary supplement that is promoted as a natural alternative to anti-anxiety drugs and sleeping pills. An analysis of six kava clinical trials found that kava (60–200 mg of kavalactones per day) produced a significant reduction in anxiety compared to placebo. Another meta-analysis found kava to be more effective than placebo in three out of seven trials. The United States Food and Drug Administration (FDA) has not made a determination about kava's efficacy for this use.

A number of cases involving liver damage (hepatitis and cirrhosis) and liver failure have been associated with commercial extract preparations of kava. In 2002, FDA issued an advisory alerting consumers and healthcare providers to the potential risk of liver-related injuries associated with the use of kava dietary supplements.

Kava dietary supplements are commonly formulated as tablets and capsules (30–90% kavalactones; 50–250 mg per capsule). Kava is also available as whole root, powdered root, extracts (powder, paste, and liquid), tea bags, and instant powdered drink mix. Kava is frequently found in products containing a variety of herbs, vitamins, or both.

Chemistry:

Kava belongs to a class of organic compounds known as dihydropyranones. Kava has a molecular formula of $C_{14}H_{16}O_3$ and a molecular weight of 232.275 g/mol. The structure of Kava is shown below:



Pharmacology:

Different varieties of kava plants possess varying concentrations of kavalactones. Pharmacologically active kavalactones are found in the lipid soluble resin of the kava rootstock. Of the 18 that were isolated and identified, the six major kavalactones are yangonin, methysticin, dihydromethysticin, dihydrokawain, kawain, and desmethoxyyangonin.

The pharmacokinetics of kavalactones have not been extensively studied. Kavalactones are thought to be absorbed relatively quickly in the gut and exhibit differences in bioavailability. The preferential sites of action of kavalactones appear to be the limbic structures, amygdala

complex, and reticular formation of the brain; however, the exact molecular mechanisms of action are unclear.

Kava has the potential for causing drug interactions through the inhibition of CYP450 enzymes that are responsible for the metabolism of many pharmaceutical agents and other herbal remedies. Chronic use of kava in large quantities may cause a dry scaly skin or yellow skin discoloration known as kava dermatopathy. Such use may also cause liver toxicity and extrapyramidal effects (e.g., tremor, abnormal body movement).

Individuals may experience a numbing or tingling of the mouth upon drinking kava due to its local anesthetic action. High doses of kavalactones can also produce central nervous system depressant effects (e.g., sedation, muscle weakness) that appear to be transient.

Illicit Uses:

Information on the illicit use of kava in the United States is anecdotal. Based on information on the internet, kava is being used recreationally to relax the body and achieve a mild euphoria. Kava is typically consumed as a beverage made from dried kava root powder, flavored and unflavored powdered extracts, and liquid extract dissolved in pure grain alcohol and vegetable glycerin. Individuals may be consuming 25 grams of kavalactones, which is approximately 125 times the daily dose in kava dietary supplements.

Intoxicated individuals typically have sensible thought processes and comprehensive conversations, but they also have difficulty coordinating movement and often fall asleep. Kava users do not exhibit the generalized confusion and delirium that occurs with high levels of alcohol intoxication. While kava alone does not produce the motor and cognitive impairments caused by alcohol, kava does potentiate both the perceived and measured impairment produced by alcohol.

The American Association of Poison Control Centers reported 106 case mentions and 75 single exposures associated with kava in 2016. In 2022, reports increased to 130 case mentions and 76 single exposures.

User Population:

Information on the user population in the United States is very limited. In the 1980s, kava was introduced to Australian Aboriginal communities, where kava quickly became a drug of abuse. Kava has since become a serious social problem in regions of Northern Australia.

Illicit Distribution

Kava is widely available on the internet. Some websites that promote and sell kava products also sell other uncontrolled, psychoactive products, such as *Salvia divinorum*. Several kava bars and lounges in the United States sell kava drinks.

The Drug Enforcement Administration's National Forensic Laboratory Information System (NFLIS) Drug database collects scientifically verified data on drug items and cases submitted to and analyzed by participating federal, state, and local forensic drug laboratories. NFLIS-Drug received the first report of kava in 2020. NFLIS-Drug also received a single report of kavain in 2019 and in 2020.

Control Status:

Kava is not controlled under the Controlled Substances Act.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 571-362-4250, Telephone 571-362-3249, or Email DPE@dea.gov.