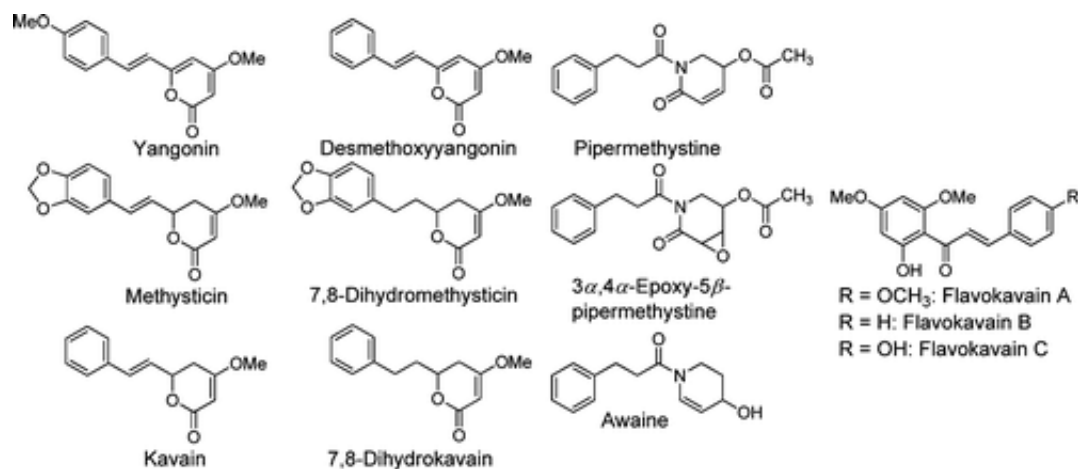


The unsolved mystery of kava toxicity

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A major new review of scientific knowledge on kava — a plant used to make dietary supplements and a trendy drink with calming effects — has left unsolved the mystery of why Pacific Island people can consume it safely, while people in the United States, Europe, and other Western cultures sometimes experience toxic effects. The article appears in ACS' journal *Chemical Research in Toxicology*.

Line Olsen and colleagues point out that for centuries, people of the Pacific Islands have safely consumed a beverage made from crushed kava roots. Kava's calming effects made it popular in Western cultures in the 1990s, when people also began to use a herbal supplement for the treatment of anxiety, emotional stress and sleep problems. But in 2001,

reports of liver damage among Westerners who took kava supplements gained widespread attention. Many Western countries, including the United States, the United Kingdom, and Canada, ban or regulate the sale of kava products. To determine why kava is toxic to some people but not to others, the researchers sifted through the scientific studies published on the topic.

Their review of 85 scientific studies on kava [toxicity](#) found no consensus on kava toxicity, despite several theories that have emerged over the years. Culprits include methods for preparing kava, the particular species of kava used, the possible toxicity of substances produced by the body when [kava](#) is digested and genetic differences among consumers. "To date, there remains no indisputable reason for the increased prevalence of kava-induced hepatotoxicity in Western countries," the researchers say.

More information: “Constituents in Kava Extracts Potentially Involved in Hepatotoxicity – A Review” Chem. Res. Toxicol., Article ASAP [DOI: 10.1021/tx100412m](https://doi.org/10.1021/tx100412m)

Abstract

Aqueous kava root preparations have been consumed in the South Pacific as an apparently safe ceremonial and cultural drink for centuries. However, several reports of hepatotoxicity have been linked to the consumption of kava extracts in Western countries, where mainly ethanolic or acetonic extracts are used. The mechanism of toxicity has not been established, although several theories have been put forward. The composition of the major constituents, the kava lactones, varies according to preparation method and species of kava plant, and thus, the toxicity of the individual lactones has been tested in order to establish whether a single lactone or a certain composition of lactones may be responsible for the increased prevalence of kava-induced hepatotoxicity in Western countries. However, no such conclusion has been made on

the basis of current data. Inhibition or induction of the major metabolizing enzymes, which might result in drug interactions, has also gained attention, but ambiguous results have been reported. On the basis of the chemical structures of kava constituents, the formation of reactive metabolites has also been suggested as an explanation of toxicity. Furthermore, skin rash is a side effect in kava consumers, which may be indicative of the formation of reactive metabolites and covalent binding to skin proteins leading to immune-mediated responses. Reactive metabolites of kava lactones have been identified in vitro as glutathione (GSH) conjugates and in vivo as mercapturates excreted in urine. Addition of GSH to kava extracts has been shown to reduce cytotoxicity in vitro, which suggests the presence of inherently reactive constituents. Only a few studies have investigated the toxicity of the minor constituents present in kava extract, such as pipermethystine and the flavokavains, where some have been shown to display higher in vitro cytotoxicity than the lactones. To date, there remains no indisputable reason for the increased prevalence of kava-induced hepatotoxicity in Western countries.

Provided by American Chemical Society

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