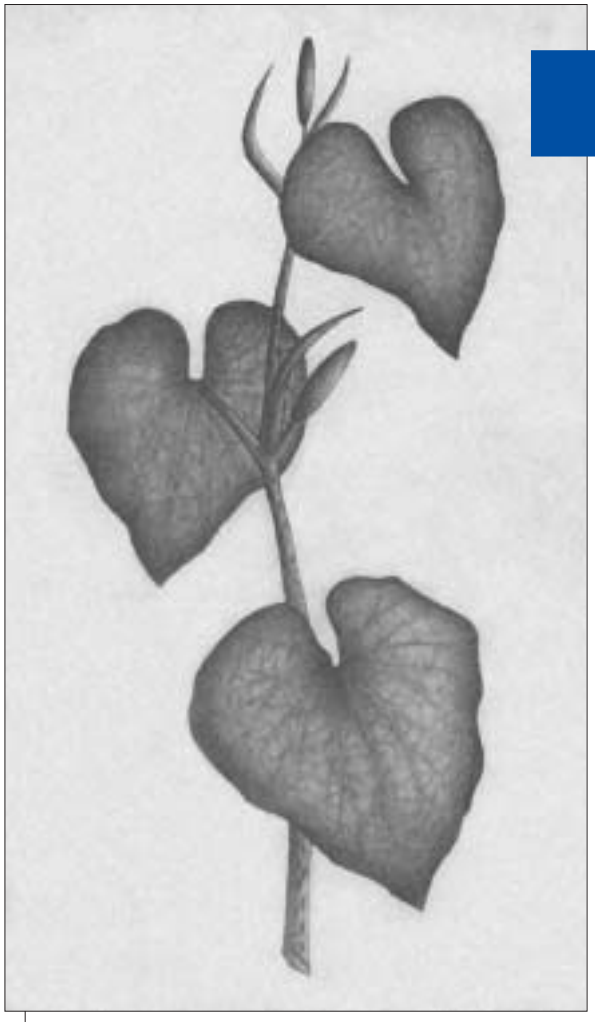

Monograph

Piper methysticum (kava kava)

Description and Constituents

Piper methysticum (kava kava) is a perennial plant native to the Pacific Island region, and has been used ceremonially for thousands of years. Traditionally, a beverage is prepared, then drunk before the evening meal. Indigenous methods of mastication of the kava root have given way to grinding or pounding the plant substance, which is then mixed with water or coconut milk.

The active constituents consist of a group of lactones, organized around an arylethylene-alpha-pyrone skeleton.[1] They are similar in structure to myristicin, which is found in nutmeg.[2] These kava lactones (AKA kava pyrones) make up 3-20 percent of the root by dry weight. Fifteen lactones have been isolated from kava, nine of which have been fully identified.

CNS Effects

Kava's exact mechanism of action on the central nervous system has not been fully elucidated. One hypothesis is that the kava lactones potentiate GABA receptors. However, a study which addressed this issue found little supportive evidence. In both *in vivo* and *in vitro* studies, only weak GABA-binding activity was observed.[3] A more recent study, however, found GABA-binding to be a mechanism for some of kava's sedative effects.[4]

In vitro studies have found that, while kava lactones were not found to efficiently block uptake of serotonin, inhibition of noradrenaline uptake was demonstrated by three lactones, providing another possible mechanism of action.[5]

In animal models, kava is known to inhibit experimentally induced convulsions.[6-8] Research indicates this anticonvulsant effect may be mediated by Na^+ channel receptor sites, a common target of anti-epileptic drugs.[9-11]

Analgesic/Anesthetic Effects

Four lactones from kava (kavain, dihydrokavain, methysticin, and dihydromethysticin) have been found to possess significant analgesic effects in animal studies. The analgesia appeared to be via non-opiate pathways.[12] A dose of 120 mg/kg of either dihydromethysticin or dihydrokavain was equivalent to 2.5 mg/kg morphine.[13]

Kavain appears to be the most effective surface anesthesia, comparable to cocaine in strength and duration of action.[14] Subcutaneous injections have been known to provide anesthesia for several hours to several days. Too high a dose, however, can induce temporary paralysis, rendering it not the most suitable local anesthetic.[15]

Psychoactive effects

Kava extracts have been found to be effective anxiolytic agents. In one double-blind, placebo controlled study, 29 subjects were treated for four weeks with 100 mg three times daily kava extract, standardized to contain 70% kava lactones. Compared to the placebo group, the kava group experienced significant decreases in symptoms of anxiety measured on the Hamilton Anxiety Scale.[16]
In a another double-blind, placebo controlled study of two groups of 20 women, using the same dosage as above, kava was found effective for decreasing anxiety associated with menopause.[17]

In a number of studies kava extracts have compared favorably to prescription medications such as benzodiazepines and tricyclic antidepressants (often used to treat anxiety disorders), and without the side-effects commonly seen with these drugs.[18,19] Not only does kava appear not to impair reaction time, it appears to improve concentration. In two separate studies, oxazepam (a common anxiolytic medication) was found to slow reaction time, while kava actually enhanced performance.[20,21]

Other Potential Applications

Kava may have application for cardio- and cerebrovascular protection. The kava lactone, kavain, has been found to reduce platelet aggregation, apparently by inhibition of cyclooxygenase, leading to inhibition of thromboxane A2.[22] An animal study found the lactone, methysticin, to protect against ischemic brain damage by decreasing the infarct area.[23]

Kava appears to have some potential antimicrobial effects. It has been used traditionally in Polynesia as an antifungal.[24] The lactone, dihydrokavain, has been noted to inhibit the growth of *Aspergillus niger*.[14]

Toxicity

The most common side-effect of heavy kava consumption is a skin rash know as "kava dermopathy." It is an ichthyosiform skin rash, with onset typically beginning in the face. Ocular photosensitivity also sometimes accompanies the rash. This type of rash is typically seen only in heavy long term consumers of the beverage, such as is seen in Polynesia. However, doses of 300-800 mg daily of the isolated lactone, dihydromethysticin, has been known to cause the rash.[25] Kava has also been known to potentiate other medications such as barbiturates, and Xanax.[14,26] It has also been noted to be a dopaminergic antagonist.[27] Claims that kava is addictive have been unsubstantiated.[14]

Dosage

The recommended dosage for kava depends upon the concentration of kava lactones. Therapeutic dosages appear to be in the range of 50-70 mg of the kava lactones three times daily, or approximately 100 mg TID of the 70-percent standardized extract. In a 30-percent concentration, the dosage would be in the range of 200 mg three times daily.

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