Rhizoma Piperis Methystici

Definition

Rhizoma Piperis Methystici consists of the dried rhizomes of *Piper methysticum* G. Forst. (Piperaceae) (*1–3*).

Synonyms

Macropiper latifolium Miq., *M. methystiscum* (G. Forst.) Hook. et Arnott, *Piper inebrians* Soland (*3*).

Selected vernacular names

Ava, ava root, awa, gea, gi, kao, kava, kavakava, kava-kava, kava-kava root, kavapipar, kawa, kawa kawa, kawa pepper, Kawapfeffer, malohu, maluk, maori kava, meruk, milik, racine de poivre enivrant, Rauschpfeffer, rhizoma de kava-kava, rhizoma di kava-kava, yagona, yaqona (*3–5*).

Geographical distribution

Indigenous to and cultivated in the islands of Oceania, from Hawaii to Papua New Guinea, with the notable exception of New Caledonia, New Zealand and most of the Solomon Islands (*5*).

Description

A perennial shrub up to 7 m high, robust and fairly succulent. Leaves cordate, pointed, smooth and green on both sides, up to 25 cm long. Root can reach 60 cm in length and 8 cm in diameter; may eventually become a heavy knotted mass, 8–25 cm wide. Petioles up to 6 cm long; flowers in irregular spadices with lateral root up to 3 m long (*5*).

Plant material of interest: dried rhizome

General appearance

Irregular, transverse and longitudinal pieces, varying considerably in size and shape: 3–20 cm long and 1–5 cm in diameter. Outer surface light yellowish or greyish-brown, longitudinally wrinkled, with large whitish circular root scars.

Fracture coarsely fibrous, inner surface yellow-white; bark thin; xylem distinctly radiate; pith large (*1*, *2*, *6*, *7*).

Organoleptic properties

Odour: slight, agreeable; taste: sweetish, pungent, sometimes slightly bitter, followed by slight numbness (*1*, *2*, *7*).

Microscopic characteristics

Transverse section through the xylem shows small channels with vascular bundles; cross section through the xylem shows narrow vessels, which are located around the pith and alternate with large pith rays. Additional vessels across the pith; xylem has tracheid-like elements; phloem has fewer and thinner-walled cells. Secretory canals contain a fine, brown resinous mass. Unpeeled rhizome has a narrow cork-layer. Primary bark contains rays of collenchyma, tissues, numerous resin and storage cells around the phloem (*1*–*3*).

Powdered plant material

Light yellow-brown. Contains large oval pith cells. Secretion canals containing yellow to red-brown masses of resin; elongated cells of the medullary rays porous and slightly lignified. Vessels lignified and reticulate; fibres slightly lignified, large lumen and occasionally branched oval ends. Xylem parenchyma, cells lignified and slightly elongated. Numerous simple or 2–3 compound starch grains, the individual grains being spheroidal or planoconvex, 10–30 µm and sometimes up to 45 µm in diameter, many showing radial or triangular central clefts. Calcium oxalate crystals absent (*1*, *2*, *7*).

General identity tests

Macroscopic, microscopic and microchemical examinations (*1*, *2*, *7*), and thin-layer chromatography for the presence of characteristic unsaturated α-pyrones known as kava pyrones (*1*, *2*, *8*).

Purity tests

Microbiological

Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on quality control methods for medicinal plants (*9*).

Foreign organic matter

Not more than 2% (*1*, *2*).

Total ash

Not more than 8% (*1*, *2*).

Acid-insoluble ash

Not more than 1.5% (*1*).

Water-soluble extractive

Not less than 5% (*1*).

Loss on drying

Not more than 12% (*2*, *3*).

Pesticide residues

The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*10*). For other pesticides, see the *European pharmacopoeia* (*10*), and the WHO guidelines on quality control methods for medicinal plants (*9*) and pesticide residues (*11*).

Heavy metals

For maximum limits and analysis of heavy metals, consult the WHO guidelines on quality control methods for medicinal plants (*9*).

Radioactive residues

Where applicable, consult the WHO guidelines on quality control methods for medicinal plants (*9*) for the analysis of radioactive isotopes.

Other purity tests

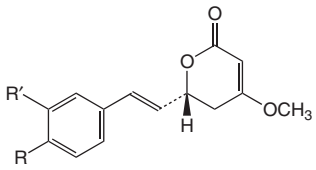
Chemical, sulfated ash and alcohol-soluble extractive tests to be established in accordance with national requirements.

Chemical assays

Contains not less than 3.5% kava pyrones, as determined by infrared absorption spectroscopy at $1705 \pm 5\,cm^{-1}$ (*2*). Complete qualitative analytical profiles can be obtained by high-performance liquid chromatography–electrospray mass spectrometry (*12*). A high-performance liquid chromatography method is also available for quantitative analysis (*3*).

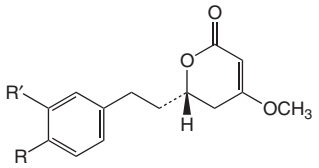
Major chemical constituents

The major constituents are kava lactones (also known as kava pyrones) with the major lactones being kawain (1.8%), methysticin (1.2%), dihydromethysticin (0.5%), demethoxyyangonin (1.0%), yangonin (1.0%) and dihydrokawain (1.0%). At least 13 other lactones, two chalcones and a number of free aromatic acids are known (*3–5*, *13*). The structures of the representative lactones are presented below.



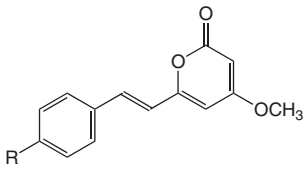
kawain R = R′ = H

methysticin R, R′ = O-CH_2-O



dihydrokawain R = R′ = H

dihydromethysticin R, R′ = O-CH_2-O



yangonin R = OCH_3

demethoxyyangonin R = H

Medicinal uses

Uses supported by clinical data

Short-term symptomatic treatment of mild states of anxiety or insomnia, due to nervousness, stress or tension (*14–24*).

Uses described in pharmacopoeias and in traditional systems of medicine

To induce relaxation, reduce weight and treat fungal infections (*5*).

Uses described in folk medicine, not supported by experimental or clinical data

Treatment of asthma, common cold, cystitis, gonorrhoea, headaches, menstrual irregularities, urinary infections and warts (*4*, *5*).

Pharmacology

Experimental pharmacology

Behavioural effects

Intraperitoneal administration of an aqueous extract of Rhizoma Piperis Methystici (62.5 mg/kg body weight) decreased the spontaneous activity of mice. This effect lasted for 2 hours without loss of muscle tone (*25*). The same extract, however, was not active in mice or rats when administered orally in single doses of 0.5–2.5 g/kg body weight. A dichloromethane extract of the rhizome (150 mg/kg body weight, administered intraperitoneally) decreased spontaneous motility by 46%, and markedly reduced motor control (by 50%)

in mice (*25*, *26*). At this dose, the extract also induced hypnosis and analgesia (*25*). Intraperitoneal administration of aqueous, dichloromethane and lyophilized aqueous extracts of the rhizome (62.5–250 mg/kg body weight) reduced spontaneous activity in mice and rats (*27*, *28*). Intraperitoneal administration of an aqueous or dichloromethane extract of the rhizome (120 mg/kg body weight) suppressed apomorphine-induced hyperactivity in rats (*25*). Intraperitoneal administration of a lipid-soluble fraction of an aqueous rhizome extract (doses up to 300 mg/kg body weight) decreased the conditioned avoidance response in rats. An aqueous extract, however, was inactive at doses up to 500 mg/kg body weight (*27*). Intraperitoneal administration of an extract of the rhizome (equivalent to 50–100 mg kava pyrones/kg body weight) or (±)-kawain, a synthetic kava lactone (10–50 mg/kg body weight), reduced muscle tone in cats (*29*).

Analgesic activity

Intraperitoneal administration of a dichloromethane extract of the rhizome (150 mg/kg body weight) produced analgesia in mice (*25*). Intraperitoneal or intragastric administration of an aqueous or lipid extract of the rhizome (150–250 mg/kg body weight) produced analgesia in mice, as measured by tail-flick reaction times and suppression of acetic acid-induced writhing (*30*). Both dihydrokawain and dihydromethysticin exhibited analgesic effects when administered intraperitoneally to rats (140 mg/kg body weight), as determined by an increase in tail-flick reaction times (*31*).

Neurological effects

Depression of the central nervous system was observed in rodents after intraperitoneal administration of an aqueous rhizome extract (50–170 mg/kg body weight) (*32*). Intraperitoneal administration of an aqueous extract (300 mg/kg body weight) or a chloroform extract (140 mg/kg body weight) of the rhizome depressed the central nervous system and potentiated the effects of barbiturates in mice. Administration of dihydromethysticin to mice potentiated pentobarbital-induced sleeping time by 400%, while dihydrokawain, yangonin and kawain were only moderately active (150–235%) (*33*). A dichloromethane extract of the rhizome administered intraperitoneally to mice (150 mg/kg body weight) induced hypnosis (*25*). The hypnotic and sedative effects of a dichloromethane rhizome extract (300 mg/kg body weight, administered intraperitoneally) were significantly prolonged in mice by the concurrent administration of ethanol (2 g/kg body weight; $P < 0.001$) (*30*). A saline extract of the rhizome had an effect on crayfish abdominal ganglia in vitro (0.05 g/ml) (*34*). Intraperitoneal administration of an extract of the rhizome (equivalent to 50–100 mg kava pyrones/kg body weight) to cats had a significant effect on EEG recordings, inducing high-amplitude delta waves, spindle-like formation, and continuous alpha- or beta-synchronization in amygdala recordings ($P < 0.001$). Hippocampal responses, following stimulation of the

amygdala nucleus, increased significantly in amplitude in cats treated intraperitoneally with the rhizome extract (equivalent to 100 mg kava pyrones/kg body weight; $P < 0.01$) or (±)-kawain (50 mg/kg body weight; $P < 0.05$) (*29*).

The neuroprotective effects of an acetone extract of the rhizome and kava pyrones have been demonstrated both in vivo and in vitro. A standardized acetone extract of the rhizome, methysticin and dihydromethysticin protected rodents against hypoxia or ischaemia-induced cerebral damage (*35*). The standardized extract also protected against neuronal damage in cultured neurons from chick embryo cerebral hemispheres (*36*).

Although the neuroprotective mechanisms of the rhizome are not well understood, recent investigations have indicated that kava pyrones may exert their effects by activating several neurotransmitter systems, such as the adrenergic (*37*), mesolimbic dopaminergic (*38*), gabaminergic (*39*), glutamatergic (*40*, *41*), and serotonergic receptor systems (*42*, *43*). An extract of the rhizome containing 58% kava pyrones enhanced the binding of [^{3}H]muscimol to γ-aminobutyric acid-A receptors in a concentration-dependent manner in rat hippocampus, amygdala and medulla oblongata in vitro (ED_{50} 200–300 µmol/l) (*39*). However, another study found no significant interaction in vitro or in vivo of a dichloromethane rhizome extract or kava pyrones with γ-aminobutyric acid (A and B) or benzodiazepine receptor binding sites (*44*). Both kawain and dihydromethysticin (10–100 µmol/l) reduced the field potential changes induced by the serotonin-1A agonist, ipsapirone, in the CA1 and CA3 areas of guinea-pig hippocampal slices in vitro. These results suggest that both compounds may modulate serotonin-1A receptor activity (*43*). Methysticin and kawain inhibited the uptake of ^{3}H-labelled norepinephrine, but not of ^{3}H-labelled serotonin, in synaptosomes prepared from the cerebral cortex and hippocampus of rats (*37*). Intragastric administration of (+)-dihydromethysticin in a single dose (100 mg/kg body weight), or chronic intragastric administration of (±)-kawain (10.8 mg/kg body weight) daily for 78 days to rats did not alter dopamine or serotonin levels in the striatal or cortical brain regions (*45*).

Anticonvulsant activity

Intraperitoneal administration of an aqueous extract (300 mg/kg body weight) or a chloroform extract (140 mg/kg body weight) of the rhizome to mice inhibited strychnine-induced convulsions (*33*). The anticonvulsant activity of methysticin and other kava pyrones against electroshock- and chemically-induced seizures has been demonstrated in mice and rats (*46–48*). Intraperitoneal administration of dihydromethysticin and dihydrokawain inhibited electroshock-induced seizures at doses of 25 and 60 mg/kg body weight, respectively, in mice and rats (*47*). Methysticin (10–100 µmol/l) was also active in different in vitro models of seizure-like events using extracellular recordings in rat temporal cortex slices containing the hippocampus and entorhinal cortex. Methysticin suppressed epileptiform activity independent of the stimulus (low calcium or magnesium, or high potassium perfusion medium), suggesting a

direct effect of the compound on neuron membranes, thus inhibiting neuron excitability (*40*). Other studies have demonstrated that (+)-kawain and (±)-kawain inhibited voltage-dependent calcium and sodium channels of rat cerebrocortical synaptosomes (*41, 49, 50*). In these synaptosomes, it was also shown that (±)-kawain inhibited the increase in intracellular calcium and glutamate release induced by veratridine and potassium chloride (*49*). Both (±)-kawain and methysticin inhibited voltage-dependent sodium channels in rat CA1 hippocampal neurons in vitro (1–400 µmol/l) (*51*).

Antispasmodic activity

An aqueous rhizome extract, kawain, dihydrokawain, methysticin and dihydromethysticin inhibited serotonin and nicotine-induced contractions of guinea-pig ileum in vitro (*52, 53*). The antispasmodic effects were attributed to a direct musculotropic action. Dihydromethysticin also inhibited contractions of rat colon and uterus in vitro induced by serotonin, acetylcholine and barium (*53*). Desmethoxyyangonin, dihydromethysticin and kawain inhibited serotonin-induced contractions of rat uterus in vitro at concentrations of 3.2, 7.5 and 10.0 µg/ml, respectively (*54*). Aqueous, dichloromethane and lyophilized extracts of the rhizome induced relaxation of rat uterus in vitro (ED_{50} 22.5 µg/ml) (*28*). The effects of an aqueous extract of the rhizome on muscle contractility and neuromuscular transmission were investigated in mouse hemidiaphragms and frog sartorius muscles in vitro using twitch tension and intracellular recording techniques. The extract (2–5 mg/ml) induced muscle relaxation by direct action on muscle contractility rather than by inhibition of neuromuscular transmission (*55*).

Antimicrobial activity

A hydroalcoholic extract of the rhizome inhibited the growth in vitro of *Aspergillus fumigatus, A. niger, Penicillium digitatum, Rhizopus nigricans, Trichophyton mentagrophytes, Candida albicans* and *Saccharomyces pastorianus* (*56*). However, an aqueous extract of the rhizome did not inhibit the growth in vitro of *Trichophyton rubrum, Microsporum canis* or *Epidermophyton floccosum* (*57*).

Clinical pharmacology

Anxiety

At least seven double-blind, controlled clinical studies have assessed the efficacy of two extracts of Rhizoma Piperis Methystici for symptomatic treatment of anxiety (*17, 18, 21–24, 58*). Two of these studies were performed with a hydroalcoholic extract standardized to contain 15% kava pyrones (*22, 58*), while the other studies used an extract standardized to contain 70% kava pyrones (*17, 18, 21, 23, 24*).

Two placebo-controlled trials investigated the effect of both standardized extracts in women with climacteric psychosomatic disturbances. In the first study, 40 such women were treated with either a placebo or 200–400 mg extract

(30–60 mg kava pyrones) daily for 8–12 weeks. Using the Kuppermann Index and Anxiety Status Index, the extract was found to be superior to the placebo (*22*). In the second study, a further 40 such women were treated with 300 mg extract (210 mg kava pyrones) daily for 8 weeks in a randomized, placebo-controlled, double-blind study. The outcome was assessed using the Hamilton Anxiety Rating Scale; the Depression Status Inventory and the Kuppermann Index were also used. The total score on the Hamilton Anxiety Rating Scale decreased after 1 week of treatment with the extract, and reached a plateau at 4 weeks. The therapeutic response to the extract was significant, as compared with the response to the placebo ($P < 0.001$) (*23*). After 8 weeks of treatment with the extract, the mean score on the Hamilton Anxiety Rating Scale decreased from 31.1 to 5.5. In the group which received the placebo, the mean score decreased from 30.15 to 22.50. The mean score on the Depression Status Inventory decreased significantly from 42.5 to 24.8 ($P < 0.01$). The mean score on the Kuppermann Index also decreased significantly from 20.35 to 3.60 ($P < 0.01$) (*23*).

A double-blind, placebo-controlled study of 58 patients with symptoms of anxiety, tension or agitation of non-psychotic origin assessed the effectiveness of the extract containing 70% kava pyrones (equivalent to 210 mg kava pyrones) daily for 4 weeks. The outcome was assessed using the total score on the Hamilton Anxiety Rating Scale, and other rating scales (the Erlanger Scale for Anxiety, Clinical Global Impressions and the Fischer Somatic Symptoms). After 1 week, patients treated with the extract showed a reduction in the total score on the Hamilton Anxiety Rating Scale as compared with the placebo group. The difference between the scores of the two groups increased after 4 weeks of treatment (*17*).

A randomized double-blind comparative study assessed the efficacy of the extract containing 70% kava pyrones in 172 patients with symptoms of anxiety, tension and agitation of non-psychotic origin. Patients received either 300 mg extract (210 mg kava pyrones), 15 mg oxazepam or 9 mg bromazepam daily for 6 weeks. The main criterion for assessment was the total score on the Hamilton Anxiety Rating Scale. No significant difference was observed between the treatments (*24*). In another randomized study which involved several centres, the efficacy of the extract containing 70% kava pyrones was tested in 100 patients with anxiety of non-psychotic origin (as defined in the *Diagnostic and statistical manual of mental disorders*, 3rd ed. (*59*)). Patients were treated with either a placebo or 300 mg extract (equivalent to 210 mg kava pyrones) daily for 24 weeks and the outcome was assessed using the Hamilton Anxiety Rating Scale. Adjunct rating scales were the Clinical Global Impressions and Von Zerssen mood scale. In patients treated with the extract, the decrease in the Hamilton Anxiety Rating Scale (mean scores of 30.7 and 9.7 at weeks 0 and 24, respectively) was significant as compared with the placebo group ($P < 0.005$). The scores on the Clinical Global Impressions and Von Zerssen mood scale also improved after 24 weeks of treatment with the extract (*21*). A randomized study of 58 patients also assessed the efficacy of the extract containing 70% kava pyrones for the treatment of anxiety of non-psychotic origin. Patients were treated with either a

placebo or 300 mg extract (equivalent to 210 mg kava pyrones) daily for 4 weeks and therapeutic efficacy was assessed using the Hamilton Anxiety Rating Scale. After 1 week, there was a significant reduction in the scores (mean scores of 25.6 and 16.2 at weeks 0 and 1, respectively) in the treated group as compared with the placebo group ($P = 0.004$) (*18*).

A randomized, double-blind pilot study investigated the effects of the extract containing 15% kava pyrones in 59 patients with pre-operative anxiety (*58*). Although improvements in mood were observed using a psychostatus score, only two doses of the extract (equivalent to 60 mg kava pyrones daily) were administered, and thus the clinical significance of this study is questionable.

An additional nine double-blind studies have been performed with (±)-kawain (*60*, *61*). Two of the studies were comparative studies and seven were placebo-controlled. Therapeutic anxiolytic activity was achieved with doses of 200–600 mg (±)-kawain daily (*60*). Kawain is available in Germany and Switzerland as an over-the-counter medication.

Insomnia

Two single-blind and four double-blind, placebo-controlled clinical trials investigated the effect of a rhizome extract standardized to contain 70% kava pyrones on EEG recordings, and intellectual and motor functions of healthy volunteers (*14*, *16*, *62–65*). Changes in EEG recordings and psychomotor test results showed no evidence of a decrease in vigilance or responsiveness in volunteers treated with 600 mg extract (equivalent to 420 mg kava pyrones) daily for 5 days (*64*, *65*). Examination of EEG recordings during sleep of healthy volunteers given a single dose of 300 mg extract (equivalent to 210 mg kava pyrones) showed an increased sleep spindle density of 20% and an increase in slow-wave sleep (i.e. deep sleep), but the rapid eye movement phase was not suppressed (*14*). Daily doses of 300 or 600 mg extract (equivalent to 210 or 420 mg kava pyrones), respectively, for 1 week increased the beta/alpha index typical for the pharmaco-EEG profile of anxiolytics. The increase in beta activity was most marked in the $beta_2$ range (*16*). In two studies, administration of 300 mg extract (equivalent to 210 mg kava pyrones) daily for either 8 or 14 days, taken with or without ethanol, had no influence on the safety-related performance of healthy volunteers (*62*, *63*).

In a randomized, double-blind crossover study involving 12 healthy volunteers, administration of daily single doses of a rhizome extract standardized to contain 30% kava pyrones (400 mg extract containing 120 mg kava pyrones) was compared with daily single doses of diazepam (10 mg) or a placebo in a 7-day trial. Changes in EEG recordings and psychometric test results showed no evidence of a decrease in vigilance in the group treated with the extract (*66*). Safety-related performance was assessed in another study after administration of an extract standardized to contain 30% kava pyrones, bromazepam or a combination of extract and bromazepam. Safety-related performance remained unaffected in healthy volunteers treated daily with 400 mg extract (equivalent

to 120 mg kava pyrones for 14 days), whereas it was impaired after treatment with bromazepam (9 mg daily) or the extract/bromazepam combination. No differences were observed following treatment with bromazepam or the combination, indicating that the extract did not have an additive effect when given in combination with bromazepam (*67*).

Contraindications

During pregnancy and lactation, and in patients with endogenous depression (*15*) or liver disease.[1]

Warnings

Rhizoma Piperis Methystici should not be taken for more than 3 months without medical advice. Even when administered within the recommended dosage range, motor reflexes and the ability to drive or operate heavy machinery may be adversely affected (*15*).

Precautions

Drug interactions

The effectiveness of centrally acting drugs such as alcohol, barbiturates and other psychopharmacological agents may be potentiated (*15*). One case of possible drug interaction between Rhizoma Piperis Methystici, alprazolam, cimetidine and terazosin has been reported (*69*). The clinical significance of this interaction has not yet been established.

Carcinogenesis, mutagenesis, impairment of fertility

Oral administration of up to 600 mg/kg body weight of a standardized extract containing 70% kava pyrones did not increase the formation of micronucleated polychromatic erythrocytes and did not lead to any change in the ratio of polychromatic to normochromatic erythrocytes. There was no increase in the number of revertants in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 with or without metabolic activation, at doses up to 2.5 mg/plate in the *Salmonella*/microsome assay (*3*).

Pregnancy: teratogenic effects

See Contraindications.

Pregnancy: non-teratogenic effects

See Contraindications.

[1] Several cases of liver toxicity have been reported in Europe following use of herbal products containing extracts of Rhizoma Piperis Methystici (*68*).

Nursing mothers

See Contraindications.

Other precautions

No information available on general precautions or precautions concerning drug interactions; drug and laboratory test interactions; or paediatric use. Therefore, Rhizoma Piperis Methystici should not be administered to children without medical supervision.

Adverse reactions

In a surveillance study involving 4049 patients who received a standardized extract of Rhizoma Piperis Methystici containing 70% kava pyrones (150 mg extract, equivalent to 105 mg kava pyrones) orally daily for 7 weeks, adverse reactions were reported in 61 patients (1.5%). The major reactions were gastrointestinal complaints or allergic skin reactions (3, *20*). In a study of 3029 patients given a standardized extract of the rhizome containing 30% kava pyrones (800 mg extract, equivalent to 240 mg kava pyrones) orally daily for 4 weeks, adverse reactions were reported in 2.3% of patients. Nine cases of allergic reactions, 31 cases of gastrointestinal complaints, 22 cases of headache or dizziness, and 11 cases of other undefined problems were reported (3, *70*). Chronic administration of the rhizome or preparations thereof may cause a transient, yellow discoloration of the skin and nails, which is reversible upon discontinuation of the drug (*15*). Excessive, chronic abuse of infusions of the rhizome has been historically associated with a scaly, eruptive dermopathy of unknown etiology (*71*). Allergic skin reactions and ichthyosis have also been reported (*72–74*). In two patients, a reaction was seen in areas rich in sebaceous glands following 3 weeks of systemic antidepressant therapy with the rhizome. The reaction resulted in the formation of papules and plaques on the face, and ventral and dorsal thorax (*75*). One study in an Australian aboriginal community found that chronic abuse of the rhizome led to malnutrition and weight loss, increased levels of γ-glutamyltransferase, decreased levels of plasma protein, and reduced platelet volume and lymphocyte numbers (*76*). In a healthy volunteer, disturbances of visual accommodation, such as enlargement of the pupils, and disturbances in oculomotor equilibrium, were reported following the ingestion of large doses of kava (*77*). Chronic consumption (6 months) of large quantities of an infusion of the rhizome (5–6 cups daily) has been reported to cause anorexia, diarrhoea and visual disturbances (*73*). A single case report of athetosis involving the limbs, trunk, neck and facial musculature, with marked athetosis of the tongue, was associated with chronic consumption of large quantities of the rhizome (*78*).

There is one report of acute hepatitis in a 39-year-old woman following ingestion of a rhizome preparation (*79*). However, the identity of the material was not authenticated.

Dosage forms

Comminuted crude drug and extracts for oral use (*15*). Store in a tightly closed container, away from light.

Posology

(Unless otherwise indicated)
Daily dosage: crude drug and extracts equivalent to 60–210 mg kava pyrones (*15*, *18*, *21–24*).

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