Piper methysticum G Forster (Kava), Piperaceae and related species

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1 Highlights

Kava is a moderately-strong nervine and anxiolytic. For a general review, see Piscopo 1997.

Kava is used primarily for anxiety and pain. Kava also has a strong affinity for the genitourinary tract, and is considered specific for interstitial cystitis pain.

Kava has no adverse effects at usual clinical doses. Chronic abuse has been associated with a particular syndrome in the Pacific. Extremely rare idiosyncratic liver damage has occurred associated with kava use.

2 Basic Clinical Information

2.1 Part Used

Fresh or dried root. Some sources suggest the rhizome is used, but kava has no rhizome.

2.2 Taste

Moderately acrid; sialagogue.

2.3 Principal Actions

- Nervine, moderate
- Anxiolytic, moderate
- Analgesic, moderate
- Skeletal muscle relaxant, central-acting

2.4 Major Organ System Affinities

Nervous system
Genitourinary tract

2.5 Major Indications

- Anxiety
- Pain
- Skeletal muscle spasms
- Insomnia (Lehrl 2004; Wheatley 2001; Emser and Bartylla 1991)
- Bladder pain
- Interstitial cystitis pain
- Chronic prostatitis pain
- Drug addiction withdrawal and relapse prevention

Two meta-analyses of multiple clinical trials confirm that kava extracts are significantly more effective than placebo and equally effective as benzodiazepines for people with mild-to-moderate anxiety (Pittler and Ernst 2001; Witte, et al. 2005). One trial has shown that kava extract is as effective as buspirone and opipramol (a tricyclic anti-anxiety drug common in Germany) for patients with general anxiety disorder (Boerner, et al. 2003). It is also useful for anxiety occurring during withdrawal from benzodiazepines (Malsch and Kieser 2001).

A pilot clinical trial found that kava could help reduce cravings for nicotine, alcohol, heroin, and cocaine (Steiner 2001).

2.6 Major Constituents

- Kavalactones
- Resin
- Alkaloids (leaf only)

2.7 Energetics

2.8 Preparations and Dose

Tincture: 1:2-1:3, 50-75% ethanol

Tincture Doses

Acute, adult: 3-5 ml every 2-3 h, adjusted for body size
Chronic, adult: 3-5 ml tid or 5-10 ml 30 before and at bedtime for insomnia
Child: as adult but adjusted for body size
Elder: as adult

Cold infusion: traditionally 30 g of peeled and chopped kava roots were extracted with 300 ml cold water. An analysis found that 10 g powdered crude root extracted with 100 ml water yielded 71.6 mg kavalactones, for a daily dose of 210 mg kavapyrones (Lazar, 1983).

Standardized extracts: extract with 30% kavalactones 70 mg tid; 210 mg 1 hr before bed for insomnia. Extracts with 70% kavalactones are available and widely used in Europe especially, but they may crowd out valuable synergistic compounds.

Isolated constituents not as effective as whole extracts as far as nervine actions go (Meyer 1979).

2.9 Adverse Effects

- Salivation
- Nausea, uncommon
- Does not depression cognitive function, and may actually enhance it (Foo and Lemon 1997; Gessner, et al. 1994)

Various reports of kava's hepatotoxicty support only that very rare, idiosyncractic liver damage can occur (Clouatre 2004; Denham, et al. 2002). Out of 78 case reports, only 27 were found to be at all associated with kava (Clouatre 2004). Another analysis of 19 cases considered potentially related to kava could only find evidence that one was actually related (Teschke, et al. 2003). No cases of hepatotoxicity have been reported in the thousands of patients exposed in clinical trials (Denham, et al. 2002). Given that millions of people are taking kava every day, this extremely low incidence of problems is not sufficient support for labeling kava hepatotoxic. Nevertheless, kava has been banned for over-the-counter sale in the European Union, Canada, and several other nations but not the United States.

"The risk-to-benefit ratio of kava extracts, nevertheless, remains good in comparison with that of other drugs used to treat anxiety." Clouatre 2004

2.10 Contraindications

- Does not interfere with ability to operate heavy machinery (Herbert 1993; Münte, et al. 1993)
- Parkinsonism, theoretically (Schelosky, et al. 1995).

2.11 Overdose

Nausea, vomiting, and sedation. Chronic abuse (4-5 cups per day each containing 210 mg kavalactones) may cause a particular skin rash (Norton and Ruze 1994). Though postulated to be the result of niacin deficiency, 100 mg nicotinamide supplementation was not more effective than placebo at reducing the rash in heavy users (Ruze 1990).

Elevated serum gamma-glutamyl transferase (GGT) and alkaline phosphatase levels have been seen in heavy users, but no sign of further liver damage and with the levels returning to normal within 1-2 weeks of abstinence (Clough, et al. 2003). In a preliminary study of 31 adult, regular kava drinkers compared to 31 non-drinkers (all healthy) in Oahu, Hawaii, serum GGT and alkaline phosphatase levels were elevated in significantly more of the kava drinkers compared to non-drinkers (Brown, et al. 2007).

2.12 Incompatibilities

None known

2.13 Adverse Drug Interactions

Studies are mixed on the effect of combining alcohol and kava. Some have found no additive problems with the combination (Herberg 1993). Others have found additive cognitive dysfunction (Foo and Lemon 1997).

There are no credible reports of negative interactions with benzodiazepines or other psychoactive medications.

Though an in vitro study of the interaction of human liver microscomes with kava extracts found numerous isozymes of cytochrome P450 (but no effect on CYP2E1), preliminary human trials have shown only a 40% inhibition of CYP2E1 (Mathews, et al. 2002; Gurley, et al. 2005). In healthy adults, 14 d intake of kava had no effect on pharmacokinetics of digoxin (Gurley, et al. 2007).

3 Botanical Information

3.1 Common Names

English Common Names: kava, kava-kava, yongona
German Common Name: Rauschpfeffer
Hawaiian Common Name: ʼawa

3.2 Botanical Description

Perennial shrub, slow-growing, that can be as tall as 3 m. Though it has dioecious flowers, the species no longer reproduces sexually. Each flower is borne on a spike and has no petals. The male flowers are axillary and solitary; female spikes are multiple. Leaves have prominent veins and are alternate and cordate, combing to an abrupt tip. The margin is wavy and entire. Each leaf petiole is around 3 cm long with stipules.

3.3 Interchangeability of Species

Kava is not clearly known to be interchangeable with any other species.

Piper wichmannii C DC (wild kava) is the only relative of kava that is at all similar to it. Wild kava is found growing up to 800 m in altitude in Vanuata, the Solomon Islands, and Papua New Guinea.

3.4 Native Habitat and Current Range

Kava is native to various Pacific islands, with a strong case having been made for Vanuata as the ultimate origin of the plant (Lebot and Siméoni 2004). It was spread by humans across the Pacific in ancient times, but has not been spread anywhere else outside the region in modern times.

3.5 Ecological Status

Widespread and stable.

3.6 Cultivation

Kava is in widespread cultivation on many Pacific islands. It is the only major crop that is grown exclusively in the pacific. Kava is susceptible to a viral disease called kava die back, which is a serious problem in Fiji primarily. Most of kava is grown intermixed with other species. Very active selection for cultivars and chemotypes based on the psychoactive properties of kava is ongoing among kava farmers.

Kava Cultivation, 1998-2001

Island	Hectares under cultivation
Vanuatu	3,000
Fiji	4,800
Samoa	1,000
Tonga	700
Pohnpei	3,000
Hawaii	50

3.7 Wildcrafting

It has been argued that there is essentially no wild kava, because all populations have been intensely managed by humans for millennia. This is emphasized by the fact that kava cannot reproduce sexually anymore and that there is a clear pattern of differences in varieties from one island to another radiating out from Vanuata closely matching human migration patterns (Lebot and Siméoni 2004). However, the cultivation of kava is generally in mixed-population wild-appearing stands, blurring the distinct between wild and cultivated.

4 Advanced Clinical Information

4.1 Additional Actions

- Analgesic by unknown (non-opiate, non-NSAID-like) mechanism (Jamieson and Duffield 1990).
- Prevent focal ischemia in brain (Backhauss and Krieglstein 1992).
- Bronchodilating on ex vivo murine bronchial tissue (Martin, et al. 2000).
- Inhibits calcium channels (voltage-gated, L-type) in vitro, helping explain spasmolytic effects on vascular smooth muscle (Martin, et al. 2002).
- GABA-A receptors in hippocampus and amygdala site of activity (Jussofie, et al. 1994; Davies, et al. 1992).
- Inhibits neuronal sodium channels, voltage-gated (Freise, et al. 1998).
- TNF-alpha release inhibition (Hashimoto, et al. 2003; Achenbach, et al. 1972).

Activities Kava Does Not Possess

- No activity on benzodiazepine receptors (Davies, et al. 1992).
- Does not inhibit eicosanoid pathways (Jamieson and Duffield 1990; Martin, et al. 2000).
- Nitric oxide synthesis not inhibited (Martin, et al. 2000).
- Not active on opioid receptors (Jamieson and Duffield 1990).

4.2 Additional Indications

- Epilepsy
- Depression
- Panic attacks
- Neuralgia
- Tremors

4.3 Constituents

Kavalactones = kava alpha-pyrones

- kavain
- yangonin
- desmethoxyyangonin
- methysticin
- dihydromethysticin

4.4 Pharmacokinetics

Isolated kavalactones not as as well absorbed into the brain as total extract (Keledjian, et al. 1988).

Isolaved kavain was 90% absorbed after oral administration to mice and almost entirely eliminated within 72 h, largely by renal excretion (Mathews, et al. 2005). Giving kavain simultaneous with kava extract significantly altered the absorption profile of kavain, greatly increasing total blood levels and peak blood levels.

4.5 Classic Formulations

None identified.

5 Other Viewpoints

5.1 Discussions in Historical Texts

Eclectic Materia Medica (Felter 1922)

PIPER METHYSTICUM.

The root of *Piper methysticum*, Forster (Nat. Ord. Piperaceae). South Sea Islands. Dose, 5 to 60 grains.

Common Names: Kava-Kava, Ava, Ava-Pepper Shrub, Intoxicating Long Pepper.

Principal Constituents.–Starch (50 per cent), methysticin ($C_{15}H_{14}O_5$), the methyl ester of methysticic acid; kavahin (methylene protocatechuic aldehyde, identical with heliotropin or piperonal); and the chief active principle, an acrid resin (2 per cent) separable into the local anesthetic alpha-resin and the less active beta-resin.

Preparation.–Specific Medicine Piper Methysticum. Dose, 5 to 60 drops.

Specific Indications.–Irritation, inflammation, or debility of the urinary passages; chronic catarrhal inflammations; vesical irritation and inflammation; vesical atony; painful micturition, strangury, and dysuria; gonorrhea, slow and intractable; gleet; anorexia; gastric atony; pale and edematous tissues, with scanty or irregular flow of urine, and indisposition to exertion; dizziness and despondency; neuralgia, idiopathic or reflex.

Action.–Piper Methysticum stimulates the salivary but not the cutaneous glands, and strongly excites the kidneys to watery diuresis, proportionately less solid material being voided in the urine. Upon the stomach it acts much like the stimulant bitters, increasing the appetite, and produces neither diarrhea nor dysentery. The central nervous system is stimulated by it to a species of intoxication, somewhat resembling but differing, however, from that caused by ethylic inebriation. Large doses will cause a drowsy and reserved intoxication, with confused dreams. The taste being agreeable, it is said one easily becomes a proselyte to its seductive qualities. The intoxicating drink prepared from it by the natives of certain Pacific islands induces an intoxication of a reserved drowsy character attended with confused dreams. Its long-continued use by them has caused more or less obscuration of vision and a dry, cracked, scaly and ulcerated skin, and lesions closely allied to leprosy.

Therapy.–Piper methysticum, "the intoxicating long pepper", is not an old medicine, though under the name of kava-kava and closely similar appellations it has been used in the preparation of a disgusting ceremonial drink among certain South Sea Islanders from early times. As a medicine it has the fourfold quality of being stimulant, sialagogue, tonic, and anaesthetic. Its field of action is upon the sensory nerves and mucous tracts of the body, more especially those of the genito-urinal and gastro-intestinal tubes.

Piper methysticum is an appetizer and tonic to the gastro-intestinal organs, this influence being especially marked when associated with urinary disorders. The patient is pale, the urinary product inconstant in quality; the tissues, especially of feet and legs, are edematous patient is indisposed to

exertion, and has the general appearance of one with Bright's disease, yet there is no albumen nor evidence of any particular disease. Such symptoms clear up quickly under this remedy, and the appetite is quickly restored. Piper methysticum augments digestion and promotes better assimilation. The glandular activity of the digestive tract is increased, natural secretion and excretion favored, constipation is overcome, and hemorrhoids, if present, are reduced. It also exerts a marked curative influence in chronic intestinal catarrh.

The best known remedial action of this drug is upon the genito-urinal tract, in which, through presumably decreasing the blood supply by contracting the capillaries, it allays irritation with its consequent pain in urination, difficult micturition, and inflammation with discharges of mucus or mucopus. Its reputation as a blennostatic in gonorrhea is well sustained, but, as with all remedies, the specific condition must be present for its best results. It relieves in that form of acute gonorrhea which is sluggish, tardy in responding to treatment, and tending toward the establishment of gleet. It is also a good agent in gleet. In the more acute cases it favorably assists the action of gelsemium, belladonna, and macrotys; while if there is marked debility it may be given with nux vomica or strychnine. Piper methysticum increases the power to urinate and, through its anaesthetic qualities, alleviates pain in the bladder and urethra, hence its value in debilitated and irritated conditions of those organs. It thus becomes an effective remedy sometimes in dysuria, painful micturition, strangury, chronic inflammation of the neck of the bladder, acute urethritis, nocturnal enuresis of old and young when due to muscular atony, and old feeble cases of catarrh of the bladder. It is also of some value in acute vaginitis, chronic bronchitis, rheumatism, and dropsy due to renal inefficiency.

Piper methysticum is a remedy for neuralgic pain, especially of the branches of the 5th nerve. It sometimes relieves ocular and aural neuralgia, toothache when not due to dental caries, neuralgia of the stomach and intestines, and neuralgic and spasmodic dysmenorrhea. Such reflex neuralgias as abdominal neuroses due to prostatic, urethral, or testicular diseases, or pectoral neuralgia arising reflexly from nervous dyspepsia are cases for the exhibition of Piper methysticum.

5.2 Ethnobotany

Used as an important ceremonial beverage and, it is believed, in more regular ceremonies or rituals to help promote harmonious relations. Its calming effects have long been known by Pacific Islanders.

Kava was first seen by Europeans in 1769 when James Cook visited Tahiti.

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7 Contributors

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