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Major Therapeutic Activity of Water-Extracted Kava

Traditional Use

Kava (*Piper methysticum*) root is, or once was, consumed in a wide range of Pacific Ocean societies, from coastal areas of New Guinea to Polynesian Hawaii. When European explorers first landed on remote Pacific islands, they encountered societies in which Kava drinking was an integral part of religious, social, political and economic life.[1]

Kava was also used as an important ingredient in the traditional medicine of many Pacific Islands societies. Kava beverage was regarded as having sedative activity, able to soothe the nerves, relax the mind and body, induce refreshing sleep and to ease pain. Uses included:[1-4]

- relief of sore throat (the root was chewed),
- insomnia, general debility,
- urinary tract problems, gonorrhoea,
- headache, colds,
- upset digestion (especially in children), constipation, leprosy,
- to relax fatigue-stiffened muscles.

In addition to sedative activity, Western traditional indications of Kava (dried root, infusion and aqueous ethanol extract) include infection and inflammation of the genitourinary tract, neuralgia, bronchitis, dyspepsia, dysmenorrhoea and rheumatism.[5,6]

Traditional Preparation

Kava was traditionally prepared by infusing masticated (chewed), pulverised or grated root with cold water or coconut milk. The solid residue was filtered out through bunches of bracken fern leaves held in a woven device, or strained through plant fibres (such as coconut fibres). In later years, it was filtered by hand with porous cotton cloth.[1,7,8] When fresh Kava is prepared kava lactones produce local anaesthesia of the chewer's mouth.[1] Traditional preparation results in an aqueous slurry containing a suspension of lipid (fatty) material in which the kava lactones are found.[9] (Chewing the root does not result in enzymatic breakdown, but instead breaks up the root thus enhancing emulsification of the resin so that it can be assimilated into the water.[10])

Active Constituents

A major constituent of Kava root is the resin which contains kava lactones. The major kava lactones are kavain, dihydrokavain, methysticin, dihydromethysticin, yangonin and desmethoxyyangonin. Extracts are often standardised for kava lactone content.[11] Other constituents include flavokavins and chalcone pigments.[12]

Kava lactones are more soluble in organic solvents such as ethanol and acetone but still can be present in water extracts. A traditional water extract (1:10) prepared from fresh, peeled roots and taken in a daily dose of 300 mL has been shown to contain 210 mg of kava lactones.[13] However, it is likely that the levels of kava lactones will vary widely, depending on how the water extract is made.

The content (and profile) of kava lactones varies with the cultivar, plant part (e.g. root, stump, basal stem), geographical area of origin and growing conditions.[14-16]

Kava lactones are responsible for the main psycho-pharmacological activity,[17] but other constituents such as those present in water extract are also likely to be required (e.g. to enhance the bioavailability of the lactones).[11]

TGA Regulations

In July 2002 the TGA (Therapeutic Goods Administration) initiated a voluntary withdrawal of all complementary medicines containing Kava following the death of a woman who was taking a herbal preparation containing Kava. A review of the safety of Kava, undertaken by an expert committee of the TGA, decided in August 2003 that only certain forms of Kava were suitable for use in listed medicines. Products must be made from water extract/dispersion or whole rhizome and the daily dosage of kava lactones must be capped (at 250 mg).

Clinical Studies

Kava lactones have demonstrated sedative and anxiolytic activity.

Acetone & Ethanol Extracts of Kava

A meta-analysis which reviewed published clinical studies to August 2002 concluded that a significant **reduction in anxiety** occurred for patients receiving Kava acetone extract compared with those receiving placebo. The dosage of kava lactones provided by the standardised extract varied (105–210 mg/day), and the duration of treatment ranged from 4 to 24 weeks. Trials included for analysis were randomised in design and measured anxiety using the Hamilton anxiety scale.[18] Two of the trials included in the meta-analysis found Kava:

- effectively treated **sleep disturbances** associated with nonpsychotic anxiety disorders (140 mg/day kava lactones);
- reduced depression and symptoms of **menopause** in addition to menopausal anxiety (210 mg/day kava lactones).

Water-Soluble Extract of Kava

A randomised, double-blind, placebo-controlled trial investigated the effect of standardised water-soluble extract of Kava in the treatment of **generalised anxiety disorder**. A significant reduction in anxiety for the Kava group compared to placebo group was found: reduction of 7.6 points on the Hamilton Anxiety Rating Scale (HAMA) for Kava compared to reduction of 4.2 points for placebo ($p = 0.046$). The dosage of Kava provided 120-240 mg/day of kava lactones, starting at the lower dosage and increasing if patients did not respond to treatment (45% of the Kava group and 55% of the placebo group did not respond and had their dose increased).[19] Kava was well-tolerated: there were no significant differences between the Kava and placebo groups for liver function tests, and no significant adverse reactions could be attributed to Kava.[20]

In a double-blind, crossover trial, patients with **chronic anxiety** received standardised water-soluble extract of Kava (providing 250 mg/day of kava lactones) or placebo. The reduction of 11.4 points over placebo on HAMA compared favourably to the effect normally achieved by benzodiazepines. Highly significant relative reductions in **depression** were also evident. No serious adverse effects were observed.[21]

Qualitative research was also conducted during this trial, and explored the subjective experiences of the patients.[22]

- The vast majority of participants wrote that they had experienced positive effects while taking the Kava tablets: lessening of anxiety, enhanced mood, **improvement in sleep** and some beneficial effects on the physical signs of anxiety. Some negative experiences were reported (Kava and placebo).
- A specific theme was identified: Kava **reduced muscular tension**.
- Four participants experienced mild gastrointestinal symptoms, including nausea, from Kava. There was a mixed effect on fatigue (some energised, some tired).

Actions

Anxiolytic, mild sedative, skeletal muscle relaxant, mild analgesic, local anaesthetic.

Indications

- Anxiety, nervous tension, insomnia, stress.
- Menopausal anxiety, mild depression.
- Skeletal muscle spasm or tension; pain of muscular or nervous origin (e.g. neuralgia, headache).
- Sexual dysfunction due to anxiety.
- Improving cognitive performance.
- Sore throat.
- May be useful to assist in withdrawal from benzodiazepines.

Cautions and Contraindications

Short-term (1–2 months) or intermittent use is recommended. For longer use suggest a liver function test every few months and discontinue if abnormal readings occur (other than mild increase in gamma-glutamyl transferase). Kava has been implicated in several rare, idiosyncratic, possibly autoimmune-related cases of liver damage in humans. Use of water extracts of Kava root is likely to further reduce this risk.

Caution is also advised in patients with a history of excessive alcohol consumption and those taking potentially hepatotoxic drugs. Contraindicated in those with pre-existing liver damage. Children under 12 and those who are pregnant or nursing are not recommended to use Kava.

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