Clinical Studies on Kava (*Piper methysticum* G. Forst.)

Anxiety

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Malsch and Kieser, 2001	Nonpsychotic nervous anxiety, tension, restlessness	R, DB, PC n=40	5 weeks	50 mg/day (week 1) 300 mg/day (after week 1)	WS 1490 (Laitan® 100)	Pretreatment of patients with benzodiazepines was tapered off over 2 weeks. Kava was superior to placebo on HAMA (p=0.01) and subjective well-being scale (p=0.002). Study confirms anxiolytic effects and good tolerance of kava, and shows that further symptom reduction is possible after changeover from benzodiazepine treatment.
Singh *et al*., 1998	Nonclinical levels of daily stress and anxiety	R, DB, PC, PG n=60	4 weeks	400 mg/day (200 mg 2x/day)	Kavatrol®	Significantly (p<0.0001) decreased daily stress due to interpersonal problems, personal competency, cognitive stressors, environmental hassles, and the sum of these varied stressors. Significantly (p<0.0001) decreased anxiety due to environmental, psychological, and personal circumstances. Significance occurred after one week of treatment with continual decline for subsequent weeks of trial, with no side effects reported.
Volz and Kieser, 1997	Anxiety and agitation caused by unspecified mental disorder	R, DB, PC, MC n=101	25 weeks	100 mg 3x/day (3 x 70 mg of kavalactones per day)	WS 1490 (Laitan® 100)	Significantly (p=0.02) reduced somatic and mental anxiety from eighth week on. Long-term treatment showed greater efficacy (p< 0.001 at week 24) than short-term treatment. Kava was well tolerated; adverse effects were rare; there were no withdrawal symptoms.
Lehmann *et al*., 1996	Anxiety, tension, and excitedness of nonmental origin	R, DB, PC n=58	4 weeks	100 mg 3x/day (3 x 70 mg of kavalactones per day)	WS 1490 (Laitan® 100)	Showed anxiolytic efficacy and significantly (p< 0.02) reduced total anxiety after one week of treatment. Efficacy increased over subsequent weeks. Did not produce any adverse reactions.
Woelk *et al*., 1993	Anxiety, tension, agitation of nonpsychotic origin	R, DB, MC, CC n=172	6 weeks	100 mg 3x/day (3 x 70 mg of kavalactones per day)	WS 1490 (Laitan® 100)	Showed equal anxiolytic efficacy as the benzodiazepines (oxazepam and bromazepam). Authors concluded WS 1490 should be included in the therapeutic possibilities to consider in conditions of anxiety, tension, and agitation of nonpsychotic origin.
Warnecke, 1991	Anxiety and depression associated with menopause and post-menopause	R, DB, PC n=40	8 weeks	100 mg 3x/day (3 x 70 mg of kavalactones per day)	WS 1490 (Laitan® 100)	Significantly reduced HAMA overall score of anxiety by an average of 50% by first week, with a continual reduction through week 4 (p<0.001). Therapeutic index for use-risk evaluation was comparable to placebo.
Kinzler *et al*., 1991	Anxiety syndrome of nonpsychotic origin	R, DB, PC n=58	4 weeks	100 mg 3x/day (3 x 70 mg of kavalactones per day)	WS 1490 (Laitan® 100)	Significantly reduced anxiety symptoms after one week of treatment, and difference between groups increased over course of study. At each checkpoint (7, 14, and 28 days) the treatment group vs. placebo had significantly lowered HAMA scores (p<0.01). Kava caused no adverse experiences.

Mental Function

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Herberg, 1996	Reaction time and safety performance	PC, CO, Cm n=18	14 days	400 mg (120 kavalactone) tablet 2x daily of kava extract alone; bromazepam alone (2 x 4.5 mg/day); kava and bromazepam combined	GITLY kava extract or bromazepam	Performance was impaired after treatment with bromazepam and the combination, but remained at the baseline level after treatment with the kava extract. The least impairment of well-being occurred with kava and the greatest with the combination.

KEY: **C** – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Kava (*Piper methysticum* G. Forst.) (cont.)

Mental Function (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Heinze *et al.*, 1994	Behavior, mental performance	DB, R, CO, Cm n=12 young healthy males, 24–37 years	5 days	200 mg 3x/day (6 x 70 mg kavalactones per day)	WS 1490 (Laitan® 100) vs. oxazepam	Kava did not alter behavior in psychometric tests, as did oxazepam. May slightly enhance mental performance associated with focal attention and processing capacity.
Munte *et al.*, 1993	Behavior, mental performance	DB, CO, Cm n=12 healthy volunteers 24–37 years	5 days	600 mg/day (200 mg 3x/day); oxazepam (10 mg/day before testing and 75 mg on morning of study); or placebo	WS 1490 (Laitan® 100) vs. oxazepam vs. placebo	Study showed nonsignificant trend toward improved cognitive function with kava. Suggests enhanced memory performance under kava. No adverse effects reported. Oxazepam produced significant decrease in quality and speed of response.
Russell *et al.*, 1987	Reaction time	Cm n=18	6 days	250 ml/day or 500 ml/day	Cold macerate of 30 g root powder	No effect on reaction time or errors with traditional or excess dosages. Consumption did not alter speed of activation of verbal information in long-term memory or reaction to warning signal.

Other

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Connor *et al.*, 2001	Safety profile	R, DB, PC n=35 adults with a 1+ month history of generalized anxiety disorder and HAMA score >16 (31–75 years of age)	6 weeks: Week 1: placebo only; Weeks 2–5: kava or placebo Week 6: No treatment, no placebo	Week 2: 140 mg kavalactones/ day or placebo Weeks 3–5: 280 mg kavalactones/ day or placebo	KavaPure® (standardized to 70 mg kavalactones)	No statistically significant differences were seen between kava and placebo groups for blood or urine studies, ECG assessments, blood pressure, heart rate, sexual function, or incidence of adverse events. No withdrawal symptoms were observed 1 week after abrupt cessation of treatment. Authors conclude kava was well-tolerated even though dosage used was higher than used in most other studies, but further studies of long term kava use are needed.
Watkins *et al.*, 2001	Vagal cardia control measured by baroreflex control of heart rate (BRC) and respiratory sinus arrhythmia (RSA)	P, DB, PC n=13 adults with a 1+ month history of generalized anxiety disorder and HAMA score >16 (35–74 years of age)	4 weeks, with assessment 1 day prior to and 4 weeks after beginning treatment	280 mg kava/day or placebo	KavaPure® (standardized to 30% kavalactones)	Kava group showed statistically significantly improved BRC vs placebo group ($p<0.05$). Degree of BRC improvement correlated significantly with clinical improvement ($p<0.05$). No change in RSA was observed in either group.
Emser and Bartylla, 1991	Sleep	PC, CO n=12 healthy people 20–31 years	4 days	150 mg/day, 50 mg 3x/day; 300mg/day, 100 mg 3x/day; or placebo	WS 1490 (Laitan®)	Kava favorably influenced sleep. Increased sleep spindle densities and duration of slow wave (deep) sleep. No effects on duration of REM sleep. Tended to decrease sleep stage 1 (falling asleep) and sleep latency (waking stage).
Warnecke *et al.*, 1990	Peri-menopausal symptoms	R, DB, PC n=20	12 weeks	One 150 mg tablet kava extract (30 mg kavalactones) 2x daily for 4 weeks, followed by 1 tablet, 1x daily starting week 5	Kavosporal®	After 4 weeks, the kava group demonstrated a highly significant ($p=0.001$) reduction in peri-menopausal symptoms. At 12 weeks, statistical sampling was not possible due to a dropout in the number of placebo-group patients.

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