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FILE: ▪Kava (*Piper methysticum*)
▪Safety
▪Toxicity

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RE: Mouse Study Shows Safety of Ethanolic Kava Extract

Sorrentino L, Capasso A, Schmidt M. Safety of ethanolic kava extract: Results of a study of chronic toxicity in rats. *Phytomed*. September 2006;13(8):542-549.

In 2002, the German health authorities banned products containing kava (*Piper methysticum*) extract based on adverse event reports of liver toxicity and liver failure allegedly associated with the use of various kava preparations. However, clinical, preclinical, and toxicological studies have failed to reveal kava-induced hepatotoxicity. Kava producers have appealed the ban. On May 12, 2005, the German health authorities (BfArM, German Federal Institute for Drugs and Medical Devices) termed the ban of registered products in Germany that contain kava "inappropriate" and changed the rejection of registration into an inactivation of registrations, which has the same effect on kava availability, or non-availability as the case may be. The purpose of this study was to test the chronic toxicity of an oral ethanolic kava extract in rats.

For 3 or 6 months, male and female rats (*n*=24 per group) were fed either a standard diet, food with 0.01% kavalactones, or food with 0.1% kavalactones. A supplier of rat food pellets created a product for the study that contained 0.01% and 0.1% total kavalactones. The kavalactone product that was added to the rat food was the same preparation that was used in Kavasedon®, Harras Pharma, Germany. [Kavasdon was a typical 96% ethanolic extract in hard gelatin capsules with 50 mg of kavalactones per capsule. Personal communication from Mathias Schmidt to Lori Glenn, October 4, 2006.] Based on an average consumption of 7.3 g of food per 100 g of body weight, this concentration was equivalent to a daily ingestion of 7.3 or 73 mg/kg body weight of kavalactones per day. Blood was drawn prior to sacrifice for hematological and biochemical parameters. The organs were examined for gross and histological abnormalities.

At both the 3 and 6-month time points, there were no significant differences in body weight gain, hematology, blood chemistry, or organ weights between the groups. The male rats consuming 0.1% kavalactones had slightly elevated cholesterol and liver

enzymes (AST and ALT) compared to control. However, the levels were still within the normal range. There were no gross pathology differences between groups. Histopathological and inflammatory changes were not specific to the kavalactone-treated rats. There were no histological changes in the hearts, adrenal glands, testes, or ovaries of any rat. Some rats were examined 3 months after stopping ingestion of kavalactones. There were no detectable behavioral withdrawal symptoms in the rats receiving 3 months treatment of kavalactones.

The authors state that there were no signs of toxicity in rats subjected to 7.3 or 73 mg/kg of kavalactones. The authors concluded that the findings rule out any harmful effect of kavalactones on organs, including the liver. The authors state that the dosage range and study duration used in this study are relevant for long-term human use. However, the high dose corresponds to only about 10 times the human equivalent dose. Most toxicology studies are conducted at doses well in excess this. However, this study was conducted in 1998 when toxicity to kava was not a topic. The object of this study was to demonstrate the safety of use doses relevant to human use as a part of drug registration.

—Heather S. Oliff, PhD

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