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FILE: ▪Kudzu (*Pueraria lobata*)
▪Alcohol Consumption
▪Puerarin

HC 090661-314

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RE: New Kudzu Extract Study Provides Better Understanding in Its Ability to Reduce Alcohol Consumption

Penetar DM, Teter CJ, Ma Z, Tracy M, Lee DY, Lukas SE. Pharmacokinetic profile of the isoflavone puerarin after acute and repeated administration of a novel kudzu extract to human volunteers. *J Altern Complement Med*. Jul-Aug 2006;12(6):543-548.

Kudzu (*Pueraria lobata*) has been used for centuries as a treatment for "alcohol related diseases."[1] The vine is considered an invasive noxious weed in the Southern United States, but it is a prized medicinal plant in Asian countries.[1] Several animal studies have demonstrated anti-alcohol effects for kudzu. Recently, the authors of the present study have shown in a small clinical trial that an extract of kudzu reduces alcohol consumption in heavy drinkers.[1] A second study by the authors (currently unpublished) has shown that subjects receiving kudzu extract for four weeks significantly reduce their alcohol consumption. These anti-alcohol effects are attributed to isoflavones found in kudzu extracts, specifically puerarin, daidzin, and daidzein. In the present study, the authors examine the pharmacokinetic profile of puerarin "after acute and repeated administration of kudzu extract."

The authors recruited 10 healthy male subjects from the Boston area for this study, which was conducted at McLean Hospital (Belmont, MA). The subjects were paid for their participation. Subjects were required to consume less than 8 drinks per week and to have a body mass index (BMI) in the range of 18-25 kg/m^2. Patients received 500 mg capsules of a kudzu extract standardized to contain 125 mg of isoflavones: 19% puerarin, 4% daidzein, and 2% daidzein (NPI-031, Natural Pharmacia, Belmont, MA). The subjects were randomly assigned to 2 studies. Participants in Study A received an acute 1 g dose of the kudzu extract (2 capsules) in 1 session and came back for a second session after receiving the 1 g dose for 3 consecutive days. Patients in Study B received an acute 2 g dose (4 capsules) of kudzu extract. For both studies, blood was drawn from the patients at regular intervals. For the acute 1 g dose, the subjects' puerarin concentrations peaked about 2 hours after consumption, and puerarin was completely eliminated within 24 hours. Doubling the acute

dose resulted in a significant increase in the time to maximum concentration (T_{max}) (P=0.048), but did not significantly affect the maximum concentration (C_{max}), area under the curve (AUC), absorption half-life ($A_{1/2}$), or elimination half-life ($E_{1/2}$). In contrast, both C_{max} and the AUC were significantly increased when the subjects took the 1 g dose for 3 days (P=0.016 and P=0.031, respectively). But, T_{max}, $A_{1/2}$, and $E_{1/2}$ were not significantly changed.

These results indicate that puerarin is probably absorbed principally in the small intestine and that a rate-limiting factor may control the maximum amount of puerarin that enters the body at one time. From the small intestine, puerarin travels in the blood to the brain without being metabolized. Most of the puerarin eliminated is unchanged, but a small amount is metabolized in the liver by cytochrome p450 and through conjugation to daidzein. The authors speculate that a delay in gastric emptying due to the increased bulk of the 4 capsules taken in the acute 2 g dose study may explain the unusual increase in T_{max}, compared with the acute 1 g dose. The results also indicate a one-compartment pharmacokinetic profile for puerarin. A daily 1 g dose of the standardized kudzu extract NPI-031 is enough to maintain steady-state levels of puerarin without accumulation of excess puerarin. The authors state that puerarin blood levels between 25 and 60 mg/ml is an effective therapeutic range for decreasing alcohol consumption. However, these levels may be difficult to attain using many commercially-available kudzu dietary supplements because they have varying range of puerarin levels. The levels of isoflavones in commercially available extracts examined by the authors ranged from less than 1% to 2 %. These levels may be too low to be biologically active. This underscores the need for adequate chemical characterization and quality control of herbal dietary supplements. In general, concentrated kudzu extracts with higher levels of puerarin are needed to achieve a therapeutic effect. Future research is needed to determine how higher or lower puerarin blood levels affect the behavior of heavy drinkers.

The authors conclude that a kudzu extract dose of up to 2 g/daily is safe and effective for "chronically" reducing alcohol intake. However, a clinical trial of a longer duration and enrolling more subjects, including women, is needed to confirm these promising initial results. Based on this study and previous studies, a daily dose of 1 g of standardized concentrated kudzu extract is advisable. A future article on the authors' four-week clinical trial on a kudzu extract and alcohol consumption is in progress.

—Marissa Oppel, MS

References

1.Oliff HS. Kudzu Extract Reduces Alcohol Consumption in Heavy Drinkers in Small Trial. *HerbalGram*. 2006; 70:28.

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