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FILE: ▪ Valerian (*Valeriana officinalis*)
▪ Cytochrome P450
▪ Herb Safety

HC 120141-272

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RE: Valerian Shows Little Effect on Cytochrome P450 Activity

Donovan JL, DeVane CL, Chavin, KD et al. Multiple night-time doses of valerian (*Valeriana officinalis*) had minimal effects on CYP3A4 activity and no effect on CYP2D6 activity in healthy volunteers. *Drug Metab Dispos*. 2004;32:1333–1336.

Valerian (*Valeriana officinalis*) root is a popular dietary supplement in the United States. Among its primary constituents are valerenic acid and its derivatives in volatile oil, which are thought to contribute to its purported sedative effects. Because of its widespread use, valerian is likely taken concomitantly with conventional medicines, the potential interactions of which are unknown. This study was conducted to determine whether the consumption of valerian alters the activities of two major drug-metabolizing enzymes: cytochrome P450 2D6 (CYP2D6) and CYP3A4. These two enzymes play a role in the metabolism of an estimated 70% of prescription and nonprescription medications.

Twelve healthy subjects (6 men and 6 women) aged 30.9 ± 7.2 (mean ± SD) were enrolled in this open-label, fixed treatment order, crossover study, which was conducted at the Medical University of South Carolina's General Clinical Research Center (Charleston, SC). The subjects served as their own controls. The probe drugs dextromethorphan (30 mg; to assess the activity of CYP2D6) and alprazolam (2 mg; to assess the activity of CYP3A4) were orally administered to the subjects at baseline and again after the consumption of 2 500-mg tablets of valerian nightly for 14 days. Each valerian tablet contained 5.51 mg valerenic acid. Dextromethorphan-to-dextrorphan metabolic ratios (DMRs) were determined in urine samples, and alprazolam pharmacokinetics were determined in blood samples collected at baseline and after valerian ingestion.

Dextromethorphan was metabolized extensively to its metabolite before and after valerian treatment in all 12 subjects; the DMRs were 0.214 ± 0.025 at baseline and 0.254 ± 0.026 after valerian treatment ($p > 0.05$). The maximum plasma concentration of alprazolam was significantly greater ($p < 0.05$) after valerian treatment (31 ± 8 ng/mL) than before valerian treatment (25 ± 7 ng/mL); none of the other pharmacokinetic parameters (area under the

curve, half-life of elimination, and time to reach the maximum plasma concentration) were significantly different between baseline and post-treatment.

The activities of the 2 drug-metabolizing enzymes studied— CYP2D6 and CYP3A4—were not significantly altered after the ingestion of 10.2 mg valerian per day for 2 weeks. This conclusion is based on the DMR data for CYP2D6 and on the lack of significant differences in pharmacokinetic parameters between baseline and post-treatment for CYP3A4. Thus, the authors conclude that "valerian is unlikely to have clinically relevant effects on the disposition of medications primarily dependent on the CYP2D6 or CYP3A4 pathways for metabolism." It should be noted, however, that this study was merely an initial investigation into the drug interaction potential of valerian. "Continued vigilance in the use of valerian and other dietary supplements is advisable, especially when used in combination with conventional medications with narrow therapeutic indices."

—Brenda Milot, ELS

The American Botanical Council has chosen not to reprint the original article.