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File: ■ Bacopa (*Bacopa monnieri*)
■ Herb-drug Interactions
■ CYP Enzymes

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RE: A Bacopa Extract May Inhibit CYP Enzymes

Ramasamy S, Kiew LV, Chung LY. Inhibition of human cytochrome P450 enzymes by *Bacopa monnieri* standardized extract and constituents. *Molecules*. February 24, 2014;19(2):2588-2601.

Bacopa (*Bacopa monnieri*) is used in Ayurvedic medicine for the support of cognitive functioning, including memory and concentration. Previous clinical trials have shown bacopa to impact cognition, and active compounds are thought to be triglycosidic saponins bacoside A3, bacopaside II, bacopaside X, and bacopasaponin C. As bacopa may be used by patients suffering from mental health conditions, it is reasonable to expect that this population may also be using prescribed pharmaceuticals. Herb-drug interactions, specifically via the liver and gastrointestinal CYP enzyme family, may lead to altered drug metabolism or efficacy. This basic research study tested a methanol extract of bacopa along with bacoside A, bacoside A3, bacopaside II, bacopaside X, bacopasaponin C, and bacopaside I on the activity of CYP1A2, 3A4, 2C9, 2C19, and 2D6 enzymes in vitro.

Enzyme activity was measured using a spectrophotometric assay. Bacopa extract was tested at concentrations ranging from 0.01-1000 µg/ml and compounds were tested at 0.01-100 µM concentrations. Concentration for the inhibition of 50% of the enzyme activity (IC_{50}) was calculated for the extract and compounds. Bacopa methanol extract (standardized to 50% bacosides) was procured from Sami Labs Ltd; Karnataka, India. Compounds were purchased from ChromaDex Inc.; Irvine, California.

From a previous study, metrics for the IC_{50} values of enzyme activity for the extract and compounds were classified as ≤ 20 µg/ml or ≤ 10 µM (potent), ≤ 20-100 µg/ml or ≤ 10-50 µM (moderate), or ≥ 100 µg/ml or ≥ 50 µM (weak).[1] Bacopa extract had the strongest inhibition of the CYP2C19 enzyme (IC_{50} = 23.67 ± 2.84 µg/ml). Bacopa extract showed moderate inhibition against the activity of CYP1A2 (IC_{50} = 52.20 ± 8.46 µg/ml), CYP3A4 (IC_{50} = 83.95 ± 12.97 µg/ml), and CYP2C9 (IC_{50} = 34.49 ± 6.60 µg/ml). Bacopa extract was considered a weak inhibitor of CYP2D6 (IC_{50} = 2061.50 ± 173.24 µg/ml). All compounds showed weak inhibition activity.

The authors estimated that, based on intestinal volume of 500 ml, a bacopa extract of 300 mg/day would result in a gastrointestinal concentration of 600 µg/ml. According to their calculations, the activities of CYP3A4, 2C9, and 2C19 would be reduced to lower than 10% of baseline levels. It is concluded that consumption of this dosage of extract may affect drug metabolism.

In conclusion, bacopa extract showed moderate inhibition at the relatively high concentrations predicted to occur in the GI tract for most of the CYP enzymes tested, with strongest inhibition and binding affinity for CYP2C19. It is surmised that the compounds tested are not likely contributing to the enzyme inhibition activity of the bacopa extract; this may be due to the chemical structure of these compounds. The authors also mention that, based on the results herein, consumption of this particular bacopa extract along with pharmaceuticals may result in herb-drug interactions. Other variables, such as specific CYP enzymes associated with the metabolism of different drugs, as well as genetic variability of CYP enzyme expression, may also play a role in potential herb-drug interactions. It is recommended that the safety and efficacy of the use of bacopa extract along with pharmaceuticals in those with mental health problems should be further investigated in vivo. Since the active constituents did not affect these enzymes, other formulations or extracts would likely have different effects on CYP enzymes. Future studies should include multiple bacopa extracts to compare herb-drug interactions.

—Amy C. Keller, PhD

Reference

[1]Kong WM, Chik Z, Ramachandra M, Subramaniam U, Raja Aziddin RE, Mohamed Z. Evaluation of the effects of *Mitragyna speciosa* alkaloid extract on cytochrome P450 enzymes using a high throughput assay. *Molecules*. 2011;16(9):7344-7356.

Referenced article can be found at http://www.mdpi.com/1420-3049/19/2/2588.