

## Inhibition of Human Cytochrome P450 Activities by Kava Extract and Kavalactones

**Mathews, J.M., Etheridge, A.S., & Black, S.R.** (2002). Inhibition of human cytochrome P450 activities by kava extract and kavalactones. *Drug Metabolism and Disposition*, 30 (11):1153-1157.



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Of the estimated 20% of Americans who use herbal remedies, most do not discuss with their doctors the use of these products along with prescribed drugs. While it is widely believed that these natural, plant-derived preparations are inherently safer than synthetic drugs, numerous reports over the last decade highlight the risks associated with their use. Interactions between drugs and herbs can occur through exaggerated pharmacological response from their combined effect at receptor sites or by affecting the activity of enzymes responsible for the degradation of drugs, among other processes.

The herb kava has been associated with numerous drug interactions, including reports that consumption of kava with the sedative alprazolam can result in coma. The prevailing hypothesis in the medical literature was that this was due to the exaggerated effects of the drug and kava components acting at the receptor site responsible for sedation.

The cytochrome P450 family of enzymes catalyzes the breakdown of drugs in the body, chiefly in the liver. The human forms of these enzymes together metabolize of 90% of drugs on the market today, and the various forms of P450 enzymes have differing specificity toward different drugs. Data on inhibition of these enzymes by drugs is so predictive of drug interactions that this information is now required in package inserts for prescriptions.

In our research at RTI we used enzyme preparations prepared from human liver and employed assays specific for P450 enzymes to discern whether kava extract could mediate degradation of different classes of drugs. This work demonstrated that kava markedly inhibited the P450 enzymes (from 55% to 90% for different enzymes). Specifically, it demonstrated that combining kava with alprazolam led to high levels of alprazolam circulating in the body and not being properly processed, or cleared, by the liver. These data indicate that kava has a high potential for causing drug interactions through inhibition of the P450 enzymes primarily responsible for the metabolism of pharmaceutical agents.

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