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Identification and Characterization of Potent CYP2B6 Inhibitors in Woohwangchungsimwon Suspension, an Herbal Preparation Used in the Treatment and Prevention of Apoplexy in and Korea

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Woohwangchungsimwon is a traditional prescription for treating with hypertension, arteriosclerosis, coma, and stroke in China and Korea. To assess the interactions of herb and drug metabolism, commercially available Woohwangchungsimwon suspension were examined for the potential to inhibit nine human cytochrome P450 enzymes activities. The Woohwangchungsimwon suspension showed strong inhibition of CYP2B6. Suspension was partitioned using hexane, ethyl acetate, dichloromethane, and each fraction was tested for the inhibitory effect of CYP2B6-catalyzed bupropion hydroxylation to identify individual constituents with inhibitory activity. Hexane fraction was shown to possess inhibitory activity, and borneol and isoborneol were identified as major constituents of hexane fraction by GC/MS analysis. These two terpenoids strongly inhibited CYP2B6-catalyzed bupropion hydroxylase activity with Ki values of 5.9 and 9.5 mM, respectively, in a competitive manner. In addition, at the same concentration in Woohwangchungsimwon suspension, reconstituted mixtures of borneol and isoborneol have comparable inhibitory potency to Woohwangchungsimwon suspension on bupropion hydroxylation. These in vitro data indicate that Woohwangchungsimwon preparations contain constituents that can potently inhibit the activities of CYP2B6 and suggest that these preparations should be examined for potential pharmacokinetic drug interactions in vivo.