Cytochrome P450 2C9 inhibition by sophoranone in human liver microsomes

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Sophora tonkinensis is a traditional medicine used for the treatment of asthma, allergic dermatitis, and throat inflammation in China and Korea. The present study was performed to evaluate the in vitro inhibitory potential of sophoranone, one of the marker components of Sophora tonkinensis, on the activities of nine human cytochrome (CYP) isoforms. Using an LC-MS/MS cocktail assay, the effects of sophoranone on specific marker reactions of the nine CYP isoforms were measured in human liver microsomes. Sophoranone showed potent inhibition of CYP2C9-mediated tolbutamide 4-hydroxylation with an IC\textsubscript{50} value of 1.21 µM and K\textsubscript{i} value of 0.418 µM in a competitive manner; this was similarly potent as a well-known typical CYP2C9 inhibitor, sulfaphenazole (K\textsubscript{i}=0.398 µM). In addition, sophoranone slightly inhibited CYP2C8 and CYP2C19 activities (IC\textsubscript{50} values of 17.8 µM and 16.4 µM). These observations indicated 13.6- and 12.5-fold decreases in inhibition potency, respectively, compared with that of CYP2C9 by sophoranone. However, no inhibition of CYP1A2, CYP2A6, CYP2B6, CYP2D6, CYP2E1, or CYP3A activities was observed. These observations suggest that sophoranone is a selective and potent inhibitor of CYP2C9 in vitro, whereas inhibition of other CYPs is substantially lower. These in vitro data support that Sophora tonkinensis extract or sophoranone as a single compound may cause herb-drug interactions via inhibition of CYP2C9, and precautions should be taken when Sophora tonkinensis extract or sophoranone is co-administered with drugs that are mainly metabolized by CYP2C9.

Biography
Soo Hyun Jang is a graduate student with major in Pharmacology/Pharmacokinetics from The Catholic University of Korea, Republic of South Korea. His research interest include: in vitro herb-drug interaction, nonclinical pharmacokinetics and bioanalysis development.

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