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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 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_{50} value of 1.21 μM and K_i value of 0.418 μM in a competitive manner; this was similarly potent as a well-known typical CYP2C9 inhibitor, sulfaphenazole (K_i=0.398 μM). In addition, sophoranone slightly inhibited CYP2C8 and CYP2C19 activities (IC_{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.

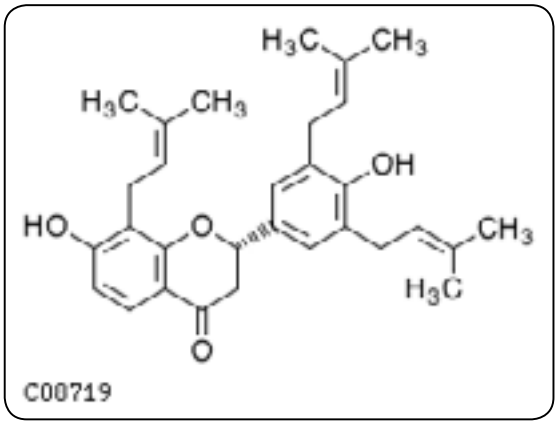

Figure 1: Chemical structure of sophoranone

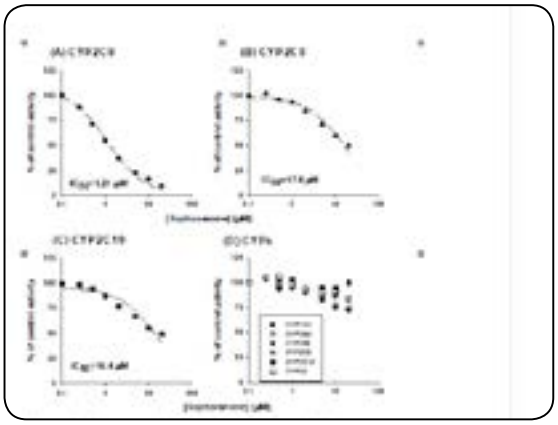

Figure 2: IC_{50} curves of sophoranone for human CYPs activities including CYP2C9 (A) CYP2C8 (B) CYP2C19 (C), and other CYPs (D) in human liver microsomes

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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