20(S)-Protopanaxatriol (Ppt) Exhibits Inhibition Towards UDP-Glucuronosyltransferase (UGT)-Catalyzed Zidovudine Glucuronidation

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SUMMARY. Drug-drug interaction (DDI) is a challenging problem for treatment of HIV-infected patients. Zidovudine (AZT), prescribed under the names Retrovir and Retrovis, is the first U.S. government-approved antiretroviral drug used for the successful treatment of HIV/AIDS infectiousness. Given that ginseng is frequently utilized in combination with AZT and AZT is mainly eliminated by UDP-glucuronosyltransferase 2B7, the aim of present study is to investigate the inhibition of UGT2B7-catalyzed AZT glucuronidation by 20(S)-protopanaxatriol type (Ppt) which is the main ginsenoside absorbed into the plasma. The results showed that ppt competitively inhibited UGT2B7-catalyzed AZT glucuronidation, and the inhibition kinetic parameter (Ki) was determined to be 24.7 μM. Using the maximum plasma concentration of ppt (Cmax), the alteration of area under the curve (AUC) of AZT was 6%. All these results provide important information for understanding ginseng-AZT interaction. However, considering the complication of herbs and individuals, the in vitro-in vivo extrapolation (IV-IVE) results should be explained with more caution.

KEY WORDS: Herb-drug interaction, Ginseng, UDP-glucuronosyltransferases (UGTs), Zidovudine (AZT).

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