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Evaluation of Inhibition of UDP-Glucuronosyltransferase (UGT) 1A1 by Demethylzeylasteral

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***SUMMARY*. Many severe clinical adverse effects can be induced through inhibition of UDP-glucuronosyltransferase (UGT) 1A1, including clinical drug-drug interactions (DDI) and metabolic disorders of endogenous substances. The present study aims to investigate the inhibition of UGT1A1 by demethylzeylasteral which is an important bioactive component isolated from *Tripterygium wilfordii* Hook F. Recombinant UGT1A1 was used as enzyme source, and 4-methylumbelliferone (4-MU) was employed as probe substrate. The results showed that the residual activity of 4-MU glucuronidation was 8.5 ± 1.1 % of the control activity at 100 μM of demethylzeylasteral for UGT1A1. Furthermore, inhibition kinetic type and parameters were evaluated. Dixon plot and Lineweaver-Burk plot showed that demethylzeylasteral non-competitively inhibited UGT1A1, and the inhibition parameter (K_i) was determined to be 21.7 μM for UGT1A1. This kind of inhibitory effect need much attention when demethylzeylasteral and demethylzeyasteral-containing herbs (e.g. *Tripterygium wilfordii* Hook F.) were co-administered with the drugs mainly undergoing UGT1A1-catalyzed metabolism.**

KEY WORDS: Demethylzeylasteral, Drug-drug interaction, UDP-glucuronosyltransferase (UGT) 1A1.

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