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Evaluation of the Inhibitory Effect of Levothyroxine Towards UDP-Glucuronosyltransferase (UGT) 2B7-Mediated 4-Methylumbelliferone (4-MU) Glucuronidation

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***SUMMARY*. Levothyroxine, a synthetic form of thyroid hormone, has been clinically used to treat thyroid hormone deficiency. Following our previous study in which the inhibition of levothyroxine towards UGT1A6 was evaluated, the aim of the present study is furtherly investigate the inhibition of levothyroxine towards another important UGT isoform, UGT2B7. The results showed that levothyroxine inhibited UGT2B7-catalyzed 4-MU glucuronidation reaction in a dose-dependent manner. Furthermore, Lineweaver-Burk and Dixon plots showed the inhibition of UGT2B7 by levothyroxine was best fit to competitive inhibition, and the inhibition kinetic parameter (K_i) was determined to be 43.1 μM. Given that UGT2B7 is one of the most important UGT isoforms catalyzing the glucuronidation reaction of many important clinical drugs, inhibition of UGT2B7 activity by levothyroxine will significantly influence the pharmacokinetic behaviour of these drugs. Therefore, clinical drug-drug interaction due to the inhibition of UGT2B7 by levothyroxine should be paid much attention.**

KEY WORDS: Levothyroxine, UDP-glucuronosyltransferase (UGT) 2B7, Drug-drug interaction.

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