



## Levothyroxine Exhibits Inhibitory Effect towards UDP-Glucuronosyltransferase (UGT) 1A6-Mediated 4-Methylumbelliferone (4-MU) Glucuronidation

Chuan-Qiang WANG\*, Ming-Zhu SONG, Hou-Wei ZHU, Jia-Jun YI,  
Ming-Chun LUAN, Ai-Yuan SHI & Yan-Qing QU

*Yantai Mountain Hospital, Yantai, Shandong province, China*

**SUMMARY.** Levothyroxine, a synthetic form of thyroid hormone, has been clinically used to treat thyroid hormone deficiency. UDP-glucuronosyltransferases (UGTs) are important phase II drug-metabolizing enzymes, and UGTs-inhibition based drug-drug interaction has been widely reported. The aim of the present study is to investigate the inhibitory effect of levothyroxine towards UGT1A6-catalyzed 4-methylumbelliferone (4-MU) glucuronidation. The results showed that levothyroxine inhibited UGT1A6-catalyzed 4-MU glucuronidation reaction in a dose-dependent manner. Furthermore, Lineweaver-Burk and Dixon plots showed the inhibition of UGT1A6 by levothyroxine was best fit to competitive inhibition, and the inhibition kinetic parameter ( $K_i$ ) was determined to be  $15.3 \mu\text{M}$ . Given that UGT1A6 is one of the most important UGT isoforms catalyzing the glucuronidation reaction of many important clinical drugs, including aspirin and serotonin, inhibition of UGT1A6 activity by levothyroxine will significantly influence the pharmacokinetic behaviour of these drugs. Therefore, clinical drug-drug interaction due to the inhibition of UGT1A6 by levothyroxine should paid much attention.

**KEY WORDS:** Drug-drug interaction, Levothyroxine, UDP-glucuronosyltransferases (UGTs).

\* Author to whom correspondence should be addressed. *E-mail:* chuanqiangwang228@gmail.com