Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **31** (7): 1060-3 (2012)

Short communication

Received: August 4, 2012
Accepted: August 7, 2012

Dihydrotanshinone I Exhibits Strong Inhibition Towards UDP-glucuronosyltransferase (UGT) 1A7

Gu GONG [1]#, Shu-Yao ZHANG [2],#, Jia-Ji LIN [3],#, Ling CAI [1], Qi WANG [4], Ru-Meng MA [4], Yong-Sheng ZHANG [4]*, & Yan-Yang TU [4]*

[1] *Department of Anesthesiology, General Hospital of the People's Liberation Army, Chengdu Military Region, Chengdu City, 610083, China*
[2] *Intravenous drug use deployment center, Cancer Hospital of Medical College, Shantou University, Shantou City, Guangdong Province, 515031, China*
[3] *Department of oral medicine, Fourth Military University, Xi'an, Shanxi, China*
[4] *Tangdu Hospital, Fourth Military Medical University, Xi'an, Shanxi, 710038, China*

SUMMARY. Inhibition of the activity of UDP-glucuronosyltransferases (UGTs) can induce severe drug-drug interaction and metabolic disorders of endogenous substances. The aim of the present study is to investigate the inhibition of important UGT isoforms by dihydrotanshinone I, which is an important bioactive component isolated from danshen. The nonselective probe substrate 4-methylumbelliferone (4-MU), and the recombinant UGT isoforms were used in the present study. The results showed that 100 M of dihydrotanshinone I inhibited the activity of UGT1A1, UGT1A3, UGT1A6, UGT1A7, UGT1A8, UGT1A10, and UGT2B7 by 32.7, 61.5, 61.1, 77.5, 47.9, 62.8, and 55.9 %, respectively. Further inhibition kinetic study was performed for the inhibition of UGT1A7 by dihydrotanshinone I. Dose-dependent inhibition of UGT1A7 by dihydrotanshinone I was detected, and Dixon and Lineweaver-Burk plots showed that the inhibition of UGT1A7 by dihydrotanshinone I was best fit to competitive inhibition type. The inhibition kinetic parameter (K_i) was determined to be 2.8 μM. Using the *in vivo* maximum plasma concentration (C_{max}) of dihydrotanshinone I (11.29 ng/mL, 0.04 μM), the the change of AUC ranged from 0.14 to 1.42 % when the contribution of UGT1A7 towards the metabolism of drugs (f_m) ranged from 0.1 to 1. Given that UGT1A7 is one of the most important gastrointestinal UGT isoforms and has high correlation with the occurence of cancer, the potential danshen-drug interaction due to the inhibition of UGT1A7 by dihydrotanshinone I should be given more attention.

KEY WORDS: Dihydrotanshinone I, Enzyme inhibition, UDP-glucuronosyltransferases (UGTs).

* Authors to whom correspondence should be addressed. *E-mail:* zhangyongsheng979@gmail.com (Y.-S. Zhang); Tu.fmmu@gmail.com (Y.-Y. Tu).

\# These authors equally contributed to this paper.

ISSN 0326-2383