Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **31** (9): 1363-6 (2012)

Short communication

Received: October 8, 2012
Accepted: October 18, 2012

Drug Metabolizing Enzymes Inhibition-Based Prediction of Celastrol-Drugs Interaction

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***SUMMARY*. Celastrol, the major bioactive ingredient isolated from *Tripterygium wilfordii* Hook F., is being developed as a promising anti-tumor drug. Given that anti-tumor drugs can be administered in combination with many drugs with narrow therapeutic windows, the potential drug-drug interaction risk due to the inhibition of UDP-glucuronosyltransferase (UGT) 1A3 might exist. Recombinant UGT1A3-catalyzed 4-methylumbelliferone (4-MU) glucuronidation reaction was used for evaluation of celastrol towards the activity of UGT1A3. Data fitting using Dixon plot and Lineweaver-Burk plot showed that celastrol is a competitive inhibitor of UGT1A3, and the second plot using the slopes of Lineweaver-Burk plot versus concentrations of celastrol was employed to calculate the inhibition kinetic parameter (K_i) to be 0.1 μM. Due to the high concentration (10-100 fold as the K_i value) of celastrol needed to reach effective anti-tumor therapy, the high risk of drug-drug interaction exists between celastrol and drugs mainly undergoing UGT1A3-mediated metabolic elimination. All these results remind us that drug-drug interaction should be paid much attention when developing celastrol as a promising anti-tumor agent.**

KEY WORDS: Celastrol, Drug-drug interaction, 4-methylumbelliferone (4-MU).

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