



Herbal Component Celastrol is an Inhibitor of UDP-Glucuronosyltransferase (UGT) 1A7

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SUMMARY. Searching the inhibitors of UDP-glucuronosyltransferases (UGTs) is an important task for identification of UGT isoforms involved in the process of drug metabolism. However, to date, few inhibitors with strong and specific inhibition ability were reported. Given that many compounds with diversified structures exist in herbs, the aim of the present study is to evaluate the inhibition of UGT1A7 by celastrol which is an important ingredient isolated from the *Tripterygium wilfordii* Hook F. The *in vitro* incubation system using recombinant UGT1A7 and non-specific substrate 4-methylumbelliferone (4-MU) was utilized. The results showed that celastrol exhibited dose-dependent inhibition towards UGT1A7-catalyzed 4-MU glucuronidation reaction. Data fitting using Dixon plot and Lineweaver-Burk plot demonstrated competitive inhibition of celastrol towards UGT1A7 activity, and the inhibition kinetic parameter (K_i) was calculated to be 8.1 μ M. All these results indicate the possible development of celastrol or the derivatives based on the core structure of celastrol as the inhibitors for UGT1A7. Additionally, the possible drug-drug interaction might occur between celastrol and the drugs mainly undergoing UGT1A7-catalyzed metabolic elimination.

KEY WORDS: Celastrol, Inhibitors, 4-methylumbelliferone (4-MU).

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