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Effect of B-Ring-Oh Numbers of 5,7-Dihydroxyflavone on the Activity of Cyp1 Enzymes

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CYP1 enzymes, CYP1A1, CYP1A2 and CYP1B1, are known to bioactivate procarcinogens particularly polyaromatic compounds. Flavonoids are a class of natural compounds that are present in edible plants. Structurally, these compounds are polyphenols with two aromatic rings (A, B) and a heterocycyclic ring (C). We observed the differential inhibition of 5,7-dihydroxyflavones which have different numbers of B-ring-OH, to the activity of ethoxyresorufin O-deethylase (EROD) in human hepatic microsomes with the IC50 values of 0.57 μM, 1.28 μM, and 3.62 μM for chrysin, apigenin, and luteolin, respectively. Thus, the effect of B-ring -OH numbers of 5,7-dihydroxyflavone on the activity of CYP enzymes was observed in this study. The inhibition of CYP1A2 was increased in the order chrysin (no -OH, IC50, 0.42 μM), apigenin (one -OH, 5.14 μM) and luteolin (two -OHs, 8.85 μM), but the activity of CYP1A1 was inhibited with the reverse rank. CYP1B1 was strongly inhibited all of them with less than 0.5 μM of IC50. All of them were shown the mixed type inhibition judging by Dixon plot. Thus, the increase of B-ring -OH number in 5,7-dihydroxyflavones was more strongly inhibited CYP1A1 compared to CYP1A2 and decreases of -OH numbers was shown the stronger inhibition of CYP1A2. These differential inhibition of CYP1 enzymes by B-ring -OH numbers of 5,7-dihydroxyflavone might due to different amino acid residue at the active site of enzymes.

Keyword : recombinant CYP1 enzyme, flavonoid, CYP1 inhibition