

【P-57】**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 heterocyclic 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 μ M, 1.28 μ M, and 3.62 μ M 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 μ M), apigenin (one -OH, 5.14 μ M) and luteolin (two -OHs, 8.85 μ M), but the activity of CYP1A1 was inhibited with the reverse rank. CYP1B1 was strongly inhibited all of them with less than 0.5 μ M 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