P20 *IN VIVO* PHENOTYPING OF CYP2A6 IN THAIS: COUMARIN VS NICOTINE

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The association between the distribution characteristics of CYP2A6 catalytic activities towards coumarin and nicotine was analyzed in 120 apparently healthy Thai volunteers. The probe drugs were given sequentially in the same subject with an approximate interval of one week. Urinary 7-hydroxycoumarin, plasma cotinine, and plasma nicotine were measured using HPLC assay. Genotyping for *CYP2A6* gene of the subjects was also performed. The distribution of 7-OHC excreted in the subsequent 8-hr urine (0.03 – 15 mg) after a single oral administration of 15 mg coumarin (Venalot®) and cotinine/nicotine ratio of the plasma concentrations (0.00 – 13.48) 2 hr after chewing a piece of nicotine chewing gum containing 2 mg nicotine (Nicorette®) showed clearly bimodality. However, the probit plot of cotinine/nicotine ratio in the plasma showed the higher number of apparent poor metabolizers (PM), in comparison to that of 7-OHC excreted in the urine. Despite the discordance in the number of PM subjects, a correlation between the *in vivo* dispositions of coumarin and nicotine was extremely closed (R = 0.92). No statistically significant difference in the CYP2A6 activities between male and female subjects was found. The results confirm that phenotyping of CYP2A6 using coumarin and that using nicotine are not metabolically equivalent. Ten subjects with known *CYP2A6* genotypes were given a tablet of 15 mg coumarin again. Liver function test was investigated just before and 24 hr after the coumarin administration. The results showed that coumarin at the challenging dose did not disturb the liver function even in the three subjects genotyped as *CYP2A6*4/*4*. Since the approximate half life of coumarin in human is only 2 hr, the probe drugs, therefore, could be theoretically given within two days consecutively. Even though both coumarin and nicotine can be clinically used as probe drugs in routine testing for CYP2A6 phenotype, our results indicate that giving coumarin and nicotine sequentially to the same subject is a better protocol for a precise CYP2A6 phenotyping.