Thesis Title Metabolic Profile of Paracetamol in Healthy Thais

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ABSTRACT

In this study, the metabolism of paracetamol in Thais was investigated. The purpose was to find the metabolic profile and magnitude of variation of the metabolism in Thai subjects. The study was carried out in 21 healthy male Thai volunteers with the average age of 21 years old. After overnight fasting, each volunteer was given a single dose of 1500 mg paracetamol tablets (Panadol®) with 200 ml water. After medication, blood samples were collected at 0, 0.5, 1, 1.5, 2, 4, 6, 8, 10, and 12 h. The collection of urine samples were at 4 intervals : 0-4, 4-8, 8-12, and 12-24 h. Paracetamol and its metabolites (glucuronide, sulfate, cysteine, and mercapturic acid conjugates) in plasma and urine were analyzed by high performance liquid chromatography (HPLC).

The absorption of paracetamol from the gastrointestinal tract was rapid with peak plasma concentration at 30 min. The peak time for glucuronide and

sulfate conjugates in plasma was at 2 h, while that of cysteine conjugate was at 4 h. In urine, fractional recovery (% of dose) of unchanged paracetamol, glucuronide, sulfate, cysteine, and mercapturic acid conjugates were 4.7, 57.7, 27.2, 3.5, and 2.8, respectively. Overall, the recovery of paracetamol in urine was 95.6% of dose. The range of paracetamol glucuronide, sulfate, and glutathione-derived conjugates (cysteine plus mercapturic acid conjugates) were 40-75, 15-35, and 3-15 % of dose, respectively.

Comparison to the data in Caucasians, it seemed that the capacity of glucuronidation and sulfation in phase II metabolism of paracetamol in Thais was higher than that in Caucasians. On the other hand, Thais had lower in oxidation of phase I metabolism compared with the Caucasians. Accordingly, it seems that Thais are less susceptible to paracetamol toxicity than Caucasians.