Thesis Title: The Study of Caffeine Pharmacokinetics in Healthy Thai Volunteers

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ABSTRACT

The widespread use of caffeine-containing beverages in Thailand has led some to suspect that it might have detrimental effects on health. It is useful to correlate the caffeine concentrations in plasma with its pharmacological effects. The present study aims to provide details of the caffeine pharmacokinetics and to determine the pharmacokinetic profiles of both natural and synthetic caffeine in healthy Thai volunteers.

The study was a crossover design with washout period of 10 days. A single dose of 200 mg of natural or synthetic caffeine was given orally to 12 healthy male Thai volunteers with the average age of 32.3 yr and weight of 66.3 kg after an overnight fasting. Blood samples were drawn at 0, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 6, 8 and 24 hr after drug administration. All samples were stored at -20°c until analyses by HPLC

method.

The present results indicated that most aspects of caffeine pharmacokinetics were generally similar to those reported previously. Some pharmacokinetic parameters of natural caffeine were shown to be significant different from those of synthetic caffeine ($p<0.05$). For natural caffeine, the mean maximum plasma concentrations (C_{max}) was 5.03 $\pm$ 0.61 ug/ml, the time to reach peak concentrations (T_{max}) was 0.85 $\pm$ 0.33 hr and areas under the curve, $AUC_{(0-8)}$ and $AUC_{(0-\infty)}$, were 21.78 $\pm$ 3.68 and 29.29 $\pm$ 7.98 ug.hr/ml, respectively. Whereas with synthetic caffeine, the C_{max} was 6.79 $\pm$ 1.56 ug/ml, T_{max} was 0.54 $\pm$ 0.22 hr and areas under the curve, $AUC_{(0-8)}$ and $AUC_{(0-\infty)}$, were 25.83 $\pm$ 6.62 and 35.81 $\pm$ 11.69 ug.hr/ml, respectively. However, the terminal elimination rate constant (β) and the terminal half-life ($T_{1/2}$) were not significantly different (0.34 $\pm$ 0.15 hr^{-1} and 2.68 $\pm$ 1.45 hr for natural caffeine, and 0.26 $\pm$ 0.14 hr^{-1} and 3.25 $\pm$ 1.07 hr for synthetic caffeine, respectively). A similar finding was also observed with clearance (CL) and the apparent volume of distribution ($V_{d(area)}$). For natural caffeine, CL was 1.85 $\pm$ 0.48 ml/min/kg and $V_{d(area)}$ was 0.45 $\pm$ 0.34 L/kg. Whereas in synthetic caffeine CL was 1.57 $\pm$ 0.54 ml/min/kg and $V_{d(area)}$ was 0.41 $\pm$ 0.12 L/kg.

A single oral administration of 200 mg caffeine from both natural and synthetic sources produced no significant adverse effects.