

Thesis Title	The Study of Pharmacokinetic and Physiological Profiles of Caffeine in Healthy Volunteers.
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ABSTRACT

The effects of caffeine on the general health of hardworking labours have been considered as one of the health problems in Thailand. However, the information is still lacking for setting up the safe limit of exposure. This study was performed to determine the pharmacokinetic parameters of synthetic caffeine and the physiological effects of caffeine as determined by changes in blood pressure (BP), heart rate (HR) and electroencephalogram (EEG). The pharmacokinetic studies in 12 healthy male subjects indicated $C_{\max} = 6.76 \pm 0.47 \mu\text{g/ml}$, $T_{\max} = 0.54 \pm 0.07 \text{ hr}$, $T_{1/2} = 5.63 \pm 0.86 \text{ hr}$, $\text{AUC}_{0 \rightarrow 8}$ and $\text{AUC}_{0 \rightarrow \infty}$ were 26.79 ± 2.20 and $45.10 \pm 7.90 \mu\text{g}\cdot\text{hr/ml}$, respectively. V_d was $0.53 \pm 0.02 \text{ l/kg}$ and CL was $1.40 \pm 0.18 \text{ ml/min.kg}$. The data suggest that caffeine is rapidly absorbed orally and

widely distributed in the body. It was also rapidly eliminated from the body.

Caffeine was shown in another group of 10 healthy male volunteers to significantly increase systolic BP at 60 min and 150 min after drug administration. Diastolic BP and mean arterial pressure showed a significantly progressive increase during 30-150 min after drug administration but no significant change in HR was demonstrated. This may be due to the fact that baroreceptor reflex is an important factor in controlling the HR.

The effects of caffeine on the CNS were determined by EEG and analysed by paired t-test. There was an indication of a caffeine effect in the form of a reduction of the amplitude (μV) of the EEG recording especially that of the alpha activity E/C LMR (8.00-12.50 Hz). With the eyes opened, the alpha rhythm was replaced by fast, irregular low-voltage activity. This phenomenon is a characteristic of the arousal or alerting response and was shown to increase with oral administration of caffeine 400 mg, whereas this effect was not observed in the case of placebo. The changes in alpha activity correlated well with the rates of change in plasma caffeine concentration.

In conclusion, caffeine at the dose of 200 mg produced statistically but not clinically significant pressor response during the period of 150 min after drug administration and exerted mild arousal effect without any evidence of excessive central stimulation as being observed when amphetamine was given.