

Thesis Title Comparative Bioavailability Study
of Paracetamol Solutions Used in
Hospitals

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ABSTRACT

The use of polyethylene glycol (PEG) as complexing and solubilizing agent has been reported to affect the bioavailability of drugs. The present study was aimed to compare the bioavailability of paracetamol in the presence of 10 % alcohol (paracetamol-alcohol liquid) to that in the presence of 10 % PEG (paracetamol-PEG liquid) since these two preparations were commonly used in hospitals.

The study was carried out in 12 healthy Thai male volunteers in randomized cross over design with a wash out period of 7 days. Following fasting over night, a single oral dose of 511 mg was given, followed by 180 ml of water and volunteer was permitted to have a normal diet 2 hours after drug administration. Blood samples were collected at 0, 5, 10, 15, 20, 30, 45, 60, 90, 120, 240, 360 and 480 minutes for analysis of paracetamol by HPLC.

The PCNONLIN two-compartment open model was used to estimate the pharmacokinetic parameters. The mean (SD) value of pharmacokinetic parameters of paracetamol-alcohol were compared to those of paracetamol-PEG as follows: the absorption rate constants (K_{01}) were 6.92 (5.26) and 5.31 (1.84) hr^{-1} , the apparent distribution rate constants (α) were 3.59 (2.28) and 3.38 (1.44) hr^{-1} , the apparent elimination rate constants (β) were 0.25 (0.07) and 0.29 (0.08) hr^{-1} , the elimination half-lives (β -HL) were 3.02 (1.12) and 2.52 (0.58) hr, the area under the curves from time zero to infinity ($AUC_{0-\infty}$) were 32.78 (7.64) and 31.37 (8.34) $\text{mcg}\cdot\text{hr}/\text{ml}$, the peak serum concentrations (C_{max}) were 12.77 (2.63) and 11.44 (3.31) mcg/ml , the time to reach peak serum concentrations (T_{max}) were 25.83 (14.43) and 23.33 (10.30) minutes, respectively.

Comparison of bioavailability indicated that paracetamol-alcohol and paracetamol-PEG were bioequivalent because C_{max} , T_{max} and $AUC_{0-\infty}$ were not significantly different ($p > 0.05$). The other pharmacokinetic parameters were not significantly different ($p > 0.05$). The pharmacokinetic parameters obtained from the two test preparations were also compared to the previous reports and found to be nearly equal.