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CHULEEKORN SIRISANGTRAGUL: PHARMACOKINETICS OF LEVOFLOXACIN IN HEALTHY THAI VOLUNTEERS. THESIS ADVISORS: SUVATNA CHULAVATNATOL, Ph.D., BUSBA CHINDAVIJAK, Ph.D., ASDA VIBHAGOOL, M.D., M.A.C.P., WINAI WANANUKUL, M.D., BOARD OF INTERNAL MEDICINE. 105 p. ISBN 974-661-953-5

Levofloxacin is a new fluoroquinolone antimicrobial agent recently launched in Thailand for the treatment of mild to moderate respiratory tract infections, community-acquired pneumonia, uncomplicated skin and soft tissue infections and complicated urinary tract infections. The recommended dose is 300 mg once daily for 7-14 days. This dose is different from that recommended in the US and Europe which is generally 500 mg once daily for 7-14 days. The present study was designed to investigate the pharmacokinetics of levofloxacin in 12 healthy Thai male subjects with an average age (SD) of 22.92 (2.50) years. A single oral dose of 300 mg or 500 mg levofloxacin was given to subjects following an 8-h overnight fast. The drug was given in a controlled, randomized, 2 x 2 crossover design with a 1 week washout period. Venous blood samples of 15 mL were drawn prior to dosing and 5 mL samples were drawn at 0.25, 0.5, 0.75, 1, 1.25, 1.5, 2.0, 2.5, 3, 4, 8, 10, 24 and 48 h after dosing. Plasma levofloxacin concentrations were determined by high performance liquid chromatography.

The pharmacokinetics of levofloxacin were well described by a linear, 2-compartment open model with first-order absorption with lag time and first-order elimination. Short lag time of 15 min occurred before systemic absorption. Mean ± SEM of C_{max} after 300 mg and 500 mg dose was 4.83 ± 0.33 and 7.75 ± 0.71 μg/mL, respectively. T_{max} ranged from 0.7 to 0.8 h for both doses. Mean + SEM of $AUC_{0-\infty}$ was 35.77 ± 2.06 μg x h/mL for 300 mg dose and 61.57 ± 2.84 μg x h/mL for 500 mg dose. High distribution with V_{ss}/F value of approximately 1.5 L/kg was demonstrated after both doses. Mean ± SEM of CL/F value was 8.64 ± 0.41 and 8.31 ± 0.37 L/h for a 300-mg and a 500-mg dose, respectively. Long $t_{1/2\beta}$ of 7 to 8 h with MRT of 10.43 ± 0.43 h and 10.49 ± 0.38 h after 300 mg and 500 mg dose, respectively, was observed. The results suggested that an oral, 300 mg dose provides sufficient C_{max} to cover most Gram-negative and atypical bacteria (median MIC_{90} 0.032-0.5 μg/mL) and Gram-positive bacteria (median MIC_{90} 0.5 μg/mL) common in the indicated infections except for severe cases or *Streptococcus pneumoniae* (MIC_{90} 2 μg/mL) infection, for which a-500 mg dose should be recommended.