

Thesis Title Norfloxacin Pharmacokinetics Determined by Micro-
Biological Analysis and Pathogenic Bacterial Susceptibility
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ABSTRACT

The comparison of pharmacokinetics of Norfloxacin containing the spray-dried rice starch (Era-tab) with Lexinor ® was studied in 12 healthy male volunteers with normal renal function and the in vitro bacterial susceptibilities of Norfloxacin was determined by the micro dilution technique.

Pharmacokinetic study of Norfloxacin and Lexinor ® was administered as two oral doses of 400 mg and 800 mg after an overnight fast. Breakfast was allowed 2 hours later. Blood samples were collected prior to drug administration and at 0.25, 1, 1.5, 2, 4, 6, 8, and 12 hours after drug administration. Plasma were separated, kept at -20^oc until analysis which were performed within 1 week of collection. The plasma concentrations of Norfloxacin and Lexinor ® were determine by microbiological assay. A two compartment open model was used to determine the pharmacokinetic

parameters. The mean \pm SEM values of time to reach peak plasma concentration (T_{max}) were 1.33 ± 0.17 hr., 1.33 ± 0.14 hr., 1.54 ± 0.11 hr., and 1.25 ± 0.18 hr., of Norfloxacin 400 mg, Lexinor® 400 mg, Norfloxacin 800 mg, Lexinor® 800 mg, respectively. The mean \pm SEM values of peak plasma concentration (C_{max}) were 1.87 ± 0.13 μ g/ml., 2.14 ± 0.18 μ g/ml., 3.09 ± 0.21 μ g/ml., and 2.83 ± 0.27 μ g/ml., of Norfloxacin 400 mg, Lexinor® 400 mg, Norfloxacin 800 mg, Lexinor®, respectively. The mean \pm SEM values of elimination half-life ($T_{1/2}$) were 9.19 ± 0.56 hr., 10.33 ± 0.52 hr., 9.16 ± 0.56 hr., and 11.09 ± 0.84 hr., of Norfloxacin 400 mg, Lexinor® 400 mg, Norfloxacin 800 mg, Lexinor® 800 mg, respectively. The mean \pm SEM values of absorption rate constant (K_a) were 1.11 ± 0.31 hr., 1.06 ± 0.17 hr., 0.96 ± 0.20 hr., and 1.12 ± 0.59 hr., of Norfloxacin 400 mg, Lexinor® 400 mg, Norfloxacin 800 mg, Lexinor® 800 mg, respectively. The mean \pm SEM values of area under the plasma concentration-time curve (AUC) were 9.18 ± 0.48 mg.hr/l., 10.30 ± 0.81 mg.hr/l., 17.70 ± 1.42 mg.hr/l., and 15.90 ± 1.66 mg.hr/l. of Norfloxacin 400 mg, Lexinor® 400 mg, Norfloxacin 800 mg, Lexinor® 800 mg, respectively. The mean \pm SEM values of the volume of distribution (V_d) were 587.57 ± 26.28 litre, 601.95 ± 38.45 litre, 650.56 ± 48.74 litre, and 983.28 ± 180.83 litre of Norfloxacin 400 mg, Lexinor® 400 mg, Norfloxacin 800 mg, Lexinor® 800 mg, respectively. The mean \pm SEM values of clearance (Cl) were 45.22 ± 2.90 ml/min, 41.26 ± 2.93 ml/min, 49.97 ± 5.96 ml/min, and 60.08 ± 8.89 ml/min of Norfloxacin 400 mg, Lexinor® 400 mg, Norfloxacin 800 mg, Lexinor® 800 mg, respectively. No significant differences were

found between mean values of all parameters of Norfloxacin and Lexinor ® except in the volume of distribution (Vd) of Norfloxacin 800 mg with Lexinor ® 800 mg where there was significant difference.

The total 250 bacterial strains of gram-negative isolated from the patients of Pra Mongkut Klao General Hospital during 1995 were used to study for susceptibility to Norfloxacin. The minimum inhibitory concentration (MIC) of isolates found by a micro dilution technique to be susceptible to Norfloxacin were: *Enterobacter spp.*, 100%; *Pseudomonas aeruginosa* and *Proteus mirabilis*, 98%; *Escherichia coli*, 96%; and *Klebsiella spp.*, 90%. No strain of *Enterobacter spp.* among studied expressed the resistance to Norfloxacin whereas 10% of *Klebsiella spp.* were resistant.