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**Repeated Dose 4-week Oral Toxicokinetic Study of DW-224a
in Rats**

Jong-Hwa Lee¹, Han-Ok Lee¹, Moon-Koo Chung¹, Dong-Rack Choi², Se-Kwang Gu²,
Yasuo Tarumoto¹, Ho-Chul Shin¹

¹*Korea Institute of Toxicology*, ²*Dong-Wha Pharm. Ind. Co., Ltd*

DW-224a is a fluoroquinolone antibiotics with a broad spectrum of activity against Gram-positive and Gram-negative bacteria. In order to clarify toxicokinetic profile of DW-224a, a 4-week repeated dose oral toxicokinetic study (dose level: 0, 63, 250, 1000 mg/kg) was conducted in groups of Sprague-Dawley rats. Studies included general observation, body weight changes, method validation, and toxicokinetic parameters. For general observation, salivation and abdominal distension were detected and these are thought to attribute to test item administration. Soft stool observed in the 1000 mg/kg treatment group was known as the adverse effect of fluoroquinolone and this was considered to be treatment related effect. For body weight measurement, statistically significant changes were not observed compared with the vehicle control. The blood samples of animals were collected from the tail vein at each time point on day 1 and on weeks 4 and toxicokinetic parameters of the peak concentration (C_{max}), time to peak concentration (T_{max}), and area under the concentration-time curve (AUC) were calculated individually. For the T_{max}, there were no significant differences between males and females. The C_{max} and AUC values showed a dose proportional increase in DW-224a in each group. The values of C_{max} and AUC were slightly changed with repeated dosing. However, these changes do not show significant nonlinear kinetics.

In conclusion, the DW-224a was absorbed rapidly, distributed and eliminated from the body with several hours of half-lives. We could not find a significant dose-dependent nonlinear kinetic properties and accumulation of the drug even though 4-week repeated dosing. This study will provide a critical information for dose range finding in long-term toxicology studies.

Keyword : DW-224a, Toxicokinetics, Repeated dose toxicity