

[P-59]**STUDIES ON THE SUBACUTE TOXICITY AND TOXICOKINETICS OF DW-224a, AFTER SINGLE AND 4-WEEK REPEATED ORAL ADMINISTRATION IN DOGS**Junghee Han¹, Shin-Woo Cha¹, Moon-Koo Chung¹ and Sang-Seop Han¹¹Department of Toxicology and Toxicokinetics, Korea Institute of Toxicology, Daejeon

The subacute toxicities and toxicokinetics of a new fluoroquinolone antibiotics, DW-224a, were evaluated after single (at the 1st day) and 4-week (at the 28th day) oral administration of the drug, in doses of 0 (to serve as a control), 10, 30 and 90 mg/kg/day, to male and female dogs (n = 3 for male and female dogs for each dose). DW-224a had an effect on the cardiovascular systems, thymus and testes. The toxic dose was 30 mg/kg and no observed adverse effect level was less than 10 mg/kg for male and female dogs. There were no significant gender differences in the pharmacokinetic parameters of DW-224a for each dose after both single and 4-week oral administration. The pharmacokinetic parameters of DW-224a were dose-independent after single oral administration; the time to reach a peak plasma concentration (T_{max}) and the dose-normalized area under the plasma concentration-time curve from time zero to 24 h in plasma (AUC_{0-24 h}) were not significantly different among three doses. The accumulation of DW-224a after 4-week oral administration was not considerable at toxic dose, 90 mg/kg/day. For example, after 4-week administration, the dose-normalized AUC_{0-24h} value at 90 mg/kg/day (7.69 and 7.05 μ g h/ml) was not significantly greater than that at 10 mg/kg/day. After 4-week oral administration, the dose-normalized C_{max} and AUC_{0-24h} at 90 mg/kg/day were not significantly higher and greater, respectively, than those after a single oral administration.

Keyword : SUBACUTE TOXICITY, TOXICOKINETICS, DW-224a, DOG