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RECLINICAL TOXICITY STUDY OF A NEW PHOSPHODIESTERASE-5 INHIBITOR (I) ACUTE TOXICITY STUDY AND MUTAGENICITY

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Single-dose toxicity of a new phosphodiesterse inhibitor-5, DA-8159, was studied in rats via oral and intravenous routes and in mice via oral route. In addition, genotoxic potential of DA-8159 was investigated by using of the battery of test; reverse mutation test on bacteria, chromosomal aberration test on cultured mammalian cells and micronucleous test on mice. Clinical signs in rats and mice after administration were similar regardless of administration routes and animal species. The observed symptoms were partially-closed eyes, hunched posture, depression, prostration and tremor. Body weight were decreased dose-dependent manner in rats after oral administration. There were no treatment-related macroscopic changes in gross necropsy. Minimal lethal dose of DA-8159 was estimatated approximately 1g/kg in oral and 100mg/kg in intravenous route, respectively. In mutagenicity study, DA-8159 did not induce his+ revertants in the Ames test and did not cause chromosomal aberrations with or without matabolic activation system. Furthermore, in micronucelous test, DA-8159 also did not show any positive response. From these results, it is concluded that DA-8159 has no mutagenic or clastogenic effects, and does not interfere with cell division.