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Estimating Benchmark Dose and Permissible Intake Level Using Subchronic Toxicity Data of Aristolochia Contorta

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Occurrence of Chinese Herbs Nephropathy (CHN) has been reported in young women who had taken a slimming pills containing some chinese herbs. Aristolochic acid (AA) known as a carcinogen, was suspected as the major causal factor of CHN. AA is major component of fruit of A. contorta was used in Korean Traditional Medicine. The national Institute of Toxicology Research had evaluated the toxicity of an aqueous extract of A. contorta in subchronic system to identify whether toxicity like AA in common usual dose prescribed to human appear or not. The animal test (male and female Sprague Dawley rat) was conducted using oral dose 21.3, 213 and 2130 mg/kg/day for a lyophilized extract for 7 days/week, 90 days. Tested dose was the equivalent value with 0.05, 0.5 and 5 mg/kg/day of AA, respectively. The lowest dose was selected from ingested daily dose for adult through general prescription of A. contorta in Korea. This study was conducted to estimate benchmark dose (BMD10) and permissible intake level (PIL) using dose-response data produced from above study. The quantal linear and quadratic models for induction of BMD was used and kidney interstitial fibrosis was selected as critical effect. Estiamted BMD10 were 151.22 mg/kg/day (female) and 459.21 mg/kg/day (male) based on kidney interstitial fibrosis. The PIL was induced from female BMD10 corresponding with NOAEL and safety factor 100 (10: from animal to human, 10: human variability). Finally, induced PIL was 1.51 mg/kg/day. This value means daily dose of A. contorta that occurrence of kidney interstitial fibrosis would not be expected.