Expression of γH2AX in urinary bladders of chemical-treated rats

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Evodia officinalis (EO) is natural product which has been used by oriental medicine and it has been known to have some pharmacologic effects such as testosterone secretion, catecholamine secretion, analgesic, anti-inflammatory, anti-obesity, vasodilatory, thermoregulatory and uterotonic effects. However, its toxicity has not been fully evaluated. In the present studies, we carried out a 90-day repeated dose toxicity study (orally five times per week at doses of 25, 74, 222, 667 and 2,000 mg/kg) using in F344 rats and genotoxicity studies (bacterial reverse mutation test in Escherichia coli WP2uvrA, Salmonella typhimurium TA98, TA100, TA1535 and TA1537, chromosome aberration test using Chinese Hamster Lung cell and micronucleus test using ICR mice) of EO. Increased liver weight in both sexes at 2,000 mg/kg (P<0.01), decreased alanine aminotransferase in males at 222, 667 and 2,000 mg/kg (P<0.01), in females at 667 and 2,000 mg/kg (P<0.01 and P<0.05, respectively), decreased total cholesterol in males at 667 and 2,000 mg/kg (P<0.01), in females at 222, 667 and 2,000 mg/kg (P<0.05, P<0.01 and P<0.01, respectively), and decreased glucose in females at 222, 667 and 2,000 mg/kg (P<0.05, P<0.01 and P<0.05, respectively) were relevant. The changes were not associated with histopathological alterations. Thus, the no-observed-adverse-effect level (NOAEL) of EO in F344 rats is considered to be greater than 2,000 mg/kg. For genotoxicity study, EO did not show the mutagenic potential, chromosome aberration and micronucleus formation.

Key word: Evodia officinalis, F344 rat, genotoxicity, repeated oral dose toxicity