【P-25】

Study on the Mechanism of Antifertility in Male Rats Treated With 3-Mcpd

Seung Jun Kwack, Soon Sun Kim, Gyu Seek Rhee, Rhee Da Lee, Ji Hyun Seok, Soo Yeong Chae, Yo Woo Choi, Yong Hyuck Won, Kwon Jo Lim, Kui Lea Park and Dae Hyun Cho

Department of Toxicology, National Institute of Toxicological Research, Korea Food and Drug Administration, Seoul, Korea

3-Monochloro-1,2-propanediol (3-MCPD) is a food contaminant, which is often found in foods containing acid hydrolyzed (AH) protein, like seasonings and savory food products. The purpose of the present study was to investigate the effects of 3-MCPD on male fertility, sperm, and hormonal levels and its antifertility mechanism. In vivo male fertility testing was performed to observe the adverse effects of 3-MCPD on the functioning of the male reproductive system and pregnancy outcome. 3-MCPD (0.01-5mg/kg) were administered daily by gavage to Sprague-Dawley (SD) male rats for 4 weeks. At the end of the pretreatment period, male rats were mated overnight with untreated females. Males successfully inducing pregnancy were sacrificed to assess sperm parameters, reproductive organ histopathology, and spermatogenesis. The resulting pregnant females were sacrificed on day 20 of gestation to evaluate pregnancy outcome. The paternal administration of 3-MCPD (5 mg/kg) was found to result in adverse effects on male fertility and pregnancy outcome without inducing remarkable histopathological changes in testes and epididymides. Additionally, 3-MCPD (5 mg/kg) significantly reduced sperm motility, and copulation, and fertility indices, and the number of live fetuses showed steep dose-response curves. 3-MCPD did not affect spermatogenesis or induce hormonal changes in the blood and testes of male rats. An in vitro hormone assay using primary isolated Leydig cells, showed no significant changes in related hormone levels after 3-MCPD treatment. To evaluate the effects of 3-MCPD on apoptotic induction and H+-ATPase levels in the testis and epididymis, 10 or 100 mg/kg of 3-MCPD was administered by gavage to male rats and testes and epididymides examined at 3, 6, 12 and 24 hr later. Apoptosis was not detected in the testes of animals treated with 100 mg/kg 3-MCPD. However, the level of H+-ATPase in the cauda

epididymis was reduced by 3-MCPD treatment. These results indicate that 3-MCPD induced a spermatotoxic effect, which was mediated by reduced H+-ATPase expression in the cauda epididymis, and suggest that an altered pH level in the cauda epididymis might lead to a disruption of sperm maturation and the acquisition of motility.

Keyword : 3-MCPD, spermatotoxicity, sperm motility, Leydig cell, ATPase