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A STUDY ON THE MUTAGENICITY OF METHAPYRILENE HYDROCHLORIDE

Hyun-Kul Lee, Yong-Hwa Kim, and Jung-Koo Roh
Toxicology Research Center, Korea Research Institute of Chemical Technology, P.O.Box 107, Yusong, Taejon 305-600, Korea

Methapyrilene hydrochloride(MPH), an antagonist of histamine H1 receptor, was used for cold and sleep aid until it was reported as a potent hepatocarcinogen in Fischer 344 rats(Lijinsky et al., 1980). In this study, a series of experiments were performed to see if the carcinogenicity of MPH could be explained by conventional or modified mutagenicity tests and other methods.

MPH was not mutagenic in the *Salmonella*/microsome reversion assays. MPH failed to induce mutations at the XGPRT locus of AS52 cells, however, MPH induced structural chromosomal aberrations in CHO-K1-BH4 and CHL cells. MPH showed no significant inhibitory effect on cell to cell metabolic cooperation in V79-4 cells. MPH did not show any synergistic effects on rat PMN-mediated induction of SCE, suggesting that MPH does not stimulate PMN to produce radicals. There was no significant increase of mutation frequency(MF) in the livers of transgenic mice treated with MPH, however, there was increase of MF in the livers of transgenic rats.

Thus, MPH does not induce gene mutations, but induces chromosomal aberrations in cultured cells. Also MPH induces mutations in rat liver but not in livers of mice. The carcinogenicity of MPH might be related to chromosomal aberration and/or *in vivo* gene mutation induced by MPH. However, it is not clear whether MPH is an initiator or a promoter.