

- P-242 EFFECTS OF DEPLETION OF EMBRYONIC GLUTATHIONE ON SELENIUM TERATOGENICITY IN CULTURED RAT EMBRYOS: Hirobumi TABATA, Makoto USAMI, Kazue SAKEMI, Kunio KAWASHIMA and Akira TAKANAKA (Div. Pharmacol., Natl. Inst. Hlth. Sci., 1-18-1 Kamiyoga, Setagaya, Tokyo 158)

We previously showed that selenium (Se) caused morphological abnormalities in specific sites in cultured rat embryos, and that their incidences changed at the reduced state of the embryonic cells, both with varied responses to different Se compounds. It was, accordingly, considered that selective cytotoxicity and the redox states of Se and embryonic cells might be involved in the mechanisms of Se teratogenicity. In the present study, we examined the effects of depletion of glutathione, the major intracellular reducing agent, on Se teratogenicity in cultured rat embryos. Rat embryos at day 9.5 of gestation were cultured for 48 h in the presence of Se as either sodium selenite (oxidation state: +4) at 10 and 20 μM or sodium selenate (+6) at 30 and 100 μM with or without the addition of 0.1 mM of L-buthionine-[S,R]-sulfoximine (BSO). With the addition of BSO, the reduced glutathione (GSH) content in the embryos was decreased to about 50%. Selenite or selenate alone increased the incidence of abnormalities of the embryos in a concentration dependent manner. The incidence of selenite-induced abnormalities of the embryos was significantly decreased with BSO. On the contrary, the incidence of selenate-induced abnormalities was significantly increased with BSO. It was concluded from these results that embryonic GSH and the Se redox state were involved in Se teratogenicity.

- P-243 INTERLABORATORY VALIDATION STUDY OF THE SKIN² DERMAL MODEL AND MTT CYTOTOXICITY ASSAY KITS: Yuzo TANIGUCHI¹, Keiji SUZUKI², Keiya NAKAJIMA³, Madoka NAKAJIMA⁴, Yoshihisa MIWA⁵, Yasushi YAMADA⁵, Matoshi SATOH⁶, Masahiro TAKEYOSHI⁷, Yasuki AKIE⁹, Matsuko MORIYASU⁹, Hitoshi YAMAMOTO¹⁰, Minoru KATAGIRI¹¹, Akemi KAZAMA¹¹ and Masami WATANABE¹² (1The Environmental Biological Life Science, 2Yokohama City University, 3The Center of Japan Biological Chemistry Co., Ltd., 4Biosafety Research Center, Foods, Drugs and Pesticides, 5Nihon Bioreserch Center Inc., 6Safety Research Institute for Chemical Compounds Co., Ltd., 7Hita Research Laboratories, Chemical Biotesting Center, Chemicals Inspection & Testing Institute, 8Fuji Life Science Inc., 9Panapharm Laboratories Co., Ltd., 10Life Science Laboratory, 11Oriental Yeast Co., Ltd., 12Nagasaki University)

Interlaboratory varidation research was designed to study the capacity of 4 chemicals to cause irritation by using Skin² Dermal Model ZK1100 kits (Skin²). The chemicals tested were SDS, CC, EtOH, and DMSO. Eleven Japanese insititutions participated in this varidation research to study the usefulness of Skin² in accordance with an identical protocol. MTT-50 values obtained with the present method correlated with DS20 values obtained with Draize method($r=0.9571$) in one of the participant institutions. The irritation study using Skin² was easy to perform and generated quantitative data. When the test was repeated, fairly good reproducibility was demonstrated with a variation of less than 2σ . It is suggested that this newly developed in vitro method would be useful in toxicity studies, and would serve as a useful alternative to the conventional methods of the eye irritation study.