Cancer Cells

Oh JiYoung°, Lee SuJung, Shin JaeHo, Kim TaeSung, Moon HyunJu, Kang IlHyun, Kim InYoung, Kim AnKeun[1], and Han SoonYoung

Endocrine Toxicology Division, National Institute of Toxicological Research, KFDA and [1]College of Pharmacy, SookMyung Women's University

Zinc is known to have an inhibitory effect on apoptosis and an antioxidative effect scavenging reactive oxygen species (ROS) under oxidative stress. We studied the influence of zinc on cadmium-induced apoptosis especially associated with ROS in MCF-7 human breast carcinoma cell line. For the determination of appropriate experimental concentration and time, we executed MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay and DNA fragmentation assay. MCF-7 cells exposed to various concentration of cadmium for 24h showed 50% cell viability at approximately 100mM. And the amount of DNA fragment significantly increased at 12h. To observe apoptosis features, we performed DNA fragmentation assay on 1.5% agarose gel, nuclei staining using DAPI (4',6-diamidino-2-phenylindole) and detection of caspase-9 protein expression by western blot. When we treated cadmium in MCF-7 cells, we observed significant nucleosomal DNA fragmentation, caspase-9 induction and an increase of apoptotic body at 12h. Positively, zinc inhibited DNA fragmentation, caspase-9 activation on cadmium-induced apoptosis. Also, we observed that cadmium (100mM, 12h) elevated peroxides level, which is thought as an apoptosis-inducing factor, and depleted antioxidative enzymes (SOD, CAT). As zinc came up to our expectations, it had ROS scavenging effect and could recover depletion of antioxidative enzymes. Cells co-treated with 100uM zinc and cadmium showed higher superoxide (SOD) level than control at 12h. Also, catalase (CAT) level was simlar to control level at 12h. These results suggest that zinc could inhibit cadmium-induced apoptosis triggered by ROS.

[PA4-34] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

TERT mRNA expression is up-regulated in MCF-7 cells and mouse mammary gland organ culture (MMOC) system by endosulfan treatment

Je KangHoon°, Nam kungWoo, Kim Kinam, Cho MyungHaing, Mar Woongchon

College of Veterinary Medicine and Natural Products Research Institute, College of Pharmacy, Seoul National University

Endosulfan is one of the organochlorine pesticides, well-known endocrine disruptors (EDs). Many EDs show the estrogenic effect. Estrogen is a group of hormones that play an important role in mammary gland function and implicated in mammary carcinogenesis. In the present study, using mouse mammary gland organ culture (MMOC) system, we studied the effects of endosulfan on nodule like alveolar lesion (NLAL) formation in the mouse mammary gland development. Additionally, we found that the telomerase catalytic subunit, TERT mRNA expression levels were increased in endosulfan-treated mammary glands in a dose-dependent manner. As it was reported that the telomerase could be activated by estrogen, we examined the effects of endosulfan on telomerase activity and found that telomerase activity in estrogen receptor-positive MCF-7 cells was up-regulated by endosulfan treatment. Moreover, this activation was accompanied by the up-regulation of TERT mRNA expression. Also, a transient expression assay using CAT reporter plasmids, which contain various fragments of TERT promoter, showed that this imperfect palindromic estrogen-responsive element is responsible for transcriptional activation by endosulfan. These results may help elucidate the endocrine disrupting mechanism of endosulfan.