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To understand mechanism of benzoquinone-induced cytotoxicity, the roles of ATP and calcium in platelet toxicity and morphology changes was investigated. Using scanning electron microscopy, morphological changes to platelets following 1,4-benzoquinone exposure consisted of membrane blebbing at 5 min which was significantly different from shape changes (pseudopod formation) observed in response to physiological agonists. Benzoquinone-induced platelet membrane bleb formation was associated with rapid depletion of intracellular ATP and independent of presence of extracellular calcium. Benzoquinone-induced platelet lysis (LDH leakage) observed between 20-30 mins was dependent on extracellular calcium and associated with increased cytosolic calcium. Benzoquinone-induced cytotoxicity was inhibited by calmodulin antagonists, suggesting that calmodulin could play a major role in 1,4-benzoquinone toxicity via protease activation. These results suggested that the progression of events for quinone-induced cytotoxicity in platelets to be as follows: quinones deplete intracellular ATP; formation of blebs occurs; calcium homeostasis is disrupted, resulting activation of calmodulin-dependent proteases; irreversible cytotoxicity occurs.

[PA4-14] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

TCDD induced micronuclei in estrogen receptor positive human breast cancer cells

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Bisphenol A (BPA, Cas no. 80-05-7), di-2-ethylhexyl phthalte (DEHP, Cas no. 117-81-7), and 2,3,7,8-tetrachlorodibenzodioxin (TCDD, Cas no. 1746-01-6) were well known endocrine disrupting chemicals (EDCs). They showed all negative results in the Standard genetic toxicology test battery recommended by ICH guideline, i.e. bacterial reverse mutation assay, chromosome aberration assay, mouse lymphoma tk+/- assay and in vivo rodent micronucleus assay (MN). In our previous study, bisphenol A and di-2-ethylhexyl phthalte induced micronucleus formation in MCF-7 cells (estrogen receptor positive). In this study, to identify the relationship between MN formation and estrogen receptor (ER), TCDD was studied using micronucleus formation in human breast MCF-7 cells (ER positive). We also performed in vitro MN to identify the role of estrogen receptors with TCDD and tamoxifen, inhibitor of estrogen receptor, in MCF-7 cells during micronucleus formation. TCDD induced MN formation in MCF-7 cells (ER positive) was 6.60 fold higher than that of MCF-10A cells (ER negative). Though TCDD induced MN in MCF-10A cells, the frequencies were weak positive. Tamoxifen inhibited TCDD-induced MN formation up to 47.3% in MCF-7 cells.

[PA4-15] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Potentiation of Agonist-Induced Platelet Aggregation by Trivalent Arsenic

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Chronic ingestions of arsenic by drinking water have been shown to induce cardiovascular disease