paper, we discuss the sample size calculation in 2 x 2 crossover design with the log-transformed data.

[OA-3] [04/18/2003 (Fri) 14:00 - 14:15 / Orchid]

Protective Effect of Biopectin on 2,3,7,8-Tetrachlorodibenzo-p-dioxin Induced Reproductive System Damage and Its Action Mechanism

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A growing body of scientific research indicates that man-made chemicals (xenobiotics) may interfere with the normal functioning of endocrine, or hormone systems. These endocrine disruptors may cause a variety of problems with development, behavior, and reproduction. Amongst the xenobiotics the World Health Organization classed 2,3,7,8-TCDD as a "known" human carcinogen. Other than carcinogenicity, the dioxins exhibit immunotoxicological, reproductive and developmental effects in mammals.
According to many reports, tissue distribution of TCDD in male Sprague-Dawley rats (240-290 g) was considered complete in 24 hr after TCDD administration. The highest levels of distribution of the chemical were found in liver (5% of dose/g tissue), followed by white fat (1% of dose/g tissue); serum was lowest at 0.01% of dose/ml serum. TCDD was mainly excreted via feces and the biological half-life of TCDD was 16.3 ± 3.0 days in rat.
Treatment of rats with TCDD resulted in a broad range of toxic effects including growth suppression, hepatomegaly, hypercholesterolemia, thymic atrophy, and increased microsomal enzyme activities.
The dioxin-induced toxic manifestations described above were reduced by water soluble biopectin administration. The hypocholesterolemic effects of pectins were studied in Sprague-Dawley rats and pectins significantly reduced plasma cholesterol levels: supplementation of pectin lowers LDL cholesterol and in some cases VLDL cholesterol rather than HDL cholesterol. The raised ratios of liver/body weight and elevated EROD activity in SD rats by TCDD were return to normal levels. Antiestrogenic effect of pectin was shown in E-screening method and trace of androgenic activity was observed in established A-screening test. Therefore, it was concluded that the lipophilic property of TCDD enhanced its adhesion to cholesterol and lowering characteristic of soluble biopectin discharge TCDD out of the body. In addition, trace of androgenic property of biopectin might help recovery of the TCDD induced male reproductive organ damage.

[OA-4] [04/18/2003 (Fri) 14:15 - 14:30 / Orchid]

Bisphenol A-induced overall immune downregulation in mice.

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This study was undertaken to assess overall effects of bisphenol A, a monomer widely used in manufacturing polycarbonate plastics or epoxy resin, exposure on immune system of mice. For in vitro evaluation, serial concentration of BPA was added into culture of various immune cells from normal female ICR mice, and for in vivo or ex vivo assessment, mice were orally exposed to BPA dissolved in olive oil as doses of 500, 1000, 2000 mg/kg b.w. for acute exposure or 100, 500, 1000 mg/kg/day b.w. 5 days a week for subacute exposure. thereafter we conducted evaluation

on immunopathology, cellular immunity, humoral immunity, and macrophages function. Liver weight was significantly increased in the mice exposed to BPA as dose-dependent manner. Hematological parameters including WBC were altered in the mice exposed to BPA. Decrease in CD3+ and CD4+CD8- cells among splenocytes as well as CD4+CD8- and CD4-CD8+ cells among thymocytes was resulted in the mice subacutely exposed to BPA. In addition to suppression of proliferation, IL-4 and IFN-γproduction of splenocytes was induced by exposure to high dose of BPA ex vivo or in vitro. Splenic IgM antibody forming response to SRBC and Serum levels of immunoglobulins were altered at the mice exposed to BPA in comparison with that of the control. In addition, BPA effected on the NO and TNF-α production ex vivo or in vitro, and decreased expression of B7-1 and B7-2 on macrophages. Overall our results suggest that BPA could affect the immune system of mice resulting in suppression of cellular immunity, humoral immunity, and peritoneal macrophages function.

Oral Presentations - Field C

[C1. Biochemistry] [C2. Microbiology] [C3. Cell Biology]

[OC-1] [04/18/2003 (Fri) 14:30 - 14:45 / Orchid]

Roles of MAPKs in H-ras-induced Invasion and Motility

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One of the most frequent defects in human cancer is the uncontrolled activation of the ras-signaling pathways. Elevated p21ras expression is associated with tumor aggressiveness in breast cancer including the extent of invasion into fat tissues, infiltration into lymphatic vessels and tumor recurrence. We demonstrate that H-ras, but not N-ras, upregulates matrix metalloproteinase (MMP)-2 expression and induces invasive phenotype in MCF10A human breast epithelial cells. We also show that H-ras-mediated invasiveness is significantly inhibited when the expression of MMP-2 is downregulated, using an oligodeoxyribonucleotide complementary to the MMP-2 mRNA, or when MMP-2 activity is blocked by its inhibitor, tissue inhibitors of matrix metalloproteinase-2 (TIMP-2). Our results show that the H-ras-induced invasive phenotype is associated more closely with the expression of MMP-2 in human breast epithelial cells. Since migration plays a crucial role in invasive, we examined motility of MCF10A cells transformed with H-ras or N-ras. We show that cell motility was increased by H-ras, but N-ras suggesting that H-ras-induced invasive phenotype may be mainly due to enhanced cell motility. We have investigated whether H-ras and N-ras differentially regulate ras effector pathways critical for cell motility and invasive phenotype. While neither H-ras nor N-ras activated JNK-1, both H-ras and N-ras effectively activated ERK-1/-2. Importantly, prominent activation of p38 was shown only in H-ras-activated cells but not in N-ras-activated MCF10A cells. Functional significance of H-ras-activated p38 in invasiveness and cell motility was evidenced by studies using SB203580, a chemical inhibitor of p38, and a dominant negative construct of p38. While inhibition of JNK-1 activity had no effect on H-ras-induced MCF10A cell invasion and motility, the inhibition of the ERK pathway using a chemical inhibitor PD98059 or dominant negative mutant of MEK-1, an activator of ERKs, significantly reduced H-ras-induced invasion and migration. We also provide evidence that p38 and, to a lesser degree, ERKs, are critical for H-ras-mediated upregulation of