Oral Presentations - Field A

[A1. Pharmacology] [A2. Therapeutics] [A3. Hygienics] [A4. Toxicology]

[OA-1] [04/18/2003 (Fri) 13:30 - 13:45 / Orchid]

Esophagitis and IL-1β-induced alteration of MAP kinase activity in esophageal smooth muscle

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We investigated whether experimental esophagitis and IL-1β could induce the activation of MAP kinases in esophageal smooth muscle. With two models of experimental esophagitis, we assessed the activity of p38 MAP kinase, p44/42 MAP kinase and JNK. In feline acute experimental esophagitis, immunoblotting of normal and esophagitis-induced smooth muscle with each types of MAP kinase antibodies revealed the slight increase of phosphorylated form of p38 MAP kinase, especially in membrane fraction. JNK activity was also increased, but the increase was detected in cytosolic fraction. The amount of phosphorylated form of p44/42 MAP kinase in esophagitis-induced smooth muscle showed the increase of activity in cytosol and the decrease in membrane fraction, compared with normal esophagus. Total PKCβII and PKCε were also increased by inflammation, especially in cytosolic fraction. Second, surgically induced reflux esophagitis of rats showed time-dependent increase of ulcer index (UI), resulting in UI 4 after 6 hours. After the increase of phosphorylation of p38 MAP kinase in 4 hours (UI = 1), it was decreased below the basal level in 6 hours. The activity of JNK was increased with accordance with the progression of esophagitis. The level of phosphorylation of p44/42 MAP kinase was increased in 1 hour and decreased in 4 hours. After 6 hours, it was recovered to the basal level. The amount of COX2 expression was not changed with the progression of esophagitis.
In cultured feline esophageal smooth muscle cells, the phosphorylated forms of p44/42 MAP kinase and p38 MAP kinase were increased 1 hour after IL-1β treatment (25ng/ml), which is maintained to 24 hours. PLC inhibitor neomycin decreased the density of p44/42 MAP kinase band to the basal level. Tyrosin kinase inhibitor tyrphostin 51 and PKC inhibitor GF109203X also reduced the IL-1β-induced MAP kinase activity.
With these results, we suggest that the each type of MAP kinases shows different features of activation and deactivation in experimental esophagitis models and IL-1β -induced MAP kinase activation might be mediated by tyrosine kinase, PLC and PKC.

[OA-2] [04/18/2003 (Fri) 13:45 - 14:00 / Orchid]

On Sample Size Calculation in Bioequivalence Trials

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Sample size calculations plays an important role in a bioequivalence trials and is determined by considering power under the alternative hypothesis. The regulatory guideline recommends that 2 x 2 crossover design is conducted and raw data is log-transformed for statistical analysis. In this

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