[PA4-9] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Studies on the Nephrotoxic Mechanism of 3-MCPD

Park ChangWon, Kim KwangJin°, Kim JaeHee, Suh SooKyong, Kim JongWon, Kim KyuBong, Park JungWon, Hwang KwanIk, Seo KyungWon, Kim JooII, Lee SunHee

Pharmacology Department, National Institute of Toxicological Research, Korea Food & Drug Administration, 5 Nokbun-Dong Eunpyung-Gu, Seoul 122-704, south Korea

3-Monochloro-1,2-propanediol (3-MCPD) produced during the acid hydrolysis of vegetable proteins (ex. soybean products) is food-contaminant material detected in acid-hydrolysed soy, bread, water, et al. 3-MCPD is currently being a matter of concern to safety. The nephrotoxicity of 3-MCPD and 3-MCPD metabolites has been reported to result from accumulating of metabolites in kidney tubules and inhibiting of renal metabolism of glucose and lactate. The major target organ of 3-MCPD toxicity is known to kidney, but the nephrotoxicity inducing mechanism of 3-MCPD has not yet been known. Therefore, we would observe the change of the nephrotoxicy on 3-MCPD single administration /co-administration with enzyme inducer and inhibitor and investigate about 3-MCPD metabolizing enzyme and neprhotoxicity inducing mechanism.
We administered for 2 weeks and 3 days in Sprague-Dawley rats with 3-MCPD(80mg/kg/day, 50mg/kg/day), 3-MCPD/phenobarbital (PB ; 30mg/kg/day, 80mg/kg/day ; cytochrome P450 Inducer), 3-MCPD/phenethyl isothiocyanate (PEITC ; 20mg/kg/day, 200mg/kg/day ; cytochrome P450 Inhibitor ; GST Inducer) and 3-MCPD/ N-acetyl cystein (NAC ; 50mg/kg/day, 300mg/kg/day ; GSH precursor) and observed body weight, relative kiney weight, BUN and creatinine value in blood, glucose and protein value, N-acetyl- -D-glucosaminidase (AGS) activity in urine, histopathology of kidney, hepatic cytochrome P450 and GSH contents.
The results are as follows. The nephrotoxicities induced by 3-MCPD were identified by body weight, relative kidney weight, BUN value in blood and histopathology of kidney. The main pathological lesion was tubule degeneration including vacuolation. As expected, we could observe increasement of hepatic cytochrome P450 contents by PB and increasement of hepatic GSH contents by PEITC and NAC. In 3-MCPD and PB co-administration group, we observed more severe toxicological finding in BUN value in blood, AGS value in urine and histopathology compared to 3-MCPD administration group. Meanwhile, we could observe that BUN value was recovered to control level by co-administration of PEITC and NAC. And the co-administration reduced toxicity in aspect the number of lesion compared to 3-MCPD administration group.
We concluded that 3-MCPD may produce toxicologically active metabolite by cytochrome P450 and the active metabolite may be eliminate by GSH. Hereafter, we consider that further studies are required to identify more detail metabolic mechanism of 3-MCPD.

[PA4-10] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Naringenin Inhibits Dimethylnitrosamine-Induced Hepatic Fibrosis in Rats

Lee MiHye°, Shin MiOk, Yoon Sik, Moon JeonOk

College of Pharmacy, Pusan National University, Changjeon-dong, Kumjeong-ku, Pusan 609-735, Korea and Department of Anatomy, College of Medicine, Pusan National University, Pusan 602-739, Korea.

Naringenin, a phytoalexin found in grapefruit, has been reported to exhibit a wide range of pharmacological properties. The aim of the present study is to evaluate the protective effect of naringenin on hepatic fibrosis induced by dimethylnitrosamine (DMN) in rats.
Fibrosis was induced by intraperitoneal injection of DMN. Naringenin was given orally at 20 mg/kg and 50 mg/kg daily for 4 weeks. Naringenin treatment essentially prevented the DMN-

induced loss in body and liver weight and inhibited its elevation of serum alanine transaminase, aspartate transaminase, alkaline phosphatase, and bilirubin. Narningenin also increased serum albumin and total protein levels and reduced the hepatic level of malondialdehyde. Furthermore, naringenin suppressed the induction of hepatic fibrosis, as determined by histological evaluation and the immunohistochemical examination showed that naringenin reduced the number of alpha-smooth muscle actin positive hepatic stellate cells.
Our results demonstrate the protective effect against hepatotoxicity and fibrosis induced by DMN suggest that naringenin may be useful in the prevention of hepatic fibrosis development.

[PA4-11] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of organic germanium and caffeic acid phenethyl ester on immune system of BALB/c mice following a 14-day oral exposure

Park JaeHyun, Lee JongKwon, Kim HyungSoo°, Chung SeungTae, Eom JunH, Kim KyungA, Paik SoonYoung, Oh HyeYoung

National Institute of Toxicological Research

The present study was conducted to determine the effects of bis-carboxyethyl germanium sesquioxide(Ge-132) and caffeic acid phenethyl ester(CAPE) on immune system in female BALB/c mice. The mice were orally exposed continuously to Ge-132 (0, 50, 100, or 200mg/kg), or CAPE (0, 5, 10, or 20mg/kg) for 14 days. Immunomodulatory activity was evaluated by assessment of body and organ weight, lymphocytes blastogenesis, splenic cell plaque forming cells (PFC) assay and lymphocyte subpopulation by flowcytometry. Even though the significant change of body weight was not observed in both treated group, exposure to Ge-132 resulted in the increase of spleen weight and cellularity of spleen at the dose of 200mg/kg, whereas the treatment of CAPE resulted in the decrease of the thymus weight and/or cellularity of thymus and spleen at the all exposed group. Mitogen lipopolysaccharide (LPS) and concannavalin A (ConA) induced Lymphocyte blastogenesis was not affected by Ge-132 and CAPE, except B-lymphocyte blastogenesis was induced at the dose of Ge-132 100mg/kg. In the case of T and B cells subpopulation in spleen, CD3+ cells were increased and CD19+ cells were decreased at the dosage group of Ge-132 100mg/kg, there was not significant change in CAPE treated group. Also, CD4+ cells were decreased in exposure to Ge-132 but increased in exposure to CAPE. The IgM antibody response to sheep red blood cell (SRBC) measured by PFC was only increased in animals treated with more than 10mg/kg of CAPE treated groups. The results of this study suggest that Ge-132 and CAPE have an immunomodulatory activity in some cases and these used methods in this study are useful to evaluate the functional foods with immunomodulatory effect.

[PA4-12] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Investigation of potential estrogenic activity of bioallethrin in vitro and in vivo assays

Kim SoonSun°, Rhee GyuSeek, Lee Rhee Da, Kwack SeungJun, Lim KwonJo, Park ChulHoon, Lee GeunShik, Jeung EuiBae, Kil KwangSup, Choi KwangSik, Park KuiLea

National Institute of Toxicological Research,KFDA/Chungbuk National University

Many pesticides possess hormonal activity and have been thus classified as endocrine disruptors. Bioallethrin is one of the pyrethroids, synthetic derivatives of naturally occurring pyrethrins. These pyrethroids including bioallethrin have been developed as insectides due to their high insecticidal potency and low mammalian toxicity. Currently, bioallethrin is used to