

Nan JiXing, Park MiRan, Kim YounChul, Sohn DongHwan, Lee ByungHoon

College of Pharmacy and Medicinal Resources Research Center, Wonkwang University

Cholestatic liver injury results from the accumulation of toxic bile salts within the liver. The aim of the present study was to understand the mechanism of bile salts-induced hepatocellular apoptosis in bile duct-ligated (BDL) rats, using Western blot and immunohistochemical analysis. The mechanisms of hepatoprotective effects of *Salvia miltiorrhiza* (SM) was also studied in this model. Apoptotic cell death was increased five-fold after three days of BDL, decreased over two weeks and remained constant thereafter. Total cellular Bax protein was increased three days after BDL and decreased over time thereafter. We observed the translocation of Bax to mitochondria and subsequent release of cytochrome c. Nuclear p53 increased three days after BDL, but most p53 was expressed in the cytoplasm after one week. The expression of c-Myc was inhibited by three days, but increased at later stages following BDL. Bcl-2 was increased over time in BDL rats. Fas expression was not changed and activation of caspase 8 did not occur. Fas immunoreactivity was exclusively observed in the cytoplasm of hepatocytes, indicating that Fas expressed in rat hepatocytes is predominantly a soluble form. Thus our data suggest that nuclear p53 regulates the expression of Bax in BDL rats. The translocation of Bax to mitochondria supports the hypothesis that this may lead to release of cytochrome c and transduce the signal for apoptotic death of hepatocytes by toxic bile salts. The lack of changes in Fas suggests that Fas may not be playing a role in apoptosis in this model.

Salvia miltiorrhiza BUNGE, a traditional chinese herbal medicine, has been commonly used to treat chronic hepatitis and liver fibrosis. However, the mechanism of action is not yet fully understood. The treatment of extract of SM to BDL rat reduced the number of TUNEL positive cells to the control level after 10 days of BDL. The expression of Bax was reduced with time by the treatment of SM. The treatment of SM accelerated the cytoplasmic sequestration of p53. The expression of Bcl-2 was increased, hence the Bax to Bcl-2 ratio was decreased significantly. These results suggest that SM may be used as hepatoprotective agent in extrahepatic cholestasis model.

[PA3-12] [10/18/2001 (Thr) 14:00 – 17:00 / Hall D]

Effect of gamma radiation on steroidogenesis and testicular function in adult mice

Chun Ki-Jung^o, Kim Jin Kyu, *Kim Jihyang, *Yoon Yong-Dal

Korea Atomic Energy Research Institute, *Hanyang University, Dept. of Life Science

The effect of radiation on testis are related to the irradiated dose resulting in temporary or permanent inhibition of spermatogenesis depending upon the radiation damaged cell types. We examined changes in testosterone production in the testis of male mice after wholebody gamma-irradiation. Eight-week-old male ICR mice were irradiated with 6.5 or 10 Gy. At days 1, 2, 3, 4 and 5 after irradiation, testes were removed and processed for paraffin sections and isolation of mRNA. We calculated the gonad index from body and testis weight, and checked testosterone levels per testicular volume. Hormonal analysis in serum and testis was performed by means of radioimmunoassay. Semiquantitative RT-PCR techniques were used to evaluate the expression kinetics of the apoptotic gene after irradiation. Gamma-irradiation in the mice showed that body weight and testosterone concentration and differential expression of the apoptotic gene were reduced compared to that of non-irradiated ones. These results demonstrate that gamma-radiation induces impairment of testicular function somewhat in adult mice.

[PA3-13] [10/18/2001 (Thr) 14:00 – 17:00 / Hall D]

Levels of PCB congeners and organochlorine pesticides in Korean adipose tissue, liver and whole blood

Yoo YoungChan, Lee SangKi^o, Yang JaYoul, Kim KiWook, Lee SuYeun, Kim DaeHyeon, Ham ByungWoo,

Chung KyuHyuck

National Institute of Scientific Investigation, Seoul, Korea, College of Pharmacy, SungKyunKwan University, Suwon, Korea

Organochlorine pesticides and polychlorinated biphenyls(PCBs) are ubiquitously distributed in the environment and belong to a group of contaminants whose occurrence in the environment is of a serious concern to environmental chemists and toxicologists. This is due to their resistance to degradation in the environment as well as their potential toxicity. The occurrence of organochlorine pesticides and PCBs in the environment and subsequently in parts of the food chain, resulting in the intake of these compounds by man and animal. The measure of the levels of organochlorine pesticides or polychlorinated biphenyls (PCBs) in tissues or blood of human populations are good markers in determining the extent of exposure and in the evaluating the hazards. So, most countries have conducted initial monitoring programs to determine organochlorine pesticides and PCBs in human tissues. But few report has been presented in Korea. In this study, organochlorine pesticides(α -BHC, β -BHC, γ -BHC, δ -BHC, p,p'-DDT, p,p'-DDD, p,p'-DDE, endrin, dieldrin, aldrin) and marker PCBs(PCB nos. 28, 52, 101, 118, 138, 153, 180) were determined in human blood, adipose tissue and liver tissues collected at autopsy of 10 men and 10 women, by using GC/ECD. From the results, the significant differences in the levels of organochlorine pesticides or PCBs between sexes, districts where they had lived and ages were also investigated.

[PA3-14] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Effects of bisphenol A on T cell and B cell population and cytokine production of splenocytes.

Byun Junga^O, Heo Yong*, Pyo Myoungyun

College of Pharmacy, Sookmyung Women's university, Seoul, College of Natural Science, Catholic University of Daegu, Daegu.*

Bisphenol A is a monomer used in the manufacturing epoxy resins and polycarbonates, and may be released into the environment through its use and handling. This study was designed to investigate the effects of BPA on the T cell population and B cell, and production of IL-4 and IFN- γ . Female ICR mice were administered to various concentrations(100, 500, 1000 mg/kg/day) of BPA for 30 days. After 2 days expose, mice were sacrificed.

Helper T cell population in spleen from exposed to BPA was decreased with increase in B cell population. The cytokines production of Con A-stimulated spleen cell from the BPA exposed mice was decreased. When normal splenocytes were activated with Con A in the presence (1, 10, 25, 50, and 100 μ M) or absence of BPA, BPA suppressed cytokines production at 50, 100 μ M. These results revealed immunotoxicity of BPA.

[PA3-15] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Bisphenol A-metabolites induces Oxidative DNA damage and reduced cell proliferation

Kim bonghee

College of Pharmacy, Chung Nam National University

Bisphenol A, a monomer of polycarbonate and epoxy resins, has been detected in canned food and human saliva. BPA stimulate cell proliferation and induces expression of estrogen-response genes in vitro. This report considers the hypothesis that BPA is converted in vivo to hydroxylated metabolites with enhanced estrogenicity and cytotoxicity. The purpose of the this study was to evaluate the cytotoxicity