processes. The purpose of the present study is to elicit molecular mechanism of tetrandrien induced apoptosis in HepG2 cells. Treatment of the cells with tetrandrine resulted in the activation of caspase 3 and subsequent cleavage of PARP at a concentration of 30 uM. It was blocked completely by the pretreatment of IETD-fmk, a specific inhibitor for caspase 8. Tetrandrine also induced caspase 8 activation. Active caspase 8 tranduces apoptotic signal to mitochondria via Bid, which is located in the cytosol and translocates to the mitochondria in a truncated form (tBid) upon caspase 8 activaiton. By the treatment of the cells with tetrandrine expression of the full length Bid was decreased, which was also inhibited by IETD-fmk. Subsequntly we observed the cytochrome c release and the decrease in the mitochondrial transmembrane potential. These results suggest that apoptosis of HepG2 cells by tetrandrine proceeds via caspase 8 induced activation of Bid which affects the mitochondrial transmembrane potential and the release of cytochrome c.

[PA3-3] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

An Anti-cancer Drug, Paclitaxel, Induces Apoptosis in MCF-7 Human Breast Cancer Cells by Generating Ceramide and Arachidonic Acid

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Accumulation of ceramide mass in MCF-7 cells by the anti-cancer agent, paclitaxel, was found to occur primarily due to activation of the de novo synthesis pathway. Morever, the addition of paclitaxel resulted in the accumulation of ceramide, which was followed by a prolonged arachidonic acid release. Participation of ceramide de novo pathway in arachidonate signaling was detected since L-cycloserine, an inhibitor of de novo synthesis, was able to inhibit the paclitaxel-induced AA release and cytotoxicity. This suggest that the production of ceramide in response to paclitaxel appears to be related with in arachidonic acid release, probably cytotoxicity. Enzymatic assays revealed that serine palmitoyltransferase, the rate-limiting enzyme in ceramide de novo pathway, was activated 1.2-fold by paclitaxel treatment. An inhibitor of glucosylceramide synthesis, 1-phenyl-2-dacanoylamino-3-morpholino-1-propanol, accumulated ceramide production and increased cytotoxicity when used in combination with paclitaxel. This data suggest that activation of serine palmitoyltransferase is responsible for increased ceramide production during de novo synthesis initiated by paclitaxel and de novo synthesis may serve a specific role in arachidonic acid release.

[PA3-4] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Effects of ascorbic acid according to administration doses on radiation induced DNA damage in mouse splenic and blood lymphocytes

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Ascorbic acid is very well known as one of various ntioxidants and is used very popular in man.Melatonin,an endogenous compound secreted by the pineal gland in human brain has been reported to act as an antioxidant nowadays. The present study was performed to obtain the differences of the radioprotective function of ascorbic acid and combination with melatonin according to the administration dose a day on radiation induced DNA damage in mouse spleen and blood.Six-week-old ICR male mice were irradiated with 8.0 Gy of γ- ray five days after oral administration of ascorbic acid(low dose:400mg/kg, high dose :2000mg/kg) and plus melatonin(250mg/kg) and were sacrificed 3 days later. Spleens and blood were taken and then isolated lymphocytes. The tail moment of DNA single-strand breaks in mouse splenic and blood lymphocytes was evaluated by the Comet

assay. Comet assay has been applied to the detection of DNA damage due to environmental toxic materials. In particular, this assay is a novel method to assess DNA single-strand breaks. In splenic lymphocytes, the administration of the ascorbic acid and combination with melatonin reduced the tail moment in the comets compared with that of the irradiated control group showed the different values according to the administration dose. In cases of two high dose administration groups, TM values showed lower than those of low dose administration ones. Combination administration of ascorbic acid and melatonin was more effective than single administration of ascorbic acid. In blood lymphocytes, TM values showed similar compared with the splenic ones. These results indicate that ascorbic acid have a little protective effects on the radiation induced DNA damage of the mouse splenic and blood lymphocytes when assessed by the Comet assay but this can be showed a little differences of radioprotective effects according to the administration doses and combination with other antioxdant like melatonin.

[PA3-5] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Changes of serum immunoglobulin in the subacute oral administration of Mancozeb

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Mancozeb, a polymeric complex of zinc and manganese salts of ethylean bisdithiocarbamate(EBDC), is used widely in agriculture as fungicides, and herbicides. Macozeb has been reported to induce teratogenic and carcinogenic effect.But the immunomodulating effects of Mancozeb exposure have not been systemically evaluated. The purpose of this study was to investigate the effects of Mancozeb on immunoglobulin production. Mancozeb at dose of 250, 1000, 1500mg/kg b.w./day with or without OVA-antigen for 30 days were orally administered to female ICR mice. Mice were sacrificed and serum was collected on day 2 following administration of BPA for 30days. Total IgG1, total IgG2a, total IgE, OVA specific IgG1,and OVA-specific IgG2a were determined and compared with those of non-treated mice. In the groups of Mancozeb with OVA antigen, total IgE, OVA-specific IgG1 and OVA-specific IgG2a were dose-dependently decreased. However, in mice treated with Mancozeb alone, OVA-specific IgG1, OVA-specific IgG2a, total IgG1, IgE, and IgG2a were not much altered. These results demonstrated the Mancozeb modulates the production of immunoglobulin.

[PA3-6] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Report on the trends of the Drug Abuse and the Mortalities related to Intoxication of Drug-Toxic Substances in the Central Area of Korea in 2001

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This presentation reports the trends of the drug abuses(DA) and the mortalities related to drug-toxicants(MDT) in the Central area of Korea in 2001. We surveyed the DA cases and MDT, which were requested to analyze the drug-toxicants in the Central district office of National Institute of Scientific Investigation.
The detected drugs on DA cases were methamphetamine, marihuana, opiates, inhalants(toluene, butane, propane), dextromethorphane, carisoprodol, benzodiazepines, nalbuphine, fenfluamine, and miscellaneous in order of cases. Men are more liable to drug abuses than women, and the most common age group was 30s. Surveys of MDT shows that the detected toxicants are paraquat(herbicide), cyanide(rodenticide or insecticide), phosphamidone(insecticide), glyphosate(herbicide), doxylamine(sedative), methomyl(insecticide), dichlorvos (insecticide), benzodiazepines(anxiolytic), and miscellaneous in order of cases. Men's intoxications by the drug-