Lee HM, Yoon EK, Choi SN, Han JY, Kim HM, Kim KH*, Kim PY

Korea Food and Drug Administration, *Duksung Women University

Aflatoxin B1(AFB1) has been found to be a potent genotoxic agent and carcinogen in many test systems and animal species with hepatotoxicity, mutagenicity, and teratogenicity(Bhat, 1996). AFB1 is a potential contaminant of many farm products such as grains, pulse and nuts that are stored under warm and humid conditions for some time. The foreign daily intake of AFB1 is very different due to various food consumption pattern.
The methodology of risk assessment was newly suggested by FAO/WHO based on it's carcinogenicity and certain genotoxicity(FAO/WHO, 1999).
This study was conducted to identify excess cancer risk of AFB1 induced by human exposure through cereal ingestion. For the risk calculation, the used cancer potency was 9 (mg/kg/day)-1 for individuals negative for hepatitis B and 230 (mg/kg/day)-1 for individuals positive for hepatitis B based on the multistage model and hepatocarcinoma dose-response data (Bowers, et al., 1993)
The human exposure dose was estimated using mean value(1997) of aflatoxin in domestic cereals (rice, barley, wheat, millet, maize), food consumption data(National Nutriton Survey Report, 1995), exposure duration(assumed value : 30, 50 years), body weight (60 kg, Korea Research Institute of Standards and Science, 1998), and averaging time(lifetime; 73 years, National Statistical Office, 1997).
The calculated cancer risk values for individuals positive and negative for hepatitis B were 1.18×10^{-3}~1.96×10^{-3} and 4.62×10^{-5}~7.7×10^{-5} respectively. This result can recommend that individuals positive for hepatitis B must be carefully attended on food ingestion due to 25 fold higher AFB1 cancer risk value than individuals negative for hepatitis B.
The futher study is needed for real risk assessment based on more representative food contamination data of AFB1.

[OA-4] [04/21/2000 (Fri) 14:55 ~ 15:10 / Rm B113, Bldg 26]

POSSIBLE INVOLVEMENT OF NF-kappa B IN PHORBOL ESTER-INDUCED EXPRESSION OF CYCLOOXYGENASE-2 AND INDUCIBLE NITRIC OXIDE SYNTHASE IN MOUSE SKIN

Chun Kyung-Soo, Keum Young-Sam, Han Seong Su, Cha Hyun-Ho, Seo Hyojoung, and Surh Young-Joon

College of Pharmacy, Seoul National University, Seoul 151-742, Korea

There has been accumulating evidence supporting that both cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) play pivotal roles in carcinogenesis as well as inflammatory processes. COX-2 and iNOS catalyze the production of PGE2 and nitric oxide (NO), respectively that are important in mediating inflammatory responses. In the present work, we found that topical application of the dorsal skin of female ICR mice with 10 nmole of the tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA) led to maximal elevation of COX-2 and iNOS proteins at 2 h and 4 h, respectively. Their mRNA expression peaked about 1 h after the TPA treatment. Pretreatment of mice with aminoguanidine, an inhibitor of iNOS, significantly suppressed the TPA-induced expression of COX-2. Recent studies have demonstrated that the eukaryotic transcription factor NF-kappa B is involved in regulation of COX-2 and iNOS expression. Topical application of 10 nmole TPA caused rapid activation of epidermal NF-kappa B as assessed by the electrophoretic mobility shift assay (EMSA), with the maximal activation observed at 1 h. TPA treatment resulted in degradation of the inhibitory protein I-kappa B with subsequent translocation of the functionally active NF-kappa B subunit p65. Furthermore, the NF-kappa B inhibitor, pyrrolidine dithiocarbamate repressed TPA-stimulated induction of COX-2, whereas iNOS expression was less influenced.

[OB-1] [04/21/2000 (Fri) 15:10 ~ 15:25 / Rm B113, Bldg 26]

Suppressive Effects of DA-9601, an Artemisia asiatica Extract, on

Dimethylnitrosamine-induced Experimental Liver Cirrhosis in Rats

Cho H°, Oh TY, Ahn BO, Kim SH, Kim WB

Research Laboratories, Dong-A Pharm. Co., Ltd., Yongin, Korea

The effect of DA-9601, an Artemisia asiatica extract, on hepatic fibrogenesis or fibrosis was evaluated using experimental liver cirrhosis induced in rats by the administration of dimethylnitrosamine (DMN) intraperitoneally three times a week for 2 weeks. DA-9601 at a dose of 30 or 100 mg was orally administered to DMN treated rats daily for 3 weeks from 1 week before the DMN. Seven days after last DMN treatment, the animals were sacrificed in order to assess the degree of hepatic fibrogenesis and damage using serum biochemical, hepatic biochemical and histopathological examination. Treatment of DA-9601 significantly reduced the elevation of serum ALT, AST and total histological score on the damaged liver ($p<0.05$). The hepatic levels of collagen and malondialdehyde (MDA), an indicative of lipid peroxidation, in DA-9601 treated rats were decreased significantly when compared to DMN-treated control ($p<0.05$). In addition, immunohistochemical examination showed that DA-9601 reduced the disposition of type I collagen in the liver than DMN-treated control. These results suggest that DA-9601 may be useful to prevent the aggravation of liver cirrhosis through the inhibition of lipid peroxidation and disposition of collagen.

[OC-1] [04/21/2000 (Fri) 10:40 - 10:55 / Rm B113, Bldg 26]

Bacterial injection induced syntheses of N-b-alanyldopamine and DOPA decarboxylase in the hemolymph of coleopteran insect, Tenebrio molitor larvae

Chang Hun JOO*, Mi Hee KIM, Mi Young CHO, Tae Hyuk KWON, Kwang Moon LEE, Tae Ho LEE*, Bok Luel LEE

College of Pharmacy, *College of Natural Sciences, Pusan National University

Injection of *Escherichia coli* into larvae of the coleopteran *Tenebrio molitor* resulted in the appearance of a dopamine-like substance on the electrochemical detector. To characterize this dopamine-like substance, we purified it to homogeneity from the immunized hemolymph and determined its molecular structure to be N-b-alanyldopamine (NBAD) by the liquid chromatographic/tandem mass spectrometric (LC/MS) method. Chemically synthesized NBAD showed the same retention time on HPLC as the purified NBAD from immunized larvae. To elucidate the molecular mechanism of NBAD synthesis in vivo, we examined the enzyme activity of DOPA decarboxylase (DDC) against *E. coli* injected hemolymph of *T. molitor* larvae. The enzyme activity of DDC dramatically increased about 8 h after injection; DDC activity of injected larvae being 10-times higher than naive larvae after 24 h. To evaluate the extent of quantitative changes of DDC in *Tenebrio* response to bacterial challenge, *Tenebrio* DDC was purified to homogeneity from the whole larvae and a cDNA clone for *Tenebrio* DDC was isolated. RNA blot hybridization revealed that expression of the DDC gene was transiently activated from 3 to 8 h after *E. coli* challenge. Immunoprecipitation experiments showed that *Tenebrio* DDC was detected from 8 to 24 h in *E. coli*-injected larval extract. Thus, bacterial injection into *T. molitor* larvae might induce transcriptional activation of a DDC gene, and then synthesis of NBAD. The synthesized NBAD might be used as a substrate by phenoloxidase during melanin synthesis in the humoral defense response or the melanotic encapsulation reaction of the cellular defense response. (*Eur.J.Biochem.*in press, 2000)

[OC-2] [04/21/2000 (Fri) 10:55 - 11:10 / Rm B113, Bldg 26]

BCL-2 ATTENUATES HYDROGEN PEROXIDE- AND BETA-AMYLOID-INDUCED OXIDATIVE PC12 CELL DEATH VIA NF-KAPPA B ACTIVATION

Jang Jung-Hee° and Surh Young-Joon