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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 its 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  $9 \text{ (mg/kg/day)}^{-1}$  for individuals negative for hepatitis B and  $230 \text{ (mg/kg/day)}^{-1}$  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 Nutrition 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  $1.18 \times 10^{-3} \sim 1.96 \times 10^{-3}$  and  $4.62 \times 10^{-5} \sim 7.7 \times 10^{-5}$  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 further 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

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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