[OA-1] [04/21/2000 (Fri) 14:10 - 14:25 / Rm B113, Bldg 26]

Protective Effect of DA-9601, an Artemisia asiatica Extract, on Experimental GERD in Rats

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The effect of DA-9601, an extract of Artemisia asiatica, which is known to possess mucoprotective action either by free radical scavenging or increase of mucus secretion, on experimental gastroesophageal reflux disease (GERD) was investigated in rats. Experimental GERD in rats was devised by the ligature of forestomach and transient stenosis of lower duodenum for 48 hrs. GERD rats were divided into 4 groups: normal, control, low and high dose of DA-9601 (30 and 100 mg/kg). DA-9601 was gavaged twice a day for 3 days before operation. Forty eight hours after operation, all animals were euthanatized and gross finding, mucosal malonedialdehyde (MDA), the electrophoretic mobility shift assay (EMSA) for detection of NFκB activation and histological changes (H&E and immune staining of nitrotyrosine or COX-2 antibody) of esophagus were examined. DA-9601 significantly reduced gross lesion score and tissue MDA compared with GERD control, in a dose-dependent manner ($p<0.05$). DA-9601 also markedly attenuated not only histologic abnormalities but activation of NFκB in esophageal tissue. These results clearly demonstrate that DA-9601 ameliorates macroscopic and hoistologic lesion of experimental GERD either through reducing oxidative stress or by attenuating NFκB involved in inflammation. DA-9601 could be a promising drug for the therapy of GERD.

[OA-2] [04/21/2000 (Fri) 14:25 - 14:40 / Rm B113, Bldg 26]

Beneficial Effect of DA-9601, an Artemisia asiatica Extract, on Dextran Sulfate Sodium-induced Colitis in Rats: Colonoscopic Evaluation

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This study was performed to examine the effects of DA-9601, an Artemisa asiatica extract, on dextran sulfate sodium (DSS)-induced colitis in Sprague Dawley rats. Experimental colitis was induced by supplementing drinking water with 4% DSS (M.W. 40,000) for 5 days. DA-9601 was administered orally at a dose of 10, 30, or 100 mg/kg twice a day for 8 days commencing 3 days before DSS drinking. Colonoendoscopic evaluation (Olympus, Japan) of anesthetized rats was done for three times on days 0, 3, and 5 of DSS drinking. During the experiment, body weight and clinical signs were examined. After sacrifice on day 6, macroscopic and microscopic findings, malondialdehyde (MDA) contents and myeloperoxidase (MPO) activity of affected colon were assessed. Before 5 days of DSS drinking, no colonoscopic alteration was noted. On day 5, however, colonoendoscopic observation showed severely damaged mucosa of colon with edema, diffuse hemorrhagic and ulcers in control animals. In contrast, animals receiving DA-9601 showed only mild edematous change of colonic mucosa. Pathologic examination revealed that DA-9601 significantly attenuated macroscopic and microscopic lesion score, formation of MDA and MPO activity, dose-dependently ($p<0.05$). The results of the present study suggest that DA-9601 can be useful for the prevention of acute flare-up symptoms of inflammatory bowel disease.

[OA-3] [04/21/2000 (Fri) 14:40 - 14:55 / Rm B113, Bldg 26]

Risk Assessment of Aflatoxin B1 in Cereals

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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 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

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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