Sixth paper

Heme oxygenase – 1 Expression in Liver and Colon of Rats Exposed to Oxidative stress and Dysplasia by a Carcinogen Diethylnitrosamine and the Possible Therapeutic Effects of Probiotic Versus Pyridazine Derivative and Chemotherapy

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Abstract

Background: Diethylnitrosamine (DENA) is dietary carcinogen. It is known as cancer initiator in various organs. The present study investigated the destructive changes of DENA in liver and colon and the possible therapeutic effects of doxorubicin (DOX); pyridazine derivative (MDP) and lactobacillus casei (LAB) against DENA induced dysplasia in liver and colon.

Methods:

Lactobacillus casei were tested for their probiotic properties and prepared for rat administration. Sixty adult male albino rats were divided into six groups. A normal control group received the vehicle; DENA group was injected intraperitoneally (ip) with 55mg/kg body weight twice per week for six weeks. DENA+MDP group received MDP at a dose of 10mg/kg (ip) twice per week for the next 4 weeks after DENA administration; DENA+DOX group received DOX at a dose of 10mg/kg (ip) twice per week for the next 4 weeks after DENA administration; DENA+LAB received LAB orally at a dose of (1.5×10^9 CFU) twice per week for the next 4 weeks after DENA administration. DENA+MDP+DOX group received both MDP and DOX as the aforementioned before. Sera, liver and colon were obtained after the end of experiment. Serum aspartate transaminase and alanine transaminase were detected as well as glutathione peroxidase (GSHPX), nitric oxide, tumor necrosis factor (TNF-α), alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA). Histo-pathological studies and immune-histochemical examination of heme oxygenase-1 (HO-1) were done. Morphometric study was performed. All measurements were followed by

statistical analysis.
Results: DENA induced significant increase in liver enzymes with significant increase in oxidation and inflammation biomarkers and AFP and CEA. Histologically, DENA showed degenerative changes in hepatocytes and dysplastic aberrant crypt foci in colon. Liver and colon displayed increased cytoplasmic and nuclear immune-expression of HO-1. Therapeutic groups showed partial improvement in biochemical parameters and histological structure. However, *Lactobacillus casei* showed the best result in attenuating pathological and biochemical changes in liver and colon.
Conclusion: *Lactobacillus casei* displayed a potential anti-tumorigenic activity against DENA in liver and colon. Thismay be exerted via HO-1 modulation and suppression of oxidation and inflammation.
Keywords: Diethylnitrosamine, dysplasia, liver, colon, *lactobacillus casei*