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THE EFFECT OF A NATURALLY SOURCED ANTIOXIDANT PRODUCT BIO-NORMALIZER ON PATIENTS WITH IDDM AND NIDDM

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Second International Conference on Natural Antioxidants and Anticarcinogens in Nutrition, Health and Disease: June 24-27, 1998, Helsinki, Finland

We have previously observed that Bio-Normalizer (BN, Sun-O International Inc., Gifu, Japan) produced by yeast and bacterial fermentation of papaya fruits and some tropical herbs, possessed the redox regulating properties in a variety of in vivo systems. Regarding diabetes mellitus as one of the most spectacular examples of free radical pathologies, we studied the effects of BN on diabetic patients and animals with streptozotocin-induced diabetes (SID). In the experimental model we found that early stages of SID were characterized by highly increased blood glucose level and acute inflammation in the rat pancreas followed by specific damage of β-islets. The tissue (pancreatic and peritoneal) macrophages isolated from SID animals produced 1.5-2 times greater than normal amount of superoxide and nitric oxide as was revealed by cyt-c reduction and Grieze reaction, respectively. At the same time, the levels of the above free radicals generated by SID circulating blood granulocytes were much lower than those in the control group. We failed to show any significant changes of iNOS expression in SID pancreatic tissue using monoclonal antibodies and immunohistochemical method. Intensity of lipid peroxidation was suppressed in SID pancreas and livers and increased in SID erythrocytes as compared with the control values. It was a good negative correlation ($r = -0.86$) between the erythrocyte GSH content and lipid peroxidation. BN, being applied intraesophagously to SID animals for 7 days (100 mg/kg weight, daily), normalized the blood glucose level with simultaneous dramatic improvement of pancreatic ultrastructure and β-cell functioning as well as NO and O_2- production by tissue macrophages. The BN administration resulted also in the increase in NO and O_2-production by blood granulocytes and the erythrocyte GSH level. However, BN did affect neither erythrocyte nor tissue lipid peroxidation. Two pilot double-blind placebo clinical trials have been carried out in Russian Center of Diabetes. Forty five infection-free patients with well controlled IDDM and NIDM were enrolled in the trial after their informed consent. The patients fulfilled the eligibility criteria were randomized into control and experimental groups each of which received the conventional treatment. Additionally, the experimental patients were given 100-150 mg/kg body weight of BN (2-3 sachets) daily for 28 days and the control patients were given 2-3 sachets containing a powder, which resembled BN in taste and design. In a strict accordance with the experimental findings, BN administration led to significant improvement of patients' redox status, namely, it increased the erythrocyte GSH level and normalized the impaired NO and O_2 production by circulating blood granulocytes. In some patients with advanced diabetic retinopathy BN decreased the MDA level in lacrimal fluid. Besides that, BN therapy had a number of beneficial clinical effects among them including the decrease in diabetic markers in blood and urine, daily insulin requirement, and vascular complications and improvement of cellular immunity. On these grounds, BN could be regarded as natural non-toxic product allowing to ameliorate diabetes-associated complications in humans.