

Preventive effect vanadium, zinc and bioflavonoids on the onset of diabetes in BB rats

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Vanadium, other trace elements and bioflavonoids have been shown to be beneficial in the treatment of animal models of type 1 and type 2 diabetes. The aim of the study was to evaluate the preventive effects of vanadate (as ammonium metavanadate), zinc chloride and bioflavonoids in prediabetic BB rats.

80 BB rats were divided into 4 equal groups. Group "V" was treated with ammonium metavanadate (0.1 mmol/l), "Z" with zinc chloride (0.1 mmol/l), and "BF" with Flavin 7® (nutrition additive with bioflavonoids, 0.2 mg/l) in drinking water from 21st day after birth to 171st day of their life, and compared with "C" – control group on pure tap water. In each group food and water intake, urine output and body mass were followed regularly. The manifestation of diabetic state was monitored through blood glucose, glycosuria and glycosylated hemoglobin determinations. Antioxidant system activity was estimated through enzyme (red cell superoxide dismutase, red cell catalase, whole blood glutathione peroxidase) as well as total antioxidant status and glutathione assays.

The age of onset of diabetes and its incidence were significantly higher in "BF" and "V" groups as compared to controls ($p < 0.001$), and zinc treated group ($p > 0.05$). In overtly diabetic rats blood glucose was higher in control group than in "V" and "BF" groups, $p < 0.001$. Decrease of parameters of the antioxidant status, at the onset of the treatment as well as immediately after its cessation showed a drop in the treatment groups, but later increased slowly and continuously until the end of the experiment. The activity of antioxidant enzymes increased slowly from the beginning of study up to the point of diabetes manifestation and decreased thereafter. The decline was less evident in rats treated with bioflavonoids.

Both bioflavonoids and vanadate delay the development and lower the manifestation rate of diabetes in BB rats which is not the case in zinc treated animals. The same compounds decrease hyperglycaemia in diabetic rats. Bioflavonoid supplementation could have a beneficial effect on antioxidant status in diabetes mellitus.

Effect of immunonutrition with omega-3 fatty acids on oxidative stress response in polytraumatized patients – Pilot-study

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A state of increased oxidative stress has been recognised in polytraumatic injury that was influenced beneficially by omega-3 fatty acids substitution in patients with type 2 diabetes mellitus. Moreover previous studies have shown that administration of omega-3 fatty acids mixed with other antioxidant substances resulted shorter postoperative periods in the intensive care unit.

We evaluate the effect of nutrition with omega-3 fatty acid on the polytraumatic injury induced oxidative stress.

13 patients were randomised to Intralipid and Omegawen groups, based on their parenteral feeding. There was difference only in omega-3 supplementation between nutrition of the two groups. Blood samples were taken on admission and during the following 5 days. We measured the level of malondialdehyd (MDA), glutathion (GSH), plasma SH groups (PSH), the activity of superoxid dismutase (SOD), catalase (KAT), and peroxidase (MPO) enzymes, and the stimulated reactive oxygen species (ROS) production of whole blood. Injury Severity Score (ISS) and Simplified Acute Physiology Score (SAPSII) were calculated on admission. Clinical data, Sequential Organ Failure Assessment Score (SOFA), Multiple Organ Dysfunction Score (MODS) were calculated every day. Primary endpoints were the duration of ICU stay and the number of mechanical ventilated days. For statistical analysis we used Mann-Whitney U test and two-way ANOVA test.

The two groups were similar initially in ISS, SAPS II, MODS, SOFA. The MDA level was significantly higher in both groups compared to the control healthy group ($p < 0.05$). We observed an elevating tendency in MPO enzyme activity in both

patients groups that was significantly higher on the 6th day compared to the controls. The induction time of ROS production was longer in the Omegaven group during the examination period than in the control group, and it was significantly longer on the 5th day compared to the Intralipid group. We detected higher catalase activity in Omegaven and in Intralipid group as well, but this activity was significantly lower on the second day in the Omegaven group versus Intralipid group. GSH and PSH levels weren't influenced by the treatment of omega-3 fatty acids.

These data suggest, that polytraumatic injury causes considerable oxidative stress, on which omega-3 fatty acid supplementation has only a moderate effect.

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***In vitro* toxicity testing of PPI dendrimers**

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Dendrimers are a new type of promising synthetic polymers characterized by a dendric branched spherical shape and a high density surface charge. The defined structure of these molecules has led to the interest in dendrimers as substrates for the attachment of antibodies or agents for applications in a number of different areas of biology and medicine. However, information on the mechanisms of dendrimer-induced cytotoxicity and a cell death is still limited. Therefore, it is necessary to undertake studies to determine biological properties of these compounds *in vitro*.

Thus, the aim of our investigation was to compare the effects of poly(propyleneimine) (PPI) dendrimers (PPI with 25% maltotriose units attached to the surface) on cultured human ovarian cancer cells (SK-OV-3) and Chinese hamster ovary cells (CHO). The cells were exposed to various concentrations of dendrimers (ranging from 1 to 300 µM). The toxicity of PPI dendrimers was studied immediately after the incubation with dendrimer (24 h) or 24 h after removing the dendrimer from the medium.

The cytotoxicity of dendrimers was studied by a MTT assay. The morphological features of apoptosis and necrosis were examined by Nomarski DIC combined with a confocal laser scanning microscope (CLSM). The level of reactive oxygen species (ROS) was evaluated with fluorescent probe: dichlorofluorescein-diacetate (H₂DCFDA) by flow cytometry. Changes in mitochondrial membrane potential were determined using JC-1.

Our studies demonstrated that PPI dendrimers exerted multiple suppressive effects on cancer SK-OV-3 cells, including proliferation inhibition, induction of an apoptotic cell death and a collapse of mitochondrial membrane potential. Most importantly, these compounds were more cytotoxic to cancer cells than to normal CHO cells.

These findings will help to understand the mechanisms of PPI dendrimer cytotoxicity in normal and tumor cells and open the possibility to use them in clinical applications.

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Bioactive compounds in *Alliums* from Vojvodina - antioxidants

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Toughout recorded history *Alliums* especially garlic and onion played rich diverse commercial, culinary, and mystic roles. Today garlic and onion are used for their flavour, aroma and taste, being prepared domestically or forming basic materials for a variety of food manufacturing processes. Onions were among the earliest vegetables to be processed, canned, dried and frozen. Many epidemiological studies have suggested that certain natural foods could prevent the development of different diseases. Garlic and onion are such natural foods. They have a variety of pharmacological effects including tumour cell growth inhibition and chemopreventive activity. Much of the data about human use came from reports of lowered rates and risks of disease (such as cancer) in people with relatively high levels of garlic or other *Alliums* consumption. People also use garlic