

## EFFECT OF *BLAUTHEROCOCCUS* AND GINSENG ON THE DEVELOPMENT OF FREE-RADICAL PATHOLOGY

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The development of the free-radical theory of aging (Emanuel, 1984; Harman, 1957; Tappel, White, 1959) roused interest in the role of processes of the nonenzymatic autooxidation of lipids and biopolymers in pathogenesis of diseases connected with aging. It was found that free-radical oxidation (FRO) was essential in pathogenesis of atherosclerosis, coronary disease, cerebral ischemia, osteochondrosis and senile cataract (Voskresensky, 1977; Voskresensky, Puzanov, 1982; Kalmykova et al., 1974; Haara et al., 1982). Along with age pathology FRO is involved in genesis of tissue injury during neuroemotional stress (Brekhan et al., 1972; Meyerson, 1984) and hypodynamia (Devyatkina, Voskresensky, 1975).

The spread of free-radical pathology, i.e. chronic noninfectious diseases of nature and senile age, in developed countries reflects the influence of factors of the scientific-technological revolution, namely the aging of the population, growth of neurohormonal stress, hypodynamia and contamination of the environment with xenobiotics - prooxidants. The problem arises to find bioregulatory substances providing for resistance of the animal organism to etiological factors of free-radical pathology and to find agents of adaptogenic action (Brekhan, 1980).

General antioxidant mechanisms of adaptogenic action agree with the unity of peroxide links of pathogenesis of free-radical pathology (Voskresensky, 1977).

The following problems were raised in the study: 1) to elucidate the role of insufficiency of bioantioxidants as natural regulators of resistance in genesis of free-radical pathology and 2) to study the protective effect of *Blautherococcus*, Ginseng and their combinations with antioxidants.

Experiments were carried out on 100 rabbits, 50 guinea pigs, 140 rats and 40 mice. Clinical examinations were conducted on 40 patients with cerebral ischemia of atherosclerotic genesis.

In experiments *in vitro* ethyl - $\alpha$ - /parachlorophenoxy/ - iso-

butyrate (clofibrate) in concentrations 0.2 or 2 mmol/ml increased definitely the peroxide hemolysis of erythrocytes as well as accumulation of YFO products, i.e. malondialdehyde during erythrocyte incubation for 3 hrs. The standard antioxidant (tocopherol acetate, 0.2 mmol/ml) when added to the incubated medium simultaneously with clofibrate prevented completely the accumulation of malondialdehyde. Thus, the prooxidant effect of clofibrate previously observed on the model autooxidation of methylcysteine by Mikitina (1983) was confirmed.

On the 100th day of chronic exposure to clofibrate (500 mg/kg body weight once a day) we observed a decrease in glutathione peroxidase activity of liver and blood, a drop of the degree of glutathione reduction in blood, a decreased tocopherol level in erythrocytes, and accumulation of acylhydroperoxides in  $\beta$ - and pre- $\beta$ -lipoproteins of blood serum and malondialdehyde in erythrocytes. An increase in processes of nonenzymatic YFO of lipids was observed also in perodontion tissues; the coefficient of exposure of molars considerably increased in comparison with intact rats and the development of spontaneous periodontosis connected with aging accelerated. Injection of  $\alpha$ -tocopherol in a dose of 5 mg/kg body weight partly inhibited the development of periodontion syndrome and aging of the perodontium.

In experiments carried out on rabbits the peroxidation syndrome was reproduced by keeping the animals for 100 days on seminatural ration without antioxidants. A decrease in the activity of physiologic antioxidant system and intensification of processes of nonenzymatic peroxidation of lipids were accompanied by the development of atherosclerosis. Daily injection of Preparation 54, a complex including lipid and water-soluble antioxidants and the powder of Ginseng root, inhibited partially the development of peroxidation syndrome, hyperlipidemia and aorta injury by atherosclerosis. However, the effect of Preparation 54 was less pronounced than the protective effect of Preparation 52, a complex of bioantioxidants without Ginseng.

A combination of antioxidants and Ginseng was studied during 3 weeks on 40 patients with cerebral ischemia of atherosclerotic genesis. Patients were divided into 2 groups. The first group consisted of those who took the limited general therapy (vasodilators and sedatives). The second group took an extra complex of

bioantioxidants including tocopherol, ascorbat, flacumine and Ginseng tincture. Somatic and neurologic status and the state of cerebral hemodynamics were examined in patients according to the data of rheoencephalography (REN) and electroencephalography (EEG). At the beginning and the end of treatment the state of lipid and peroxide exchange as well as indices of the physiologic antioxidant system were studied in all patients. Clinical improvement and certain normalization of cerebral hemodynamics according to REN were observed in patients taking a complex of bioantioxidants with Ginseng. Biochemical investigations revealed a reliable decrease in the level of total cholesterol,  $\beta$ - and pre- $\beta$ -lipoproteins, content of acylhydroperoxides in the atherogenic lipoproteins and increase in the level of hydrophilic and lipid antioxidants in the blood.

Experiments in vitro with incubation of erythrocytes in a medium containing water-alcohol dispersions of the active agents of liquid Eleutherococcus extract (EE) and Ginseng tincture (in concentrations corresponding to 0.00025-0.00025 ml/ml of incubative medium) showed a direct antioxidant effect of Eleutherococcus. EE decreased spontaneous hemolysis of erythrocytes from  $18 \pm 1.4\%$  to  $12 \pm 0.9\%$  ( $P < 0.002$ ) and accumulation of malondialdehyde by the 3rd hr of incubation (control  $216 \pm 5.6\%$  of the initial value, in test -  $191 \pm 2.6\%$ ,  $P < 0.002$ ).

The effect of EE on survival of mice during cooling stress was studied. Animals were kept 20 days on the antioxidant-free semisynthetic diet or usual vivarium food. One group of animals received liquid EE in a dose 0.05 ml/20 g body weight, and the other received a combination of EE with a complex of antioxidants. Mice with the antioxidant inadequacy died during the 1st hr of hypothermia more frequently than intact animals: 30 and 20%, respectively, of the total number of animals in the groups. All the animals treated with the EE or EE with antioxidants endured cooling for 1 hr. By the end of the 2nd hr of the experiment all the intact mice with antioxidant insufficiency perished. The EE and its combination with antioxidants facilitated the survival of 22 and 43% of mice, respectively.

The data obtained testify to the monodirectional protective effects of Eleutherococcus, Ginseng and a complex of bioantioxidants. It is of particular interest that the complexes of com-

younds (Preparations 52, 54) or natural combinations of physiologically active substances (glycosides in the form of Kleutherooccus or Ginseng preparations) display pronounced adaptogenic action at free-radical pathology. The systematic inhibition of FRO makes it necessary to supply various components of the physiologic antioxidant system during adaptation diseases (Voskresensky, 1977). The use of compositions of antioxidants of direct and indirect action or galenic plant preparations containing natural combinations of glycosides - inhibitors of FRO (Kipnya et al., 1983) and inducers for synthesis of antioxidant enzymes complies with such a requirement (Khasina et al., 1983).

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