DISTURBANCES OF DEAMINATION OF NITROGEN COMPOUNDS IN HEART MUSCLE IN EXPERIMENTAL ATHEROSCLEROSIS

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In experimental atherosclerosis the rate of deamination of tyramine [10], β-phenylethylamine, benzylamine, and tryptamine [1] in the heart muscle is reduced. The decrease in the rate of deamination of amines which are substrates for monoamine oxidases (MAO) may be partly the result of qualitative modification (transformation) of the catalytic properties of the MAO, leading to the appearance of ability to deaminate certain nitrogen compounds (for example, histamine, cadaverine, or adenylic acid), which usually are not attacked by MAO [2]. The phenomenon of MAO transformation often occurs in tissues of the liver, kidneys, and other organs in pathological states accompanied by stimulation of lipid peroxidation, such as in atherosclerosis [8]. However, no evidence of MAO transformation (the appearance of ability to deaminate histamine coupled with a decrease in the rate of deamination of monoamines) has been observed [1] in heart muscle in atherosclerosis.

The aim of the present investigation was to study the possibility of qualitative modification of the properties of MAO in the heart muscle in atherosclerosis, in view of the reversible character of this modification, which is of great importance in connection with the question of experimental treatment of atherosclerosis [6].

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male rabbits weighing 2200-3500 g. Experimental atherosclerosis was induced by daily injection of cholesterol emulsion (c.e.) in cottonseed oil into the animals' stomach through a flexible tube in a dose of 0.3 g/kg body weight daily for 30, 60, and 90 days [9]. The development of atherosclerosis was judged on the basis of the time course of changes in the serum cholesterol, triglyceride, and β-lipoprotein levels [8]. The methods and conditions of isolation of mitochondrial fractions, and of determining the rate of deamination of the nitrogen compounds and the protein concentration were described previously [8]. The preparation of ladyginoside, generously provided by the Laboratory of Glycoside Chemistry, Institute of Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, consisting of total water-soluble triterpene glycosides from the root of the plant *Ladyginia bucharica*, growing in Central Asia [7], was injected into the rabbits in a dose of 10 mg/kg daily [5]. The antioxidant dibunol (2,6-di-tert-butyl-4-methylphenol), generously provided by Professor E. B. Burlakova (Institute of Chemical Physics, Academy of Sciences of the USSR), was injected into the animals' stomach through a flexible tube in the form of a 3% emulsion in cottonseed oil, in a dose of 30 mg/kg daily.

EXPERIMENTAL RESULTS

The data showing a statistically significant increase in serum levels of cholesterol, triglycerides, and β-lipoproteins in rabbits fed with cholesterol (Fig. 1) are evidence of the development of atherosclerosis under these experimental conditions, and this was confirmed by morphometric investigations of the aorta [6, 8] and by the intravital discovery of characteristic cardiac arrhythmias [6].

Predominantly a fall in the rate of deamination of serotonin — one substrate of type A MAO [2] — was found in the mitochondrial fraction isolated from heart muscle tissues of

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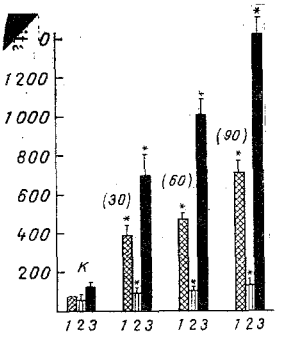

Fig. 1

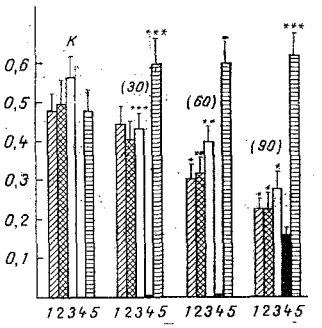

Fig. 2

Fig. 1. Serum lipid concentration (in mg %) in rabbits during development of experimental atherosclerosis. 1) Cholesterol; 2) triglycerides; 3) β-lipoproteins. Duration of experiment (in days) shown in parentheses. *P < 0.001 compared with intact animals (K). Each group contained 7-11 rabbits.

Fig. 2. Deamination of some nitrogen compounds (in μmoles NH_3/mg protein/45 min) on incubation with mitochondrial fraction of rabbit heart muscle during development of experimental atherosclerosis. 1) Serotonin; 2) benzylamine; 3) tyramine; 4) cadaverine; 5) AMP. *P < 0.001, **P < 0.01, ***P < 0.05. Remainder of legend as to Fig. 1.

the experimental rabbits. During the development of atherosclerosis the intensity of this phenomenon and the decrease in the rate of deamination of benzylamine (a specific substrate for type B MAO) and tyramine, usually placed in the category of "mixed" substrates of both types of MAO, gradually increased until the 90th day of the experiment. Meanwhile a qualitatively new property appeared in this same mitochondrial fraction: ability to deaminate the diamine cadaverine at a very high velocity, reaching 68% of the maximal velocity of serotonin deamination under optimal conditions of measurement (Fig. 2). These data are evidence of the possible qualitative modification (transformation) of MAO not only in the liver and kidneys [8], but also in the heart muscle under conditions of manifest, biochemically confirmed, experimental atherosclerosis. The increase in the rate of hydrolytic deamination of AMP in the mitochondrial fraction of heart muscle in experimental atherosclerosis, although statistically significant, did not increase further in the course of development of atherosclerosis. Possibly the intensified deamination of AMP which was observed was not due to transformation of MAO, but might have been connected with activation of adenylate deaminase [3, 4].

The pathogenetic importance of MAO transformation in heart muscle in atherosclerosis is unknown. According to our previous data, administration of the antioxidant dibunol [6] or of the preparation ladyginoside, which have a hypocholesterolemic action [5], caused a marked decrease in the intensity of the characteristic morphological, physiological, and biochemical manifestations of atherosclerosis (lesions of the aortic intima, disturbances of the cardiac rhythm, an increase in the serum lipid concentration) but, at the same time, prevented or abolished disturbances of the relative rates of deamination of nitrogen compounds, indicating reversible qualitative modification of MAO activity. However, a relationship of cause and effect between these phenomena has not yet been established.

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