Antiatherosclerotic Effects of Polysaccharide of Animal Origin

M. M. Rasulov, M. V. Velikaya, A. G. Zabozlaev, I. G. Kuznetsov, and M. G. Voronkov

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Atherosclerosis is now the most prevalent cardiovascular disease, and severe disorders of lipid metabolism are generally acknowledged to be the principal factor in its pathogenesis. A heparinlike drug, atheroid, characterized by an antiatherosclerotic effect, has been developed and is in clinical use in the West. The technology for preparing an analog of this drug from porcine duodenum has been developed at the Research Institute of the Meat Industry, and collaborative studies have demonstrated the appurtenance of the new drug to heparinlike polysaccharide and its complete safety.

In the present study we investigated the effects of polysaccharide from porcine duodenum on the lipid metabolism of animals with experimental atherosclerosis.

MATERIALS AND METHODS

Male rabbits weighing 2.5-3 kg were used in the experiments. Atherosclerosis was induced after N. N. Anichkov and S. S. Khalatov by adding cholesterol to the food in a dose of 250 mg/kg daily for 30 days [2].

The animals were divided into 4 groups: 1) rabbits administered oral polysaccharide in a daily dose of 200 mg/kg in parallel with the hypercholesterol diet starting from the first day of the experiment; 2) rabbits administered oral atheroid in a daily dose of 10 mg/kg in parallel with the hypercholesterol diet starting from the first day of the experiment; 3) rabbits administered oral polysaccharide in a daily dose of 200 mg/kg one month after the start of the hypercholesterol diet; 4) rabbits administered oral atheroid in a daily dose of 10 mg/kg one month after the start of the hypercholesterol diet. Control animals were fed the hypercholesterol diet over the course of the experiment. Hence, groups 1 and 2 were administered the drugs for prophylaxis. Blood serum cholesterol, β-lipoproteins, and triglycerides were measured by standard methods before the experiment and 2 months after its start. The animals were then sacrificed by air embolism, and the cholesterol and triglyceride levels were measured in the liver and thoracic aorta. The index of atherosclerotic plaque involvement of the aorta was assessed as described

TABLE 1. Parameters of Lipid Metabolism in Rabbits with Experimental Atherosclerosis Administered Polysaccharide

Group	Parameter, mg%		
	cholesterol	triglycerides	β-lipoproteins
1 (control)	796.0±96.4	549.2±67.8	96.8±15.6
2	801.5±111.0	534.6±75.4	102.5±21.8
3	412.9±56.4*	298.7±32.4*	37.1±9.3
4	440.0±37.5*	270.8±46.2*	32.5±7.4*

Note. Here and in Tables 2 and 3: asterisk: $p<0.05$ vs. control group; each group consisted of 5 animals.

Irkutsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences; RAMIT Company, Moscow

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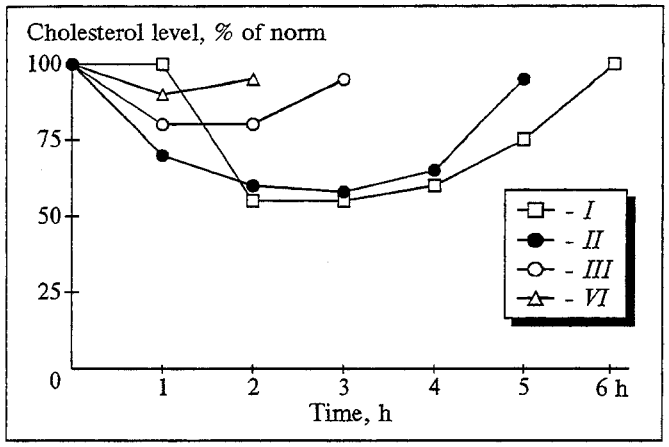

Fig. 1. Dose effects of polysaccharide on blood cholesterol level. Abscissa: cholesterol level, % of norm; ordinate: time, h. Curves: time course of cholesterol (Ch) level for administration of atheroid (*I*), polysaccharide in a dose of 500 mg/kg (*II*), polysaccharide in a dose of 100 mg/kg (*III*), and polysaccharide in a dose of 20 mg/kg (*IV*).

previously [1,3]. A special series of experiments was carried out to study the dose effects of porcine duodenum polysaccharide after its single oral administration to intact rabbits. These effects were compared with the effects of oral atheroid administered in a single dose of 10 mg/kg. Blood cholesterol, triglycerides, and β-lipoproteins were measured every hour for six hours after drug administration. The results were statistically processed using the Student test.

RESULTS

A single oral administration of atheroid induced a reduction of the serum levels of cholesterol (Fig. 1), β-lipoproteins (Fig. 2), and triglycerides (Fig. 3) in intact rabbits. Porcine duodenum polysaccharide in a dose of 500 mg/kg had a similar effect.

TABLE 2. Cholesterol and Triglyceride Levels in Tissue of Thoracic Aorta in Rabbits with Experimental Atherosclerosis

Group	Parameter, mg%	
	cholesterol	triglycerides
1 (control)	27.5±2.3	15.7±2.0
2	23.4±3.1	16.4±2.8
3	19.2±1.7*	12.3±1.5
4	16.9±1.8*	8.9±0.9*

Both atheroid and porcine duodenum polysaccharide had a marked effect on the lipid metabolism of animals with induced hyperlipidemia, manifested in inhibition of the development of experimental atherosclerosis for prophylactic administration of these agents. There was a tendency for the cholesterol level to drop under the influence of atheroid and polysaccharide in manifest hypercholesterolemia. At the same time, a marked effect of polysaccharide on plasma triglycerides is noteworthy in such a case (Table 1).

Measurements of cholesterol and triglycerides in the liver and thoracic aorta showed their reduction in all the test groups in comparison with the controls. This difference was most expressed in animals administered atheroid and polysaccharide starting from the first day of the experiment (groups 1 and 2) (Table 2). The index of atherosclerotic plaque involvement of the aorta was reliably lower in these groups as well (Table 3).

Note the similar direction of atheroid and polysaccharide effects on lipid metabolism; the difference in the doses needed to attain a lipolytic effect may be explained by the fact that atheroid tablets are coated and porcine duodenum polysac-

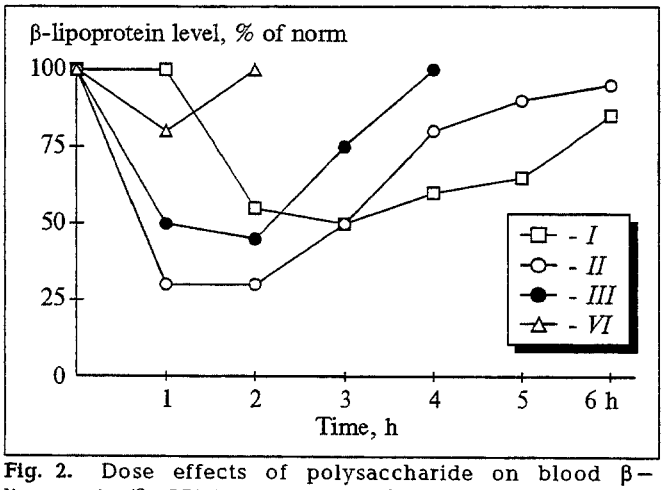

Fig. 2. Dose effects of polysaccharide on blood β-lipoprotein (β-LP) level. Abscissa: β-lipoprotein level, % of norm; ordinate: time, h. Curves: time course of β-lipoprotein level for administration of atheroid (*I*), polysaccharide in a dose of 500 mg/kg (*II*), polysaccharide in a dose of 100 mg/kg (*III*), and polysaccharide in a dose of 20 mg/kg (*IV*).

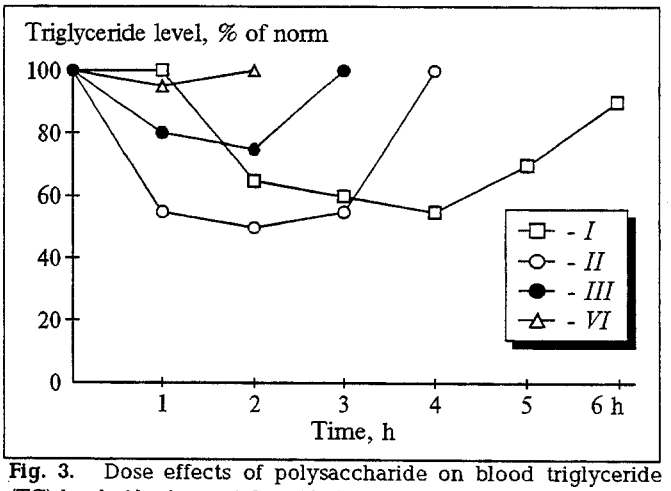

Fig. 3. Dose effects of polysaccharide on blood triglyceride (TG) level. Abscissa: triglyceride level, % of norm; ordinate: time, h. Curves: time course of triglyceride level for administration of atheroid (*I*), polysaccharide in a dose of 500 mg/kg (*II*), polysaccharide in a dose of 100 mg/kg (*III*), and polysaccharide in a dose of 20 mg/kg (*IV*).

TABLE 3. Index of Atherosclerotic Plaque Involvement of Thoracic Aorta in Animals with Experimental Atherosclerosis Administered Polysaccharide

Group	Index of aortic involvement, %
1 (control)	41.3±5.4
2	38.2±7.1
3	24.3±4.7*
4	20.7±2.9*

charide is a substance which evidently loses its potency under the effect of gastric juice.

Hence, oral polysaccharide has a marked antiatherosclerotic effect, manifested in the delayed development of experimental atherosclerosis and in the reduction of atherosclerotic lesions of the aorta. The latter effect is indicative of angioprotector properties. The polysaccharide is less effective in manifest hypercholesterolemia. In a certain dose this substance is not inferior in specific activity to atheroid and has a similar effect on the lipid spectrum. Porcine duodenum polysaccharide can thus be considered promising material for the development of an antiatherosclerotic drug.

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Functional and Morphological Interventricular Relationships during Chronic Overload of the Primarily Intact Left Heart in a Model of Experimental Vasorenal Hypertension

P. Ramdawon, G. A. Drozdova, V. L. Bakhilov, and V. A. Frolov

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Modern cardiology is characterized, above all, by the accumulation of rich experience in conservative and surgical management of various types of damage to the left and right heart. Nevertheless, studies of the operating mechanisms of each of the ventricles are most frequently performed separately, which contradicts the principle of an integral approach to the investigation of the heart as a unified system of organs, and makes it difficult to reveal both general and individual patterns of activity of each of the ventricles.

The aim of our study was to explore the functional and morphological relationships between the ventricles during hemodynamic overload of the primarily intact left heart on an experimental model of vasorenal hypertension.

Department of Pathological Physiology, Russian Peoples' Friendship University, Moscow

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