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MOLECULAR-BIOLOGICAL PROBLEMS OF DRUG DESIGN AND MECHANISM OF DRUG ACTION

INFLUENCE OF POLYURONIDES ON BIOLOGICAL OXIDATION, LIVER ANTITOXIC FUNCTIONS, AND ERYTHROCYTE MEMBRANE CONDITION IN LEAD-INTOXICATED RATS

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The influence of pectin and laminarid NP complex on biological oxidation processes in lead-intoxicated rats was estimated using parameters such as oxidative phosphorylation, ATP synthesis, activities of biological oxidation enzymes, lipid peroxidation, and erythrocyte resistance to osmotic shock and oxidation by oxygen in air, liver antitoxic function, and blood hematological indices. It was established that the polyuronides exhibited antihypoxic, antioxidant, and membrane-stabilizing action.

Keywords: polyuronides, biological oxidation, intoxication with Pb(II) ions, pharmacological activity.

Heavy-metal cations are known to exhibit toxicity by destroying the structural integrity of membranes or increasing their permeability for protons, disrupting tissue respiration and oxidative phosphorylation processes, forming free radicals of oxygen and fatty acids that damage the membranes of cells including erythrocytes, developing hemolytic anemia, and destroying enzyme activity and DNA metabolic processes [1]. Polyuronides found in beet pectin and the polysaccharide—amino-acid complex Laminarid NP possibly influence the aforementioned toxic effects by accelerating the elimination of heavy metals. However, this requires experimental verification, which is the goal of the present research.

The goal of the research was to study the influence of polyuronides and lead (Pb) intoxication on biological oxidation processes such as oxidative phosphorylation, free-radical oxidation indices, the condition of erythrocyte membranes, and hematological parameters.

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EXPERIMENTAL PART

The following substances were studied:

Beet pectin (Scientific-Production Co. Pekto, Nalchik, Kabardino-Balkaria Republic) of average molecular mass 3.2 kg/mol corresponding to requirements of VFS 42-3433-99 "Pectin" and containing five polysaccharide constituents with molecular-mass distribution (35 ± 1.0) kDa, (4.5 ± 0.2)%; (11.5 ± 0.5) kDa, (20.3 ± 0.6)%; (8.7 ± 0.4) kDa, (7.9 ± 0.3)%; (8 ± 0.4) kDa, (19.9 ± 0.4)%; and (5 ± 0.2) kDa, (47.4 ± 1.0)%. Of these, two were neutral (galactans, arabinans) and three, acidic (rhamnogalacturonan I, rhamnogalacturonan II, and homogalacturonan) with D-galacturonic acid contents of (17 ± 0.7), (31 ± 0.9), and (100 ± 2)%, respectively [2, 3];

Laminarid NP polysaccharide—amino-acid complex isolated from *Laminaria saccharina* (L.) at Arkhangelsk Test Alga Combine had average molecular mass (89.7 ± 1.9) kg/mol and corresponded to requirements of FS 42-2462-87 "Laminarid". It consisted of alternating blocks of 1→4-bonded β-L-glucuronic and α-D-mannuronic acids in a 1:2 ratio

with (9.1 ± 0.3)% free carboxylates and (0.9 ± 0.04)% methylated carboxylates [4].

Polyuronide solutions were prepared in normal saline (pH ~ 7.0). The studies used 70 Wistar white male rats (180-220 g).

Animals were administered orally and daily first Pb(II) acetate solution (Berlin-Chemie, Germany) at a dose of 75 mg/kg per day for one week [1] and then polyuronide solutions of beet pectin (1%, pH 3.49) or laminarid NP (1%, pH 5.2) at a dose of 500 mg/kg per day (optimum dose for acute Pb-intoxication in rats [5]) for one month [5]. The heavy-metal ion Pb(II) was chosen because of its very high toxicity [1]. The control group of rats (Wistar males, 180 – 220 g) received isotonic saline (1 mL) instead of the polyuronides. A group of untreated animals was also studied. Thus, the following animal groups were used: 1, untreated animals; 2, animals receiving Pb(II) acetate; 3, animals receiving Pb(II) acetate and isotonic saline (control); 4, animals receiving Pb(II) acetate and pectin; 5, animals receiving Pb(II) acetate and laminarid NP; 6, animals receiving pectin without Pb-intoxication; 7, animals receiving laminarid NP without Pb-intoxication. Each group consisted of 10 animals. Animals were maintained on a standard feeding regime during the experiment. Animals were decapitated under light ether anesthesia at the end of the tests. Blood, liver, and femoral muscle were used as the experimental biological substrates.

The following metabolic parameters were determined:

Liver oxidative phosphorylation and ATP contents in liver and femoral muscle {from loss of inorganic phosphate (Pi) using photometry and the reaction with ammonium molybdate [6, 7]};

Relative activity of Cu-containing monooxygenases of the liver endoplasmic network and acetylating activity of enzymes involved in conjugation of metabolites (from amidopyrine metabolite contents in urine [7]);

Lipid peroxidation (LPO) rate of erythrocyte membranes with and without pro-oxidants, i.e., easily oxidized compounds [thiobarbituric acid (TBA)] {from the reaction of the final oxidation product malondialdehyde (MDA) with TBA using photometry [8]};

Blood catalase index {permanganate determination of the amount of undecomposed H_2O_2; calculated as catalase number relative to the number of erythrocytes (10^6 per mm^3) [9]};

Reduced glutathione content and total SH contents of proteins calculated as cysteine [9] in blood serum (iodometry with preliminary determination of the blood serum protein content using UV spectrophotometry [7]);

Osmotic resistance of erythrocytes to hypotonic (0.5%) and isotonic saline [10];

Erythrocyte spontaneous hemolysis (Jager method [7, 8]);

Number of blood erythrocytes and leukocytes (by a unified counting method in a Goryaev chamber [8]);

Blood hemoglobin content (by hemoglobin cyanide method [8]);

Haptoglobin content (by photometry from the excess of hemoglobin after precipitation of the hemoglobin—haptoglobin complex by Rivanol [7]);

Hemic indices such as color index {ratio of the two fractions obtained by dividing the amount of hemoglobin by the amounts of erythrocytes in normal (166.7 g/L : 5×10^{12}/L [8]) and test blood; calculated by multiplying the amount of hemoglobin by 30 and dividing by the first four digits of the number of counted erythrocytes} and hemoglobin content per erythrocyte {ratio of hemoglobin concentration (g/L) to the number of erythrocytes (10^6) in the same blood sample expressed in picograms (pg) [8]};

Antihypoxic activity in Pb intoxication models and acute hemic hypoxia induced by a single i.m. administration to rats of sodium nitrite at a dose of 300 mg/kg [11] [antihypoxic index (AHI) calculated as the ratio of the lifespans of one group of animals to another]; the reference drugs were sodium hydroxybutyrate (solution for injection in ampuls, Moskhimfarmpreparaty) and gutimin (guanylthiourea, solution for injection in ampuls, ICN Polypharm) [12].

TABLE 1. Influence of Pectin and Laminarid NP on Oxidative Phosphorylation and Liver Enzyme Activities

Animal group	Oxidative phosphorylation in liver (loss of inorganic phosphate), μmol	ATP content, μmol of inorganic phosphate per g		Relative activity of liver monooxygenase, %	Acetylating activity of enzymes involved in conjugation of amidopyrine metabolites, %
		in liver	in femoral muscle		
1	0.93 ± 0.10	1.80 ± 0.10	0.36 ± 0.04	8.72 ± 0.41	84.92 ± 4.01
2	0.32 ± 0.03*	0.30 ± 0.05*	0.19 ± 0.02*	5.01 ± 0.50*	59.22 ± 3.11*
3	0.36 ± 0.04*	0.32 ± 0.05*	0.19 ± 0.02*	6.61 ± 0.40$^{*\times}$	63.03 ± 5.81*
4	1.31 ± 0.10$^{*\times\circ}$	2.11 ± 0.19$^{*\times\circ}$	0.57 ± 0.05$^{*\times\circ}$	10.21 ± 0.50$^{*\times\circ}$	97.22 ± 3.81$^{*\times\circ}$
5	1.30 ± 0.12$^{*\times\circ}$	1.50 ± 0.10$^{*\times\circ}$	0.26 ± 0.02$^{*\times\circ}$	9.62 ± 0.51$^{\times\circ}$	79.52 ± 4.21$^{\times\circ+}$

Here and in Tables 2 and 3: $p < 0.05$ compared with group 1 (*), 2 ($^{\times}$), 3 ($^{\circ}$), and 4 ($^{+}$).
Differences between all parameters for groups 3 and 4 were statistically significant ($p < 0.001$); for groups 3 and 5, except for ATP content in femoral muscle and acetylating activity of the enzymes, where they were less significant ($p < 0.05$).

Results were processed by multiple statistics using the Student parametric criterion. The arithmetic mean and its standard deviation and the probability of differences (p) between results of compared groups were determined.

RESULTS AND DISCUSSION

Table 1 presents results for the influence of the polyuronides on oxidative phosphorylation and liver enzyme activity in Pb-intoxicated rats.

Table 1 shows that Pb(II) ions slowed oxidative phosphorylation by 66%. ATP synthesis also declined in liver by 83%; in femoral muscle, by 48%. Pb(II) ions inhibited tissue respiration [2] and blocked polar groups, e.g., SH groups at enzyme catalytic sites [13]. As a result, the enzyme—inhibitor complex could not bind substrate so that its transformation stopped. Thus, oxidative phosphorylation was slowed by 66%. ATP formation in liver was suppressed by 83%; in femoral muscle, by 47%. Liver oxidative phosphorylation accelerated by four times if pectin and laminarid NP were used with Pb-intoxication. This increased the ATP content in liver by 7 and 5 times; in muscle, by 3 and 1.4 times, respectively, as compared with animals that received Pb(II) acetate. Administration of pectin and laminarid NP to Pb-intoxicated animals accelerated oxidative phosphorylation in liver by 3.7 and 3.6 times, respectively, as compared with the control. This caused ATP synthesis to accelerate in liver by 6.5 and 4.7 times; in muscle, by 3 and 1.4 times, respectively. Apparently, the use of polyuronides with Pb-intoxication helped to expel Pb(II) cations from the enzyme—inhibitor complex. As a result, tissue respiration processes were restored. Pectin accelerated ATP formation in liver by 1.4 times as compared with laminarid NP; in muscle, by 2.2 times.

The influence of Pb(II) cations and polyuronides on enzymes was studied in order to assess liver antitoxic functions. It was found that intoxication by Pb(II) acetate reduced the relative activity of liver monooxygenases by 42.5%; enzyme acetylating activity, by 30%, i.e., enzymatic oxidation and conjugation occurring during amidopyrine metabolism was slowed. These same liver enzyme functions were reduced by 24 and 26%, respectively, as compared with the control. This same mechanism probably also explained the increased relative activity of liver monooxygenases and the enzyme acetylating activity by pectin by 2 and 1.6 times and by laminarid NP by 1.9 and 1.3 times, respectively. Pectin increased liver acetylating activity by 18% more than laminarid NP. The influences of both polyuronides on the relative activity of liver monooxygenases were of the same magnitude.

Table 2 presents results for the influence of the polyuronides on the LPO rate in erythrocyte membranes, blood

TABLE 2. Influence of Polyuronides on MDA Formation Rate in Erythrocyte Membranes, Blood Catalase Activity, Glutathione Content, and SH Groups of Blood Proteins of Pb-intoxicated Rats

Parameter	Animal group						
	1	2	3	4	5	6	7
1. MDA formation rate, nmol/h							
with pro-oxidants	57.72 ± 3.91	74.92 ± 5.11*	70.01 ± 3.80*	38.21 ± 2.70$^{*\times\circ}$	43.62 ± 3.11$^{*\times\circ}$	53.11 ± 3.01$^{\times\circ}$	53.52 ± 3.21$^{\times\circ}$
without pro-oxidants	51.41 ± 3.21	68.82 ± 4.91*	67.32 ± 4.31*	34.41 ± 2.91$^{*\times\circ}$	38.81 ± 3.20$^{*\times\circ}$	45.32 ± 3.40$^{\times\circ}$	45.12 ± 3.20$^{\times\circ}$
2. Blood catalase activity							
catalase number	5.01 ± 0.25	0.10 ± 0.01*	0.20 ± 0.02$^{*\delta}$	2.20 ± 0.11$^{*\times\circ}$	1.50 ± 0.08$^{*\times\circ+}$	8.50 ± 0.34$^{*\times\circ+}$	5.71 ± 0.23$^{\times\circ+}$
number of erythrocytes ($\times 10^{-8}$/mm^3)	6.71 ± 0.40	3.71 ± 0.30*	3.81 ± 0.30*	6.21 ± 0.50$^{\times\circ}$	5.31 ± 0.50$^{*\times\circ}$	5.31 ± 0.50$^{*\times\circ}$	5.21 ± 0.50$^{*\times\circ}$
catalase index ($\times 10^{9}$)	7.42 ± 0.60	0.38 ± 0.001*	0.44 ± 0.04*	3.51 ± 0.30$^{*\times\circ}$	2.70 ± 0.20$^{*\times\circ+}$	16.11 ± 1.20$^{*\times\circ}$	10.91 ± 1.01$^{*\times\circ}$
3. Blood glutathione content, mg%							
total	46.72 ± 3.30	58.91 ± 3.20*	57.12 ± 2.70*	49.22 ± 2.30$^{\times\circ}$	50.02 ± 1.71$^{\times\circ+}$		
reduced	36.42 ± 1.80	3.61 ± 0.40*	3.71 ± 0.40*	34.62 ± 2.50$^{\times\circ}$	42.03 ± 1.80$^{*\times\circ+}$		
oxidized	10.42 ± 0.80	55.33 ± 5.30*	53.32 ± 5.31*	14.51 ± 1.10$^{*\times\circ}$	8.02 ± 0.71$^{*\times\circ+}$		
4. SH group content, mg% of cysteine							
total	35.41 ± 2.20	13.50 ± 1.00*	16.51 ± 1.10*	29.72 ± 1.40$^{*\times\circ}$	39.32 ± 2.91$^{\times\circ+}$		
residual	24.01 ± 1.90	6.12 ± 0.52*	8.31 ± 0.71$^{*\delta}$	15.72 ± 1.31$^{*\times\circ}$	21.82 ± 1.80$^{\times\circ+}$		
protein	147.74 ± 7.42	120.73 ± 6.13*	126.23 ± 6.22*	174.64 ± 9.61$^{*\times\circ}$	198.34 ± 10.13$^{*\times\circ}$		
5. Blood serum protein content, %							
	7.71 ± 0.41	6.11 ± 0.41*	6.51 ± 0.31*	8.02 ± 0.41$^{\times\circ}$	8.82 ± 0.51$^{\times\circ}$		

catalase activity, and glutathione and SH groups of blood serum proteins with Pb-intoxication.

The least significant differences ($p < 0.05$) between groups 3 and 4 were found for total blood glutathione content; more significant differences, for blood serum protein content ($p < 0.02$), number of erythrocytes and content of protein SH groups ($p < 0.01$); and substantial differences ($p < 0.001$), for all other parameters.

The least significant differences ($p < 0.05$) between groups 3 and 5 were found for the number of erythrocytes and total blood glutathione content; more significant differences ($p < 0.01$), for blood serum protein content; and substantial differences ($p < 0.001$), for all other parameters.

Induced free-radical oxidation in erythrocyte membranes was increased by 29.7% after administration of Pb(II) acetate to the animals; spontaneous free-radical oxidation, by 33.7% as compared with the untreated control. Practically the same effect was observed after subsequent administration to the animals of isotonic saline. Pb(II) ions and several other redox-active metal ions are known to cause the formation of fatty-acid and peroxide radicals, i.e., reactive particles that accelerate peroxidation chain reactions of unsaturated phospholipids in biological membranes [14]. Pectin and laminarid NP are natural complexants that bind Pb(II) ions [15] and slow induced LPO by 45 and 38%; spontaneous LPO, by 49 and 42%, respectively, as compared with the control. Apparently, they reduce the permeability of cell membranes with Pb-intoxication and increase their stability. Use of polyuronides without Pb-intoxication does not affect LPO processes and; therefore, erythrocyte membrane permeability and stability.

Pb-intoxication diminished sharply the activity of the biochemical system for protecting membranes from LPO. This was evident in the decrease of the parameters for blood catalase by 95%, reduced glutathione by 90%, protein SH groups in blood serum by 18%, and blood serum protein contents by 21%. This agreed with the literature [1, 13], according to which Pb(II) ions decreased the reduced glutathione concentration. Subsequent administration to the animals of isotonic saline did not change these parameters. The observed toxic effects of Pb(II) acetate could be explained by blockage by Pb(II) ions of protein and enzyme active sites [1, 13], as a result of which the enzymes were inactivated. The literature indicates [16] that Pb(II) ions are bound to membrane SH, phosphate, and carboxylate groups, increase the membrane rigidity, and destabilize them with respect to osmotic shock. Studies with erythrocytes [17] showed that Pb(II) ions altered the membrane permeability and blocked active sites (SH, phosphate, carboxylate), i.e., pumps.

Pectin helped to increase the reduced glutathione level to normal and the protein-SH concentration to 18% over normal when administered to animals in our tests with Pb-intoxication. The catalase index was eight times greater than that of the control and half of the value for untreated rats. Administration of laminarid NP after Pb-intoxication resulted in reduced glutathione contents that were increased by 15%; protein SH groups, by 34% compared with untreated animals. The catalase index did not reach the level of untreated rats but increased by six times compared with the control.

TABLE 3. Influence of Polyuronides on Osmotic Resistance, Yager Erythrocyte Spontaneous Hemolysis, and Hematological Parameters in Pb-intoxicated Rats

Parameter	Animal group						
	1	2	3	4	5	6	7
1. Osmotic resistance of erythrocytes (degree of hemolysis), %:							
with hypotonic solution	4.41 ± 0.30	32.11 ± 2.90*	13.21 ± 1.10$^{*\delta}$	8.41 ± 0.90$^{*\times\circ}$	8.31 ± 1.10$^{*\times\circ}$	3.50 ± 0.20$^{*\times\circ}$	3.40 ± 0.30$^{*\times\circ}$
with isotonic solution	2.51 ± 0.30	11.12 ± 0.91*	6.21 ± 0.50$^{*\delta}$	4.21 ± 0.50$^{*\times\circ}$	2.71 ± 0.11$^{\times\circ+}$	1.71 ± 0.11$^{*\times\circ}$	1.61 ± 0.20$^{*\times\circ}$
2. Erythrocyte spontaneous hemolysis (degree of hemolysis), %:	9.82 ± 1.11	44.02 ± 4.22*	27.02 ± 2.61$^{*\delta}$	13.51 ± 1.20$^{*\times\circ}$	12.81 ± 0.71$^{*\times\circ}$	7.11 ± 0.51$^{*\times\circ}$	7.01 ± 0.60$^{*\times\circ}$
3. Erythrocyte content, 10^{12}/L	6.71 ± 0.50	3.71 ± 0.40*	3.81 ± 0.40*	6.92 ± 0.51$^{\times\circ}$	5.21 ± 0.40$^{*\times\circ+}$	6.83 ± 0.41$^{\times\circ}$	6.54 ± 0.46$^{\times\circ}$
4. Hemoglobin content, g/L	121.24 ± 6.12	94.42 ± 5.11*	96.02 ± 4.11*	144.54 ± 7.83$^{*\times\circ}$	109.44 ± 4.42$^{\times\circ+}$		
5. Haptoglobin content, g/L	2.01 ± 0.11	1.02 ± 0.10*	1.01 ± 0.10*	2.22 ± 0.20$^{*\times\circ}$	1.80 ± 0.20$^{\times\circ}$		
6. Color index	0.54 ± 0.04	0.76 ± 0.04*	0.75 ± 0.03*	0.63 ± 0.03$^{\times\circ}$	0.64 ± 0.03$^{\times\circ}$		
7. Hemoglobin content per erythrocyte, pg	18.12 ± 1.01	25.21 ± 1.30*	25.12 ± 1.20*	21.02 ± 1.31$^{\times\circ}$	21.21 ± 1.20$^{\times\circ}$		
8. Leukocyte content, L^{-1}	6.10 ± 0.31	7.71 ± 0.40*	7.11 ± 0.30*	5.61 ± 0.41$^{\times\circ}$	5.71 ± 0.40$^{\times\circ}$		

A comparison of the activities of pectin and laminarid NP with each other showed that the influence of pectin with Pb-intoxication was 28% more efficacious than that of laminarid NP. Laminarid NP was 21% more active than pectin for increasing the reduced glutathione level. Both polyuronides had equal influences on the LPO rate in erythrocyte membranes and content of protein SH groups. Another reason for the increased catalase activity could be the fact that both polysaccharides contained Mn ions [15] that functioned as redox-cofactors in Mn-catalase. The catalase index also increased without Pb-intoxication by 2.2 and 1.5 times as compared to untreated rats if pectin and laminarid NP, respectively, were administered to the animals.

Table 3 presents results for the influence of the polyuronides on osmotic resistance and Jager spontaneous hemolysis of erythrocytes and hematological parameters for Pb-intoxicated rats.

The least significant differences ($p < 0.05$) between groups 3 and 4 were found for hemoglobin per erythrocyte; more significant differences, for osmotic resistance of erythrocytes in isotonic saline, color index, and leukocyte content ($p < 0.02$) and osmotic resistance of erythrocytes in hypotonic saline ($p < 0.01$); and substantial differences ($p < 0.001$), for all other parameters.

The least significant differences ($p < 0.05$) between groups 3 and 5 were found for erythrocyte contents, hemoglobin, color index, and hemoglobin per erythrocyte; more significant differences, for osmotic resistance in hypotonic saline and leukocyte contents ($p < 0.02$) and haptoglobin ($p < 0.01$); and substantial differences ($p < 0.001$), for osmotic resistance in isotonic saline and spontaneous erythrocyte hemolysis.

The results suggested that administering Pb(II) acetate to the animals assisted the development of hemolytic anemia, i.e., reduced the osmotic resistance of the erythrocytes by seven times and increased spontaneous erythrocyte hemolysis by 4.5 times. Pectin and laminarid NP with Pb-intoxication assisted the reduction of the erythrocyte hemolysis level by 3.8 and 3.9 times and spontaneous hemolysis, by 3.3 and 3.4 times, respectively. Also, laminarid NP normalized the extraerythrocytic hemoglobin level. Isotonic saline had an influence analogous to those of the polyuronides but less pronounced (by 36 – 53%) on the hemolysis level. Pectin and laminarid NP with or without Pb-intoxication increased the resistance of erythrocytes to hemolysis by 26 and 29%, respectively, as compared with untreated animals.

Hematological parameters in rats after administration of Pb(II) acetate showed decreases in the blood contents of hemoglobin and haptoglobin by 22 and 50%, respectively, as compared with untreated animals. The reduced blood hemoglobin content was combined with a decrease of 44% in the erythrocyte concentration. Also, sharp changes in the erythrocyte indices were observed. The color index increased by 41%; hemoglobin per erythrocyte, by 39%. This depended exclusively on the change of erythrocyte volume and not on increased saturation of them by hemoglobin [8]. All these changes with Pb-intoxication were indicative of anemia. The hemoglobin and haptoglobin contents reached that of untreated rats if an excess of laminarid NP was administered to them. They were even higher than normal by 19 and 13% if pectin was used. These changes caused the erythrocyte contents to increase and the erythrocyte indices to normalize.

Leukocytosis in addition to anemia was assisted by intoxication with Pb(II) acetate. The blood leukocyte contents grew by 26%. Further administration of isotonic saline to the animals reduced the leukocyte level to 16%. Administration of the polyuronides to rats with Pb-intoxication reduced the leukocyte content to normal. Both polyuronides exhibited the same effect.

The antihypoxic effect of the polyuronides was confirmed in additional studies using an acute hemic hypoxia model induced by sodium nitrite (Table 4).

TABLE 4. Antihypoxic Activity of Polyuronides

Rat group	Lifespan after sodium nitrite injection, min	For groups			
		untreated	control	sodium hydroxybutyrate	gutimin
Untreated	16.31 ± 1.31		0.70	0.56	0.58
Isotonic solution	$23.21 \pm 1.80^{*}$	1.42		0.80	0.82
Pectin	$37.12 \pm 3.11^{*\circ}$	2.28	1.60	1.28	1.32
Laminarid NP	$32.41 \pm 2.80^{*\circ}$	1.99	1.40	1.11	1.15
Sodium hydroxybutyrate (500 mg/kg per day [11])	$29.01 \pm 1.80^{*\circ+}$	1.78	1.25		1.03
Gutimin (500 mg/kg per day [11])	$28.21 \pm 1.31^{*\circ+}$	1.73	1.22	0.97	

$p < 0.05$ vs. untreated animals (*), animals receiving isotonic solution (°), animals receiving laminarid NP ($^{+}$).
Differences for animals receiving pectin were more significant ($p < 0.01$) than those for animals receiving laminarid NP ($p = 0.02$) vs. those receiving isotonic solution.

The results confirmed the antihypoxic effect of the polyuronides that was established using the Pb-intoxication model. The lifespan of animals with acute hemic hypoxia induced by sodium nitrite increased compared with untreated animals by 2.3 and 2 times and by 1.6 and 1.4 times compared with the control for preliminary administration of pectin and laminarid NP, respectively. The effect of pectin was 1.3 times greater than those of sodium hydroxybutyrate and gutimin whereas that of laminarid NP was at the level of the reference drugs.

Possible reasons for the different influence of the polyuronides on several metabolic indicators could be:

Differences in the compositions. Pectin consisted of polygalacturonic acid whereas laminarid NP was a mixture containing alginic acid salts (consisting of polymannuronic and polyguluronic acids), laminaran polysaccharide, the six-atom alcohol mannitol, and amino acids [2]. The medium molecular-mass polysaccharides in laminarid NP and the predominant accumulation of alginates as the calcium salts contrasted with pectin with a smaller molecular mass and lack of metal salts [2] and were responsible for the prolonged swelling and moderate solubility of laminarid NP in H_2O and, possibly, it lower bioavailability;

Differences in the degree of dialysis through the parietal layer of the rat peritoneum [2]. The value for pectin (3.64×10^{-3} h^{-1}) was 2.6 times greater than that for sodium alginate (1.41×10^{-3} h^{-1}) and 1.7 – 1.9 times greater than those for polyguluronic (2.09×10^{-3} h^{-1}) and polymannuronic (1.89×10^{-3} h^{-1}) acids;

Differences in diffusion coefficients through lecithin membranes [2]. The coefficient of pectin (9×10^{-6}) was higher than those of sodium alginate (10^{-6}), polyguluronic acid (2.5×10^{-6}), and polymannuronic acid (2×10^{-6});

More pronounced absorption capacity for Pb(II) ions of pectin (by 10.7%) as compared with laminarid NP, in which alginates are partially blocked by amino acids [2];

The poorer ability of pectins than laminarid NP to bind radionuclides. The ratio of the absorption and desorption parameters for Sr-90 in tests on rats were 4.63 for pectin and 17.63 for laminarid NP [2];

Differences in the stability constants of Pb(II) polyuronates. The values are 3.2×10^3 L/mol for pectinates and 2.8×10^3 L/mol for alginates [2];

Differences in exchange constants of Ca^{2+} by Pb^{2+} in calcium polyuronates (formed due to the prevalence of Ca^{2+} in laminarid NP and the small amount of Ca^{2+} in pectin). The values are 2.0 for pectin calcium salts, 1.5 for alginic acid, 4.2 for polyguluronic acid, and 0.75 for polymannuronic acid [2]. The selectivity for Pb(II) ions is relatively low because the alginates contained in laminarid NP have a polyguluronic:polymannuronic ratio of 1:3.5 (22%:78%) [2].

Pectin and laminarid NP had a normalizing influence on biochemical processes, induced an antihypoxic effect, and prevented the development of anemia.

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