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Lipid -Lowering Effect of Polysaccharide (Pectin) of *Viscum album L.* Plant in Rats

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Abstract

Disturbances of lipid metabolism is a predisposing factor of cardiovascular diseases. which are accompanied by high mortality rates of the population - ischemic heart disease and ischemic stroke. Plant polysaccharides can be promising remedies for correction of lipid imbalanceIn this regard. the aim of the study was to assess the hypolipidemic activity of polysaccharides isolated from the leaves of mistletoe.

The test-object was the leaves of the white mistletoe (*Viscum album L.*) growing on the apple (*Malus domestica Borkh*.). and the pear (*Pyrus communis L.*). Polysaccharides (water-soluble polysaccharides and pectin substances) were quantitatively determined by the gravimetric method followed by reprecipitation from ethanol. The qualitative composition was evaluated by thin layer chromatography. Functional groups in polysaccharides were determined by titrimetric method. The hypolipidemic activity of the obtained polysaccharides was determined under oral administration at a dose of 100 mg / kg in *Wistar* rats by the change of the concentration of total cholesterol. triglycerides. LDL and HDL cholesterol. The change of the content of cholesteryl ester transfer protein and Niemann-Pick C1-Like1 protein was also determined.

As a result. it was found that among the polysaccharides in the leaves of mistletoe. pectin substances are predominate. which belong to the group of low-esterified pectins. A significant content of free carboxyl groups in pectins from the leaves of mistletoe was also found. The study of hypolipidemic activity showed that. among the polysaccharides of mistletoe leaves. pectin substances exert a more pronounced effect on lipid metabolism. the use of which reduced the content of triglycerides. total cholesterol and LDL cholesterol with an increase in LDL cholesterol in rats. probably due to a decrease in the activity of cholesteryl ester transfer protein and Niemann-Pick C1-Like1 protein. At the same time. at the level of the trend. mistletoe pectins showed a higher level of activity than analogous compounds obtained from the leaves of host-plants. It should be noted that the severity of the pharmacological effect of mistletoe pectins did not depend on the host-plants.

Thus. based on the obtained results. it can be assumed that pectins obtained from the mistletoe leaves can be a potentially effective and safety hypolipidemic agent.

Keywords: Plant polysaccharides. Pectin substances. Cholesterol-lowering activity. CEPT. NPCL1.

Introduction

White mistletoe (*Viscum album L.*) is a semi-parasitic plant. as it is able to synthesize organic matter through photosynthesis. and receives moisture and minerals from the phloem of the affected plant - the host with the help of a special vascular body. penetrating its roots deep under the bark[(1-3)].

Most often. *Viscum album* parasitizes: *Populus nigra. Pyrus communis. Malus domestica*; less often on *Carpinus betulus. Quercus robur. Juglans regia. Robinia pseudoacacia*; extremely rarely on *Juniperus communis. Abies sibirica. Pinus sylvestris*[(3-5)].

The leaves of hemiparasite - white mistletoe are of significant interest for medicine and are diverse in chemical composition. The main biologically active substances of mistletoe leaves: flavonoids (quercetin. 3-methyl ester of quercetin. rhamnetin. isorhamnetin. rhamnazine. 3.7-dimethyl ester of quercetin). phenol carboxylic acids (caffeic and sinapic acids). carotenoids. organic acids. lectins. phenols and their derivatives. nitrogen-containing compounds and others[(1-4)]. In ethnomedicine. mistletoe leaves are used for angina pectoris and chronic osteoarthritis treatment and as a hemostatic. astringent. painkiller. In scientific medicine. an aqueous extract in an experiment delays the growth of a cancerous tumor. inhibits the growth and development of metastases. is able to regulate metabolism. and nonspecifically increases the body's resistance[(1)]. Abroad. in the treatment of malignant neoplasms. mistletoe medication are widely used – Iscador. Abnoba viscum. Iscucin. Helixor. Isorel. Viscum compositum. which have high immunomodulatory and antitumor activity.

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Recent scientific studies have shown that Iskador is an effective therapeutic agent for the treatment of chronic viral hepatitis [4,6,7].

Polysaccharides are vital plant metabolites and promising therapeutic agents. Until recently. the study of the pharmacological activity of plant polysaccharides was very limited. but recently there has been significant progress in this area. So *Yin. et al.. 2019* established the presence of immunoregulatory properties in natural polysaccharides. which were expressed in an increase in the activity of macrophages[8].

Huang et al.. 2019. showed that plant polysaccharides have a pronounced antioxidant effect. Moreover. the antioxidant properties of polysaccharides were realized through the effect on the enzymatic component of the endogenous antioxidant defense system - superoxide dismutase and glutathione peroxidase[9]. It was also found that polysaccharides isolated from plants prevent the effect of ionizing radiation on the body. while improving the immune status. hematopoietic function and preventing DNA damage[10]. Thus. the high therapeutic potential of plant polysaccharides makes it relevant to study other aspects of the pharmacological activity of these compounds.In this regard. the aim of the study was investigate the polysaccharides in the leaves of the plant - the semi-parasite of mistletoe (*Viscum album L.*). and the leaves of host plants - the apple (*Malus domestica Borkh*.) and the pear (*Pyrus communis L.*).

Materials and Methods

Test objects

The test object was the leaves of the white mistletoe (*Viscum album L.)* growing on the apple (*Malus domestica Borkh*.). Collected in the Stavropol region. and the leaves of the white mistletoe (*Viscum album L*.). growing on the pear (*Pyrus communis L* .). collected on the territory of the Belorechensky district of the Krasnodar region. The raw material is the leaves of both plants. collected during the fruiting phase. The leaves of host-plants were also studied[1. 5]. The studied samples of mistletoe and host plants were identified by specialists of the Department of Pharmacognosy and Botany with the course of technology of phytopreparations (Head of the department Doctor of Science (Pharm.) Konovalov D.A.) with the assignment of the number of the herbarium fund PMPIG 17506 - PMPIG 17510.

Method of gravimetric separation of water-soluble polysaccharides (WSP) and pectin substances (PS).

The quantitative determination of these fractions was determined gravimetrically[11-14]. The removal of high molecular weight compounds was carried out by reprecipitation in ethyl alcohol and centrifugation (1000g. 15 min.) of the resulting precipitate [11. 12].

To the investigation the qualitative monomeric composition of the isolated fractions. hydrolysis by sulfuric acid was carried out in 10 hours for WSP and in 48 hours for PS at t = 100°C. Then. neutralization was carried out by barium carbonate solution using a universal indicator paper to pH = 7. filtered and evaporated in a water bath to a small residue[11, 13, 15, 16]. The monosaccharide composition of the fractions was established by ascending thin layer chromatography using standard witness samples. The mobile phase was the solvent systems: pyridine-ethyl acetate-water (1: 2: 2) and n-butanol-acetic acid-water (4: 1: 5). and the stationary phase was FN-7 paper (Germany). Aniline phthalate reagent was used as a developer[11, 16].

Quantitative analysis of functional groups in pectin substances

The percentage of functional groups in pectin substances was determined by the titrimetric method [14, 17, 18, 19].

To determine free carboxyl groups (Kc) the test-samples of the PS near 1.0 g (accurately weighed) and was placed in conical flasks with a capacity of 300 ml. moistened with 95% ethyl alcohol (to avoid clumping). added 100 ml of distilled water. stirred and left night for complete dissolution of PS. Then the resulting mixtures were titrated with a solution of sodium hydroxide (0.1 mol / L) until a red color appeared. which did not disappear within a minute. when 6 drops of Hinton's indicator were added.

The percentage of free carboxyl groups was calculated using the formula:

$$Kc.\ \% = a/m \times 0.45$$

where: a - the volume of sodium hydroxide solution (0.1 mol / L) in ml used for titration; m - is an amount of pectin substances.

The percentage of methoxylated carboxyl groups (Km.%) was calculated by the formula:

$$Km.\% = b/m \times 0.45$$

where: b - the volume of sodium hydroxide solution (0.1 mol / L) in ml for the second titration; m - is an amount of pectin substances.

The total number of carboxyl groups (Co) is equal to the sum of free and methoxylated carboxyl groups (in percent).

$$Co.\% = Kc.\% + Km.\%$$

The degree of methoxylation (esterification) of pectins was found as the ratio of the content of methoxylated carboxyl groups to the total amount of carboxyl groups (in percent):

$$\lambda = Km / Ko \cdot 100\%$$

The percentage of methoxyl groups (CH_3O) was calculated using the formula:

$$CH_3O.\% = Km \times (31/45)$$

where: Km - the content of methoxylated carboxyl groups in pectin powder.%; 31 - equivalent weight of CH_3O groups; 45 - is the equivalent weight of COOH groups.

Pharmacological study

Experimental animals

The work was performed on 100 male Wistar rats weighing 200-220 grams. 3 months old. The animals were obtained from the «Rappolovo laboratory animal nursery» (Russia. Leningrad region) and during the experiment were kept under controlled conditions in the laboratory of living systems of the Pyatigorsk Medical and Pharmaceutical Institute. Conditions of detention: ambient temperature - 22 ± 2^0C. relative humidity - 60 ± 5%. with a 12-hour change of the daily cycle. The rats were housed by 5 animals in macrolon cages on a granular hardwood bedding with free access to water and full diet feed. Working with experimental animals was in accordance with generally accepted protocols of experimental ethics: Directive 2010/63 / EU of the European Parliament and of the council on the protection of animals used for scientific purposes. September 22. 2010 and ARRIVE 2.0 guidelines. The local ethical committee (protocol # 21 dated 06.16.2020) approved the work.

Hypercholeterolemia model

Rats were set on Paigen's high cholesterol diet (15% natural fat (sunflower oil). 1.25% cholesterol (Panreac) and 0.5% cholic acid (Panreac)) for 6 weeks. After the specified time the biomaterials were taken for research [20].

Study design

In the course of the work. the following experimental groups (summary 10 groups) were distinguished (by 10 animals in each group): SO - sham-operated rats. NC - negative control; PSpc — a group of rats that received pectin from pear; PSmd - a group of rats that received pectin from a apple tree; PSva/pc - a group of rats that received pectin substances from mistletoe collected from pear; PSva/md - a group of rats that received pectin substances from mistletoe collected from apple tree; WSPpc - a group of rats that received soluble pear polysaccharides; WSPmd - a group of rats that received water soluble polysaccharides from apple tree; WSPva/pc - a group of rats that received water-soluble polysaccharides of mistletoe collected from common pear; WSPva / md - a group of rats that received water-soluble polysaccharides of mistletoe collected from apple tree. The test-compounds were administered at a dose of 100 mg / kg[21]. *per os*. daily for 6 weeks in water solution form. After 6 weeks of administration the plasma lipoprotein profile and cholesteryl ester transfer protein (CEPT) concentration was determined. Also. the small intestine was harvested from the rats to obtain the supernatant and assess the change of the Niemann-Pick C1-Like1 protein (NPCL1) content was investigated.

Biomaterial sampling

Blood was collected from the abdominal part of the aorta into a citrate-filled syringe. Then. whole blood was centrifuged at 1000 g for 10 min. to obtain a serum. in which the concentration of total cholesterol (TC). low density lipoprotein cholesterol (cLDL). high density lipoprotein cholesterol (cHDL). triglycerides (TG) and CEPT was determined. The small intestine was freed from the contents and washed in phosphate buffer solution - PBS (pH = 7.4). The intestine were homogenized in a mechanical Potter homogenizer in PBS (pH = 7.4) in a 1:7 ratio. The resulting homogenate was centrifuged at 10.000 g for 15 min to obtain a supernatant. in which the NPCL1 content was determined.

Determination of TC content.

The principle of the method is based on the spectrophotometric detection of the quinonimine dye. which is formed as a result of the oxidative azocoupling reaction of 4-aminoantipyrine with phenol. which occurs in the participation of hydrogen peroxide. which undergoes the oxidation of cholesterol to 4-cholesten-3-one. The color intensity of the reaction environ is proportional to the cholesterol content in the test material and is determined photometrically at a wavelength of 500 nm.

Determination of cHDL content.

The principle of the method is based on the fact that chylomicrons. very low density lipoproteins and low density lipoproteins are precipitated when phosphotungstic acid and Mg^{2+} ions are added to the test sample. After centrifugation (4000 g for 10 minutes). only cHDL remains in the supernatant. the concentration of which is determined similarly to the concentration of TC.

Determination of cLDL content.

The principle of the method is based on the fact that after adding heparin to the test sample. LDL are deposited at their isoelectric point at pH 5.1. After centrifugation (4000 g for 10 minutes). cholesterol of chylomicrons. very low density lipoproteins and HDL remains in the supernatant. The cLDL concentration is determined by the difference in total cholesterol and supernatant cholesterol.

Determination of TG content.

The principle of the method is based on the detection of colored products of conjugaiuon reactions of lipase-mediated hydrolysis of fatty acids and oxidative azo coupling of 4-aminoantipyrine and phenol with the formation of a quinonimine dye. which has an absorption maximum at 500 nm.

Determination of the concentration of CEPT and NPCL1.

The content of CEPT and NPCL1 was determined by the method of enzyme-linked immunosorbent assay. Assay kits were obtained from *Cloud Clone* (USA). The assay progress was in accordance with the kit manufacturer's instructions. The spectrophotometric signal was detected using an Infinite F50 plate reader (Tecan. Austria).

Statistical analysis

The results of experiment were statistically processed. The software package STATISTICA 6.0 (StatSoft. USA) was used in the work. Statistical significant differences between the groups were determined by the ANOVA method with the Newman-Keulse post-test. at a significance level of $p < 0.05$.

Results

Isolation and investigation of polysaccharide complexes in mistletoe and host-plants leaves

The quantitative determination of polysaccharide fractions was determined gravimetrically.

Table 1. Qualitative and quantitative composition of polysaccharides isolated from leaves of white mistletoe. apple tree and pear

Test-object	Polysaccharides content% (n=6)	Monosaccharides and its mobility coefficients in thin layer chromatography (n=4)							
		Galactose (Gal)		Galacturonic acid (Gal A)		Arabinose (Ara)		Rhamnose (Rha)	
		Solutions systems							
		1	2	1	2	1	2	1	2
Leaves of mistletoe collected from apple tree	WSP – 1.84±0.06	0.15± 0.01	0.25± 0.02	0.18± 0.01	0.35± 0.02	0.25± 0.02	0.45± 0.02	0.38± 0.02	0.57± 0.02
	PS – 5.86±0.22	0.15± 0.01	0.26± 0.02	0.18± 0.01	0.35± 0.02	0.26± 0.02	0.44± 0.02	0.38± 0.02	0.55± 0.02
Leaves of apple tree	WSP – 2.08±0.06	0.14± 0.01	0.25± 0.02	0.18± 0.01	0.37± 0.02	0.27± 0.02	0.44± 0.02	0.37± 0.02	0.56± 0.02
	PS – 7.86±0.36	0.15± 0.01	0.25± 0.01	0.17± 0.01	0.36± 0.02	0.26± 0.02	0.45± 0.02	0.39± 0.02	0.55± 0.02
Leaves of mistletoe collected from pear	WSP – 3.86±0.07	0.14± 0.01	0.23± 0.02	0.17± 0.01	0.36± 0.02	0.26± 0.02	0.44± 0.02	0.39± 0.02	0.55± 0.02
	PS – 6.44±0.30	0.15± 0.01	0.24± 0.02	0.17± 0.01	0.35± 0.02	0.27± 0.02	0.43± 0.02	0.38± 0.02	0.56± 0.02
Leaves of pear	WSP – 5.27±0.08	0.14± 0.01	0.25± 0.02	0.16± 0.01	0.37± 0.02	0.25± 0.02	0.45± 0.02	0.39± 0.02	0.56± 0.02
	PS – 12.02±0.37	0.14± 0.01	0.24± 0.02	0.17± 0.01	0.36± 0.02	0.26± 0.02	0.46± 0.02	0.40± 0.02	0.56± 0.02

Note: Mobility coefficients of standard samples in solvent systems: (1 - pyridine - ethyl acetate - water (1: 2: 2)): 0.15 ± 0.01 (Gal); 0.17 ± 0.01 (Gal A); 0.27 ± 0.02 (Ara) 0.38 ± 0.02 (Rha); (2- n-butanol - acetic acid - purified water (4: 1: 2)): 0.24 ± 0.02 (Gal); 0.37 ± 0.02 (Gal A); 0.45 ± 0.02 (Ara); 0.56 ± 0.02 (Rha); WSP-water soluble polysaccharides; PS - pectin substances.

After acid hydrolysis of the obtained fractions. it can be concluded that these fractions are characterized by a similar monomer composition.

Quantification of functional groups of pectin substances

The study of the qualitative characteristicsof pectin substances and the determination of functional groups was of interest to substantiate the possibility of their use for medical purposes.

Table 2. Content of functional groups in pectin substances isolated from leaves of white mistletoe. apple tree and pear

Test-objects / Functional group	$К_с$. %	$К_м$. %	$К_о$. %	$-OCH_3$. %	(λ). %
PS isolated from:					
Leaves of mistletoe collected from apple tree	7.02	2.17	9.19	1.49	23.61
Leaves of apple tree	9.63	4.10	13.73	2.82	29.86
Leaves of mistletoe collected from pear	7.43	1.53	8.96	1.05	17.09
Leaves of pear	8.64	3.83	12.47	2.64	30.69

The investigated pectin substances belong to the group of low esterified pectins (23.61%. 29.86%. 17.09%. 30.69%). because the degree of esterification of carboxyl groups is less than 50%. The significant content of free carboxyl groups (7.02%. 9.63%. 7.43%. 8.64%) indicates their rather high complexing ability and the possibility of using pectin substances as detoxicants.

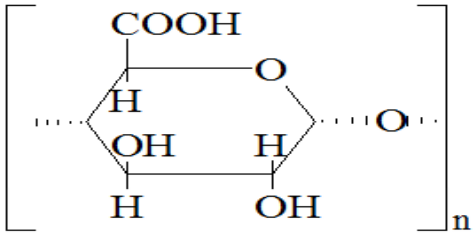

Figure 1. A structural fragment of polygalacturonic acid. which is part of the studied pectin substances

Hypolipidemic activity of pectin substances and water-soluble polysaccharides obtained from mistletoe and host-plants leaves

The block of pharmacological tests showed that in the NC group of rats under conditions of experimental hypercholesterolemia (Table 3). an increase in the concentration of total cholesterol. cLDL and TG was noted in relation to the SO group of animals by 2.2 times ($p < 0.05$); 4.1 times ($p < 0.05$) and 1.6 times ($p < 0.05$) respectively. with a decrease of cHDL content by 54.5% ($p < 0.05$). Against the background of the administration of pectin substances obtained from the pear in relation to the NC group of rats. a decrease in the concentration of TC - by 21.7% ($p < 0.05$); cLDL - by 29.3% ($p < 0.05$) and TG - by 15.8% ($p < 0.05$) was observed. At the same time. the content of cHDL in animals that received pectin substances from pear increased by 40.0% ($p < 0.05$) relative to the NC group of rats (Table 3). Against the administration of pectin substances from the apple tree. there was a decrease of the concentration of TC. cLDL and TG in relation to the NC group of animals by 23.9% ($p < 0.05$); 30.5% ($p < 0.05$) and 15.8% ($p < 0.05$). respectively. with an increase in cHDL content by 30.0% ($p < 0.05$). When animals were treated by pectin substances obtained from white mistletoe. which was collected from pear. a decrease in the concentration of TC. cLDL and TG relative to the NC group of animals by 32.6% ($p < 0.05$); 43.9% ($p < 0.05$) and 21.1% ($p < 0.05$) was noted. with an increase in cHDL by 60% ($p < 0.05$). In rats that were treated by pectin substances obtained from mistletoe. which was collected from a apple tree. the concentration of TC. cLDL and TG was lower than that of the NC group of animals by 30.4% ($p < 0.05$). 43. 9% ($p < 0.05$) and 26.3% ($p < 0.05$). respectively. while the content of cHDL increased by 80% ($p < 0.05$). It should be noted that the administration of water-soluble polysaccharides did not have a significant effect on the change in the lipid profile of blood serum in animals.

Table 3. Influence of the test-substances on the change in the lipid profile of blood plasma in rats under conditions of experimental hypercholesterolemia

Group	TC. мM/L	LDL. мM/L	HDL. мM/L	TG.мM/L
SO	2.1±0.17	1±0.1	1.1±0.22	1.2±0.21
NC	4.6±0.25#	4.1±0.13#	0.5±0.19#	1.9±0.26#
PSpc	3.6±0.14*	2.9±0.24*	0.7±0.22*	1.6±0.17*
PSmd	3.5±0.13*	2.8±0.09*	0.7±0.24*	1.6±0.24*
PSva/pc	3.1±0.24*	2.3±0.25*	0.8±0.22*	1.5±0.14*
PSva/md	3.2±0.29*	2.3±0.18*	0.9±0.15*	1.4±0.29*
WSPpc	4.2±0.21	3.8±0.24	0.4±0.15	1.7±0.29
WSPmd	4±0.28	3.5±0.11	0.5±0.23	1.9±0.16
WSPva/pc	4.4±0.18	4.1±0.19	0.5±0.24	1.8±0.29
WSPva/md	4.1±0.12	3.6±0.28	0.5±0.16	1.9±0.09

Note: SO - sham-operated rats. NC - negative control; PSpc — a group of rats that received pectin from pear; PSmd - a group of rats that received pectin from a apple tree; PSva/pc - a group of rats that received pectin substances from mistletoe collected from pear; PSva/md - a group of rats that received pectin substances from mistletoe collected from apple tree; WSPpc - a group of rats that received soluble pear polysaccharides; WSPmd - a group of rats that received water soluble polysaccharides from apple tree; WSPva/pc - a group of rats that received water-soluble polysaccharides of mistletoe collected from common pear; WSPva / md - a group of rats that received water-soluble polysaccharides of mistletoe collected from apple tree. # - statistically significant relative to the SO group; * - statistically significant relative to the NC group.

Also during the work it was found that the administration of pectin substances contributed to a decrease in the concentration of CEPT and NPCL1. Thus. in the NC group of rats. the content of CEPT and NPCL1 was 2.6 times ($p < 0.05$) and 2.9 times ($p < 0.05$). respectively higher. than in SO animals. Against the background of the PSpc. PSmd. PSva / pc and PSva / md administration. a decrease in the concentration of CEPT in relation to NC in the group of animals by 28% ($p < 0.05$); 23.4% ($p < 0.05$); 38.6% ($p < 0.05$) and 40.1% ($p < 0.05$). respectively (Fig. 2) and NPCL1 (Fig. 3) by 25.7% ($p < 0.05$); 24.9% ($p < 0.05$); 37.3% ($p < 0.05$) and 40% ($p < 0.05$). respectively was noted. At the same time. the content of CEPT and NPCL1 in rats treated by water-soluble polysaccharides did not statistically significantly differ from that in the NC group of animals.

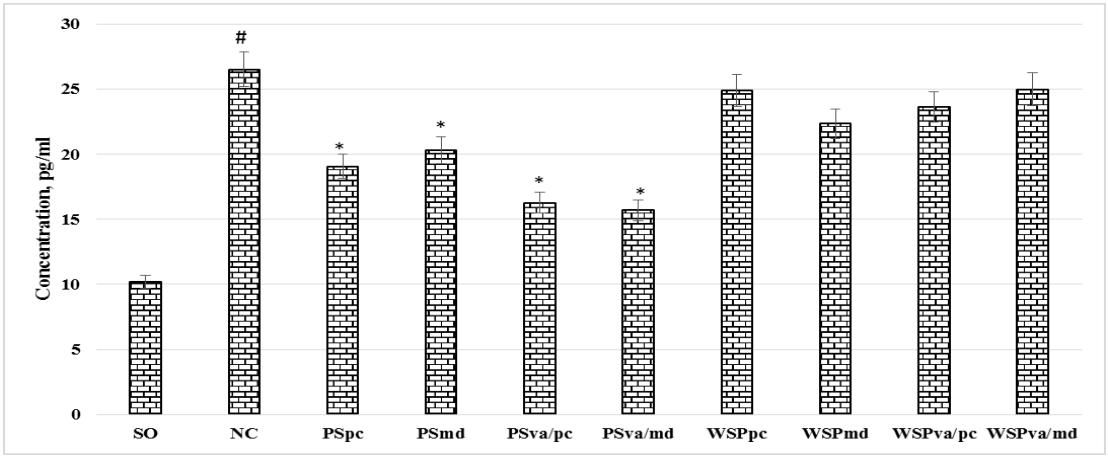

Figure 2. The effect of the test substances on the change in the concentration of CEPT in the blood of rats under conditions of experimental hypercholesterolemia.

Note: SO - sham-operated rats. NC - negative control; PSpc — a group of rats that received pectin from pear; PSmd - a group of rats that received pectin from a apple tree; PSva/pc - a group of rats that received pectin substances from mistletoe collected from pear; PSva/md - a group of rats that received pectin substances from mistletoe collected from apple tree; WSPpc - a group of rats that received soluble pear polysaccharides; WSPmd - a group of rats that received water soluble polysaccharides from apple tree; WSPva/pc - a group of rats that received water-soluble polysaccharides of mistletoe collected from common pear; WSPva / md - a group of rats that received water-soluble polysaccharides of mistletoe collected from apple tree. # - statistically significant relative to the SO group; * - statistically significant relative to the NC group.

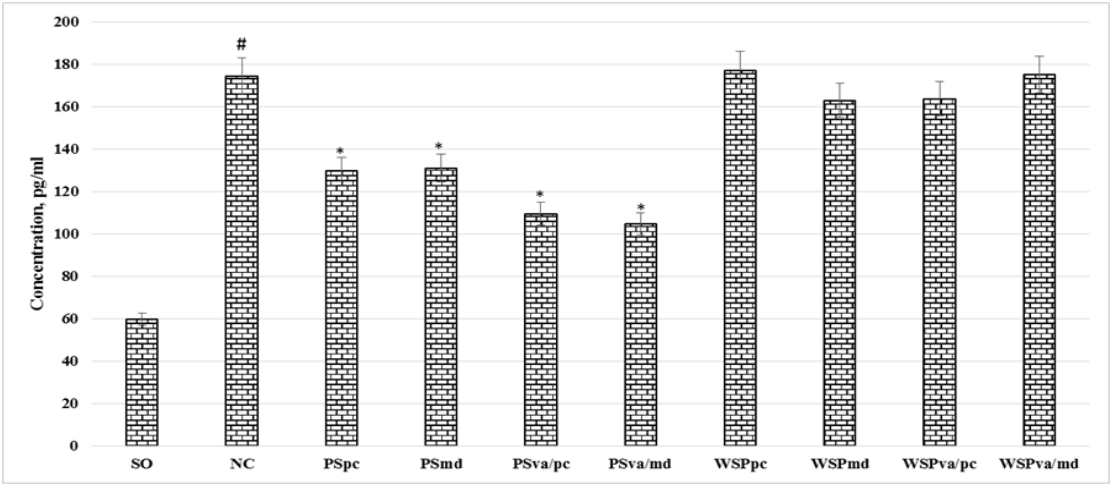

Figure 3. The influence of the test substances on the change in the concentration of NPCL1 in the blood of rats under conditions of experimental hypercholesterolemia.

Note: SO - sham-operated rats, NC - negative control; PSpc — a group of rats that received pectin from pear; PSmd - a group of rats that received pectin from a apple tree; PSva/pc - a group of rats that received pectin substances from mistletoe collected from pear; PSva/md - a group of rats that received pectin substances from mistletoe collected from apple tree; WSPpc - a group of rats that received soluble pear polysaccharides; WSPmd - a group of rats that received water soluble polysaccharides from apple tree; WSPva/pc - a group of rats that received water-soluble polysaccharides of mistletoe collected from common pear; WSPva / md - a group of rats that received water-soluble polysaccharides of mistletoe collected from apple tree. # - statistically significant relative to the SO group; * - statistically significant relative to the NC group.

Discussion

Lipid metabolism disorders leading to atherosclerosis are among the most common metabolic disorders and underlie the pathogenesis of a large number of diseases. The two leading non-infectious causes of mortality in the population (according to WHO) are ischemic heart disease and ischemic stroke. which are directly associated with progressive atherosclerosis and hyperlipidemia. In turn. hyperlipidemia is associated with an imbalance in the metabolism of cholesterol and triglycerides: in the lipid profile of blood serum. LDL cholesterol predominates. the concentration of triglycerides is increased. and the content of HDL is reduced. Today. a wide range of medicines are used to treat mixed hypercholesterolemia. ranging from statins to newer PCSK9 inhibitors. The available medicines generally show excellent levels of efficacy and. when used rationally. can reach target blood cholesterol and triglyceride levels fairly quickly. However. despite the high efficiency. the use of statins is associated with the development of serious side effects. As pointed out by *Ward et al. 2019*. deviation from the mode of use or dosing violation of drugs of the statin group is accompanied by the development of adverse reactions from the skeletal muscle (myopathy). liver (hepatotoxicity) and kidneys (myoglobin nephropathy) [22]. PCSK9 inhibitors are a new group of highly selective cholesterol-lowering agents that can reduce LDL cholesterol levels by more than 70%. To date. the use of available agents of this group. alirocumab and evolocumab. is associated with an increased risk of developing upper respiratory tract infections [23] . A significant number of adverse reactions of the main cholesterol-lowering medicines makes urgent the search for alternative methods of lowering the concentration of cholesterol and triglycerides in the blood. One of such approaches may be the use of natural pectin substances.

Pectin's are complex polysaccharides of the plant cell wall. localized in specific vacuoles. unevenly distributed. Pectin's play an important role in plant morphogenesis and physiology. and are also potentially effective therapeutic agents [24]. *Li. et al. 2020* found that pectins isolated from *Abelmoschus esculentus* prevent the development of fatigue by increasing the amount of glycogen. glucose and. accordingly. ATP in skeletal muscle [25]. The immunosuppressive and antiallergic properties of pectin's. in particular galactan. arabinan. and apiogalacturonan. have also been investigated [26]. There is information about the antibacterial activity of pectin's. on multi-resistant strains [27].

The hypolipidemic activity of some pectin's also has been studied. A work by *Hu. et al.. 2019* showed that the use of pectin's obtained from citrus fruits reduced the level of LDL cholesterol in C57BL / 6 mice [28]. Similar results for pectin substances were presented in a review by *Zhang et al.. 2021* [29].

This study also established the hypocholesterolemic activity of pectin's obtained from the leaves of the hemiparasite plant - white mistletoe and host-plants - pear and apple tree. At the same time. the use of pectin substances from mistletoe leaves contributed to a more pronounced (at the level of tendency) decrease of the concentration of TC. cLDL and TG. as well as an increase of cHDL. It should be noted that the administration of water-soluble polysaccharides to animals did not have a significant effect on the change in the lipid profile of blood plasma. Analyzing the possible mechanisms of cholesterol and triglyceride reduction under the influence of the test pectin substances. it was suggested that these compounds can affect the function of CEPT and NPCL1.

CEPT is a hydrophobic glycoprotein that provides bi-directional transfer of cholesterol and triglycerides between plasma lipoproteins. The increased activity of CEPT leads to an increase in the transport of cholesterol and triglycerides from HDL to LDL. thereby increasing their amount and promoting atherogenesis [30]. Currently. several CEPT inhibitors are in 3 stage of clinical trials: torcetrapib. dalcetrapib. evacetrapib. and anacetrapib [31]. In the course of the study. it was found that the administration of the test pectin substances contributed to a decrease in the concentration of CEPT. which contributed to the restoration of the balance of cLDL / cHDL.

The transport protein NPCL1 controls the absorption of cholesterol in the intestine and is a pharmacological target for some medicines. for example. ezetimibe[32]. In the present study. it was shown that the studied pectin substances reduced the concentration of NPCL1 in the small intestine. which can mediate impaired absorption of cholesterol and. accordingly. the hypocholesterolemic effect. Also. one cannot exclude the possibility of the formation of difficult-to-absorb complexes of cholesterol with the studied pectin's. since the latter have a sufficiently high adsorption capacity.

Conclusion

This work showed no differences between the total content of polysaccharides in the leaves of the white mistletoe (*Viscum album L.*) growing on the apple tree (*Malus domestica Borkh.*) and the leaves of the white mistletoe (*Viscum album L.*) growing on the pear (*Pyrus communis L.*). A study of the pharmacological activity of the isolated polysaccharides showed that pectin substances have a hypolipidemic effect. which is expressed in a decrease in the concentration of total cholesterol. LDL cholesterol and an increase in HDL cholesterol. as well as a decrease in triglycerides levels. At the tendency level. pectin substances obtained from white mistletoe had a more pronounced effect than analogous compounds isolated from carrier plants. At the same time. the ability of pectin substances to reduce the level of cholesterol and triglycerides in blood may be based on a decrease in the function of CEPT and NPCL1. It should be noted that water-soluble polysaccharides did not exhibit cholesterol-lowering activity.

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