Dietary supplement-wheat germ's effect on the spectrum of lipoproteins and fatty acids in the blood of experimental hyperlipidemic animals

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Abstract---Objective: *The present study was designed to investigate the effect of dietary supplement- wheat seedling on the serum of blood lipids and the fatty acid composition in animals with experimental hyperlipidemia model.*

Material and methods: *Thirty male rabbits – Chinchilla breed were divided into 5 groups: intact rabbits, animals with experimental model of hypercholesterolemia, adjustment of experimental hypercholesterolemia statin, adjustment of experimental hypercholesterolemia of wheat seedling, adjustment of experimental hypercholesterolemia statin and wheat seedling. The experimental hypercholesterolemia was reproduced by intragastric daily administration of cholesterol of 0.2 g per kg of mass for 2 months. During treatment ultrox and wheat seedling were administered at 0.6 mg/kg and 142 mg/kg for 30 days respectively. While the comparative evaluation wheat seedling and statin of ultrox in blood serum on the automated biochemical analyzer (RX Daytona/Randox, Great Britain) the content of triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol(HDL), low-density lipoprotein, very low-density lipoprotein (LDL) were determined and the atherogenic coefficient (AC) was calculated.*

Results: *There was a significant decrease in the saturated blood content and an increase in polyunsaturated fatty acids such as linoleic and linolenic acids. The use of both the ultrox and wheat seedling had a distinct positive effect on the spectrum of high- and low-density lipoproteins, more significant lipid-lowering effect.*

Conclusion: *The present study indicates that wheat seedling can be prescribed to reduce the dose of statin in their blood*.

Keywords---*wheat seedlings, fatty acid composition, cholesterols level, blood analysis, polycosanol.*

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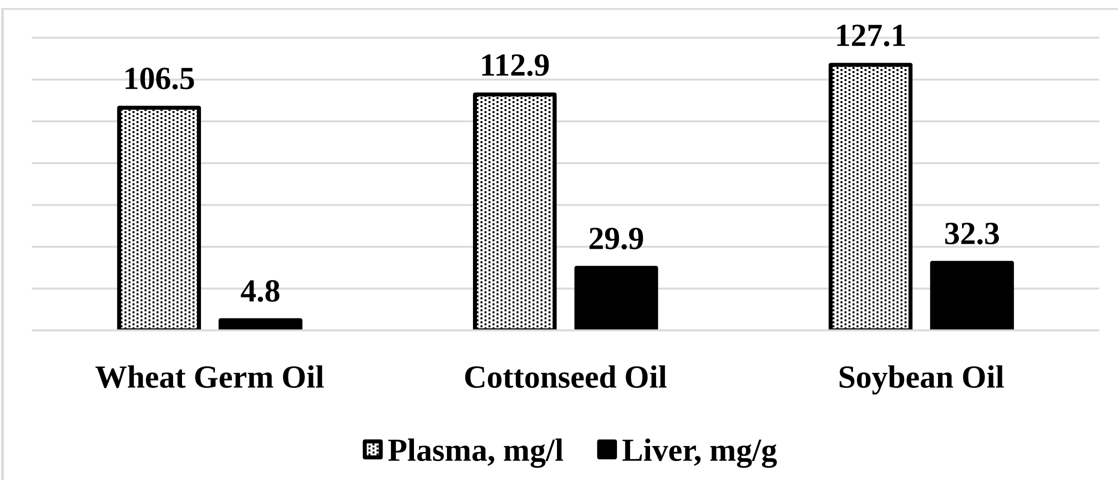
I. INTRODUCTION

Nowadays, it is very evident that the hypercholesterolemia is transforming into a global non-communicable epidemy. According to the Ministry of Health of the Republic of Uzbekistan 2014, diseases of the circulatory system are about 5800 per 100 thousand people and tend to increase. Ischemic heart disease (IHD), being the most common cause of death, accounts for 22,300 deaths per year (Karimov et al., 2014) .

Hypercholesterolemia (HCL) plays an important role in the pathogenesis of atherosclerosis and IHD (Shpagina, 2008). Prescribing cholesterol-lowering drugs is a priority in the treatment of IHD and HCL. The inhibitors of 3-hydroxy-3-methyl-glutaryl-CoA reductase are most effective in reducing low-density lipoprotein cholesterol (LDL-C) and mortality from atherosclerosis and IHD (JAMA, 2011). In many statins, an effective therapeutic daily dose causes the occurrence of side effects – an increase in hepatic enzymes of aspartic and alanine transaminases (ALT, AST), myalgia, myopathy with an increase in creatine phosphokinase (CPK) (Hippisley-Cox, 2010). Therefore, the search for new drugs with a lower daily dose, safer, prolonged action and effective for x-reducing action is conducted.

In recent years, wheat germ and wheat germ flour are causing some interest in researchers. To a certain extent, a prerequisite for testing wheat germ oil (WGO) and wheat germ flour effects, in the clinic of different diseases of cardiovascular system, foreign data about the impact of WGO, and wheat germ on the content of cholesterol in the blood and liver was used. As can be seen from the data presented in Fig.1, the cholesterol content in the blood and liver of rats is significantly reduced with the use of wheat germ oil compared to the use of cottonseed or soybean oil (Shpagina, 2008).



1-fig. The effect of wheat germ oil on cholesterol in blood and liver of rats[20].

Analysis of changes in biochemical composition of the blood showed that the use of wheat germ oil in patients with coronary heart disease gives a more accurate hypolipidemic effect (reduction of lipids and β-lipoproteins). Thus, assessment of clinical picture in patients who received additional wheat germ oil showed that the number of angina attacks decreased by 4 times (in the control group by 2.5 times) and, accordingly, the consumption of nitroglycerin decreased. It is noted that using wheat germ oil in the treatment is accompanied by a decrease of high blood clotting, which is very important from a pathogenetic point of view(Arruzazabala, 2010).

According to Shpagina et al., in patients receiving a combined lipid-lowering diet and wheat germ oil there was a significant improvement; a decrease in clinical symptoms and positive dynamics in the spectrum of blood lipids. At the same time, the lipid-lowering effect was stable and persisted even after 3 months of therapy. Therefore, the analysis of

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works devoted to the study of the effect of wheat germ oil and flour on the level and spectrum of blood lipids in hyperlipidemia indicates the presence of a significant and stable lipid-lowering effect, which is a prerequisite for further targeted research in this direction.

II. MATERIALS AND METHODS

The study of the antiatherogenic effects of wheat seedling on the model of hypercholesterolemia in rabbits

In connection with the foregoing, we conducted an experimental study to investigate the effects of dietary supplement- wheat seedling (hereinafter WS) on the spectrum of blood lipids and the composition of fatty acids in animals with experimental hypercholesterolemia model.

The experiments were performed on 30 male rabbits of the breed "Chinchilla" from the original mass of 2500-3000 g. They were divided (depending on the purpose of the study and method of treatment) into 5 groups (6 animals): 1- (control) – intact rabbits; 2– animals with experimental model of hypercholesterolemia; 3 – adjustment of experimental hypercholesterolemia statin; 4 – adjustment of experimental hypercholesterolemia of WS; 5 – adjustment of experimental hypercholesterolemia statin and WS.

The model of experimental hypercholesterolemia was reproduced by intragastric daily administration of cholesterol of 0.2 g per kg of mass for 2 months (Anichkov&Khalatov, 1913). Treatment of experimental animals was started after 2 months of introduction of the cholesterol. Statin ultrox (Nobel Farm) was used, which was administered at 0.6 mg/kg for 30 days, and WS142 mg/kg for 30 days. The studied drugs were administered intragastrically using an atraumatic probe daily in the morning and evening hours in the volume, calculated based on the weight of the rabbit. The object of the study was blood serum.

All studies were conducted in accordance with the principles indicated in “the Convention about the protection of vertebrates for experimental and other purposes” (Strasbourg, 1986).

For the comparative evaluation of the drug, plant origin of WS and statin of ultrox in blood serum on the automated biochemical analyzer (RX Daytona/Randox, Great Britain) the content of triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol(HDL), low-density lipoprotein, very low-density lipoprotein (LDL) were determined and the atherogenic coefficient (AC) was calculated.

***Method to determinethe fatty acid composition of blood serum*.**

The fatty acid composition of blood serum was determined in the scientific laboratory of the Republican scientific and practical center of sports medicine at the National Olympic Committee of Republic of Uzbekistan on a triple quadrupole chromato-mass spectrometer with a gas chromatograph (GC-MS/MS) TRACE 1310 TSQ 8000 and a robotic autosampler CTC TriPlus RSH of Thermo Fisher Scientific(USA).

In order tocarry out this, the blood serum was separated from the red blood cells by centrifugation of whole blood at 2000 rpm for 6 min. Then 0.5 ml of supernatant (blood plasma) was transferred to 1.5 ml of graduated Eppendorf tubes and 0.4 ml of acetone was added to precipitate the protein fraction. The mixture was thoroughly mixed on vortex for 0.5-1 min and then centrifuged at 15,000 rpm for 10 min. After that, the supernatants in a volume of 0.3-0.4 ml were transferred to the new Eppendorf tubes and 0.25 ml hexane was added for the extraction of fatty acids. The mixture was thoroughly mixed on the vortex and left for a few minutes to completely separate the water and hexane layer. The hexane layer of the mixture was transferred to the new Eppendorf tubes, and the extraction process was repeated two more times for the complete extraction of chemicals of lipid nature. The resulting hexane layers were evaporated on a microconcentrator until

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they got dry, and then the resulting precipitates were dissolved in 0.5 ml of hexane volume and transferred to glass vials for analysis in GC-MS.

The chromatography conditions were set as follows: capillary column (0.2 µm x 0.25mmx 30 m), impregnated 5% nymbiphenyl-dimethylsiloxane; gas-carrier helium with a constant flow of 1 ml/min. The initial temperature of thermostat column was 40ºCwith a delay of 1 min. Then the thermostat was heated until 280º C with a speed of 20ºC/min with a delay of 3 min at 280ºC, with a subsequent decrease in temperature to the initial state within 6 min at a speed of 40ºC. The temperature of the injector and the mass spectrometric detector was set to 250 ° C. The extract was injected in a volume of 1 µl in split mode (split) flow. The ionization method was carried out by an electron impact at 20 eV. The registration of the chromatographic profile was performed 3 minutes after the start to remove the solvent signal. The chromatography process was controlled by the XCalibur program in the range of limits of m/z 50-1500. Identification of components was performed using the library of reference mass-spectra of natural compounds “NIST”.

Digital material was processed statistically on a personal computer using a package of applications for statistical analysis.

Ethical approval

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 2008 Declaration of Helsinki.

III. RESULTS

The data obtained are given in table 2. The content of rabbits on a cholesterol diet during 60 days of the experiment led to the development of severe hypercholesterolemia (295,0±1,45 mg/DL). Treatment with the use of ultrox and food additive WS reduced the content of TC, 2.08 and 1.49 times(p<0.05), respectively. With the combined use of ultrox and WS, the content of total cholesterol decreased more clearly.

Table 2.Lipid metabolism indices in rabbits with experimental HCL, n=6

indicator	controlgroup	animals with experimental HCL	After treatment		
			Ultrox	wheat seedling	combined treatment
TC, mg/dl	71,8±0,78	295±1,45	142±0,66	179±1,77	131±1,2
TG, mg/dl	14,6±0,6	28,1±0,36	29,4±0,66*	37,3±0,54	25,6±0,12
C HDL, mg/dl	26,7±0,98	17,8±0,8	29,6±0,7	25,3±1,08	34,8±0,75
C VLDL mg/dl	2,92±0,07	6,98±0,15	5,9±0,22	7,46±0,21 *	5,12±0,68
C LDL mg/dl	40,78±0,86	270,3±2,8	106,7±0,68	146±1,88	91,08±0,14
AC	1,37±0,02	15,6±0,43	3,83±0,14	6,16±0,12	2,76±0,44

Note. * – p<0.05 compared to untreated animals.

It is important to note that in groups of animals treated with ultrox and WS, reduction of cholesterol level was comparable. In all experimental groups, compared with the control, after 30 days of combined administration of drugs,

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there was a significant difference in the level of TC by 7.75-26.8% ($p<0.05$), which indicates good cholesterol reducing-effect of the combined use of ultrox and WS.Thus, the combined use of ultrox with WS has a higher effect on the blood lipid levels of the experimental animals with HCL than that of these two drugs used separately.

The study of other indicators of blood lipids in animals with HCL, in particular, the content of TG shows that the value of the latter was 1.92 times ($p<0.05$) higher than in the control group. No significant changes in the content of TG were observed against the background use of ultrox. At the same time, under the influence of WS triglycerides content increased by 32.4%, and the combined administration of ultrox and WS, in contrast, declined by 8.9% compared with the untreated group. The results indicate that ultrox and WS, and their combination do not have an influence on the content of TG. Our data coincide with the data of Y. I. Ragino et al.(2010), who studied the effect of singali on the model of hypercholesterolemia in rabbits (Ragino et al.).

The study of HDL cholesterol in animals with HCL indicates a decrease in its level by 33.4% compared with the control group. While in the group of animals treated with ultrox and WS, the level of this indicator increased, compared with HC animals not receiving these drugs, 66.3 and 42.1%, respectively. It should be noted that their combined administration contributes to a more significant increase in the level of C in HDL, which in comparison with control and untreated animals increases by 30.3 and 95.5%, respectively.

Experimental HCL is accompanied by an increase in the content of VLDL cholesterol by 2.4 times ($p<0.05$). Also, if the use of ultrox reduces its content by 15.5%, then the use of a food additive-wheat seedling does not cause significant changes in the content of LDL in comparison with the untreated group. At the same time, with the combined administration of ultrox and WS, the content of LDL-C in comparison with the untreated group is reduced by 26.7%. The results obtained by us confirm the data (Tolstikova, 2006) about the effect of pharmacological synergism in the combination of certain pharmacological compounds. Experimental HCL is characterized by a more notable increase in LDL-C content compared to the control group (270.3 ± 2.8 at the control of 40.78 ± 0.86 mg/DL, $p<0.05$). Treatment with ultrox and WS within 30 days leads to a decrease in the content of LDL cholesterol compared with the untreated group, 2.53 and 1.85 times, respectively. It must be emphasized that the combination of ultrox and WS proved to be more effective than introducing them separately. Co-administration decreased the content of LDL-C 2.97 times compared with the untreated group. It must be noted, that the content ofLDL-C is 2.23 times higher compared to the control group ($p<0.05$).

In atherosclerosis, the determination of the atherogenic coefficient (AC) is of great importance. In the animals of the control group, this coefficient was equal to 1.37 ± 0.02. The experimental HCL caused a sharp increase in this coefficient compared to the control (11.4 times). Ultrox and wheat seedling compared to untreated animals reduced AC, at 4.0 and 2.5 times, respectively. At the same time, the combined administration of the used drugs led to a decrease in this coefficient by 5.6 times.

Thus, the creation of a multicomponent biologically active substance with lipid-lowering properties is relevant not only for potential use in mild forms of lipid metabolism disorders, but also in combination with statins in order to reduce the dose of the latter, and consequently their side effects.

The influence of dietary supplement- wheat seedling on fatty acid composition of blood (further results)

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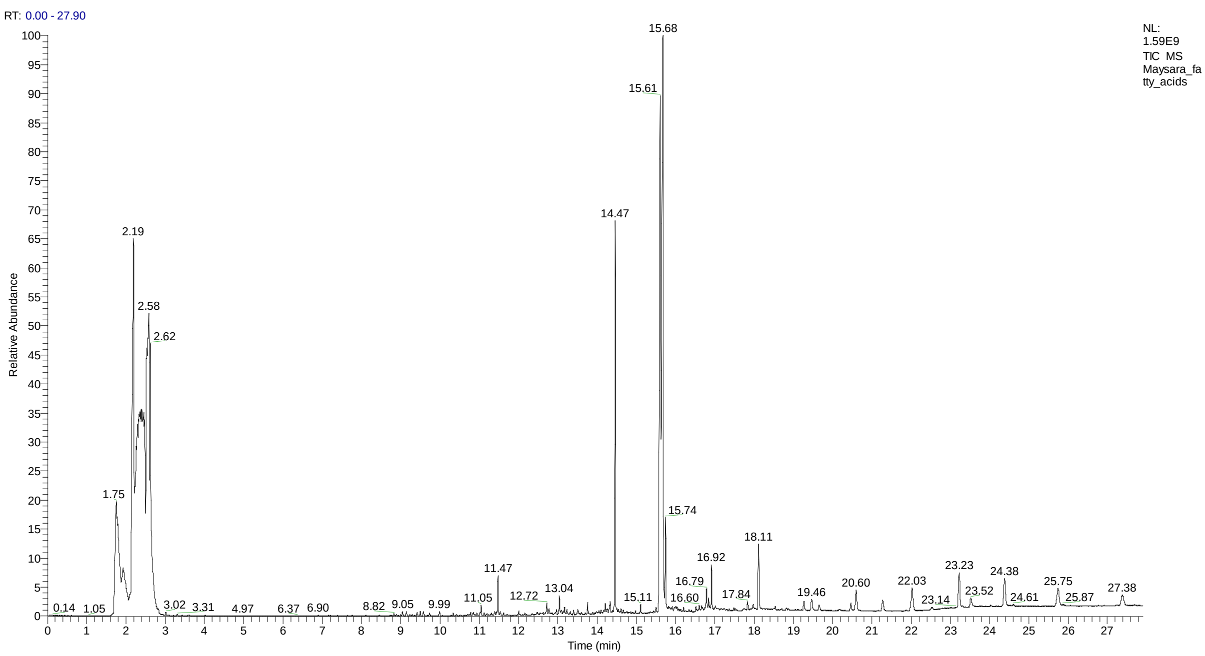
To study the effect of WS on the content of fatty acids in serum, in the first place food additive WS's fatty acid composition was studied. The results of the study are presented in fig.2. In WS saturated fatty acids are mainly represented by palmitic and stearic acids. At the same time, in the structure of fatty acids, the highest proportion is represented by linoleic (31.3%) and linolenic acids (39.8%). Consequently, a significant amount of fatty acids, including unsaturated ones, falls on the shares of linoleic and linolenic acids, which are of great physiological importance for the body (Guseva et al., 2010).

It is known that from the point of physiological effects linoleic acid is considered to be the main one. As this acid is converted in the body to arachidonic acidwhich is an important element of lipid metabolism. This occurs with A and E vitamins.

It is also known that linoleic acid belongs to the omega-6 family, and linolenic acid to – omega-3. Although the family of omega-6 and omega-3 consists of 11 polyunsaturated fatty acids (tab. 3).



Fatty acid analysis of wheat seedling

9.73 min – decanoic acid methyl ester

11.05 min – Eicosane

13.04 min. –Tetradecanoic acid

13.76 min – Pentadecanoic acid

14.34 min –9-hexanoic acid

14.47 min – palmitic acid

15.61 min – Linoleic acid

15.68 min – Linolenic acid (α-form) (omega-3)

15.74 min – stearic acid

16.52 min – 9-cis, 11-trans, 13-trans-octadecatrienoic acid

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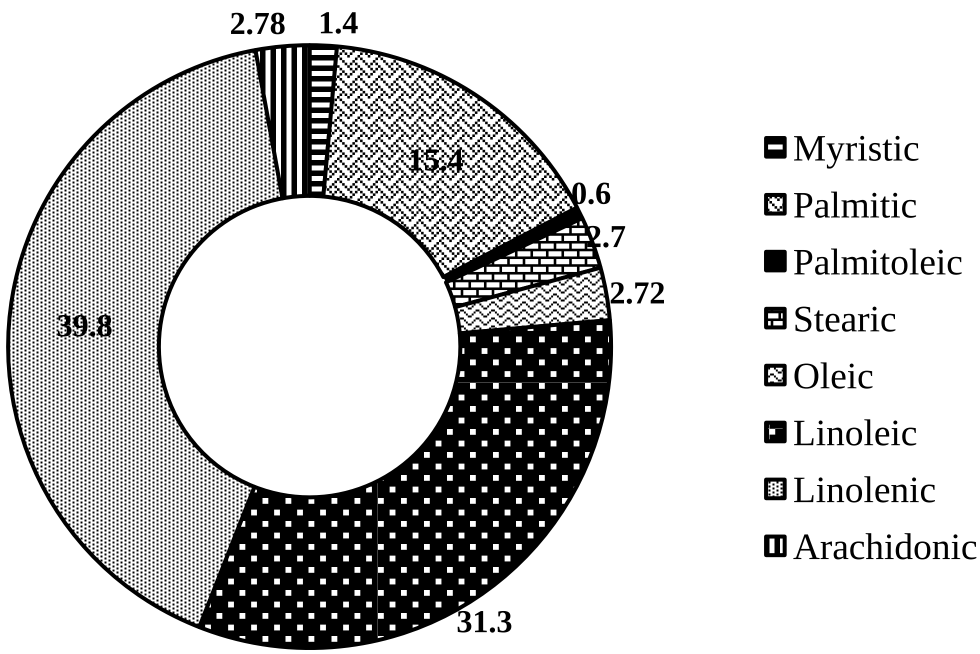
16.79 min – 10,13-eicosadiene acid

16.84 min – 6,9,12,15-docosatetraenic acid

16.92 min – Eicosanic acid



2-fig. Fatty acid composition of wheat seedling in % per 1 mg of the substance.

Table 3. Structure of the omega-6 family of polyunsaturated fatty acids

№	Name of polyunsaturated fatty acids	Chemical structure
1.	Linoleic acid	18:2ω6, *all-cis*-9,12-octadecadienoic acid
2.	γ-linolenic acid	18:3ω6, *all-cis*-6,9,12-octadecatrienoic acid
3.	Calendic acid	18:3ω6, 8E,10E,12Z-octadecatrienoic acid
4.	Eicosadienoic acid	20:2ω6, *all-cis*-11,14-eicosadienoic acid
5.	Dihomo-γ-linolenic acid	20:3ω6, *all-cis*-8,11,14-eicosatrienoic acid
6.	Adrenic acid	20:4ω6, *all-cis*-7,10,13,16-docosatetraenoic acid
7.	Docosadienoic acid	22:2ω6*all-cis*-4,7,10,13,16-docosapentaenoic acid
8.	Adrenic acid	22:4ω6, *all-cis*-7,10,13,16-docosatetraenoic acid
9.	Docosapentaenoic acid	22:5ω6, *all-cis*-4,7,10,13,16-docosapentaenoic acid
10.	Tetracosatetraenoic acid	24:5ω6, *all-cis*-6, 9,12,15,18-tetracosatetraenoic acid
11.	Tetracosapentaenoic acid	24:5ω6, *all-cis*-6,9,12,15,18-tetracosapentaenoic acid

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Table 4.Structure of the omega-3 family of polyunsaturated fatty acids

№	Name of polyunsaturated fatty acids	Chemical structure
1.	Hexadecatrienoic acid	16:3ω3, *all-cis*-7,10,13-hexadecatrienoic acid
2.	α-Linolenic acid	18:3ω3, *all-cis*-9,12,15-octadecatrienoic acid
3.	Stearidonic acid	18:4ω3, *all-cis*-6,9,12,15-octadecatetraenoic acid
4.	Eicosatrienoic acid	20:3ω3, *all-cis*-11,14,17-eicosatrienoic acid
5.	Eicosatetraenoic acid	20:4ω3, *all-cis*-8,11,14,17-eicosatetraenoic acid
6.	Eicosapentaenoic acid	20:5ω3, *all-cis*-5,8,11,14,17-eicosapentaenoic acid
7.	Heneicosapentaenoic acid	21:5ω3, *all-cis*-6,9,12,15,18-heneicosapentaenoic acid
8.	Docosapentaenoic acid	22:5ω3, Clupanodonic acid *all-cis*-7,10,13,16,19-docosapentaenoic acid
9.	Docosahexaenoic acid	22:6ω3, *all-cis*-4,7,10,13,16,19-docosahexaenoic acid
10.	Tetracosapentaenoic acid	24:5ω3, *all-cis*-9,12,15,18,21-tetracosapentaenoic acid
11.	Tetracosahexaenoic acid	24:6ω3, *ll-cis*-6,9,12,15,18,21-tetracosahexaenoic acid.

Our study of the fatty acid composition of food additives WS shows that the structure of the fatty acids found in other members of the family of omega-3 and omega-6 polyunsaturated fatty acids, such as docosatetraenoic (arachidonic acid) (omega-6), eicosapentaenoic acid (omega-3) and octadecatrienoic acid (omega -6). However, it should be noted that among them linoleic and linolenic acids have the highest specific weight. The presence in the food supplements-WS of these representatives of polyunsaturated fatty acids determines their physiological significance in the body. Indeed, polyunsaturated fatty acids have a positive effect, especially fat metabolism which accelerates the intensity of lipid oxidation. Besides, it involves detoxification of the body from toxins, supports the immune system and hormonal balance in the body. Thus, it has a positive effect on the functioning of many organs and systems, digestive, cardiovascular, endocrine, nervous, etc.

A number of studies have convincingly shown and confirmed the positive extensive effects of omega-6 and omega-3 fatty acids on human. In the metabolic processes occurring in the body, the ability of unsaturated bonds of these acids is widely used for the synthesis of many important regulatory molecules for the life of the cell and the body as a whole (Schacky et al., 2004).

In the human body, omega-3 fatty acids are involved in the formation of eicosanoids - hormone-like substances that perform a bioregulatory function. It also participates in the regulation of numerous biochemical processes occurring in the cells and tissues of the body. These polyunsaturated fatty acids are a component of the membranes of brain cells, blood vessels, heart, retina, and others. Even if omega-3 fatty acids accumulate in adipose tissue to a much lesser extent than saturated fats, they contribute to the mobilization of accumulated fats. Moreover, these acids take part in the process of energy formation; they become, like other fatty acids, the main supplier of the energy of the body. They help to reduce

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total cholesterol in the blood, increase the level of high-density lipoproteins and reduce low-density lipoproteins. Apparently, due to this mechanism in the conditions of our study, positive changes in the spectrum of blood lipids were obtained (table.2). Along with the lipid-lowering effect, omega-3 fatty acids have a beneficial effect on the coagulation system by reducing platelet aggregation, as well as increasing the flow of oxygen to the tissues and reduce hypertension. This occurs as a result of the expansion of blood vessels due to the action of eicosanoids. At the same time, due to the content of omega-3 fatty acids in the membranes of the heart muscles and nerve cells, the work of the heart and metabolism in the nervous system are more effectively carried out. This helps to reduce the risk of arrhythmia, myocardial infarction, coronary heart disease, atherosclerosis, and stroke, as well as more effective nerve impulses, which causes the normal functioning of the brain and nervous system as a whole.

Omega-6 polyunsaturated fatty acids, like omega-3 acids, also have many physiological properties. Their derivatives accelerate regenerative processes in tissues, participate in the regulation of the immune system and, most importantly, reduce cholesterol in the blood, which contributes to reducing the risk of atherosclerosis. Perhaps these effects are due to the positive dynamics in the spectrum of blood lipids, which is obtained by us in conditions of hypercholesterolemia (table 2).

Along with the presence relatively high level of polyunsaturated fatty acids, the food additive WS contains many water-soluble and fat-soluble vitamins. The structure and content of these vitamins are shown in figure 3 and 4.

As it can be seen from the figure, the food additive- WS contains a lot of representatives of vitamins. Out of the water-soluble vitamins vitamin B_9 - folic acid has the highest portion of weight, which contains more than 2/5 of the water-soluble vitamins. At that time, other vitamins from B group are almost equal in specific weight. Meanwhile, if the specific weight of Biotin – vitamin B_7 is 15.39%, then the specific weight of vitamin B_2 is 15.11%, and vitamin B_6 and B_1 are 13.84% and 12.22%, respectively. Consequently, the composition of water-soluble vitamins in the studied food additive is quite diverse and useful for physiological processes in the body. At the same time, fat-soluble vitamins are mainly represented by vitamins K, E, and A (Fig.4). Also, more than 90% of the specific weight of these vitamins is represented by vitamin K and E. It should be noted that a fairly high proportion of vitamin E is necessary for the conversion of linoleic acid into arachidonic acid. With these all, the vitamin composition of the studied product indicates its important usefulness for the body.

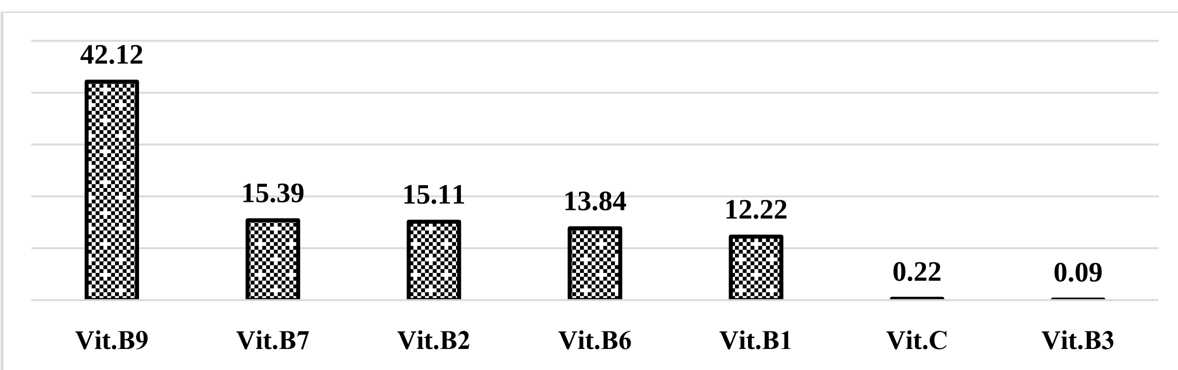

Fig.3. Structure and content (in%) of water-soluble vitamins in extracts of food additive- wheat seedling.

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Indeed, vitamin E – α-tocopherol has a hypolipidemic effect by reducing cholesterol in the blood and prevents the formation of blood clots, has a protective effect on the walls of blood vessels and contributes to the normalization of blood pressure, has a positive effect on the cardiovascular system, improves the functional state of the muscular system and significantly prevents premature aging of the human body.

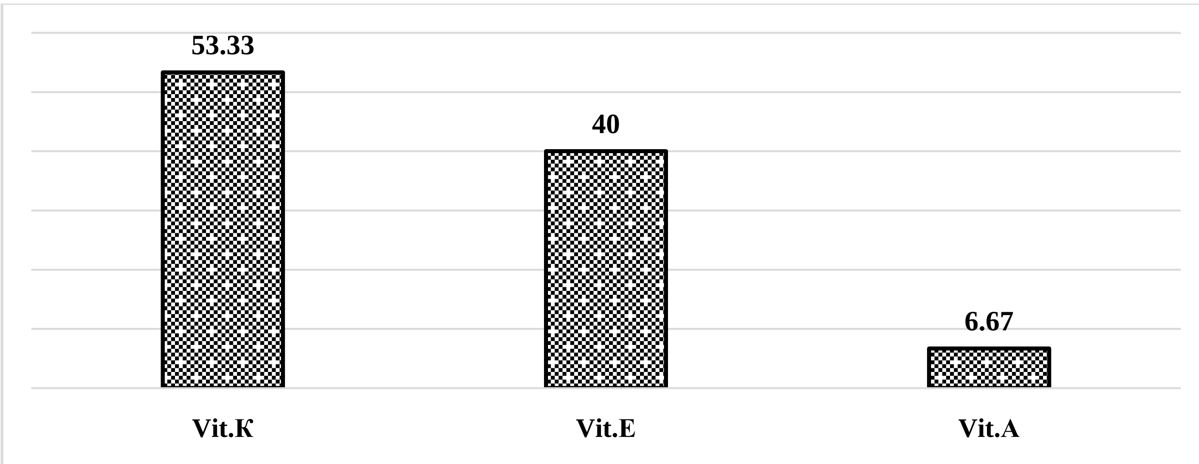

Fig.4. Structure and content (in%) fat-soluble vitamins in extracts of wheat seedling food additives.

Vitamin B_9 – folic acid, which has the highest proportion of water-soluble vitamins (fig.3). It is an active participant in the synthesis of a wide range of biologically active substances that are important for the life of cells and tissues. Folic acid in conjunction with vitamin B_{12} is involved in hematopoiesis. Vitamin B_9 plays an important role in fetal and neonatal development because it contributes to protein synthesis and the formation of new cells in children, especially during their rapid growth. It should be noted that folic acid actively participates in the reproduction of DNA that is necessary for the formation and functioning of red blood cells.

Other vitamins in the WSfrom group B also have an important role in maintaining adequate metabolism in the body. For instance, Vitamin B_1 - thiamine has a significant effect on biochemical reactions involving carbohydrates, accompanied by energy release. With age, the human body requires a significant amount of vitamin B1 regulating the process of carbohydrates conversion into energy.

Vitamin B_2 is involved in the biochemical processes of splitting proteins and the formation of enzymes that are responsible for the transfer of oxygen to tissues and organs of the body. This vitamin promotes more effective use of vitamin B_6 by the body. Riboflavin (vitamin B_2) has a positive effect on the metabolic processes occurring in the skin and hair. Furthermore, vitamin B_3 has a beneficial effect on fat metabolism, reduces the level of cholesterol in the blood, has a vasodilating effect and enhances the body's immunity. Promotes recovery in diseases of the nervous system, gastrointestinal tract, hepatitis, atherosclerosis;accelerates wound healing. Niacin together with vitamins B_2 and B_6 takes part in the formation of energy, in addition, it has a beneficial effect on the state of skin, strengthens hair and eyelashes, protects the body from anemia and reduces blood cholesterol. Likewise, Vitamin B_6 gets involved in metabolic processes, prevents nervous diseases, atherosclerosis, liver, and gastrointestinal diseases, reduces the effects of radiation sickness. This vitamin protects from anemia, prevents toxicosis in pregnant women.Apparently, the basis of the positive effects of dietary supplement- WS is not only the presence of a favorable profile of fatty acids, but also a fairly wide range of both water-soluble and fat-soluble forms of vitamins that are necessary for the life of the body.

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The results of the conducted studies on the food additive WS on the fatty acid composition of the blood of animals with hypercholesterolemia showed that there are noticeable shifts in their composition. As can be seen from the chromatograms presented, in the dynamics of treatment with this product compared to the original (Fig.5), there are significant shifts in the blood fatty acid spectrum of experimental animals. This is especially evident by the end of the second month of treatment (Fig.6).

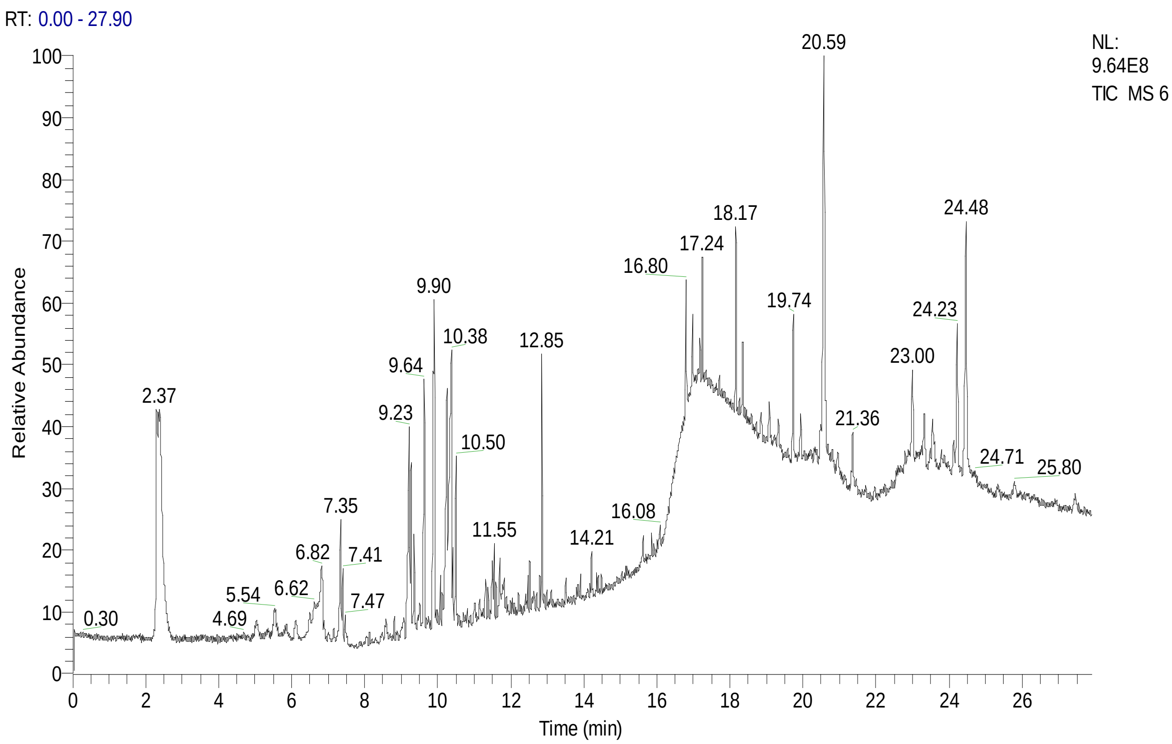

Fig.5. Fatty acid composition of the blood of experimental animals with hypercholesterolemia before the drugs used

A quantitative analysis of individual fatty acids in animals with hypercholesterolemia receiving food additives WS compared with animals that did not receive this product shows (Fig.7) that the content of saturated and monounsaturated fatty acids such as palmitic, palmitoleic, stearic and oleic acids were reduced compared to the unsaturated group of animals by 46.0%, 64.0%, 37.7% and 20.0%, respectively. Meanwhile, the content of polyunsaturated fatty acids like linoleic and linolenic acids, on the contrary, increased by 29% and 141%, respectively. Consequently, the use of food additives wheat seedling in animals with hyperlipidemia contributes to a noticeable decrease in the saturated blood content and an increase in polyunsaturated fatty acids such as linoleic and linolenic acids.

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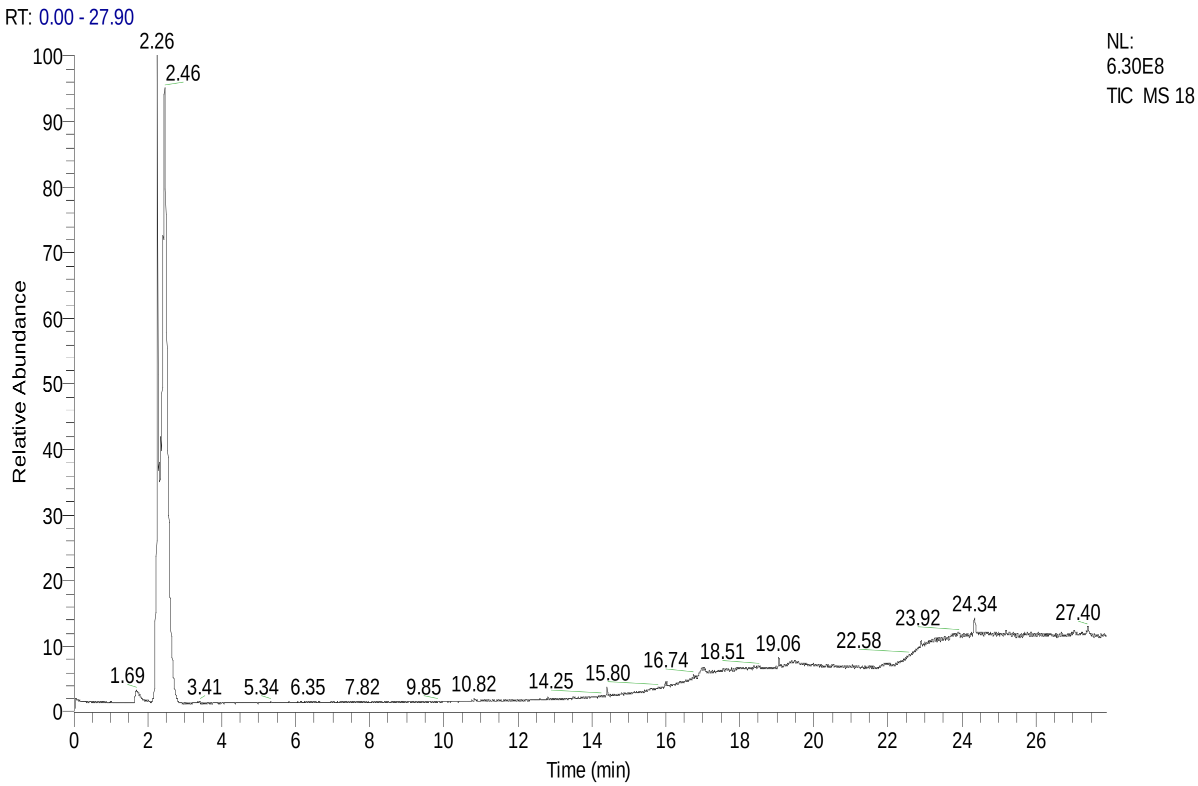

Fig.6. **Fatty acid composition of blood of experimental animals with hypercholesterolemia amid use of wheat seedling for 1 month**.

If we consider that these acids belong to the family of omega-6 and omega-3 fatty acids, it becomes obvious that they have arole in metabolism in the body as a whole, and in cholesterol metabolism in particular. Presumably, we have identified shifts in the fatty acid composition of the blood of experimental animals with hypercholesterolemia and what is the basis of positive changes in the spectrum of low- and high-density lipoproteins against the background usage of food additive- WS.

The study conducted by us with healthy individuals to study the effects of dietary supplements- WS also testified about the existence of similar picture in the fatty-acid composition of blood.

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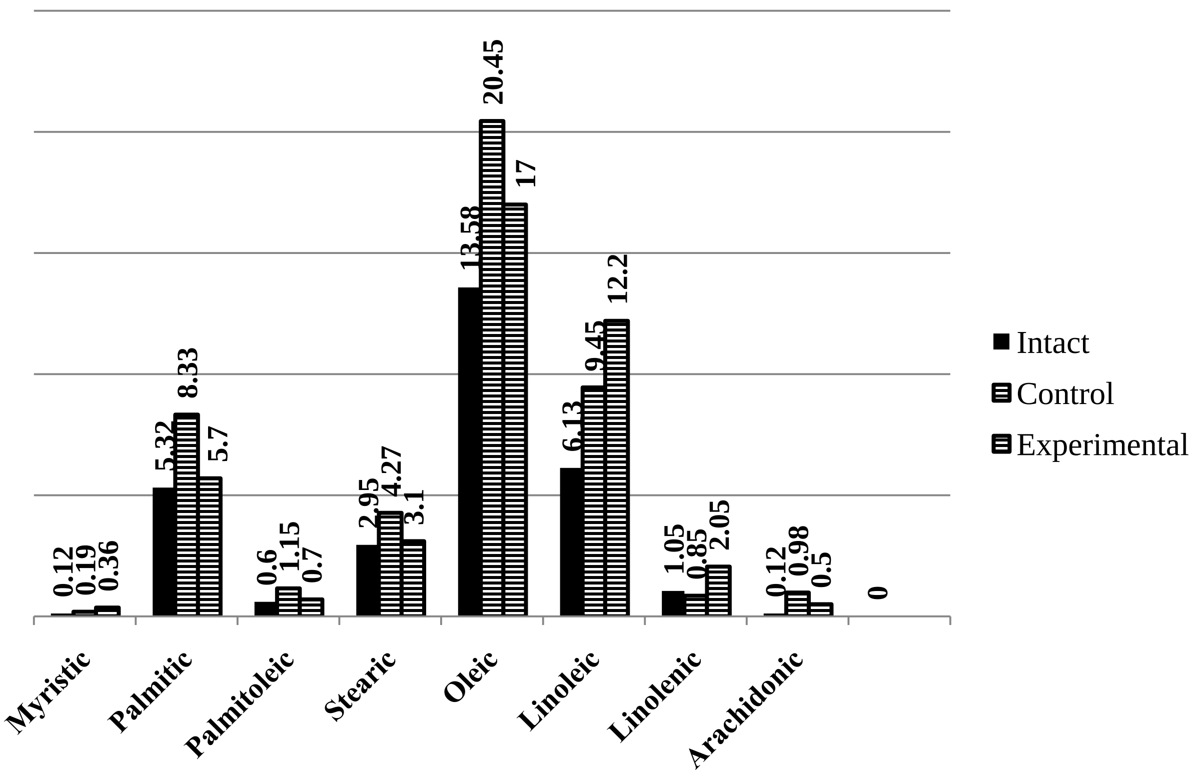

Fig.7. Comparative content of individual fatty acids in the blood of experimental animals with hypercholesterolemia during 1 month.

As can be seen from the data presented in Fig.8, the quantitative analysis of individual fatty acids in healthy individuals receiving dietary supplement-WS compared with the initial data shows that the content of palmitic acid after two months of treatment initiation is reduced by almost two times. At the same time, the content of polyunsaturated fatty acids such as linoleic and linolenic acids increases 3.5 times and 2.6 times, respectively. The content of arachidonic acid also increases (Fig.8). However, the degree is less pronounced.

Consequently, the results of the studies suggest that the product we used in healthy individuals also contributes to an increase in the blood content of polyunsaturated fatty acids, in particular linoleic, linolenic and arachidonic acids, which once again confirms the positive effect of dietary supplements of WS on lipid metabolism.

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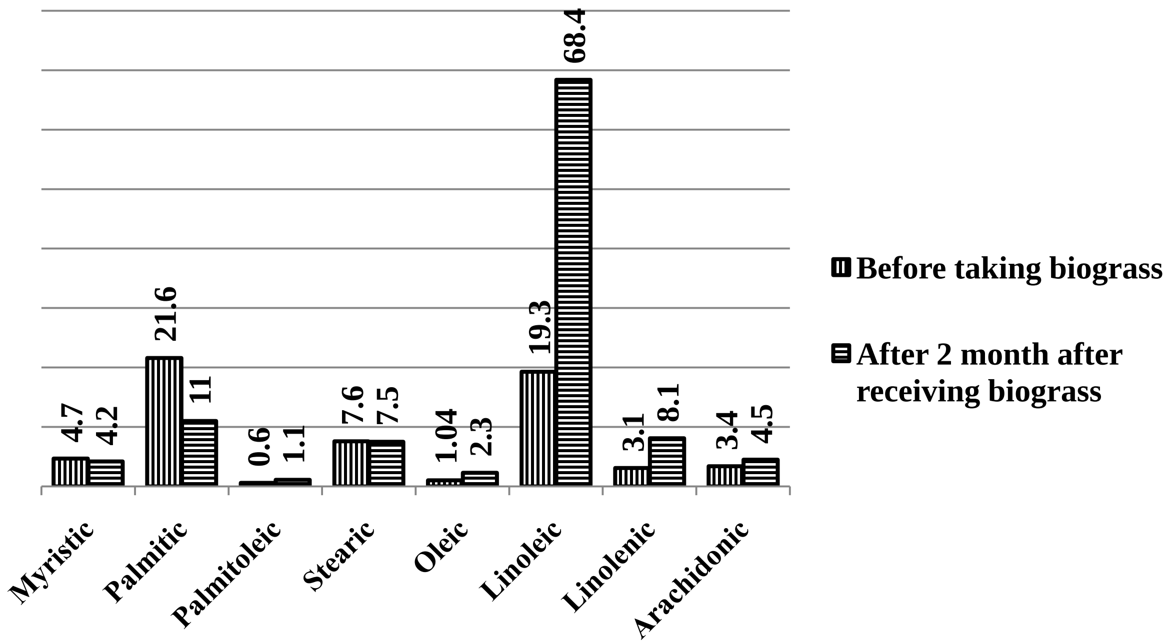

Fig.8. Comparative content of individual fatty acids in the blood of healthy individuals on the background use of biomass during 2 months.

In this way, the results of the studies suggest that the use of both the hypolipidemic drug ultrox and the dietary supplement from wheat germ- WSin animals with hypercholesterolemia have a distinct positive effect on the spectrum of high and low density lipoproteins. Also, their combined use contributes to a more significant lipid-lowering effect. Since ultrox belongs to the statins and their lipid-lowering effect is well known (Lankin et al. 2009) , the mechanism of positive action of it does not require an explanation. At the same time, a similar effect of food additive- WS remains outstanding. What mechanisms underlie the positive effect of this product on the lipid spectrum of the blood? This is due to the favorable composition of fatty acids or the presence of a fairly wide range of vitamins such as water-soluble and fat-soluble or mineral composition with the presence of a wide range of macro-and micronutrients. Outwardly, all of these, which form the basis of the natural product - wheat germ and bring us about to identify the results in relation to lipid metabolism. Perhaps there are other mechanisms contributing to the lipid-lowering effect of this product. Albeit, it is known that in wheat germ oil a valuable essential component –polycosanol was found (Arruzazabala et al., 2012).

Polycosanol is a mixture of high molecular weight aliphatic alcohols with a long chain of 20 to 36 carbon atoms. The main part of polycosanol wheat germ oil is aliphatic alcohols such as octacosanol, hexacosanol, and tetracosane. Exactly with the presence of these aliphatic alcohols, modulation of HMG-CoA reductase, absorption of bile acids and partial utilization of lactic acid are conditioned. Polycosanoland its active ingredients help to slow down the formation of cholesterol. It should be noted that these aliphatic alcohols have a targeted effect on the metabolism of low-density lipoprotein cholesterol. In this case, polycosanol increases the receptor-dependent effect on low-density lipoproteins by increasing their binding to its receptor. This results in improved transport of low-density lipoproteins to liver cells. As a result, it significantly increases the cleavage of low-density lipoprotein cholesterol. Along with a reduction in low-density lipoprotein, it has place under the action of polycosanol, increasing the level of high density lipoprotein. Moreover, these aliphatic alcohols protect low-density lipoproteins from the destructive action of free radicals. Apparently, this contributes

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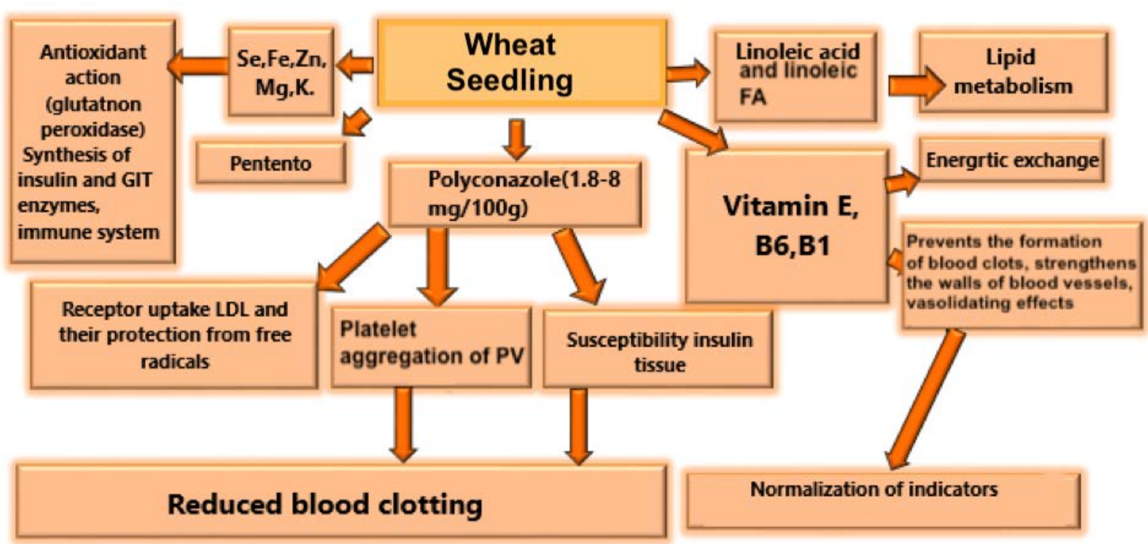
to the high content of polyunsaturated fatty acids, which act as acceptors for free radicals. All this prevents the development of atherosclerotic disorders and their consequences. The presence of such important component in the composition of wheat germ oil along with a positive effect on lipid metabolism contributes to the emergence of other positive effects such as improving tissue susceptibility to insulin, accelerating the proliferation of muscle cells, stimulation of oxygen consumption by tissues during exercise, improving neuromuscular function, reducing motor response time, increasing physical endurance, increasing glycogen stores in muscle and decreasing the symptoms of stress (Rodionova et al., 2013). In addition, oilcake and germ oil contain a high amount of pentosans - up to 10%, which are part of a wide range of ribonucleic acids, and coenzymes.

These compounds likepolycosanol, have a beneficial influence on many functions of the body (Makarov & Belyakov, 2013).

Currently, the analysis of the research results of many scientists has confirmed the high effectiveness of the wheat germ products usage for medical purposes. L. K. Dudnikova and others researched on reducing the effects of diabetes on the human body. Under the leadership of L. M. Yashinain Chelyabinsk city, lipid center conducted research on the impact of these products on the lipid spectrum in patients with hypertension and coronary heart disease. There, it was also shown that wheat germ products were effective means for the treatment of atherosclerosis and increased levels of anti-pathogenic lipid fractions, in particular, high-density lipoprotein cholesterol. Results of I. E. Trubitsina's research in the Central Research Institute of Gastroenterology (Moscow) to study the effect of wheat germ oil on the gastrointestinal tract showed that the use of even one oil approximately halves the healing time of ulcers. The use of wheat germ oil in combination with other agents significantly improved the general condition of patients and accelerated the treatment of peptic ulcer disease (Rodionova, 2013)



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IV. CONCLUSION

During the experimental HCL in the serum of rabbits, the level of atherogenic lipoproteins of LDL and VLDL increased, and the content of antiatherogenic HDL decreased, compared with intact animals. Monotherapy with ultrox at a dose of 0.5 mg/kg and WS statistically significantly reduced the levels of cholesterol and LPNP in comparison with the untreated animal group. The combined use of the drugs indicated a significant decrease in the level of LDL, VLDL. This action of WS can be associated with polycosanol. An important component of wheat germ oil is the presence of a valuable essential component – polycosanol. Polycosanol is a mixture of high molecular weight aliphatic alcohols with a long chain of 20 to 36 carbon atoms, which'sa main part is octacosanol, and also includes tetracosanol and hexacosanol. According to various reports, wheat germ oil contains from 1.5 to 8.0 mg/100 g policosanol.

The mechanism of action of polycosanol is based on modulation of HMG-CoA reductase, on the absorption of bile acids and partial utilization of lactic acid. The active components of polycosanol slow down the production of cholesterol. It is important that polycosanol has an exceptional effect on the metabolism of low-density lipoprotein (LDL) cholesterol. In particular, polycosanol increases the receptor-dependent LDL processing by increasing the binding of LDL with its receptor, improving the transport of LDL into liver cells, greatly increasing thus the breakdown of LDL cholesterol.

On the basis of these studies, a theoretical basishas been developed to give recommendations for patients with hyperlipidemic therapy who are difficult to treat statins andtreat them with a biologically active additive (BAA) of wheat seedling to reduce the dose of statins.

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Conflict of Interest

The authors declared that there is no conflict of interest.

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