JOURNAL OF ADVANCED SCIENTIFIC RESEARCH

ISSN: 0976-9595

Journal of Advanced Scientific Research (ISSN: 0976-9595)
Vol.3. Issue 1 page 8
Impactfactorsearch 8.4

Editorial Team

C/O Advanced Scientific Research,
8/21 Thamotharan Street,
Arisipalayam, Salem

Journal of Advanced Scientific Research (ISSN: 0976-9595)
Vol.3. Issue 1 page 9
Impactfactorsearch 8.4

Influence of biomays on the oxidant -antioxidant system in hypercholesterolemia

Azizova D.M. [1] , Sabirova R.A. [1] , Ishigov I.A. [2] ,Ismoilova R.[3] Isamatova E.O.[1]

[1.] Tashkent Medical Academy, Republic of Uzbekistan
[2.] International Kazakh-Turkish University named after Kh.A.Yasavi
[3] The Kimyo International University in Tashkent

Abstract: In combined treatment of rabbits with experimental hypercholesterolemia ultrax and biomaysa found a more pronounced decrease in the content of MDA on the 70th, 80th and 90th days of the experiment compared with the control group of animals, and it amounted to 25.1; 27.5 and 25.3% respectively. The content of dienes in this group of animals is reduced by 2.2; 2.3 and 2.4 times, respectively, compared to the control group. The activity of SOD after combined treatment in the indicated terms increases by 28.6; 31.4 and 15.6% compared to the control group. Compared to SOD, catalase activity increased most pronouncedly during the studied periods of the experiment compared to the control group, and it amounted to 36.8; 35.4 and 32.9% respectively. Based on the results obtained, it can be concluded that biomaysa, used in the treatment of experimental hypercholesterolemia, is able to activate the antioxidant system.

Keywords: hypercholesterolemia, free radical oxidation, wheat germ

Introduction. The study of the mechanisms underlying the processes occurring in the body in normal and pathological conditions, deciphering the molecular basis of the pathogenesis of diseases is one of the main areas of modern medicine. To date, it has been established that free radical (FR) processes play an extremely important role in the vital activity of cells, being a necessary step in various metabolic processes [**1]**. Free radical oxidation (FRO) contributes to the destruction of obsolete cells, the elimination of xenobiotics , prevents malignant transformation of cells, models energy processes by influencing the activity of the respiratory chain in mitochondria, cell proliferation and differentiation, ion transport, participates in the regulation of cell membrane permeability, in the destruction of damaged chromosomes to ensure the action of insulin. The participation of SR is necessary for the synthesis of prostaglandins, prostacyclins, thromboxanes , leukotrienes [2] . At the same time, the intensification of FR processes is one of the leading mechanisms of cellular pathology, including cardiovascular diseases, various malignant processes, autoimmune diseases, chronic inflammation, neurodegenerative diseases, and others [3,4] .

Thus, in the body of humans and animals, vitally important free radical reactions constantly occur, the rate of which is maintained at a certain level. FRO processes are under the control of the body's antioxidant system. However, with excessive generation of reactive oxygen species (ROS), due to the action of ionizing radiation, infectious agents, toxins, ischemia, and other pathological factors, the FRO process takes on a cascade character, which leads to lipid-lipid and protein -lipid disorders, uncoupling of the processes of oxidative phosphorylation and associated tissue respiration. and, as a result, to a severe imbalance of cellular metabolism [5].

Thus, the pro- and antioxidant systems are in a state of dynamic equilibrium, which is supported by a certain organization of plasma and cellular lipids, a dynamic

system for the exchange of membrane phospholipids and cholesterol, which determine the initial level of rigidity and oxidizability of cell membranes **[** 6]

Excessive activation of free radical processes entails a whole cascade of negative reactions and pathological processes that underlie a number of diseases. The damaging action of free radicals and peroxide compounds in the body is resisted by a complex multicomponent antioxidant system that provides binding and modification of radicals, prevents the formation or destroys hydroperoxides. [7].

Most studied free radical pathologies to date are atherosclerosis, coronary heart disease, arterial hypertension, in the development of which uncontrolled generation of peroxides is of great importance [8] dyslipidemia , in which atherogenic lipids contained in high concentrations in the blood serve as an easy substrate for peroxidation [9].

Recently, speaking about the mechanisms of atherogenesis , many authors attach great importance to the peroxide modification of low-density lipoproteins (LDL) - lipid-protein complexes that provide cholesterol transport to endothelial cells. In modified low-density lipoproteins, catabolism slows down, which causes the development of dyslipidemia. They acquire the ability to bind to endothelial receptors faster and transport more cholesterol to the endothelium [10]. The accumulation of peroxide-modified lipoproteins (LP) in endothelial cells , which include oxidized cholesterol, as well as the chemotactic effect of thrombin and a number of other coagulation factors activated by lipoperoxides, stimulate the migration of monocytes into the endothelium from the bloodstream and the uptake of cholesterol. Macrophages that have penetrated the intercellular spaces begin to intensively capture modified LPs, while modified LPs are captured ten times faster than conventional ones. Macrophages supersaturated with cholesterol turn into foam cells, the vast majority of which quickly die, as a result of which accumulated esterified cholesterol (ECH), non- esterified cholesterol (NECH), crystals of cholesterol monohydrate are poured into the intima, and lipid infiltration of the arterial wall is formed. The death of foam cells is facilitated by peroxides that violate the structural integrity of the cell and plasma membranes [11]. Lipoperoxides, cholesterol, platelet and fibroblast growth factors accumulated in the intima stimulate the migration of smooth muscle cells from the media, followed by their proliferation, which ultimately leads to the formation of an atherosclerotic plaque. Evidence of the dominant role of peroxide- modified LDL in the development of atherosclerosis is the fact that in experimental studies on cell culture in vitro inactivation of LDL oxidation with natural or synthetic antioxidants prevented the migration of macrophages into intima, delayed the formation of atherosclerotic plaque.

. The developments of domestic and foreign scientists have shown that complex molecular-cellular studies of the mechanism of action of herbal and domestic preparations for the treatment of atherosclerosis are of paramount importance in practical medicine in order to reduce the risk to public health . [12] The use of antioxidants (probucol) in rabbits with hypercholesterolemia also prevented the development of atherosclerosis, while LPO was inactivated both in hepatocytes and

in the vascular intima. In patients with atherosclerosis, the use of the antioxidant probucol prevented the development of restenosis after angioplasty [13].

To date, approaches to the prevention of cardiovascular complications in hypercholesterolemia remain insufficiently developed. Existing therapeutic methods do not provide full correction of lipid peroxidation processes .

Material and methods of research: Experiments were carried out on 30 male rabbits divided into 5 groups. Experimental hypercholesterolemia was reproduced by daily intragastric administration of cholesterol at 0.2 g per kg of body weight for 2 months. The first group consisted of intact animals, the second - experimental hypercholesterolemia . 3rd, 4th and 5th groups of animals were treated for 30 days . Ultrox (Nobel Farm) was used as a statin and was administered at 0.6 mg/kg. Biomaisa was administered at the rate of 142 mg/kg. Biomaisa is a wheat germ powder and was provided by ORION-SKORPION OOO .

Malonic dialdehyde (MDA) in blood serum was determined by the method of L.I. Andreeva et al . (1989). Products reacting with thiobarbituric acid were calculated from the molar extinction coefficient of malonic dialdehyde equal to 1.5 6x10 ^{5} mM $^{-1}$ cm $^{-1}$ and recalculated per mg of microsomal protein. The content of diene conjugates was determined by the method of Khyshiktuev B.S. et al . (1996). [14] The state of AOS was assessed by the activity of its main enzymes, catalase and superoxide dismutase (SOD). Catalase activity was determined by the method of M.A. Korolyuk et al . (1988) [15] , based on the ability of hydrogen peroxide to form a stable yellowish color with molybdenum salts. The intensity of staining was measured on SF-46 at a wavelength of 410 nm , the results were expressed in μat /min/mg of protein. SOD activity was determined by the percentage of reduction of nitrotetrazolium blue in an alkaline medium and expressed in conditional units per min/mg of protein by the Mirsa method . P. _ H. , Fridovich I. _ (1972) [16] . The protein content was determined by the Lowry method. O. _ H. _ et . all (1975) [17] .

Mathematical and statistical processing of the obtained data was carried out using the STATISTICA 7.0 software package. Quantitative data are presented as median (Me) and upper and lower quartiles (25%; 75%). Qualitative variables were compared using the chi-square test or Fisher's exact method . Comparison of quantitative variables with a normal distribution of a trait was carried out using the Student's t-test, and in the case of a distribution different from normal, using the Wilcoxon rank test for dependent variables and the Mann-Whitney U-test 18 for independent groups. The Kruskal-Wallis test was used to compare several independent groups . Correlation analysis using the nonparametric Spearman test and linear regression analysis were used to study the relationships between traits.

Purpose of work: To study the effectiveness of complex treatment with biomaysa and statin on the process of oxidative stress in animals with experimental hypercholesterolemia .

Results of the study and their discussion: The results of the study of LPO and AOS indicators are presented in Table No. 1.

Table №1

Changes in LPO and AOS in the dynamics of development of experimental hypercholesterolemia (n =12)

Indicators	Intact group	Study days				
		20	40	6 0	80	90
MDA (mmol/ml)	2.85±0.2	3.64±0.04	3.91 ± 0.04 _	4.07 ± 0.0 2	.3±0.04	6.1±0.02
Dienes (nmol /ml)	1.31±0.04	1.85±0.08	2.68±0.02	3.48 ± 0.24 _	4.35±0.03	5.9±0.03
COD (U /mg protein)	1.33±0.01	1.07±0.01	0.87±0.01	0.7±0.02	0.57±0.01	0.47±0.01
Catalase (mkat /mg protein)	35.45±0.59	31.4±0.45	28.03±0.04	23.3±0.7	19.4±0.5	16.1±0.93

Note: In all cases, P <0.05 in relation to the intact group

On the 20th day of cholesterol administration, the content of MDA and dienes increased by 27.7 and 41.2%, respectively, compared with the intact group. On the 40th and 60th days of the study, the content of MDA and dienes, compared with the 20th day of the study, increased by 7.4; 11.8 and 44.7; 88.1% respectively. On days 80 and 90 of the development of hypercholesterolemia, the content of MDA and dienes was significantly increased by 1.76; 2.1 and 3.3; 4.5 times, respectively, compared with the intact group.

Thus, with the development of hypercholesterolemia , the increase in lipid peroxidation depends on the timing of the study, the most pronounced increase in these indicators was established on days 80 and 90 of experimental hypercholesterolemia . These data indicate a trend towards an increase in the level of active carbonyl compounds in the body of rabbits as a result of oxidative changes.

SOD activity on days 20, 40 and 60 of experimental hypercholesterolemia decreases by 19.6; 34.6 and 47.4%, respectively, compared with the intact group. The most pronounced decrease in SOD activity was found on days 80 and 90 of the development of experimental hypercholesterolemia and it was 2.3 and 2.8 times, respectively, compared with the intact group.

Catalase activity on days 20, 40 and 60 of experimental hypercholesterolemia decreases by 11.4; 20.9 and 34.3%, respectively, compared with the intact group. On days 80 and 90 of the development of experimental hypercholesterolemia , the decrease in catalase activity was 1.8 and 2.2 times, respectively, compared with the intact group.

Thus, with the development of experimental hypercholesterolemia , the activity of enzymes of the antioxidant system decreases depending on the duration of the study. SOD activity decreases more pronouncedly compared to catalase activity. In experimental animals, the maximum severity of oxidative processes and lipid peroxidation is noted along with a decrease in the activity of antioxidant protection. The current clinical experience and the results of experimental studies indicate the important role of oxidative stress in the formation and progression of cardiovascular

pathology and the need for its early, systematic and comprehensive antioxidant correction. [9]

Treatment of experimental animals hypercholesterolemia began after the 60th day of cholesterol administration. The results of treatment with Ultrox and Biomaysa are shown in Table No. 2. The study of the results of treatment was carried out on the 70th, 80th and 90th days of the experiment and compared the data with the results of the 60th day of cholesterol administration.

Table 2

Influence of Ultrox and Biomaysa on the oxidant -antioxidant system in the development of experimental hypercholesterolemia (n =12)

group of animals	MDA (mmol/ml)	dienes (nmol /ml)	COD (U /mg protein)	catalase (mkat /mg protein)
Intact	2.85 ±0.2	1.31 ± 0.03 _	1.33 ±0.01	35.45 ±0.2
Control (60th day)	4.07 ±0.01	3.48 ±0.04	0.7 ±0.02	23.3 ±0.3
ultrox treatment				
70th day	3.46 ±0.02	1.62 ±0.01	1.15 ±0.03	29.46 ±0.02
80th day	3.45±0.01	1.75±0.11	1.1±0.04	30.11±0.95
90th day	3.81±0.02	1.8±0.13	1.2±0.01	27.15±0.35
biomaysa treatment				
70th day	3.34±0.03	1.74±0.07	1.24±0.01	26.1±0.92
80th day	3.2±0.11	1.7±0.08	1,20,08	27.88 ± 0.4
90th day	3.18±0.11	1.67±0.15	1.28±0.12	27.47±0.76
combined treatment				
70th day	3.05±0.2	1.55±0.08	1.2±0.01	31.89±0.93
80th day	2.95 ±0.01	1.49 ±0.02	1.18 ±0.01	31.56 ±0.34
90th day	2.92 ±0.02	1.46 ±0.023	1.29 ±0.24	30.91 ±0.4

Note: In all cases, P <0.05 in relation to the control group

In the treatment with Ultrox , the content of MDA on the 70th, 80th and 90th days is reduced by 15; 15.3 and 6.4%, respectively, compared with animals of the 60th day of hypercholesterolemia . During these periods of the study, the content of dienes in treated animals with Ultrox decreases by a factor of, respectively, compared with the untreated group. The activity of SOD on the 70th, 80th and 90th days of treatment increases by 1.64; 1.57 and 1.71 times, respectively, compared with the control group of animals. At the same time, the activity of catalase in these animals increases by 1.26; 1.29 and 1.16 times, respectively, compared with the control group of animals. These data indicate that Ultrox does not effectively affect the oxidant - antioxidant system in the development of hypercholesterolemia . According to Pedersen T. R.[18] Suppression of cholesterol biosynthesis by statins with a decrease in the effectiveness of antioxidant protection can lead to an increase in free radical oxidation of LDL particles, provoking atherogenic damage in the vascular

wall. The direct antioxidant effect of statins has not been established, however, there are reports in the literature about the "antioxidant" effect of statins .

In the treatment of biomaysa , the content of MDA on the 70th, 80th and 90th days of the experiment is reduced by 17.3; 21.4 and 21.9%, respectively, compared with the control group of animals. The content of dienes in the same group of animals is reduced by 2; 2.04 and 2.08 times, respectively, compared with the control group. SOD activity after treatment with biomaysa on the 70th, 80th and 90th days of the study increased by 71.42-82.5%, respectively, compared with the control group. The activity of catalase in animals of this group compared with the control group is increased by 12.01; 19.65 and 17.89% respectively .

Thus, the results of the studies showed that when correcting experimental hypercholesterolemia biomaysa , consisting of wheat germ powder, has been found to have an antioxidant effect.

With combined treatment with ultrox and biomaysa , we found a more pronounced decrease in the content of MDA on the 70th, 80th and 90th days of the experiment compared with the control group of animals, and it amounted to 25.1; 27.5 and 25.3% respectively. The content of dienes in this group of animals is reduced by 2.2; 2.3 and 2.4 times, respectively, compared to the control group. The activity of SOD after combined treatment in the indicated terms increases by 28.6; 31.4 and 15.6% compared to the control group. Compared to SOD, catalase activity increased most pronouncedly during the studied periods of the experiment compared to the control group, and it amounted to 36.8; 35.4 and 32.9% respectively.

Thus, complex treatment with the use of biomaysa against the background of standard therapy with ultrax in animals with experimental hypercholesterolemia leads to a decrease in the severity of oxidative stress and an increase in the activity of the antioxidant system than with the separate use of these drugs . The main group of drugs that can resist oxidative stress are antioxidants that inactivate free radicals and prevent their formation, are involved in the restoration of antioxidants, or drugs that have mediated antioxidant activity. The latter are not directly antioxidants, but can either activate the antioxidant system, or increase the efficiency of natural antioxidants, or prevent the oxidation of potential substrates. Based on the results obtained, it can be concluded that the biomayse used by us in the treatment of experimental hypercholesterolemia is able to activate the antioxidant system.

1.
2. I.E. Okrut , D.A. Dautova post-graduate student of the UNN N.I. Lobachevsky Nizhny Novgorod, Russian Federation Nitric oxide as an indicator of free radical oxidation activity in metabolic syndrome International scientific journal "Innovative Science" No. 8/2015 ISSN 2410-6070 1
3. Sisein EA Biochemistry of free radicals and antioxidants / EA Sisein // Scholars Academic Journal of Biosciences. - 2014. - Vol. 2, no. 2. - P. 110-118. 2/.
4. Lankin V.Z. The role of lipid peroxidation in the etiology and pathogenesis of atherosclerosis / V.Z. Lankin [et al.] // Cardiology. - 2000. - T. 7. - S. 48-57.
5. Makeeva A.V. Study of the effect of thioctic acid on free radical homeostasis in rat tissues with pathologies associated with oxidative stress : diss …. Cand. Biol. Nauk / A.V. Makeev. - Voronezh, 2007. - 203 p.]
6. Evstratova O.R., Kharitonova A.S., Lushchik M.V. THE ROLE OF FREE RADICAL OXIDATION PROCESSES IN THE DEVELOPMENT OF PATHOLOGIES // Proceedings of the VIII International Student Scientific Conference "Student Scientific Forum"
7. Golikov A.P., Boytsov S.A., Mikhin V.P. and others. Free radical oxidation and cardiovascular pathology: correction with antioxidants // Attending Doctor - 2003. - No. 4.
8. Sabirova R.A., Shukurov I.B. The role of oxidant and antioxidant systems in the development of acute pancreatitis and ways of its correction // Problems of Biology and Medicine 2022, No. 2 (135)
9. Bioradicals and Antioxidants 2016 Volume 3, No. 3 217 I.E. Okrut 1 , K.N. Kontorshchikova , D.A. Dautova EFFECT OF OZONE THERAPY ON THE CONCENTRATION OF NITROGEN OXIDE IN ARTERIAL HYPERTENSION
10. Zenkov, N.K. oxidative stress. Biochemical and pathophysiological aspects / N.K. Zenkov , V.Z. Lankin , E.B. Menshikov. - M: MAIK "Nauka / Interperiodika", 2001. - 343 s]
11. Golikov A.P., Boytsov S.A., Mikhin V.P., Polumiskov V.Yu. C Free-radical oxidation and cardiovascular pathology: correction with antioxidants. Attending physician 2003;4:70-74
12. *Lankin VZ, Tikhaze AK, Belenkov Yu. N. Free radical processes in normal and pathological conditions. - M., 2001. - 78 p .*
13. Lankin VZ, Tikhaze AK The role of oxidative stress in the genesis of atherosclerosis and diabetes mellitus: a personal view of 50 years of research. Curr asing Sci . 2017; 10(1):18-25. https :// doi.org/10.2174/1874609809666160926142640
14. I.R. Mavlyanov , R.A. Sabirova , M.U. Kulmanova , A.B. Soliev , G.Zh. Zharylkasynova "Development of new approaches to the correction of hyperlipidemia , taking into account changes in the fatty acid composition of blood serum" Health Risk Analysis 2020 No. 2, pp. 152-163.
15. Khyshiktuev B.S., Khyshiktueva N.A., Ivanov V.N. Methods for determining lipid peroxidation products in exhaled air condensate and their clinical significance. Clinical laboratory diagnostics. 1996 No. 3 S.13-15.
16. Korolyuk M.A., Ivanova L.I., Mayorova I.G., Tokarev V.E. Method for determining catalase activity//Moscow., Medicine .- P.16-18
17. Mirsa PH, Fridovich I. The role of superoxide anion in the antioxidation of epinephrine and a simple assay for superoxide dismutase. // J. Biol. Chem. - 1972. - V. 247.- №10.- P.3170-3175
18. Lowry OH, Rosenbrouch HG, Farr AL, Randall R., Protein measurement with the folin
19. Pleotropic effects of statins: evidence against benefits beyond LDL-cholesterol lowering. Am J Cardiovasc Drugs. 2010;10 (Suppl 1):10-7, https://doi.org/10.2165/1158822-S0-000000000-00000