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Change of Lipid Profile Indicators and their Correction Under Chronic Radiation in Rabbits of Different Ages

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Annotation: The article analyzes the state of the lipid profile in rabbits under the influence of chronic irradiation and provides data on the correction of the identified shifts in the lipid spectrum after using ASD as a corrector. Under the influence of chronic irradiation, it was noted that rabbits of all ages showed a statistically significant decrease in lipid profile, total cholesterol, and especially LDL compared with the intact group. It was found that after treatment with ASD, the amount of TG and HDL in rabbits of all ages approached the values of the original intact group ($p<0.05$). As a result of the treatment of ASD, it was possible to match the HDL index with the initial intact group, as a result of which a significant decrease in the CA index was achieved.

Keywords: Atherosclerosis; chronic radiation sickness, lipid profile; HDL; LDL; TG; KA; ASD.

Enter. It is known that in the era of globalization, as a result of the increase in the number of x-ray equipment and therapeutic methods in medicine, the operation of many nuclear power plants, and the increase in our need for many technologies that emit radioactive rays in our daily life, the risk of radiation poisoning is increasing. It is known that the molecular effect of radiation is that as a result of radiation's cytotoxic effect on cells, first of all, active oxygen radicals appear and cause various mutations due to cell DNA damage [12]. In this case, various enzymes are activated to repair the DNA. If the repair process fails to restore DNA for a certain period of time, the mechanisms that trigger cell apoptosis, particularly p53-induced apoptosis, are triggered [16].

As a result of exposure to radiation on the body, all organs and tissues experience light-induced alterations and dysfunctions. A positive correlation between radiation poisoning and atherosclerosis and ischemic heart disease has been proven by several studies [8, 19]. Although this situation is recognized by many scientists, the mechanism by which radiation poisoning induces atherosclerosis has not been clearly proven. There are different opinions in explaining the pathogenesis of light-induced atherosclerosis. According to some scientists (in particular, Little and his colleagues), the endothelial cells of blood vessels are altered as a result of the toxic effect of ionizing radiation, and as a result, the inflammatory process and the increased permeability of altered endotheliocytes to ZPLP and other substances create conditions for the development of radiation-induced atherosclerosis [11, 15].

On the other hand, increased non-specific immune response and hyperproduction of cytokines under the influence of radiation damage endothelial cells in many organs and tissues, including the cardiovascular system [1]. Hyperproduction of cytokines, especially inflammatory cytokines, dysfunction of endotheliocytes, changes in the expression of proteins responsible for adhesion, migration of many leuko-lymphocytes to the vascular intima, proliferation of vascular myocytes, development of many pro-coagulation factors increase the risk of developing atherosclerosis [4].

It is known that ASD biostimulant consists of sub-molecular components obtained from the breakdown of animal tissue and has a comprehensive effect on our body. In particular, it has an immunomodulatory effect on the specific and non-specific immune response, phagocytosis and the complement system, normalizes the amount of V-lymphocytes and related immunoglobulins, as well as the proportion of T-lymphocyte subpopulations [5]. In addition, according to other literature, ASD has a multifaceted effect on animals and humans, in particular, it normalizes the central and peripheral nervous system, activates cell growth and metabolism, accelerates the elimination of altered foci by strengthening regenerative and reparative processes, and improves digestion in the gastrointestinal system. the effect of regulating the activity of the cardiovascular and respiratory system organs, the effect of eliminating the general acidosis and increasing the general resistance of the body are recognized [2, 3].

Based on the above, the purpose of the work: changes in the lipid profile in rabbits of different ages under the influence of chronic radiation and correction of the observed changes with ASD.

Material and methods. For research, 150 healthy rabbits of different ages were selected and grouped by age. As a result, there are 10 in each group, namely 3 months (first group), 6 months (second group), 9 months (third group), 12 months (fourth group) and 24 months (fifth group) a group of rabbits was created. 100 rabbits of different ages were irradiated from 1 gray for 10 days. In irradiated rabbits, ASD drug was administered orally for 10 days at a dose of 1.0 ml to correct the dyslipidemia induced by radiation. Then, 24 hours after the last day of treatment, the rabbits were bled again, and serum total triglycerides, total cholesterol, ZPLP and ZYuLP cholesterol levels were measured on a MINDRAY BA-88A (China) analyzer using CYPRESS Diagnostics (Belgium) reagents. From the obtained results, the atherogenic coefficient was calculated using the formula [Kak=(total cholesterol (mmol'/l) – ZYuLP (mmol'/l))/ZYuLP (mmol'/l)]. The obtained results were statistically processed.

The obtained results and their analysis. As shown in Table 1, it was found that the amount of all parameters specific to the lipid profile in the blood serum of the first group, 3-month-old rabbits that received radiation, decreased under the influence of radiation. In particular, compared to the results of intact rabbits of the same age, total cholesterol - 1.16 ($p<0.05$); It was observed that the amount of cholesterol in ZYuLPs decreased by 1.49 ($p<0.01$) and the amount of triglycerides by 1.24 ($p<0.01$). A tendency to reduce the amount of cholesterol in ZPLPs was found. In the 6-month-old group of irradiated rabbits, the amount of total cholesterol, cholesterol in ZULPs and triglycerides decreased statistically significantly by 1.16 ($p<0.05$) compared to the parameters of intact rabbits during the same period; A decrease of 1.76 ($p<0.01$) and 1.15 ($p<0.01$) was observed. Even in this group, the amount of cholesterol in ZPLPs did not change much under the influence of light. In 9-month-old rabbits, chronic exposure to radiation was similar to the above-mentioned groups. After irradiation, the amount of total cholesterol and cholesterol in ZYuLPs in the blood serum of rabbits decreased statistically significantly by 1.19 ($p<0.05$) and 1.76 ($p<0.01$) times compared to the values of intact rabbits of the same age. In this group, the amount of cholesterol in ZPLPs, similar to the previous groups, did not change much. Unlike the previous groups, the amount of triglycerides in the irradiated animals did not differ from the values of the intact group.

Table 1 Changes in lipid indicators in rabbits of different ages compared to the results of intact rabbits under the influence of light M±m

Groups of rabbits by age	Total cholesterol (mmol'/l)	Cholesterol in ZPLPs (mmol'/l)	Cholesterol in ZYuLPs (mmol'/l)	Amount of triglycerides (mmol'/l)
Intact rabbits				
3 monthly	2,06 ± 0,023	1,25 ± 0,022	0,55 ± 0,009	0,572±0,010
6 monthly	2,29 ± 0,037	1,41 ± 0,039	0,58 ± 0,013	0,682 ± 0,009
9 monthly	2,37 ± 0,047	1,48 ± 0,020	0,51 ± 0,028	0,840 ± 0,011
12 monthly	2,42 ± 0,048	1,55 ± 0,030	0,47 ± 0,027	0,902 ± 0,020
24 monthly	2,36 ± 0,031	1,51 ± 0,022	0,40 ± 0,031	0,985 ± 0,009
Lighted rabbits				
3 monthly	1,79 ± 0,100[a]	1,21 ± 0,088	0,37 ± 0,025[a]	0,462 ± 0,060[a]
6 monthly	1,97±0,060[a]	1,36 ± 0,055	0,33 ± 0,018[a]	0,594±0,023[a]

9 monthly	2,00±0,019[a]	1,36 ± 0,015	0,29±0,008[a]	0,780±0,023[a]
12 monthly	2,04±0,040[a]	1,39±0,036[a]	0,28±0,018[a]	0,814±0,050[a]
24 monthly	1,93±0,040[a]	1,27±0,035[a]	0,26±0,020[a]	0,879±0,035[a]

Indication: a – the differences between the indicators of the intact and irradiated groups at the same age are significant, p <0.05.

As can be seen from Table 1, irradiation of 12-month-old rabbits for 10 days significantly reduced total cholesterol, low- and high-density lipoprotein cholesterol, and triglycerides by 1.19 (p<0.05); 1.12 (p<0.05); It led to a decrease of 1.68 (p<0.01) and 1.19 (p<0.05) times. And finally, exposure to light in 24-month-old rabbits compared to the indicators of conditionally healthy rabbits of the same age significantly increased total cholesterol, cholesterol in low- and high-density lipoproteins, and triglycerides in blood serum by 1.22 (p<0.05); 1.19 (p<0.05); We can observe that it decreased by 1.54 (p<0.01) and 1.12 (p<0.015) times.

So, irradiating rabbits of different ages at 1 gray for 10 days leads to a decrease in the amount of lipids in the blood serum of animals. The strongest changes in the amount of cholesterol in ZYuLPs were observed in the 9-12 months of the experiment. Decreased serum triglycerides were more common in young animals.

Accordingly, we calculated the AK using the obtained results and presented the results graphically (see Figure 1.

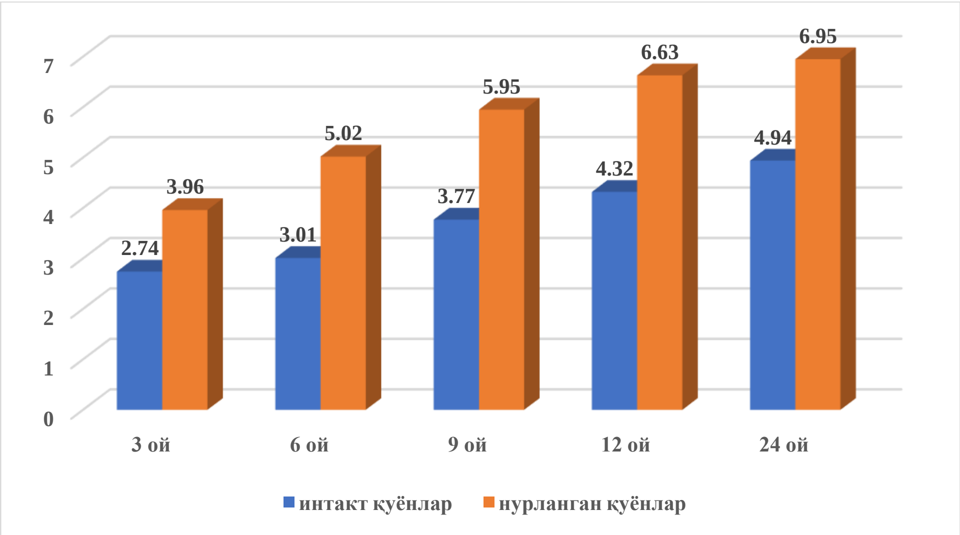

Figure 1.Dynamics of change of atherogenic coefficient in intact and irradiated rabbits of different ages.

As can be seen from Figure 1, AK was significantly increased by exposure to light at all ages. In particular, in 3-month-old rabbits, AK changed from 2.74±0.06 to 3.96±0.29 (1.4 times, p<0.05), and in 6-month-old rabbits, this indicator was 3.01±0, increased from 11 to 5.02±0.26 (1.67 times, p<0.01). And in 9-month-old rabbits, AK changed statistically significantly from 3.76±0.18 to 5.95±0.16 after light exposure (increased by 1.58 times, p<0.01). In 12-month-old rabbits, under the influence of light, AK increased 1.53 times (p<0.01) and increased from 4.32±0.21 to 6.63±0.5. And finally, in two-year-old rabbits, the amount of AK changed from 4.93±0.17 to 6.95±0.57, that is, it increased by 1.41 times (p<0.05).

Therefore, in irradiated rabbits, there is an increase in blood pressure independent of age, which indicates that they undergo atherosclerotic changes in the endothelial layer of blood vessels. Analyzing the obtained results, we can say that the decrease in the amount of cholesterol and total cholesterol in ZPLPs induced by radiation has been recognized by many studies [1, 17]. Radiation-induced hypolipidemia (hypocholesterolemia) and a sharp decrease in cholesterol in ZYuLPs, in our opinion, are related to radiation-induced liver dysfunction, and chronic radiation damage to hepatocytes causes a significant decrease in cholesterol synthesis, ZPLP and, especially, ZYuLP, and their apo-protein synthesis. may have been [9]. In particular, radiation-induced apoptosis in hepatocytes occurs as a result of radiation-induced DNA damage in hepatocytes, oxidative stress and the generation of aggressive radicals, as well as hyperproduction of cytokines [6. 13, 18]. On the other hand, as a result of chronic radiation-induced liver injury, along with the death of many hepatocytes, it initiates the proliferation of myofibroblast cells and causes liver fibrosis [6, 10]. In turn, a decrease in the amount of ZYuLP causes a violation of the normal utilization of cholesterol and ZPLP from peripheral organs, and the accumulated ZLPP increases the risk of developing atherosclerosis by causing them to be swallowed by mononuclear phagocytic cells through scavenger receptors and accumulate in the vascular intima [14]. Therefore, we can say that as a result of radiation-induced liver dysfunction, the decrease in ZYuLP concentration may be one of the main reasons for increasing the risk of developing radiation-induced atherosclerosis and ischemic heart disease.

We can see that in 3-month-old rabbits with chronic radiation sickness, ASD treatment normalized lipid parameters and approached the results of the intact group at the same age (see Table 2). In particular, with the help of ASD treatment, total cholesterol, cholesterol content in low and high density lipoproteins, and triglycerides in blood serum increased by 1.11 ($p<0.05$) compared to the untreated group; 1.06 ($p>0.05$); We observed an increase of 1.27 ($p<0.05$) and 1.09 ($p<0.05$) times. If total cholesterol and cholesterol in ZLPPs were close to the values of the intact rabbit group and did not differ from them, cholesterol content in ZYuLPs remained statistically reliable 1.18 ($p<0.05$) and 1.14 ($p<0.05$) times lower than them. Similar changes were also observed in 6-month-old rabbits: total cholesterol and cholesterol in ZYuLPs were statistically significantly increased by 1.16 ($p<0.05$) and 1.48 ($p<0.01$) times compared to the untreated group, while cholesterol and triglycerides in ZYuLPs did not affect the amount much. While the amount of total cholesterol, cholesterol and triglycerides in ZLPPs approached the norm, the amount of cholesterol in ZYuLPs remained 1.18 ($p<0.05$) times lower than them. In 9-month-old irradiated rabbits, total cholesterol and cholesterol in ZULPs were statistically significantly increased by 1.09 ($p<0.05$) and 1.31 ($p<0.01$) times compared to the untreated group, but the other lipid parameters were not significantly affected. It is worth mentioning that although positive results were observed in the treatment of ASD in irradiated rabbits of this age, total cholesterol and cholesterol in ZYuLPs were statistically significant 1.09 ($p<0.05$) and 1.34 ($p<0.01$) times lower than the values of intact rabbits. was preserved.

Table 2 Irradiated rabbits of different ages with ASD effect of treatment on serum lipid indicators, M±m

Groups of rabbits by age	Total cholesterol (mmol'/l)	Cholesterol in ZPLPs (mmol'/l)	Cholesterol in ZYuLPs (mmol'/l)	Amount of triglycerides (mmol'/l)
Intact rabbits				
3 monthly	2,06±0,02	1,25±0,02	0,55±0,01	0,57±0,01
6 monthly	2,29±0,04	1,41±0,04	0,58±0,01	0,68±0,01
9 monthly	2,37±0,05	1,48±0,02	0,51±0,03	0,84±0,01
12 monthly	2,42±0,05	1,55±0,03	0,47±0,03	0,90±0,02
24 monthly	2,36±0,03	1,51±0,02	0,40±0,03	0,99±0,01
Lighted rabbits				
3 monthly	1,79±0,10^{a}	1,21±0,09	0,37±0,03^{a}	0,46±0,06^{a}
6 monthly	1,97±0,06^{a}	1,36±0,05	0,33±0,02^{a}	0,59±0,02^{a}
9 monthly	2,00±0,02^{a}	1,36±0,02	0,29±0,01^{a}	0,78±0,02^{a}
12 monthly	2,04±0,04^{a}	1,39±0,04^{a}	0,28±0,02^{a}	0,81±0,05^{a}
24 monthly	1,93±0,04^{a}	1,27±0,03^{a}	0,26±0,02^{a}	0,88±0,03^{a}
Rabbits treated with ASD				
3 monthly	1,98±0,02^{б}	1,28±0,02^{б}	0,47±0,01^{a}	0,50±0,01^{б}
6 monthly	2,20±0,05^{a}	1,40±0,03^{б}	0,49±0,02^{a}	0,67±0,13^{б}

9 monthly	$2,17 \pm 0,02^{a}$	$1,42 \pm 0,02^{a}$	$0,38 \pm 0,01^{a}$	$0,81 \pm 0,01^{б}$
12 monthly	$2,23 \pm 0,05^{a}$	$1,42 \pm 0,03^{б}$	$0,39 \pm 0,03^{a}$	$0,91 \pm 0,02^{б}$
24 monthly	$2,05 \pm 0,03^{a}$	$1,31 \pm 0,03^{б}$	$0,30 \pm 0,01^{б}$	$0,94 \pm 0,03^{б}$

Indication: a – the differences between the indicators of the intact and irradiated groups at the same age are reliable, $p < 0.05$; b - the differences between the indicators of the treated and untreated groups are reliable.

Thus, in 12-month-old irradiated rabbits treated with ASD, the total cholesterol, cholesterol and triglycerides in ZYuLPs were statistically significant 1.09 ($p<0.05$) compared to the untreated group; An increase of 1.39 ($p<0.01$) and 1.12 ($p<0.05$) was observed. Normalization of serum lipid parameters was found in this group. Only the amount of cholesterol in ZYuLPs remained 1.21 ($p<0.05$) times lower than that of intact rabbits. Finally, treatment of 24-month-old irradiated animals with ASD did not significantly affect serum lipid parameters. We observed a statistically significant increase in the cholesterol content of only ZYuLPs by 1.15 ($p<0.05$) times compared to the values of the untreated group. Total cholesterol in the blood serum of this group, cholesterol in LPLP and ZYuLP compared to the parameters of intact rabbits is 1.15 ($p<0.05$); 1.15 ($p<0.05$) and 1.33 ($p<0.01$) times remained low.

Such positive shifts in cholesterol metabolism prevented the acute increase in AK detected in irradiated animals (see Figure 2). High AK in irradiated animals statistically significantly reduced the cholesterol content of ZYuLPs due to ASD exposure. In particular, AK in 3-month-old rabbits decreased by 1.12 ($p<0.05$) times and reached 3.27±0.1 under the influence of ASD, but remained 1.19 ($p<0.05$) times higher than the values of intact rabbits.

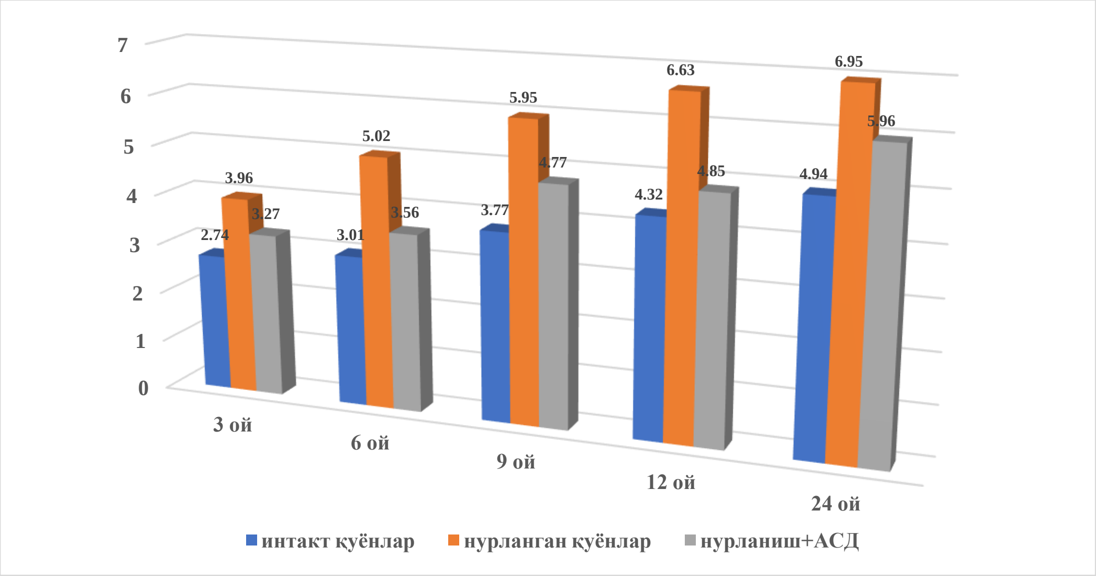

Figure 2. Effect of ASD on atherogenicity ratio in treated irradiated rabbits.

6-month-old irradiated rabbits had an AK of 5.02±0.26, after treatment with ASD, this indicator decreased by 1.42 ($p<0.01$) times and became 3.56±0.14, which is 1.3 times higher than the standard values ($p<0.05$) remained high. After treatment with ASD in 9-month-old rabbits, AK decreased by 1.24 ($p<0.05$) times and remained 4.77±0.21, 1.26 ($p<0.05$) times higher than standard values. Similar changes were observed in 12-month-old irradiated rabbits, after treatment 1.37 ($p<0.01$) times decreased to 4.85±0.31, but remained 1.12 ($p<0.05$) times higher than normal values. And finally, introduction of ASD to 24-month-old irradiated rabbits for 10 days decreased this indicator by 1.17 times ($p<0.05$) and reached 6.95±0.57. It remained 1.21 ($p<0.05$) times higher than the indicators of intact rabbits.

The obtained results showed that ASD had a positive effect on the serum lipid spectrum of irradiated rabbits. Basically, ASD has a positive effect on total cholesterol and cholesterol in ZYuLPs, bringing their amount closer to the norm. Positive changes were clearly observed in rabbits aged 6-12 months.

As mentioned above, the restorative and endurance-increasing effect of the ASD drug on the body has been proven in many studies. Therefore, ASD drug can correct the radiation-induced lipid profile imbalance in irradiated rabbits, especially by normalizing liver function and accelerating the regeneration of endothelial system, through its antiatherogenic effect. In particular, a reliable increase in the concentration of total cholesterol and cholesterol in ZYuLPs, whose concentration constant depends on liver function ($p<0.05$), indicates that the ASD drug accelerates the recovery processes occurring in the body after radiation. On the other hand, according to some scientists, ASD drug also has immunomodulatory properties [5]. Perhaps, therefore, the correcting effect of the ASD biostimulant on the lipid profile caused by radiation-induced immune dysfunction, in particular, the hyperproduction of cytokines and the acceleration of cell apoptosis, is related to its immunomodulatory effect.

Based on the obtained results, we made the following conclusions:

1. Irradiation of rabbits of different ages for 10 days at 1 gray led to a decrease in the amount of lipids in the blood serum of animals. The strongest changes in the amount of cholesterol in ZYuLPs were observed in the 9-12 months of the experiment. Decreased serum triglycerides were more common in young animals. Such changes indicate an increase in the coefficient of atherogenicity and atherosclerotic changes in the endothelial layer of blood vessels.
2. Treatment of irradiated rabbits with ASD had a positive effect on the serum lipid spectrum of the animals. Basically, ASD has a positive effect on total cholesterol and cholesterol in ZYuLPs in the blood serum of 6-12-month-old rabbits, bringing their amount closer to the norm, reducing the atherogenic coefficient.
3. In our opinion, ASD shows that there is a positive effect on regenerative and reparative processes in the body of irradiated animals.

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