J Biochem Technol (2023) 14(1): 50-56
https://doi.org/10.51847/GGLSMMHC5s
ISSN: 0974-2328

Physiological Changes in the Erythrocytes of an Aging Organism Experiencing Physical

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Received: 20 November 2022 / Received in revised form: 09 March 2023, Accepted:12 March 2023, Published online: 17 March 2023

Abstract

All aging rats included in the study had standard signs of aging. As a result of regular physical activity during 60 days of observation, the existing manifestations of aging weakened in these rats. Initially, in aging rats, the processes of lipid peroxidation in erythrocytes were enhanced due to a decrease in the activity of erythrocyte antioxidant protection. Against the background of increased physical activity in the structures of erythrocytes of aging rats, the amount of lipid peroxidation products gradually decreased and after 60 days of observation approached control level 2. In aging rats, an initially low content of erythrocyte-discocytes in the blood was found. At the same time, their blood contained an excess content of reversibly and irreversibly altered erythrocytes. As a result of regular physical activity, these indicators gradually approached the control level of 2. Initially, aging rats had a high amount of erythrocytes in the aggregates and a large number of erythrocyte aggregates with a low number of isolated erythrocytes. By the end of the experiment, these indicators in the experimental group approached levels close to control 2. Systematic feasible muscle loads were able to lead aging rats to the weakening of the existing microrheological disorders of their erythrocytes.

Keywords: Aging, Rats, Erythrocytes, Physical activity

Introduction

Aging is one of the most common phenomena in nature. It affects all structures of the mammalian body (Vakhtin, 2009). For the further development of medical science, it is necessary to continue studying the manifestations and mechanisms of aging, which can be most successfully done under experimental conditions (Klebanov *et al*., 2019). The study of various aspects of aging in different body systems is of great scientific and practical importance for the development of medicine (Bespalov *et al*., 2018).

Modern biological science is trying to study in detail the stages of the aging process, considering its main mechanisms and its course on various models (Zavalishina *et al*., 2019), taking into account the processes of formation of age-related pathology (Abualhamayel *et al*., 2021; Mikhailovna *et al*., 2021). Recently, great importance in this process has been attached to the state of functional and rheological features of blood cells and, first of all, their most numerous group, erythrocytes (Zavalishina *et al*., 2018). The importance of such observations is that aging affects the state of all systems and organs (Alghamdi *et al*., 2021; Alshehri *et al*., 2021). It is also often accompanied by a weakening of their work, the appearance of dysfunctions in them, and often an obvious pathology (Dontsov *et al*., 2010).

It has been noted that in the course of aging, primarily aggravated by obvious pathological processes, there is an increase in the functional activity of platelets, which can adversely affect other blood parameters (Vatnikov *et al*., 2018). This situation can worsen the course of microcirculation and slow down the metabolism in the cells of the whole organism. At the same time, the features of the microrheological properties of erythrocytes at the final stages of ontogenesis remain insufficiently studied (Adlan *et al*., 2021).

Rats are a very popular object of study in gerontology. This object is of particular interest since it is very often addressed by theoretical biologists and practical biologists. It is customary to find out and check various biological facts and clarify the mechanisms for the implementation of any processes in the body, including aging, with an assessment of the effectiveness of any optimizing effects on a living organism (Usha *et al*., 2019).

Concerning age-related changes in a living organism, the significant effectiveness of non-drug effects, including in the form of regular muscle loads, was previously noted (Karpov *et al*., 2020). At the same time, a decrease in the severity of several age-related disorders against their background was found earlier. In earlier clinical observations and experiments, the effect of physical activity on the functionality of platelets, including age, was established (Kulikov *et al*., 2020). At the same time, the question of the nature of the impact of regular physical activity on the dynamics of the microrheological properties of erythrocytes in an aging organism remains not fully clear. It is most convenient to

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clarify this information in the experimental conditions on rats. This information will be in great demand in the course of subsequent studies that can clarify the timing of the most scientifically based start of health effects on the aging body (Mikhaylova *et al*., 2021). In this regard, the aim of the work is to evaluate changes in the rheological properties of erythrocytes in aging rats under conditions of experimental regular muscle loads.

Materials and Methods

The work was carried out in strict accordance with ethical standards and fundamentals of humane work with laboratory animals, which are set out in the European Convention for the Protection of Vertebrate Animals that can be used in any experiments or for any scientific purposes.

The study included 88 healthy outbred male rats aged 24 months. During their lifetime, these rats did not get sick and did not participate in any experiments, acute or chronic.

Old rats were randomly divided into experimental group (45 rats) and control group 1 (43 rats). The rats that made up the experimental group for the next 60 days received regular daily physical activity carried out on a TORNEO horizontal treadmill from KETLER. This track was moving at a speed of 5m/min. Each animal was placed separately in a special section of a rectangular wooden frame installed on the surface of the treadmill. It was divided by wooden partitions into three parts. This allowed individual placement of rats on the track. During the first day, the duration of physical activity reached 1 minute. Subsequently, physical activity increased by 1 minute per day. The duration of the load was brought up to 25 minutes per day and subsequently, its duration remained unchanged throughout the entire observation.

Rats included in control group 1 were examined twice - when taken into the study and at the age of 26 months, that is, at the same time when the observation of the rats of the experimental group that experienced regular physical activity ended.

Also, 32 outbred healthy male rats were examined at the age of 3 months and made up of control group 2. They were examined twice: initially and at the age of 5 months, that is, at the same time with the completion of observation of old rats. Due to the absence of statistically significant differences between the data found in both surveys in the control group 2, the digital values in the work are represented by one figure - their arithmetic mean.

The intensity of lipid peroxidation occurring in the plasma of rats was monitored, taking into account the substances contained in it, capable of reacting with thiobarbituric acid, using the set of Agat-Med (Russia) and by the numberof acyl hydroperoxides contained in it. In all rats, the level of antioxidant activity of blood plasma was determined. The state of lipid peroxidation processes in erythrocytes was monitored by the amounts of malondialdehyde and acyl hydroperoxides in them. In their composition, using the enzymatic method with a set of reagents produced by Vitaldiagnostikum (Russia), the level of total cholesterol was determined and the content of the total level of phospholipids was determined by the amount of phosphorus present in the structures of erythrocytes with the calculation of the ratio of total cholesterol to total phospholipids. In the structures of erythrocytes, the level of activity of the catalase enzyme and the superoxide dismutase enzyme was recorded. The levels of activity of enzyme catalase and enzyme superoxide dismutase were recorded in the structures of erythrocytes.

The surface properties of the membranes of red blood cells were recorded during light-phase contrast microscopy. There were three variants of the form of erythrocytes: discocytes, reversibly altered erythrocytes, and irreversibly transformed erythrocyte forms. The ability of erythrocytes to aggregate erythrocytes was determined using a light microscope and a Goryaev camera. To do this, we took into account the number of their aggregatesand the number of red blood cells that entered into aggregation and did not start this process out of the total number of erythrocytes after their washing and resuspension.

The data obtained were processed by calculating Student's t-test and applying systemic multivariate analysis.

Results and Discussion

Initially, aging rats showed standard external signs of aging. They had to fadeand thinning of the coat, which decreased appetite and interest in the environment. As a result of regular running loads in rats of the experimental group, these signs were eliminated. These rats became similar in appearance to the rats of control group 2, differing from them only in the larger size. In control group 1, no changes in appearance were found by the end of the study.

In aging rats, high content of acyl hydroperoxides in plasma was found and reacted with thiobarbituric acid. Providing rats of the experimental group with regular exercise led to a decrease in the amount of acyl hydroperoxides in their plasma, approaching the control level and reaching 1.61±0.028 D_{233}/1 ml by the end of the observation. Plasma concentrations of products capable of reacting with thiobarbituric acid in physically exercised rats experienced similar dynamics and reached the level characteristic of control 2. The marked increase in lipid peroxidation in aging rats was possibly due to a decrease in plasma antioxidant protection. Regular running training led to an increase in the value of this indicator from 24.2±0.57% initially to 28.4±0.32% by 60 days of physical activity, which caused this indicator to approach the value of control 2 **(Table 1)**. Observation of the animals of control group 1 showed no dynamics in the levels of lipid peroxidation and plasma antioxidant protection.

In aging rats, the cholesterol content in the structures of erythrocytes turned out to be increased (up to 1.03±0.032 μmol/10^{12} erythrocytes) with a somewhat reduced amount of total phospholipids in their membranes (up to 0.64±0.027 μmol/10^{12} erythrocytes). This caused a slightly elevated erythrocyte cholesterol/total phospholipid gradient. In the group of animals that experienced regular running loads, there was a gradual decrease in cholesterol and an increase in phospholipids in erythrocytes, which led to a decrease in the ratio of erythrocyte cholesterol/total phospholipids to control level 2. In erythrocytes of rats of control group 1, throughout the entire observation, the amount and ratio of cholesterol and total phospholipids remained at baseline.

With aging in rats, an increase in lipid peroxidation was noted in erythrocytes, which was caused by a decrease in the activity of their antioxidant system. Under conditions of regular muscle loads in aging rats, the numberof acyl hydroperoxides in the structures of erythrocytes gradually decreased and after 60 days of observation reached the control level 2. The same dynamics wereexperienced during the observation period in experimental rats by the concentration of erythrocyte malonic dialdehyde, which reached by 60 days of running loads 0.90±0.018 nmol/10^{12} erythrocytes. The achieved level fully corresponded to the level in control group 2. The found changes in the level of lipid peroxidation in erythrocytes in aging rats during running loads occurred due to the dynamics of the functional capabilities of the antioxidant system of these blood cells. Its state in the work was judged by the biological capabilities of erythrocyte catalase and superoxide dismutase. In aging rats, their functionality in erythrocytes was somewhat reduced, while during exercise they reached a level close to that in control 2 due to their activation by 24.5% and 9.6%, respectively **(Table 1)**. In control group 1, the intensity of lipid peroxidation and the activity of catalase and superoxidase in erythrocytes remained without significant changes during the observation period.

Table 1. Dynamics of hematological parameters in observed rats

Registered indicators	A group of aging rats doing regular forced runs, M±m, n=45				Control group 1, M±m, n=43		Control group 2, M±m, n=32
	initial state	20 days of loads	40 days of loads	60 days of loads	initial state	condition after 60 days of observation	
Level of acyl hydroperoxides in plasma, D_{233}/1ml	1.96±0.037 p<0.01	1.84±0.024 p<0.01	1.77±0.027 p<0.05	1.61±0.028	1.94±0.032 p<0.01	2.11±0.023 p<0.01	1.56±0.023
The content of thiobarbituric acid-active products in plasma, µmol/l	4.31±0.042 p<0.01	4.05±0.036 p<0.05	3.75±0.031	3.70±0.025	4.29±0.039 p<0.01	4.48±0.041 p<0.01	3.67±0.028
Plasma antioxidant potential, %	24.2±0.57 p<0.01	25.5±0.48 p<0.05	27.3±0.34 p<0.05	28.4±0.32	24.3±0.47 p<0.01	28.8±0.33 p<0.01	29.1±0.42
Erythrocyte cholesterol level, µmol/10^{12} erythrocytes	1.03±0.032 p<0.05	0.99±0.027 p<0.05	0.96±0.029	0.92±0.022	1.03±0.029 p<0.05	1.04±0.024	0.91±0.038
The level of total erythrocyte phospholipids, µmol/10^{12} erythrocytes	0.64±0.027	0.65±0.022	0.67±0.026	0.68±0.019	0.65±0.029	0.63±0.021 p<0.05	0.69±0.020
Cholesterol/total erythrocyte phospholipids ratio	1.61±0.017 p<0.01	1.52±0.014 p<0.05	1.43±0.018 p<0.05	1.35±0.024	1.58±0.036 p<0.01	1.65±0.017 p<0.01	1.32±0.032
The number of erythrocyte acyl hydroperoxides, D_{233}/10^{12} erythrocytes	3.42±0.030 p<0.01	3.22±0.027 p<0.01	3.01±0.026 p<0.05	2.74±0.035	3.43±0.028 p<0.01	3.63±0.021 p<0.01	2.71±0.041
The amount of malonic dialdehyde in erythrocytes, nmol/10^{12} erythrocytes	1.12±0.028 p<0.01	1.05±0.021 p<0.01	0.98±0.023 p<0.05	0.90±0.018	1.14±0.036 p<0.01	1.23±0.017 p<0.01	0.88±0.027
Erythrocyte catalase activity, IU/10^{12} erythrocytes	7920.0±12.7 p<0.01	8300.0±14.3 p<0.01	8940.0±11.9 p<0.05	9860.0±12.6	7940.0±15.7 p<0.01	7870.0±9.94 p<0.01	9920.0±9.5
Erythrocyte superoxide dismutase activity, IU/10^{12} erythrocytes	1650.0±3.86 p<0.05	1710.0±4.25 p<0.05	1760.0±5.47	1810.0±5.11	1660.0±6.11 p<0.05	1630.0±5.83 p<0.05	1870.0±7.6
The content of erythrocytes-discocytes, %	72.2±0.57 p<0.01	76.5±0.43 p<0.05	79.9±0.45 p<0.05	84.6±0.36	73.0±0.52 p<0.05	71.8±0.29 p<0.01	85.1±0.53
Number of reversibly altered erythrocytes, %	18.2±0.32 p<0.01	14.9±0.30 p<0.01	12.0±0.26 p<0.01	9.6±0.19	17.9±0.41 p<0.01	18.5±0.22 p<0.01	9.3±0.26
Number of irreversibly altered erythrocytes, %	9.6±0.16 p<0.01	8.6±0.23 p<0.01	8.1±0.20 p<0.01	5.8±0.12	9.1±0.24 p<0.01	9.7±0.17 p<0.01	5.6±0.17
The total number of all erythrocytes in the aggregate, cells	48.5±0.07 p<0.01	45.1±0.04 p<0.01	41.2±0.09 p<0.05	38.1±0.06	47.9±0.12 p<0.01	49.8±0.09 p<0.01	36.5±0.09
Number of aggregates, units	12.1±0.06 p<0.01	11.0±0.05 p<0.01	9.7±0.07 p<0.05	8.7±0.08	12.3±0.10 p<0.01	13.0±0.08 p<0.01	8.5±0.10
The number of free erythrocytes, cells	220.7±0.83 p<0.05	229.3±0.72 p<0.05	237.2±0.56	246.2±0.43	222.0±0.69 p<0.05	215.3±0.57 p<0.05	251.3±0.32

Symbols: p –the significance of differences between the recorded indicators and the level in the control group 2.

In aging rats, a significantly lower content of erythrocyte-discocytes in the blood than in control 2 was noted. It reached control level 2 for 60 days of daily running loads. This was accompanied in these rats on the background of physical exertion by a decrease in the blood content of erythrocytes changed reversibly and irreversibly (up to 9.6±0.19% and 5.8±0.12%, respectively) to the control level 2. During the observation in the blood of rats in control group 1, no dynamics of the number of different forms of erythrocytes werefound. In the blood of aging rats, there was an increase in the total number of erythrocytes included in the aggregates and an increase in the content of these aggregates. This was accompanied by a decrease in the number of erythrocytes not involved in the process of aggregation. All these indicators approached the levels of similar indicators of control group 2 after 60 days of running loads **(Table 1)**. In control group 1, the indicators of erythrocyte aggregation did not have significant dynamics, experiencing only a tendency to increase.

The processing of the results obtained in the work using a systemic multivariate analysis in the observed rats made it possible to calculate the value of the pro-aggregation potential of erythrocytes and the value of the disaggregation potential of erythrocytes, to determine the degree of impact on them of all the indicators taken into account, and also to calculate the value of the total aggregation potential of erythrocytes.

In the pro-aggregation potential of erythrocytes in aging rats, the average size of the erythrocyte aggregate (Pi = 579.3), the number of erythrocyte aggregates in the blood (Pi = 481.3), the level of irreversibly altered erythrocytes (Pi = 433.6) and the total the number of erythrocytes in the aggregates (Pi=411.6). The value of the weighted average pro-aggregation potential of erythrocytes, reflecting, in general, the processes of erythrocyte aggregation in aging rats, reached 0.109. The activity of erythrocyte superoxide dismutase (Pi=526.4), the blood level of erythrocyte-discocytes (Pi=524.3), and the enzymatic activity of catalase (Pi=518.7) turned out to be very significant in the composition of the disaggregation potential of erythrocytes in aging rats. The value of the weighted average disaggregation potential of erythrocytes, which reflects the total ability of the mechanisms that inhibit aggregation of erythrocytes, in aging rats was 0.086, while the value of the total aggregation potential of erythrocytes in these rats reached 0.023.

In the pro-aggregation potential of erythrocytes in rats of the experimental group, by the end of regular physical activity, the average aggregate value (Pi=457.2), the number of erythrocyte aggregates (Pi=431.6), the level of irreversibly altered erythrocytes (Pi=389.6) and the sum of erythrocytes in the aggregate (Pi=367.8). The value of the weighted average pro-aggregation potential of erythrocytes, which comprehensively assesses the severity of the processes of realization of erythrocyte aggregation during physical exertion, in aging rats was 0.098, which was close to control group 2.

Of great importance in the disaggregation potential of erythrocytes in rats experiencing regular running loads was the content in their blood of erythrocytes with a discoid shape (Pi=612.3), as well as the enzymatic activity of catalase (Pi=596.8) and superoxide dismutase in erythrocytes (Pi=589.7). The value of the weighted average disaggregation potential of erythrocytes, which comprehensively assesses the severity of disaggregation of erythrocytes in exercised aging rats, reached 0.094 with a total erythrocyte aggregation potential of 0.004, which was close to the level of the control group 2.

In control group 1, by the end of the observation, the weight of individual indicators almost did not change, leaving the values of the pro-aggregation potential of erythrocytes (0.110), the disaggregation potential of erythrocytes (0.083) and the total aggregation potential of erythrocytes (0.027) at a level close to the outcome.

Recognizing the aging process as the result of a complex interaction between the genetic program and environmental influences, the monitored changes in the rheological properties of erythrocytes in aging rats and the attempt to influence them can be considered a very informative physiological model (Dontsov & Krutko, 2019). The aging process in rats is similar to that in other mammals, and the biological phenomena found during the aging of this living object can be transferred to other mammals with some caution (Kishkun, 2008).

Aging is accompanied by a weakening of the antioxidant activity of the blood, which leads to an increase in the molecules of acyl hydroperoxides and products capable of reacting with thiobarbituric acid, which can disrupt tissue metabolism. The intensification of lipid peroxidation processes in plasma contributes to the development of alteration of the inner lining of blood vessels and the surface of blood cells. All this is quite true for their most numerous group - erythrocytes, whose functions under these conditions can be significantly impaired (Tabeeva, 2019). This situation can be exacerbated by the development of hypoxia that occurs in rats during aging. In many respects, it is associated with membranopathies that are formed in erythrocytes, associated with an increase in the amount of cholesterol in them and a decrease in the content of phospholipids and an increase in lipid peroxidation in the erythrocyte membranes.

The emerging situation leads to the inevitable loss of a certain part of the erythrocytes of their optimal shape, which slows down the movement of their bulk through the capillaries. The upcoming changes in the structure of erythrocytes lead to an increase in the blood content of their reversibly and irreversibly disturbed forms. This led to the fact that in aging rats, the content in the blood of erythrocytes changed by echinocytosis into spheres, with the development of spines of any size on their surface, and erythrocytes changed by stomatocytosis to the shape of a unilaterally curved disc significantly exceeded that in control group 1. These forms subsequently rapidly pass into spheroechinocytes, spherostomatocytes, and spherocytes capable of rapidly degrading (Zavalishina *et al*., 2018).

The increase in erythrocyte aggregation found in aging rats is largely due to changes in the charge of the outer membrane of these cells due to the activation of lipid peroxidation as a result of the degradation of some of the negatively charged glycoproteins on it. Increased formation of reactive oxygen species in aging rats, even under standard conditions, leads to oxidative alteration of different membrane loci and disturbances in the tertiary structure of globular plasma proteins. These damages enhance the interaction of damaged plasma proteins with individual erythrocytes, facilitating the activation of their aggregation. The products of lipid peroxidation accumulating under these conditions contribute to the acceleration of erythrocyte aggregation due to obvious oxidative damage to the structures of their membranes and to an increase in the threshold of erythrocyte disaggregation due to increased binding of erythrocytes in the aggregates (Vatnikov *et al*., 2018).

The increase in erythrocyte aggregation in aging rats found in the course of the study is also caused by the effect on their surface of catecholamines, the level of which in the blood during aging, as a rule, gradually increases. This circumstance exacerbates the course of aging, contributing to the development of various age-related pathologies (Dyleva *et al*., 2023). Under these conditions, the activity of α_1-receptors increases with an increase in the function of the Ca^{2+}-calmodulin system and the inclusion of phosphatidylinositol in the activation processes inside erythrocytes. The increase in the activity of α_2-adrenergic receptors of erythrocytes is realized largely as a result of depression of adenylate cyclase in them, activation of cytoplasmic Gi proteins through agonist receptors. All this additionally enhances the process of erythrocyte aggregation due to the upcoming decrease in the level of cytoplasmic cyclic adenosine monophosphate and activation of Ca^{2+} entry into erythrocytes (Zavalishina *et al*., 2018).

An increase in the level of suspended erythrocyte aggregates in the blood of aging rats contributes to damage to the endothelial layer of their vessels, which leads to an increase in the availability of subendothelial structures for blood, activates the mechanisms of hemostasis, and slows down the movement of blood through the vessels (Zavalishina *et al*., 2019). An increasing number of aggregates in the blood disrupts the perfusion of part of the vasa vasorum. (Najim *et al*., 2023). This contributes to the inhibition of metabolism in the walls of blood vessels, leading to a significant reduction in the level of synthesis in endothelial cells of substances that have disaggregation properties.

Activation of the antioxidant protection of blood plasma and erythrocytes was very significant for improving the microrheological characteristics of erythrocytes in rats that received regular muscle loads, which caused a significant weakening of lipid peroxidation in them (Zavalishina *et al*., 2021). Under conditions of regular physical activity in aging rats, an increase in the capabilities of the plasma antioxidant system was found, leading to a decrease in the concentrations of acyl hydroperoxides and products interacting with thiobarbituric acid. The revealed weakening of lipid peroxidation in plasma can lead to an improvement in the structure of the vascular endothelium and the functioning of receptors on it and the surface of blood cells. The current situation contributes to a pronounced improvement in the parameters of erythrocyte membranes, optimizing their rheological characteristics. The increasing activity of the antioxidant defense of erythrocytes inhibited all lipid peroxidation processes in them, further improving their rheological properties (Kotova *et al*., 2017).

Running loads for 60 days in aging rats ensured the normalization of the shape of the main part of erythrocytes with a drop in the number of altered erythrocytes in their blood to the values present in control group 2. Daily physical loads had a positive effect on the structure of the membranes of the bulk of erythrocytes, apparently due to an improvement in the condition of their protein cytoskeleton. Normalization of the shape of the main part of erythrocytes can be achieved by optimizing the state of the spectrin network with the majority of erythrocytes achieving the distance between individual spectrin molecules. The activation of ATP synthesis that develops in erythrocytes occurs largely due to the weakening of lipid peroxidation, the intensification of the work of ion pumps and the normalization of the level in the cytoplasm of erythrocytes of the most significant ions: Ca^{2+}, Na^{+} and K^{+}(Karpov *et al*., 2021).

Changes in the composition of rat erythrocytes occurring against the background of a running load inevitably caused a decrease in the content of erythrocytes in the blood of animals, which have a reversibly and irreversibly changed cell shape. In aging rats that began to experience physical activity, the number of erythrocytes in the blood that reached the state of an echinocyte, that is, a sphere with spikes of various lengths and shapes on the surface, significantly decreased. Under these conditions, the process of transition of normal erythrocytes to the state of stomatitis to the disk, which has a one-sided advantage, was very pronouncedly weakened. These changes largely contributed to the significant facilitation of the movement of erythrocytes through vessels of any diameter (Vorobyeva *et al*., 2018).

Erythrocyte aggregation in aging rats that received rational physical activity for sixty days gradually returned to normal (Albhair & Bugis, 2023). This was greatly facilitated by a change in the charge level of their surface as a result of optimization of the amount of negatively charged glycoproteins on the outer part of their membrane due to a decrease in the intensity of lipid peroxidation. A significant weakening of the peroxide alteration of plasma globular proteins, capable of connecting at different ends with neighboring erythrocytes, ensured a decrease in the intensity of their aggregation. A decrease in the content of peroxidation products in the plasma composition and in the structures of erythrocytes led to an increase in their ability to disaggregate, largely due to a weakening of the erythrocyte bond in the composition of newly emerging aggregates (Zavalishina, 2020; AlHumaidi *et al*., 2022).

The inhibition of erythrocyte aggregation in aging rats during forced runs is significantly associated with a decrease in the effect of catecholamines on their structures, the concentration of which in the blood always decreases under conditions of physical exertion (Dorontsev *et al*., 2022). This also occurred as a result of a decrease in the number of α_1-adrenergic receptors on erythrocytes, which weakened the functionality of the Ca^{2+}-calmodulin system and the metabolic transformations of phosphatidylinositol. In addition, a decrease in the functional activity of α_2-adrenergic receptors causes activation of adenylate cyclase activity in erythrocytes due to the weakening of the stimulating effects of these receptors on Gi proteins. This leads to an increase in the content of cyclic adenosine monophosphate in the erythrocyte cytoplasm, inhibiting the entry of calcium ions into it and contributing to the weakening of erythrocyte aggregation (Zdravomyslova, 2022).

A decrease in the number of erythrocyte aggregates floating through the blood of physically loaded aging rats to the control level 2 provides conditions for high preservation of their intravascular endothelial lining. This minimizes the expression of subendothelial structures in the blood of these animals and significantly weakens the activity of hemostasis mechanisms in them. The current situation contributes to a significant facilitation of general hemocirculation (Yashkichev, 2018). This effect is especially important for the implementation of hemocirculation in the lumen of the vasa vasorum, which ensures a sufficient level of trophism of all cellular elements of the vascular wall and in maintaining conditions for high production of disaggregation active substances in them: nitric oxide and prostacyclin (Zavalishina *et al*., 2018).

Between 24 and 26 months of life, standard conditions of keeping with the lack of regular physical activity in rats of control group 1 were accompanied by a tendency to aggravate the initially existing hematological disorders, which was associated with the natural progression of the aging process. Developing disorders were largely caused by increased membranopathy in erythrocytes and intense damage to all their structures inside and out, intensified by lipid peroxidation. (Deisy *et al*., 2023).

Conclusion

In aging rats in the blood, a decrease in the number of erythrocytes having a discoid shape, an increase in the content of erythrocyte varieties with the reversibly and irreversibly changed structure of the membrane surface, and an increase in the severity of their ability to aggregatewasfound. In many ways, this occurs during an increase in the ratio of cholesterol to total phospholipids in the structures of erythrocytes, a decrease in the antioxidant protection of their structures, and an increase in lipid peroxidation processes in them. Systematic adequate muscle loads carried out in the form of jogging helped in aging rats to bring the microrheological parameters of erythrocytes closer to the level of these parameters in young rats .At the same time, in aging rats, a decrease in the number of erythrocyte aggregates and the number of individual cells involved in them developed in the blood to a level characteristic of young animals (Mustarichie & Saptarini, 2023). This suggests that conditions are created in aging rats under conditions of physical exertion to minimize injury to the endothelial lining of blood vessels, which leaves their subendothelial structures inaccessible to blood and keeps the activity of hemostasis at a low level. The information established in the course of the study gives grounds to draw the attention of biologists working with older mammals to the high optimizing potential of feasible physical activity for microrheological disorders that appear during aging (Deana *et al*., 2022; Feghhi *et al*., 2023).

Acknowledgments: The team of authors thanks the administration of the Russian State Social University for the opportunity to research its basis.

Conflict of interest: None

Financial support: None

Ethics statement: The study was approved by the local ethics committee of the Russian State Social University on September 15, 2018 (protocol №11).

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