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STUDY OF THE EFFECT OF IMMOBILIZATION STRESS ON ERYTHROCYTE MEMBRANES

This article discusses the effect of acute and chronic immobilization stress on erythrocyte membranes. The intensive development of science and technology has brought into human life, along with positive phenomena, a number of unfavorable factors: hypodynamia, excessive nervous, physical exertion, professional and household stresses. Among them, hypodynamia is a lifestyle characterized by a decrease in motor activity, which negatively affects human health. This is a common situation nowadays. Hypodynamia leads to metabolic and energy disorders in the body, cardiovascular diseases, diseases of the gastrointestinal tract, overweight, early aging, a decrease in the body's ability to resist various diseases, changes in the general condition of the body, etc. Such a stressful effect is observed at the cellular and molecular level. As stress increases, metabolic disorders appear, activation of free radical oxidation leads to disruption of the main: barrier, receptor, catalytic functions of biological membranes. As a result, it leads the human body to various pathological conditions. Currently, more attention is being paid to an integrated approach to the treatment and prevention of diseases. This article discusses the effect of acute and chronic immobilization stress on erythrocyte membranes. As a result of the research, it was found that the effect of immobilization stress leads to a decrease in the osmotic and peroxide resistance of erythrocytes and an increase in the hemoglobin yield. The use of vitamin E reduces the damaging effect of both acute and chronic immobilization stress. Consequently, antioxidants can protect the body from the damaging effects of stress factors.

Key words: erythrocyte membrane, acute and chronic immobilization stress, hemolysis, vitamin E.

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Эритроцит мембраналарына иммобилизация стресінің әсерін зерттеу

Бұл мақалада эритроцит мембраналарына жедел және созылмалы иммобилизация стресінің әсері қарастырылған. Ғылым мен техниканың қарыштап дамуы адамзат тіршілігіне жағымды құбылыстармен бірге бірқатар қолайсыз факторларды, яғни гиподинамия, шектен тыс жүйке, физикалық жүктемелерді, кәсіби және тұрмыстық күйзелістерді енгізді. Осылардың ішінде гиподинамия қимыл белсенділігінің төмендеуімен сипатталатын, адам денсаулығына кері әсер ететін өмір салты болып табылады. Бұл қазіргі кезде кең таралған жағдай. Гиподинамия организмдегі зат және энергия алмасудың бұзылуына, жүрек-тамыр ауруларына, асқазан-ішек жолдарының ауруларына, артық салмаққа, ерте қартаюға, организмнің әртүрлі ауруларға қарсы тұру қабілетінің төмендеуіне, организмнің жалпы күйінің өзгеруіне және т.б. әкеледі. Мұндай стресс әсері клеткалық және молекулалық деңгейде байқалады. Стресс артқан сайын метаболизмдік ауытқуларды тудырады, бос радикалдардың тотығуының активтенуі биологиялық мембраналардың негізгі: тосқауылдық, рецепторлық, каталитикалық қызметтерінің бұзылуына әкеледі. Нәтижесінде әртүрлі патологиялық жағдайлар пайда болады. Қазіргі уақытта ауруларды емдеу мен алдын алудың кешенді тәсіліне көбірек көңіл бөлінуде. Бұл мақалада эритроциттердің мембраналарына жедел және созылмалы иммобилизациялық стресстің әсері қарастырылады. Зерттеу нәтижесінде иммобилизациялық стресстің эритроциттердің осмостық және асқын тотықтық төзімділігін төмендететіні және гемоглобиннің босап шығуын жоғарылататыны анықталды. Е витаминін қолдану жедел және созылмалы иммобилизациялық стресстің зиянды әсерін төмендетеді. Сондықтан антиоксиданттар организмді стресс факторларының зиянды әсерінен қорғай алады.

Түйін сөздер: эритроцит мембранасы, жедел және созылмалы иммобилизациялық стресс, гемолиз, Е-витамині.

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Изучение влияния иммобилизационного стресса на мембраны эритроцитов

Интенсивное развитие науки и техники внесло в жизнедеятельность человечества наряду с положительными явлениями ряд неблагоприятных факторов: гиподинамию, чрезмерные нервные, физические нагрузки, профессиональные и бытовые стрессы. Среди них гиподинамия – образ жизни, характеризующийся снижением двигательной активности, что отрицательно сказывается на здоровье человека. Это распространенная ситуация в наше время. Гиподинамия приводит к нарушениям обмена веществ и энергии в организме, сердечно-сосудистым заболеваниям, заболеваниям желудочно-кишечного тракта, избыточному весу, раннему старению, снижению способности организма противостоять различным заболеваниям, изменениям общего состояния организма, и т.п. Такое стрессовое воздействие наблюдается на клеточном и молекулярном уровне. По мере нарастания стресса появляются метаболические нарушения, активация окисления свободных радикалов приводит к нарушению основных: барьерной, рецепторной, каталитической функций биологических мембран. В результате возникают различные патологические состояния. В настоящее время все больше внимания уделяется комплексному подходу к лечению и профилактике заболеваний. В данной статье рассматривается влияние острого и хронического иммобилизационного стресса на мембраны эритроцитов. В результате исследований установлено, что действие иммобилизационного стресса приводит к снижению осмотической и перекисной резистентности эритроцитов и увеличению выхода гемоглобина. Применение витамина Е снижает повреждающее действие как острого, так и хронического иммобилизационного стресса. Следовательно, антиоксиданты могут обеспечить защиту организма при повреждающем действии стрессовых факторов.

Ключевые слова: мембрана эритроцитов, острый и хронический иммобилизационный стресс, гемолиз, витамин Е.

Introduction

The scientific and technological revolution, together with progressive phenomena, introduced into the life of mankind a number of stress factors, primarily hypodynamia, excessive nervous loads, professional and domestic stress, unfavorable environmental, social, economic, conditions, disorders of a healthy lifestyle, etc. [1]. Hypodynamia, or hypokinesia, is a limitation of the general motor activity of the body due to the peculiarities of lifestyle, professional (employees of banking, office, administrative and managerial, public service centers) activities, distance education and services, weightlessness of a person in space [2, 3]. Conditions of forced state of the body during work, local physical exertion, monotony of activities or conditions, daily use of transport and irrational Organization of rest lead to hypodynamia. It is a very common condition that is observed in many people [4-6]. Some researchers claim that now physical activity has decreased 100 times compared to past centuries.

It should be noted that hypodynamia does not damage only one organ in isolation, it is the cause of several disorders, diseases that strengthen each

other in the body: diseases of the cardiovascular, gastrointestinal tract, overweight, premature aging, a decrease in the body's ability to resist various diseases, a change in the general state of the body, etc. [7, 8].

Under the influence of a very strong and long-acting stimulus, the body's stress response turns from a general adaptation syndrome into a factor of pathogenesis. As the stress effects increase, regardless of the type of stressor, there is a violation of the vegetative and humoral balance, which is observed due to fluctuations in various processes of tissue metabolism: a violation of biological oxidation and the accumulation of reduced compounds, a decrease in the activity of the antioxidant system, a lack of energy resources [9-13]. Energy deficiency, in turn, causes secondary metabolic shifts, that is, the activation of free radical oxidation in the cell. It leads to a violation of the main functions of biological membranes: barrier, receptor, catalytic [14, 15]. As a result, functional and structural damage to tissues and organs occurs, which leads to a decrease in the quality of life, loss of ability to work, disability. Currently, more and more attention is paid to an integrated approach to the treatment and Prevention of diseases. Antioxidants are of

great importance for the human body [16, 17]. Their effective use makes it possible to avoid a number of pathological processes [18].

In this regard, the use of antioxidants in the prevention of membrane-damaging effects of stress factors is one of the most pressing problems. The purpose of the research work is to determine the effects of immobilizing stress on the erythrocyte membrane and the effectiveness of vitamin E (or γ -tocopherol) in increasing the body's resistance to the stress factor.

Materials and Methods

Physiological and biochemical properties of erythrocytes of adult laboratory rats weighing 200 ± 20 g were studied *in vitro* in order to achieve the set goals and objectives.

In the research work were used methods of red blood cell division, determination of osmotic fragility of erythrocytes (OFT), peroxide-erythrocyte hemolysis [19].

Experiments were performed on 20 animals in 3 groups in the research part. Animals of Group 1-group exposed to acute immobilizing stress (4 individuals: 2 Control, 2 experience versions); animals of Group 2 – group exposed to chronic immobilizing stress (8 individuals: 2 Control, 6 experience versions); Group 3-group exposed effect of vitamin E on group animals (8 individuals: 2 Control, 6 Experience versions) subjected to chronic immobilization stress was studied. Rats of experimental groups were exposed to stress factors. Immobilizing stress (is) was created by placing rats in specially designed pens.

The animals of group 1 were immobilized once a day for 3 hours in a specially designed pen to induce acute immobilization stress.

Group 2 animals were subjected to a 15-day experiment to induce chronic immobilization stress. On the 1st day of the experiment, the animals were placed in a specially made pen for 5 minutes, on the 2nd day for 15 minutes, on the 3rd day for 20 minutes, on the 4th day for 30 minutes, and on the 5th-15th day for 60 minutes. In the experiments, indicators of the effect of stress on 1, 7, 15 days were determined.

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In experiments on increasing the resistance of animals of the 3rd group to the effects of chronic immobilization stress, 6 rats were injected with the biologically active substance of vitamin E before stress exposure. 10 mg of E-vitamin per 100 g of animal body weight (15 days) were taken into account. From the next day, the animals were subjected to chronic immobilization stress factor.

Statistical processing of the results was carried out by calculating the arithmetic mean, standard deviation and error of the arithmetic mean using the Microsoft Excel program. Taking into account the Fisher-Student test, the registered changes in indicators were considered significant at $p \leq 0.05$.

Results and Discussion

Currently, changes in the structure and functions of the membrane are considered as the main universal type of damage under the adverse effects of stress factors, as well as in the pathogenesis of various diseases [20]. Data on changes in the permeability of erythrocyte membranes can be considered as indicators of the permeability of the membranes of the body as a whole. One of the methods for studying the permeability of erythrocyte membranes is to determine their osmotic resistance.

On fig. 1 shows the effect of the acute immobilization stress factor on the osmotic resistance of erythrocytes. Osmotic resistance (tolerance) of erythrocytes was determined by osmotic hemolysis. The level of hemolysis in a concentrated solution of 0.1 g/100 ml Na_2CO_3 was calculated as 100% and the osmotic resistance of erythrocytes in solutions of 0.35-0.9 g/100 ml NaCl was determined. With an increase in the concentration of the solution, the level of hemolysis of erythrocytes decreased, and their resistance increased. In the results of studying the effect of stress factors on the osmotic tolerance of erythrocytes, the rate of hemolysis in a solution of 0.35 g/100 ml of sodium chloride was clearly observed and compared with a solution of 0.45 g/100 ml.

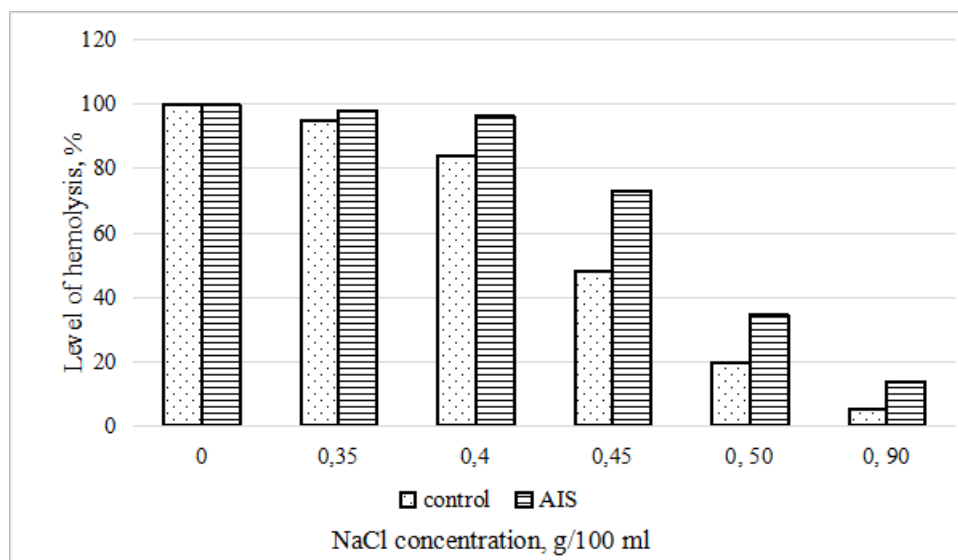


Figure 1 – Effect of acute immobilization stress (AIS) on osmotic hemolysis of erythrocytes

The level of hemolysis of erythrocytes in a 0.35 g/100 ml solution of sodium chloride was 98.1%, in a solution of 0.45 g/100 ml it was 73.2%, the level of hemolysis rate reduced by 24.9%. And was found that this indicator in sodium chloride solution of 0.90 g/100 ml showed 13.9% and reduced the degree of hemolysis by 84.2%. This can be explained as follows: under the influence of unfavorable factors, the double-layer structure of the erythrocyte membrane is disturbed, phospholipids are oxidized, as a result, the permeability of the membrane changes, and the release of hemoglobin from erythrocytes increases. Under the influence of various stress factors, tissue cells of many organs, as well as erythrocyte membrane undergo structural and functional changes.

Figure 2 shows the results of research on the determination of the peroxidation tolerance of animal erythrocytes during acute immobilization stress. The level of hemolysis of erythrocytes of control and experimental group animals increased as H_2O_2 concentration increased.

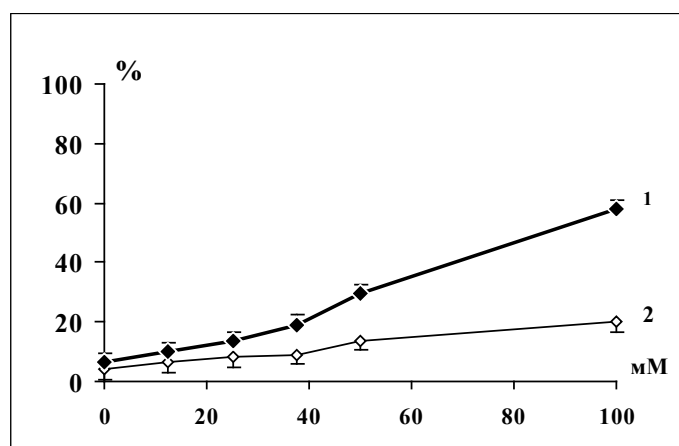
Hydrogen peroxide (H_2O_2) is an active form of oxygen, like superoxide anion radical ($\cdot O_2^-$) and hydroxyl radical ($\cdot OH$). The formation of the active form of oxygen, which is considered a stronger oxidant than the oxygen molecule, is the basis of the lipid peroxidation process [21-23]. Currently, lipid peroxidation processes are considered as the main mechanisms of cell membrane structure damage not only in various pathological conditions,

but also under the influence of extreme factors [24, 25].

According to the results of the experiments conducted to determine the hyperoxidation tolerance of erythrocytes, acute immobilization stress increased hemolysis of erythrocytes. It may be the result of increased rate of peroxidation of membrane phospholipids during stress on the body.

At a concentration of 12.5 mm of H_2O_2 solution, erythrocyte peroxide hemolysis in the control sample was 6.28%, in the AIS sample-10.12%, and the degree of hemolysis increased by 3.84%. In the control sample at a concentration of 100 mm of solution, it can be seen that the erythrocyte peroxide hemolysis was 19.87%, while in the AIS sample it was 58.20%, increasing the peroxide hemolysis by 3 times.

So, the results of our research showed that acute immobilizing stress leads to damage to the red blood cell membrane, as a result of which the release of hemoglobin from red blood cells increases, and therefore the resistance of red blood cells decreases. A decrease in the resistance of the membrane under the influence of stress factors is associated with the course of pathological reactions in the cell. Violation of the structure of the membrane can occur due to the rapid breakdown of its constituent parts, i.e. lipids and proteins, due to lack of energy, a decrease in the formation of membrane proteins and lipids, and an increase in free radical oxidation of cell membrane lipids.



Abscissa axis: H₂O₂ concentration, mM. 1 – AIS, 2 – control. Ordinate axis: level of hemolysis, %.

Figure 2 – Effects of acute immobilization stress (AIS) on peroxidative hemolysis of erythrocytes

Experiments to determine the effect of chronic immobilizing stress factors on the osmotic resistance of red blood cells were depicted in Figures 3, 4. The osmotic resistance (resistance) of red blood cells was determined by osmotic hemolysis. The hemolysis rate in a solution with a concentration of 0.1 g/100 ml of Na₂CO₃ was calculated as 100% and the osmotic resistance of red blood cells in solutions of 0.35-0.9 g/100 ml of NaCl was studied. The effect of chronic immobilizing stress lasted for 15 days, as described in the research method. To determine the effect of stress, test indicators for the 1st, 7th and 15th day were taken.

Figure 3 shows the effects of 1 and 7 daily stress. In sodium chloride solutions of 0.35 g/100 ml, the level of hemolysis was 94.8% in the control group, 95.2% on the 1st day of chronic immobilization stress (CIS), and 96.9% on the 7th day of the SIS. And, in 0.45 g/100 ml solutions, the level of hemolysis was 48.1% in the control group, 58.9% on the 1st day of CIS, and 64.9% on the 7th day of CIS. That is, the rate of hemolysis increased by 1.5-2 times in 0.35 g/100 ml sodium chloride solution compared to 0.45 g/100 ml solution.

During the study of the effects of 1 and 15 days of stress, this pattern was observed (Figure 4). It was found that as the concentration of the solution increases, the level of hemolysis decreases and, accordingly, the tolerance of erythrocytes increases.

As the duration of exposure to the stress factor increased, the level of hemolysis of erythrocyte membranes increased accordingly, and on the 15th day, compared to the 1st day, it had a significant

harmful effect. As a result, it was observed that the stability of erythrocyte membranes decreased.

The next stage of our experimental work was to determine the peroxide resistance of animal erythrocytes during the effects of chronic immobilization stress. The results of the study are shown in Figures 5 and 6. Chronic immobilization lasted 15 days, as described in the method for studying the effects of stress. In order to determine the effect of stress, test results were obtained on 1, 7 and 15 days.

As shown in the figures, the peroxidic hemolysis of erythrocytes at a low concentration of hydrogen peroxide (H₂O₂) was 8.6% in the control group, 9.8% on the 1st day of chronic immobilization stress (CIS), 13.2% on the 7th day, and 17.2% on the 15th day. Compared to the control group, it was found that on the 1st day of SIS, peroxidic hemolysis increased by 1.2%, on the 7th day by 3.4%, and on the 15th day by 8.6%.

At a high concentration of H₂O₂, erythrocyte superoxide hemolysis was 17.2% in the control group, 27.1% on the 1st day of SIS, 30.9% on the 7th day, and 60.5% on the 15th day. Compared to the control group, peroxidase hemolysis increased by 9.9% on the 1st day of SIS, on the 7th day by 13.7%, and on the 15th day by 33.4%. The level of hemolysis of erythrocytes of control and experimental group animals increased as the H₂O₂ concentration increased. The results of the experiments showed that depending on the duration of exposure to stress, the resistance of membranes decreases.

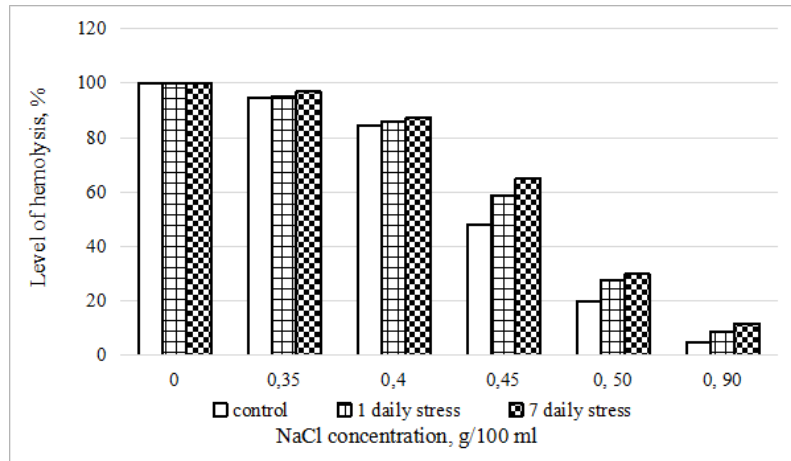


Figure 3 – Effect of chronic immobilization stress (AIS) on osmotic hemolysis of erythrocytes

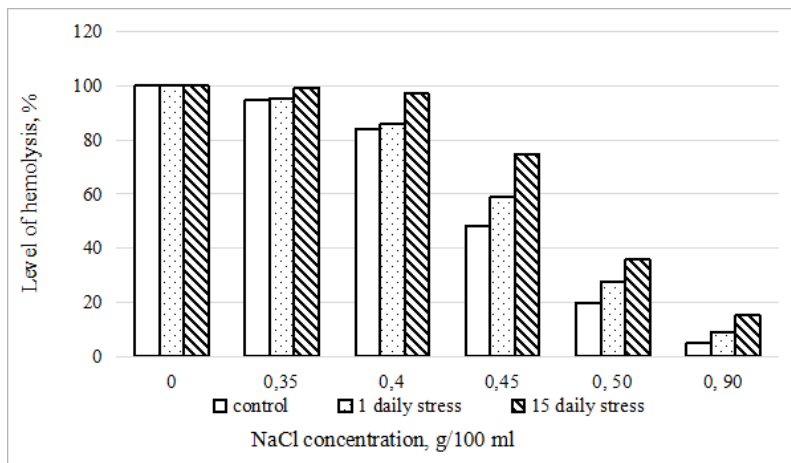
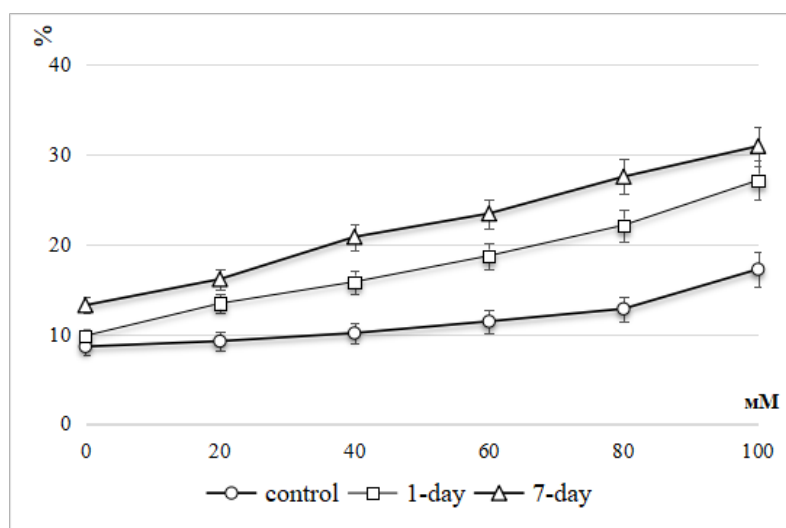
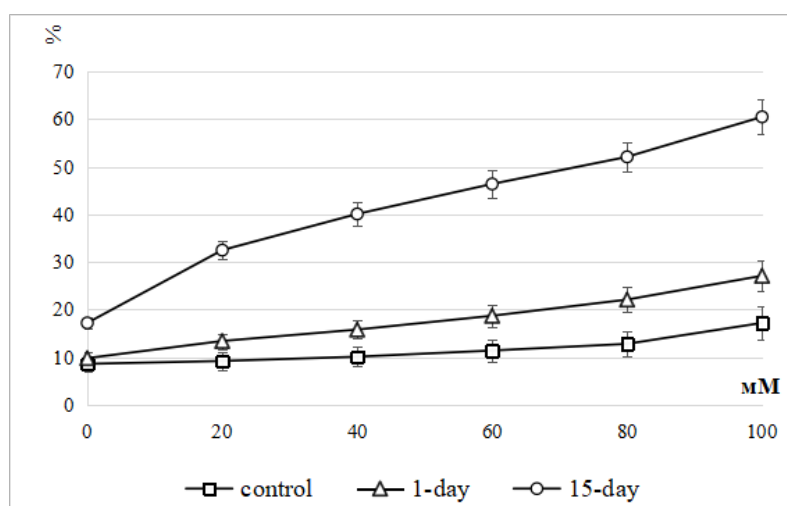


Figure 4 – Effect of chronic immobilization stress on osmotic hemolysis of erythrocytes



Abscissa axis: H₂O₂ concentration, mM. Ordinate axis: level of hemolysis, %.

Figure 5 – Peroxide hemolysis of erythrocytes in chronic immobilization stress effect



Abscissa axis: H₂O₂ concentration, mM. Ordinate axis: level of hemolysis, %.

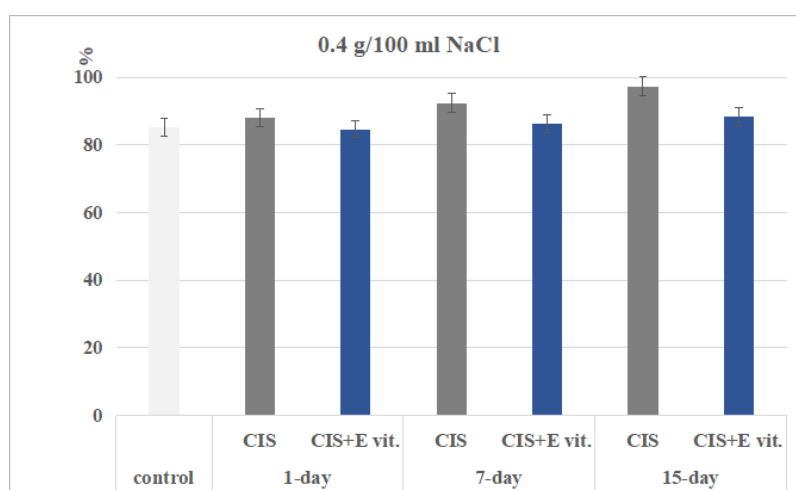
Figure 6 – Peroxide hemolysis of erythrocytes in chronic immobilization stress effect

Figures 7 and 8 show the indicators obtained from research experiments on the possibility of increasing the osmotic stability of the erythrocyte membrane with vitamin E or α -tocopherol under the influence of chronic immobilization stress.

In general, it is known that vitamin E (α -tocopherol) has membrane-stabilizing, antioxidant properties and reduces oxidative hemolysis of erythrocytes caused by free radicals. It is due to this property that α -tocopherol increases the tolerance of the erythrocyte membrane to the stress factor.

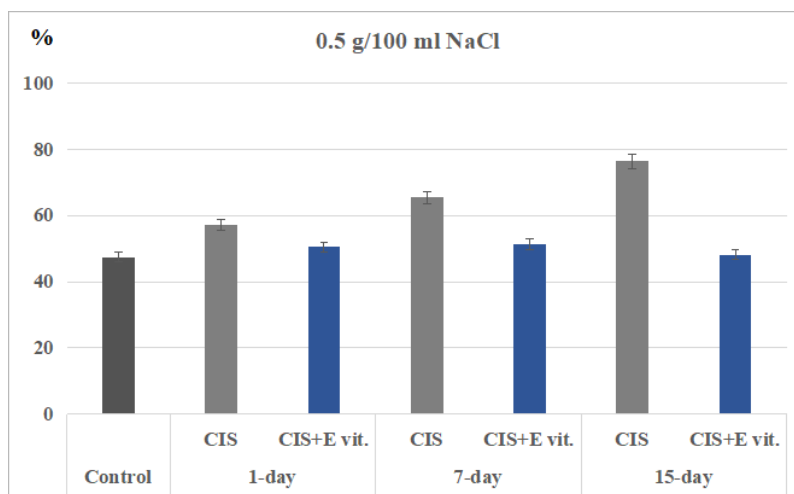
As shown in Figure 7, the level of osmotic hemolysis of erythrocytes of animals exposed

to stress was 85.3% in the control group in a solution of 0.4 g/100 ml of sodium chloride. And, in the version of SIS on the 1st day, the value of hemolysis is 88.2%, CIS+Evit. it was observed that vitamin E reduced the level of osmotic hemolysis of erythrocytes by 3.5%, making it 84.7%. On the 7th day, hemolysis was 92.4% in the CIS version, 86.2% in the |CIS+Evit version, and vitamin E reduced osmotic hemolysis by 6.2%. It was found that hemolysis in the SIS version on the 15th day of the experiment was 97.4%, in the CIS+Evit version it was 88.3%, and vitamin E reduced osmotic hemolysis by 9.1%.



Abscissa axis: CIS – chronic immobilization stress; CIS+E vit. – the effect of vitamin E during stress. 0.4 g/100 ml NaCl. Ordinate axis: level of hemolysis, %.

Figure 7 – Effect of vitamin E on osmotic hemolysis of erythrocyte membrane during chronic immobilization stress



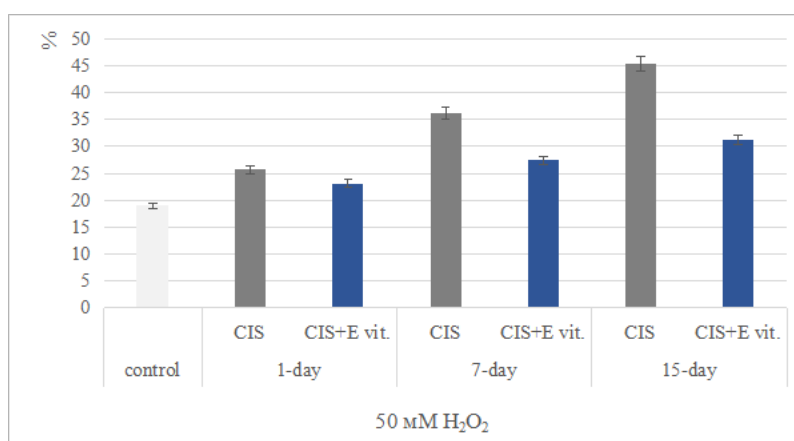
Abscissa axis: CIS – chronic immobilization stress; CIS+E vit. – the effect of vitamin E during stress. 0.5 g/100 ml NaCl. Ordinate axis: level of hemolysis, %.

Figure 8 – Effect of vitamin E on osmotic hemolysis of erythrocyte membrane during chronic immobilization stress

In the experiment of determining the effect of vitamin E on the osmotic hemolysis of the erythrocyte membrane in a 0.5 g/100 ml solution of sodium chloride during chronic immobilization stress (Figure 8), this law was observed. However, the rate of hemolysis decreased in 0.5 g/100 ml sodium chloride solution compared to 0.4 g/100 ml solution. Vitamin E increased the resistance of the erythrocyte membrane to chronic immobilization stress.

The results of the study showed that the long-term effect of vitamin E was more dominant than the short-term effect in increasing the resistance of the erythrocyte membrane during immobilization stress.

The indicators of the results of the study of the peroxide hemolysis of erythrocytes at concentrations of 50 mM and 100 mM of hydrogen peroxide are shown in Figures 9-10.

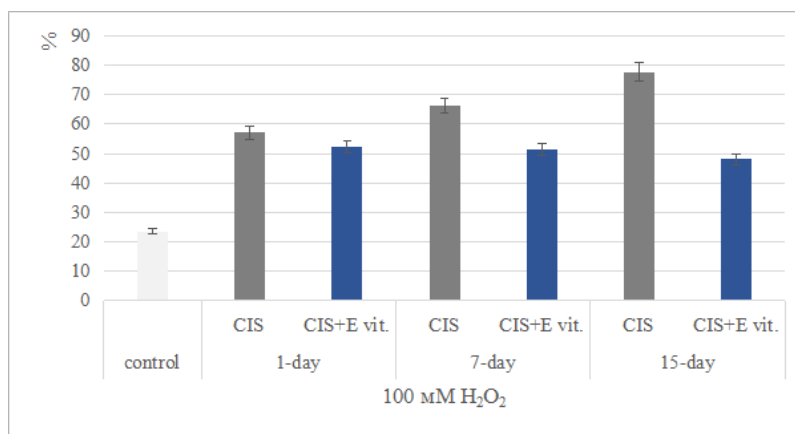


Abscissa axis: SIS – chronic immobilization stress; CIS+E vit. – the effect of vitamin E during stress. 50 mM H₂O₂. Ordinate axis: level of hemolysis, %.

Figure 9 – Effect of vitamin E on peroxidic hemolysis of erythrocyte membrane during chronic immobilization stress

Peroxide hemolysis of erythrocytes in a 50 mM solution of hydrogen peroxide (H_2O_2) was 18.9% in the control version. And, in the version of chronic immobilization stress (CIS) on the 1st day, 25.7%, CIS+E vit. made 23.1% in the version, and reduced the level of hemolysis by 2.6%. On the 7th day,

superoxide hemolysis in CIS variant was 36.2%, CIS+E vit. showed 27.4% in the version and reduced the level of hemolysis by 8.8%. On the 15th day, superoxide hemolysis in CIS variant was 45.4%, CIS+E vit. in version 31.2%, it was found that the level of hemolysis decreased by 14.2% (Fig. 9).



Abscissa axis: CIS – chronic immobilization stress; CIS+E vit. – the effect of vitamin E during stress. 100 mM H_2O_2 . Ordinate axis: level of hemolysis, %.

Figure 10 – Effect of vitamin E on peroxidic hemolysis of erythrocyte membrane during chronic immobilization stress

Peroxide hemolysis of erythrocytes in a 100 mM H_2O_2 solution was 23.5% in the control version. And, in the version of CIS on the 1st day, 57.1%, CIS+E vit. made 52.4% in the variant and reduced hemolysis level by 4.7%. On the 7th day, superoxide hemolysis in CIS variant was 66.3%, CIS+E vit. showed 51.5% in the variant and reduced the level of hemolysis by 14.8%. On the 15th day, superoxide hemolysis in CIS version was 77.7%, CIS+E vit. in the version, it was 48.1%, and it was observed that the hemolysis level decreased by 29.6% (Fig. 10).

After adding vitamin E to animal feed, resistance of erythrocytes increases. The biological activity of the vitamin E is evaluated by increasing the resistance of erythrocytes to hemolysis. Thus, vitamin E increased the membrane-stabilizing properties of the erythrocyte membrane under the influence of chronic immobilization stress.

Conclusion

According to the results of the research, under the influence of acute immobilization stress, the osmotic and superoxide hemolysis of the erythrocyte membrane increased, and the resistance of the membrane decreased. During the study of the effect of chronic immobilization stress on erythrocyte membranes, osmotic and superoxide hemolysis of erythrocyte membranes increased on the 1st, 7th and 15th days. The role of vitamin E in increasing the membrane-stabilizing property of the erythrocyte membrane against the harmful effects of chronic immobilization stress depended on the duration of its administration. Therefore, vitamin E can be used to prevent diseases caused by free radical damage to biomembranes.

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