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STATE OF THE ANTIOXIDANT PROTECTION SYSTEM IN RATS ERYTHROCYTES UNDER THE INFLUENCE OF HISTAMINE AND SODIUM HYPOCHLORITE

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Sodium hypochlorite is used in medicine as a detoxifier due to oxidation of toxins and metabolites. This substance is officially used for disinfection of tap water. The widespread use of drugs for the release and histamine metabolism in medical practice is based on the use of two groups of drugs: histamine receptor blockers and plasma cell membrane stabilizing. However, the negative side effect causes the search for other safe paths of inactivation and reduction of histamine content in biological tissues. Thus, it is important to study the safety of the use of sodium hypochlorite for the treatment of patients with allergic manifestations. The excessive allocation of histamine, which is easily oxidized, mast cells and blood basophils should be also taken into account. Study of safety using the sodium hypochlorite for treatment the patients with allergic manifestation and the excessive allocation of histamine is an acute problematic nowadays.

The purpose of the study was to investigate the influence of histamine (in doses of 1 and 8 μg/kg of body weight of animals) and sodium hypochlorite (in concentrations 5 and 20 mg/l), as well as their simultaneous action on the enzyme and non-enzymatic levels of the antioxidant system of red blood cells in rats.

Material and methods. The test substances were administered to animals for 14 days. On the 1st, 7th, 14th and 21st (rehabilitation) days animals were decapitated. We took blood red cells samples by centrifugation and conducted their hemolysis. In hemolysates, the activity of glutathione peroxidase was studied, catalase, glutathione-S-transferase, amount of reduced glutathione. The dispersion analysis was also conducted.

Results and discussion. The histamine in erythrocytes leads to a decrease in the activity of investigated enzymes and the content of reduced glutathione during the experiment, except for the 7th day of the experiment. Sodium hypochlorite causes the initial growth of activity of glutathione peroxidase with the next decreasing the activity. Glutathione-S-transferase is the least sensitive to the action of this substance. Sodium hypochlorite on the background of action of histamine disrupts the work of enzymes. At the first day of the experiment, a histamine influence on the activity of glutathione peroxidase, catalase, and the content of reduced glutathione was dominant, whereas the simultaneous administration of histamine and sodium hypochlorite was significantly influenced by glutathione-S-transferase activity.

Conclusion. The combined administration of substances had a significant effect on the activity of glutathione peroxidase on the 7th and 14th days of the experiment. Sodium hypochlorite affected the activity of catalase and the content of reduced glutathione.

Keywords: histamine, sodium hypochlorite, erythrocytes.

Research relation to the plans, programs and department themes. The work is a fragment of the research work "Prooxidant-antioxidant homeostasis and systems of membrane transport of bioobjects under the influence of physical and chemical factors" (scientific leader: Dr. of biological sciences, professor Sanahursky D.I., State registration number: 0116U001633).

Introduction. The primary function of erythrocytes is the delivery of oxygen, nitric oxide to the periphery, and carbon dioxide in the lungs. At the same time, these cells act as a circulating inactivator (sink) of products of oxidative and nitrosyl stress. In erythrocytes there is a high level of compounds that belong to the antioxidant system of protection: reduced glutathione, thioredoxin, vitamins C and E, superoxide dismutase, thioredoxin reductase, catalase, glutathione peroxidase, glutathione reductase, oxydoreductase of the plasmatic membrane, methemoglobin reductase [1]. Glutathione antioxidant system, which includes glutathione peroxidase, glutathione-S-transferase, glutathione reductase, reduced glutathione, prevents the accumulation of toxic products of lipid peroxidation, plays an important role in detoxification, degradation and excretion of heterologous organic substances

from the body [2]. Glutathione peroxidase neutralizes hydrogen peroxide, which is also intercepted by catalase.

Histamine, the first established mediator of allergy, is synthesized from the amino acid of histidine by decarboxylation. Histamine is found in granules of mast cells and basophils in the form of a complex with proteoglycans. The concentration of histamine in cells of the mucous coat is high (5 mg/100 cells). In thrombocytes and basophils it is significantly less (1 mg/100 cells). The amount of histamine in the blood fluctuates during the day and averages 300 pg/ml. The peak of histamine action in 1–2 minutes after its release, the duration of action is up to 10 minutes. The main inactivation pathways of the biogenic amine are the deamination by histaminase and methylation with N-methyltransferase. A part of histamine binds to proteins of serum blood. Released from the depot, histamine acts via H1-, H2-, H3-, H4-receptors. For example, stimulation of H1-receptors causes a contraction of smooth muscles of the bronchus and gastrointestinal tract increased vascular permeability, increased secretion of mucus by the glands of the nasal mucosa, paresis of peripheral pre-capillaries of the skin, irritation of the nerve endings and itching. Histamine plays an important role in the regulation of the immune response, since H2-receptors are present on cytotoxic T-lymphocytes and basophils, and stimulation of this receptor by histamine leads to the activation of T-suppressors [3]. Matthew C. Wagner et al. showed that the release of histamine contributes to the attachment of falx cells of erythrocytes to the endothelium in postcapillary veins and vasocclusion. The adhesion of the falx cells of erythrocytes caused by histamine is dependent on the simultaneous stimulation of histamine H2- and H4-receptors and the expression of endothelial P-selectin [4]. There are a number of inflammatory mediators that are produced by leukocytes, mainly neutrophils, with bacterial invasion. Neutrophils produce and release eosinophilic cationic protein and histamine, two important mediators of inflammation. In patients with periodontitis, neutrophils form histamine in response to the action of lipopolysaccharides [5]. Nowadays, it remains unknown whether there are erythrocyte receptors for histamine, whether erythrocytes can adsorb histamine, and also how histamine acts on the antioxidant defense system in them.

Sodium hypochlorite (SH) used in medicine as a detoxifier due to oxidation of toxins and metabolites. This substance is officially used for disinfection of tap water [6]. The widespread use of drugs for the release and histamine metabolism in medical practice is based on the use of two groups of drugs: histamine receptor blockers and plasma cell membrane stabilizing. However, the negative side effect causes the search for other safe paths of inactivation and reduction of histamine content in biological tissues [7]. Thus, it is important to study the safety of the use of SH for the treatment of patients with allergic manifestations, and also the excessive allocation of histamine, which is easily oxidized, mast cells and blood basophils.

SH reduces its content in the blood of people in the case of severe poisoning with psychopharmacological substances [8]. The literature does not contain information on the direct effect of histamine on the antioxidant state of erythrocytes. Unresolved remains the issue of mutual action of histamine and SH. Previously, we studied the influence of histamine and SH on various tissues of the body: lungs, heart, blood plasma, kidneys, liver [9, 10].

The Purpose of our Work was to investigate the influence of histamine and SH, as well as their simultaneous action on the enzymatic and non- enzymatic levels of the antioxidant system of red blood cells in rats.

Material and Methods. Experiments were conducted on outbred white male rats (Rattus norvegicus f. Domesticus) for 21 days. The weight of animals was 180-220 g. The animals were selected on the basis of analogies, 20 animals in each group. The 1st control group included intact animals. The animals of the second and third groups received subcutaneous injections of histamine solutions in doses of 1 and 8 μg/kg of body weight of animals (0,01% histamine dihydrochloride solution was used as a stock solution; manufacturer – Limited Liability Company «Immunolog», Ukraine, Vinnytsya) respectively. The chosen doses corresponded to those causing pathological manifestations in experimental conditions [11]. Animals of the 4th and 5th groups were given a solution of SH (5 and 20 mg/l, respectively, made at the Ukrainian State Chemical Technology University, Dnipropetrovsk) during this period. In addition, four more groups were formed. The animals of these groups were simultaneously injected by histamine and sodium hypochlorite in different combinations of the indicated concentrations. On the 1^{st}, 7^{th}, 14^{th} and 21^{st} (rehabilitation) days five animals from each group were decapitated under light ether anesthesia in compliance with the European Convention for the Protection of vertebrate animals used for experimental and scientific purposes (Strasbourg, France 1986) and according to the recommendations of the "Bioethical examination of preclinical and other scientific researchers performed on animals" (Kyiv, Ukraine, 2006). We took blood red cells samples by centrifugation and conducted their hemolysis with distilled water. In hemolysates, the activity of glutathione peroxidase was studied (EC 1.11.1.9; glutathione: hydrogen-peroxide-

oxydoreductase) [12], catalase (EC 1.11.1.6; hydrogen-peroxide:hydrogen-peroxide-oxydoreductase) [13], glutathione-S-transferase (EC 2.5.1.18; RX:glutathione-R-transferase) [14], amount of reduced glutathione (GSH) [15]. The amount of protein in each sample was determined by Lowry method.

Statistical processing of the research results and two-factor dispersion analysis were performed using the Excel-2010 program for Windows. The significance probability of the difference between the statistical characteristics of two alternative sets of data was estimated by calculating Student coefficient. The significant difference was considered for $p \geq 0,95$, $p \geq 0,99$, $p \geq 0,999$.

Results and Discussion. It is known that erythrocytes possess high sensitivity to chemicals substances [16]. We found out that the histamine in concentrations of 1 and 8 μg/kg in rats' erythrocyte hemolysates led to decreasing the activity of glutathione peroxidase at 1st and 14th day of the experiment (on 89 and 46% – 1st day, 53 and 63% – 14th day respectively). After the rehabilitation period, the activity of this enzyme decreased (**Fig. 1, A**). Histamine caused a decreasing in the activity of catalase in the 1st and 21st (rehabilitation) days of the experiment.

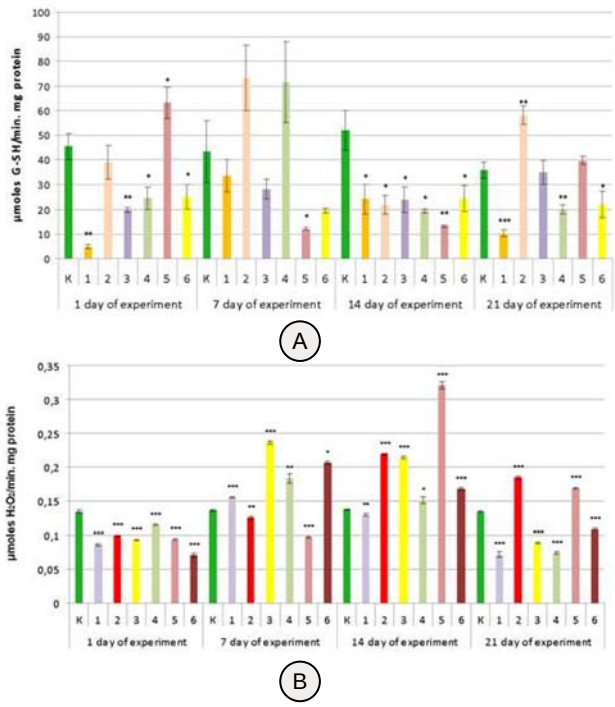

Fig. 1 – The activity of glutathione peroxidase (A) and catalase (B) in rats erythrocyte hemolysates on 1st, 7th, 14th and 21st day of the experiment. Here and on Fig. 2:
K – control; **1, 4** – for the histamine action, respectively, at a dose of 1 and 8 μg/kg body weight of animals; **2, 5** – with simultaneous exposure to sodium hypochlorite (5 mg/l) and histamine (1 and 8 μg/kg body weight of animals, respectively); **3, 6** – with simultaneous exposure to sodium hypochlorite (20 mg/l) and histamine (1 and 8 μg/kg body weight of animals, respectively). * $p \geq 0,95$; ** $p \geq 0,99$; *** $p \geq 0,999$

However, on the 7th, the growth of catalase activity was found to be 13% and 35%, respectively, due to histamine effects of lower and higher concentrations in accordance. At the 14th day of the action of the biogenic amine in a low concentration, a slight, but a significant reduction in the activity of catalase was detected (by 6%), while in high concentration we detected the increased activity of catalase by 10% (**Fig. 1, B**). The simultaneous decrease in the activity of glutathione peroxidase and catalase indicates a decreasing the content of hydrogen peroxide in erythrocytes, as well as lipid hydroperoxides since these enzymes intercept hydrogen peroxide and glutathione peroxidase also neutralizes hydroperoxides. At the 7th day, an increase in the activity of catalase on the background of the normal work of glutathione peroxidase was detected. This indicates that a significant amount of H_2O_2 is formed at this time. It is known that glutathione peroxidase neutralizes small amounts of hydrogen peroxide, while catalase activity increases at significant concentrations of this substrate.

We also noticed a reduction in the activity of glutathione-S-transferase at the 7th and 14th day of the experiment after injection of histamine at a concentration of 1 μg/kg. Biogenic amine in higher concentrations caused a decrease (by 57%) the activity of this enzyme at the 7th day, as well as after the rehabilitation period (58%, **Fig. 2, A**). The glutathione-S-transferase and reduced glutathione play an important role in the detoxification function of red blood cells. Thus, aldehyde dehydrogenase, aldehyde reductase, and glutathione-S-transferase are involved in the removing of aldehydes (which are capable of interacting with proteins and nucleic acids, changing their functional properties). However, the main path of catabolism is conjugation with glutathione [17]. It should be noted that this enzyme also neutralizes drugs, harmful compounds. Reduced glutathione-S-transferase activity in erythrocytes due to histamine exposure is a negative phenomenon since in this case the detoxification function of these cells is disturbed.

The content recovered glutathione significantly decreased in erythrocytes by the histamine action in both concentrations during the experiment. It was noted every day, except for the 7th day, when its content rose (by 21 and 13% accordingly to at a concentration of 1 and 8 μg/kg; **Fig. 2, B**).

The decreased activity of glutathione peroxidase by histamine action was due to a lowered content of reduced glutathione. It is well-known that glutathione peroxidase works in the presence of sufficient amounts of glutathione in the medium. Probably histamine leads to the formation of reactive oxygen

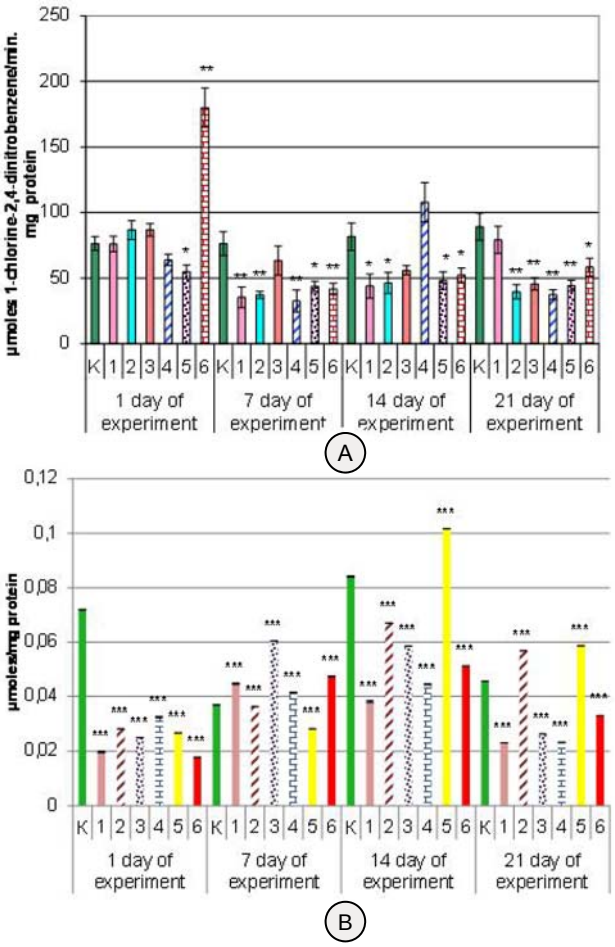

Fig. 2. The glutathione-S-transferase activity (A) and the content of reduced glutathione (B) in rats erythrocyte hemolysates on 1st, 7th, 14th and 21st day of the experiment.
* p ≥ 0,95; ** p ≥ 0,99; *** p ≥ 0,999

species and harmful compounds in the plasma, which adsorbs by erythrocytes and neutralizes by GSH, reducing its pool. Significant oxidation of intracellular GSH promotes oxidative damage to proteins and lipids and also endangers the structural integrity and viability of red blood cells. The GSH redox status of erythrocytes not only contributes to the growth of their oxidative potential and increases hemolysis, but also reduces the bioavailability of nitric oxide in zones of oxidative damage [1]. The histamine had a special (more adaptive) effects on the antioxidant system of red blood cells on the 7th day of the experiment. These effects consisted in returning to the normal activity of glutathione peroxidase, increasing activity of catalase decreasing glutathione-S-transferase activity and increasing GSH content. The concentration of reduced glutathione in erythrocytes is 2–4 mM. Approximately 99,5% of GSH blood is present in erythrocytes in the amount of 8,77 mg/g hemoglobin, or at a concentration of 2,73–3,50 mmol/l [1]. It was shown that the glutathione peroxidase activity, glutathione-S-transferase, glutathione reductase and GSH content significantly decreased in experimental animals after 3 hours after administration of 0,1 ml of histamine in the middle ear as a proinflammatory factor for the development of otitis, in samples of red blood cells from the middle ear inflammatory fluid guinea pigs compared to control [18]. Consequently, our studies are consistent with the literature data. Ucuncu H. suggests that histamine causes the inflammatory process, during which reactive oxygen species are formed, and the glutathione link of the antioxidant system reacts in protocols with histamine otitis and with the use of antioxidant agents on the background of inflammatory reactions [19].

Thus, histamine in erythrocytes causes a predominant decreasing in the activity of antioxidant system enzymes during the experiment, except for the 7th day of the experiment.

The SH in a concentration of 5 mg/l lead to increase the activity of glutathione peroxidase by 229% on the 7th day, with next decreasing the activity on the 14th day (by 51%). Along with this, the activity of catalase in erythrocytes of rats is insignificant, but decreases reliably both on 1st, and on the 7th day of the experiment. After 14-day using water with SH (5 mg/l) for the drink, the activity of catalase increased by 81% compared with control. Probably SH in this concentration on the 7th day of the experiment neutralizes large amounts of hydroperoxides. The action of SH (5 mg/l) after the fourteen-day led to the formation of significant amounts of hydrogen peroxide, resulting in an increase in catalase activity at that time (**Fig. 3, A, B**). The action of SH at a concentration of 20 mg/l led to the activity of glutathione peroxidase increases for 1 day (80%), however, at the 7th and 14th day showed the opposite effect. At the first and the 14th day the activity of the catalase enzyme increases by 9 and 73%, respectively, with the action of the SH at the higher concentration. Consequently, the action of SH in the concentration of 20 mg/l caused a negative oxidative effect at the initial stage of the study. Notice that SH at both concentrations led to the formation of higher concentration of hydrogen peroxide more than normal after the prolonged action. Hydrogen peroxide in the blood may be formed outside the erythrocytes. H_2O_2 can penetrate them through diffusion, where it is deactivated by catalase [20]. Fe^{2+} hemoglobin is oxidized to Fe^{3+} (methemoglobin, MetHB) under the action of oxidants (amyl nitrite, aniline, nitrobenzene, nitrates and nitrites, thiosulfates, ferricyanide). Probably the SH accompanies such a process because it acts as a strong oxidizer. Every day 0.5% of all hemoglobin is converted into methemoglobin in the body. But in erythrocytes, there is an enzyme called methemoglobin reductase, which catalyzes the restoration of

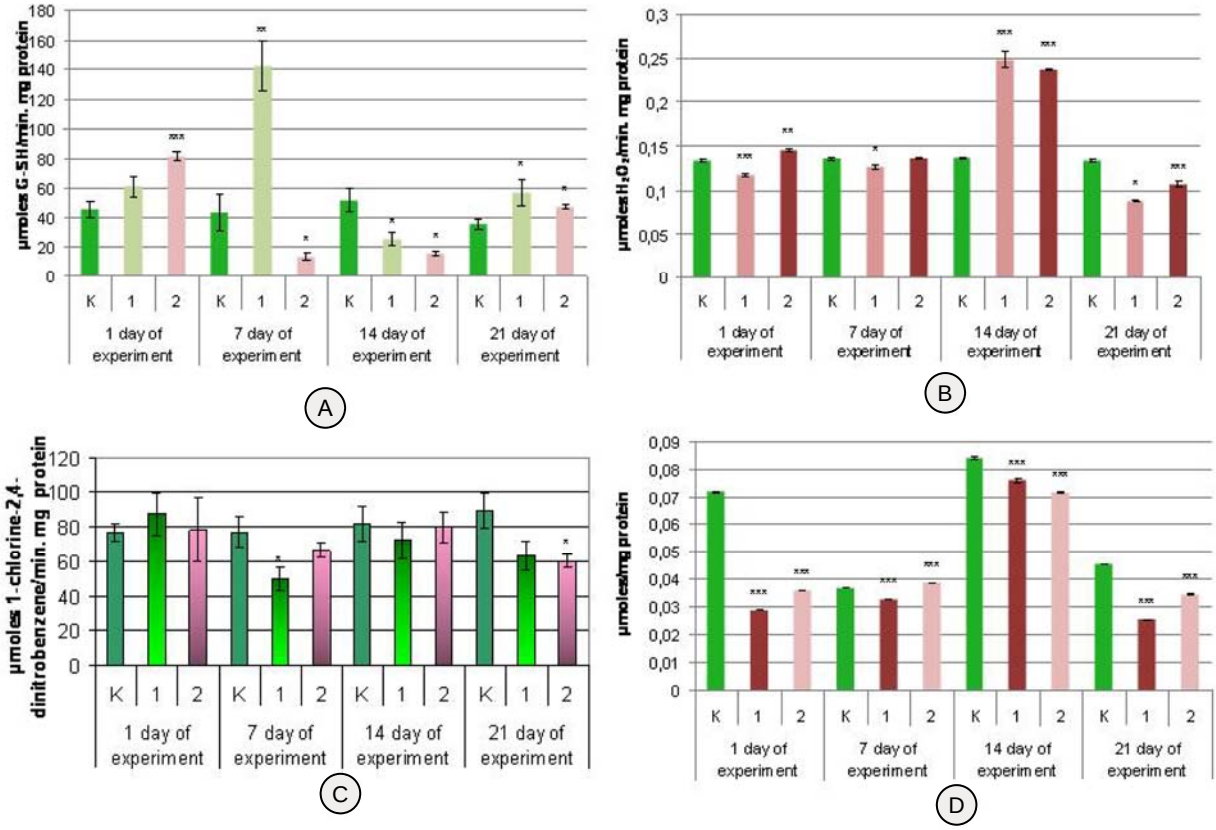

Fig. 3 – The activity of glutathione peroxidase (A), catalase (B), glutathione-S-transferase (C) and the content of reduced glutathione (D) in rats erythrocyte hemolysates on 1st, 7th, 14th and 21st day of the experiment. **K** – control; **1, 2** – for the sodium hypochlorite action, respectively, at a concentrations 5 i 20 mg/l. * p ≥ 0,95; ** p ≥ 0,99; *** p ≥ 0,999

methemoglobin to hemoglobin, so the actual concentration of methemoglobin in the blood is normally low. The oxidation of hemoglobin to methemoglobin by oxygen causes the formation of a superoxide anion radical ($O2^{\cdot-}$). Superoxide radical, which exhibits toxic activity under the action of superoxide dismutase, is converted into H_2O_2. The latter decomposes under the influence of catalase and peroxidase of red blood cells. After seven days of rehabilitation, the activity of glutathione peroxidase increases, while catalase it decreases (**Fig. 3, A, B**). This time, the work of the antioxidant system in the erythrocytes is probably aimed at the destruction of hydroperoxides, and excessive formation of hydrogen peroxide no longer occurs.

By studying the activity of glutathione-S-transferase, it was found out that SH only at a concentration of 5 mg/l caused the decrease its activity on the 7th day by 35%. Such results indicate that in erythrocytes, the action of SH does not produce harmful substrate compounds for this enzyme. It is important to note that SH caused a decreasing in the content of reduced glutathione during the experiment, except for the effect of this compound at a concentration of 20 mg/l on the 7th day (increasing by 5%). Therefore, we may conclude that the influence of SH in the red blood cells formed substances that intercept the recovered glutathione and its pool is reduced (**Fig. 3, C, D**). We may include aldehydes to these substances.

Thus, SH causes the initial growth of activity of glutathione peroxidase with its subsequent decrease. The fourteen-day administration of this substance causes an increase in the activity of catalase, while the content of reduced glutathione decreases during the experiment. After rehabilitation, the activity of glutathione peroxidase increased, and the activity of catalase and the content of reduced glutathione decreased compared to control group in erythrocytes. The most inert to this investigating substance was glutathione-S-transferase. After analysis of these research results, we suppose that in erythrocytes, SH acts as an oxidizer, resulting in the formation of various active forms of oxygen and free radicals, which are intercepted by the enzymatic and non-enzymatic links of the antioxidant system. The formation of hypohalites in this case (by the effect on red blood cells of control rats) probably does not occur, as evidenced by the activity of glutathione-S-transferase, an enzyme that neutralizes harmful substances. There is also no damage to the structure of enzymes, since their

activity fluctuates throughout the experiment and their work can be interconnected.

We had found out that the combined action of SH at the concentration of 5 mg/l and histamine at the concentration of 8 μg/kg led to the violation of the activity of glutathione peroxidase from the first day. So, at this day, the activity of the enzyme increased by 39%, but already at the 7th, it decreased by 72% compared with to the control. Reduction of glutathione peroxidase activity occurred on the 14th day in the groups of rats, that were administered the histamine in both concentrations and SH (5 mg/l) simultaneously. When we studied catalase in erythrocytes it was noted that its activity decreased on the 7th day by about 30%, however, since the 14th day, was found the opposite effect the action of SH in the concentration 5 mg/l and histamine (1 and 8 μg/kg). After analyzing the work of these two enzymes, we assumed that the concentration of hydrogen peroxide significantly increases in erythrocytes since the 14th day and catalase reacts with it. The administration of SH (5 mg/l) on the background of histamine action of both concentrations caused a decreasing the activity of glutathione-S-transferase over the course of the experiment by an average of 50%. It should be noted that the activity of this enzyme is lowered by the action of histamine, while the simultaneous effect of biogenic amine and SH (5 mg/l) only enhances such an effect. We established a decreasing in the content of reduced glutathione till the 7th day by the action of histamine and SH (5 mg/l). By the 14th day of the experiment, the content of reduced glutathione had already increased by 21% with simultaneous exposure SH (5 mg/l) and histamine at a concentration of 8 μg/kg. After the rehabilitation period, the GSH content increased in the groups of rats that received histamine in both studied concentrations and SH (5 mg/l). Consequently, SH at the concentration of 5 mg/l against the background of histamine action violated function the antioxidant system with a predominant inhibition of glutathione-related enzymes (**Fig. 1, 2**). The most pronounced negative action was on glutathione-S-transferase.

The combined action of SH at a concentration of 20 mg/l and histamine (1 and 8 μg/kg) resulted to decrease in the activity of glutathione peroxidase, catalase and reduced glutathione on the 1st day of the experiment in erythrocytes hemolysates. On the 7th day the simultaneous action of the studied substances, the activity of glutathione peroxidase returns to the limits of control, and the activity of catalase and the content of reduced glutathione – increase. The growth of GSH content can be explained by not using glutathione peroxidase and glutathione-S-transferase, as well as the absence of substrate compounds for it. After two weeks of substances administration in erythrocyte hemolysates, the activity of glutathione peroxidase, glutathione-S-transferase and the content of reduced glutathione decreased, while the activity of catalase remained high. The growth of the activity of catalase, as already noted, indicates the formation of the high hydrogen peroxide concentrations.

It is known that in erythrocytes there is a high content of catalase [21]. After the rehabilitation period, the activity of the studied enzymes and the content of GSH were reduced (**Fig. 1, 2**). Consequently, SH at a concentration of 20 mg/l on the background of histamine action caused a more pronounced negative effect (compared to the simultaneous action of low concentration of SH) on the antioxidant defense system, as evidenced by the increasing activity of catalase (and hence the formation of high concentrations of hydrogen peroxide) and decreasing activity of glutathione peroxidase and glutathione-S-transferase. Glutathione peroxidase, an enzyme that depends on selenium micronutrients, plays a decisive role in lowering lipids and hydrogen peroxide. If the activity of glutathione peroxidase decreases, the content of hydrogen peroxide increases, which leads to direct damage to the cells and activates the proinflammatory pathways [22]. In the cell, the role of glutathione-S-transferase is to provide oxidative-reducing homeostasis by restoring the cysteine residues of proteins, which prevents their degradation after the action of endogenous (oxidative or nitrous) or exogenous (xenobiotic) factors, and ligament binding to the kinase pathways (in particular, JNK), that is, the signaling mechanisms of survival and death of cells [23].

It was noted that SH at a concentration of 0,1 mg/l in the 7th day in *Solea senegalensis* causes hypertrophy, oxidative stress [24]. Sodium hypochlorite (NaClO), which is discharged by the power plants in the receiving waters, causes 1, 3, 7 and 14 days of *Mytilus galloprovincialis* in the digestive gland and gland of the moth, pathological reaction, as well as changes in the activity of glutathione-S-transferase enzymes, catalase, acetylcholinesterase and level peroxide oxidation of lipids. Influence of NaClO causes a toxicological reaction [25]. We assume that simultaneous administration of histamine to rats and SH in the body produce harmful substances that damage the enzymes (glutathione-S-transferase, glutathione peroxidase). These include nitriles and carbonyl compounds, as well as chloramines.

The two-factor dispersion analysis showed that at the 1st day of the experiment, the dominant influence of histamine was on the activity of glutathione peroxidase, catalase and the content of reduced glutathione where the share of influence of the factors were 46.66 and 41% respectively. Probably the short-term action of histamine causes the formation of free radicals due

to the violation of the prooxidant-antioxidant homeostasis of blood, in particular, erythrocytes. Thus, the simultaneous administration of histamine and SH (share of influence of the factor is equal to 46%) significantly influences the activity of glutathione-S-transferase. The combined effect of histamine and SH induces a change in the activity of glutathione peroxidase at the 7th and 14th day of the experiment (share of influence of the factors are 44 and 30%, respectively). At these days of the experiment, the SH had a major influence on the activity of catalase and the content of reduced glutathione. NaClO is a powerful oxidizer, due to which free radicals are formed, which are inactivated precisely by catalase and reduced glutathione. GSH is an important factor in the formation of the thiol component of the redox buffer of most differentiated cells, including erythrocytes [1]. A significant part of the effects on the activity of glutathione peroxidase and glutathione-S-transferase in rat erythrocytes was unaccounted factors (**Fig. 4**).

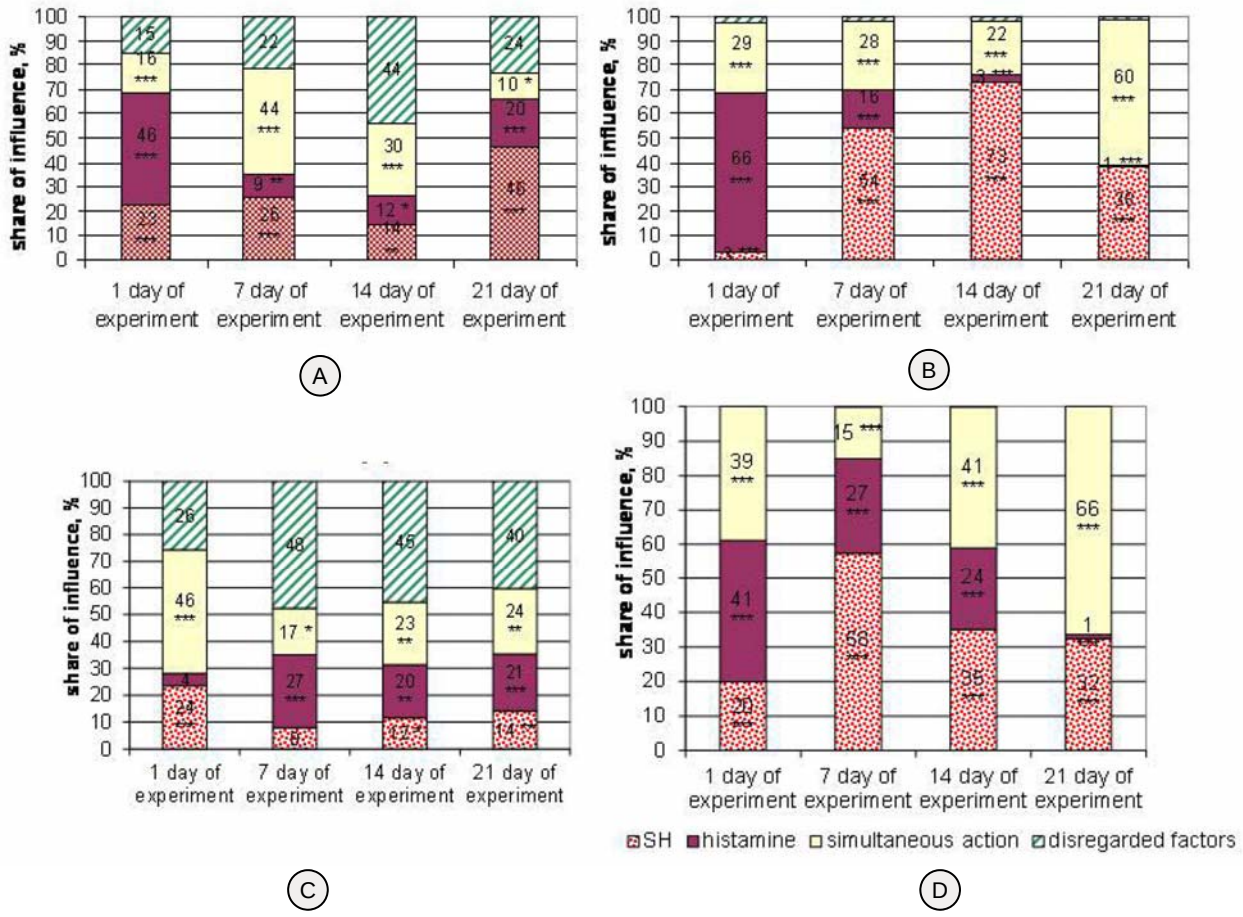

Fig. 4. – Results of two-factor dispersion analysis of indicators of antioxidant state (A – glutathione peroxidase; B – catalase; C – glutathione-S-transferase; D – reduced glutathione) in rats erythrocyte hemolysates for the histamine and sodium hypochlorite action. * p ≥ 0,95; ** p ≥ 0,99; *** p ≥ 0,999

Conclusion. Consequently, histamine in erythrocytes leads to a predominant decrease in the activity of enzymes of the antioxidant system and the content of reduced glutathione during the experiment, except for the 7th day. SH caused the initial growth of activity of glutathione peroxidase with its subsequent decreasing. At the fourteenth-day injection of SH led to increasing the activity of catalase, but the content of reduced glutathione decreased during the experiment. The least sensitive to the action of SH was glutathione -S-transferase. SH at a low concentration (5 mg/l) against the background of histamine action violates the function of enzymes antioxidant system with the predominant inhibition of glutathione-related enzymes. SH at a high concentration (20 mg/l) on the background of histamine action had a more pronounced negative effect on the antioxidant defense system, as evidenced by the increased activity of catalase and decreased the activity of glutathione peroxidase and glutathione-S-transferase. The dispersion analysis

showed that on the 1st day of the experiment histamine had the main effect on the activity of glutathione peroxidase, catalase and on the content of reduced glutathione, whereas, the simultaneous administration of histamine and SH had the effect on the activity of glutathione-S-transferase. The combined administration of histamine and SH had a powerful effect on the activity of glutathione peroxidase on the 7th and 14th day of the experiment, SH acted on the activity of catalase and the content of reduced glutathione.

Prospects of further research. In future the perspective direction of research is in determination of intensity of lipid peroxydation in erythrocytes of rats under the action of histamine and sodium hypochlorite.

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СТАН СИСТЕМИ АНТИОКСИДАНТНОГО ЗАХИСТУ В ЕРИТРОЦИТАХ ЩУРІВ ЗА ДІЇ ГІСТАМІНУ ТА ГІПОХЛОРИТУ НАТРІЮ

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Резюме. Важливим є вивчення безпечності застосування гіпохлориту натрію для лікування пацієнтів, які мають алергічні прояви, а значить і надмірне виділення гістаміну. Метою роботи є дослідити вплив гістаміну та гіпохлориту натрію, а також одночасну їхню дію на ензиматичну і неензиматичну ланки антиоксидантної системи еритроцитів щурів. Вивчали активність глутатіонпероксидази, каталази, глутатіон-S-трансферази, вміст відновленого глутатіону. Проводили двофакторний дисперсійний аналіз. У еритроцитах щурів гістамін призводить до пониження активності досліджуваних ензимів та вмісту відновленого глутатіону впродовж досліду, крім 7-ї доби. Гіпохлорит натрію спричиняє першопочаткове зростання активності глутатіонпероксидази з наступним її пониженням. Найменш чутливою до дії цієї речовини є глутатіон-S-трансфераза. Гіпохлорит натрію на фоні дії гістаміну порушує роботу ензимів. На 1-шу добу досліду на активність глутатіонпероксидази, каталази і вміст відновленого глутатіону чинить головний вплив гістамін, тоді як на активність глутатіон-S-трансферази значно діє одночасне введення гістаміну і гіпохлориту натрію. Поєднане введення речовин справляє значний вплив на активність глутатіонпероксидази на 7-му і 14-ту доби досліду. На активність каталази і вміст відновленого глутатіону впливає гіпохлорит натрію.

Ключові слова: гістамін, гіпохлорит натрію, еритроцити.

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СОСТОЯНИЕ СИСТЕМЫ АНТИОКСИДАНТНОЙ ЗАЩИТЫ В ЭРИТРОЦИТАХ КРЫС ПРИ ДЕЙСТВИИ ГИСТАМИНА И ГИПОХЛОРИТА НАТРИЯ

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Резюме. Важным является изучение безопасности применения гипохлорита натрия для лечения пациентов с аллергическими проявлениями, а значит и чрезмерным выделением гистамина. Целью работы является исследовать влияние гистамина и гипохлорит натрия, а также одновременное их действие на ферментативные и неферментативные звена антиоксидантной системы эритроцитов крыс. Изучали активность глутатионпероксидазы, каталазы, глутатион-S-трансферазы, содержание восстановленного глутатиона. Проводили дисперсионный анализ. В эритроцитах крыс гистамин приводит к понижению активности исследуемых ферментов и содержания восстановленного глутатиона в течение опыта, кроме 7-го дня опыта. Гипохлорит натрия вызывает первоначальное повышение активности глутатионпероксидазы с последующим ее понижением. Наименее чувствительной к действию этого вещества является глутатион-S-трансфераза. Гипохлорит натрия на фоне действия гистамина нарушает работу энзимов. На 1-е сутки опыта на активность глутатионпероксидазы, каталазы и содержание восстановленного глутатиона оказывает ведущее влияние гистамин, тогда как на активность глутатион-S-трансферазы значительно действует одновременное введение гистамина и гипохлорита натрия. Совместное введение веществ оказывает значительное влияние на активность глутатионпероксидазы на 7- и 14-е сутки опыта. На активность каталазы и содержание восстановленного глутатиона влияет гипохлорит натрия.

Ключевые слова: гистамин, гипохлорит натрия, эритроциты.

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