УДК 619.615
DOI 10.11603/mcch.2410-681X.2023.i1.13714

B. V. Gutyj[1], I. S. Varkholiak[1], B. M. Verveha[2], T. V. Martyshuk[1], Kh. Ya. Leskiv[1]
STEPAN GZHYTSKYI NATIONAL UNIVERSITY OF VETERINARY MEDICINE AND BIOTECHNOLOGIES, LVIV[1]
DANYLO HALYTSKY LVIV NATIONAL MEDICAL UNIVERSITY[2]

THE ANTIOXIDANT PROTECTION SYSTEM STATE OF RATS UNDER EXPERIMENTAL DOXORUBICIN INTOXICATION AND THE EFFECTS OF CORRECTING FACTORS

Introduction. *The doxorubicin model was used for research, which, according to many authors, most adequately reproduces heart failure of varying degrees of severity. Doxorubicin is an antibiotic that has a cytostatic effect. The mechanism of its action consists of interaction with DNA, formation of free radicals, and inhibition of nucleic acid synthesis. The doxorubicin action and the development of hypoxia are accompanied by the activation of oxidative stress, the strengthening of free radical processes, and changes in the metabolism of carbohydrates, proteins, and lipids.*

The aim of the study *– the effect of the drug "Bendamine" on the indicators of antioxidant protection of the body of rats under experimental simulation of heart failure.*

Research Methods. *Modeling of heart failure was performed on sexually mature male Wistar rats with a body weight of 180–200 g. In blood and myocardial homogenate, the level of lipid peroxidation products, the activity of antioxidant enzymes, and the level of reduced glutathione were determined against the background of doxorubicin intoxication and when using the drug "Bendamine".*

Results and Discussion. *During doxorubicin intoxication, LPO processes are enhanced in rats, which is indicated by the increased lipid hydroperoxides, diene conjugates, and TBA-active products in the blood and the homogenate of the rat myocardium of the first experimental group. It is worth noting that the inhibition of the antioxidant defense system was also established in intoxicated rats, as indicated by the low level of both enzymatic and non-enzymatic links of the antioxidant system. It was established that bendamine has a corrective effect on rats' oxidative stress conditions inherent in doxorubicin-induced heart failure. The drug "Bendamine" inhibits the excessive formation of POL products in pathologically changed tissues of the heart of rats and has an inducing effect on the system of antioxidant protection.*

Conclusions. *The influence of the drug "Bendamine" on the indicators of antioxidant protection of the body of rats under experimental simulation of heart failure was studied. Its antioxidant properties have been proven.*

KEY WORDS: **antioxidant system; doxorubicin; intoxication; free radical oxidation; phosphodiesterase-3 inhibitor; ethylmethylhydroxypyridine succinate.**

INTRODUCTION. Redox reactions occupy an important place in the system of metabolic transformations, and their disturbances play a significant and sometimes decisive role in developing pathological processes [1]. Oxidation processes in the liver are of particular importance, where the organ performs its main functions with their participation, in particular, detoxification of endo- and exotoxins [2, 3].

According to many scientists, the primary pathogenetic shifts in the formation of cardiovascular system pathology are closely interrelated with the overstrain of mechanisms for utilizing reactive oxygen species and the degree of disturbances in the POL–AOS system. They are primarily determined by the state of the body's immune system [4–6]. Their imbalance is the basis of metabolic disorders in general, which predominantly affects the state of cell membranes. In addition, among the metabolism indicators during the development of pathology, the POL–AOS system is distinguished by early deviations [1, 7, 8]. They have a leading role in the processes of adaptation of a healthy body to extreme conditions and the development of significantly severe disorders under pathology [9–11]. In particular, it is considered proven that changes in the course of LPO processes are one of the pathogenetic mechanisms of the development of cardiovascular pathology [12].

The pathogenesis of the development of heart failure caused by the administration of doxorubicin is diverse. Some authors suggest that damage to

the myocardium occurs due to the formation of free radicals and reactive oxygen species, leading to damage to cell membranes, the development of apoptosis, and necrosis of cardiomyocytes. The cardiotoxic effect of doxorubicin is accompanied by a gradual increase in the number of damaged cardiomyocytes, a decrease in the contractility of the myocardium of the left ventricle, and its eccentric remodeling [13, 14].

Violating the system of antioxidant protection of the body of dogs under the influence of toxic substances and its correction when using various combinations of pharmacological and natural antioxidants is relevant and timely.

In veterinary medicine, one of the most promising drugs from the group of antioxidants are derivatives of 3-oxy pyridine, particularly ethylmethylhydroxypyridine succinate – a direct antioxidant [15]. The mechanism of action of this drug consists of antioxidant and membrane-protective action. It suppresses lipid peroxidation processes and increases the activity of superoxide dismutase, which neutralizes the starting radical of free radical processes [16]. Under conditions of tissue ischemia, this drug enhances the compensatory activation of aerobic glycolysis, reduces the degree of inhibition of oxidative processes in the Krebs cycle, and promotes the activation of ATP synthesis. Under the influence of ethylmethylhydroxypyridine succinate, a specific protein that accelerates apoptosis, was found to decrease in cardiomyocytes. Transmembrane ion currents are also modulated: the slow current through calcium channels is slowed down, the blockade of fast sodium channels and the rapidly activated potassium current component of delayed rectification (JKR) is reversed [17, 18].

The methylhydroxypyridinexypyridine succinate has a complex effect on the metabolism of the myocardium of animals.

A combined approach for treating animals with heart failure, based on using a phosphodiesterase-3 inhibitor and antioxidants, is relevant. Antioxidant compounds can protect healthy cells and tissues in dogs from developing unwanted side effects caused by the development of heart failure. In addition, it is known that the development of this pathology is characterized by oxidative stress, which determines the particular metabolic activity of antioxidants.

The aim of the study is to investigate the effect of the drug “Bendamine” on the indicators of antioxidant protection of the body of rats under experimental simulation of heart failure.

RESEARCH METHODS. The research was conducted on sexually mature male Wistar rats with a body weight of 180–200 g, which were kept on a standard ration of the institute vivarium of the State Research Control Institute of Veterinary Medicines and Feed Additives. The rats were kept on a balanced diet throughout the experiment containing all the necessary components. In addition, the animals received drinking water without restrictions from 0.2-liter glass drinking bowls.

Experimental studies were carried out following the requirements of a medicinal and biological experiment for the selection of analogs, the establishment of controls, compliance with the same feeding and maintenance conditions during the experiment, and the recording of results.

To create a model of doxorubicin-induced cardiomyopathy, 24 male rats were selected. Animals were divided into 3 groups of 6 animals each: control group – intact animals; experimental group E_2, in which animals were modeled doxorubicin-induced cardiomyopathy by intraperitoneal administration of doxorubicin at a dose of 2.5 mg/kg 3 times a week for two weeks; experimental group E_2, in which the animals, after the injection of doxorubicin, were intragastrically injected with the drug “Bendamine” at a dose of 20 mg/kg. The drug "Bendamine" contains a phosphodiesterase-3 inhibitor and ethylmethylhydroxypyridine succinate.

The content of LPO products – lipid hydroperoxides, diene conjugates, and TBA-active products, the activity of antioxidant enzymes – superoxide dismutase, glutathione peroxidase, and glutathione reductase, the level of reduced glutathione, were determined according to the methods [19].

All animal manipulations followed the European Convention for the Protection of Vertebrate Animals Used for Experimental and Scientific Purposes (Strasbourg, 1986).

The research results were analyzed using the Statistica 7.0 software package. Student's t-test assessed the probability of differences. The results were considered reliable at $P \leq 0.05$.

RESULTS AND DISCUSSION. Based on the conducted studies, it was established that the processes of peroxide oxidation of lipids and the formation of reactive oxygen species grow in animals under chronic experimental intoxication with doxorubicin. Thus, in the blood of rats of the first experimental group, an increase in lipid hydroperoxides by 47.4 % compared to the control was established. Furthermore, the level of diene conjugates and TBA-active products in the blood of this experimental group of rats was also high. In contrast, compared to the control group, it was higher by 21.4 and 24.9 %, respectively (Fig. 1).

Similar changes are observed when determining the intensity of lipid peroxidation in the homogenate

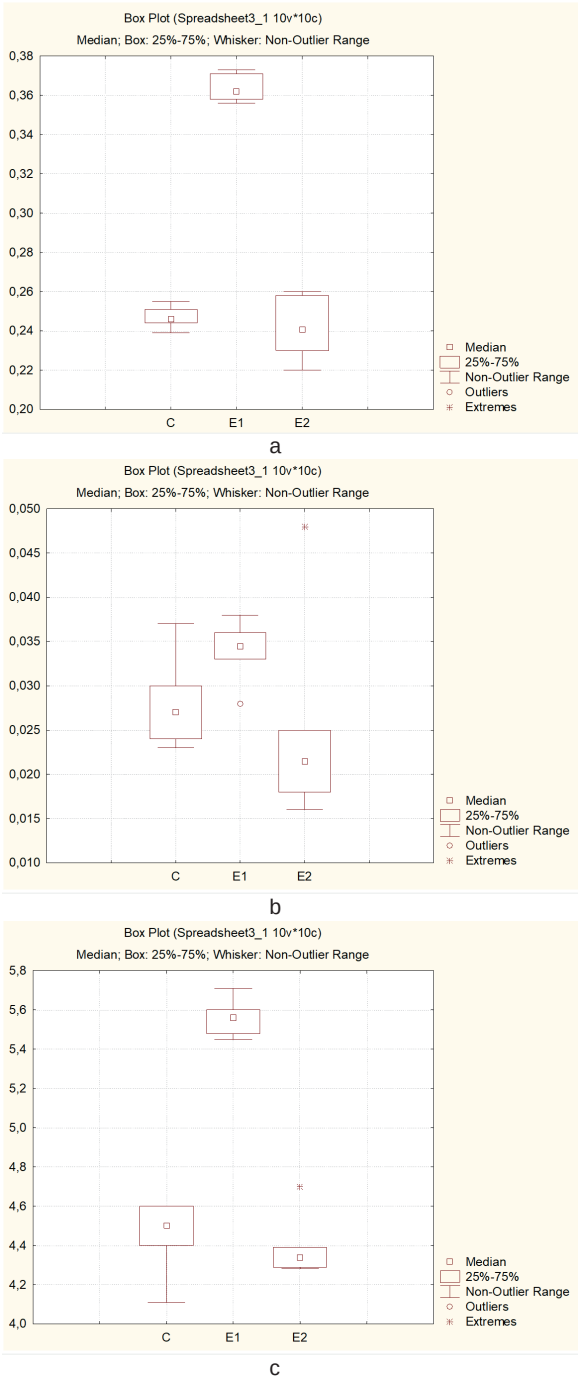


Fig. 1. Indicators of the intensity of lipid peroxidation in the blood of rats under experimental simulation of heart failure and the action of corrective factors: a) hydroperoxides of lipids, units/ml; b) diene conjugates, mmol/l; c) TBA act. products, mmol/l.

of the myocardium of rats under experimental simulation of heart failure (Fig. 2). The obtained data indicate that the intensification of free radical oxidation processes in the myocardium accompanies the administration of doxorubicin to the experimental animals of the research group. It was established that the level of diene conjugates in the homogenate of the rat myocardium of the first experimental group was (8.56±0.39) μmol/g, while in control, this indicator was (6.45±0.13) μmol/g. The level of TBA-active products in the myocardium homogenate of the first experimental group increased by 37.6 % compared to the indicators of the control group of rats.

Consequently, animals with simulated cardiomyopathy developed excessive activation of lipid peroxidation, as indicated by a high level of primary, intermediate, and end products. These results are consistent with literature data on the activation of free radical reactions and LPO processes in the blood of animals under the influence of doxorubicin.

An increase in the content of LPO products: lipid hydroperoxides, diene conjugates, and TBA-active products in the blood of rats with experimental doxorubicin intoxication indicates the development of oxidative stress.

Oxidative damage to proteins leads to a disturbance in the metabolism of cardiomyocytes. Thus, under the conditions of intensifying free radical oxidation, free radicals suppress the enzymatic link of the antioxidant system, thereby increasing oxidative stress in the myocardium. The

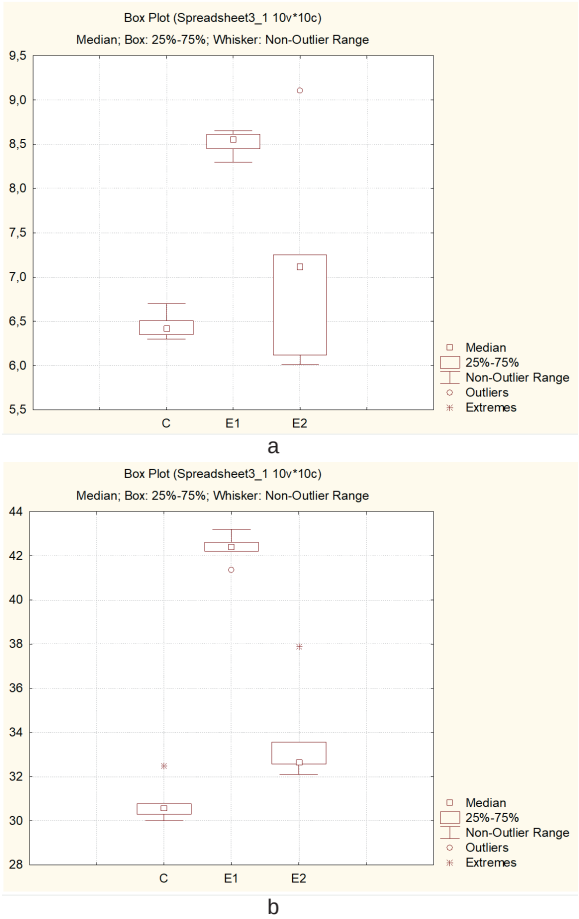


Fig. 2. Indicators of the intensity of lipid peroxidation in rat myocardium homogenate under experimental simulation of heart failure and the action of corrective factors: a) diene conjugates, mmol/l; b) TBA act. products, mmol/l.

negative effect of oxidatively modified proteins in the cell is related to oxidized proteins acting as a source of free radicals that deplete the reserves of cellular antioxidants.

When the rats of research group E_2 were given Bendamine, the level of lipid hydroperoxides in their blood decreased by 33.5 % compared to the first group of rats, which were experimentally induced cardiomyopathy by administering doxorubicin. The level of diene conjugates and TBA-active products in the blood of the second experimental group fluctuated within physiological values, so compared to the first experimental group of rats, their level decreased by 26.5 and 21.0 %, respectively.

In the homogenate of the rat myocardium of the second experimental group, a decrease in lipid peroxidation products was also established compared to the first experimental group, where the level of diene conjugates decreased by 16.8 % respectively. The level of final products of POL in the homogenate of the myocardium of rats of the second experimental group was (33.57±2.47) mmol/g, while in the first experimental group, it was (42.36±2.11) mmol/g. The lowest level of TBA-active products was in rats of the control group, where it was (30.79±4.500 mmol/g respectively.

These research results indicate the antioxidant properties of the drug "Bendamine", which contributed to the inhibition of LPO processes and the reduction of its products in the blood of experimental rats.

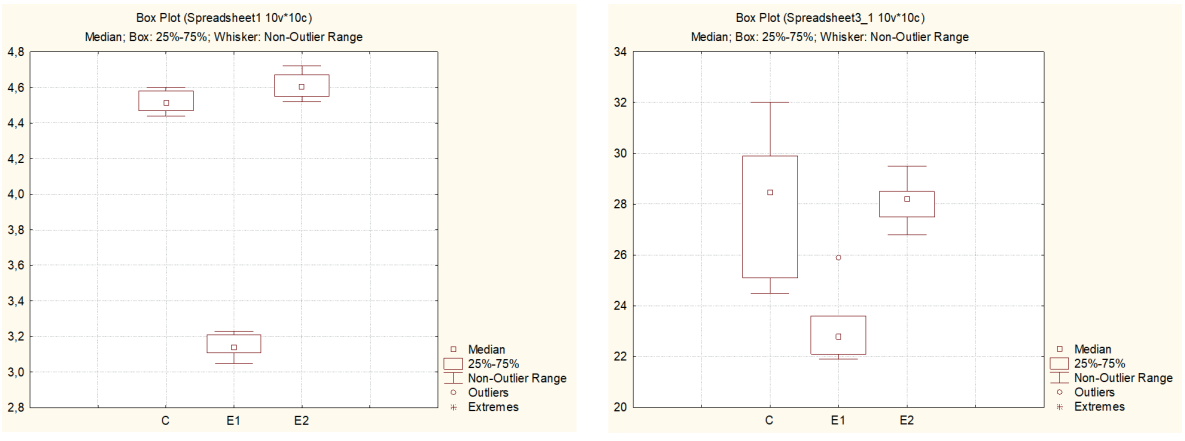
Therefore, the drug “Bendamine” inhibits the excessive formation of LPO products in pathologically changed heart tissues of rats, has an inducing effect on the antioxidant defense system and thus protects the structural and functional integrity of cell biomembranes.

Administration of doxorubicin to the rats of the experimental groups was accompanied by stress on the antioxidant defense system, which was indicated by a decrease in both enzymatic and non-enzymatic links of the antioxidant system. In the blood of the rats of the first experimental group, a decrease in superoxide dismutase activity was established by 30.3 %, and in the homogenate of the myocardium – 61.4 % compared to the control indicators.

An essential link of the antioxidant defense system is the glutathione system. It comprises reduced glutathione and several enzymes, namely glutathione oxidase and glutathione reductase. The coordinated action of all its components (reduced glutathione, glutathione peroxidase, glutathione reductase) contributes to establishing the optimal content of peroxide compounds and preserving antioxidant homeostasis.

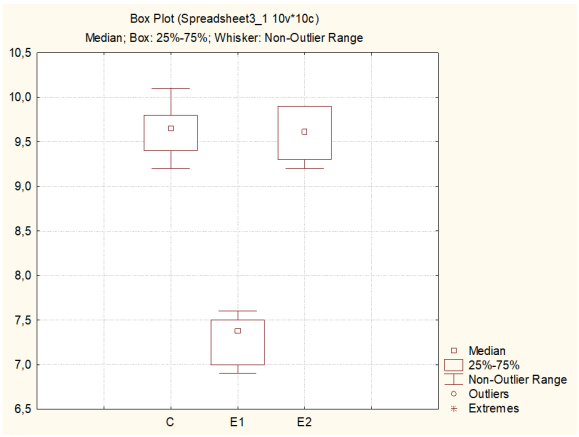
Regarding the study of the glutathione system of antioxidant protection of the body of rats, a decrease in the level of reduced glutathione in the blood of the first experimental group was established by 16.3 %, glutathione peroxidase activity by 17.4 %, and glutathione reductase activity by 24.3 % compared to the indicators of the control group (Fig. 3). When studying these indicators of the glutathione system in the myocardium homogenate, it was established that the level of reduced glutathione decreased by 45.3 %, and the activity of glutathione peroxidase and glutathione reductase decreased by 26.1 and 33.3 %, respectively (Fig. 4).

Good antioxidant properties were demonstrated by the drug “Bendamine”, which, when administered to rats of the second research group under the conditions of doxorubicin intoxication, increased the activity of glutathione peroxidase in their blood to (28.12±1.42) nmol of glutathione/min per 1 mg of protein and the activity of glutathione reductase to (9.59±0.77) nmol of NADRN/min per 1 mg of protein.

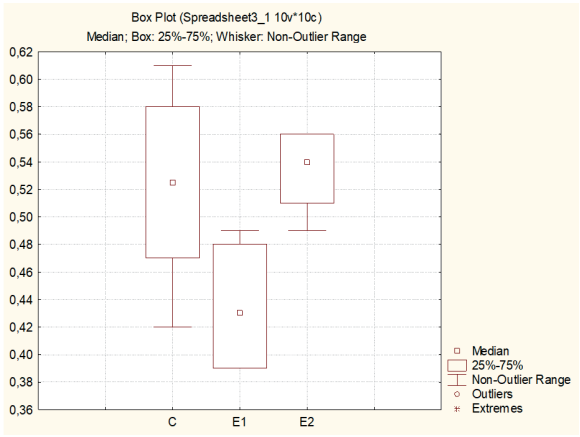


a b

Fig. 3. Indicators of the system of antioxidant protection of the body of rats under experimental modeling of heart failure and the action of corrective factors: a) Superoxide dismutase, um. units/1 mg. protein; b) Glutathione peroxidase, nmol of glutathione/min per 1 mg of protein.

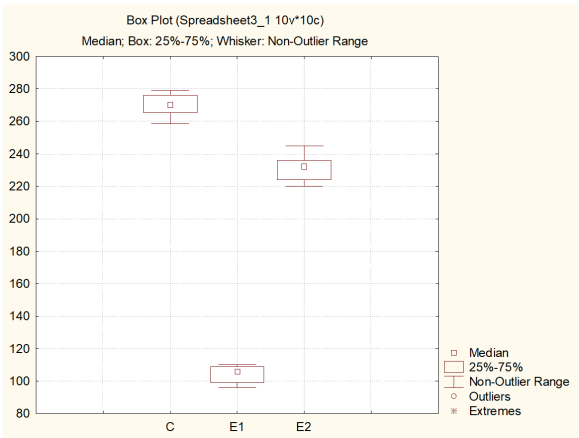


c

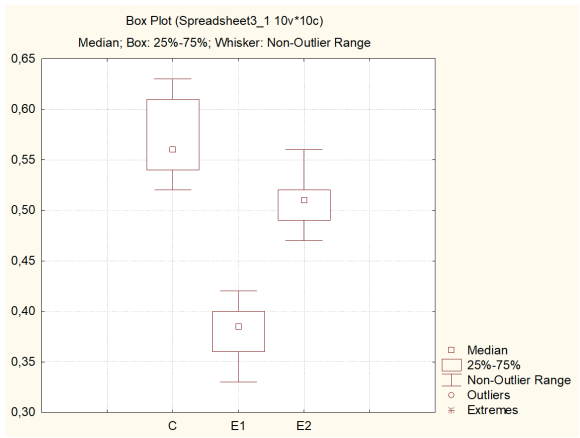


d

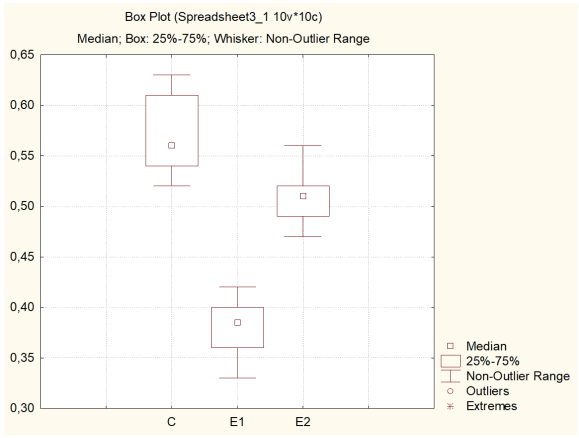
Fig. 3. Indicators of the system of antioxidant protection of the body of rats under experimental modeling of heart failure and the action of corrective factors (continuation): c) Glutathione reductase, nmol of NADPH/min per 1 mg of protein; d) Reduced glutathione, μmol/ml.



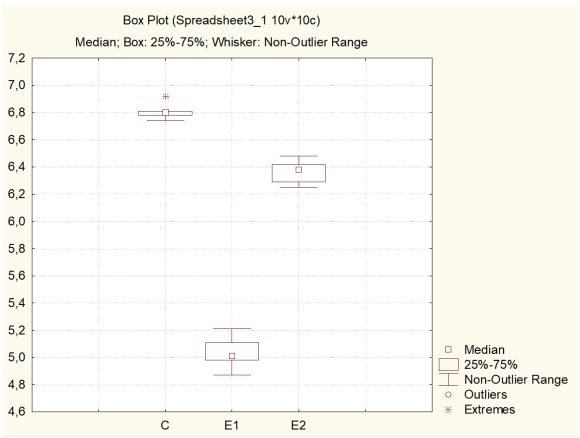
a



b



c



d

Fig. 4. Indicators of the antioxidant protection system in rat myocardium homogenate under experimental simulation of heart failure and the action of corrective factors: a) Superoxide dismutase, c.u./(mg·min); b) Reduced glutathione, μmol/g; c) Glutathione peroxidase, nmol/min×mg of protein; d) Glutathione reductase, μmol/min×mg protein.

When studying the activity of glutathione peroxidase in the myocardium of rats of the experimental groups, it was established that it was the highest in the second experimental group of rats that were given the drug “Bendamine”. Accordingly, the activity of this enzyme was higher by 26.6 % concerning intoxicated rats that were not treated. Furthermore, glutathione reductase activity was also higher in the second experimental group, which was (0.51±0.10) μmol/min×mg protein. In contrast, this indicator was (0.38±0.12) μmol/min×mg protein in the first experimental group.

Glutathione is a central component of the antioxidant defense system of almost all cells and organs. Its antioxidant action is associated with the transfer of sulfhydryl groups. It was found that when the drug "Bendamine" was administered to rats, the level of reduced glutathione in the blood of the animals of the second experimental group probably increased by 22.2 % compared to the first experimental group. In the homogenate of the rat myocardium of this research group, the level of the studied indicator was also higher, respectively, by 34.5 %.

An increase in the activity of superoxide dismutase in blood and myocardial homogenate of rats of experimental group E_2 was established by 46.3 and 122 % compared to rats subjected to experimental intoxication with doxorubicin.

Therefore, based on the conducted studies of the influence of the drug "Bendamine" on the indicators of the antioxidant system of the myocardium of experimental rats under the conditions of doxorubicin intoxication, it was established that this drug has a corrective effect in the conditions of oxidative stress inherent in doxorubicin-induced heart failure in rats. The results of the conducted studies enrich the pharmacological characteristics of bendamine, indicate a sufficiently pronounced protective effect on the myocardium during experimental doxorubicin intoxication, and are convincing proof of the feasibility of using the drug mentioned above in the practice of veterinary medicine.

CONCLUSIONS. The action of doxorubicin and the development of a hypoxic state in rats are accompanied by the activation of oxidative stress and the strengthening of free radical processes, which is indicated by the increased level of intermediate and final products of lipid peroxidation, as well as the suppression of the activity of the antioxidant defense system.

The benefit of the drug "Bendamine" in the rats of the second experimental group helped strengthen the enzymatic and non-enzymatic link of the antioxidant system, protecting cell biomembranes' structural and functional integrity.

LITERATURE

1. Prooxidant-antioxidant balance in the organism of bulls (young cattle) after using cadmium load / B. Gutyj, V. Stybel, L. Darmohray [et al.] // Ukrainian Journal of Ecology. – 2017. – **7**, No. 4. – P. 589–596.

2. The effect of milk thistle, metiphen, and silimevit on the protein-synthesizing function of the liver of laying hens in experimental chronic cadmium toxicosis / M. I. Bashchenko, O. V. Boiko, O. F. Honchar [et al.] // Ukrainian Journal of Ecology. – 2020. – **10**, No. 6. – P. 164–168. DOI: 10.15421/2020_276

3. Dang X. Silybum marianum seed extract supplementation positively affects the body weight of weaned piglets by improving voluntary feed intake / X. Dang, S. Cho, I. H. Kim // Journal of Animal Science and Technology. – 2022. – **64,** No. 4. – P. 696–706. DOI: 10.5187/jast.2022.e39

4. Effect of Butaselmevit-Plus on the immune system of piglets during and after weaning / T. V. Martyshuk, B. V. Gutyj, M. M. Zhelavskyi [et al.] // Ukrainian Journal of Ecology. – 2020. – **10,** No. 2. – P. 347–352. DOI: 10.15421/2020_106

5. Trofimiak R. Diagnostic value of echocar-diographic indices of left atrial and ventricular morphology in dogs with myxomatous mitral valve disease (MMVD) / R. Trofimiak, L. Slivinska // Ukrainian Journal of Veterinary and Agricultural Sciences. – 2021. – **4**, No. 1. – P. 16–23. DOI: 10.32718/ujvas4-1.04.

6. Oxidative stress in oocyte aging and female reproduction / L. Wang, J. Tang, L. Wang [et al.] // Journal of Cellular Physiology. – 2021. – **236**, No. 12. P. 7966–7983. DOI: 10.1002/jcp.30468.

7. Olfat N. Riboflavin is an antioxidant: a review update / N. Olfat, M. Ashoori, A. Saedisomeolia // British Journal of Nutrition. – 2022. – **128**, No. 10. – P. 1887–1895. DOI: 10.1017/S0007114521005031

8. The antioxidant system response to drought-stressed Diospyros lotus treated with exogenous melatonin / P. Zhang, Y. Hu, R. Zhou [et al.] // Peer J. – 2022. – **10**. – P. e13936. DOI: 10.7717/peerj.13936.

9. Mitochondrial Oxidative Stress-A Causative Factor and Therapeutic Target in Many Diseases / P. Kowalczyk, D. Sulejczak, P. Kleczkowska [et al.] // International Journal of Molecular Sciences. – **22**, No. 24. – P. 13384. DOI: 10.3390/ijms222413384

10. Natural Antioxidant Evaluation: A Review of Detection Methods / J. D. S. Mendonça, R. C. A. Guimarães, V.A. Zorgetto-Pinheiro [et al.] // Molecules. – 2022. – **27**, No. 11. – P. 3563. DOI: 10.3390/molecules27113563

11. Slobodian S. O. The level of lipid peroxidation products in the rats blood under prolonged cadmium and lead loading / S. O. Slobodian, B. V. Gutyj, K. Y. Leskiv // Ukrainian Journal of Veterinary and Agricultural Sciences. – 2019. – **2**, No. 3. – P. 15–18. DOI: 10.32718/ujvas2-3.04.

12. The effect of the drug "Bendamine" on the clinical and morphological parameters of dogs in heart failure / I. S. Varkholiak, B. V. Gutyj, D. F. Gufriy [et al.] // Ukrainian Journal of Veterinary and Agricultural Sciences. – 2021. – **4**, No. 3. – 76–83. DOI: 10.32718/ujvas4-3.13.

13. Трофім'як Р. М. Діагностика хронічної серцевої недостатності собак – існуючі методи та подальші

перспективи / Р. М. Трофім'як, Л. Г. Слівінська // Наук. вісн. ЛНУВМБ імені С. З. Ґжицького. Серія "Ветеринарні науки". – 2016. – **18**, № 71. – С. 130–133.

14. Експериментальна оцінка токсичності кардіологічного препарату на основі інгібітора фосфодиестерази-3 та етилметилгідроксипіридину сукцинату / І. С. Вархоляк, Б. В. Гутий, О. Б. Золотоцька [та ін.] // Наук. вісн. ЛНУВМБ імені С. З. Ґжицького. Серія "Ветеринарні науки". – 2022. – **24**, № 105. – С. 109–119.

15. Oxidative stress in the pathogenesis of stroke and its correction / M. Y. Martynov, M. V. Zhuravleva, N. S. Vasyukova [et al.] // Zh. Nevrol. Psikhiatr. Im. S. S. Korsakova. – 2023. – **123**, No. 1. – P. 16–27. DOI: 10.17116/jnevro202312301116.

16. Movsisyan A. B. Use and outcomes of antioxidant therapy in ophthalmic practice / A. B. Movsisyan, Z. G. Oganezova, E. A. Egorov // Vestn Oftalmol. – 2022. – **138**, No. 5. – 126–132. DOI: 10.17116/oftalma2022138051126

17. Voronina T. A. Geroprotective effects of ethylmethylhydroxypyridine succinate in an experimental study / T. A. Voronina // Zh. Nevrol. Psikhiatr. Im. S. S. Korsakova. – 2020. – **120**, No. 4. – P. 81–87. DOI: 10.17116/jnevro202012004181.

18. Efficacy and safety of ethylmethylhydroxypyridine succinate in patients with ischemic stroke / M. V. Zhuravleva, I. A. Shchukin, M. S. Fidler [et al.] // Zh Nevrol Psikhiatr Im S S Korsakova. – 2020. – **120**, No. 12. – 60–66. DOI: 10.17116/jnevro202012012260.

19. Лабораторні методи досліджень у біології, тваринництві та ветеринарній медицині : довідник / [В. В. Влізло, Р. С. Федорук, І. Б. Ратич та ін.] ; за ред. В. В. Влізла. – Львів : Сполом, 2012. – 764 с.

REFERENCES

1. Gutyj, B., Stybel, V., Darmohray, L., Lavryshyn, Y., Turko, I., Hachak, Y., Shcherbatyy, A., Bushueva, I., Parchenko, V., Kaplaushenko, A., & Krushelnytska, O. (2017). Prooxidant-antioxidant balance in the organism of bulls (young cattle) after using cadmium load. *Ukrainian Journal of Ecology*, 7 (4), 589-596.

2. Bashchenko, M.I., Boiko, O.V., Honchar, O.F., Gutyj, B.V., Lesyk, Y.V., Ostapyuk, A.Y., Kovalchuk, I.I., & Leskiv, K.Y. (2020). The effect of milk thistle, metiphen, and silimevit on the protein-synthesizing function of the liver of laying hens in experimental chronic cadmium toxicosis. *Ukrainian Journal of Ecology*, 10 (6), 164-168. DOI: 10.15421/2020_276

3. Dang, X., Cho, S., & Kim, I.H. (2022). Silybum marianum seed extract supplementation positively affects the body weight of weaned piglets by improving voluntary feed intake. *Journal of Animal Science and Technology*, 64 (4), 696-706. DOI: 10.5187/jast.2022.e39

4. Martyshuk, T.V., Gutyj, B.V., Zhelavskyi, M.M., Midyk. S.V., Fedorchenko, A.M., Todoriuk, V.B., Nahirniak, T.B., Kisera, Ya.V., Sus, H.V., Chemerys, V.A., Levkivska, N.D., & Iglitskej, I.I. (2020). Effect of Butaselmevit-Plus on the immune system of piglets during and after weaning. *Ukrainian Journal of Ecology*, 10 (2), 347-352. doi: 10.15421/2020_106

5. Trofimiak, R., & Slivinska, L. (2021). Diagnostic value of echocar-diographic indices of left atrial and ventricular morphology in dogs with myxomatous mitral valve disease (MMVD). *Ukrainian Journal of Veterinary and Agricultural Sciences*, 4 (1), 16-23. DOI: 10.32718/ujvas4-1.04.

6. Wang, L., Tang, J., Wang, L., Tan, F., Song, H., Zhou, J., & Li, F. (2021). Oxidative stress in oocyte aging and female reproduction. *Journal of Cellular Physiology*, 236 (12), 7966-7983. DOI: 10.1002/jcp.30468.

7. Olfat, N., Ashoori, M., & Saedisomeolia, A. (2022). Riboflavin is an antioxidant: a review update. British Journal of Nutrition, 128 (10), 1887-1895. DOI: 10.1017/S0007114521005031.

8. Zhang, P., Hu, Y., Zhou, R., Zhang, X., Hu, H., Lang, D. (2022). The antioxidant system response to drought-stressed Diospyros lotus treated with exogenous melatonin. Peer J, 10, e13936. DOI: 10.7717/peerj.13936

9. Kowalczyk, P., Sulejczak, D., Kleczkowska, P., Bukowska-Ośko, I., Kucia, M., Popiel, M., Wietrak, E., Kramkowski, K., Wrzosek, K., & Kaczyńska, K. (2021). Mitochondrial oxidative stress – a causative factor and therapeutic target in many diseases. *International Journal of Molecular Sciences*, 22 (24), 13384. DOI: 10.3390/ijms222413384

10. Mendonça, J.D.S., Guimarães, R.C.A., Zorgetto-Pinheiro, V.A., Fernandes, C.D.P., Marcelino, G., Bogo, D., Freitas, K.C., Hiane, P.A., de Pádua Melo, E.S., Vilela, M.L.B., Nascimento, V.A.D. (2022). Natural Antioxidant Evaluation: A Review of Detection Methods. *Molecules*, 27 (11), 3563. DOI: 10.3390/molecules27113563

11. Slobodian, S.O., Gutyj, B.V., & Leskiv, K.Y. (2019). The level of lipid peroxidation products in the rats blood under prolonged cadmium and lead loading. *Ukrainian Journal of Veterinary and Agricultural Sciences*, 2 (3), 15-18. DOI: 10.32718/ujvas2-3.04

12. Varkholiak, I.S., Gutyj, B.V., Gufriy, D.F., Sachuk, R.M., Mylostyvyi, R.V., Radzykhovskyi, M.L., Sedilo, H.M., & Izhboldina, O.O. (2021). The effect of the drug "Bendamine" on the clinical and morphological parameters of dogs in heart failure. *Ukrainian Journal of Veterinary and Agricultural Sciences*, 4 (3), 76-83. DOI: 10.32718/ujvas4-3.13

13. Trofimjak, R., & Slivinska, L. (2016). Diagnosis of chronic heart failure dogs – existing methods and future prospects. *Scientific Messenger of LNU of Veterinary Medicine and Biotechnologies. Series: Veterinary Sciences*, 18 (71), 130-133 [in Ukrainian]. DOI: 10.15421/nvlvet7129.

14. Varkholiak, I.S., Gutyj, B.V., Zolototska, O.B., Goralskyi, L.P., Sokulskyi, I.M., Khalak, V.I., Parchenko, V.V., Shcherbatyy, A.R., Martyshuk, T.V., & Guta, Z.A. (2022). Experimental assessment of the toxicity of a cardiac drug based on a phosphodiesterase-3 inhibitor and ethylmethylhydroxypyridine succinate. *Scientific Messenger of Lviv National University of Veterinary*

Medicine and Biotechnologies. Series: Veterinary sciences, 24 (105), 109-119 [in Ukrainian]. DOI: 10.32718/nvlvet10516

15. Martynov, M.Y., Zhuravleva, M.V., Vasyukova, N.S., Kuznetsova, E.V., & Kameneva, T.R. (2023). Oxidative stress in the pathogenesis of stroke and its correction. *Zh Nevrol Psikhiatr Im S S Korsakova*, 123 (1), 16-27. DOI: 10.17116/jnevro202312301116.

16. Movsisyan, A.B., Oganezova, Z.G., & Egorov, E.A. (2022). Use and outcomes of antioxidant therapy in ophthalmic practice]. *Ophtalmology Bulletin*, 138 (5), 126-132. DOI: 10.17116/oftalma2022138051126

17. Voronina, T.A. (2020). Geroprotective effects of ethylmethylhydroxypyridine succinate in an experimental study. *Journal of Neur. Psychiatry by S. S. Korsakov*, 120 (4), 81-87. DOI: 10.17116/jnevro202012004181

18. Zhuravleva, M.V., Shchukin, I.A., Fidler, M.S., Prokofiev, A.B., Serebrova, S.Y., Vasyukova, N.S., Demchenkova, E.Y., & Arkhipov, V.V. (2020). Efficacy and safety of ethylmethylhydroxypyridine succinate in patients with ischemic stroke. *Zh Journal of Neur. Psychiatry by S. S. Korsakova*, 120 (12), 60-66. DOI: 10.17116/jnevro202012012260.

19. Vlislo, V.V. (2012). *Laboratory methods of research in biology, animal husbandry and veterinary medicine.* Spolom, Lviv [in Ukrainian].

Б. В. Гутий[1], І. С. Вархоляк[1], Б. М. Вервега[2], Т. В. Мартишук[1], Х. Я. Леськів[1]
ЛЬВІВСЬКИЙ НАЦІОНАЛЬНИЙ УНІВЕРСИТЕТ ВЕТЕРИНАРНОЇ МЕДИЦИНИ ТА БІОТЕХНОЛОГІЙ ІМЕНІ С. З. ҐЖИЦЬКОГО[1]
ЛЬВІВСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ ІМЕНІ ДАНИЛА ГАЛИЦЬКОГО[2]

СТАН СИСТЕМИ АНТИОКСИДАНТНОГО ЗАХИСТУ ОРГАНІЗМУ ЩУРІВ ЗА УМОВ ЕКСПЕРИМЕНТАЛЬНОЇ ДОКСОРУБІЦИНОВОЇ ІНТОКСИКАЦІЇ ТА ДІЇ КОРИГУВАЛЬНИХ ЧИННИКІВ

Резюме

Вступ. *Для досліджень використовували доксорубіцинову модель, яка, на думку багатьох авторів, найбільш адекватно відтворює серцеву недостатність різного ступеня тяжкості. Доксорубіцин – антибіотик, що має цитостатичний ефект. Механізм його дії полягає у взаємодії з ДНК, утворенні вільних радикалів і пригніченні синтезу нуклеїнових кислот. Дія доксорубіцину та розвиток гіпоксії супроводжуються активацією оксидативного стресу і посиленням вільнорадикальних процесів, а також зміною обміну вуглеводів, білків та ліпідів.*

Мета дослідження *– вивчити вплив препарату "Бендамін" на показники антиоксидантного захисту організму щурів за умов експериментального моделювання серцевої недостатності.*

Методи дослідження. *Моделювання серцевої недостатності проводили на білих статевозрілих молодих щурах-самцях лінії Вістар масою 180–200 г. У крові та гомогенаті міокарда визначали рівень продуктів пероксидного окиснення ліпідів, активність антиоксидантних ензимів та рівень відновленого глутатіону на тлі доксорубіцинової інтоксикації і при використанні препарату "Бендамін".*

Результати й обговорення. *За умов доксорубіцинової інтоксикації у щурів посилювалися процеси пероксидного окиснення ліпідів, на що вказувало збільшення вмісту гідроперекисів ліпідів, дієнових кон'югатів і ТБК-активних продуктів як у крові, так і в гомогенаті міокарда тварин першої дослідної групи. Варто зазначити, що в інтоксикованих щурів також спостерігали пригнічення системи антиоксидантного захисту, про що свідчило зниження рівня як ензимної, так і неензимної ланок антиоксидантної системи. Встановлено, що препарат "Бендамін" проявляв коригувальну дію за умов оксидативного стресу, притаманного доксорубіциніндукованій серцевій недостатності у щурів. Він гальмував надмірне утворення продуктів пероксидного окиснення ліпідів у патологічно змінених тканинах серця тварин, мав індукуючий вплив на систему антиоксидантного захисту.*

Висновки. *Вивчено вплив препарату "Бендамін" на показники антиоксидантного захисту організму щурів за умов експериментального моделювання серцевої недостатності. Доведено його антиоксидантні властивості.*

КЛЮЧОВІ СЛОВА: **антиоксидантна система; доксорубіцин; інтоксикація; вільнорадикальне окиснення; інгібітор фосфодіестерази-3; етилметилгідроксипіридину сукцинат.**

Received 20.01.23

Address for correspondence: *B. M. Verveha, Danylo Halytsky Lviv National Medical University, Pekarska str., 69, Lviv, 79010, Ukraine, e-mail: danaverveha@gmail.com.*